

**SEVENTEENTH HEALTH SCIENCES CENTRE  
POSTER CONFERENCE 2012**

**Under the Patronage of  
The President of Kuwait University**



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## **17<sup>th</sup> HSC Poster Conference 2012**

### **Organizing Committee**

- Prof. Widad Al-Nakeeb, Vice Dean Research & Postgraduate Studies, FOM
- Prof. Yunus Luqmani, Chairman & Coordinator; Scientific Sub-Committee, Dept. of Pharmaceutical Chemistry, FOP
- Prof. Ludmil Benov, Dept. of Biochemistry, FOM
- Prof. Raj Raghupathy, Coordinator, Printing & Information Technology Sub-Committee, Dept. of Microbiology, FOM
- Prof. Saeed Akhtar, Coordinator, Social & Logistics Sub-Committee, Dept. of Community Medicine & Behavioral Sciences, FOM
- Prof. Majedah Al-Azemi, Coordinator, Finance Sub-Committee, Dept of Obstetrics & Gynecology, FOM
- Prof. Chacko Mathew, Dept. of Medical Lab Sciences, Faculty of Allied Health
- Dr. Sulaiman Al-Sabah, Dept. of Pharmacology, FOM
- Dr. Iqbal Siddique, Dept. of Medicine, FOM
- Dr. Faisal Al-Sayegh, CME Officer, Dept. of Medicine, FOM
- Dr. Rajaa Marouf, Dept of Pathology, FOM
- Dr. Sisko Honkala, Dept. of Developmental & Preventive Sciences, FOD
- Dr. Anwar Al-Awadhi, Dept. of Medical Lab Science, FAHS
- Mr. Jassim Al-Khorafi, Administration Manager, FOM
- Mr. Dheya H A Al-Hasan, Finance Manager, FOM
- Mrs. Amna Safar, Technical Service Administration, HSC

### **Special Acknowledgements**

- Prof. Adel K Ayad, Dean, Faculty of Medicine
- Mr. Adel Al-Moosad, Director, Service Department
- Mrs. Teena Sadan, Technical Staff, CRC, Faculty of Medicine



## Photograph of Organizing Committee



**Prof. Widad Al-Nakib, Vice Dean for  
*Research & Postgraduate Studies***



**Prof. Yunus Luqmani  
*Chairman & Coordinator,  
Scientific Sub-Committee***



**Prof. Ludmil Benov**



**Prof. Raj Raghupathy,  
*Coordinator, Printing & Information  
Technology***



**Prof. Saeed Akhtar  
*Coordinator, Social & Logistics  
Sub-Committee***



**Prof. Majedah Al-Azemi,  
*Coordinator Finance***



**Prof. Chacko Mathew**



**Dr. Suleiman  
Al-Sabah**



**Dr. Iqbal Siddique**



**Dr. Faisal Al-Sayegh**  
*CME Officer*



**Dr. Rajaa Marouf**



**Dr. Sisko Honkala**



**Dr. Anwar Al-Awadhi**



**Mr. Jassim Al-Khorafi**



**Mr. Dheya HA Al-Hasan**

## Message from the Dean, Faculty of Medicine



It gives me a great pleasure to write the introductory message for the 2012 Health Sciences Center Poster Conference. This event which has become a landmark activity in our academic year. The Faculty of Medicine has been organizing this conference since 1996 for the Academic Staff and students in order to present some of their research work. The total number of abstracts this year is 270, which reflects the great interest this event has made among professionals in Kuwait.

The basic objective of this Poster Conference is firstly to provide an opportunity for academic staff, medical students, and Ministry of Health doctors to present their research findings. Secondly, it facilitates the development of collaborative efforts between researchers. Thirdly, it provides an advancement in knowledge and future development in research and scientific discussions.

The invited Keynote Speaker for this year is Professor Barry McGrath from Monash University, Australia. He will be addressing a lecture entitled “Cardiovascular Health in th 21<sup>st</sup> Century”.

The Annual Health Sciences Poster Day is organized through the office of the Vice-Dean for Research and Postgraduate Studies. I take this opportunity to thank the Vice-Dean Prof. Widad Al Nakib for his enthusiasm and hard work. We are also grateful to the Chairman of the Organizing Committee, Professor Yunus Luqmani, his colleagues on the organizing committee, and the Abstract Review Committee Members for their commitment and outstanding effort to maintain the quality of this important academic activity.

**Professor Adel K. Ayed**  
Dean, Faculty of Medicine



## **Message from the Vice Dean for Research & Postgraduate Studies Faculty of Medicine**



The first Poster Conference was introduced in April 1996 in the Faculty of Medicine. We have since held this conference annually with great success with staff and students of all the faculties of the Health Sciences Centre participating and presenting their research. Today, the Poster Conference is held by many Faculties in the University of Kuwait. This is because of the success of our Poster Conference. Through this important event, students, scientists and doctors in the Health Sciences Centre exchange scientific communications between them and hence stimulate research. I cannot emphasize more, that strong research is a prerequisite for academic excellence.

In continuing the tradition of inviting internationally recognized scientists whose work has great impact upon the Health Sciences, this year we would like to welcome Prof. Barry P. McGrath, Adjunct Professor of Medicine, Monash University, Australia, who will give the keynote speech on “Cardiovascular Health in the 21<sup>st</sup> Century”. This year we have 270 poster abstracts and I have no doubt the 17<sup>th</sup> HSC Poster Conference will be a great success. I thank Kuwait University for the continuing support and sponsorship of the Poster Conference and Prof. Barry McGrath for accepting our invitation as a keynote speaker in this year’s Poster Conference. I would like to express my appreciation to the Vice-President Health Sciences Centre, Deans of different Faculties of HSC for their encouragement and support and to all HSC technical and support staff who assisted in the organization and implementation of this meeting. I am especially very grateful to the Chairman and the members of the Organizing Committee for their commitment and efforts to make this a very successful event.

### **Prof. Widad Al-Nakib**

Vice-Dean for Research & Postgraduate Studies  
Faculty of Medicine

**Message from the Chairman,  
17<sup>th</sup> HSC Poster Conference Organizing Committee**



The Poster Day Conference initiated in 1996 has now become enshrined as an annual event in the HSC academic calendar. It is most heartening to see that it has been consistently supported by the active and enthusiastic participation of not only the researchers of the HSC and Science Faculties of the University but as well by other institutions and hospital departments in Kuwait, and even from some outside of the country. In the last few years the consistency in the number of submissions attest to the success of this endeavour, with discernible improvements in quality of presentations as a result of more rigorous standards.

Basic science and clinical research by academics and clinicians is the backbone of a reputed medical university but another vital activity for future development is the contribution of students to research output. Our efforts in this respect are proving successful. This year 25% of the Posters are from undergraduate, postgraduate MSc and PhD students and clinical graduate residents, and as usual cover a wide subject area. We hope this will encourage both themselves and their successors, and provide impetus for more innovative work.

It may be pertinent to remind participants that the original aim of this occasion was to provide a forum for dissemination and exchange of information and ideas for mutual benefit. With increasing reliance on technology, collaboration has become essential, and we hope this event will offer such opportunities.

We are privileged with this year's distinguished keynote speaker, Prof Barry McGrath (our first invitee from the southern hemisphere) who will talk on a subject of particular concern to Kuwait, and hopefully provide some suggestions for reducing cardiovascular risk with lifestyle modifications.

I thank my colleagues in the Organising Committee for giving their time. Our task has been greatly facilitated with the complete financing of the event by



the University and the establishment in the HSC of the Centre for Research Support and Conferences under the Vice Dean Research FOM. We are particularly indebted to Ms Teena Sadan and her team for their efficient administrative assistance, to the judges for their unenviable but rewarding task of selecting outstanding posters, and to all participants for sharing their work.

**Prof Yunus Luqmani**

Chairman, 17th HSC Poster Conference

## Keynote Speaker

### Professor Barry Patrick McGrath

*Adjunct Professor of Medicine, Monash University, Australia*



Barry McGrath is a physician who was a full-time clinical academic at Monash University for 33 years until 2010. His research leadership is reflected in an extensive list of publications (author or co-author of 6 books, 11 book chapters, 220 papers in referred journals); student supervision (11 completed PhDs) and post-doctoral supervision (10), grants obtained, and invited international presentations in Europe, Canada, China, Japan and South Africa. His research interests include hypertension, arterial disease and heart failure. He has a lead educator role in the Australian Medical Council and is currently Director of Medical Education, Southern Health, Australia.



## Keynote Abstract

### Cardiovascular Health in the 21<sup>st</sup> Century

*Professor Barry P McGrath, Adjunct Professor of Medicine,  
Monash University, Australia.*

Over the past ten years in Australia cardiovascular causes of death have declined from 38 to 32%, cancer is unchanged, whilst dementia as a cause of death has more than doubled (5 to 13%). Advances in therapeutics have been striking. Treatment of cardiovascular risk rather than individual risk factors has become the new focus and combination therapeutics is the new norm. We have witnessed the definition of the human genome, although progress on genetic causes of common cardiovascular disorders has been somewhat disappointing. Non-invasive monitoring of arterial blood pressure and arterial function, and wonderful advances in vascular and cardiac imaging have greatly increased our understanding of the pathogenesis of disease and offer new hope in early detection, personalised medicine, intervention and monitoring responses to therapy. Extensive research data from home and ambulatory blood pressure monitoring has changed the way we define and manage hypertension. There is now compelling evidence that central pulse wave velocity is a very good surrogate marker of cardiovascular risk. The challenge to today's clinician is how to incorporate these new methodologies. However a warning needs to be sounded about the rush to superspecialisation. The pendulum has swung too far and we need to focus on defined roles and rewards for well-trained generalists as conductors of the cardiovascular disease management orchestras of the future.



## ***Best Poster Award Winners -2011***

### **Dr. Nael Al-Naqeeb Award for Best Undergraduate Research**

Al-Mogahwi AW, Bin Essa NE, Al-Sayed Ahmed DM, Al-Zanki SO, Al-Lahu R, Al-Shaleh M, AlSabah RN; Primary caregiver and child's perception, attitude and coping in pediatric cancer.

### **Graduate Research in Basic Sciences (MSc)**

AlFadhli S, Sidky A, Bahbahani A, Alkuraya F, Al-Hajri A; Autosomal dominant congenital cataract of a consanguineous Kuwaiti family revealed genetic and clinical heterogeneity discovered to have novel mutations in CRYGB gene.

### **Graduate Research in Basic Sciences (PhD)**

Al-Turab M, Chehadeh W, Al-Mulla F, Al-Nakib W; Role of Human Metapneumovirus in Respiratory Tract Infections in Kuwait.

### **Graduate Research for Resident Doctors**

Alali MA; Patients presenting to secondary emergency services: A comparison study between Kuwait and Ireland.

### **Basic Sciences**

- Ezeamuzie CI, Shihab PK; Potentially useful interactions between Theophylline and Salbutamol on cytokine release in human monocytes.
- Renno WM\*, Rao MS; Green tea extract (-)-epigallocatechin-3-gallate (EGCG) promotes spinal neuroprotection and axon regeneration in sciatic nerve crush model of nerve injury: A light and electron microscopic study.

### **Clinical Sciences**

- Mojiminiyi OA, Abdella NA, Al-Kharyef D, Al-Mulla F, Pinto C, George S, Al-Mohammed H; Prospective longitudinal study of factors associated with progression/regression of microalbuminuria in patients with Type 2 diabetes mellitus.
- Kapila K, Anim JT, Francis IM, George SS, Behbehani A, Al Mulla F; Expression of progesterone receptor (PR) and its isoforms PRAB and PRB in fine needle aspirates from breast carcinoma.



- Al-Azemi MK, Al-Jassar W, Omu FE, Omu AE; Features of Polycystic Ovarian Syndrome in Adolescent Women and management with Metformin.

### **Case Report**

Shaaban H, El Kabany M, Amanguno HG, Hebbar HG, Jassar A, Francis IM, Kapila K; Signet ring cell adenocarcinoma of the rectum with bilateral breast metastasis: A case report and review of literature.



## Past Poster Day Keynote Speakers and Lectures

2011

Cardiovascular Outcome Trials in Diabetes.

Prof. Rury Holman, Director of the University of Oxford Diabetes Trials Unit,  
University of Oxford, Canada

2010

New mycobacterial vaccine candidates: from lab to clinical trials.

Prof. Abu Salim Mustafa, PhD, FRC Path. Department of Microbiology, Faculty of Medicine, Kuwait University

2009

Evidence-Based Medicine and Knowledge Translation Research for Better Health Care.

Prof. Brian Haynes, Professor of Clinical Epidemiology and Medicine, Chief of the Health Information Research Unit at McMaster University, Hamilton Ontario, Canada

2008

What Ails The World? How Do We Respond?

Prof. Abdallah S Daar, D.Phil (Oxon), FRSC, FRCP (Lon), FRCS (Eng), FRCS (Ed), FRCS (C), Director of Ethics and Policy, McLaughlin Centre for Molecular Medicine, Professor of Public Health Sciences and Professor of Surgery, Senior scientist and Co-director, Program on Life Sciences, Ethics and Policy, McLaughlin Rotman Centre for Global Health, University of Toronto, Ontario, Canada

2007

From Molecular Imaging to Molecular Medicine.

Prof. Henry N. Wagner, Jr. MD, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

2006

Stem cell research.

Prof. Sir Martin Evans FRS, DSc (Nobel Laureate), Director of the School of Biosciences and Professor of Mammalian Genetics at Cardiff University, UK.



## **Past Poster Day Keynote Speakers and Lectures, Cont.**

2005

How Corticosteroids Work in inflammatory Diseases: New Molecular Insights.  
Prof. Peter Barnes is of Thoracic Medicine at the National Heart and Lung Institute, Head of Respiratory Medicine at Imperial College and Honorary Consultant Physician at Royal Brompton Hospital, London, UK.

2004

The Nitric Oxide/Cyclic GMP Pathway: Targets for Drug Development Prof. Ferid Murad, Nobel Prize recipient, Chairman, Department of Integrative Biology and Pharmacology, Director, Institute of Molecular Medicine, University of Texas Medical School, Houston, Texas, USA

2003

The Post-Genomic Era: Global Impact on Medicine and Health Care Delivery  
Prof. Seyed E. Hasnain, Director, Centre for DNA Fingerprinting & Diagnostics (CDFD) Hyderabad, India

2002

Genetics and World Health: Fact or Fantasy Prof. (Sir) David J Weatherall, Emeritus Professor, Weatherall Institute of Molecular Medicine, University of Oxford, UK

2001

Genomic View of Human History Prof. Mary-Claire King, American Cancer Society Research Professor, Department of Medicine and Genetics, University of Washington, Seattle, Washington, USA

2000

Molecular Mechanisms and Biomedical Implications of Apoptotic Cell Death  
Dr. Sten Orrenius, Professor and Chairman, Division of Toxicology, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden



## **Past Poster Day Keynote Speakers and Lectures, Cont.**

1999

Nutrition, Immunity and Infection: Basic Considerations and Public Health Significance Dr. Ranjit Kumar Chandra, Professor & Director, Allergy, Asthma and Immunology Centre, Gurgaon, India

1998

Futurology in Biomedical Research: From Crystallography to Crystal Gazing Prof. Jasbir S. Bajaj, All India Institute of Medical Sciences, New Delhi, India

1997

The Impact of Research on the Development of an Academician Dr. Elia Ayoub, Distinguished Professor of Pediatrics, Department of Pediatrics, Pediatric Immunology and Infectious Diseases, College of Medicine, University of Florida USA.



## **Original Research Abstracts List By Subject Area**



## **Allied Health**

**1**

\*Joshi RM, Rawdhan H, Madbouly N, Nair S: Distribution and antimicrobial susceptibility of *Stenotrophomonas maltophilia*: Six years study

**2**

\*Mohammad Q, Christo P: Treatment length in ICU after cardiovascular surgery

**3**

\*Saafan AM: Assessment of bactericidal effect of photodynamic therapy on *Streptococcus mutans*

## **Anatomy**

**4**

\*Lucas PW, Ziscovici C: Fracture toughness of sea otter enamel

**5**

Mousa AMA, \*Elshahat M: Effect of developmental lead exposure on neurogenesis in wistar rats

**6**

\*Mousa AMA, Al-Fadhli A, Rao MS, Kilarkaje N: Intrauterine lead nitrate exposure induces apoptosis in rat fetal cerebellum

## **Behavioral Sciences**

**7**

\*Al-Isa AN: Prevalence of metabolic syndrome among female adolescents using two criteria

**8**

\*Al-Osaimi A, Obaid O, Al-Asfour Y, Yousef A, Razouki M, Rajab SH: The acute effect of SHISHA Smoking on oxygen saturation level and heart rate

## **Biochemistry**

**9**

\*Abu Ghefreh A, Khan I: The role and regulation of colonic sodium/hydrogen exchanger isoforms 1 and 3 in spontaneous hypertensive rats

**10**

\*Al-Ansary M, Benov L, Craik J: A new discovery in G6PD deficiency explains favism, drug sensitivity and resistance to malaria

**11**

\*Madhu D, Zamoon J: RAGE a deterrent force in the pathogenesis of cardiovascular complications in diabetes



**12**

\*Majdalawieh AF, Bogachev O, Pan X, Zhang L, Ro HS: Adipocyte Enhancer-Binding Protein 1 (AEBP1) is a pro-atherogenic factor in mice

**13**

\*Thomas M, Batinic-Haberle I, Benov L: Fe-porphyrins: Superoxide scavengers and anti-bacterials

### **Community Medicine**

**14**

\*Al-Ateeqi AM: Evaluation of coordination between Ministry of Health and other governmental agencies of Kuwait in providing public health services

**15**

\*Al-Enezi BS, Al-Mutairi AY, Al-Arbeed AA, Al-Obaidan A, Al-Jenfawi MK, Al-Ajmi AS, Akhtar S: The prevalence of and factors associated with work-related sleep disturbance in working population of Kuwait

**16**

\*Al-Faddagh A, Al-Fadaghi A, Abdulrida M, Al-Fadhli J, Al-Otaibi F, Al-Hajery N, Moussa M: Knowledge, attitude, and screening practice among Kuwaiti adult males at risk regarding prostate cancer

**17**

\*Al-Haddad F, Al-Farhan M, Behbehani J, Karimi M, Asem M, Thalib L: Disability, pain and quality of life in relation to low back pain among teachers in Kuwait

**18**

Al-Kanderi A, Al-Eidan S, Al-Juaidi F, Al-Safi A, \*Taqi S, Bouhaimed M: Prevalence of vitamin D deficiency among adults at the Health Sciences Centre in Kuwait

**19**

\*Al-Mazidi A, Al-Hajeri M, Al-Juwaisri N, Al-Jassar R, Al-Khalifa S, Al-Rayes S, Shah N: Self-reported prevalence and correlates of ADHD among Kuwait University Students

**20**

Al-Mubarak SJ, Al-Refaie AT, Behbehani LA, \*Abul MF, Longenecker JC: Infertility and the use of assisted reproductive techniques among employed Kuwaiti women

**21**

\*Al-Sulaiten N, Al-Anteri E, Al-Thaher F, Fareh F, Al-Rashidi F, Najem N, Al-Taiar A: Patterns and determinants of current breastfeeding among mothers with children under one year of age in Kuwait

**22**

\*Badr H, Shah N, Shah M: Obesity among Kuwaitis aged 50 years or older: Prevalence, correlates and comorbidities



**23**

AlFarhan H, AlTourah L, AlGhanim M, AlEnezi N, \*AlMutar S, Moussa M: Occupational stress and mental health among general medical practitioners and general surgeons

**24**

\*Thalib L, Al-Taiar A: Respiratory and asthma admissions to hospitals in relation to dust storms events in Kuwait

## **Dentistry**

**25**

\*Abuhaloob L: Dental fluorosis: Knowledge and public perception in the Gaza Strip

**26**

Al Abbas K, Fahl R\*, Qudeimat M: Association between body mass index and dental caries among Kuwaiti children attending the 6th Grade

**27**

\*Al-Asfour A, Andersson L, Dahlin C, Tengvall P: Histological analysis of Titanium Dioxide-Impregnated extra-cellular matrix membrane

**28**

\*Al-Mashaan S, Al-Sabah Y, Qudeimat M: Space maintainers: Uses, survival and factors affecting longevity at KUDC

**29**

\*Al-Mutawa S, Shyama M, Al-Nafisi M, Soparkar P: Prevalence of malocclusions in schoolchildren by Governorate in Kuwait

**30**

\*Al-Nafisi M, Al-Menayekh R, Al-Mutawaa S, Nazar H, Ariga J: Oral cancer knowledge, practices and opinion of dentists attending KUDR

**31**

\*Altarakemah Y, AlSane M, Ismail A, Kingman A, Lim S: A new approach to reliability assessment of dental caries examinations

**32**

\*Barari S, Roohollahi MR, F Assefzadeh F, Valizadeh S, Shahed: Effect of preparation design on stress distribution in FRC inlay bridges

**33**

Behbehani F, \*Roy R, Alsayegh F: Differences in extraction decision between users of conventional bracket system versus passive self ligation system

**34**

\*Ben-Ali RA, Al-Juwaihel SF, Al-Kabbaz A: Compliance of smokers and non-smokers to non-surgical periodontal therapy



**35**

\*Darvell BW: Early strength of dental silver amalgam

**36**

Honkala S, \*Al-Ansari JM, Honkala E: Dental pain experience among pregnant women in Kuwait

**37**

\*Honkala S, Honkala E, Humphris G, Freeman R: Association between dental fear and oral health habits in Kuwait

**38**

\*Hmaidouch R, Mueller W, Lauer H, Weigl P: Evaluation of microhardness of Y-TZP for fully-anatomic Zirconia Crowns

**39**

Mohammad RS, \*Halboub ES, Mashlah AM: Increased salivary IgA levels in acute and quiescent aphthous stomatitis

**40**

\*Kocani FK, Kamberi B: Root and canal morphology of the first human maxillary premolar

**41**

\*Moeini M, Khayam E: Antegonial and mental indices vs. age, gender, and dental status

**42**

\*Qasem JA, Qasem AA: Molecular detection of helicobacter pylori in dental plaques of Kuwaiti diabetic patients, as a possible source of re-infection

**43**

\*Schütz P, Ibrahim HH: Frontal bone fractures and management of frontal sinus

**44**

\*Shyama M, Al-Mutawa S, Al-Duwairi Y, Soparkar P: Risk factors for caries, fluorosis and malocclusions in Kuwaiti schoolchildren

**45**

Tabatabaei MH, \*Valizadeh S, Barari S, Sadraei S: Monomers elution from composites by food-simulating liquids

## **Environmental Sciences**

**46**

\*Ali AH, Nair VS, Al-Shoumer KAS: Effects of lifestyle and environmental factors on bone mineral density in healthy Kuwaiti females



**47**

\*Al-Mujaibel L, Kilarkaje N: Lead acetate modulates AP-1, c-Myc and NF-kB signaling in hepatocytes

### **Genetics**

**48**

\*Al-Ahmad M, Al-Bustan SA, Al-Qattan K: A genetic association study of Angiotensin Converting Enzyme (ACE) polymorphisms and essential hypertension in the Kuwaiti population

**49**

\*Ismael F, Al-Bustan SA, Al-Rashdan I: Selective genetic markers in association with the development of coronary heart disease in the Kuwaiti population

### **Medical Education**

**50**

\*Al-Fouzan R, Al-Ajlan S, Marwan Y, Al-Saleh M: Factors affecting future specialty choice among medical students in Kuwait

**51**

\*Hassan SH, Al-Sharqawi N, Dashti F, AbdulAziz M, Abdullah A, Shukkur M, Thalib L: Level of empathy among Kuwait University medical students and its correlates

**52**

\*Marwan Y, Al-Saddique M, Hassan A, Karim J, Al-Saleh M: Are medical students accepted by patients in teaching hospitals?

**53**

\*Marwan Y, Karim J, Dawas A, Akhtar S: Self-confidence of medical students in performing clinical skills acquired during their surgical rotation: an assessment of a new teaching curriculum

### **Medicine**

**54**

\*Abdella NA, Mojiminiyi OA, Al-Mohammedi H, Pinto C, Al-Rammah T: Could gender dimorphism explain the controversial associations between RBP-4 and Cardiometabolic risk factors in obese subjects?

**55**

\*Abdelghani A, Hussain N: Evaluation of quality of care in Mubarak Al-Kabeer hemodialysis unit

**56**

Abdelwahab O, \*El-Barky E, Khalil M, Kamar A: Resistive index of prostatic blood flow In benign prostatic hyperplasia



**57**

\*Al-Ati T, Preston T, Al-Hooti S, Al-Hamad N, Al-Ghanim J, Al-Khulifi F, Al-Lahou B: Establishing stable isotope facilities for assessment of childhood obesity in Kuwait

**58**

\*Al-Adsani AMS, Hassanein REA, Khouzam SYA, Abd elkareem MRK, Shalla HA : Risk factors associated with diabetic foot complications in Kuwait

**59**

\*Alazmi W, Omar S, Altourah L: Prevalence of adenomatous colorectal polyps in Kuwait: A retrospective analysis

**60**

\*AlAzmi W, AlTourah L, Omar S: Prevalence of pancreas divisum in Kuwait

**61**

\*Al-Azmi W, Siddique I, Al-Ali J, Al-Fadli A, Memon A: Ulcerative colitis in an Arab population: Epidemiology and clinical course

**62**

Al Otaibi T, \*Gheith O, Halim M, Said T, Nair MP, Balaha MA, Abd-el-tawab K, Zakareya Z, Hosni W, Nampoory MRN: Critical illness polyneuromyopathy in renal transplant recipients: Risk factors and outcome

**63**

\*Ali H, Forraz N, McGuckin CP, Jurga M, Lindsay S, Ip BK, Trevelyan A, Basford C, Habibollah S, Ahmad S, Clowry GJ, Bayatti N: Making cortical neurons from umbilical cord blood stem cells

**64**

\*Al Mutairi SS, Mojiminiyi OA, Abdella NA, Al-alawi A, Al-Ramah T: Should glycated haemoglobin (HbA1c) be performed routinely in non diabetic patients with Obstructive Sleep Apnea (OSA)

**65**

\*Al-Shammri SN, Akanji AO, GirgisM, Mathew R, Bhattacharya A, Madala C: Kuwaiti patients with multiple sclerosis have demonstrable metabolic bone disease

**66**

Al-Shammri SN, Girgis M, \*Bhattacharya A, Mathew R, Madala C, Sharma P, Akanji AO: Environmental and socio-cultural risk factors associated with multiple sclerosis in Kuwait- A preliminary hospital based study.

**67**

\*Alessa T, Szeto A, Chacra W, Mendez A, Goldberg R: Elevated level of high density lipoprotein-cholesterol is common in adults with Type 1 Diabetes



**68**

\*Akanji AO, Al-Shammri SN, Bhattacharya A, Mathew R, Girgis M, Madala C: Functional derangement in Vitamin D and bone homeostasis in Arab patients with multiple sclerosis

**69**

\*Alsaadoun W, Bouhaimed M: Eyeopening look at eye makeup hygiene: Practice, risk factors, ocular symptoms and microbiological evidence

**70**

Bhattacharya A, Al-Shammari SN, Mathew R, Girgis M, Madala C, \*Akanji AO: Evidence for sub-clinical malnutrition in Kuwaiti patients with multiple sclerosis: Relationship with clinical phenotypes, disease activity and outcome.

**71**

\*Awadain WH, Hassan A, El-Deeb S, Hassan N, El-Agroudy A, Fouda A, Ghoneim M: Single center experience in steroid resistant acute cellular rejection: Risk factors and impact on graft and patient survival

**72**

\*Awadain WH, Nair MP, Nampoory MRN, Said T, Halim MA, Moneim MA, Vareed B, El-sayed A, Al-Otaibi T: A single centre experience postrenal transplants Zero-HLA mismatch

**73**

\*Al-Youha DS, Al-Nami ND, El-Ghandour NM, Al-Fahad FW, Mohammed AM, Al-Huwais SH, Al-Taiar AM: Association between oral hygiene practices and coronary heart disease in Kuwait

**74**

\*Gheith O, Zakareya Z, Al-Otaibi T, Halim M, Nampoory MRN: Impact of positive BK virus-kidney donors on renal transplant recipient outcome and possible protective HLA Loci

**75**

\*Hasan EA, Olusi SO, Mokaddem K, Sharma PN, Alawadhi A: Disease activity and serum lipid profile in patients with rheumatoid arthritis treated with Rituximab: A cohort study

**76**

\*Hasan EA, Olusi SO, AlAwadhi A, Mokaddem K, Sharma PN, George S: Effects of rituximab treatment on the serum concentrations of vitamin D and interleukins 2, 6, 7, and 10 in patients with rheumatoid arthritis

**77**

\*Hussain N, Abdelghani A: Spectrum of peritonitis in continuous ambulatory versus automated peritoneal dialysis in Mubarak Al Kabeer Hospital

**78**

\*Longenecker JC, Estrella MM, Sethi A, Ugarte R, Mohamed GA: Risk factors for renal disease progression after orthotopic liver transplantation



**79**

\*Mosaad AM, Hamdy AF, Hassan NM, Donia AF, Gheith O, Salem ME, El-Shahawy EM, Bakr MA, Ghoneim MA: Evaluation of growth in low-body-weight kidney transplant children: 25-year experience

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## **Original Research Abstracts By Subject Area**



**Allied Health**

*Category: Clinical*

**1**

**Distribution and antimicrobial susceptibility of *Stenotrophomonas maltophilia*: Six years study**

\*Joshi RM<sup>1</sup>, Rawdhan H<sup>2</sup>, Madbouly N<sup>1</sup>, Nair S<sup>1</sup>

<sup>1</sup>Microbiology Unit, Radiology, Nuclear Medicine & Laboratory Center, Yiacco Medical Co. K.S.C.C;

<sup>2</sup>Intensive Care Unit, Al-Adan Hospital

**Introduction:**

*Stenotrophomonas maltophilia* is a Gram negative bacillus widely distributed in nature. Hospitalized patients may get colonized and medical instrumentation may introduce the organism to normally sterile sites. Most infections are nosocomial and include bacteremia, wound infections, pneumonia and urinary tract infections. Organism is intrinsically resistant to most commonly used antimicrobials including betalactams. There is need to differentiate between colonization and infection caused by this opportunistic pathogen for the prudent use of antimicrobials. We present six years (Nov.2005 to Nov. 2011) data on *S.maltophilia* from Yiacco, Al- Adan Hospital.

**Methods:**

Study included 197 patients. Their demographic details were recorded. Cultures were done on routine bacteriological media. After recording colony characters, Gram stain, catalase and oxidase test findings, bacterial identification and antimicrobial susceptibility testing was done in MicroScan using NUC 35 and NBPC 34. *Pseudomonas aeruginosa* ATCC 27853 was used as a control strain.

**Results:**

Of 226 isolates of *S.maltophilia*, 29.20% were from ICU, 16.81% from Pediatric wards and 53.98% from other Wards/OPDs. Respiratory samples topped with 47.79%, while urine, blood and other body sites comprised 11.06%, 9.73% and 31.42% respectively. Majority of the isolates were resistant to three or more major groups of antimicrobial agents. While resistance to gentamicin, ciprofloxacin, tetracycline, ceftazidime and amikacin was seen in 83.19%, 80.97%, 76.99%, 76.55% and 73.45% respectively, it was encountered only in 7.96% to levofloxacin and 5.31% to trimethoprim/sulfamethoxazole.

**Conclusions:**

*S.maltophilia* is widely distributed in hospital environments. Nearly half of the isolates were recovered from respiratory specimens and about one third isolates from ICU patients. Almost 95% isolates were susceptible to trimethoprim/sulfamethoxazole which remains the drug of choice for treating *S.maltophilia* infections

*Key Words: Distribution; Antimicrobial susceptibility*

*Funding Agency: None*



**Allied Health**

Category: *Clinical*

2

## **Treatment length in ICU after cardiovascular surgery**

\*Mohammad Q, Christo P

Chest Disease Hospital, Ministry of Health, Kuwait

### **Introduction:**

Cardiovascular Surgery (CS) is frequently done in Kuwait to treat complications of Ischemic Heart Disease, to correct Congenital Heart Disease, or treat Valvular Heart Disease. Time plays an important role for Physical therapy (PT) in the ICU because patient assessment has to be done in order to start the rehabilitation program phase I.

Objectives: Determine the period of time a patient stays in ICU after CS, and the number of days it takes the PT to do an assessment of the post surgical patient to fit to phase I PT program.

### **Methods:**

Retrospective study (2003-2007) was done with 1929 patients with CS. All of them were followed during their ICU stay after CS. The length of stay in ICU was calculated for patients with and without complications using Statistical Package Social Sciences (SPSS) program.

### **Results:**

Data show that the average length of time that patients stayed in ICU after surgery was 2.5 days and for patients with complications it was 11 days. It was recorded that the longest a patient stayed was after valve replacement and other types of surgeries for the Arabic non-Kuwaiti 2.5 and 2.9 respectively. Both Kuwaitis and non-Kuwaitis shared the same time of days 2.4 PO after Valve Replacement , but in other types 2.6 days for Kuwaitis and 2.1 days for non-Kuwaitis. Statistics shows that Kuwaiti patients with Coronary Artery Bypass Surgery spend 2.6 days, more than Arabic and non-Kuwaiti. The same results were recorded for the last six months.

### **Conclusions:**

The results showed that the average number of days for PO patient in ICU is less than the number of days approved in the PT protocol in ICU from the ministry of health for doing the assessment .Modification needs to be taken in PT ICU protocol to fit the time that has been suggested in this study.

*Key Words: Cardiovascular surgery; ICU; Physical therapy*

*Funding Agency: None*



**Allied Health**

*Category: Undergraduate*

**3**

## **Assessment of bactericidal effect of photodynamic therapy on streptococcus mutans**

\*Saafan AM

Medical laser application, Laser Institute -Cairo University, Cairo, Egypt

### **Introduction:**

To assess the bactericidal effect of photodynamic therapy (PDT) on *Streptococcus mutans*.

### **Methods:**

Forty five children with simple class one carious molar were divided into three groups. Methylene blue (MB) was applied to the carious cavities (concentration of 100 ug/ml). Diode laser (650nm) was applied with average energies 4.8 J (group I), 9.6 J (Group II) and 14.4 J ( group III) respectively. Dentine samples were collected using a sterile sharp spoon excavator before and after laser irradiation for microbiological study.

### **Results:**

Statistical analysis of the collected data revealed a significant bactericidal effect of all the treated groups with maximum bactericidal effect (85.6%) with 14.4 J irradiation and minimum effect with 4.8 J irradiation (38.8).

### **Conclusions:**

Under the circumstances of this study, we can conclude that photodynamic therapy can be considered as a promising effective technique, that may play a role in the atraumatic restorative dentistry.

*Key Words: Caries; Lasers and PDT*

*Funding Agency: None*



**Anatomy**

Category: Basic Sciences

4

**Fracture toughness of sea otter enamel**

\*Lucas PW<sup>1</sup>, Ziscovici C<sup>2</sup>

<sup>1</sup>Department of Bioclinical Sciences, Faculty of Dentistry, Kuwait University;

<sup>2</sup>Department of Anthropology, George Washington University

**Introduction:**

We tested the fracture behaviour of the enamel of a carnivore in chipping tests.

**Methods:**

Sea otter (*Enhydra lutris Mustelidae*) teeth were obtained, still within jaws (from Melissa Miller, California Fish and Game, with full permission). Teeth were excised and their roots embedded in epoxy resin blocks. Teeth were kept hydrated prior to experiment and cut so that a flat enamel (transverse) surface was obtained. A Vickers pyramid, ground onto the end of a 6-mm diameter tungsten carbide rod, was fixed in a mechanical tester with its tip directed vertically to contact the enamel at a distance  $h$  from the tooth edge. The load was gradually increased until, at a peak force  $P_F$ , a scallop-shaped chip broke away from the enamel. Previous work on chipping fine-grained ceramic materials and human enamel suggests that  $P_F = 9.3Th^{1.5}$ , where  $T$  is fracture toughness. Log-log plots of  $P_F$  versus  $h$  for varying  $h$  were constructed such that the gradient could reveal  $T$  for sea otter enamel. Enamel structure was examined by LM and ESEM.

**Results:**

Data for 12 chips were obtained. Plots of  $\log P_F$  vs.  $\log h$  were linear, but with substantial scatter. The apparent average toughness of sea otter enamel was 1.8 Mpa  $m^{1/2}$ , close to double that in the human. However, there was considerable plasticity under the indenter. Structural study by LM confirmed that prism decussation of the inner enamel of sea otters was greater than in humans, extending close to the enamel surface. Crack paths observed using ESEM showed that fractures often crossed enamel rods.

**Conclusions:**

Sea otters appear to have tougher enamel than humans. As carnivores suffer frequent dental fractures, it is logical to suppose that their teeth have been under strong selective pressure to combat fracture damage.

This abstract was previously presented at the IADR AMER meeting in Abuja, Nigeria 2011.

*Key Words: Dental anatomy; Hard tissue properties; Fracture mechanics*

*Funding Agency: None*



**Anatomy**

*Category: Basic Sciences*

**5**

**Effect of developmental lead exposure on neurogenesis in wistar rats**

Mousa AMA, \*Elshahat M

Faculty of Medicine, Kuwait University

**Introduction:**

Lead (Pb) is a neurotoxic heavy metal that continues to be a major public health problem. It particularly affects the developing nervous system. The present study examined the temporal effect of perinatal lead exposure on neurogenesis during development.

**Methods:**

0.5% lead acetate was administered to pregnant Wistar rats on the first day of pregnancy and continued through the whole period of experiment. Control animals received deionized water. Animals were grouped as follows: gestational day (GD) 18 and 21 and postnatal day (PD) 7, 14, 21 and 28 in both control and experimental groups. 5 $\mu$ m sections were stained with cresyl violet or immunostained with anti-PCNA or GFAP.

**Results:**

At 18GD and 21GD, significant ( $P < 0.05$ ) increase in PCNA-positive nuclei per 100  $\mu$ m<sup>2</sup> was observed in the ventricular and subventricular zones of lateral ventricle in the experimental group. However, the number of mitotic figures in these regions did not show significant difference between the two groups. Postnatally, the number of PCNA-positive nuclei was markedly decreased especially after the first week. The experimental groups showed significant ( $P < 0.05$ ) decrease in PCNA-positivity in comparable to control. The mitotic figures were also slightly less in lead exposed animals than control. In the sensorimotor cortex the number of PCNA-positive nuclei was significantly ( $P < 0.05$ ) lower in lead exposed groups than control at 7, 14, and 21PD. However, the decrease was not significant by 28PD. The neuron density in experimental group was comparable to control till the second postnatal week. At 21PD the experimental group showed significant ( $P < 0.05$ ) decrease in neurons density. By 21PD, GFAP –positive reaction was significantly higher in experimental groups.

**Conclusions:**

Lead exposure may have a trophic effect on neurogenesis and gliogenesis prenatally and inhibitory effect postnatally.

*Key Words: Neurogenesis; Rat development*

*Funding Agency: None*



**Anatomy**

Category: *Basic Sciences*

6

## **Intrauterine lead nitrate exposure induces apoptosis in rat fetal cerebellum**

\*Mousa AMA, Al-Fadhli A, Rao MS, Kilarkaje N  
Kuwait University

### **Introduction:**

Lead is a ubiquitous environmental toxicant known to interact with almost all organ systems. The present study was designed to investigate putative pro-apoptotic effects of lead on fetal rat cerebellum.

### **Methods:**

Female Sprague–Dawley rats were divided into two groups (N=3/group); Group 1- control and group 2- treated with 1% of lead nitrate for three weeks before conception and during pregnancy and sacrificed on gestational day 21. The fetal cerebella were separated, weighed and prepared for immunohistochemical study for the expression of p53, Bax, Bcl-2, Caspase 3 and glial fibrillary acidic protein (GFAP). Slides were scanned by a light microscope and images were captured with a digital camera. Ten random microscopic fields were evaluated in each slide by using an image analyzer (AnalySIS Life Science, Germany). The slides were evaluated at 40X magnification; the area of one field equals 2284543.06  $\mu\text{m}^2$ . The blue color was separated and the threshold was set at 110-198 and brown area was measured. The mean density value was measured for each animal. Finally, the percentage of immunohistochemically positive area/field was measured to obtain an index of intensity of staining. Data were expressed as mean + SD for each group and subjected to statistical analysis by One-way ANOVA.

### **Results:**

Lead exposure results in decrease in fetal brain weight compared to control ( $P<0.05$ ). Lead nitrate but not the control induces structural damage, up-regulation of Bax ( $P<0.001$ ), caspase 3 ( $P<0.05$ ) and down-regulation of Bcl-2 ( $P<0.01$ ) but did not affect p53 activities. The GFAP expression was significantly down-regulated in lead-exposed group ( $P<0.01$ ) compared to control group.

### **Conclusions:**

Decreased GFAP immunoreactivity suggests a glia-mediated response to lead. Up-regulation of pro-apoptotic proteins indicates lead-induced apoptosis of cerebellar neurons.

*Key Words: Lead; Apoptosis; p53, Bax, Bcl-2, Caspase 3*

*Funding Agency: NONE*



**Behavioral Sciences**

*Category: Basic Sciences*

7

**Prevalence of metabolic syndrome among female adolescents using two criteria**

\*Al-Isa AN

Department of Community Medicine & Behavioural Sciences, Faculty of Medicine, Kuwait University

**Introduction:**

The prevalence of overweight and obesity are high in Kuwait. Metabolic Syndrome is associated with both. It is expected to find the syndrome to be high. The objective is to assess the prevalence of MS using two different diagnostic criteria, the International Diabetes Federation (IDF) and the National Cholesterol Education Program-Third Adult Treatment Panel Modified for age (NCEP- ATP III).

**Methods:**

Data for this multi-stage random sample study was collected from a sample of 303 male Kuwaiti adolescents, 10-19 years of age, selected from four randomly selected, two intermediate and two high schools, one from each governorate, the Capital and Hawally, selected randomly. Anthropometric measurements and biochemical tests on blood samples were carried out. The IDF and the ATP III criteria were used to test for the presence of MS parameters.

**Results:**

Each of the two criterion revealed that the prevalence of MS was 14.8 and 19.5%, using the IDF and the ATP III criteria, respectively.

**Conclusions:**

Significant implications may be drawn from these results, especially when it comes to being at risk of type 2 diabetes (T2D), hypertension and cardiovascular disease (CVD).

*Key Words: Metabolic Syndrome; Female; Kuwaiti*

*Funding Agency: None*



**Behavioral Sciences**

Category: Undergraduate

8

## **The acute effect of Shisha smoking on oxygen saturation level and heart rate**

\*Al-Osaimi A, Obaid O, Al-Asfour Y, Yousef A, Razouki M, Rajab SH  
Department of Community Medicine, Faculty of Medicine, Kuwait University

### **Introduction:**

Previous studies have shown that shisha smoking is associated with chronic health problems. However, very few studies have addressed the acute effects of shisha smoking, such as oxygen saturation and heart rate. The aim of this study was to assess the acute changes in oxygen saturation and heart rate following shisha smoking.

### **Methods:**

This concurrent cohort study enrolled 220 shisha smokers from 22 shisha houses in Kuwait. Personal data were collected using questionnaires. Oxygen saturation and heart rate were measured at baseline (using a hand-held oximeter) and at 30 minutes after initiation of shisha smoking. The main outcome variables were change from baseline in oxygen saturation and heart rate.

### **Results:**

Compared to baseline, oxygen saturation decreased by 0.39% ( $p < 0.001$ ). The only variables associated with change in oxygen saturation (more than 2% decrease) after adjustment for age and gender was asthma (OR=3.4 [95% Confidence Interval, 1.3–9.3] and history of smoking (OR=2.4 [1.02, 5.7]). Heart rate increased from baseline by an average of 15 bpm ( $p < 0.001$ ). Factors associated with increase in heart rate ( $>15$  bpm) after adjustment, included male gender, younger age, frequent shisha smoking, and change in head weight  $>4$  grams. A minority of participants (6.4%) had a very large increase in heart rate ( $>50$  bpm), and 8 (3.6%) participants had a heart rate over 200 bpm after 30 minutes of shisha smoking.

### **Conclusions:**

Shisha smoking was significantly associated with an increase in heart rate and a decrease in oxygen saturation. Extreme increases in heart rate were found in a small group of participants, suggesting that some shisha smokers may be vulnerable to the sympathomimetic effects of shisha smoking.

*Key Words: SHISHA Smoking; Heart rate; Cohort study*

*Funding Agency: None*



**Biochemistry**

Category: Graduate MSc (Basic Science)

9

**The role and regulation of colonic sodium/hydrogen exchanger isoforms 1 and 3 in spontaneous hypertensive rats**

\*Abu Ghefreh A, Khan I.

Department of Biochemistry, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

Role of colonic Na-H exchanger (NHE) isoforms-1 and 3 which regulate water and electrolyte absorption from GI-tract and kidneys is poorly investigated in hypertension. Further to elucidate the underlying mechanism of regulation of NHE, the expression of NHERF-1 and cGK-II, and sodium pump which regulate the activity of NHE were also examined.

**Methods:**

In this study 12 week old spontaneously hypertensive rats (SHR) and WKY rats as normal controls were used. Groups of animals were also treated with captopril (CAP) starting from week 4 after birth till week 12. Levels of NHE-1, NHE-3, NHERF and cGKII proteins were examined using ECL western blot analysis.

**Results:**

SHR animals showed a significant proteinuria and increase in kidney and heart weights, and a decrease in the urine output as compared to WKY controls. Myeloperoxidase activity was also significantly increased in SHR colon. Expression of NHE-1, NHE-3, and NHERF-1 and activity of sodium pump was significantly decreased, while that of cGK-II was increased in SHR colon as compared to WKY controls. CAP was able to partially reverse these in SHR. Yield of microsomal protein was not different in the test and the control groups.

**Conclusions:**

We demonstrated hypertension-induced inflammation in SHR colon. Suppression of NHE-1, 3 protein and NHERF-1 expression, increase in cGK-II protein expression, and decrease in sodium pump activity would suppress uptake of water and NaCl from GI-tract and hence may be a counteracting response of GI-tract to the development of hypertension.

*Key Words: Hypertension; Sodium/hydrogen exchangers; Inflammation*

*Funding Agency: Kuwait University Research Administration (Grant YM06/10), and College of Graduate Studies.*



**Biochemistry**

Category: Graduate MSc (Basic Science)

10

**A new discovery in G6PD deficiency explains favism, drug sensitivity and resistance to malaria**

\*Al-Ansary M, Benov L, Craik J

Department of Biochemistry, Kuwait University

**Introduction:**

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most prevalent inherited enzyme deficiency worldwide. G6PD activity is required to maintain levels of the cellular antioxidant reduced glutathione. Affected individuals may suffer from episodic hemolytic anemia following infection or ingestion of certain foods ('Favism') and drugs. However, not all G6PD-deficient subjects are sensitive to fava beans; some severely G6PD-deficient individuals can ingest fava beans without harm. This 'favism mystery' has challenged investigators for the last 50 years.

**Methods:**

Immunoblotting techniques were used to measure expression of erythrocyte membrane proteins. Nucleoside transport rates were estimated using <sup>3</sup>H-uridine radiotracer. Statistical analysis was undertaken with SPSS. Extreme pathway analysis (Wilbeck&Palsson, 2002) was used to track possible effects of reduction of hENT1 and G6PD deficiency on 39 routes of erythrocyte metabolism.

**Results:**

Immunoblot analysis showed significant and variable decrease in expression of hENT1 nucleoside transporter ( $p < 0.005$ ), but not of glucose transporter (Glut1) or anion transporter (AE-1), in G6PD-deficient cells. Uridine flux measurements showed significant decrease in nucleoside transport activity ( $p < 0.05$ ).

**Conclusions:**

G6PD-deficient individuals show 20-80% reduction of hENT1 with associated decreases in nucleoside transport. Pathway analysis suggests that G6PD-deficiency and low hENT1 expression causes suppression of more than 70% of important metabolic routes, while individuals with high hENT1 expression are suggested to have more metabolically active erythrocytes. We suggest a new answer of drug sensitivity which could be due to drug-hENT1 interactions. Our hypothesis fits a concept of increased resistance of G6PD-deficient individuals against the malaria parasite *Plasmodium falciparum*. We suggest a novel solution to the 'Favism mystery' based upon variable deficiency of hENT1 expression.

*Key Words: Erythrocyte pathways; G6PD deficiency anemia; Favism*

*Funding Agency: Research Administration Kuwait University*



**Biochemistry**

Category: Basic Sciences

11

## **RAGE a deterrent force in the pathogenesis of cardiovascular complications in diabetes**

\*Madhu D, Zamoony J.

Department of Biological Sciences, Faculty of Science, Kuwait University

### **Introduction:**

hRAGE (human Receptor for advanced glycation end products) is a multi-ligand cell surface receptor belonging to IgG superfamily. It plays a vital role in both inflammatory diseases and cardiovascular diseases, and its malfunction has been linked directly to vascular injury in diabetes. Studies reveal that the cytoplasmic region, which is essential for intracellular signalling, is linked directly to diabetes complications. So the main objective is to decipher the structure of transmembrane and cytosolic domain by NMR.

### **Methods:**

Molecular biology techniques were performed to produce a recombinant plasmid and confirmation by DNA sequencing. Then the optimal cell line to express the recombinant protein was chosen based on our test expression screen. This was followed by trial purifications. Affinity chromatography was performed to isolate the fusion protein proceeded by test cleavages to separate the target protein from the affinity tag. The separated protein of interest was then subjected to size exclusion chromatography to get the purified form of the hRAGE protein. Finally the purified protein was characterized by several biophysical analysis such as NMR, mass spectroscopy and fluorescence.

### **Results:**

Affinity chromatography by amylose column was optimized to get the intact purified hRAGE. Test cleavages separated the affinity tag (MBP) from the hRAGE. It was then subjected to size exclusion chromatography to obtain the pure fraction. This was followed by characterization of RAGE by mass spectroscopy analysis (MALDI TOF-TOF) and NMR that confirmed the integrity of the target protein and established it as having an intrinsically disordered region.

### **Conclusions:**

Our efforts at the level of molecular biology, protein chemistry and preliminary biophysical analysis such as NMR screening and mass spectroscopy have revealed which of our RAGE constructs to be most amenable for further structure determination.

*Key Words: IMAC; NMR*

*Funding Agency: Kuwait University RA project RS01/09*



**Biochemistry**

Category: Basic Sciences

12

**Adipocyte Enhancer-Binding Protein 1 (AEBP1) is a pro-atherogenic factor in mice**

\*Majdalawieh AF<sup>1</sup>, Bogachev O<sup>2</sup>, Pan X<sup>2</sup>, Zhang L<sup>2</sup>, Ro HS<sup>2</sup>

<sup>1</sup>Faculty of Arts & Sciences, Department of Biology, Chemistry and Environmental Sciences, American University of Sharjah, Sharjah, United Arab Emirates; <sup>2</sup>Faculty of Medicine, Department of Biochemistry & Molecular Biology, Dalhousie University, Halifax, Nova Scotia, Canada

**Introduction:**

Atherogenesis is a long-term process that involves inflammatory response coupled with metabolic dysfunction. Adipocyte enhancer-binding protein 1 (AEBP1) has been shown to impede macrophage cholesterol efflux, promoting foam cell formation, via PPAR $\gamma$ 1 and LXRA down-regulation. The objective of this study was to assess the role of macrophage AEBP1 in promoting atherosclerosis.

**Methods:**

Atherosclerotic lesion formation and macrophage infiltration were assessed using AEBP1<sup>-/-</sup>/LDLR<sup>-/-</sup> double-knockout mice, en face analysis, bone marrow (BM) transplantation, and immunohistochemistry of aortic cryosections. mRNA and protein levels were assessed by real-time PCR and immunoblotting, respectively.

**Results:**

AEBP1-transgenic mice (AEBP1TG) with macrophage-specific AEBP1 over-expression exhibit hyperlipidemia and develop atherosclerotic lesions. Consistently, ablation of AEBP1 results in significant attenuation of atherosclerosis in the AEBP1<sup>-/-</sup>/LDLR<sup>-/-</sup> double-knockout mice. BM transplantation experiments further revealed that LDLR<sup>-/-</sup> mice reconstituted with AEBP1<sup>-/-</sup>/LDLR<sup>-/-</sup> BM cells (LDLR<sup>-/-</sup>/KO-BM chimera) display significant reduction of atherosclerosis lesions compared to control mice reconstituted with AEBP1<sup>+/+</sup>/LDLR<sup>-/-</sup> BM cells (LDLR<sup>-/-</sup>/WT-BM chimera). Furthermore, transplantation of AEBP1TG BM cells with normal ApoE gene into ApoE<sup>-/-</sup> mice (ApoE<sup>-/-</sup>/TG-BM chimera) leads to significant atherogenesis despite the restoration of ApoE expression. Macrophages from ApoE<sup>-/-</sup>/TG-BM chimeric mice express reduced levels of PPAR $\gamma$ 1, LXRA, ABCA1 and ABCG1 and increased levels of the inflammatory mediators IL-6 and TNF $\alpha$  compared to macrophages of control chimeric mice (ApoE<sup>-/-</sup>/NT-BM) that received AEBP1-non-transgenic (AEBP1NT) BM cells.

**Conclusions:**

These data strongly suggest that macrophage AEBP1 plays critical regulatory role in atherogenesis. We anticipate that AEBP1 may serve as a potential therapeutic target for the treatment of atherosclerosis.

*Key Words: Macrophages; Atherosclerosis; Bone Marrow transplantation*

*Funding Agency: None*



**Biochemistry**

Category: Basic Sciences

13

## **Fe-porphyrins: Superoxide scavengers and antibacterials**

\*Thomas M<sup>1</sup>, Batinic-Haberle I<sup>2</sup>, Benov L<sup>1</sup>

<sup>1</sup>Department of Biochemistry, Faculty of Medicine, Kuwait University, Kuwait; <sup>2</sup>Department of Radiation Oncology, Duke University Medical Center, Durham, USA

### **Introduction:**

Mn N-alkylpyridylporphyrins (MnPs) are among the most powerful catalytic antioxidants (AO). Fe porphyrins (FePs), in contrast, are considered potentially dangerous because Fe can participate in the Fenton reaction producing hydroxyl radicals. In addition, FePs may interfere with bacterial heme transport and metabolism and thus act as bacteriostatics. The aim of this study was to investigate the physico-chemical properties, catalytic and biological activities of ortho and meta FeP isomers.

### **Methods:**

The FePs were synthesized as previously described (Batinic-Haberle, et al. 2011). FePs were characterized using Uv/vis spectroscopy, electrospray ionization mass spectrometric analysis and cyclic voltametry. Biological tests were done on wild E. coli and mutants carrying deletions of superoxide dismutases (SOD), and of the oxyR regulon. All experiments were repeated at least 3 - 5 times with 3 replicates. Results are expressed as means  $\pm$  S.E.

### **Results:**

Series of ortho and meta Fe(III) N-alkylpyridylporphyrins (alkyl = methyl, ethyl, butyl, hexyl, octyl) were synthesized and characterized. Metal-centered reduction potentials of ortho isomers, E1/2 were more positive than that of their respective meta analogs. The superoxide dismutating activity, expressed as  $k_{cat}$  ( $O_2^{\cdot-}$ ), was higher for both ortho and meta FePs compared to their respective MnP analogs. Irrespective of their higher superoxide scavenging abilities, FePs exert bacteriostatic effects and induce catalases/peroxidases via activation of the oxyR regulon.

### **Conclusions:**

Differences in the axial coordination of the metal site play a critical role in the thermodynamics and kinetics of superoxide dismutation catalysis. The observed antibacterial activity can be attributed in part to generation of hydrogen peroxide via redox-cycling.

*Key Words: Iron-porphyrin; Superoxide scavenger; Antibacterial*

*Funding Agency: Grant MB01/09 from Kuwait University*



**Community Medicine**

*Category: Graduate (Resident)*

14

**Evaluation of coordination between Ministry of Health and other governmental agencies of Kuwait in providing public health services**

\*Al-ateeqi AM

Department of Community Medicine & Behavioral Sciences, Faculty of Medicine, Kuwait University

**Introduction:**

The Ministry of Health (MOH) in Kuwait, has distributed many of its public health tasks to other governmental agencies. However, coordination between the MOH and these agencies has remained a major challenge. In this study, we aimed to evaluate the level of coordination between the MOH and different public sector agencies. We report our findings based on survey with key decision makers in MOH & Public Authority of Agriculture and Fish Resources (PAAF) in relation to diagnosis and management of zoonotic diseases in Kuwait.

**Methods:**

From January to May 2010, we used a qualitative approach in a semi-structured interview with a number of key administrators in the MOH and PAAF, to collect data on different aspects of coordination between the two organizations in relation to zoonotic diseases.

**Results:**

All participants agreed that there were lack of planning and coordination. Despite of the existence of a committee that constituted in 1987, which supposed to meet quarterly at least to coordinate between MOH & PAAF, committee has not convened for more than 11 months, at the time of data collection, Furthermore of 36 cases of human brucellosis and 582 human cases of animal bite registered in MOH, expected to be reported to PAAF to investigate the animal source of brucellosis and take the precautionary measures in cases of animal bite, only 1 and 10 were respectively reported to PAAF. Additionally MOH was un-aware of an on-going outbreak of Glanders - a notifiable zoonotic disease, identified by PAAF for more than 1 year prior to data collection for this study.

**Conclusions:**

There appears to be a lack of coordination between MOH and PAAF that affect the control of zoonotic diseases in Kuwait. Therefore urgent efforts are needed in updating the regulations and strengthening the coordination between different entities to provide better public health services.

*Key Words: Zoonotic diseases; Coordination; Public health*

*Funding Agency: None*



**Community Medicine**

Category: Undergraduate

15

**The prevalence of and factors associated with work-related sleep disturbance in working population of Kuwait**

\*Al-Enezi BS, Al-Mutairi AY, Al-Arbeed AA, Al-Obaidan A, Al-Jenfawi MK, Al-Ajmi AS, Akhtar S  
Faculty of Medicine, Kuwait University

**Introduction:**

Sleep disturbance is a worldwide problem. This study aimed to assess i) to assess the prevalence of work-related sleep disturbance in working population and ii) to evaluate the factors associated with sleep disturbance.

**Methods:**

This cross-sectional study was conducted to assess the prevalence of work-related sleep disturbance in a sample of working population of three of 16 ministries in public sector of Kuwait. Also, we evaluated the factors associated with sleep disturbance. Employees of any gender, age or nationality, or nature of the office work were eligible for inclusion in the study sample. The participant was considered to have suffered from sleep disturbance, if he or she responded 'every day' to the question 'In the past three months how often have you had difficulty sleeping because thoughts about have kept you awake?'

**Results:**

In the three ministries, we approached 620 workers, 603 (97.3%) of whom consented to participate in the study. The prevalence of work-related sleep disturbance among working population of Kuwait was 17.1%. Gender was statistically significantly ( $p = 0.019$ ) associated with sleep disturbance and the prevalence of sleep disturbance among males was 20.1% higher than among females (12.8%). Other factors significantly ( $p < 0.05$ ) associated with work-related sleep disturbance on univariate logistic regression analyses were taking office work to home, suffering daily headache, diagnosed with thyroid disease, anxiety/ stress, feeling very exhausted after work

**Conclusions:**

Prevalence of work-related sleep disturbance among employees in the public sector of Kuwait is quite high 17.1%. A cohort study of sleep disturbance and associated factors in this and other working population including shift workers is suggested. An educational campaign to increase the public health awareness about work-related sleep disturbance and its associated factors may reduce the problem in this population.

*Key Words: Sleep disturbance; Risk factors; Working population*

*Funding Agency: None*



## **Community Medicine**

Category: Undergraduate

16

### **Knowledge, attitude, and screening practice among Kuwaiti adult males at risk regarding prostate cancer**

\*Al-Faddagh A, Al-Fadaghi A, Abdulrida M, Al-Fadhli J, Al-Otaibi F, Al-Hajery N, Moussa M  
Department of Community Medicine, Faculty of Medicine, Kuwait University

#### **Introduction:**

To assess the level of knowledge, attitude and screening practices among adult Kuwaiti men at risk of prostate cancer (Pca) as well as their relationship with sociodemographic characteristics.

#### **Methods:**

This cross-sectional study involved 209 adult Kuwaiti men above the age of 50 years. Data were collected via a personal interview which included sociodemographic characteristics (reported as a score), knowledge about Pca (based on risk factors and PROCASE knowledge index), attitude towards Pca screening (using the theory of planned behavior questionnaire), and screening practices. Logistic regression analysis was used to assess the association between low level of knowledge or screening practices with characteristics and attitude after adjusting the confounding.

#### **Results:**

Less than 15% of participants had high knowledge score regarding risk factors and the PROCASE knowledge index. Moreover, 95.7% of participants had positive attitude towards prostate cancer screening, despite the low reported prostate cancer screening practice (25.8% of the sample). The majority of screening practices were done in governmental hospitals. Neither knowledge nor attitude were associated with screening practices. Additionally, the participants' level of knowledge regarding Pca was not associated with their attitude. The logistic regression analysis showed that age (adjusted odds ratio, aOR=2.5, p=0.018), smoking (aOR= 2.2, p=0.048) and knowledge score about symptoms/tests (adjusted OR= 1.2, p=0.033) were significantly and independently associated with screening practice. Age (aOR=6.3, p=0.001), smoking (aOR=2.8, p=0.01), and socioeconomic status score (aOR=0.8, p=0.045) were independently associated with low level of knowledge with statistical significance.

#### **Conclusions:**

Low proportion of Kuwaiti men above 50 years of age have high knowledge about Pca, and screening practices, despite the positive attitude towards screening. Neither knowledge nor attitude towards screening

*Key Words: Prostate cancer; Screening; Knowledge and attitude*

*Funding Agency: None*



**Community medicine**

Category: Undergraduate

17

**Disability, pain and quality of life in relation to low back pain among teachers in Kuwait**

\*Al-Haddad F, Al-Farhan M, Behbehani J, Karimi M, Asem M, Thalib L  
Faculty of Medicine, Kuwait University

**Introduction:**

To quantify the prevalence of low back pain (LBP), identify the risk factors as well as explore the effects of LBP on disability, quality of life and pain among teachers in Kuwait.

**Methods:**

A cross sectional survey was conducted using multi-stage cluster sampling method with a sample size of 599. Our participants were drawn from 18 different schools in three governorates in Kuwait. Data were collected through a self-administered questionnaire that consisted of validated and standardized tools including Roland-Morris disability assessment, NRS rating scale for pain severity and SF-12 for quality of life assessment. The questionnaire also consisted of risk factor profiles such as socio-demographic, lifestyle, clinical history and workload. We evaluated LBP using a standardized low back pain assessment tool. Risk factors, quality of life, disability and pain were compared between those teachers with LBP, versus those without, using appropriate statistical tests. We also reported the odds ratios (OR) and 95% confidence intervals along with the P values.

**Results:**

The lifetime and 12 months prevalence of LBP were 52.7% and 47.1%, respectively. We also found 39.2% of the teachers were currently in pain at the time of our study. We found the teachers with LBP had significantly decreased quality of life with a significantly higher level of disability. We also identified a number of other risk factors associated with low back pain. That included co-morbidities such as asthma, neck pain and spinal deformities in addition to lack of exercise and smoking.

**Conclusions:**

We found an alarming level of LBP among the teachers indicating a significant public health problem, perhaps with little attention.

*Key Words: Low back pain; Kuwait; Teachers*

*Funding Agency: None*



**Community Medicine**

*Category: Undergraduate*

**18**

**Prevalence of vitamin D deficiency among adults at the Health Sciences Centre in Kuwait**

Al-Kanderi A, Al-Eidan S, Al-Juaidi F, Al-Safi A, \*Taqi S, Bouhaimed M

Department of Community Medicine and Behavioural Sciences, Faculty of Medicine, Kuwait University

**Introduction:**

Vitamin D is not simply needed for healthy bones; it is responsible for many physiologic processes which help to regulate muscle function, immune function, insulin synthesis, cell proliferation, cell apoptosis and control of malignant cell growth. All the diseases reported in the literature to be associated with vitamin D deficiency are prevalent in Kuwait and result in high morbidity and mortality. The main objective of this study was to estimate the prevalence of vitamin D deficiency among apparently healthy adult population at the Health Sciences Center in Kuwait.

**Methods:**

A cross sectional study using convenience sampling was designed to estimate the prevalence of vitamin D3 deficiency among adults (students and employees both Kuwaitis and non Kuwaitis). A total of 330 participants were studied using a self-administered questionnaire and analysis of serum Vitamin D3 (Elecys assay). A subgroup analysis of total Vitamin D was performed in 10% of the original sample using the LIAISON assay.

**Results:**

The estimated prevalence is 98.2% by serum vitamin D3 assessment (cut off point <50 nmol/L) which is currently used by the Ministry of Health in Kuwait. This prevalence will hypothetically be lower at 83.1% if a lower cut off point of <25 nmol/L is to be used following the NICE guidelines. This prevalence will hypothetically be even less at 75% when measuring the total vitamin D and not the D3 levels. Multiple regression models after stratifying by gender showed that age and amount of milk consumption were the only significant factors associated with deficiency in males while age and supplement consumption were significant among females.

**Conclusions:**

There is a very high prevalence of vitamin D deficiency among this group of apparently healthy adults despite the use of different laboratory tests and different cut-off levels. Standardizing the tests for proper assessment and management of vitamin D deficiency is highly recommended.

*Key Words: Vitamin D3; Total Vitamin D; Adults*

*Funding Agency: None*



**Community Medicine**

Category: Undergraduate

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## **Self-reported prevalence and correlates of ADHD among Kuwait University students**

\*Al-Mazidi A, Al-Hajeri M, Al-Juwaisri N, Al-Jassar R, Al-Khalifa S, Al-Rayes S, Shah N  
Community Medicine Department, Faculty of Medicine, Kuwait University

### **Introduction:**

Attention Deficit Hyperactivity Disorder (ADHD) starts in early childhood and may persist into adulthood. This disorder is of a great importance due to its likely impact on academic, behavioral, and social outcomes.

Objectives: (1) To estimate the prevalence of self-reported ADHD and its socio-demographic and behavioral correlates among Kuwait University students. (2) To assess the academic and other probable consequences of ADHD.

### **Methods:**

A sample of 1035 students was selected from four faculties of Kuwait University. A self-administered questionnaire was used to evaluate the prevalence, associated factors, and probable consequences of ADHD. An 18 item ASRS-V1.1 symptom checklist was used to measure ADHD. This scale has two subtypes, inattentive and hyperactive, each consisting of 9 items.

### **Results:**

Out of 1104 distributed questionnaires, 1035 (93.8%) were completed. The prevalence of inattentive and hyperactive ADHD among Kuwait University students was 7.9% and 7%, respectively. Living with persons other than both parents increased the likelihood of ADHD. Students who had parents with a lower educational level were more likely to report a high level of inattentive ADHD. Eating more chocolate bars per day was positively associated with the likelihood of both ADHD subtypes. Fish consumption was inversely related with the inattentive subtype only. Among students who were highly likely to have inattentive ADHD, 50% were absent for five or more lectures compared with 28.8% who were unlikely to have it. For both subtypes, significantly larger percentages of individuals with high ADHD scores reported failing two or more courses and sleeping less than 6 hours per night, compared with those unlikely to have ADHD.

### **Conclusions:**

Self-reported ADHD was significantly associated with poorer educational achievements and higher amounts of sleep difficulties. These findings highlight the need for raising awareness through education programs among the population.

*Key Words: ADHD; Prevalence; Correlates*

*Funding Agency: None*



## **Community Medicine**

Category: Undergraduate

20

### **Infertility and the use of assisted reproductive techniques among employed Kuwaiti women**

Al-Mubarak SJ, Al-Refaie AT, Behbehani LA, \*Abul MF, Longenecker JC.

Department of Community Medicine, Faculty of Medicine, Kuwait University, Kuwait.

#### **Introduction:**

Assisted Reproductive Techniques (ART) are medications and procedures used to aid infertile couples to conceive a child. The aim of this study is to assess the knowledge of, attitudes towards and factors associated with the experience with ART.

#### **Methods:**

This cross-sectional study enrolled 636 Kuwaiti women, working in Kuwaiti government ministries. The study questionnaire consisted of 44 questions divided into 4 sections (sociodemographic information, general knowledge of ART, reproductive history, and attitudes towards ART).

#### **Results:**

The prevalence of ART use among woman in their last attempt to get pregnant was 27.9%. Of those, 40% used ART before attempting pregnancy for 12 months. The commonest type of ART being used was fertility drugs (82%). Factors associated with ART use include having no children (OR 3.7;  $p < 0.001$ ), the age group of 26 to 34 (OR 1.9;  $p = 0.05$ ). ART use was associated with higher report of complications in pregnancy (vaginal bleeding, C-section, multiple pregnancy, pre-mature child, and low birth weight). ART was not associated with education, cultural background, occupation and income. There was no association found between the type of doctor and the use of ART; however 68% of woman indicated they chose private hospital doctors to care for their pregnancy. The majority of women (over 67%) were aware of fertility drugs, IUI, and IVF, but ICSI, ZIFT, and GIFT were less commonly known. A common misconception among woman was that ART was used to have twins (61%). Most women (~90%) thought that ART is socially acceptable and not against their religious beliefs. Around 80% felt there is social pressure to use ART.

#### **Conclusions:**

Our study suggests that ART maybe overused by young Kuwaiti woman. A large percentage of women are seeking ART use before completing a year of trying to conceive a child, and many report high social pressure to use ART. These data can guide public health programs aimed at increasing knowledge of the risks of ART.

*Key Words: Infertility; Assisted Reproductive Techniques; Kuwait*

*Funding Agency: None*



**Community Medicine**

Category: Undergraduate

21

**Patterns and determinants of current breastfeeding among mothers with children under one year of age in Kuwait**

\*Al-Sulaiteen N, Al-Anteri E, Al-Thaher F, Fareh F, Al-Rashidi F, Najem N, Al-Taiair A  
Department of Community Medicine and Behavioral Sciences, Faculty of Medicine, Kuwait University

**Introduction:**

Although the benefits of breastfeeding to both infants and mothers are well recognized, breastfeeding practices remain less than optimal in many countries. In Kuwait, as in many other countries in the Gulf region, there is a lack of data on the current breastfeeding practices and the factors associated with these practices.

Objectives: This study aimed to assess the prevalence of breastfeeding initiation in the youngest child, and the prevalence of current breastfeeding and exclusive breastfeeding among mothers with children  $\leq 6$  months as well as to investigate the determinants of current breastfeeding.

**Methods:**

A cross-sectional study on 488 mothers with children under one year of age, who attended health centers to vaccinate their child, was conducted. Data were collected by a face-to-face interview using a structured questionnaire in seventeen health centers distributed in 6 governorates.

**Results:**

Out of 521 mothers approached, 488 (93.7%) completed the interview. The prevalence of breastfeeding initiation was 92.8% (95% CI:90.1%-95.0%) among mothers with children  $<$  one year, while the prevalence of current breastfeeding was 56.1% (95% CI:49.8%-62.3%) and 57.2% (95% CI:49.6%-64.6%) among mothers with infants  $\leq 6$  months and  $\leq 4$  months, respectively. The prevalence of exclusive breastfeeding was 5.9% (95% CI:3.4%-9.6%) and 7.2% (95% CI:3.9%-12.0%) among mothers with infants  $\leq 6$  months and  $\leq 4$  months, respectively. Factors significantly associated with current breastfeeding among mothers with infants  $\leq 6$  months were mother's nationality, father's age, mother's income and admission of the index child to the neonatal care.

**Conclusions:**

Despite the high initiation of breastfeeding after birth, the prevalence of breastfeeding declined quickly, thus efforts should be made to keep mothers breastfeeding for at least the first 6 months of birth. Efforts should also be made to promote exclusive breastfeeding which is extremely low in our setting.

*Key Words: Initiation; Exclusive*

*Funding Agency: None*



## **Community Medicine**

*Category: Basic Sciences*

22

### **Obesity among Kuwaitis aged 50 years or older: Prevalence, correlates and comorbidities**

\*Badr H, Shah N, Shah M

<sup>1</sup>Department of Community Medicine & Behavioural Sciences, Faculty of Medicine, Kuwait University; <sup>2</sup>Globe Consultancy, Kuwait

#### **Introduction:**

Our objectives are to assess the prevalence of overweight and obesity among elderly Kuwaitis aged 50 or older, examine their socio-demographic correlates, and analyze the association between obesity and its comorbidities.

#### **Methods:**

A cross-sectional face to face interview survey using a structured questionnaire was conducted among 2443 Kuwaiti men and women aged 50 or older. Height and weight were measured and body mass index (BMI) was calculated. According to World Health Organization, overweight and obesity are defined when BMI is 25-29.9 and  $\geq 30$  respectively.

#### **Results:**

About 36% (n=868) of respondents were overweight (46% men and 29% females) and 46% (n=1115) were obese (30% men and 56% females). Mean BMI was 30.0 (31.2 for women and 28.1 for men). Multinomial logistic regression analysis revealed that relatively young elderly (50-59) were 1.7 and 2.3 times more likely to be overweight and obese respectively compared to those aged 70 or older. Married individuals had 2.3 times higher risk to be overweight or obese than non-married individuals. Gender as a significant correlate was found associated with only obesity but not overweight. Women were 2.3 times more likely to suffer from obesity than men. Overweight and obesity were found to be independent risk factors for hypertension (OR=1.3 & 1.9 respectively), diabetes (OR=1.4), and osteoarthritis (OR=1.8 & 1.6 respectively).

#### **Conclusions:**

Prevalence of overweight and obesity is alarmingly high among elderly Kuwaitis. The associated disease burden is substantial. Stakeholders should address the problem and launch national extensive health promoting campaigns targeting perceptible lifestyle changes.

*Key Words: overweight and obesity; Kuwaiti elderly; obesity comorbidity*

*Funding Agency: Kuwait Foundation for Social Sciences [grant number KFAS 2003-1302-02].*



**Community Medicine**

Category: Undergraduate

23

**Occupational stress and mental health among general medical practitioners and general surgeons**

AlFarhan H, AlTourah L, AlGhanim M, AlEnezi N, \*AlMutar S, Moussa M  
Community Medicine Department, Faculty of Medicine, Kuwait University

**Introduction:**

Assess occupational stress & mental health among general surgeons and general medicine practitioners

**Methods:**

Cross-sectional sample survey conducted in March and April of 2010 including 365 participants. Data was collected through a self-administered questionnaire including sociodemographic, health & work-related aspects; occupational stress using the Specialist Doctors' Stress Inventory (SDSI); & general mental health using the 12 item General Health Questionnaire (GHQ-12). The SDSI scale was categorized into three levels: low (1st tertile <65), medium (2nd tertile 65-74) and high (3rd tertile >74). Chi-square test was used to assess the association between two qualitative variables, the Spearman rank correlation was used for quantitative variables & Mann-Whitney U test was used to compare medians of quantitative & binary variables. Binary logistic regression was used to assess the association between mental health score and various predictors after adjustment for partial confounders (0 for GHQ < 4, 1 for GHQ ≥ 4)

**Results:**

There were no significant differences in general health (surg=2, med=3) or Stress (surg=71, med=70) median scores except in personal confidence, one of the four domains of stress; the median personal confidence score for surgery was significantly higher than that of medicine respondents (22 vs. 20, p=0.035). There was significant association of stress score with mental health score, p<0.001. There is a trend toward increase in poor mental health as level increases from low to high. As the stress score level increases, the risk for mental health increases (adjusted OR for medium stress, & high stress levels were 1.871, 2.965) respectively in reference to low stress level

**Conclusions:**

The study supported one of our hypotheses, namely: there is a significant association between occupational stress and mental health; while it did not support the hypothesis that work-related stress is more prevalent among general surgeons than medicine practitioners

*Key Words: Stress; General Physicians and Surgeons*

*Funding Agency: None*



**Community Medicine**

Category: Basic Sciences

24

**Respiratory and asthma admissions to hospitals in relation to dust storms events in Kuwait**

\*Thalib L, Al-Taiar A

Dept. Community Medicine and Behavioural Science, Faculty of Medicine, Kuwait University

**Introduction:**

Arabian Peninsula is one of the largest sources of global dust, yet there is no data on the impact of this on human health. Our study aimed to investigate the impact of dust storms on hospital admissions due to asthma and respiratory causes over a period of five-year (1996 to 2000) in Kuwait.

**Methods:**

A population-based retrospective ecological study of daily emergency admissions due to respiratory and asthma causes in the public hospitals in Kuwait were analyzed in relation to dust storm events. Dust storms days were defined as the mean daily PM10 > 200 µg/m<sup>3</sup> based on measurements obtained from all six monitoring sites in the country. A Poisson regression with Generalized Additive Model framework was used to estimate the age-stratified risk ratios between cause specific admissions and dust storm events after adjusting for potential confounders including weather variables and long term trends.

**Results:**

During the five-year study period, 569 (33.6%) days had dust storms events and they were significantly associated with an increased risk of same-day asthma and respiratory admission, adjusted RR 1.04 (95%CI:1.02–1.06) and 1.06 (95%CI:1.05–1.07), respectively. This was particularly evident among children; adjusted RR 1.04 (95%CI:1.01 – 1.07) for asthma admission and 1.07 (95%CI:1.06–1.09) for respiratory admission; and young adults; adjusted RR 1.04 (95% CI:1.01–1.08) for asthma and 1.06 (95%CI:1.04–1.07) for respiratory.

**Conclusions:**

Our findings have significant public health implications and we recommend implementation of prevention measures to protect people's health during dust storms and reduce the burden on health services due to dust events.

*Key Words: Dust storms; Sandstorms; Asthma*

*Funding Agency: Kuwait University Research Grant MXS001 funded by the Environment Public Authority of Kuwait.*



**Dentistry**

*Category: Basic Sciences*

**25**

**Dental fluorosis: Knowledge and public perception in the Gaza Strip**

\*Abuhaloob L

Palestinian Ministry of Health, Gaza Strip, Palestine, West Bank and Gaza

**Introduction:**

The high prevalence and severity of dental fluorosis (DF) have been serious dental problems for decades in the Gaza Strip, Palestine (GS). Objective: to estimate DF prevalence and severity, to study the knowledge of DF and its causes, and to study the public perception of DF in Palestinian children and their mothers in the GS.

**Methods:**

Ethical approval was secured. A cross-sectional study recruited stratified cluster random samples of 350 children aged 12-18 y and their mothers. DF prevalence and severity were determined using the Thyllstrup-Fejerskov Index (TFI). Data on knowledge and public perception of DF were collected through interview questionnaires.

**Results:**

Prevalence of DF was 78%: 63.4% suffered from moderate DF (1-4 TFI score) while 14.6% suffered from severe DF (5-8 TFI score). Most children (99.4%) and all mothers did not know what DF was and had not received any information about it. The majority (99.7%) did not know DF's causes, how to prevent it or minimize its severity. Concerning the public perception of DF, 87.7% of the children and 88.6% of mothers did not have a problem with fluorosed teeth colour, and 86.6% of the children and 87.4% of mothers did not want to treat fluorosed teeth in order to have a better appearance. Although all respondents felt that others with fluorosed teeth did not have good appearance, 96.9% of children did not hide their smile. Most of the participating mothers (99.7%) thought that the government should find an immediate solution to this problem; they were ready to participate in solving the problem but the participation would not be monetary.

**Conclusions:**

Lack of knowledge about dental fluorosis and its causes increases the risk of having DF and suggests the importance of developing immediate governmental preventive interventions for DF in affected communities in the GS.

*Key Words: Fluorosis; Gaza Strip*

*Funding Agency: None*



**Dentistry**

*Category: Graduate (Resident)*

**26**

**Association between body mass index and dental caries among Kuwaiti children attending the 6th Grade**

Al Abbas K, \*Fahl R, Qudeimat M

Department of Developmental & Preventive Sciences, Kuwait University, Faculty of Dentistry

**Introduction:**

Obesity and dental caries are two health issues in Kuwait that affect children's function and development. This study investigates: 1.the association between body mass index (BMI) and dental caries and plaque index among Kuwaiti children and 2.the role of children's life style and eating habits in their oral health status.

**Methods:**

A cross-sectional study was conducted. Two schools (girls and boys attending the 6th grade) from the six governorates were randomly selected using a computer software. After obtaining a written consent from the parents, questionnaires investigating the family's demographic data, physical activities, the diet and oral hygiene practices of the children were distributed. Dental caries experience (DMFT/dmft and DMFS/dmfs) and plaque index were recorded under day light, using disposable dental mirrors and periodontal probes, according to the WHO criteria. Heights and weights were recorded, using a measuring tape and a digital scale, respectively. Calculated BMI was plotted against charts and reference percentiles previously determined for Kuwaiti children.

**Results:**

Of studied 127 children, 104 (82%) were in the normal/underweight category (group 1) and 23 (18%) were in the overweight/obese category (group 2). There was a statistically significant positive association between the child's BMI and family income and a statistically significant inverse relationship between the BMI and parents' perception of body weight and time spent on outdoor activities. Total DMFT/dmft for group 1 was 5.6 (SD=3.7) and 4.9 (SD=3.0) for group 2 ( $p>0.05$ ). Total DMFS/dmfs was 10.5 (SD=9.0) for group 1 and 6.9 (SD=4.9) for group 2 ( $p>0.05$ ). The mean plaque index for group 1 was 1.6 (SD=0.8) and for group 2 1.2 (SD=0.6) ( $p<0.02$ ).

**Conclusions:**

No significant association between BMI and dental caries experience was found. However, plaque index among the overweight/obese group was statistically lower than among the normal/underweight group.

*Key Words: Dental caries; Obesity; Kuwait*

*Funding Agency: None*



**Dentistry**

*Category: Basic Sciences*

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**Histological analysis of titanium dioxide-impregnated extra-cellular matrix membrane**

\*Al-Asfour A<sup>1</sup>, Andersson L<sup>1</sup>, Dahlin C<sup>2</sup>, Tengvall P<sup>2</sup>

<sup>1</sup>Department of Surgical Sciences, Faculty of Dentistry, Kuwait University; <sup>2</sup>Department of Biomaterials, University of Gothenburg, Gothenburg, Sweden

**Introduction:**

Objectives: To study the histological feasibility and biological impact of titanium dioxide (TiO<sub>2</sub>) impregnation of an extra-cellular matrix membrane (ECM) product in guided bone regeneration.

**Methods:**

Eighteen adult New Zealand white rabbits were used. Bilateral bone defects (5 x 8 x 3 mm<sup>3</sup>) were created in edentulous areas of the maxilla. The defects were filled with demineralized freeze-dried bone (DFDB). ECMs (Dynamatrix®) were randomly pretreated with a suspension of 3 mg TiO<sub>2</sub> granules in saline. An untreated membrane served as control on the contralateral side. Healing was allowed for 2, 4 and 8 weeks. Histological and histomorphometric analysis were performed. The variables assessed were (1) zone of inflammatory cells adjacent to the ECM, (2) presence of cellular ingrowth into the ECM, and (3) presence of TiO<sub>2</sub> particles within the ECM.

**Results:**

In general, no adverse reactions towards either group of ECMs was found. The TiO<sub>2</sub> particles remained within the ECM after 8 weeks of healing, making histological detection of the ECM easy to perform. No migration or adverse reaction was found. Histomorphometric analysis revealed low numbers of inflammatory cells adjacent to the ECM surface.

**Conclusions:**

The histological evaluation of the ECM demonstrated adequate preservation and integration of the barrier. Contrasting TiO<sub>2</sub> particles in the ECM can be useful for the detection of similar biological materials in vivo. This method could be further developed and applied in a number of environments. TiO<sub>2</sub> particles in the ECM can be considered useful for detection of similar materials when studied in vitro.

*Key Words: Dental materials; Implantology and Oral surgery*

*Funding Agency: None*



**Dentistry**

Category: Graduate (Resident)

28

**Space maintainers: Uses, survival and factors affecting longevity at KUDC**

\*Al-Mashaan S, Al-Sabah Y, Qudeimat M  
Faculty of Dentistry, Kuwait University, Kuwait

**Introduction:**

To investigate retrospectively the use, success, median survival time (MST) and factors affecting longevity of space maintainer appliances fitted at the Faculty of Dentistry, Kuwait University.

**Methods:**

Records were identified of 267 patients (137 male and 130 female) who had space maintainers fitted at Kuwait University Dental Clinics between January 2005 and September 2011 and who fulfilled the selection criteria. Data regarding 493 space maintainers fitted in those patients during the study period were collected.

**Results:**

The age range of patients was 3.9 - 14 years (mean  $7.7 \pm 1.5$  years). The main indication for fitting a space maintainer was premature loss of primary teeth due to caries and its consequences (81%). The most commonly-used design was band and loop (56%). Of all appliances, 339 (69%) were fitted in 6- to 9-year-old children. Glass ionomer was the most commonly used luting agent (79%). Failures occurred in 255 (52%) space maintainers. Breakages accounted for 34% of failure, followed by complete loss of the space maintainer (20%) and decementation (11%). MST for all space maintainers was 14 months. Crown and loop appliances had a statistically-significant higher MST (32 months), followed by band and loop (20 months), Nance appliances (15 months) and lower lingual holding arches (9 months). Space maintainers fitted in boys less than 6 years old, subjects with fair or poor oral hygiene, and those cemented by senior undergraduate students, had a statistically significantly higher MST. Luting agent and cooperation of the child at the cementation appointment did not have a significant effect on the MST.

**Conclusions:**

This study determines the need for a more detailed and careful assessment of the use of space maintainers in a teaching institute setting.

*Key Words: Children; Pedodontics; Teeth; Human*

*Funding Agency: None*



**Dentistry**

Category: Basic Sciences

29

## **Prevalence of malocclusions in schoolchildren by governorate in Kuwait**

\*Al-Mutawa S<sup>1</sup>, Shyama M<sup>1</sup>, Al-Nafisi M<sup>1</sup>, Soparkar P<sup>2</sup>

<sup>1</sup>National School Oral Health Program, Ministry of Health, Kuwait; <sup>2</sup>Forsyth Institute, Boston, MA

**Introduction:**

To determine the prevalence of malocclusions in schoolchildren in the various governorates of Kuwait.

**Methods:**

A national epidemiologic survey of 5-14 year-old children (n = 4, 588) was conducted in the five governorates of Kuwait (Ahmadi, Farwaniya, Hawalli, Jahra, Capital). Malocclusion was identified according to WHO criteria. Two levels of anomaly were registered: slight malocclusion (such as one or more rotated or twisted teeth, crowding or spacing); and severe malocclusion, that is, anomalies that cause an unacceptable effect on facial appearance, significant reduction in masticatory function, impairment of speech, or one or more of the following conditions of the incisors: maxillary overjet  $\geq 9$  mm, mandibular overjet  $\geq$  one full tooth depth, open bite, midline shift  $\geq 4$  mm, crowding or spacing  $\geq 4$  mm.

**Results:**

The prevalence of severe malocclusion was 5.3% and that of slight malocclusion was 62.3%. There were significant differences in the occurrence of malocclusions by governorate ( $p < 0.001$ ). Severe malocclusions were highest in Ahmadi (10.3%) and lowest in Jahra (1.7%) ( $p < 0.001$ ). Slight malocclusions were highest in Hawalli and Capital (89.0%) and lowest in Jahra (20.5%) ( $p < 0.001$ ). There was a significant difference in the occurrence of malocclusions by age ( $p = 0.001$ ). Severe malocclusions were highest in 14-year-olds (10.6%) and lowest in 5-year-olds (3.4%) ( $p = 0.001$ ). Slight malocclusions were highest in 8-year-olds (68%) and lowest in 5-year-olds (43.2%) ( $p = 0.001$ ). Severe malocclusions were higher in girls (8.1%) than boys in Farwaniya (4.3%) ( $p < 0.001$ ). Slight malocclusions were higher in boys (24.3%) than girls in Jahra (16.6%) ( $p = 0.02$ ).

**Conclusions:**

There are variations in the prevalence of malocclusions between governorates. Severe malocclusion was less prevalent among these children than had been reported for previous national oral health surveys in Kuwait.

*Key Words: Epidemiology; Malocclusion*

*Funding Agency: None*



**Dentistry**

Category: Basic Sciences

**30**

**Oral cancer knowledge, practices and opinion of dentists attending  
KUADR**

\*Al-Nafisi M, Al-Menayekh R, Al-Mutawaa S, Nazar H, Ariga J  
National School of Oral Health Program, Ministry of Health, Kuwait

**Introduction:**

Early detection of oral cancer can improve the prognosis and the 5-year survival rate. Oral cancer screening should be a routine procedure at primary oral health care clinics. Objectives: To assess the level of knowledge, practices and opinion of dentists who attended the KUADR meeting in Kuwait regarding oral cancer.

**Methods:**

Self-reporting questionnaires, distributed during a break between presentations at the KUADR meeting in Kuwait during December 2010, included questions on knowledge, practices and opinions about oral cancer.

**Results:**

Of forty dentists, who answered the questionnaire, 26 were Kuwaiti dentists, 12 were from other different countries and 2 of them did not mention their nationality. Seventy seven percent (77%) were males and 23% were females. Mean age of dentists was 33 years. Half of the dentists had bachelor degree and 25% had PhD. Majority of dentists answered the knowledge questions correctly (82%). Only 25% of dentists thought they have adequate training to perform oral cancer screening. Approximately, half of the dentists refer their patient with suspicious lesion to a specialist. Thirty two percent (32%) of dentists reported that they assessed the use of tobacco and alcohol consumption.

**Conclusions:**

Most dentists showed a good knowledge of various aspects of oral cancer. They lacked experience because of limited exposure to oral cancer cases in this part of the world. More continuing education programmes should be arranged to increase the knowledge of such cases.

*Key Words: Epidemiology; Preventive dentistry; Oral cancer*

*Funding Agency: None*



**Dentistry**

Category: Basic Sciences

**31**

**A new approach to reliability assessment of dental caries examinations**

\*Altarakemah Y<sup>1</sup>, AlSane M<sup>2</sup>, Ismail A<sup>3</sup>, Kingman A<sup>4</sup>, Lim S<sup>3</sup>

<sup>1</sup>University of Kuwait, Kuwait City, Kuwait; <sup>2</sup>Kuwait University, Kuwait City, Kuwait; <sup>3</sup>Temple University, Philadelphia, PA; <sup>4</sup>NIDCR, NIH, USA, Bethesda, MD

**Introduction:**

To evaluate reliability of the ICDAS caries detection system and identify sources of disagreement among 12 Kuwaiti dentists with no prior knowledge of the system.

**Methods:**

A 90-minute introductory e-course was given, followed by an examination of extracted teeth using the ICDAS coding system, on the first day. Then 3 sessions of clinical examinations were performed. This study only used data from the last session where 705 tooth surfaces of 10 patients were examined to assess bias in caries examination and on which codes the examiners had the highest disagreement. Compared with the gold standard, we evaluated the bias of ICDAS coding using 3 approaches: Bland-Altman plot, Maximum kappa statistic, and Bhapkar's  $\times 2$  test. Linear kappa statistics were computed to assess inter-examiner reliability.

**Results:**

Marginal ICDAS distributions for most examiners were significantly different from that of the gold standard (bias present). The primary source of these marginal differences was misclassification of sound surfaces as non-cavitated lesions. Inter-examiner reliability of the 3-level ICDAS (codes 0, 1-2, and 3-6) classification ranged between 0.43 and 0.73, indicating evidence of substantial inconsistency between examiners. The primary source of examiner differences was lack of agreement on the diagnosis of non-cavitated lesions.

**Conclusions:**

This study highlights the importance of assessing both systematic and random sources of examiner agreement to correctly interpret kappa measures of reliability.

*Key Words: Cariology; Diagnosis*

*Funding Agency: None*



**Dentistry**

*Category: Basic Sciences*

**32**

**Effect of preparation design on stress distribution in FRC inlay bridges**

\*Barari S<sup>1</sup>, Roohollahi MR<sup>1</sup>, F. Assefzadeh F<sup>1</sup>, Valizadeh S<sup>2</sup>

<sup>1</sup>Shahed University, Tehran, Iran; <sup>2</sup>Tehran University, Tehran, Iran

**Introduction:**

To evaluate stress distribution in two designs of fibre-reinforced composite inlay fixed partial dentures (FRC-FPD): dovetail and simple box preparations.

**Methods:**

Two 3-dimensional finite element (FE) models of a 3-unit FPD from maxillary central incisor to maxillary canine (intended to replace the maxillary lateral incisor) were developed. Dovetail and simple box preparations were designed on retainers and loaded to 155 N (at 45°) to the point between the middle and cervical third of the pontic and retainers. The stress distribution and maximum principal stress were calculated for each.

**Results:**

Stress concentrations were located in the connectors in both designs. The maximum principal stress was lower for the dovetail than the simple box. Stress was distributed better in FRC-FPDs with dovetail preparation design.

**Conclusions:**

The dovetail design provided a more even stress distribution than the simple box.

*Key Words: Finite element; Stress*

*Funding Agency: None*



**Dentistry**

*Category: Clinical*

**33**

**Differences in extraction decision between users of conventional bracket system versus passive self ligation system**

Behbehani F<sup>1</sup>, \*Roy R<sup>2</sup>, Alsayegh F<sup>2</sup>

<sup>1</sup>Kuwait University, Faculty of Dentistry; <sup>2</sup>Ministry of Health, Kuwait

**Introduction:**

Despite the claims for the advantages of self ligation bracket system, other studies have found no difference in treatment plan and results when comparing conventional versus self ligation bracket systems.

**Methods:**

Questionnaire and pretreatment records for a Class I crowding case were circulated among 64 orthodontists. The orthodontists were asked about their treatment plan and the bracket system they use.

**Results:**

The majority of orthodontists (56%) proposed to extract premolars. All of those who planned extraction (N=36) are users of the conventional ligation system (CLS), while all of the orthodontists who use passive self ligation system (PSLS) planned non extraction (N=7). Statistical test indicates that the PSLS users tend to plan extraction less often than CLS users.

**Conclusions:**

Usage of PSLS could expand the envelope of nonextraction protocol in Class I borderline extraction cases.

*Key Words: Self ligation; Non extraction; Orthodontics*

*Funding Agency: This Research was supported by Kuwait University Grant No. DD04/10*



**Dentistry**

*Category: Graduate (Resident)*

**34**

**Compliance of smokers and non-smokers to non-surgical periodontal therapy**

\*Ben-Ali RA, Al-Juwaihel SF, Al-Kabbaz A  
Kuwait University, Faculty of Dentistry

**Introduction:**

Smoking is one of the main risk factors for the development of periodontal disease. In addition, cigarette smoking has been associated with an impaired response to periodontal treatment.

Objective: To assess the response of smokers to non-surgical periodontal therapy and compare them with non-smokers.

**Methods:**

From patient records of the Dental Clinics of Kuwait University were extracted socio-demographic data, medical history, smoking history and periodontal findings before and after non-surgical periodontal therapy.

**Results:**

232 healthy patients' records (107 smokers and 125 non-smokers) were included. Only 46% of smokers reported brushing  $\geq 2$  per day as compared with 56% of non-smokers ( $p < 0.045$ ). There was a significant difference between smokers and non-smokers regarding all periodontal findings. Smokers had higher plaque score ( $75 \pm 53$ ) compared to non-smokers ( $57 \pm 29$ ). In addition, 36% of smokers were diagnosed with severe periodontitis, compared with only 15% of non-smokers ( $p < 0.001$ ). Following periodontal therapy, statistically significant differences were found between smokers and non-smokers regarding the reduction in plaque index and number of sites with pocket depth  $\geq 5$  mm. Regression analysis showed that age, smoking and bleeding score were the most significant variables associated with severe periodontal destruction.

**Conclusions:**

The results suggest that periodontal health is compromised by smoking. Providing non-surgical periodontal therapy effectively improved periodontal status in smokers and non-smokers. Non-surgical periodontal therapy and supportive periodontal care should be provided more frequently to smokers.

*Key Words: Periodontal therapy; Smokers*

*Funding Agency: None*



**Dentistry**

*Category: Clinical*

**35**

**Early strength of dental silver amalgam**

\*Darvell BW

Kuwait University, Bioclinical Sciences, Health Sciences Centre

**Introduction:**

To characterize the development of strength during the setting process of dental silver amalgam in the context of 'early strength' measurements for standards compliance testing in relation to patient instructions, and to demonstrate the applicability of the Hertzian 'ball on disc' method.

**Methods:**

Thirteen dental silver amalgam products were tested using the 'ball on disc' protocol at 1, 2, 3, 4 and 24 h after setting at 37°C in air. The materials were mixed according to manufacturer's instructions, packed into a tapered steel disc mould (10 mm diameter, 3 mm thick) resting on a glass surface, slightly overfilled and carved level with a sharp edge, then ejected at ~10 min and placed immediately into an incubator at 37°C. Testing was in Hertzian mode, using a 20 mm steel ball, with the specimen resting on a disc of glass-filled polyamide ( $E = 10$  GPa) at a cross-head speed of 0.2 mm/min on a universal testing machine (E3000, Instron). The load at first crack was recorded, as was the number of radial cracks produced.

**Results:**

Radial cracking into 2-4 pieces, in a clinically relevant (non-explosive) mode was observed in all cases. Considerable disparity was found in the strength at 1 h, reflecting the variation in setting rate. Otherwise, very little difference is apparent at 24 h, despite the variations between products in composition, particle type and size distribution.

**Conclusions:**

The Hertzian protocol provides a simple and relevant means of characterizing amalgam. However, testing early strength at 1 h (especially for standards compliance purposes) may be inappropriate. It is suggested that a 2-h value may be more effective.

*Key Words: Corrosion; Saliva; Strength*

*Funding Agency: Kuwait University Research Grant DB01/10.*



**Dentistry**

*Category: Clinical*

**36**

**Dental pain experience among pregnant women in Kuwait**

Honkala S<sup>1</sup>, \*Al-Ansari JM<sup>2</sup>, Honkala E<sup>1</sup>

<sup>1</sup>Department of Developmental & Preventive Sciences, Faculty of Dentistry, Kuwait University;

<sup>2</sup>Department of Oral and Dental Hygiene, College of Health Sciences, Kuwait

**Introduction:**

Hormonal and vascular changes during pregnancy have been suggested to predispose women to oral diseases, such as gingivitis, periodontal disease and dental decay. The aim of this study was to describe perceived dental pain of pregnant women in Kuwait.

**Methods:**

A cross-sectional study with an anonymous structured questionnaire was conducted among 650 pregnant women during a six-weeks period in the biggest government maternity hospital in Kuwait city. The response rate was 93% (n=603). Cross-tabulation with the chi-squared test was used to evaluate the differences between different variables. Statistical significance was set at the p-value of less than 0.05.

**Results:**

The mean age of the women was 30 years (range between 18 and 56 years). Every fourth had her first pregnancy, while 35% already had three or more children. Dental pain experience was reported by 35% of the pregnant women at the time of filling in the questionnaire; 65% of them thought that they had dental caries, 50% believed to have periodontal problems, and 70% had experienced dental pain also during the last 6 months ( $p < 0.001$ ). Almost half of those women who had current pain, had also visited a dentist recently because of pain. The main reasons for the latest appointment had been a need for treatment (48%) and pain (37%). Only 14% of them visited dentist just for a check-up or teeth cleaning. The dental pain experience was more common among the women who brushed their teeth infrequently ( $p = 0.026$ ). No statistical significant differences were found between perceived dental pain and women's age, education, occupation or number of deliveries in the past.

**Conclusions:**

Over one-third of pregnant women reported experiencing dental pain at the time of the filling in the questionnaire, and half of them had visited a dentist recently because of pain. Preventive professional oral health care and self-care should be emphasized during pregnancy.

*Key Words: Dental pain; Pregnancy; Preventive Dentistry*

*Funding Agency: None*



**Dentistry**

Category: *Basic Sciences*

37

**Association between dental fear and oral health habits in Kuwait**

\*Honkala S<sup>1</sup>, Honkala E<sup>1</sup>, Humphris G<sup>2</sup>, Freeman R<sup>3</sup>

<sup>1</sup> Developmental and Preventive Sciences, Faculty of Dentistry, Kuwait University; <sup>2</sup>Bute Medical School, University of St Andrews, Health Psychology, St Andrews, United Kingdom; <sup>3</sup>Dental Health Services Research Unit, University of Dundee, Dundee, United Kingdom

**Introduction:**

To determine whether self-reported dental fear is associated with oral health habits among adolescents in Kuwait.

**Methods:**

School children from grades 8 and 9 (aged 13 to 15 years) from one Government girls' school (n = 371) and two boys' schools (n = 427) were invited to participate in the study. Self-administered structured questionnaires in Arabic were completed anonymously during regular classes supervised by teachers and researchers. Questions on age, gender, nationality, oral home-care and dental visiting habits were included. One question, 'How afraid are you of visiting a dentist?', measured dental fear. A chi-square test was used for analyses and the critical value was set at 0.05.

**Results:**

The response rate was 94%. One third of the girls and 6% of the boys reported to be very much afraid of visiting a dentist, 26.3% of girls and 62.9% of boys being not at all afraid ( $p < 0.001$ ). Comparing being afraid (a little or very much) with not being afraid of visiting a dentist, significant associations were found among girls for dental visits (over a year ago being more afraid;  $p = 0.013$ ), tooth-brushing frequency (brushing  $\leq 1$  per day being more afraid;  $p = 0.014$ ), and soft-drinks consumption (more-than-once-a-day drinkers being more afraid;  $p = 0.014$ ). Among boys, the only statistically significant association was found between the grades: older boys reported to be more afraid of visiting a dentist than the younger ones ( $p = 0.045$ ). Those who had visited a dentist because of decay or tooth pain reported to be more afraid of dental visits than those given any other reason for their visit.

**Conclusions:**

Detrimental oral health habits seemed to be associated with self-reported dental fear among adolescents in Kuwait. Also, experiencing dental problems seemed to increase reported fear.

*Key Words: Anxiety; Diet; Oral hygiene; Utilization/demand*

*Funding Agency: KU DI01/10*

**Dentistry***Category: Basic Sciences***38****Evaluation of microhardness of Y-TZP for fully-anatomic zirconia crowns**\*Hmaidouch R<sup>1</sup>, Mueller W<sup>2</sup>, Lauer H<sup>3</sup>, Weigl P<sup>4</sup>

<sup>1</sup>Johann Wolfgang Goethe University, Department of Prosthodontics and Geriatric Dentistry; <sup>2</sup>Charité Medical University of Berlin, Department of Prosthodontics and Geriatric Dentistry, Laboratory for Dental Materials and Biomaterial Research; <sup>3,4</sup> J.W. Goethe University, Dept. of Prosthodontics, Berlin, Germany

**Introduction:**

To evaluate the microhardness of Y-TZP for fully-anatomic zirconia crowns and to compare it with classical veneered Y-TZP crowns.

**Methods:**

Thirty bar-shaped zirconia specimens (Zirluna®, Amberg, Germany) measuring 30 x 6 x 2 mm<sup>3</sup> were fabricated and divided into 3 groups (n = 10). The first 10 specimens in Group A were glazed using GC Initial™ IQ Lustre Pastes NF (GC America, Alsip, USA) without being veneered. The specimens in Groups B and C were veneered with feldspathic ceramic Vita VM9 (Vita Zahnfabrik, Germany). Specimens in Group B were then glazed using Vita glaze, and those in Group C glazed using DenseoHIQ glaze (Denseo, Aschaffenburg, Germany). The microhardness was evaluated with a Vickers measuring tester (Wezler, Germany). Loads of 2.94, 4.90 and 9.81 N were sequentially applied with a dwell time of 15 s, repeated 6 times for each specimen. Data were submitted to one-way ANOVA ( $\alpha = 0.05$ ).

**Results:**Mean microhardness (N/mm<sup>2</sup>)

Group	Load (N)		
	2.94	4.90	9.81
A	577.99	604.00	641.28
B	558.94	521.73	523.26
C	563.92	524.34	510.93

At the higher loads, the microhardness of unveneered Y-TZP increased significantly. However, that of veneered Y-TZP did not. At 2.94 N there were no significant difference between unveneered and the veneered Y-TZP. However, at 4.95 and 9.81 N the unveneered Y-TZP showed a significantly higher microhardness compared to veneered Y-TZP, regardless of the type of glaze.

**Conclusions:**

Using a glazing procedure, the hardness of the surface of unveneered Y-TZP became comparable to the hardness of the veneered Y-TZP. The increased load probably removed the glazing layer, allowing the unveneered Y-TZP to show its higher microhardness.

*Key Words: Ceramics; Hardness; Occlusion**Funding Agency: None*



**Dentistry**

*Category: Basic Sciences*

**39**

**Increased salivary IgA levels in acute and quiescent aphthous stomatitis**

Mohammad RS, \*Halboub ES, Mashlah AM  
Oral Medicine Department, Damascus University, Damascus, Syria

**Introduction:**

Despite many studies of the aetiopathogenesis of recurrent aphthous stomatitis (RAS), no definite cause has been identified. Objectives: To determine the potential changes of salivary IgA and salivary flow rate in RAS patients.

**Methods:**

Resting whole salivary flow rate and IgA level in 33 patients in the acute and remission (quiescent) phases of the minor form of RAS, and 33 matched healthy controls, were determined in resting whole saliva. IgA was measured using enzyme-linked immunosorbent assay (ELISA).

**Results:**

Salivary IgA was significantly increased in the acute phase of RAS [median (interquartile range): 124.94 µg/mL (106.22 - 136.31)] in comparison with the healthy controls [88.92 µg/mL (76.85 - 93.91;  $P < 0.001$ )] and with the levels in the remission phase [102.4 µg/mL (84.6 - 120.16;  $P = 0.01$ )]. Even during the disease-free period (remission phase), salivary IgA remained significantly higher than in the healthy controls ( $P = 0.01$ ). Salivary flow rate, on the other hand, was not affected by the health state (healthy versus RAS), RAS phase (acute versus remission), or patient sex.

**Conclusions:**

To our knowledge, this is the first time that a marked increase in salivary IgA in both the acute and remission phases of RAS has been reported. Therefore, a potential role for this immunoglobulin in the pathogenesis of RAS is strongly indicated.

*Key Words: Immunology; Mucosal diseases; Oral medicine; Saliva*  
*Funding Agency: Faculty of Dentistry, Damascus University*



**Dentistry**

Category: Basic Sciences

40

**Root and canal morphology of the first human maxillary premolar**

\*Kocani FK, Kamberi B

University of Prishtina, Faculty of Medicine, Dept. of Stomatology, Dental Pathology and Endodontics, Kosovo

**Introduction:**

To examine the root and canal morphology of the first human maxillary premolar with completely formed root apices. The length of tooth, the number of roots, the direction of the root curvature, and the form of the external surface of the roots were observed and recorded; the root canal morphology (root canal system) was classified according to the Vertucci system.

**Methods:**

Two hundred and twenty-one first maxillary premolar teeth which had been extracted due to periodontal disease or for orthodontic reasons, were examined using an operating microscope (OP), computed by dental radiography (CDR) and a stereomicroscope. The root canal systems were classified according to the classification of Vertucci.

**Results:**

Of the 221 first maxillary premolar teeth, 70.1% (n = 155) had two roots, 21.7% (n = 48) had one root, and 8.1% (n = 18) had three roots. One hundred and fifty-five (70.1%) of the specimens with two roots (Table 2) of which 16.3% (n = 36) had bifurcation on apical third, 21.7% (n = 48) had bifurcation on middle third, and 32.1% (n = 71) had bifurcation on cervical third. The distribution of the number of canals on a single rooted first premolar were: one canal, 8.9%, two canals 1.1%. According to the Vertucci classification of the type of canal, 64.8% (#31) were type IV (2 separated canals), 26.3% (#13) type II (2-1), and 8.9% (#4) type I (1).

**Conclusions:**

Most maxillary first premolar teeth showed a higher prevalence of two-root morphology (70.1%), with one root (21.7%), and with three roots 8.1%. On single-rooted premolars were found one canal of 8.9% (Type I), two canals 91.1% (Type IV 64.8%; Type II 26.3%). A deep longitudinal depression on the proximal surface with one root was observed on the mesial root surface of 74.8%, and a slight one on 48.1% of the distal root surface.

*Key Words: Endodontics Pulp; Root*

*Funding Agency: None*



**Dentistry**

Category: Basic Sciences

**41**

**Antegonial and mental indices vs. age, gender, and dental status**

\*Moeini M, Khayam E

Yazd University of Medical Sciences, Dental Radiology, Yazd, Iran

**Introduction:**

There is evidence that panoramic indices can be utilized as tools in the detection of low mineral bone density. Objectives: To evaluate the correlation of mental and antegonial indices with age, gender, and dental status.

**Methods:**

This historical cohort study was conducted between March 2005 and December 2006 in the School of Dental Medicine, Shaheed-Beheshty University of Medical Sciences, Tehran, Iran. The sample included patients 40-79 years of age who were referred for evaluation by panoramic radiography for dental treatment purposes. The correlation of mental and antegonial indices with age, gender and dental status was evaluated.

**Results:**

A total of 212 people were studied: 118 females (55.7%) and 94 males (44.3%). Antegonial index (AI) showed a statistically-significant decrease with age in females ( $P < 0.05$ ). However, in males AI increased until age 60 years, after which there was a statistically-significant decrease ( $P < 0.05$ ). Mental index was statistically lower in females aged 60 or older compared with males ( $P < 0.05$ ). In males, this index increased until age 60 and decreased thereafter, as observed for AI. Dentate persons had statistically higher AI means compared with partially dentate and edentulous persons in all age groups ( $P < 0.05$ ). There was no relationship between MI and dental status ( $P > 0.05$ ).

**Conclusions:**

The results indicate that the antegonial index is influenced by dental status. Therefore, the index is not sufficient for determining bone loss. Future studies for determining the relationship between MI and BMD are recommended.

*Key Words: Bone; Radiology; Digital image analysis*

*Funding Agency: None*



**Dentistry**

Category: Clinical

42

**Molecular detection of *Helicobacter pylori* in dental plaques of Kuwaiti diabetic patients, as a possible source of re-infection**

\*Qasem JA<sup>1</sup>, Qasem AA<sup>2</sup>

<sup>1</sup>The Public Authority for Applied Education and Training, College of Health Sciences, Department of Applied Medical Sciences; <sup>2</sup>Abu-Fatira Dental Clinic, Ministry of Public Health, Kuwait

**Introduction:**

*Helicobacter pylori* infection is considered as one of the most prevalent infectious diseases throughout the world. Oral infection with *H. pylori* is usually associated with *H. pylori* infection of the stomach therefore it has been speculated that oral bacteria are responsible for stomach re-infection. The objective of this study is to elucidate the prevalence of *H. pylori* infection in dental plaques of type 2 diabetic subjects with and without gastritis.

**Methods:**

Supragingival and subgingival samples were collected from 70 patients with chronic periodontitis, 15 of whom were also suffering from gastritis, 26 from diabetic, 9 from both gastritis and diabetic, and 2 from ischemic heart disease, diabetic and gastritis. The samples were analyzed by PCR using two Random sequence nt 4835-5041 primer. DNA extraction was done using the Gentra PureGene DNA isolation Kit

**Results:**

*H. pylori* was detected in 40% of the patients. The prevalence of *Helicobacter pylori* in dental plaques was 60% in gastritis patients and 31% in patients with diabetes only. Patients with gastritis and diabetes had 56% PCR positivity in gastritis patients with ischemic heart diseases and 100% with diabetes, compared to 24% among the control patients (healthy with no gastritis, diabetes or heart diseases). Interaction of age and infection was not significant but the prevalence of *H. pylori* in dental plaque of both diabetic and gastritis male patients were higher than among female patients.

**Conclusions:**

The prevalence of *H. pylori* in the dental plaque of gastritis patients was high and the alterations of glucose metabolism in diabetes seems to promote the *Helicobacter pylori* colonization in the dental plaques of the diabetic patients. The oral cavity may be a reservoir for *H. pylori* infection, it is therefore suggested that professional plaque removal and oral hygiene procedure be performed, along with the antibiotic treatment of *H. pylori*

*Key Words: Helicobacter pylori; Dental plaque; Diabetic*

*Funding Agency: Public Authority for Applied Education and Training (HS-01-10)*



**Dentistry**

*Category: Clinical*

**43**

**Frontal bone fractures and management of frontal sinus**

\*Schütz P, Ibrahim HH

Oral & Maxillofacial Surgery Unit, Al-Adan Dental Center, Kuwait

**Introduction:**

Frontal bone fractures (FBFs) make up between 5 and 12 % of all maxillofacial fractures. Treatment of FBFs is strongly influenced by degree of involvement of the frontal sinus (FS). The objective of the current study is to investigate incidence of different fracture patterns and their impact on treatment strategies.

**Methods:**

Records of all patients diagnosed with FBFs in Al-Adan Hospital from 2004 till 2011 were retrieved from computer database and tabulated. Microsoft Excel software was used to produce descriptive statistics and analysis.

**Results:**

There were 160 male and 19 female patients aged between 1 and 53 years (average=27, SD=13). The most frequent cause of injury was road traffic accident (n=80), followed by fall from height (n=49). Associated injuries were diagnosed in 102 patients, mostly intracranial bleeding and brain contusions (n=69). We were able to distinguish 10 different patterns of FBFs. Fractures outside FS (n=43) and non-displaced fractures involving FS walls (n=51) were excluded. In remaining 85 patients operative treatment was indicated, but only 51 patients were really treated. Patients with fractures of anterior wall FS received reconstruction preserving FS in most cases (n=18). Only in 4 cases of severe disruption of fronto-nasal ostium FS was obliterated. Patients with posterior wall disruption received cranialization (n=29). The reasons for non operating indicated cases were refusal by patients or their families (n=13), medical unfitness (n=9), disagreement on indication with neurosurgeon (n=7) and transfer abroad (n=3). Two patients from group indicated for surgical treatment died before treatment.

**Conclusions:**

About 50% of patients in our series required operative treatment. For different reasons substantial number of them were not operated. These individuals are possibly subject to the risk of late complications. Long term clinical studies are needed to improve decision algorithms and consensus on indications.

*Key Words: Frontal sinus; Frontal bone fracture; Cranialization of frontal sinus*

*Funding Agency: None*



**Dentistry**

*Category: Basic Sciences*

44

**Risk factors for caries, fluorosis and malocclusions in Kuwaiti school-children**

\*Shyama M<sup>1</sup>, Al-Mutawa S<sup>1</sup>, Al-Duwairi Y<sup>2</sup>, Soparkar P<sup>3</sup>

<sup>1</sup>National School Oral Health Program, Ministry of Health, Kuwait; <sup>2</sup>Dental Administration, Ministry of Health, Kuwait; <sup>3</sup>Forsyth Institute, Boston, MA

**Introduction:**

The present study was carried out to determine the risk factors for caries, fluorosis and malocclusions in Kuwaiti schoolchildren.

**Methods:**

A national epidemiological survey of children 5-14 years (n = 4, 588) was conducted in five governorates of Kuwait. Clinical examinations were carried out by calibrated dentists. Dental caries and malocclusions were scored by using WHO criteria, dental fluorosis by Dean's index. Multivariate analysis (logistic regression) was used to assess the risk factors for the occurrence of caries, fluorosis and malocclusions. Odds ratios (OR) and their confidence intervals (95% CI) were estimated.

**Results:**

About half of the children (48%) were caries-free. The mean DMFT increased from 0.4 at the age of 6 to 3.9 at the age of 14 (p<0.001). The corresponding mean DFS was 0.4 to 5.2. Poor oral hygiene (OR = 2.0; p<0.0001) and increasing age (OR = 1.4; p<0.0001) were significantly associated with caries risk. Fluorosis was seen in 2.6% of the children. Living in Jahra governorate (OR = 22.9; p<0.0001), increasing age (OR = 2.4; p=0.0001) and male gender (OR = 1.8; p=0.001) were associated with higher occurrence of dental fluorosis. About 5.3% of the children had severe malocclusion. Children in Ahmadi governorate (OR = 6.8; p<0.0001), Farwaniya governorate (OR = 3.8; p<0.0001) and increasing age (OR = 1.1; p=0.001) had a higher risk for the occurrence of severe malocclusion.

**Conclusions:**

Caries levels are similar to those in neighbouring and other Middle East countries. Fluorosis and severe malocclusions were quite rare. An extensive prevention program in schoolchildren is now in place to prevent caries. Oral hygiene measures need to be reinforced for the schoolchildren and should form part of the school curriculum.

*Key Words: Children; Malocclusion; Risk factors; Fluorosis*

*Funding Agency: None*



**Dentistry**

*Category: Basic Sciences*

**45**

**Monomers elution from composites by food-simulating liquids**

Tabatabaei MH<sup>1</sup>, \*Valizadeh S<sup>2</sup>, Barari S<sup>3</sup>, Sadraei S<sup>2</sup>

<sup>1</sup>Tehran University of Medical Sciences, Pasdaran, Tehran, Iran; <sup>2</sup>Tehran University, Tehran, Iran;

<sup>3</sup>Shahed University, Tehran, Iran

**Introduction:**

There are concerns about the possibility of release of unpolymerized monomers from light-cured composite resins. Objectives: To evaluate the effect of food-simulating fluids on monomer elution from a nanofilled composite resin at various immersion times.

**Methods:**

140 discs (5 mm diameter and 3 mm height) were prepared from a nanohybrid composite resin (Supreme 3M), polymerized with a halogen light-curing unit and then soaked in distilled water (control), citric acid and lactic acid solutions, and 75% ethanol. The discs were removed after 24, 48 and 72 h, 1 week, and 1 and 3 months. The solutions were analysed with HPLC for detection of released Bis-GMA, TEGDMA, UDMA and Bis-EMA. Data were processed with ANOVA and post hoc (Tukey HSD) for significance.

**Results:**

Ethanol released significantly more monomer, and distilled water less, than the other groups. Leaching of monomers in lactic acid and citric acid solutions compared with distilled water was significantly greater but there was no significant difference between those two. Immersion time in ethanol increased the release of monomer, but this did not occur for distilled water or the lactic and citric acid solutions.

**Conclusions:**

The food- and drink-simulating liquids used increased the amount of some of the monomers released from the composite resin.

*Key Words: Chemical, Composites; Dental materials; Polymerization*

*Funding Agency: None*



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**Environmental Sciences**

Category: Graduate MSc (Basic Science)

46

**Effects of lifestyle and environmental factors on bone mineral density  
in healthy Kuwaiti females**

\*Ali AH<sup>1</sup>, Nair VS<sup>1</sup>, Al-Shoumer KAS<sup>1,2</sup>

<sup>1</sup>Division of Endocrinology & Metabolic Medicine, Department of Medicine, Faculty of Medicine, Kuwait University; <sup>2</sup>Mubarak Al-Kabeer Hospital, Kuwait

**Introduction:**

It is well known that genetic, lifestyle and environmental factors may affect bone health. Data on the effects of lifestyle and environmental factors on bone health in Kuwaiti subjects are unavailable.

**Methods:**

Bone strength was studied in 140 healthy Kuwaiti females. Subjects were included if they were not taking any medication and had no previous illnesses for at least 12 months. Bone strength was assessed by measuring bone mineral density (BMD) using dual-energy X-ray absorptiometry (DXA). BMD of L2-L4 spine, femurs and distal forearms were measured. Information on lifestyle and environmental factors were gained from a questionnaire on education, occupation, diet, exercise, smoking and sun exposure.

**Results:**

The (mean±SEM) age and BMI, of the 140 studied females, were 44±1 years and 28.8±0.5 kg/m<sup>2</sup>. 64% Were employed; 76% were graduate; 17% were smokers; 14% were on diet; 50% were on daily exercise; and 79% were exposed to sun < 10 min daily. BMD at right distal forearm was significantly higher in graduates than undergraduates (p=0.014), at left femur total was significantly lower in smokers than non-smokers (p=0.04), at left femur neck was significantly higher in subjects exposed to sun 10-30 min than those exposed < 10 min daily (p=0.0001), and at right neck trochanter was significantly higher in those on daily exercise (p=0.044).

**Conclusions:**

Reduced level of education, smoking, limited sun exposure and exercise are associated with a reduced bone mineral density at certain areas of skeleton in healthy Kuwaiti females.

*Key Words: Lifestyle/environment; Bone; Kuwaiti females*

*Funding Agency: College of Graduate Studies, KU*



**Environmental Sciences**

Category: Graduate MSc (Basic Science)

47

**Lead acetate modulates AP-1, c-Myc and NF-κB signaling in hepatocytes**

\*Al-Mujaibel L, Kilarkaje N

Department of Anatomy, Faculty of Medicine, Kuwait University

**Introduction:**

Lead imparts severe structural, biochemical and molecular effects on hepatocytes. Consequently, lead-induced hepatotoxicity has become a universal public health problem. The present study investigated AP-1 (c-Jun and c-Fos), c-Myc and NF-κB signaling in lead acetate exposed hepatocytes.

**Methods:**

Adult Wistar rats (13-15-week-old; N=8/group) were exposed to 0, 0.5% and 1% lead acetate for 3d, 14d and 35d and the livers were sampled the next day. The expression of c-Jun, c-Fos, c-Myc and NF-κB was evaluated by Western blotting (quantified by densitometry) and immunohistochemistry/confocal microscopy. Data were analyzed by one way ANOVA followed by LSD and P<0.05 was considered significant.

**Results:**

The expression of c-Jun and c-Myc was down-regulated in all groups (P<0.05) except in the 1% group on 36d and that of c-Fos and NF-κB was unaffected during early days of lead exposure but was up-regulated (P<0.05) in 1% group on 36d. The signaling of c-Jun, c-Fos and NF-κB did not show any particular dose- or time-dependent pattern of changes but that of c-Myc did show only on 36d. C-Jun and c-Fos were localized in the nucleus whereas c-Myc and NF-κB were localized both in cytoplasm and nucleus of hepatocytes.

**Conclusions:**

Down-regulated c-Jun and c-Myc signaling is pro-apoptotic but up-regulated c-Myc signaling after a long-term exposure is pro-cell survival. Lead imparts fewer effects on c-Fos signaling during early exposure, but the signaling is up-regulated after a long-term exposure indicating its pro-cell survival function. The NF-κB signaling is indifferent to lead exposure during initial stage of lead exposure, but gets up-regulated after a long-term exposure in conjunction with infiltration of leukocytes.

*Key Words: Liver; Transcription factors; Cell death*

*Funding Agency: YS05/09 and GM01/01 & GM01/05*



## **Genetics**

*Category: Graduate MSc (Basic Science)*

48

### **A genetic association study of angiotensin converting enzyme (ACE) polymorphisms and essential hypertension in the Kuwaiti population**

\*Al-Ahmad M, Al-Bustan SA, Al-Qattan K

Department of Biological Sciences, Faculty of Science, Kuwait University

#### **Introduction:**

Angiotensin converting enzyme (ACE) is a vital component of the renin-angiotensin system (RAS), a key regulator of blood pressure. This study aimed to investigate the association of specific ACE polymorphisms (ACE I/D, ACE6 and ACE8) and risk factors with essential hypertension in the Kuwaiti population.

#### **Methods:**

DNA samples were extracted from whole blood collected from 154 Kuwaiti essential hypertensive patients and 115 normotensive Kuwaiti controls matched based on gender and age. Genotyping of the ACE polymorphism were done using AS-PCR and PCR-RFLP where the products were used to construct haplotypes. The Hardy-Weinberg equilibrium (HWE) and linkage disequilibrium (LD) was performed on the genotype and allele frequencies and statistical analysis including logistic regression was used to investigate the association of ACE polymorphisms with hypertension and its associated risk factors.

#### **Results:**

All allele and genotype frequencies were found to be in HWE and were in LD however did not show direct segregation with hypertension. A significant association ( $p < 0.05$ ) was observed between the ACE polymorphisms and family history of hypercholesterolemia where the frequency of the ACE I/D II genotype was found to be 38.9% followed by the ACE6 CT genotype (27%) then by the ACE 8 GG genotype (32.2%). Logistic regression analysis of ACE8 genotypes showed a strong association with hypercholesterolemia ( $p = 0.005$ ); whereas the ACE6 polymorphism revealed a significant ( $p < 0.05$ ) increase to the risk of essential hypertension and other variables such as family history of hypertension where the increased risk was three folds.

#### **Conclusions:**

This study suggests that ACE polymorphisms could be related with the increased risk for essential hypertension in the Kuwaiti population. It is strongly recommended that a larger sample size and other polymorphisms and factors be investigated to assess the genetic predisposition to develop essential hypertension.

*Key Words: Hypertension; ACE polymorphisms; Kuwait*

*Funding Agency: Kuwait University Graduate School*



**Genetics**

Category: Graduate MSc (Basic Science)

49

**Selective genetic markers in association with the development of coronary heart disease in the Kuwaiti population**

\*Ismael F<sup>1</sup>, Al-Bustan SA<sup>1</sup>, Al-Rashdan I<sup>2,3</sup>

<sup>1</sup>Department of Biological Sciences, Kuwait University Faculty of Science;

<sup>2</sup>Department of Medicine, Kuwait University Faculty of Medicine; <sup>3</sup>Chest Hospital, Kuwait

**Introduction:**

CHD is a complex disorder that involves both environmental and genetic factors. Apolipoproteins including APOAV c.56C>G, APOB signal peptide and APOCIII 3238C>G gene polymorphisms may influence plasma lipids resulting in fatty deposits on the arterial wall and plaque formation leading to CHD. This study aimed to provide an insight on the association of APOAV c.56C>G, APOB-SP and APOCIII 3238C>G with CHD among the Kuwaiti population.

**Methods:**

Total gDNA was extracted from blood samples obtained from a total of 735 Kuwaiti's including CHD patients (n=375) and matched controls (n=363). AS-PCR and Real-Time PCR were used to genotype the DNA samples. Statistical analysis including Hardy-Weinberg equilibrium (HWE) was performed to investigate the association of the polymorphisms with risk factors and CHD in the samples collected.

**Results:**

The analysis revealed significant association of gender, the metabolic syndrome and smoking with CHD in the samples studied consistent with those reported previously on the Kuwaiti population; a highly significant association between CHD and ethnicity ( $P \leq 0.001$ ) was also observed. A significant association between the genotype and allele frequency distribution with CHD was only observed for the APOAV and APOB polymorphism. Unlike APOCIII, both the APOAV and the APOB polymorphisms showed a significant deviation from HWE ( $P < 0.05$ ) in the patient group only further supporting their association with CHD.

**Conclusions:**

Among the genotypes observed, the CC genotype of the APOAV contributed the highest risk for CHD while the DD genotype of the APOB was found to be mainly associated with Arab Bedouin CHD patients. The current study is the first to report an extensive genetic analysis of CHD and its risk factors in the Kuwaiti population with findings that strongly support the role of genetic factors in the increased risk to develop CHD among the Kuwaiti population which may prove beneficial in the prevention and management of CHD.

*Key Words: Genetic Polymorphisms; CHD; Kuwait*

*Funding Agency: Kuwait University College of Graduate Studies Kuwait University (YS06/09) and Kuwait University Research Administration (GS01/02)*



**Medical Education**

Category: Undergraduate

50

**Factors affecting future specialty choice among medical student in Kuwait**

\*Al-Fouzan R, Al-Ajlan S, Marwan Y, Al-Saleh M

Department of Surgery, Faculty of Medicine, Health Sciences Center, Kuwait University, Kuwait

**Introduction:**

Choosing a medical specialty can be a daunting and confusing experience for some medical students and junior doctors or could be a foregone conclusion to others. The aim of this study is to evaluate factors affecting future specialty choice among medical students in Kuwait University.

**Methods:**

A self-administered questionnaire was used to collect data from medical students registered in Kuwait University during the academic year 2011/2012. Chi-square test and logistic regression were used to test the association between deciding a future specialty and students' sociodemographic and academic factors.

**Results:**

Of 422 students approached, 387 (91.7%) decided to participate. One hundred and forty four (37.2%) students had decided a future medical specialty. Pediatrics (18; 12.5%), general surgery (17; 11.8%) and cardiology (16; 11.1%) were the most desired specialties. Only 61 (42.4%) students of those who selected a future specialty received advices regarding their choice. Looking for good treatment outcomes on patients (66; 45.8%) and a challenging specialty (58; 40.3%) were the most influencing incentives to select a future specialty. Students in the clinical phase of their study were 3.01 (95% CI: 1.498 – 6.065) more likely to report deciding a future specialty compared to students in the basic medical sciences phase (p-value 0.002).

**Conclusions:**

A variety of factors appeared to inspire medical students in Kuwait to choose a future medical specialty. When identified, these factors can be used by mentors of medical students and directors of residency training programs to motivate students to choose specialties that are scarce in Kuwait.

*Key Words: Specialty choice; Medical students; Future career*

*Funding Agency: None*



**Medical Education**

Category: Basic Sciences

51

**Level of empathy among Kuwait University medical students and its correlates**

\*Hassan SH, Al-Sharqawi N, Dashti F, AbdulAziz M, Abdullah A, Shukkur M, Thalib L  
Department of Community Medicine, Kuwait University Faculty of Medicine

**Introduction:**

Empathy is defined as the “objective awareness of and insight into the feeling, emotions and behavior of another person”. The Importance of empathy among doctors is clearly palpable as there is mounting evidence to suggest that empathy is significantly associated with better health outcomes. Our objective was to evaluate the level of empathy in Kuwait University medical students and its association with personality, stress level and sociodemographic factors.

**Methods:**

A cross-sectional study was carried out on a sample of 264 medical students in Kuwait University, Faculty of Medicine using a self-administered questionnaire. Empathy was measured using the Jefferson Scale of Physician Empathy, medical student version. Personality type was assessed using the Zuckerman-Kuhlman Personality Questionnaire and the Perceived Stress Scale was utilized to quantify the stress levels. Factors associated with empathy were tested using t-test/ANOVA in case of categorical independent variables, and correlation and regression approach was used to test the association between empathy scores and continuous explanatory variables.

**Results:**

The mean empathy score was 104.6 (SD: 16.3). Empathy scores were significantly associated with gender, year of study, academic performance, mothers’ education, satisfactory relationship with the mother and stress levels. Male medical students with lower academic performance, as well as those in later years of medical education, had significantly lower empathy levels. Stress scores were significantly and positively correlated to empathy ( $r = 0.129$ ;  $p = 0.041$ ). Although personality types were not significantly associated, those who scored higher on the aggressiveness scale tended to have lower levels of empathy.

**Conclusions:**

Lower empathy levels among medical students in Kuwait compared to that of our counterparts is a cause for concern and may require educational intervention and revision of our medical curriculum.

*Key Words: Empathy; Stress; Personality*

*Funding Agency: None*



## **Medical Education**

*Category: Undergraduate*

52

### **Are medical students accepted by patients in teaching hospitals?**

\*Marwan Y<sup>1</sup>, Al-Saddique M<sup>2</sup>, Hassan A<sup>2</sup>, Karim J<sup>1</sup>, Al-Saleh M<sup>1</sup>

<sup>1</sup>Department of Surgery, Faculty of Medicine, Health Sciences Center, Kuwait University; <sup>2</sup>Royal College of Surgeons in Ireland

#### **Introduction:**

Worldwide, patients are the cornerstone of bedside teaching of medical students. In this study, the authors aimed to assess patients' acceptability toward medical students in teaching hospitals of the Faculty of Medicine of Kuwait University.

#### **Methods:**

Nine hundred and ninety five patients were approached in 14 teaching hospitals; 932 patients agreed to participate (refusal rate is 6.3%). A self-administered questionnaire was used to collect data. Data were analyzed using descriptive and chi-square methods.

#### **Results:**

In general, higher acceptance of students by patients was found when there is no direct contact between the patient and the student (e.g. reading patients' files, presenting in outpatient clinic, observing doctors performing examination or procedures) compared to other situations (e.g. performing physical examination or procedures). Pediatrics patients showed higher acceptance of students compared to patients in other specialties, while Obstetrics/Gynecology patients showed the highest refusal of students. Gender of patients (especially females) and students appeared to affect the degree of acceptance of medical students by patients. Majority of the patients (436; 46.8%) believed that the presence of medical students in hospitals improves the quality of health care.

#### **Conclusions:**

Patients are an important factor of bedside teaching. Clinical tutors must take advantage of patients who accept medical students. Clinical tutors and medical students should master essential communication skills to convince patients in accepting students, thus improving bedside teaching. Also, using simulation and standardization should be considered to address scenarios that most patients are unwilling to allow students to participate.

*Key Words: Bedside teaching; Teaching hospitals; Patients' acceptability*

*Funding Agency: None*



**Medical Education**

Category: Undergraduate

53

**Self-confidence of medical students in performing clinical skills acquired during their surgical rotation: an assessment of a new teaching curriculum**

\*Marwan Y, Karim J, Dawas A, Akhtar S

Departments of Surgery and Community Medicine and Behavioural Sciences, Faculty of Medicine, Health Sciences Center, Kuwait University

**Introduction:**

Clinical skills are practiced routinely by medical doctors. Therefore, having a high self-confidence in performing these skills is essential. The authors aimed to assess self-confidence of clinical years' medical students of Kuwait University in performing the clinical skills/procedures that they were supposed to acquire during their surgical rotation.

**Methods:**

A questionnaire was used to collect data from students who at least completed 11 weeks of surgical rotation. Students were requested to report their level of self-confidence in performing specific skills/procedures that they were supposed to master during their surgical rotation of the 1st clinical year. Confidence level of 60% or more was considered acceptable.

**Results:**

The mean confidence level in performing all skills/procedures was 34.8%. The mean confidence level in history taking and physical examination skills was 65.4%, but it dropped to 24.6% for skills required in performing diagnostic and treatment procedures. The highest confidence level was in performing abdominal examination, while the lowest level was in caring of a Jackson-Pratt (JP) drain site and emptying the drain bulb.

**Conclusions:**

Medical students appeared to have poor self-confidence in performing clinical skills/procedures. Curriculum planners should look for potential reasons, and methods of improvement, for the low confidence level among medical students in performing skills/procedures they were expected to learn during their surgical rotation.

*Key Words: Clinical skills; Bedside teaching; Self-confidence*

*Funding Agency: None*



## Medicine

Category: Clinical

54

### Could gender dimorphism explain the controversial associations between RBP-4 and cardiometabolic risk factors in obese subjects?

\*Abdella NA<sup>1</sup>, Mojiminiyi OA<sup>2</sup>, Al-Mohammed H<sup>3</sup>, Pinto C<sup>1</sup>, Al-Rammah T<sup>2</sup>

<sup>1</sup>Departments of Medicine; <sup>2</sup>Pathology, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Medicine, Mubarak Al-Kabeer Hospital, Kuwait

#### Introduction:

Retinol-binding protein 4 (RBP4) RBP4 is an adipokine associated with insulin sensitivity in mice but data from clinical studies are controversial. Recent reports suggest that adipose tissue RBP4-mRNA expression is regulated by leptin and gender specific. This study evaluates gender specific differences in the associations of RBP4.

#### Methods:

Fasting RBP4, leptin, insulin, glucose, lipid profile, ALT, LH, FSH, estradiol (E2), testosterone, SHBG, and Free androgen index (FAI) were determined in 191 (82 males 109 females) healthy first degree relatives of Type 2 diabetic patients with mean (SD) age of 28 (8) years. Insulin resistance (IR) was assessed with the homeostasis model (HOMA-IR). Subjects were classified by IDF criteria for Metabolic syndrome (MetS). Linear and binary regression analyses were used to determine the associations of RBP4 with other variables, IR and MetS.

#### Results:

Mean RBP4 (26 vs 23 µg/ml) was significantly higher in males but leptin (43 vs 19 ng/ml) was significantly higher in females despite similar anthropometric indices (AI). Mean RBP4 was significantly higher in females with IR (23 vs 20 µg/ml) but not in males. RBP4 was not significantly correlated with AI and leptin and showed gender dimorphisms in correlations with other variables – in males significant correlations with only FAI ( $r=0.7$ ), Triglycerides (Tg) ( $r = 0.4$ ), creatinine ( $r = 0.4$ ) and ALT ( $r = 0.2$ ); in females, significant correlations with only age (0.2), E2 ( $r=0.3$ ) and Tg (0.3). RBP4 showed stepwise increase with increasing number of MetS criteria and was mildly but significantly associated with MetS in males (Odds Ratio (OR) = 1.091 and females (OR = 1.037). RBP4 was significantly associated with IR in females (OR = 1.17) but not in males (OR = 0.98).

#### Conclusions:

Leptin and AI are not related to RBP4 which shows gender dimorphisms in associations with cardiometabolic risk factors. These may account for the controversies on the potential roles of RBP4 in humans.

*Key Words: Retinol-binding protein 4; Insulin resistance; Gender dimorphism*

*Funding Agency: KFAS grant 2004-1302-03*



**Medicine**

*Category: Clinical*

**55**

**Evaluation of quality of care in Mubarak Al-Kabeer hemodialysis unit**

\*Abdelghani A, Hussain N

Nephrology Department, Mubarak al Kabeer Hospital, Ministry of Health, Kuwait

**Introduction:**

The quality of care provided to dialysis patients is under increasing scrutiny. Earlier studies revealed striking differences among countries which are not fully explained by the differences in patients' characteristics suggesting variations in the quality of care provided. The aim of this study was to evaluate the quality of care delivered to hemodialysis patients in view of the international guidelines.

**Methods:**

A retrospective study conducted in Mubarak Al Kabeer Hospital. Clinical and laboratory data of the chronic hemodialysis (HD) patients for the year 2010 were reviewed to find the extent of adherence to the kidney diseases outcome quality initiative guidelines.

**Results:**

A total of 162 HD patients (53.1% males) were included in the study with mean age  $54.9 \pm 15.4$  years. An arteriovenous fistula was the vascular access in 52.5% of cases, and a permanent catheter was used in 47.5%. 92.7% were using dialyzers with surface area  $\geq 1.6$  m<sup>2</sup>. The mean Kt/V was  $1.18 \pm 0.2$  Kt/V was  $>1.1$  in 68.1%. The mean predialysis blood pressure was  $\leq 140/90$  in 78.2% of cases. The mean hemoglobin level was  $11.6 \pm 1.3$  g/dL; 88.4% had a hemoglobin level  $\geq 11$  g/dL. The mean serum albumin level was  $30.91 \pm 5.2$  g/L; 47.3% had serum albumin  $\geq 35$  g/L. The mean parathormone level was  $50.13 \pm 28.32$  pmol/L; 39.5% had the target range, and the mean calcium level was  $2.28 \pm 0.02$  mmol/L; 89.5% had the target range while the mean serum phosphorus level was  $1.7 \pm 0.2$  mmol/L; 63.9% had the target range. The prevalence of hepatitis C and B virus-positive patients was 14.8% and 1.8%, respectively. The annual mortality rate was 11.3%.

**Conclusions:**

Our study showed an acceptable quality of care for HD patients in the field of hemoglobin, Ca and phosphorus levels, blood pressure control, and dialysis adequacy. On the other hand, this study showed the need for improving the nutritional status of patients through more dietary counseling, nutritional education, and early management for nutritional problems.

*Key Words: Hemodialysis; Quality assessment; Guidelines*

*Funding Agency: None*



**Medicine**

*Category: Clinical*

**56**

**Resistive index of prostatic blood flow in benign prostatic hyperplasia**

Abdelwahab O, \*El-Barky E, Khalil M, Kamar A

Urology Department, Banha Faculty of Medicine, Banha University

**Introduction:**

The aim of this work is to study the resistive index (RI) of prostatic blood flow by transrectal power Doppler sonography in benign prostatic hyperplasia (BPH) to determine its correlation with other parameters of BPH.

**Methods:**

Eighty two male patients aged 48-84 years with lower urinary tract symptoms (LUTS) due to BPH were included in this study. Patients with prostate cancer, neurogenic bladder, or associated with other pathology e.g. prostatitis, bladder stone were excluded from the study. All patients were evaluated by full history including International Prostate Symptoms Score (IPSS), general and local examination (DRE), neurologic examination, uroflowmetry, laboratory investigations including urine analysis, routine laboratory tests and serum prostate specific antigen (PSA). Transrectal ultrasonography was used to calculate the total prostatic volume. Transrectal Power Doppler ultrasound (PUD) was used to identify the capsular and urethral arteries of the prostate and to measure its RI value.

**Results:**

There was highly significant increase in the RI of capsular arteries (right & left) and urethral arteries with the degree of obstruction (P value<0.001), severity of symptoms (P value<0.001) and also with the prostatic volume, (P value<0.001).

**Conclusions:**

Resistive index of the prostatic blood flow can be applied as an easy and non-invasive tool to evaluate the lower urinary tract obstruction due to BPH.

*Key Words: Power Doppler; Resistive index; BPH*

*Funding Agency: None*



**Medicine**

Category: Basic Sciences

57

## **Establishing stable isotope facilities for assessment of childhood obesity in Kuwait**

\*Al-Ati T<sup>1</sup>, Preston T<sup>2</sup>, Al-Hooti S<sup>1</sup>, Al-Hamad N<sup>3</sup>, Al-Ghanim J<sup>1</sup>, Al-Khulifi F<sup>1</sup>, Al-Lahou B<sup>1</sup>

<sup>1</sup>Biotechnology Department, Kuwait Institute for Scientific Research, Kuwait; <sup>2</sup>The University of Glasgow, Scottish Universities Environmental Research Center, Scotland, UK; <sup>3</sup>Food and Nutrition Administration, Ministry of Health, Kuwait city, Kuwait

### **Introduction:**

Isotope ratio mass spectrometer (IRMS) is the gold standard method for measuring total body water (TBW), allowing for accurate assessment of body composition. A stable isotope facility was established in Biotechnology Department at Kuwait Institute for Scientific Research for a collaborative study with International Atomic Energy Agency (IAEA). Objectives: To use IRMS in an observational study of body composition in Kuwaiti children.

### **Methods:**

The study was approved by the Joint Committee for the Protection of Human Subjects in Research at the Kuwait Institute of Medical Specialization of the Ministry of Health. A convenient sample of 187 children (5-10 years) met the inclusion criteria of being Kuwaiti and healthy. Children <35 Kg drank a water dose with 1 grams of 99.8% deuterium oxide (D<sub>2</sub>O), while those ≥35 Kg drank 3 grams of 99.8% D<sub>2</sub>O.

### **Results:**

IRMS measured deuterium enrichment in urine samples of 82 boys (6yr:2mo-10yr:5mo) and 89 girls (5yr:10mo-9yr:10mo). The measured TBW was used to calculate fat free mass (FFM), fat mass (FM) and fat mass index (FMI). On average boys had a TBW of 16.36±3.18 kg, FFM of 21.34±4.2 kg, FM of 12.81±7.6 kg and FMI of 7.37±4 kg/m<sup>2</sup>. Girls had on average TBW of 15.59±3.7 kg, FFM of 20.12±4.8 kg, FM of 14.34±14.3 kg, and FMI of 8.25±3.6 kg/m<sup>2</sup>. According to the WHO classification (Cole classification in parenthesis) 1 girl was underweight, 42 (44) boys and 36 (39) girls with normal weight, 6 (11) boys and 14 (13) girls were overweight, and 34 (27) boys and 38 (37) girls were obese.

### **Conclusions:**

The deuterium dilution technique has been established at the Kuwait Institute for Scientific Research (KISR) for the first time in Kuwait. Among others, the stable isotope facility at KISR can be used to validate conventional methods and evaluate intervention studies in obesity related research studies.

*Key Words: Stable isotope; Deuterium dilution; Childhood obesity*

*Funding Agency: Kuwait Institute for Scientific Research. International Atomic Energy Agency (IAEA)*



**Medicine**

*Category: Clinical*

**58**

**Risk factors associated with diabetic foot complications in Kuwait**

\*Al-Adsani AMS, Hassanein REA, Khouzam SYA, Abd elkareem MRK, Shalla HA  
Diabetes Unit, Department of Medicine, Al-Sabah Hospital, Kuwait

**Introduction:**

Foot ulcers and amputations are a major cause of morbidity, disability, as well as emotional and economic costs. Early recognition and management of independent risk factors for ulcers and amputations can prevent or delay the onset of adverse outcomes. This study is conducted to identify the risk factors associated with diabetic foot complications (DFC).

**Methods:**

Demographic and clinical data were collected for a sample of 55 diabetic patients who presented to Surgical Department with DFC from February to October 2011. Controls were selected from a pool of diabetic patients followed up in the diabetic outpatient clinic, and they were matched by gender, nationality, and type of diabetes.

**Results:**

The mean age was  $59.8 \pm 11.7$  and  $57.8 \pm 10.4$  years for cases and controls respectively. Cases had a notable longer duration of diabetes compared to controls ( $17.7 \pm 9.6$  vs.  $14.2 \pm 9.7$  years,  $p=0.063$ ). Among the studied cases, foot ulceration was the main presentation in 37 patients (67.3%), and ten patients (18.2%) had gangrene. The majority of the cases (98.2%) had type 2 diabetes, 56.4% were male, 65.5% were Kuwaitis, and 9.1% were current smokers. Amputation was done for 14 cases. Longer duration of diabetes (+20years), current smoking, and presence of diabetic neuropathy (DN), peripheral vascular disease (PVD), retinopathy, and treatment with insulin were the significant factors associated with DFC in both the univariate and multivariate regression analyses. DN and PVD were the strongest significant factors ( $p < 0.001$ ).

**Conclusions:**

DN and PVD were the strongest risk factors for DFC. Other factors included longer duration of diabetes, current smoking, treatment with insulin, and presence of retinopathy. Identifying patients at highest risk for developing DFC can improve the quality of diabetes services by targeting these patients for early prevention and treatment, thereby reducing the disability and costs associated with diabetic foot disease.

*Key Words: Diabetes; Foot Complication; Risk Factors*

*Funding Agency: None*



**Medicine**

Category: Clinical

59

**Prevalence of adenomatous colorectal polyps in Kuwait:  
A retrospective analysis**

\*Alazmi W, Omar S, Altourah L

Faculty of Medicine, Kuwait University

**Introduction:**

A decrease in the prevalence of colorectal cancer (CRC) in Western countries is noticed and mainly attributed to the detection of the precancerous adenomatous lesions; however, it is increasing in other parts of the world, including Kuwait. Our aim is to investigate the prevalence and endoscopic and histological features of colorectal polyps.

**Methods:**

A total of 1300 patients who underwent colonoscopy for various indications were retrospectively evaluated over a period of 13 months.

**Results:**

Among 1129 eligible patients, 159 (14.1%) had 204 colorectal polyps, of which 166 (81.4%) were adenomatous detected in 124 (11%) of patients. Histopathological examination of the adenomatous colorectal polyps revealed 16 (9.6%) villous adenomas and 150 (90.4%) tubular and/or tubulovillous. Advanced adenomas were detected in 29 (17.5%) polyps. The rate of adenomatous colorectal polyps detection was significantly associated with older age ( $p < 0.05$ ), male sex ( $p = 0.004$ ) and past history of colonic polyps ( $p < 0.001$ ); proximal polyps were more likely to be adenomatous ( $p = 0.002$ ).

**Conclusions:**

This study shows a trend towards the increase in the prevalence of adenomatous colorectal polyps and accordingly colorectal cancer in Kuwait.

*Key Words: Polyps; Prevalence; Colorectal Cancer (CRC)*

*Funding Agency: None*



**Medicine**

*Category: Clinical*

**60**

**Prevalence of pancreas divisum in Kuwait**

\*AlAzmi W, AlTourah L, Omar S

Faculty of Medicine, Kuwait University

**Introduction:**

The rate of pancreas divisum (PD) detection has increased with advancement of ERCP. No data reflects its prevalence in the Middle East region. The aim of the study is to assess the prevalence of PD in the state of Kuwait.

**Methods:**

A retrospective analysis was conducted on 1091 patients who underwent ERCP over 31 months.

**Results:**

Among 1091 patients who underwent ERCP, 478 were eligible candidates and had pancreatogram; of these, 303 (63.4%) were Kuwaitis. PD was detected in 7 patients (1.46%): 4 (1.32%) were Kuwaitis and 3 (1.71%) were non-Kuwaitis. Complete PD was identified in 5 patients. The indications of ERCP among PD patients were: suspected or retained CBD stones (4), traumatic pancreatic fistula (1), obstructive jaundice (1), and recurrent acute pancreatitis (1).

**Conclusions:**

This study is the first to explore PD prevalence in Kuwait. Prevalence of PD in Kuwait was lower than the Western world and comparable to that of the Southeastern countries.

*Key Words: Pancreas divisum; Prevalence*

*Funding Agency: None*



**Medicine**

Category: Clinical

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**Ulcerative colitis in an Arab population: Epidemiology and clinical course**

\*Al-Azmi W<sup>1,2</sup>, Siddique I<sup>1,2</sup>, Al-Ali J<sup>1,3</sup>, Al-Fadli A<sup>3</sup>, Memon A<sup>4</sup>

<sup>1</sup>Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait; <sup>2</sup>Thunayan Al-Ghanim Gastroenterology Center, Al-Amiri Hospital, Kuwait; <sup>3</sup>Mubarak Al-Kabeer Hospital, Kuwait; <sup>4</sup>Division of Primary Care and Public Health, Brighton and Sussex Medical School, Brighton, United Kingdom

**Introduction:**

There has been an increase in the incidence of ulcerative colitis (UC) among Arabs in recent years. We conducted this study to determine the clinical epidemiology of UC in Kuwait.

**Methods:**

Sociodemographic and clinical information was collected for a continuous series of 182 Arab patients with UC, and age at diagnosis, extent and severity of disease was determined according to the Montreal classification.

**Results:**

Among the 182 patients, 91 (50.0%) were males. The mean age at diagnosis ( $\pm$  SD) was  $28.9 \pm 13$  years. Family history of UC was reported by 26 (14.3%) patients. The disease was limited to the rectum in 34 (18.7%) patients, whereas in 67 (36.8%) it extended up to the splenic flexure and in 81 (44.5%) it extended proximal to the splenic flexure. At the time of inclusion in the study, 127 (69.8%) patients were in clinical remission, 53 (29.1%) had mild to moderate disease and 2 (1.1%) had severe colitis. In the multivariate analysis, adjusted for age and gender, the use of biologic therapy or need for surgery was not significantly associated with age at diagnosis, duration or extent of disease, smoking or family history of IBD.

**Conclusions:**

Our data show that compared with other populations, UC among Arabs is equally common in males and females, and is more likely to be limited to the rectosigmoid or the left side of the colon. There also appears to be less need for surgery for the disease in the Arab population.

*Key Words: Ulcerative colitis; Inflammatory bowel disease; Arab*

*Funding Agency: None*



**Medicine**

*Category: Clinical*

**62**

**Critical illness polyneuromyopathy in renal transplant recipients: Risk factors and outcome**

Al Otaibi T, \*Gheith O, Halim M, Said T, Nair MP, Balaha MA, Abd-el-tawab K, Zakareya Z, Hosni W, Nampoory MRN

Hamed Al-Essa Organ Transplant Center, Kuwait

**Introduction:**

Critical illness polyneuromyopathy (CIP/CIM) commonly accompanies patients with multi-organ failure and sepsis. Distal muscle weakness and loss of deep tendon reflexes are usually found with sparing the cranial nerves musculature. Many risk factors had been identified specially hypoxia, hypotension, hyperpyrexia, and age. Other independent risk factors that had been reported as female gender, severity of illness, duration of organ dysfunction, renal failure and renal replacement therapy, hyperosmolality, parenteral nutrition, low serum albumin, duration of ICU stay, catecholamine support, and central neurologic failure. Hyperglycemia also has been identified as an independent risk factor, with an important potential impact in terms of prevention. Herein, we reported the development of such syndrome in 7 out of 22 renal transplant recipients who were weaned successfully from ventilator for bronchopneumonia.

**Methods:**

Out of 45 renal allo-transplant recipients who developed persistent bronchopneumonia- between August 2009 and Marsh 2010–22 of them necessitated mechanical ventilation following diagnostic bronchoscopic aspiration and lavage. We failed to wean seven patients from mechanical ventilation. Critical illness polyneuromyopathy was suggested.

**Results:**

Our lines of management were supportive, consisted of aggressive pulmonary hygiene in addition to prevent secondary complications of immobility such as bed sores, deep venous thrombosis and superimposed compressive neuropathies. As a long term management, rehabilitation program-active and passive exercises- were started beside assistive devices, and medication for neuropathic pain, if present.

**Conclusions:**

CIP/CIM is a rare complication and this is the first report among renal transplant recipients. Clinical suspicion and electrophysiological studies are the tools for early diagnosis .Proper management including correction of risk factors especially diabetes and long term measures of rehabilitation might be beneficial.

*Key Words: Critical illness; Neuropathy; Renal transplant*

*Funding Agency: None*



**Medicine**

Category: Basic Sciences

63

**Making cortical neurons from umbilical cord blood stem cells**

\*Ali H<sup>1,2</sup>, Forraz N<sup>3</sup>, McGuckin CP<sup>3</sup>, Jurga M<sup>3</sup>, Lindsay S<sup>2</sup>, Ip BK<sup>2</sup>, Trevelyan A<sup>4</sup>, Basford C<sup>2</sup>, Habballah S<sup>2</sup>, Ahmad S<sup>2</sup>, Clowry GJ<sup>4</sup>, Bayatti N<sup>4</sup>.

<sup>1</sup>Institute of Genetic Medicine, Newcastle University, Newcastle-upon-Tyne, UK; <sup>2</sup>Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait; <sup>3</sup>Cell Therapy Research Institute (CTI-Lyon), Parc Technologique de Lyon-Saint Priest, Saint Priest, France; <sup>4</sup>Institute of Neuroscience, Newcastle University, Newcastle upon Tyne, UK.

**Introduction:**

Neurogenesis of excitatory neurons in the developing human cerebral neocortex is a complex and dynamic set of processes and the exact mechanisms controlling the specification of human neocortical neuron subtypes are poorly understood due to lack of relevant cell models available. It has been shown that the transcription factors Pax6, Tbr2 and Tbr1, which are sequentially expressed in the rodent neocortex, regulate and define corticogenesis of glutamatergic neocortical neurons. In humans the homologues of these genes are generally expressed in a similar pattern, but with some differences.

**Methods:**

In this study, we used purified human umbilical cord blood stem cells, expressing pluripotency marker genes (OCT4, SOX2 and NANOG), to model human neocortical neurogenesis in vitro. We analyzed the expression patterns of PAX6, TBR2 and TBR1, at both protein and mRNA levels, throughout the 24 days of a sequential neuronal induction protocol and compared them with their expression patterns across the human neocortex.

**Results:**

The expression patterns of the umbilical cord and stem cells correlated with those found in the developing human neocortex where they define different developmental stages of neocortical neurons. The derived cord blood neuron-like cells expressed a number of neuronal markers. They also expressed components of glutamatergic neurotransmission including glutamate receptor subunits and transporters, and generated calcium influxes upon stimulation with glutamate.

**Conclusions:**

We have demonstrated that it is possible to model neocortical neurogenesis using cord blood stem cells in vitro. This may allow detailed analysis of the molecular mechanisms regulating neocortical neuronal specification, thus aiding the development of potential therapeutic tools for diseases and injuries of the cerebral cortex.

*Key Words: Stem cell; Brain; Umbilical cord blood*

*Funding Agency: Novus Sanguis Consortium and Fondation Jérôme Lejeune, France, NS/2008A /2/07. Joint MRC, UK, G0700089. Wellcome Trust, UK, GR082557. Kuwait University, Kuwait, UG365-06-60543*



**Medicine**

*Category: Clinical*

64

**Should glycated haemoglobin (HbA1c) be performed routinely in non diabetic patients with obstructive sleep apnea (OSA)**

\*Al Mutairi SS<sup>1</sup>, Mojiminiyi OA<sup>2</sup>, Abdella NA<sup>3</sup>, Al-Alawi A<sup>4</sup>, Al-Ramah T<sup>5</sup>

<sup>1</sup>Department of Medicine, Faculty of Medicine, Kuwait University; <sup>2</sup>Department of Pathology, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Medicine, Faculty of Medicine, Kuwait University; <sup>4</sup>Department of Medicine, Al-Amiri Hospital, Ministry of Health; <sup>5</sup>Department of Pathology, Faculty of Medicine, Kuwait University.

**Introduction:**

Obstructive sleep apnea (OSA) is a sleep disorder that is associated with insulin resistance, glucose intolerance and risk of type 2 diabetes among overweight and obese individuals. Therefore there is need to screen for diabetes in subjects with OSA. Hemoglobin A1c (A1C) is now a recommended diagnostic test for diabetes and identification of subjects with high risk for the disease. The main aim of this study was to evaluate the use of HbA1c as a screening test for undiagnosed diabetes and other categories of glucose intolerance in patients with OSA.

**Methods:**

Venous blood was collected for determination of HbA1c in 77 subjects with previously undiagnosed diabetes and provisional diagnosis of OSA. All subjects had overnight polysomnography and spirometry; subjects were classified on the basis of polysomnographic findings as normal, mild, moderate or severe OSA. Clinical and anthropometric data were recorded and the American Diabetes Association (ADA) cut-off points for HbA1c were used to classify the patients as diabetic (HbA1c  $\geq$ 6.5% (48 mmol/mol)); prediabetic (HbA1c 5.7–6.4% (39–46 mmol/mol)) or normal (HbA1c < 5.7% (<39 mmol/mol)). Binary logistic regression was used to determine the risk associations of HbA1c with OSA.

**Results:**

25% of the subjects were normal, 41% had mild OSA, 21% had moderate OSA and 13% had severe OSA. Mean (SD) HbA1c in normal, mild, moderate and severe OSA were 5.5 (1.2)%; 8.7(3)%, 9.1 (1.6)% and 9.4 (3)% respectively. Using ADA HbA1c cut-offs, 84% of subjects with OSA had diabetes, 8% had pre-diabetes and 8% had normal glucose status. Binary logistic regression analysis showed that the odds ratio of the association of HbA1c with OSA was 1.7 (95% CI: 1.4-2.03).

**Conclusions:**

HbA1c is significantly associated with OSA and could be used to detect previously undiagnosed diabetes and other categories of glucose intolerance that require intervention. We recommend routine estimation in patients with suspected OSA

*Key Words: Obstructive sleep apnea; HbA1c; Non diabetics*

*Funding Agency: Kuwait university grant MM01/07*



**Medicine**

Category: *Clinical*

65

**Kuwaiti patients with multiple sclerosis have demonstrable metabolic bone disease**

\*Al-Shammri SN<sup>1,3</sup>, Akanji AO<sup>2</sup>, GirgisM<sup>3</sup>, Mathew R<sup>2</sup>, Bhattacharya A<sup>1</sup>, Madala C<sup>1</sup>

<sup>1</sup>Departments of Medicine, Kuwait University, Faculty of Medicine; <sup>2</sup>Department of Pathology, Kuwait University, Faculty of Medicine; <sup>3</sup>Departments of Medicine, Mubarak Al Kabir Hospital, Kuwait

**Introduction:**

Multiple sclerosis(MS) is a neurodegenerative disease characterized by immune dysregulation causing inflammatory demyelination of the myelin sheaths and axon damage. This disease is typically progressive. It is typically accompanied by bone dysfunction that is currently poorly understood. This study aims to evaluate the determinants of bone osteolytic/osteoblastic markers in relation to severity of the disease in MS.

**Methods:**

2 groups of subjects were studied. Group A: 29 age matched healthy controls; Group B: 37 Kuwaiti MS patients (14 males and 23 females) who attended the Neurology Clinic at the Mubarak-Al-Kabeer Hospital, Kuwait, whose clinical, demographic and anthropometric parameters were noted at recruitment. Fasting blood and urine samples were collected for evaluation of osteolytic/osteoblastic markers as well as CRP (C-Reactive Protein) as an index of systemic inflammation.

**Results:**

There was no age difference between patients and controls ( $p>0.05$ ), although the patients tended to be heavier with greater BMI and WHR (both  $p<0.05$ ). While levels of CRP (marker of systemic inflammation), osteocalcin and BAP (markers of osteoblastic activity) did not differ between the two groups, the patients had lower levels of the osteolytic markers (NTX and DPD) (both  $p<0.05$ ). Additionally, PTH levels were higher in the patients ( $p<0.05$ ). These parameters appeared variably influenced by disease severity, as indicated by EDSS.

**Conclusions:**

The dynamic interaction between levels of PTH and bone osteolytic markers is disturbed in patients with MS of varying severity. These observations have potential therapeutic implications.

*Key Words: Multiple Sclerosis (MS); Demyelination; Osteolytic/osteoblastic*  
*Funding Agency: MM 03/09*

**Medicine***Category: Clinical***66****Environmental and socio-cultural risk factors associated with multiple sclerosis in Kuwait- A preliminary hospital based study**Al-Shammri SN<sup>1,3</sup>, Girgis M<sup>3</sup>, \*Bhattacharya A<sup>1</sup>, Mathew R<sup>2</sup>, Madala C<sup>1</sup>, Sharma P<sup>5</sup>, Akanji AO<sup>2,4</sup><sup>1</sup>Departments of Medicine, Kuwait University, Faculty of Medicine; <sup>2</sup> Department of Pathology, Kuwait University, Faculty of Medicine; <sup>3</sup>Departments of Medicine, Mubarak Al Kabir Hospital, Kuwait; <sup>4</sup>Clinical Biochemistry, Mubarak Al-Kabir Hospital, Kuwait; <sup>5</sup>Office of the Vice Dean of Research, Kuwait University Faculty of Medicine**Introduction:**

Multiple sclerosis (MS) is a chronic, demyelinating disease of unknown etiology. Immunological, genetic and environmental factors are thought to play an important role in incidence and prognosis of this disease. Objective of this study is to identify different socio-cultural and demographic risk factors associated with MS in Kuwait.

**Methods:**

In this cross-sectional study, 167 Kuwaiti MS patients fulfilling Mc Donald criteria were followed up in a national MS clinic at Mubarak Al-Kabir Hospital and 29 healthy age and sex matched controls were clinically evaluated, and interviewed through a pre-designed questionnaire. Routine laboratory tests were also carried out according to international protocol.

**Results:**

The mean age and age at presentation of the MS patients was 33.4 years ( $\pm 10.1$ SD) and 27.1 ( $\pm 9.6$ SD) respectively, having a male to female ratio of 1:1.49. The median duration of the disease was 5 years (Inter-quartile range 2-10 years). Smoking [patients (26%) vs controls (4%),  $p < 0.011$ ] and sun exposure of  $< 10$  minutes/day [patients (70%) vs controls (42%),  $p < 0.012$ ] were found to be significant risk factors. Family history of MS (27% vs 14%, RR=1.9) and inactive life style (18% vs 4%, RR=4.9) also seems to contribute in the incidence of disease. Male MS patients had significantly higher solar exposure time than females ( $p < 0.05$ ). Majority of patients and controls use partial or fully covered dressing (74.3% vs 65.5%). Birth frequency of MS patients was higher during summer (October-February; bfr=15.2/month) than winter (March-Sept; bfr=12.10/month).

**Conclusions:**

Young age ( $< 35$  years), smoking, family history as well as solar exposure and inactive life style could be the important risk factors among Kuwaiti MS patients. More research is needed to focus on these factors for environmental and socio-cultural values among Kuwaiti population

*Key Words: Multiple sclerosis; Solar exposure**Funding Agency: Kuwait University, MM 03/09*



**Medicine**

Category: *Clinical*

67

**Elevated level of high density lipoprotein-cholesterol is common in adults with type 1 diabetes**

\*Alessa T<sup>1</sup>, Szeto A<sup>2</sup>, Chacra W<sup>1</sup>, Mendez A<sup>1,2</sup>, Goldberg R<sup>1</sup>

<sup>1</sup>Division of Endocrinology, Diabetes and Metabolism, University of Miami Miller School of Medicine; <sup>2</sup>Diabetes Research Institute, University of Miami Miller School of Medicine.

**Introduction:**

The observation that High Density Lipoprotein-Cholesterol (HDL-C) is frequently elevated in Type 1 diabetes mellitus (T1DM) was well noted, but not been consistently observed in all studies. We therefore re-assessed the prevalence and features of high HDL-C in a large group of subjects with T1DM.

**Methods:**

We reviewed the charts of 194 confirmed T1DM subjects (83 men and 111 women) in our Diabetes Clinic and extracted demographic, metabolic, and clinical data. Cutpoints for high HDL-C were arbitrarily set at >60mg/dL for men and >70mg/dL for women, both corresponding to the 85th percentiles of the National Health and Nutrition Examination Survey III report on population distribution of HDL-C.

**Results:**

The mean (+SEM) HDL-C was higher in women (68mg/dL+2mg/dL) than in men (57mg/dL+2mg/dL;  $p<0.001$ ). The prevalence of high HDL-C was similar in women (38%) and in men (36%). For both men and women, HDL-C level correlated positively with age ( $r=0.262$ ,  $p<0.05$ ;  $r=0.377$ ,  $p<0.001$ , respectively) and negatively with triglycerides ( $r=-0.246$ ,  $p<0.05$ ;  $r=-0.350$ ,  $p<0.001$ , respectively); and inversely with body mass index in women only ( $r=-0.246$ ,  $p<0.01$ ). In a linear regression model, the increase in HDL-C per year of aging was 0.47mg/dL in women ( $R^2=0.142$ ) and 0.30mg/dl in men ( $R^2=0.069$ ). There was no correlation between glycosylated hemoglobin and HDL-C.

**Conclusions:**

This study confirms that high HDL-C is common in adults with T1DM. The basis for mean value difference between genders is unknown. Age was a significant determinant of HDL-C level in both genders, suggesting a unique interaction between aging and the underlying mechanism causing high HDL-C in T1DM. This finding of a high prevalence of elevated HDL-C level in T1DM raises the question as to its functionality, given the excess risk of cardiovascular disease in these subjects. Detailed studies of HDL structure and function in T1DM are therefore needed to evaluate the prognostic significance of these findings.

*Key Words: HDL-C; Type 1 Diabetes; Hyperalphalipoproteinemia*

*Funding Agency: None*



## **Medicine**

Category: Clinical

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### **Functional derangement in vitamin D and bone homeostasis in Arab patients with multiple sclerosis**

\*Akanji AO<sup>2,4</sup>, Al-Shammri SN<sup>1,3</sup>, Bhattacharya A<sup>1</sup>, Mathew R<sup>2</sup>, Girgis M<sup>4</sup>, Madala C<sup>1</sup>

<sup>1</sup>Departments of Medicine, Kuwait University, Faculty of Medicine; <sup>2</sup>Department of Pathology, Kuwait University, Faculty of Medicine; <sup>3</sup>Departments of Medicine, Mubarak Al Kabir Hospital, Kuwait; <sup>4</sup>Clinical Biochemistry, Mubarak Al-Kabir Hospital, Kuwait.

#### **Introduction:**

Vitamin D is potentially important in pathogenesis of multiple sclerosis (MS), prevalence of which is increasing in Kuwait. This study attempted to evaluate vitamin D levels in Kuwaiti MS patients and healthy controls, and in former, investigate potential impact of any derangements, on bone homeostatic parameters.

#### **Methods:**

In a cross-sectional design, we recruited 105 MS patients (diagnosed by standard criteria) and 29 healthy controls. Each patient and control was interviewed by questionnaire, and clinically evaluated and also gave a fasting blood and early morning urine sample for assessment for: (i) serum calcium, PO<sub>4</sub>, alkaline phosphatase (ALP), intact parathyroid hormone (iPTH), total 25-OHvitamin D, bone osteoblastic markers-osteocalcin, bone specific alkaline phosphatase (BAP), and C-reactive protein (CRP); (ii) bone osteolytic markers-urine pyridinoline (PYD), deoxypyridinoline (DPD); type I collagen N-terminal telopeptides (NTx).

#### **Results:**

Results were available for 37 patients (we excluded 68 patients who were on vitamin D or multivitamin supplements) and 29 controls, median duration of disease since diagnosis was 6yr (range 1-13). Vit D levels were low in both patients and controls (median < 30 nmol/L) and did not differ significantly between them. However, serum Ca, PO<sub>4</sub> and ALP levels were lower in patients (P < 0.001). In addition, iPTH was higher in patients than controls, while levels of bone osteolytic markers-urinary NTx and DPD were lower in patients than controls (all p < 0.05) even when levels of osteoblastic markers, BAP, and serum osteocalcin, as well as CRP (marker of continuing inflammation), were similar for two groups.

#### **Conclusions:**

Although total 25-OH Vit D levels were deficient in both MS patients and healthy controls, there was a greater tendency to pathophysiological derangements in calcium and bone metabolism in former, manifesting as low Ca, PO<sub>4</sub> and high iPTH (early secondary hyperparathyroidism) and reduced levels of urinary osteolytic bone markers

*Key Words: Multiple Sclerosis (MS); Bone homeostatic parameters.*

*Funding Agency: Kuwait University, MM03/09*



**Medicine**

Category: Graduate (Resident)

69

**Eyeopening look at eye makeup hygiene: Practice, risk factors, ocular symptoms and microbiological evidence**

\*Alsaadoun W<sup>1</sup>, Bouhaimed M<sup>1,2</sup>

<sup>1</sup>Al-Bahar Eye Centre, Ibn Sina Hospital-Ministry of Health, Kuwait;

<sup>2</sup>Department of Community Medicine and Behavioural Sciences, Faculty of Medicine, Kuwait University

**Introduction:**

Blepharitis is the most common chronic condition seen by ophthalmologists in which the eyelid margins get inflamed secondary to excess growth of bacteria, blockage of the eyelid's oil glands, and allergies. There are many systemic and local risk factors associated with this high prevalence. In this study we looked specifically at the risk factors associated with eye makeup (mascara) hygiene. Most women use eye makeup to a certain extent and knowledge of their potential harm can be an eyeopener.

**Methods:**

A cross sectional study including 50 female students at the Health Science Centre was conducted using a questionnaire and microbiological analysis of their eye mascara. Swabs from the brush of the mascara were taken using sterile swabs and were sent to the laboratory using biohazard bags. Gram Kits for staining, Catalase and Coagulase tests were used. Inoculation and subcultures on to different agar plates were done using sterile disposable loops. Analytical Profile Index was used for staphylococcus identification. Finally, Kirby-Bauer disc diffusion method was used to detect bacterial sensitivities.

**Results:**

There were 14 positive cultures of bacterial growth (28%) with Staph. epidermidis, aures, xylosus, and diphtheroids. In practice, 86% were using mascara older than one month, 54% were sharing their mascara, and only 58% always remove their eye makeup. Interestingly, 32% were using false lashes (ranging from 1 day to one year). Ocular symptoms ranging from red eyes to photophobia were present to a variable degree. Current irritation from dust or smoke is correlated with having positive mascara cultures (p-value = 0.004). Contact lens were used by 32 participants (11 with positive cultures).

**Conclusions:**

Despite the small sample size and the participants' background, transferring bacteria back and forth from the eye into the mascara tube was evident with many associated risk factors.

*Key Words: Eye makeup hygiene; Ocular symptoms; Microbiological evidence*

*Funding Agency: None*



**Medicine**

Category: Clinical

70

**Evidence for sub-clinical malnutrition in Kuwaiti patients with multiple sclerosis: Relationship with clinical phenotypes, disease activity and outcome**

Bhattacharya A<sup>1</sup>, Al-Shammari SN<sup>1,3</sup>, Mathew R<sup>2</sup>, Girgis M<sup>3</sup>, Madala C<sup>1</sup>, \*Akanji AO<sup>2,4</sup>  
<sup>1</sup>Departments of Medicine, Kuwait University, Faculty of Medicine; <sup>2</sup> Department of Pathology, Kuwait University, Faculty of Medicine; <sup>3</sup>Departments of Medicine, Mubarak Al Kabir Hospital, Kuwait; <sup>4</sup>Clinical Biochemistry, Mubarak Al-Kabir Hospital, Kuwait

**Introduction:**

Multiple sclerosis (MS) is a chronic, immune-mediated demyelinating disorder of central nervous system, influenced by different genetic and environmental factors. Some findings suggest that MS Patients suffer from malnutrition which is often unrecognized causing fatigue and worsening of major symptoms; many patients also use different dietary supplements in order to improve their health. This study aimed to investigate the level and patterns of changes in nutritional markers in relation to clinical phenotypes in patients with MS.

**Methods:**

In this cross-sectional study, 116 MS patients fulfilling Mc Donald criteria and 29 age and sex matched healthy controls were included. Each patient and control was interviewed by a questionnaire & clinically evaluated. Fasting blood sample was collected to assess different :i) nutritional markers namely: serum albumin (Alb), prealbumin (Palb), urea, iron (Fe), Ferritin (Fr); and ii) inflammatory marker: C reactive protein (CRP).

**Results:**

Results were available for 37 patients [79 patients taking VitD or multivitamin supplements were excluded] and 29 controls. Patients had significantly higher ( $P<0.001$ ) BMI and waist-hip ratio, than controls. Most patients (94.65%) had relapsing remitting (RR)MS and were on immune-modulatory therapies (94.3%). Majority of them (83.8%) had an expanded disability status scale $<3$  with the serum levels of nutritional markers did not differ according to clinical phenotypes. Serum Alb, Palb, and urea ( $P<0.001$ ) and serum Fe levels ( $P<0.05$ ) were lower in patients than controls, while serum Fr levels were higher in patients ( $P<0.001$ ). CRP levels were similar for both groups.

**Conclusions:**

These results suggest an abnormality in release of circulating iron from the tissue ferritin in MS patients. This change is associated with subclinical malnutrition as indicated by reduced pre-albumin and albumin level in the patients. These observations have potential therapeutic implications.

*Key Words: Multiple Sclerosis [MS]; Clinical phenotypes; Nutritional markers*

*Funding Agency: Kuwait University, MM 03/09*



**Medicine**

Category: Clinical

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**Single center experience in steroid resistant acute cellular rejection:  
Risk factors and impact on graft and patient survival**

\*Awadain WH<sup>1</sup>, Hassan A<sup>2</sup>, El-Deeb S<sup>2</sup>, Hassan N<sup>3</sup>, Gheith O<sup>3</sup>, El-Agroudy A<sup>3</sup>, Fouda A<sup>3</sup>, Ghoneim M<sup>3</sup>

<sup>1</sup>Hamed Al Essa Organ Transplant Center Kuwait; <sup>2</sup>Zagazeeg University Egypt; <sup>3</sup>Urology & Nephrology Center, Mansoura, Egypt

**Introduction:**

Acute rejection in renal transplantation is considered a risk factor for short and long-term allograft survival. The expected reversal rate for the first acute cellular rejection-by steroid pulse- ranged between 60 to 100%, and lack of improvement within one week after treatment was defined as steroid-resistant rejection. The aim of this work was to evaluate factors that lead to steroid-resistant acute cellular rejection among patients with first live-donor renal allotransplant and its impact on graft and patient survival.

**Methods:**

Patients with improvement of serum creatinine was considered as control group I (n=106); while others were considered as steroid-resistant group (SRACR) II (n=101). Both groups were matched regarding demographic data.

**Results:**

Patients with below target CsA level were significantly higher in group II (p=0.02). We found no significant differences between the 2 groups regarding post-transplant complications (P>0.05). However, the mean hospital stay was longer in group II (p=0.021). Living patients with functioning graft were more prevalent in group I while those who live on dialysis were more prevalent in group II. The two groups were comparable regarding long-term patient and graft survival despite significantly lower creatinine in patients of group I till the end of 6 months (P= <0.001).

**Conclusions:**

Prebiopsy low cyclosporine trough level and associated chronic changes represented the most important risk factors for SRACR. Rescue therapies improve short term graft outcome, however they did not affect either patient or long term graft survival after 5 years of follow up.

*Key Words: Steroid resistant; Rejection; Renal transplant*

*Funding Agency: None*



## **Medicine**

*Category: Clinical*

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### **A single centre experience postrenal transplants Zero-HLA mismatch**

\*Awadain WH, Nair MP, Nampoory MRN, Said T, Halim MA, Moneim MA, Vareed B, Gheith O, Elsayed A, Al-Otaibi T.

Organ Transplant Centre, Kuwait

#### **Introduction:**

The evidence that HLA system provide the major barrier to acceptance of renal transplants was first obtained with living-related transplants. We aimed to analyze the outcome of zero-mismatched renal transplants done in our centre

#### **Methods:**

This study is retrospective study from 1993 to 2010, 1050 renal transplants were performed in our centre, including 40 (3.8%) zero-HLA mismatched kidney recipients. We studied the cases regarding demographic data, original kidney disease, immunosuppression, rejection episodes, and graft and patient outcome. Males represented (52.5%) while females represented (47.5%) with their mean recipient age was 28.8±2.1 years. The primary renal disease was chronic glomerulonephritis (GN) in 17 (42.5%), chronic tubulointerstitial disease in 12 (30%), diabetes mellitus in 2 (5%) and unknown in 9 (22.5%). All recipients had negative B and T cell lymphocytotoxicity cross match at the time of transplantation.

#### **Results:**

Mean follow up period was 8.76±1.1 years and the mean serum creatinine on last follow-up was 112±20.1umol/L. Graft survival was, 100% at 1 year, 97.2% at 3 years, 93.9% at 5 years and 84% at 10 years with a patient survival of 100% after 10 years. Four grafts were lost during the mean follow up period due to chronic rejection. There were only 2 (5%) episodes of biopsy proven acute rejection which occurred during the 1st year after transplantation and responded completely to steroid treatment. There were in total, 3 (7.5%) cases of post transplant GN, 2 being recurrent diseases ( lupus nephritis, IgA nephropathy) and the third, a case of de novo membranous GN. There were no cases of post transplant malignancy.

#### **Conclusions:**

The long term outcome of zero-mismatched renal transplantation in our centre shows excellent results.

Key Words: Zero mismatch; Renal transplant; Outcome

Funding Agency: None



**Medicine**

Category: Undergraduate

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**Association between oral hygiene practices and coronary heart disease in Kuwait**

\*Al-Youha DS, Al-Nami ND, El-Ghandour NM, Al-Fahad FW, Mohammed AM, Al-Huwais SH, Al-Ta'iar AM

Department of Community Medicine, Faculty of Medicine, Kuwait University

**Introduction:**

The relationship between periodontitis and coronary heart disease (CHD) although remains controversial- is of great interest as it postulates a role of poor oral health as an emerging risk factor for CHD. Self-reported oral hygiene practices have been shown to be a valid indicator of clinically confirmed periodontal disease but it remains unclear whether better self-reported oral hygiene practices are associated with a decrease in the risk of CHD. This study aimed to investigate the association between self-reported oral hygiene practices and CHD in Kuwait.

**Methods:**

A hospital-based case-control study was conducted in which 127 CHD cases were compared to 127 controls who had other acute conditions “patient-controls” and 134 healthy participants visiting the hospitals “visitor-controls”. Controls were frequency matched with CHD cases by age. Data on self-reported oral hygiene practices and the main risk factors of CHD, and other potential confounders were collected by face-to-face interview using structured pre-coded questionnaire. Poor oral hygiene practices were defined as those who brush their teeth less than twice a day.

**Results:**

A significant association between self-reported poor oral hygiene practices and CHD was found when cases were compared to visitor-controls after adjusting for potential confounders, odds ratio 2.26 (95%CI:1.13-4.51) (p=0.02). When cases were compared to patient-controls, there was a weak statistically non-significant association between self-reported poor oral hygiene practices and CHD, odds ratio 1.21 (95%CI:0.56-2.63) (p=0.62). Any use of dental floss was negatively associated with CHD, whether cases were compared to patient-controls or visitor-controls but the statistical significance was lost after adjusting for potential confounders.

**Conclusions:**

There is an association between self-reported oral hygiene practices and CHD, although it was not statistically significant. Large scale prospective studies are needed to investigate this relationship and ascertain whether programs aimed to improve oral hygiene practices have spin off benefits as CHD prevention.

Key Words: Periodontitis; Coronary heart disease

Funding Agency: None



**Medicine**

*Category: Clinical*

74

**Impact of positive BK virus-kidney donors on renal transplant recipient outcome and possible protective HLA Loci**

\*Gheith O, Zakareya Z, Al-Otaibi T, Halim M, Nampoory MRN

Hamed Al-Essa Organ Transplant Center, Inb-Sina Hospital, El-Sabah Area, Ministry of Health, Kuwait

**Introduction:**

BK nephropathy is increasing problem in renal transplant recipients. It has been correlated with newer immunosuppressive agents and the decline in acute rejection rates. However, the combinations of early detection, prompt diagnosis, and appropriate reduction in maintenance immunosuppressive therapy have been associated with better outcome. We aimed to evaluate the impact of BK positive kidney donors on the outcome of kidney transplant recipients after mean follow up period of 21 months.

**Methods:**

Out of 18 positive-BK kidney donors, 5 were found fit for donation. Here in we present 5 kidney transplant recipients who received kidney allografts from such donors with mean age of  $35\pm 3$  years. We try to assess the impact of donor BK on patient and graft survival after mean follow up period of 21 months.

**Results:**

All patients-except one –were males with mean age  $49.4\pm 4.2$  years; mean body weight  $68.2\pm 4$  kgm and mean follow up duration  $21.6\pm 4$  months. The original kidney disease was diagnosed in 4 cases as autosomal dominant polycystic kidney disease (APCKD), chronic interstitial nephritis, focal segmental glomerulosclerosis (FSGS) and diabetic nephropathy while the 5th case was idiopathic. All patients –except one - received thymo induction and steroid, tacrolimus, MMF as maintenance therapy; and ureteric stenting was a routine procedure in each case .HLA-CW7 was detected in 4 out of 5 recipients and the 5th was detected in the donor .Three patients were biopsied and acute tubular necrosis was the corner stone in all biopsies; however one patient was managed successfully with plasma exchange for antibody mediated rejection. Moreover, at last follow up all patients are enjoying functioning grafts without evidence of recurrence of BK infection.

**Conclusions:**

BK positive persons can be accepted safely for kidney donation especially with HLA-CW7. Further longer term and larger randomized studies are needed to evaluate this issue.

*Key Words: BK virus; Kidney donor; Outcome*

*Funding Agency: None*



**Medicine**

*Category: Clinical*

**75**

**Disease activity and serum lipid profile in patients with rheumatoid arthritis treated with Rituximab: A cohort study**

\*Hasan EA<sup>1</sup>, Olusi SO<sup>2</sup>, Mokaddem K<sup>1</sup>, Sharma PN<sup>3</sup>, Alawadhi A<sup>4</sup>

Rheumatic Disease Unit, Department of Medicine, Al-Amiri Hospital, Ministry of Health, Kuwait; Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait; Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

To investigate the effects of Rituximab (RTX) therapy on disease activity and serum lipid levels in patients with rheumatoid arthritis (RA).

**Methods:**

Forty-seven patients, aged 25-78 years, were enrolled into a cohort prospective study. All patients were treated with intravenous RTX. Disease activity and lipid profile were assessed at baseline and after 1, 3, and 6 months of treatment.

**Results:**

Disease activity score-28 (DAS-28), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and health assessment questionnaire (HAQ) score significantly decreased in patients with active RA at all follow-up assessments ( $p < 0.01$ ). RTX significantly increased high density lipoprotein (HDL)-cholesterol from median 1.10 (range 0.60-1.90) to 1.30 mmol/L (0.70-2.00) ( $p < 0.05$ ) and decreased atherogenic index from 4.40 (2.42-14.67) to 3.80 (2.26-9.75) ( $p < 0.05$ ) at the end of the study. The increase in serum HDL-C correlated negatively with DAS28, CRP, and ESR. Total cholesterol, Low density lipoprotein (LDL)-cholesterol, and triglycerides did not change during treatment.

**Conclusions:**

Our findings suggest a favorable effect of RTX treatment on disease activity and HDL-C in patients with RA.

*Key Words: Rheumatoid arthritis; Serum lipid profile; Rituximab*

*Funding Agency: None*



**Medicine**

*Category: Clinical*

**76**

**Effects of rituximab treatment on the serum concentrations of vitamin D and interleukins 2, 6, 7, and 10 in patients with rheumatoid arthritis**

\*Hasan EA, Olusi SO, AlAwadhi A, Mokaddem K, Sharma PN, George S

Rheumatic Disease Unit, Amiri Hospital; Department of Pathology and Medicine, Faculty of Medicine, Kuwait University; Computer Unit, Health Science Center, Kuwait University, Kuwait.

**Introduction:**

Rituximab, a monoclonal antibody that selectively targets CD20-positive B-lymphocytes, is used for the treatment of patients with rheumatoid arthritis (RA) with an inadequate response or tolerance to tumor necrosis factor inhibitors. The objective of this study was to investigate the effects of rituximab treatment on the serum concentrations of vitamin D, interleukin (IL) 2, IL-6, IL-7, and IL-10 in patients with rheumatoid arthritis (RA).

**Methods:**

Forty-five patients, aged 25–78 years, were enrolled into a cohort prospective study. All patients were treated with intravenous rituximab. Disease activity score-28 (DAS-28) and serum concentrations of rheumatoid factor (RF), C-reactive protein (CRP), anticyclic citrullinated peptide (anti-CCP), erythrocyte sedimentation rate (ESR), health assessment questionnaire (HAQ), vitamin D, IIs 2, 6, 7, and 10 were estimated in the patients before and after treatment with rituximab.

**Results:**

DAS-28, HAQ score, and serum concentrations of CRP, RF, anti-CCP, IL-2, IL-6, IL-7, IL-10, and ESR significantly decreased after treatment. All 45 patients had vitamin D deficiency before treatment and this did not significantly change after treatment. However no significant association was found among serum vitamin D concentration and any of the IIs.

**Conclusions:**

We concluded from this study that although rituximab treatment of patients with RA significantly reduced their disease activity and serum concentrations of IL-2, IL-6, IL-7, and IL-10, it did not significantly alter their vitamin D status. Furthermore, no significant association was found among serum vitamin D concentration and any of the IIs.

*Key Words: Vitamin D; Rituximab; Rheumatoid arthritis*

*Funding Agency: None*



**Medicine**

*Category: Clinical*

77

**Spectrum of peritonitis in continuous ambulatory versus automated peritoneal dialysis in Mubarak Al Kabeer Hospital**

\*Hussain N, Abdelghani A

Nephrology Department, Mubarak Al Kabeer Hospital, Ministry of Health, Kuwait

**Introduction:**

Catheter related infections (peritonitis, tunnel and exit site) are among the most common serious complications of peritoneal dialysis. The aim of this study was to find the difference in the incidence as well as the spectrum of catheter related infections among peritoneal dialysis patients in Mubarak Al Kabeer Hospital.

**Methods:**

All patients on Peritoneal dialysis in 2011 were retrospectively reviewed to determine the difference in the spectrum and incidence of Catheter related infections in continuous ambulatory peritoneal dialysis (CAPD) versus automated peritoneal dialysis (APD).

**Results:**

106 patients underwent peritoneal dialysis in 2011. 41 of them were using APD and 65 were doing CAPD. 27 episodes of peritonitis were reported in 17 CAPD patients versus 25 episodes in 13 APD patients. Regarding CAPD peritonitis the commonest organism was Staph. epidermidis (29.6%) followed by streptococcus infection (14.4%) while culture negative peritonitis was reported in 25.9% of cases. None of the patients required catheter removal to treat peritonitis. Regarding APD patients 9 and 4 episodes of recurrent peritonitis were reported in two different patients necessitating catheter removal and shifting them to hemodialysis. In contrast to CAPD Staph. epidermidis was isolated in a single episode of peritonitis. The commonest organism was staph. hemolyticus (20%) followed by streptococcus infection in 16% of episodes, whereas culture negative peritonitis was reported in 28% of episodes. Two cases need catheter removal. The incidence of peritonitis was 8.06/100 patient month treatment in CAPD patients and 5.12/100 patient month treatment.

**Conclusions:**

The incidence of peritonitis was more in CAPD patients than APD patient yet both are within the acceptable range according to the international guidelines. The commonest causative organism was staph epidermidis in CAPD related peritonitis whereas staph. hemolyticus was the commonest organism in APD related peritonitis.

*Key Words: Peritonitis; Spectrum; Rate*

*Funding Agency: None*



## **Medicine**

*Category: Clinical*

**78**

### **Risk factors for renal disease progression after orthotopic liver transplantation**

\*Longenecker JC<sup>1</sup>, Estrella MM<sup>2</sup>, Sethi A<sup>2</sup>, Ugarte R<sup>3</sup>, Mohamed GA<sup>2</sup>

<sup>1</sup>Kuwait University, Faculty of Medicine, Dept. of Community Medicine, Kuwait; <sup>2</sup>Johns Hopkins University School of Medicine, Department of Medicine, Baltimore, MD; <sup>3</sup>University of Maryland Medical Center, Dept. of Medicine, Baltimore, MD.

#### **Introduction:**

Chronic kidney disease (CKD) is an important long-term complication in orthotopic liver transplantation (OLTx) patients. Few studies have assessed risk factors for CKD progression in post-Tx patients in the era of the Model for End-Stage Liver Disease (MELD).

#### **Methods:**

Using medical record and UNOS registry data from May 1995 to April 2009, this non-concurrent prospective cohort study followed 419 primary OLTx adults at a tertiary hospital for up to 2 years. Pre-Tx and 3-, 6-, 12-, and 24-month post-Tx glomerular filtration rates were estimated (eGFR, using the CKD-Epi formula), along with other baseline clinical parameters. The pre-MELD era was defined as time until February 2002. Statistical adjustment was made for age, gender, MELD Score, hepatorenal syndrome, and hepatic carcinoma, ( $\pm$ baseline eGFR).

#### **Results:**

The mean age was 51 years, 67% of the cohort was male, and 61% received OLTx in the pre-MELD era. The median pre-transplant and 12-month post-Tx eGFRs were 82 and 63 ml/min/1.73m<sup>2</sup>, respectively, representing a 20% decline in eGFR. After 24 months, the median eGFR was 59. Over 12 months, eGFR declined >33% in 31% of participants; and for those followed for 24 months, 42% declined >33%. Among those with pre-Tx eGFR  $\geq$ 90, 60-89, and 30-59 ml/min/1.73m<sup>2</sup>, 70%, 52%, and 9% declined to a lower eGFR category over 12 months, respectively. Decline in eGFR primarily occurred in the first three months post-Tx. Progression to a lower eGFR category was associated with age >55 years (adjusted odds ratio versus age <45, AOR=8.0 [3, 21] p<0.001), and marginally associated with hemodialysis in the post-Tx period (AOR=4.8 [0.8, 29] p=0.08), and diabetes (AOR=1.9 [0.9, 2.9] p=0.09). No association was present with gender, race, hepatorenal syndrome, hypertension, or hepatitis C virus.

#### **Conclusions:**

Renal function declined substantially after OLTx, and was associated with older age, post-Tx hemodialysis requirement, diabetes, pre-MELD era, and higher pre-Tx eGFR.

*Key Words: Renal disease progression; Liver transplantation; Kidney disease progression*

*Funding Agency: None*



**Medicine**

*Category: Clinical*

**79**

**Evaluation of growth in low-body-weight kidney transplant children:  
25-year experience.**

\*Mosaad AM, Hamdy AF, Hassan NM, Donia AF, Gheith O, Salem ME, El-Shahawy EM, Bakr MA,  
Ghoneim MA.  
Organ Transplant Centre

**Introduction:**

Identification of problems associated with kidney transplantation in low-body-weight children is an essential step toward improving graft function and patient survival as well as quality of life. We aimed to assess factors which were associated with growth retardation in renal transplant children.

**Methods:**

This study comprised 63 renal transplant children weighing 25 kg or less at time of transplantation. All children received a living donor renal allotransplant between December 1984 and March 2009. They were retrospectively evaluated regarding their survival, graft survival as well as physical growth.

**Results:**

Our patient and graft survival rates at 1, 5 and 10 years were 98.4%, 96.8% and 96.8%, and 94.9%, 82.6% and 58.4%, respectively. Significant risk factors for growth retardation post renal transplant were identified and included older age at time of transplant ( $p=0.019$ ), female sex ( $p=0.010$ ), retarded growth at time of transplant ( $p=0.011$ , by univariate analysis, and  $p=0.028$ , by multivariate analysis), incidence of chronic rejection ( $p=0.012$ ), higher steroid cumulative dose ( $p=0.013$ ) and graft dysfunction ( $p=0.009$ , by multivariate analysis).

**Conclusions:**

The final height of low-body-weight transplant children has remained suboptimal. Post-transplant growth retardation is multifactorial and its management should start before transplantation, with optimal care of growth in children with chronic kidney disease. Moreover, optimizations of post-transplant graft function with minimal steroid exposure especially with new immunosuppression medications.

*Key Words: Pediatric; Kidney transplant; Outcome*

*Funding Agency: None*



**Medicine**

*Category: Basic Sciences*

**80**

**Placental transport kinetics of deoxy glucose in vitro in toxemia model human placenta**

\*Nandakumaran M<sup>1</sup>, Al-Shammari M<sup>1</sup>, Al-Hijji J<sup>2</sup>, Susan G<sup>1</sup>, Al-Saleh E<sup>1</sup>

<sup>1</sup>Obstetrics & Gynecology Department, Faculty of Medicine, University of Kuwait; <sup>2</sup>Obstetrics & Gynecology Department, Adan Hospital, Kuwait

**Introduction:**

Previous reports from our laboratory had shown that maternal-fetal transport kinetics of model nutrients and reference markers were altered in toxemic pregnancies. This study was meant to explore whether transport kinetics of a non-metabolisable glucose analogue, deoxy-glucose were altered in toxemia model placental states.

**Methods:**

Human placenta from control pregnancies were collected post-partum. 14-C labelled Deoxy glucose (specific activity: 9.25 MBq/mmol, Amersham, UK) along with tritiated water (specific activity 185 MBq/mmol, Amersham, UK) as reference marker were then injected as a single bolus (100ul) into the maternal arterial circulation of perfused placental lobules & perfusate samples collected from maternal and fetal circulations over a period of 5 minutes. After a control perfusion phase, toxemia like situation was induced by artificial reduction of maternal perfusate flow by 50% of control flow rate & perfusion protocol performed as before. National Culture and Tissue Collection medium, diluted with Earle's buffered salt solution was used as perfusate. Concentration of labelled substances in perfusate samples in control & toxemia model perfusion phases was assessed by scintillation spectrometry (LKB Wallac Scintillation Spectrometer, Denmark). Transport kinetics of substances studied were computed using standard parameters.

**Results:**

Transport rates of deoxy glucose & tritiated water in 8 perfusions differed significantly (Student's t-test;  $p < 0.05$ ) for all fractions studied in control & study perfusion phases. Transport Fraction index of deoxy glucose averaged 36.2% in control perfusions ( $n=8$ ) & 22.90% in toxemia model perfusions ( $n=8$ ) respectively. Absorption rate: elimination rate indices of deoxy glucose differed significantly between control & study groups (Student's t-test;  $p < 0.05$ ).

**Conclusions:**

Our studies show altered transport behaviour & kinetics of deoxy glucose in toxemia model perfusions

*Key Words: Toxemia Model; Deoxy Glucose*

*Funding Agency: Kuwait University Grant M0026*



**Medicine**

Category: *Clinical*

**81**

**Back to basics: Ankle reflex in the evaluation of peripheral neuropathy in type 2 diabetes mellitus**

\*Shehab DK<sup>1</sup>, Al-Jarallah KF<sup>1</sup>, Abraham M<sup>1</sup>, Mojiminiyi OA<sup>2</sup>, Al-Mohamedy H<sup>3</sup>, Abdella NA<sup>1</sup>

<sup>1</sup>Departments of Medicine; <sup>2</sup>Pathology, Faculty of Medicine, Kuwait University; <sup>3</sup> Department of Medicine, Mubarak Al-Kabeer Hospital, Kuwait.

**Introduction:**

Ankle reflex is a simple screening tool frequently used in the detection of peripheral neuropathy.

Aim: The purpose of this study is to assess the performance characteristics of ankle reflex in detecting diabetic peripheral neuropathy (DPN) by evaluating the sensitivity, specificity and the predictive ability of the ankle reflex, a component of Neuropathy Disability Score (NDS) with reference to Nerve Conduction Studies (NCS).

**Methods:**

151 patients with type 2 diabetes were assessed (47 males, 104 females). Grading of neuropathy was done using Neuropathy Symptom Score (NSS), NDS and NCS. Patients were divided into two groups, those with abnormal NCS (Group 1) and those with normal NCS (Group 2). Demographic characteristics, biochemistry, NSS and NDS were assessed between the two groups. Taking NCS as the gold standard, sensitivity, specificity and predictive ability of the ankle reflex were calculated and compared with other tests included in NDS, namely vibration sense, superficial pain and temperature sensation.

**Results:**

There were 59 (39.1%) patients in Group 1 and 92 (60.9%) in Group 2. NSS and NDS demonstrated strong positive association with NCS. Taking NCS as the gold standard, ankle reflex yielded the highest sensitivity and specificity (91.5% and 67.4% respectively), closely followed by that of vibration sense.

**Conclusions:**

Ankle reflex is a powerful screening tool with high sensitivity and negative predictive value, but a combination of ankle reflex and vibration sense has superior sensitivity and specificity compared to either of them done alone for detection of DPN in clinical settings.

*Key Words: Diabetic peripheral neuropathy; Ankle reflex & Sensitivity; Specificity; Nerve Conduction Studies*

*Funding Agency: None*

**Medicine***Category: Clinical*

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***H. pylori* genotypes and their association with severity of gastric mucosal inflammation and interleukin-8 induction**\*Siddique I<sup>1,2</sup>, Memon A<sup>3</sup>, Al-Qabandi A<sup>4</sup>, Al-Azmi W<sup>1,2</sup>, Al-Ali J<sup>1,5</sup>, Mustafa AS<sup>6</sup>, Junaid TA<sup>4</sup>

<sup>1</sup>Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait; <sup>2</sup>Thunayan Al-Ghanim Gastroenterology Center, Al-Amiri Hospital, Kuwait; <sup>3</sup>Division of Primary Care and Public Health, Brighton and Sussex Medical School, Brighton, United Kingdom; <sup>4</sup>Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait; <sup>5</sup>Mubarak Al-Kabeer Hospital, Kuwait; <sup>6</sup>Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

The virulence of *H. pylori* (HP) is determined by its genotype and ability to induce interleukin-8 (IL-8). The aim of this study was to determine the association between the *cagA*, *vacAs1* and *vacAs2* genotypes of HP, severity of gastritis and peptic ulcer disease (PUD) and correlate these with IL-8 level in gastric mucosa.

**Methods:**

Gastric biopsies obtained in patients presenting for endoscopy were examined. The severity of chronic gastritis was documented using the updated Sydney system. HP *vacA* or *cagA* genotypes were determined by PCR. The IL-8 levels were measured by ELIZA in the gastric mucosal biopsy.

**Results:**

99 (mean age 38.4±12.9; 72 males) patients were found to have HP *vacA* or *cagA* genotypes, of whom 52 (52.5%) were positive for *cagA*, 44 (44.4%) for *vacAs1* and 39 (39.4%) for *vacAs2*. 70 (70.7%) patients had PUD on endoscopy. The severity of inflammation in gastric mucosa was increased with *vacAs1* ( $p<0.05$ ) and decreased with *vacAs2* ( $p<0.05$ ), while *cagA* had no association. The degree of neutrophil activity in the gastric biopsies was not associated with either *cagA* or *vacAs1*, and decreased with *vacAs2* ( $p<0.05$ ). The presence of PUD was increased in patients with *cagA* ( $p<0.005$ ) and *vacAs1* ( $p<0.05$ ), and decreased in those with *vacAs2* ( $p<0.05$ ). The level of IL-8 was increased with *vacAs1* ( $p<0.05$ ) and lower with *vacAs2* had a lower level of IL-8 ( $p<0.05$ ). Higher levels of IL-8 were also found in patients with a more severe chronic inflammation ( $p<0.05$ ), neutrophil activity ( $p<0.05$ ) and those with PUD ( $p<0.05$ ).

**Conclusions:**

Presence of *vacAs1* genotype of *H. pylori* is associated with more severe chronic inflammation and higher levels on IL-8 induction in the gastric mucosa, as well as higher frequency of PUD. Patients with *vacAs2* have less severe gastritis, lower levels of IL-8 and is associated with lower rates of PUD. The presence of *cagA* genotype is not associated with the severity of gastritis or IL-8 induction in the gastric mucosa.

*Key Words: Helicobacter pylori; Gastritis; Interleukin-8 (IL-8)*

*Funding Agency: None*



**Medicine**

*Category: Clinical*

**83**

**Crohn's disease in an Arab population: Epidemiology and clinical course**

\*Siddique I<sup>1,2</sup>, Al-Ali J<sup>1,3</sup>, Al-Azmi W<sup>1,2</sup>, Al-Fadli A<sup>3</sup>, Memon A<sup>4</sup>

<sup>1</sup>Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait; <sup>2</sup>Thunayan Al-Ghanim Gastroenterology Center, Al-Amiri Hospital, Kuwait; <sup>3</sup>Mubarak Al-Kabeer Hospital, Kuwait; <sup>4</sup>Division of Primary Care and Public Health, Brighton and Sussex Medical School, Brighton, United Kingdom

**Introduction:**

There has been an increase in the incidence of Crohn's disease among Arabs in recent years. We conducted this study to determine the clinical epidemiology of CD in Kuwait.

**Methods:**

Sociodemographic and clinical information was collected for a continuous series of 206 Arab patients with CD, and age at diagnosis, location and behavior of disease was determined according to the Montreal classification.

**Results:**

Among the 206 patients, 100 (48.5%) were males and 106 (51.5%) females. The mean age at diagnosis ( $\pm$  SD) was  $21.9 \pm 10$  years. Family history of CD was reported by 39 (18.9%) patients. The disease was limited to the ileum in 115 (55.8%) patients, whereas in 28 (13.6%) it involved the colon and in 63 (30.6%) it involved both the ileum and colon. The behavior of the disease was non-stricturing, non-penetrating in 146 (70.9%) patients, whereas 49 (23.8%) had stricturing and 11 (5.3%) penetrating disease, respectively. Perianal disease was present in 41 (19.9%) patients. In the multivariate analysis, the use of biologic therapy and duration of the disease for  $\geq 6$  years were significantly associated with the presence of perianal disease; and the need for surgery was significantly associated with stricturing and penetrating disease behavior.

**Conclusions:**

Crohn's Disease among Arabs is equally common in males and females, presents at a relatively younger age, and in about half of the patients limited to the small bowel. These features may indicate an underlying genetic predisposition for the disease in this population, which need further investigation.

*Key Words: Crohn's disease; Inflammatory bowel disease; Arab*

*Funding Agency: None*



***Microbiology, Virology and Immunology***

*Category: Graduate PhD (Basic Science)*

**84**

**Detection of bacterial endotoxin in drinking tap and bottled water in Kuwait**

Abdulraheem A, Mustafa S, \*Al-Saffar N, Shahjahan M  
Public Authority for Applied Education and Training (PAAET), Kuwait

**Introduction:**

This study was carried out to measure and compare the concentration of bacterial endotoxin in a variety of samples from drinking tap and bottled water available in Kuwait by using the Limulus Amoebocyte lysate test.

**Methods:**

A total of 29 samples were tested. Samples were collected from a variety of locations throughout the six governorates of Kuwait and 23 brands of local and imported bottled water samples were collected from the local market. The concentration of bacterial endotoxin was measured by using the standard Limulus Amoebocyte lysate test, gel clot method. Differences between mean values were tested for significance using Students t-test. The difference was assumed to be significant when  $p < 0.05$

**Results:**

This study showed that measured endotoxin concentrations in tap drinking water varied from 2.4 to 33.8 EU/ml with the average endotoxin concentration of 14.2 EU/ml. While the results of endotoxin concentrations in the bottled water were  $< 0.03$  to 20.1 EU/ml with an average of 1.96 EU/ml. The average concentration of endotoxin in bottled water is 13.5 % of the average concentration of endotoxin in tap drinking water.

**Conclusions:**

This experimental investigation has proved that drinking bottled water has less endotoxin as compared to tap water in Kuwait. It is also demonstrated that the endotoxin concentration did not exceed the acceptable level in drinking tap water.

*Key Words: Endotoxin; Tap water; Bottled water*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

Category: Basic Sciences

85

**Development of a simple PCR-RFLP-based method for rapid detection of flucytosine-resistant clinical *Candida dubliniensis* isolates**

\*Ahmad S, Joseph L, Theyyathel A

Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

*Candida dubliniensis* is an emerging pathogen that shares many phenotypic features with *Candida albicans* but exhibits reduced susceptibility to azoles and frequent resistance to 5-flucytosine (5-FC). 5-FC-resistant *C. dubliniensis* strains contain S29L mutation, while 5-FC-susceptible isolates contain wild-type codon 29 in cytosine deaminase (CdFCA1). The aim of this study was to develop a simple, PCR-RFLP-based method for rapid detection of S29L mutation in CdFCA1 gene.

**Methods:**

Clinical *C. dubliniensis* isolates (n=72) identified by Vitek2 yeast identification system and direct DNA sequencing of internally transcribed spacer (ITS) region of rDNA and reference strain CD36 were used. Susceptibility to 5-FC was determined by Etest. The CdFCA1 gene codon 29 region was amplified by PCR and the amplicons were digested with Dpn II to yield RFLP patterns specific for isolates containing wild-type or mutant codon 29 of CdFCA1 or sequenced to confirm the results of RFLP.

**Results:**

PCR amplification with FCA1F and FCA1R primers yielded an amplicon of 340 bp from all *C. dubliniensis* strains, as expected. Restriction digestion of amplicons from 5-FC-susceptible *C. dubliniensis* strains (n=47) with Dpn II yielded three (176 bp, 119 bp and 45 bp) DNA fragments, which is characteristic of isolates containing wild-type (TCA, Serine) at CdFCA1 codon 29. On the contrary, restriction digestion of PCR amplicons from 5-FC-resistant *C. dubliniensis* strains (n=25) with Dpn II yielded only two (295 bp and 45 bp) DNA fragments, which is characteristic of isolates containing TTA (Leucine) at CdFCA1 codon 29 (S29L mutation). The results were confirmed by DNA sequencing of PCR amplified DNA fragments.

**Conclusions:**

A simple, PCR-RFLP-based method has been successfully developed to facilitate detection of S29L mutation in CdFCA1 gene that confers resistance to 5-FC in *C. dubliniensis* strains. The assay will help in early recognition of 5-FC-resistant *C. dubliniensis* strains.

*Key Words: Candida dubliniensis; 5-Flucytosine resistance; PCR-RFLP*

*Funding Agency: Supported by KURA grant MI 01/08.*



**Microbiology, Virology and Immunology**

Category: Basic Sciences

86

**Immunisation with cholera toxin (CT) affords protection against *Campylobacter jejuni* infection in an adult mouse colonisation model**

\*Albert MJ, Islam A, Haridas S, Mustafa AS

Department of Microbiology, Kuwait University, Faculty of Medicine

**Introduction:**

We demonstrated that the major outer membrane protein (MOMP) of *Campylobacter jejuni*, a major cause of diarrhoea, cross-reacts with antibody to CT. We addressed the question of whether immunisation with CT would protect against *C. jejuni* infection in an adult mouse colonization model. If protection can be shown by immunisation with CT, the possibility of controlling *C. jejuni* diarrhoea with the licensed oral cholera vaccine (which contains CT-B subunit) exists.

**Methods:**

A group of 9 adult BALB/c mice were immunised with four oral doses of CT (10mcrg, 15mcrg, 15mcrg and 15mcrg) given a week apart. Control mice received phosphate buffered saline (PBS). A week after the last dose, serum and faeces were collected for antibody estimation and groups of mice were separately challenged orally with three different serotypes of *C. jejuni* (strain 48 [serotype 19], strain 75 [serotype 3], strain 111 [serotype 1, 44]). Faecal shedding of the challenge organism was studied every day for nine days. Antibodies to CT and Sarkosyl-purified MOMP of all three *C. jejuni* serotypes were studied in sera and faecal extracts of the mice by ELISA or immunoblot.

**Results:**

CT induced a robust antibody response against itself in serum (mean IgG end point titre of  $22756 \pm 5644$  in test mice versus titre of  $<200$  in control mice,  $n=9$ ) and faeces ( $>2$ -fold increase in IgA antibody/total IgA in test mice in comparison with control mice,  $n=9$ ), but a weak antibody response against MOMP from the strain 111 (mean OD at lambda 405 of  $0.58 \pm 0.15$  in test mice versus  $0.33 \pm 0.08$  in control mice in serum and  $<2$ -fold increase in IgA antibody/total IgA in comparison control mice,  $n=9$ ). Post-immune sera and faeces reacted with MOMP from all three serotypes in immunoblot. Vaccination with CT reduced faecal load and colonisation with all three serotypes. The protective efficacies varied between 34-49% ( $P<0.001$ ).

**Conclusions:**

The CT vaccine provided significant protection against *C. jejuni* infection justifying further studies.

*Key Words: Cholera toxin; Vaccination*

*Funding Agency: Kuwait University Grant No. MI04/10*



**Microbiology, Virology and Immunology**

Category: Clinical

87

**Evaluating the performance of GeneXpert in screening pregnant women for *Streptococcus agalactiae***

\*Alfouzan W, Dhar R

Microbiology Unit, Department of Laboratories, Farwaniya Hospital, Kuwait

**Introduction:**

*Streptococcus agalactiae* or group B streptococcus (GBS) is a common flora of the gastrointestinal and female the genitourinary tract. Babies born to mothers colonized with the organism are at risk of developing invasive infection. We aim to assess the diagnostic accuracy of GeneXpert GBS (Xpert® GBS, Cepheid, Sunnyvale, CA, USA) in detecting GBS as compared to culture method.

**Methods:**

High vaginal swabs (HVS) collected from women attending obstetrics and gynecology out-patient clinics, in-patients using transport swab (Copan, Italy). For patients in the labour wards swabs (Venturi Transystem transport swab, Copan, Italy), which came in duplicate form were used for GeneXpert and the other for culture on 5% sheep blood agar (BA). The BA plates were incubated at 37°C for 24 hour and examined for growth of GBS which were identified by gram stained smear, catalase and grouping (Streptococcal grouping kit, Oxoid Ltd., United Kingdom).

**Results:**

During the period of 3 months, a total of 485 HVS were processed in our laboratory. Of these 87 were found to be positive for GBS by culture giving the prevalence rate was 17.9% in the female genital tract. Of 84 HVS received from labour ward 23 (27%) tested positive by culture as well as GeneXpert and 56 were found to be negative by both methods. The sensitivity, specificity, positive and negative predictive values for GeneXpert were 95.8%, 98.2%, 95.8% and 98.2%, respectively.

**Conclusions:**

GeneXpert is considered a highly accurate point of care test to identify intrapartum GBS carriers. Not only does it helps to identify candidates who require intrapartum antibiotic prophylaxis, but also excludes the non-carriers. Its role in decreasing unnecessary antibiotic consumption in pregnant women is valuable.

*Key Words: Group B streptococcus; S.agalactia; GeneXpert*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

Category: Graduate MSc (Basic Science)

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**Correlation of cytokine responses with pathological ocular changes in murine *Toxoplasma* infection.**

\*Al-Awadhi M<sup>1</sup>, Iqbal J<sup>2</sup>, Raghupathy R<sup>3</sup>

Department of Microbiology, Kuwait University Faculty of Medicine

**Introduction:**

*Toxoplasma gondii* causes significant ocular damage and mortality mainly in fetuses during pregnancy and in immunocompromised individuals. The main objective of this study was to determine dynamics of cytokines in blood and tissue (ocular and spleen) during infection and correlate it with the pathological changes seen in the tissues.

**Methods:**

BALB/c and MF1 mice were infected with virulent *T. gondii* Rh strain by 1) direct intraocular injection and 2) by oral gavage followed 4 days later by the ocular route. A total of 400 mice were injected with the parasite. Sequential analysis of blood and aqueous humor (eye) was done for cytokine IL-17, IFN- $\gamma$ , TNF- $\alpha$ , Fas-L, TGF- $\beta$  1, IL-10, and MIP-1 $\alpha$  and for serum anti-toxoplasma antibodies using ELISA kits. Eyes were enucleated, sectioned, stained and examined for pathological changes.

**Results:**

Ratios of pro-inflammatory to anti-inflammatory cytokines show that ocularly inoculated BALB/c mice produced a stronger pro-inflammatory response compared to oral plus ocularly inoculated mice. On the other hand, oral plus ocularly inoculated MF1 mice showed a stronger pro-inflammatory response as compared to ocularly inoculated MF1 mice. The antibody levels peaked much earlier in MF1 than in BALB/c mice. Histopathological examination of retinal layers of BALB/c mice showed dilated blood vessels within the ganglion cell layer and the characteristic formation of lacunae in the inner nuclear layer by day 8, and by day 26 and 35, alterations in the outer nuclear layer were clearly visible as protruding humps, disrupting the rods and cones layer. Retinal tissue damage in MF1 was observed on day 8 and 11 including the parasites.

**Conclusions:**

Our results show that the genetic background of the host and related immunity may play a key role in determining the tissue damage in *T. gondii* infection.

*Key Words: Cytokines; Ocular pathology*

*Funding Agency: Kuwait University Research Grant No. YM 02/10*



**Microbiology, Virology and Immunology**

Category: Clinical

89

**Evaluation of the Speed-oligo Mycobacteria assay for rapid differentiation of *Mycobacterium tuberculosis* from non-tuberculous mycobacteria in fresh liquid cultures from human clinical samples**

\*Al-Mutairi NM, Ahmad S, Mokaddas E

Department Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

Species-specific identification is of clinical relevance since treatment varies according to the Mycobacterium species causing infection. This study evaluated the ability of a novel DNA strip assay (Speed-oligo Mycobacteria, SpO-M), based on multiplex PCR and double-reverse hybridization on a dipstick using probes bound to colloidal gold and to the membrane, to correctly identify most frequently isolated Mycobacterium spp. From clinical samples.

**Methods:**

Fresh liquid cultures of mycobacterial isolates (n=81) grown with MGIT 960 system from human clinical samples and reference strains of Mycobacterium spp. were tested. The DNA from liquid cultures was extracted and was amplified by multiplex PCR using PCR mix supplied with the SpO-M kit. Following amplification, PCR products were detected by using the dipstick according to kit instructions and results were interpreted by identification of 7 specific bands. A multiplex PCR able to differentiate NTM from MTC members was also used. PCR-sequencing of 16S-23S rRNA region was used as gold standard to confirm the results of SpO-M.

**Results:**

The SpO-M correctly identified 34 of 34 isolates as *M. tuberculosis*, 15 of 16 isolates as *M. avium-intracellulare-scrofulaceum* complex, 11 of 11 as *M. fortuitum* complex, 10 of 10 as *M. chelonae/M. abscessus* complex (including 1 *M. immunogenum* isolate), 8 of 9 as *M. kansasii*, 1 of 1 as *M. goodii* and 1 isolate as Mycobacterium species (identified as *M. lentiflavum* by sequencing). One *M. kansasii* isolate yielded inconclusive results since probe 4 also reacted weakly in addition to probe 3. There was only 1 major discrepancy, misidentification of *M. parascrofulaceum* as *M. tuberculosis*, verified by sequencing.

**Conclusions:**

The SpO-M is a reliable oligochromatographic test for rapid detection and identification of most frequently isolated human mycobacteria in primary liquid cultures and is suitable for clinical microbiology laboratories equipped with basic PCR technology

*Key Words: Speed-oligo Mycobacteria; Mycobacterial identification; 16S-23S rRNA sequencing*

*Funding Agency: Supported in part by KURA grant M102/04*



**Microbiology, Virology and Immunology**

Category: Graduate MSc (Basic Science)

90

**The prevalence of norovirus infection among patients with gastroenteritis in Kuwait**

\*Al Rashidi A, Albert MJ, Chehadeh W, Szucs G

Department of Microbiology, Kuwait University, Faculty of Medicine

**Introduction:**

Norovirus is considered to be the second most common cause of acute gastroenteritis worldwide. The impact of this virus infection is not fully known in Kuwait. Our study aimed to identify the etiology of norovirus gastroenteritis in Kuwait and to identify the circulating genotypes.

**Methods:**

A total of 171 stool samples were collected from patients with gastroenteritis of different age groups (from 1M to 60Y), at 3 hospitals in Kuwait: Al-Adan, Al-Farwaniya, Mubarak Al-Kabir hospitals, during 2005-2011. These samples were negative for bacterial pathogens. The stool samples were screened for norovirus using ELISA and reverse transcriptase polymerase chain reaction (RT-PCR). Direct sequencing and phylogenetic analysis were performed on the RNA-dependent RNA polymerase.

**Results:**

Norovirus was found to be the cause of 8.18% of non-bacterial gastroenteritis. Norovirus infection was mostly (85.7%) detected in children under 5 years of age. Phylogenetic tree analysis has shown that 50% of the norovirus strains belonged to the genotype GII.4, and the prevalent strain was GII.4 2006b. Other genotypes detected were GII.12, GII.b, GII.3, GII.8, GII.7, GII.4-2004, and GII.4-2006a.

**Conclusions:**

This study highlighted the importance of screening for norovirus infection in acute gastroenteritis, and the importance of having a reporting system to identify sources of infection and to better understand the epidemiology of norovirus infection in Kuwait.

*Key Words: Norovirus; Gastroenteritis; Kuwait*

*Funding Agency: Collage of Graduate Studies*



**Microbiology, Virology and Immunology**

Category: Graduate MSc (Basic Science)

91

**Molecular genetic characterization and antifungal susceptibility profile of clinical *Aspergillus flavus* section flavi isolates in Kuwait**

\*Al-Wathiqi FA, Ahmad S, Khan ZU

Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

Phenotypically similar *Aspergillus flavus* section flavi isolates, second most important agents of invasive aspergillosis (IA) in humans, have recently been placed into several closely related species which differ in their virulence and susceptibility to antifungal drugs. This study determined species spectrum and antifungal drug susceptibility (ADS) of *A. flavus* section flavi isolates recovered from clinical specimens from patients in Kuwait.

**Methods:**

Clinical isolates (n=93) phenotypically identified as *A. flavus* during 1995-2011 were studied and their identity was confirmed by *A. flavus* section Flavi-specific PCR. PCR sequencing of ITS and/or D1/D2 regions of rDNA, beta-tubulin and calmodulin phylogenetic markers was done for species delineation. Phylogenetic relationships were deduced by neighbor-joining tree with bootstrap analysis (1000 replicates) using MEGA4. Etest was used for ADS for amphotericin B (AmB), voriconazole, posaconazole, anidulafungin, micafungin and casofungin and disk (1 µg and 100 µg) diffusion test (DDT) was used for amphotericin B and voriconazole.

**Results:**

Sequencing studies identified 92 isolates as *A. flavus* and 1 as *A. tamari*. Other pathogenic species of *A. flavus* section flavi were not detected. Only beta-tubulin and calmodulin gene sequences showed slight variations. Phylogenetic trees showed close evolutionary relationships among isolates. MIC<sub>90</sub>/mean MIC values for all drugs except AmB were within susceptible range. Posaconazole showed higher activity than voriconazole (p <0.001). Micafungin and anidulafungin were more potent than casofungin (p <0.001).

**Conclusions:**

A molecular approach based on multiple gene loci accurately identified clinical isolates belonging to *A. flavus* section Flavi in Kuwait. Variations in ADS patterns showed voriconazole as the best antifungal agent for treatment and management of cases of IA by *A. flavus*. Micafungin alone or in combination with voriconazole may also be beneficial in some patients.

*Key Words: Aspergillus flavus section flavi; Species-specific identification; Antifungal drug susceptibility*

*Funding Agency: College of Graduate Studies and KURA grant YM03/09*



**Microbiology, Virology and Immunology**

Category: Graduate PhD (Basic Science)

92

**INFINITI RVP-Plus microarray assay for simultaneous detection and genotyping of a panel of respiratory viruses in patients with respiratory tract infections in Kuwait**

\*Al-Turab M<sup>1</sup>, Chehadeh W<sup>1</sup>, Al-Mulla F<sup>2</sup>, Al-Nakib W<sup>1</sup>

<sup>1</sup>Departments of Microbiology; <sup>2</sup> Pathology, Faculty of Medicine, Kuwait University, Kuwait

**Introduction:**

Respiratory infections are considered as a major cause of morbidity and mortality especially in infants, children, and the elderly. A sensitive, fast and high throughput diagnostic test is needed for the detection of respiratory viruses that may assist in the clinical management as well as in the reduction of inappropriate therapy. This study aimed to detect and genotype a panel of respiratory viruses in patients with respiratory tract infections by the use of a commercial multiplex PCR assay based on microarray technology the INFINITI Respiratory Viral Panel Plus Assay (RVP-Plus).

**Methods:**

A total of 200 respiratory samples were collected from 185 hospitalized patients with either upper or lower respiratory tract infections, from December 2010 to February 2011. They were tested by the INFINITI RVP-Plus assay for the detection of 25 common respiratory viruses including subtypes (influenza A, Swine H1N1 and B, human parainfluenza virus (HPIV) 1, 2, 3 and 4, rhinovirus A and B, enterovirus A, B, C and D, coronavirus (HKU1, OC43, NL63, 229E), human metapneumovirus (hMPV) A and B, human respiratory syncytial virus (HRSV) A and B, and adenovirus A, B, C and E.

**Results:**

Out of 185 patients, 31 (17%) were positive for viral respiratory tract infections; 11 (35%) of them were positive for HRSV (9 HRSV-A, 2 HRSV-B), 9 (29%) were positive for hMPV (8 hMPV-A, 1 hMPV-B), 6 (19%) were positive for adenoviruses (5 ADV-B, 1 ADV-C), 5 (16%) were positive for influenza viruses (2 Flu-A, 1 H1N1, 2 Flu-B), 3 (10%) were positive for rhinovirus-A, and 1 (3%) was positive for coronavirus-OC43. Most of positive patients had lower respiratory tract infection (71%), and 48% were infants less than 2 years, and 53% of these infants presented with pneumonia.

**Conclusions:**

The INFINITI RVP-Plus assay is a sensitive, rapid, automated and high throughput diagnostic test for simultaneous detection and genotyping of common viral respiratory tract infections.

*Key Words: Respiratory viruses; Detection; Microarray*

*Funding Agency: Supported by College of Graduate Studies and Research Administration, Grant # YM 05/09, Kuwait University*

**Microbiology, Virology and Immunology***Category: Clinical***93****Antibiotic resistance and misuse: a survey of physicians' knowledge, perception and behavior in Kuwait**\*Aly NY<sup>1,3</sup>, Hassan SG<sup>2,4</sup>, Al-Mousa HH<sup>1</sup>

<sup>1</sup>Directorate of Infection control; <sup>2</sup>Department of Health promotion, Ministry of Health, Kuwait; Departments of <sup>3</sup>Tropical Medicine and Hygiene, Faculty of Medicine; <sup>4</sup>Health Education and Behavioral Sciences, High Institute of Public Health, University of Alexandria, Egypt

**Introduction:**

Improper use of antibiotics (Abs) has been linked to the emergence and spread of resistant organisms. In this study, we aimed to evaluate the physicians' knowledge, perception and behavior towards antibiotic resistance (ABR) and use.

**Methods:**

A cross-sectional survey was conducted on 1242 physicians in public hospitals and primary healthcare centers (PHC) between March and June 2011. On a questionnaire format, data were collected regarding physicians' knowledge and perception about ABR and their prescribing behavior. The knowledge and behavior were scored as total mean percent of correct choices to the queries presented in the questionnaire. Perception was assessed as percentage of agree responses to evaluating statements on a 3 point Likert scale: "agree", "not sure" and "disagree".

**Results:**

The knowledge score was 79.5% ±18.7 and behavior 51.4% ±23.8. Of all physicians, 79.1% perceived ABR as a national problem, and 55.1% considered it a problem in their daily practice. Despite 87% believe that misuse of Abs by the public is a cause of ABR, 81% agree that the physicians themselves prescribe Abs more than necessary. Overprescribing was primarily due to deficient understanding regarding proper AB use (77.1%) and seeking patient satisfaction or meeting his expectation (61%). Patient satisfaction concern was more perceptible among PHC physicians than hospital physicians (75.5% vs. 52.9%, P<0.001). The most significant drive for AB prescribing was the lack of time to perform a required investigation (70.3%), and fear of complications (69%). In logistic regression, age below 40 years (p = 0.004), suboptimal knowledge (p = 0.002) and being a registrar (p = 0.024) were predictors of poor antibiotic prescribing behavior among hospital physicians.

**Conclusions:**

There was a wide gap between physicians' knowledge on ABR and their perception and behavior related to antibiotic use. Prompt interventions to optimize antibiotic prescribing are recommended.

*Key Words: Antibiotics; Physicians; Behavior*

*Funding Agency: None*



*Microbiology, Virology and Immunology*

Category: *Clinical*

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**Parasitological diagnosis of lymphatic filariasis by detecting Og4C3 antigen by Immunochromatographic Technique (ICT): Comparison with wet-mount and thick blood film methods**

\*Ali Sher<sup>1</sup>, Latif SA<sup>2</sup>, Al-Mufti S<sup>3</sup>, Mandkar Y<sup>4</sup>

<sup>1</sup>Malaria Laboratory, Ports & Borders Health Division; <sup>2</sup>40 - 1591 South Parade Court, Mississauga, Ontario, Canada, <sup>3</sup>Virology Laboratory; <sup>4</sup>Department of Public Health, Ministry of Health, Kuwait;

**Introduction:**

Parasitological diagnosis of lymphatic filariasis is performed by using wet-mount, Giemsa stained thick blood film, Knott's concentration, membrane filtration and counting chamber methods. All the tests require night blood samples to detect the nocturnally periodic *Wuchereria bancrofti* microfilaria. This study was done to evaluate the performance of immunochromatographic test (ICT) that detects circulating filarial antigen Og4C3 and compare with wet-mount and thick blood film methods among immigrants.

**Methods:**

Over a period of two years, January 2010 to December 2011, a total of 502, 578 immigrants were screened and 148 were found positive for microfilaria of *W. bancrofti* in Giemsa stained thick blood film. Out of 148 infected individuals only 133 individuals were available for further studies in wet-mount, thick blood film and ICT filariasis tests.

**Results:**

A total of 502, 578 immigrants were screened and 148 (0.03%) were found positive for microfilaria of *W. bancrofti*. Most of these infected individuals were from India (78%) and Nepal (20%) and in the age group of 25 – 35 years. Out of 148 positive cases only 133 cases were available for further studies. All 133 (100% sensitivity) patients were positive in ICT-filariasis test, 106/133 ( 80.0%) were positive in thick blood film and 90/133 (68.0%) were positive in wet-mount. Thirty individuals were used as controls from endemic and non-endemic countries. ICT-filariasis test detected Og4C3 antigen in 5/30 (17.0%) individuals used as endemic controls (belongs to filaria endemic countries) whereas all the individuals from non-filaria endemic countries were negative for Og4C3 antigen.

**Conclusions:**

ICT-filariasis test is very sensitive and specific, very simple and does not require a well developed laboratory for the diagnosis of filaria. The biggest advantage is that the blood sample may be taken at any time of the day. The test may be used in epidemiological surveys and also for monitoring filariasis control programme.

Key Words: Filaria; Immunochromatographic test; Antigen

Funding Agency: Ministry of Health, Kuwait



**Microbiology, Virology and Immunology**

Category: *Basic Sciences*

95

**Reassessment of susceptibility profile of *Candida* bloodstream isolates for fluconazole using harmonized CLSI-EUCAST clinical breakpoints**

\*Chandy R, Vayalil S, Al-Musallam O

Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

The minimum inhibitory concentration clinical breakpoints (CBPs) for *Candida* spp. have recently been revised and harmonized by Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) to achieve improved detection of fluconazole resistance. The aim of this study was to determine if there is any evidence of emergence of resistance to fluconazole among bloodstream *Candida* spp. isolates in Kuwait using these revised CBPs.

**Methods:**

A total of 1,263 bloodstream isolates recovered over a 12-year (2000-2011) period and representing *Candida albicans* (n=552), *Candida parapsilosis* (n=492) and *Candida tropicalis* (n=219) were included in the study. Antifungal susceptibility to fluconazole was determined by Etest. The susceptibility data were analyzed using newly agreed CBPs breakpoints for fluconazole, which are defined as follows: susceptible, <2 mcg/ml; susceptible dose-dependent (S-DD), 4 mcg/ml; and resistant >8 mcg/ml.

**Results:**

Employing these newly agreed harmonized CLSI-EUCAST clinical breakpoints, resistance to fluconazole was detected in 8 (1.4%) of 552 isolates of *C. albicans*, 2 (0.40%) of 492 isolates of *C. parapsilosis*, and 2 (0.91%) of 219 isolates of *C. tropicalis*. Likewise, the distribution of S-DD isolates was 6 (1.1%), 15 (3.0%), and 3 (1.4%) in *C. albicans*, *C. parapsilosis* and *C. tropicalis* isolates, respectively. A comparison of geometric mean of MICs revealed that there is no significant increase in MIC levels to fluconazole during the 12-year study period.

**Conclusions:**

Antifungal susceptibility testing of fluconazole against *Candida* spp. Is a useful adjunct for optimizing treatment of candidiasis. Employing these newly agreed CBPs, our data show that there is no evidence of development of acquired resistance among bloodstream isolates of *C. albicans*, *C. parapsilosis*, and *C. tropicalis* in Kuwait.

Key Words: *Candida* species; Fluconazole resistance; New clinical breakpoints

Funding Agency: None



**Microbiology, Virology and Immunology**

Category: Clinical

96

**First molecular characterization of human BK and JC polyomaviruses circulating in Kuwait among potential kidney donors and post-transplant kidney recipients**

\*Chehadeh W<sup>1</sup>, Kurien SS<sup>1</sup>, Szucs G<sup>1</sup>, Al-Qaseer M<sup>1</sup>, Nampoory MRN<sup>2</sup>, Said T<sup>2</sup>, Al-Otaibi T<sup>2</sup>, Al-Nakib W<sup>1</sup>

<sup>1</sup>Department of Microbiology, Kuwait University, Faculty of Medicine; <sup>2</sup>Division of Nephrology, Hamed Al-Essa Organ Transplantation Centre, Ibn Sina Hospital

**Introduction:**

BK and JC viruses are human polyomaviruses that cause asymptomatic latent infections. However, virus reactivation may be brought about by immunosuppression or other factors. Such reactivation accompanying kidney transplantation is a leading cause of nephropathy and allograft failure. Our aim was to identify the types and subtypes of polyomaviruses circulating in potential kidney donors and post-transplant kidney recipients.

**Methods:**

A total of 1410 serum and urine samples were collected from potential healthy kidney donors and from kidney recipients. The detection of polyomavirus infection was carried out using semi-nested PCR and real-time PCR. The identification of polyomavirus types and subtypes was determined by direct sequencing of the major capsid protein VP1, followed by phylogenetic analysis.

**Results:**

Two (1.3%) samples from pre-transplant patients, 98 (9.9%) samples from post-transplant recipients, and 38 (14.3%) samples from potential kidney donors, were tested positive for polyomavirus DNA. Viremia was higher in post-transplant recipients than in potential kidney donors. BK virus was more detected in post-transplant recipients (75.8%) than in potential kidney donors (34.3%). On the contrary, JC virus was more detected in potential kidney donors (65.7%) than in post-transplant recipients (24.2%). Phylogenetic analysis of polyomavirus VP1 sequences indicated that the majority of detected BK sequences were belonging to subtypes I and IV, whereas 52% of JC sequences were belonging to the subtypes 1 and 3.

**Conclusions:**

This study mainly offers a glimpse of the different polyomavirus subtypes which may be present in Kuwait. It is likely that additional subtypes other than classical subtypes of polyomaviruses may be present because of the highly mixed ethnicity and mixed-race marriages.

*Key Words: Polyomavirus; Transplantation; Subtypes*

*Funding Agency: Research Administration Grant No MI05/08*



**Microbiology, Virology and Immunology**

Category: *Clinical*

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**Evaluation of rapid diagnostic methods used for identification of staphylococcus species in blood culture samples**

\*Dhar R, Al Fouzan W

Microbiology Unit, Department of Laboratories, Al Farwania Hospital, Al Farwania, Kuwait

**Introduction:**

Presence of Gram-positive cocci in clusters (GPCC) as observed in a direct Gram-stained smear from a positive blood culture bottle may take several days for identification and antimicrobial susceptibility testing resulting in delay in initiating appropriate antimicrobial therapy. The present study was undertaken to assess the utility of using direct Dnase test and a commercial molecular method vs. the conventional methods for identification of staphylococcal strains in blood samples.

**Methods:**

Over a period of 7 months (May-November, 2011) blood cultures positive for GPCC were examined by conventional methods, direct Dnase test and a commercial rapid PCR, GeneXpert. Specific identification of colonies was done by coagulase test, Dnase test and susceptibility to cefoxitin (30 µg). For performing direct Dnase test, a drop of sample from positive blood culture bottle was inoculated on to a DNA agar plate and incubated at 35°C overnight. The method recommended by the manufacturer was used to identify the staphylococcal isolates from positive blood culture by GeneXpert.

**Results:**

By conventional methods 168 blood culture bottles, which were positive for GPCC, yielded growth of coagulase-negative staphylococci (CoNS), methicillin-susceptible *S. aureus* (MSSA), and methicillin-resistant *S. aureus* (MRSA) in 140, 22, and 6 samples, respectively. Only 131 CoNS and all of *S. aureus* strains were tested and identified correctly by direct Dnase test. Similarly, CoNS (114), MSSA (19), and MRSA (6) were tested and identified correctly by GeneXpert, giving 100% sensitivity and 100% specificity for both the methods.

**Conclusions:**

Even though both the methods proved excellent for enhanced reporting of positive blood cultures for Staphylococci in our laboratory, the latter tool is faster (50 min.), reliable and thereby allows early optimization of antibiotic therapy for the patient. Cost may be the only constraint in the use of the PCR-based commercial method.

*Key Words: Blood culture; Staphylococcus spp.; Identification*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

Category: Graduate MSc (Basic Science)

98

**Humoral and cellular immune responses against ORF3 and ORF6 proteins of *Mycobacterium tuberculosis*-specific region of difference 1 using recombinant *Mycobacterium vaccae* constructs**

\*Ebrahimi B, Amoudy HA, Mustafa AS

Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

**Introduction:**

The failure of BCG vaccine in providing consistent protection against tuberculosis (TB) has spurred the need for improved vaccines. To identify new vaccine candidates, a nonpathogenic mycobacterial species (*M. vaccae*), was transformed with recombinant shuttle plasmids containing the genes of two *M. tuberculosis*-specific antigens, i.e. ORF3 (PE35) and ORF6 (CFP-10), and the recombinant constructs were evaluated for induction of antigen-specific cellular and humoral immune responses in mice.

**Methods:**

Wild-type *M. vaccae* cells were transformed with recombinant plasmids (pDE22-ORF3 and pDE22-ORF6) by electroporation. The presence of desired genes in transformed *M. vaccae* was confirmed by growing on selective media and PCR using insert-specific primers. The expression of recombinant proteins in in vitro grown *M. vaccae* was determined by SDS-PAGE and western immunoblotting. The in vivo expression and immunogenicity of proteins was determined by immunizing mice with constructs and studying antigen-specific cellular immune responses using splenocytes in proliferation assays and cytokine ELISAs, and sera in ELISA for humoral immune responses.

**Results:**

The western immunoblotting suggested the expression of corresponding protein by recombinant *M. vaccae*-pDE22-ORF3 grown in vitro. Furthermore, antigen-specific proliferation of splenocytes from immunized mice suggested the in vivo expression of both ORF3 and ORF6 proteins. However, antigen-specific secretion of cytokines, IFN- $\gamma$ , IL-5, and IL-10, could not be detected in culture supernatants of splenocytes stimulated with ORF3 or ORF6. Moreover, antibodies specific to ORF3 and its individual peptides were detected in sera of mice immunized with corresponding recombinant *M. vaccae*.

**Conclusions:**

The study shows the expression and immunogenicity of *M. tuberculosis*-specific RD1 ORF3 and ORF6 antigens by using recombinant constructs of *M. vaccae*, thus suggesting their potential as new anti-TB vaccine candidates

*Key Words: Vaccine; Recombinant technology*

*Funding Agency: Kuwait University, YM08/15*



**Microbiology, Virology and Immunology**

Category: Basic Sciences

99

**Rapid differentiation of *Candida dubliniensis* from *Candida albicans* by early D-xylose assimilation**

\*Ellepolá ANB<sup>1</sup>, Joseph BK<sup>1</sup>

<sup>1</sup>Faculty of Dentistry, Kuwait University; <sup>2</sup>Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

Previous reports have indicated that assimilation patterns for D-xylose (XYL) and  $\alpha$  methyl-D-glucoside (MDG) may be useful for differentiation of *C. dubliniensis* from *C. albicans* after 72 h of incubation at 30°C. It was therefore of interest to determine if XYL and MDG assimilation could be used reliably as a rapid test to differentiate *C. dubliniensis* from *C. albicans* at an earlier time point, rather than requiring 72 h to determine the outcome. Therefore, the aim of this study was to determine XYL and MDG assimilation, beginning as early as 2 h after inoculation of the isolates into the API 20C AUX yeast identification system.

**Methods:**

Thirty isolates each of *C. albicans* and *C. dubliniensis* were used. All isolates were inoculated into the API 20C AUX yeast identification system and incubated at 30°C. Results of XYL and MDG assimilation were read at 2 h intervals, beginning 2 h after the initial inoculation and up to 24 h of incubation. Thereafter, assimilation results were read after 48 and 72 h.

**Results:**

97% of *C. albicans* isolates had assimilated XYL at 16 h and by 24 h, all *C. albicans* isolates were positive for XYL assimilation. In contrast, none of the *C. dubliniensis* isolates assimilated XYL at any time point studied. Examination of MDG assimilation revealed that 24, 40, 92 and 100% of *C. albicans* isolates became positive after 16, 24, 48 and 72 h of incubation, respectively, whereas only 3% of *C. dubliniensis* isolates assimilated MDG after 72 h.

**Conclusions:**

Foregoing data indicate that it is possible to differentiate the large majority of *C. albicans* and *C. dubliniensis* isolates using the API 20C AUX carbohydrate assimilation kits after 16 h of incubation and 100% of isolates by 24 h of incubation at 30°C, based on the XYL assimilation patterns of these two species. Further studies with a larger number of isolates are warranted to evaluate the efficacy of the XYL assimilation test preferably in conjunction with molecular methods.

*Key Words: D-xylose; C. dubliniensis; C. albicans*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

*Category: Clinical*

**100**

**Evaluation of the use of *origanum majorana* as an organic food preservative in chicken, meat products, milk products and cereals**

\*Farouk N, Gheith O, Farahat M, EL-Derea H, EL-Moneim, AL-Ahwal A

Dasman Institute, OTC, Alex

**Introduction:**

Many food products are perishable by nature and require protection from spoilage during their preparation, storage and distribution to give them the desired shelf-life. We aimed to evaluate the use of *origanum majorana* as an organic food preservative from the microbiological, pH and organoleptic points of views in different food products after their storage for different periods.

**Methods:**

After getting sufficient amount of food products (ras, white and Kareesh cheeses); (minced meat, beef burger and deboned chicken meat) and (wheat and corn); we divided each food product into 10 parts; the first three parts were mixed with 3 levels of oil, the second were mixed with 3 levels of hydrosol and the third were mixed with 3 levels of ground leaves and the remaining tenth part was used as control. All samples of meat were stored frozen; dairy products were stored below 5°C; while cereals were stored at room temperature till the end of the study.

**Results:**

There were inverse relationships between the concentration of different forms of *origanum* and the mean score and acceptance percentages in most of the studied organoleptic properties of food products especially meat and milk products. We noticed a trend toward early reduction in pH values of all samples of food products especially in chicken, minced meat, beef burger and ras cheese. By time pH values returned back to more or less the baseline values. These pH changes in our samples were reflected microbiologically by decreasing bacterial and mold counts with the advance of storage period. *Origanum* oil was more effective than other forms. Moreover, oil and leaves showed antibacterial activity against *Staphylococcus aureus* but the hydrosol did not show any activity.

**Conclusions:**

We recommended the use of *origanum majorana* as an organic food biopreservative in different food products especially dairy products.

*Key Words: Food preservative; Origanum majorana; Storage*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

Category: Graduate MSc (Basic Science)

101

**Sequencing of intergenic spacer 2 of rDNA reveals genotypic heterogeneity among clinical *Candida glabrata* isolates in Kuwait**

\*Fayadh A, Ahmad S, Khan ZU

Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

*Candida glabrata* is an important pathogen causing mucosal and blood stream infections. Phenotypically identified *Candida glabrata* isolates represent a complex of three species, i.e., *C. glabrata*, *C. nivariensis* and *C. bracarensis*. This study determined the frequency of *C. nivariensis* and *C. bracarensis* among phenotypically identified *C. glabrata* isolates in Kuwait and molecular fingerprinting was performed to determine genotypic relatedness among clinical isolates.

**Methods:**

*C. glabrata* isolates (n=214) identified by Vitek2 were tested by multiplex PCR (mPCR) that yields species-specific amplicons from *C. glabrata* (360 bp), *C. nivariensis* (250 bp) and *C. bracarensis* (180 bp) and then by uniplex PCR using species-specific primers targeting rDNA. Molecular fingerprinting of selected 80 *C. glabrata* isolates was done by PCR sequencing of variable intergenic spacer region 2 (IGS2) of rDNA. Genotypic relationship among the isolates was deduced by constructing neighbor joining phylogenetic tree using bootstrap analysis with interior branch test of phylogeny by MEGA4 software.

**Results:**

None of 214 *C. glabrata*-complex isolates was identified as *C. nivariensis* or *C. bracarensis* as they yielded *C. glabrata*-specific amplicons in both, mPCR and uniplex PCR with *C. glabrata*-specific primer pair. Results for 30 selected isolates were confirmed by DNA sequencing of rDNA. Fingerprinting of 80 *C. glabrata* isolates identified 68 isolates as unique strains while 12 isolates were grouped in 5 clusters with two or three isolates in each cluster.

**Conclusions:**

All 214 clinical *C. glabrata*-complex isolates in Kuwait were identified as *C. glabrata* indicating that *C. nivariensis* and *C. bracarensis* are not clinically important species among patients with *Candida* infections in Kuwait. Fingerprinting data showed that vast majority of *C. glabrata* isolates were unique strains implying that nosocomial transmission is not a major mechanism of *C. glabrata* infections in Kuwait.

*Key Words: Candida glabrata; Species-specific identification; Genotypic heterogeneity*

*Funding Agency: College of Graduate Studies/KURA grant YM 24/09*



**Microbiology, Virology and Immunology**

Category: Graduate PhD (Basic Science)

102

**Reduced natural killer cell activity after dietary supplementation with eicosapentaenoic acid**

\*Hanan AK

Kuwait Institute for Scientific Research

**Introduction:**

There has been interest in the enrichment of poultry meat with long chain n-3 polyunsaturated fatty acids (PUFA) in order to increase their consumption by humans. There is concern that high levels of n-3 PUFA may have detrimental effects on immune function in chickens. Objective: To determine the effects of various dietary sources of n-3 PUFA on the natural killer (NK) cell activity of splenocytes peripheral blood leukocytes (PBMCs) in chickens.

**Methods:**

One-day-old male Ross 308 broiler chicks (n=20) were fed a common starter diet for 21 days. Then, birds were randomly allocated to 4 dietary treatments. The broilers were fed for 33 days on one of four sources of n-3 PUFA: echium-, algal DHA, fish oil (FO)-and linseed-enriched diets. Chickens were sacrificed between 41 and 43 days of age. Lipid profile of splenocytes and PBMCs was analyzed by gas chromatography. NK cell activity assay was conducted against LSCC-RP9 cell line on splenocytes and PBMCs.

**Results:**

The greatest enrichment of EPA (eicosapentaenoic acid) was observed in the broilers fed FO, followed by those fed algal DHA, while broilers fed linseed or echium oil had low levels of EPA in their lymphocytes. Splenocytes and PBMCs from FO-fed chicks exhibited the lowest NK cell activity while those from linseed oil-fed chicks exhibited the highest NK cell activity.

**Conclusions:**

The lowest NK cell activity was observed in chickens fed fish oil. This means that EPA, but not docosahexaenoic acid (DHA) or  $\alpha$ -linoleinic acid, may be responsible for the suppressive effect of NK cell activity. These studies highlight the need for the poultry industry to consider the health status of poultry when poultry meat is being enriched with n-3 PUFA.

*Key Words: Polyunsaturated fatty acids (PUFA); Natural killer (NK) cell activity; Eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA)*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

Category: Basic Sciences

103

**Immunization of mice with recombinant pUMVC6 and pUMVC7, containing RD1 and RD9 genes of *Mycobacterium Tuberculosis*, induces antigen-specific antibodies**

\*Hanif SNM, Al-Attayah R, Mustafa AS

Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

**Introduction:**

To study the antigen-specific antibody responses in mice immunized with recombinant DNA vaccine constructs of pUMVC6 and pUMVC7, containing RD1 and RD9 genes of *Mycobacterium tuberculosis*.

**Methods:**

Mice were immunized with the recombinant and parent plasmids and sera were tested for antibodies against pure proteins, peptide mixtures of each ORF and individual peptides of RD1 ORF3, ORF5, ORF6 and ORF7, and RD9 ORF3 using enzyme-linked immunosorbent assays (ELISA). The optical density (OD) values were measured at 405 nm. E/C (OD in antigen-coated wells/OD in antigen uncoated wells) were calculated, and the values of  $E/C > 2$  were considered positive.

**Results:**

Antigen-specific antibodies were not detected in the sera of mice immunized with parent plasmids pUMVC6 and pUMVC7. However, RD1 and RD9-antigen-specific antibodies were detected in sera of all groups of mice immunized with the recombinant DNA vaccine constructs ( $E/C > 2.0$ ). With respect to peptides, only P6 of RD1 ORF3, and P18 and P24 of ORF5 showed antibody reactivity with sera of mice immunized with the recombinant pUMVC6 and/or pUMVC7 DNA vaccine constructs.

**Conclusions:**

These results confirm *in vivo* expression and immunogenicity of the genes cloned in both DNA vaccine vectors. Furthermore, the results suggest that some of the epitopes recognized by antibodies were linear.

*Key Words: ELISA; Antigens; Antibodies*

*Funding Agency: Research Administration grant YM01/03*



**Microbiology, Virology and Immunology**

Category: Basic Sciences

104

**Rapid molecular identification of agents of zygomycosis: A fulminant disease of immunocompromised patients**

\*Joseph L, Khan ZU

Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

Zygomycetes include a phenotypically diverse group of molds that have assumed increasing clinical importance in immunocompromised patients as agents of fatal infections. Species-specific identification is crucial for improved prognosis since treatment varies for different agents of zygomycosis. Since phenotypic identification is time-consuming and lacks specificity, PCR sequencing of internally transcribed spacer (ITS) region of rDNA was studied for species-specific identification of a diverse group of zygomycetes isolated from clinical specimens in Kuwait.

**Methods:**

Initial identification of clinical and reference isolates (n=37) of zygomycetes was based on phenotypic and morphological characteristics. PCR sequencing of ITS region of rDNA was done for species delineation. Results for selected isolates were validated by PCR sequencing of 28S rRNA. Species-specific identification and genotypic relationships were derived by comparing sequences in BLAST searches and by constructing phylogenetic tree using MEGA4 phylogenetic software.

**Results:**

PCR sequencing identified all isolates and six different species/species-complexes were represented which formed six distinct clusters. *Rhizopus* spp. (*R. microsporus*, n=11 and *R. oryzae*, n=10) were most common. While 9 of 10 isolates of *R. oryzae* had identical ITS region sequences, five clusters were apparent among *R. microsporus*. Three of 4 *Mucor circinelloides* isolates had identical sequences while those of *Actinomucor elegans*-complex (n=6) varied slightly. Sequences of 4 *Syncephalstrum recemosum* and 2 *Lichthemia ramosa* isolates were more divergent.

**Conclusions:**

PCR sequencing of ITS region of rDNA is useful for rapid and accurate identification of clinical isolates of zygomycetes. The data also show that ITS region sequences of *Syncephalstrum* and *Lichthemia* species are more divergent than other agents of zygomycosis. Rapid species-specific identification will help in prompt initiation of specific antifungal therapy.

*Key Words: Zygomycetes; rDNA sequencing; Species-specific identification*

*Funding Agency: Supported by KURA grant MI 01/09*



**Microbiology, Virology and Immunology**

Category: Clinical

105

**Emergence of *Candida lusitanae* as a significant nosocomial pathogen in Kuwait**

\*Khan ZU, Mokaddas E, Chandy R, Joseph L

Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

*Candida lusitanae* is known to exhibit intrinsic resistance to amphotericin B. Acquired resistance of *C. lusitanae* to amphotericin B has also been reported to develop in neutropenic patients during treatment. Despite these concerns, amphotericin B has been used to successfully treat *C. lusitanae* fungemia in immunocompromised patients. The objective of this study was to highlight the emergence of *C. lusitanae* as a nosocomial pathogen in Kuwait and to provide information on its antifungal susceptibility profile.

**Methods:**

All *Candida lusitanae* isolates received from various hospitals for identification and/or antifungal susceptibility testing or recovered from various clinical specimens in Mycology Reference Laboratory during 2000-2010 were included. They were identified by Vitek2 Yeast identification system. Blood culture isolates were also confirmed by mating studies and/or by PCR sequencing of ITS region of rDNA. Antifungal susceptibility against amphotericin B and fluconazole was determined by Etest.

**Results:**

Of 125 *C. lusitanae* strains recovered during the study period, majority (58, 46.4%) were isolated from respiratory specimens. The remaining isolates were obtained from urine (24), blood (18), nasogastric tube aspirate (8), peritoneal fluid (5), rectum (4), and other sources (8). The rate of recovery of *C. lusitanae* among *Candida* bloodstream isolates increased from 2 of 467 (0.42%) during 2000-2005 to 16 of 807 (1.98%) during 2006-2010. No isolate was resistant to amphotericin B and fluconazole.

**Conclusions:**

Our data highlight the increasing role of *C. lusitanae* in bloodstream infections in Kuwait. Although no specific reasons for this increased occurrence were apparent, the data are in line with the worldwide trend suggesting a greater role of non-*albicans* *Candida* species in bloodstream infections. A better understanding of the epidemiology and associated predisposing factors for *C. lusitanae* infections is warranted.

*Key Words: Candida lusitanae; Bloodstream pathogen; Emerging significance*

*Funding Agency: KURA grant No. MI01/08*



**Microbiology, Virology and Immunology**

Category: Basic Sciences

106

**Leukocyte expression of inflammatory cytokines, heat shock proteins, and adiponectin in osteoarthritis-afflicted type 2 diabetics**

Mahmoud F<sup>1\*</sup>, Haines D<sup>2,4</sup>, Al-Awadhi A<sup>3</sup>, El-Shazly S<sup>1</sup>, Tosaki A<sup>4</sup>

<sup>1</sup>Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, Kuwait University, Kuwait; <sup>2</sup>Department of Molecular Biology, University of Connecticut, Storrs, CT, USA; <sup>3</sup>Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait; <sup>4</sup>Department of Pharmacology, Faculty of Pharmacy, University of Debrecen, Debrecen, Hungary

**Introduction:**

The present study profiles peripheral blood CD3+ T lymphocyte subpopulations contributing to T2DM-associated osteoarthritis (OA), hemoxygenase-1 (HO-1) a major cytoprotective enzyme; heat shock proteins (HSP) 70 and 90 which maintain cell viability; and adiponectin, a glucose- and fatty acid-regulatory hormone.

**Methods:**

Peripheral blood mononuclear cells from 15 T2DM-OA patients; 15 non-OA T2DM patients; and 10 healthy control subjects were evaluated by 2-color flow cytometry for representation of CD3+ T cells producing interferon-gamma (IFN- $\gamma$ ), tumor necrosis factor alpha (TNF- $\alpha$ ); ineterleukin-6 (IL-6) and ineterleukin-1beta (IL-1 $\beta$ ). HO-1, HSP70, HSP90 and adiponectin were assayed using Enzyme-Linked Immunoassay.

**Results:**

Non-OA T2DM blood did not contain significantly increased inflammatory T cell phenotypes versus control blood. However, CD3+IFN- $\gamma$  and CD3+TNF- $\alpha$  cells were elevated in T2DM-OA blood relative to controls ( $p < 0.05$ ); and to non-OA afflicted diabetics ( $p < 0.05$ ). HO-1 and adiponectin expression in blood from both OA and non-OA T2DM patients was significantly lower than in healthy subjects ( $p < 0.05$ ); and HSP 70 was elevated in OA-afflicted diabetics relative to controls ( $p < 0.05$ ), however no significant differences were noted in these 3 metabolites in OA versus non-OA diabetic blood. Finally, Pearson correlation coefficient analysis revealed significantly inverse correlation between HO-1 and TNF- $\alpha$  ( $r = -0.886$ ,  $p = 0.008$ ); and HO-1 and IL-1 $\beta$  ( $r = -0.923$ ,  $p < 0.009$ ).

**Conclusions:**

The present study demonstrates correlation between potentially pathogenic T cell phenotypes and regulators of diabetes-associated response to oxidative stress: HO-1 and adiponectin. These results serve as guidelines for design of therapies that act by modulating these mediators.

*Key Words: Inflammatory cytokines; Heat shock proteins; Type 2 diabetes*

*Funding Agency: TAMOPS 4.2.2-08/1-2008-007; 4.2.1/B-09/KONV-2010-0007; 4.2.2/B-10/1-2010-0024*



**Microbiology, Virology and Immunology**

Category: Basic Sciences

107

**Delayed-type hypersensitivity skin responses to recombinant proteins encoded by genes present in *Mycobacterium tuberculosis*-specific genomic regions of difference**

\*Mustafa AS, Shaban F

Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

Tuberculosis (TB) is a major infectious disease of local and international concern. The early and specific diagnosis of active and latent TB is hampered due to non-availability of specific, cost-effective and easy to administer tests. Such tests should be able to differentiate TB infection from BCG vaccination and exposure to environmental mycobacteria. In this study, the proteins encoded by *Mycobacterium tuberculosis*-specific regions of difference (RD) genes, which are absent in BCG and most non-tuberculous mycobacteria, were studied for delayed-type hypersensitivity (DTH) skin responses in guinea pigs infected with *M. tuberculosis*.

**Methods:**

The genes of RD1 (CFP10 and ESAT-6), RD7 (Rv2346 and Rv2347) and RD9 (Rv3619 and Rv3620) proteins were cloned in plasmid vectors and expressed as recombinant proteins in *Escherichia coli*. The recombinant RD proteins were purified to homogeneity using glutathione Sepharose and Ni:NTA affinity columns. Guinea pigs were injected with  $1 \times 10^{10}$  heat-killed *M. tuberculosis*; and phosphate buffered saline (PBS), as a placebo control. After four weeks of injection, all the animals were tested for DTH skin responses by intradermal injection with PBS (negative control), purified protein derivative (PPD) and sonicates of *M. tuberculosis* (positive control), and purified recombinant proteins.

**Results:**

PBS failed to induced DTH responses in any group, whereas PPD, *M. tuberculosis* sonicates and the recombinant proteins induced positive DTH responses in animals injected with heat-killed *M. tuberculosis*, but not in PBS-injected animals.

**Conclusions:**

The results suggest that purified RD proteins are active in inducing DTH responses in vivo, and, therefore, may be useful in specific diagnosis of TB

*Key Words: Tuberculosis; DTH response; Diagnosis*

*Funding Agency: Funded by Kuwait University, Research Administration grant MI01/10*



**Microbiology, Virology and Immunology**

Category: Clinical

108

**Comparison of two nucleic acid amplification assays, the ProbeTec ET assay and Xpert MTB/RIF assay, for detection of *Mycobacterium tuberculosis* in pulmonary and extrapulmonary specimens**

Mokaddas EM\*, Ahmad S, Eldeen HS, Hanif SNM

Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

The ability of ProbeTec ET and Xpert MTB/RIF assays to rapidly detect *Mycobacterium tuberculosis* in pulmonary and extrapulmonary specimens was evaluated against the gold standard culture technique.

**Methods:**

Smear microscopy for acid-fast bacilli, culture by automated BACTEC MGIT 960 system and direct detection of *M. tuberculosis* by ProbeTec ET and Xpert MTB/RIF systems were performed on 989 pulmonary and 454 extrapulmonary specimens from January 2010 to August, 2011. Drug susceptibility to rifampicin by BACTEC MGIT 960 system was compared with Xpert.

**Results:**

Of 989 pulmonary specimens, 90, 66 and 833 were; smear positive-culture positive, smear negative-culture positive and smear negative-culture negative, respectively. Both molecular tests detected *M. tuberculosis* in 81 of 90 smear positive-culture positive samples, one sample was negative by both molecular tests while 8 samples yielded non-tuberculous mycobacteria (NTM) with a sensitivity of 99%. The ProbeTec and Xpert detected *M. tuberculosis* in 46 and 43 of 66 smear negative-culture positive samples, respectively with sensitivity of 70% and 65%. Of 454 extrapulmonary specimens, 25, 1, 58 and 370 were; smear positive-culture positive, smear positive-culture negative, smear negative-culture positive and smear negative-culture negative, respectively. Both molecular tests detected *M. tuberculosis* in 23 of 25 smear positive-culture positive samples while 2 samples yielded NTM with 100% sensitivity. One smear positive-culture negative sample was from a leprosy patient. The ProbeTec and Xpert detected *M. tuberculosis* in 33 and 50 of 58 smear negative-culture positive samples, respectively with sensitivity of 57% and 86%. All smear negative-culture negative pulmonary and extra-pulmonary samples were negative by both molecular tests with 100% specificity. Xpert correctly detected rifampicin resistance in 13 of 14 samples with a sensitivity of 93%.

**Conclusions:**

Both, ProbeTec and Xpert offer rapid and sensitive detection of *M. tuberculosis* and its resistance to rifampicin in pulmonary and extrapulmonary specimens.

*Key Words: Gene-Xpert; Proptec; TB*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

Category: *Clinical*

109

**Clinical evaluation of Bruker Microflex MS versus bioMerieux VITEK MS methods for the identification of pathogens**

\*Rotimi VO<sup>1,2</sup>, Saleem R<sup>2</sup>, Jamal W<sup>1,2</sup>, Pazhoor A<sup>2</sup>, Khan ZU<sup>1,2</sup>, Albert MJ<sup>1,2</sup>

<sup>1</sup>Departments of Microbiology, Faculty of Medicine, Kuwait University; <sup>2</sup>Mubarak Al Kabir Hospital, Kuwait

**Introduction:**

Fast and cost-effective matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF)-based systems are replacing biochemical and other phenotypic systems for routine identification (ID) of bacteria. Our objective was to evaluate two MALDI-TOF MS systems for ID of clinical pathogens.

**Methods:**

Clinically isolates were subjected to ID by the Bruker MMS® and bioMerieux VMS® in parallel VITEK 2. For MMS, the isolates were tested in duplicates directly and after pretreatment while with VMS, single deposits of the same sets of isolates were tested in duplicates directly on MALDI-plate. Identification was according to manufacturer's protocols. Discrepant results were resolved by 16S rRNA gene sequencing.

**Results:**

A total of 1007 pathogens were tested. MMS and VMS correctly identified 98.1% and 99.3%, and 92.8% and 96.3% of the isolates to genus and species levels, respectively. Both systems correctly identified all species of the family Enterobacteriaceae, *Pseudomonas* spp., *Acinetobacter baumannii* and all Gram-positives to genus level. *Candida albicans* and other species were correctly identified by both systems. Discrepant results were resolved by 16S rRNA sequencing more in favor of VMS. MMS misidentified 2 *S. mitis* isolates as *S. pneumoniae*. One strain identified as *Ralstonia picketti* by VITEK 2 and VMS was identified as *R. insidiosa* by MMS and *R. solanacearum* by sequencing.

**Conclusions:**

Both systems performed excellently in terms of providing accurate diagnosis 24-48h earlier than the CPS. Both are user-friendly (bioMerieux VMS>Bruker MMS) and can be easily incorporated into routine diagnostic procedures.

*Key Words: Identification; Clinical pathogens; MALDI-TOF systems*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

Category: Basic Sciences

110

**Comparative performance of bioMerieux VITEK MS, Bruker Microflex MS and API AN methods for identification of anaerobes**

Shahin M\*, Jamal W, Pazhoor A, Rotimi VO

Mubarak Hospital, Jabriya

**Introduction:**

Matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF)-based systems are state-of-the-art automated systems developed for routine identification (ID) of bacteria. Our objective was to compare the performance of two MALDI-TOF MS and API AN systems for ID of clinically relevant anaerobes.

**Methods:**

A selection of 274 clinical isolates representing 4 genera and 14 species, obtained during a 7-month period, were subjected to ID by the bioMerieux VITEK MSTM (VMS), Bruker MICROFLEX MSTM (MMS) and API 20 AN (CPA). For VMS and MMS, isolates were tested in duplicates directly on MALDI-plate and for the API 20 AN, routine protocol was followed. ID interpretation was according to manufacturer's protocols. 16S rRNA gene sequencing was used as reference standard to resolve discrepant results

**Results:**

VMS, API and MMS correctly ID all species of Porphyronomas, Prevotella, Clostridium and Peptostreptococcus, confirmed by sequencing. BioMerieux VMS and API were in agreement in the ID of all (100%) *B. fragilis* and *B. thetaiotaomicron* isolates, two of which Bruker MMS misidentified as *Malika spinosa* and *Propionibacterium acne*. The 2 discrepant results were resolved by 16S rRNA sequencing in favor of VMS and API AN. Log scores of 9 isolates (2 *B. thetaiotaomicron*, 1 *B. fragilis*, 1 *P. bivia*, 1 *B. ovatus*, 1 *B. vulgatus*, 1 *C. difficile*, 1 *C. sporogenes* and 1 *P. assacharolyticus* gave unreliable ID of <1.7 in the Bruker MMS. Likewise, another 24 could be validated only to genus level in the Bruker MMS with scores of 1.7-<2.0, whereas VMS and API ID all isolates with scores of 99.9 and 99.4-99.9, respectively.

**Conclusions:**

VMS and API performed slightly better than MMS in the identification of anaerobic bacteria. However, both VMS and MMS are completely automated and easier to manipulate than API

*Key Words: MALDI-TOF MS; Identification; Anaerobes*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

Category: *Clinical*

111

**Pattern of bacterial pathogens in burn wound infections: A 6 year study**

\*Shetty SA, Abdullah AA, Mokaddas E

Department of Laboratory Medicine, Ibn Sina Hospital

**Introduction:**

Rapidly emerging nosocomial pathogens and the problem of multi-drug resistance necessitates periodic review of pattern of bacterial pathogens. This six year retrospective study was done at the Al-Babtain Center for Burns to determine the microbial etiology of burn wound infections. The antimicrobial susceptibility pattern of *Acinetobacter baumannii* and *Pseudomonas aeruginosa* to a range of antibiotics and the number of extended spectrum beta lactamase (ESBL) producers in Enterobacteriaceae were determined.

**Methods:**

All clinically significant Gram-positive and Gram-negative bacteria isolated from burn wound swabs from January 2005 to December 2010 were included. The isolates were identified by Vitek 2 (Biomérieux, France). Antimicrobial susceptibility pattern of *Acinetobacter baumannii* and *Pseudomonas aeruginosa* was done by Vitek 2 and confirmed by E-test (AB Biodisk, Solna, Sweden) whenever required. ESBL production in Enterobacteriaceae was detected by the E-test method.

**Results:**

Out of a total of 8372 clinically significant burn wound isolates evaluated over the study period, 3238 (38.6%) and 5134 (61.3%) were Gram-positive and Gram-negative bacteria, respectively. Methicillin resistant *Staphylococcus aureus* (MRSA) accounted for 54.9% of the Gram-positive isolates. *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and Enterobacteriaceae accounted for 1882 (36.6%), 536 (10.4%) and 2623 (51%) of the Gram-negative isolates, respectively. Twenty two percent of the Enterobacteriaceae isolates were ESBL producers. *Acinetobacter baumannii* showed an increase in the antimicrobial resistance to both amikacin and carbapenems from 38% in 2005 to 65% in 2010 while in *Pseudomonas aeruginosa* it was uniform over the years.

**Conclusions:**

In this study, a high prevalence of carbapenem resistant *Acinetobacter baumannii* was encountered, which calls for continuous surveillance, rational use of antibiotics and stringent infection control measures.

*Key Words: Burn Wound; Microbial aetiology; Antimicrobial susceptibility*

*Funding Agency: None*



**Microbiology, Virology and Immunology**

Category: Basic Sciences

112

**Development of a multiplex allele-specific PCR assay targeting *cyp51A* codon 98 mutations for rapid detection of azole-resistant *Aspergillus fumigatus* isolates**

\*Theyyathel A, Ahmad S

Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

*Aspergillus fumigatus*, the principal etiologic agent of invasive aspergillosis is intrinsically resistant to fluconazole, however, new triazoles (itraconazole and voriconazole) are active and are common choice for primary therapy of IA. Mutations at codon 98 (L98H) of *cyp51A* (*cyp51A98*) encoding 14- $\alpha$ -sterol demethylase have been detected in triazole-resistant clinical *A. fumigatus* isolates. This study developed a multiplex allele-specific PCR (MAS-PCR) assay targeting *cyp51A98* mutations for rapid detection of azole-resistant *Aspergillus fumigatus* isolates for proper patient management.

**Methods:**

Reference *A. fumigatus* strains (wild-type and with L98H mutation at *cyp51A98*) were used for establishing MAS-PCR. MAS-PCR was done by using three primers designed to detect the presence of CTC (wild-type) or CAC (mutant) allele at *cyp51A98*. Clinical and environmental isolates of *A. fumigatus* (n=60) were used to evaluate MAS-PCR. Drug susceptibility testing (DST) of *A. fumigatus* isolates to triazoles and other antifungal drugs was determined by Etest. Results of MAS-PCR were confirmed by direct DNA sequencing of *cyp51A98* region from selected isolates.

**Results:**

The MAS-PCR performed with reference *A. fumigatus* strains carrying wild-type (CTC) and CTC to CAC (L98H) mutation at *cyp51A98* yielded varying amplicon patterns in agarose gels, as expected. None of the clinical *A. fumigatus* isolate was resistant to itraconazole or voriconazole as their MIC values were below the cut-off defining resistant strains. The MAS-PCR analyses showed that all clinical isolates contained wild-type sequence at *cyp51A98* and the results were verified by DNA sequencing.

**Conclusions:**

A simple, MAS-PCR assay has been successfully developed to facilitate rapid detection of L98H mutation in *cyp51A* gene that confers resistance to triazoles in *A. fumigatus* strains. The assay will help in early recognition of triazole-resistant *A. fumigatus* strains for proper management of patients with IA.

*Key Words:* Triazole-resistant *A. fumigatus*; MAS-PCR; Rapid Detection

*Funding Agency:* Supported by KURA grant MI 01/09

**Microbiology, Virology and Immunology**Category: *Clinical*

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**Emergence and characterisation of community-associated Methicillin-resistant *Staphylococcus aureus* at a neonatal special care unit**Udo EE <sup>1\*</sup>, Al-Sweih N<sup>1,2</sup>, Khan S<sup>2</sup>, Mathew B<sup>1</sup>, Noronha B<sup>1</sup>, Verghese T<sup>1</sup>.<sup>1</sup>Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait;<sup>2</sup>Maternity Hospital, Kuwait**Introduction:**

Community-associated methicillin-resistant *S. aureus* (CA-MRSA) is an emerging healthcare problem among pregnant women and neonates worldwide. This study was conducted to determine the genetic relatedness of MRSA isolated from neonates admitted to special care units of the Maternity hospital in Kuwait.

**Methods:**

A total of 21 MRSA were isolated from 20 neonates between October and December 2011. They were characterized using antibiogram, pulsed-field gel electrophoresis (PFGE), SCCmec typing and spa typing and screened for the carriage of genes for Panton Valentine leukocidin (PVL) and capsular polysaccharide types 5 and 8.

**Results:**

All isolates were susceptible to vancomycin, teicoplanin and mupirocin but were resistant to trimethoprim (13/21), gentamicin and kanamycin (7/21), ciprofloxacin (5/21), erythromycin and clindamycin (2/22), tetracycline (2/22) and fusidic acid (2/22). PFGE identified seven pulsotypes and subtypes with nine isolates belonging to one cluster (type A). Pulsotypes B, D, E, C, F and G consisted of four, three, two and one isolates respectively. Spa typing differentiated the isolates into 11 spa types with five isolates belonging to spa type t3935, followed by spa types t6269 (3 isolates) and t 6892 (3 isolates), t1084 (2 isolates) and t2962 (2 isolates). Spa types t339, t1548, t5801, t1340, t2810 and t4410 occurred in single isolates. Twenty isolates contained SCCmec IV or V genetic elements that are characteristic of CA-MRSA while one isolate contained SCCmec III element characteristic of healthcare-associated MRSA. Seven isolates spanning four pulsotypes and five spa types contained genes for PVL. Fifteen and six isolates carried genes for types 5 and 8 capsular polysaccharide respectively.

**Conclusions:**

This study highlighted the heterogeneous emergence of CA-MRSA in the neonatal special care unit which warrants the implementation of a rapid screening protocol for mothers and babies to prevent the establishment and further spread of CA-MRSA.

*Key Words: Community-associated MRSA; Epidemiological typing*

*Funding Agency: Funded by Kuwait University Research Administration*



*Neuroscience*

*Category: Clinical*

**114**

**Lumbar drainage in severe bacterial meningitis: A retrospective cohort study**

\*Abulhasan YB<sup>1</sup>, Al-Jehani H<sup>2</sup>, Valiquette MA<sup>2</sup>, Mc Manus A<sup>2</sup>, Dolan-Cake M<sup>2</sup>, Ayoub O<sup>2</sup>, Teitelbaum J<sup>2</sup>, Angle M<sup>2</sup>

<sup>1</sup>Faculty of Medicine, Health Sciences Center, Kuwait University, Kuwait; <sup>2</sup>Neurological ICU, Montreal Neurological Institute and Hospital, McGill University, Montreal, Quebec, Canada.

**Introduction:**

Despite medical management with early antibiotic therapy and steroids, severe bacterial meningitis in adult patients requiring an ICU admission still carries a high rate of morbidity and mortality. We studied the use of lumbar drains as an adjuvant modality and compared it to the standard treatment of this uncommon patient population in our institution.

**Methods:**

We conducted a retrospective chart review of all patients above the age of 18 years, with severe bacterial meningitis and alteration in mental status, requiring admission to the Neurological ICU (Neuro-ICU) from January 2000 till December 2010. A total of 37 patient episodes of meningitis were analyzed. We classified patients as following: lumbar drain (LD) group (n=11) and non-lumbar drain (non-LD) group (n=27). The primary outcome was mortality and severe morbidity in the acute phase. The secondary outcome included ICU stay and Glasgow Outcome Scale (GOS) at 1 to 3 months.

**Results:**

All patients (n=37) had an altered mental status and were started on broad-spectrum antibiotics while 84% were started on steroids. The opening pressure was high in all patients in the LD group. Mean time-to-insertion of the lumbar drain was 37 hours, coinciding with the time of admission to the Neuro-ICU. The lumbar drains were open with a mean daily drainage of 129 mls to achieve an ICP less than 10 mmHg. In the LD group, there was no mortality and 91% of the patients achieved a GOS of 4-5 while in the non-LD group, there was 15% mortality and 60% achieved a GOS of 4-5.

**Conclusions:**

In a single-center, retrospective, non-randomized study, the use of lumbar drainage as an adjuvant therapy in adult patients with severe bacterial meningitis is a significant contributor to reduced mortality and severe morbidity.

*Key Words: Meningitis; Lumbar Drainage; Cohort Study*

*Funding Agency: None*



**Neuroscience**

Category: Basic Sciences

115

**Enhancement of cell proliferation and survival in vitro culture and *in vivo* transplant by green tea extract**

\*Rao MS

Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait

**Introduction:**

Green tea extract (GTE) has been shown to have neuroprotective and antioxidant properties. Objective of the present study was to investigate the role of aqueous GTE in proliferation and survival of fetal hippocampal cells in vitro cell culture and in vivo transplantation.

**Methods:**

For in vivo study, primary culture of fetal hippocampal tissue (E19) was done. Control cultures(n=6) remained without any treatment, experimental cultures(n=6) were treated with aqueous GTE (50µl/ml). Cultures were terminated on 7th day, cell survival was analyzed by counting no.of cells in randomly selected fields using a phase contrast microscope. For transplantation, single cell suspension of fetal hippocampal tissue(E19) was transplanted into the lateral ventricles of the adult rats(n=12) using a stereotaxic apparatus. Experimental group of transplanted rats were treated with aqueous GTE (1ml/day, orally, n=6) for 1 week and sacrificed at the end of 4 weeks. Brain sections were stained with cresyl violet, doublecortin and GFAP immunostaining. Number of cells in the transplant were quantified by counting the cells under a light microscope. Data were analyzed with Student's t-test.

**Results:**

There was a significant increase in the number of surviving cells in the cultures treated with GTE. Significantly large number of cultured cells expressed glial marker (GFAP, 80%) and neuronal marker (Doublecortin, 20%) in treated culture compared to control culture, (P<0.01). Transplants in treated rats had significantly more (40%) number of neurons compared to control transplants, (P<0.01). Significantly less(30%) number of transplanted cells expressed GFAP, and transplants contained significantly higher(40%) number of newly generated neurons, (P<0.05, P<0.01).

**Conclusions:**

In vitro and in vivo data suggest cell proliferative role and facilitation of transplant survival by GTE. GTE may be used for enhancing the survival, growth and differentiation of fetal neural cells in the transplants.

*Key Words: Hippocampus; Transplantation; Green tea*

*Funding Agency: None*



***Nuclear Medicine and Radiology***

*Category: Graduate MSc (Basic Science)*

**116**

**Molecular investigation of the degree of environmentally-induced DNA damage in Kuwaiti women with breast cancer**

\*Al-Enezi BM, Saleh F, Al-Bader M

Faculty of Medicine, Kuwait University

**Introduction:**

The number of Kuwaiti women developing breast cancer has increased significantly over the past 10 years. Environment (referring to air, water, soil, food/diet, lifestyle, climate, occupation, and socio-economic status) plays a crucial role in causing the disease. This thesis investigates extent of environmentally-induced DNA damage in peripheral blood lymphocytes (PBLs) of newly-diagnosed breast cancer patients by examining two parameters-micronucleus formation and HPRT gene mutation. It also investigates association between these parameters, and markers of environmentally-induced DNA adducts in the breast cancer tissue of patients and in the fibroadenoma tissue of matching controls.

**Methods:**

0.5ml of peripheral blood from 42 newly-diagnosed breast cancer patients, and 45 age-matched controls was examined for chromosomal damage (using Cytokinesis Block Micronucleus technique) and for mutant frequency of the HPRT gene (using HPRT gene mutation test). Immunohistochemistry was performed using antisera against 4-ABP (3C8) and PAH-DNA adducts (5D11) for 10 of these patients on 4 micron paraffin sections As controls we used sections from ten women, whose breast biopsies showed fibroadenoma.

**Results:**

We found that Kuwaiti women newly-diagnosed with breast cancer, as compared to those with fibroadenoma had the following characteristics: (1), their PBLs had significantly more micronuclei formation (2), such formation was significantly associated with the disease (3), nuclear division index of their PBLs was significantly higher (4), HPRT gene mutation frequency was not significantly different from controls and (5), their tumor exhibited significantly higher degree of expression of PAH and 4-ABP-DNA adducts, and this was significantly associated with the disease.

**Conclusions:**

This thesis highlights existence of environmentally-induced DNA damage in newly-diagnosed Kuwaiti breast cancer patients.

*Key Words: Breast Cancer and Kuwaiti women; PAH-DNA adducts; HPRT Gene Mutation*

*Funding Agency: None*



**Nuclear Medicine and Radiology**

Category: Basic Sciences

117

**Choline administrations affect the liver reticuloendothelial system and plasma fatty acid profile in diabetic rats**

\*Al-Saeedi F<sup>1</sup>, Cheng B<sup>2</sup>

<sup>1</sup>Nuclear Medicine Department, Faculty of Medicine, Kuwait University; <sup>2</sup> Biochemistry Department, Faculty of Medicine, Kuwait University.

**Introduction:**

This study was undertaken to investigate effects of choline-administrations on hepatic reticuloendothelial function, hepatobiliary function, and plasma fatty acid profile, in diabetic rats.

**Methods:**

Diabetes was induced by streptozotocin (STZ, 55 mg/kg, ip). Untreated and some of STZ-treated rats were administered choline (5 g/kg, iv) for two five-consecutive-days, with a 2-day-interval in between. Rats received saline injections only served as controls. The hepatic functions were investigated using non-invasive <sup>99m</sup>Tc Tin (II) colloid (TIN), and <sup>99m</sup>Tc mebrofenin (BrIDA), imaging. Ratios of TIN-uptake in heart, liver, and spleen, and ratios of BrIDA-uptake in liver, biliary tree, and abdomen, to whole body were obtained following the imaging studies. Plasma fatty acids were analyzed by GC/MS after methylation. Student's t-test and ANOVA were employed to determine statistical significance.

**Results:**

Diabetic rats showed: (a) a decreased TIN-uptake-ratio in liver, with co-increases of the ratios in heart and spleen, choline-administrations abolished these changes; (b) elevations in BrIDA-uptake-ratios in biliary tree and abdomen, but not in liver, choline-administrations did not attenuate the elevations; (c) decrease in plasma palmitoleic acid and oleic acid, reflecting an impaired stearoyl CoA desaturase (SCD) activity; choline administrations did not affect the diminutions, but caused decreased arachidonic acid with co-increased linoleic acid.

**Conclusions:**

Choline-administrations to diabetic rats affected their hepatic reticuloendothelial function and plasma fatty acid profiles, but not the hepatobiliary function. The diabetes-deactivated SCD activity is known as a self-correcting device for enhancing insulin receptor (IR) sensitivity. Because arachidonic acid and linoleic acid are both inhibitory to SCD activity, whether the choline-induced alterations in these fatty acids would further sensitize IR require further investigations.

*Key Words: Phagocytic function; Diabetes; STZ-treated rats*

*Funding Agency: MN01/07*



**Nuclear Medicine and Radiology**

Category: Basic Sciences

118

**Assessment of tracer  $^{99m}\text{Tc}$ -(V)DMSA uptake as a measure of tumor cell proliferation**

\*Al-Saeedi FJ<sup>1</sup>, Luqmani YA<sup>2</sup>, Mathew PM<sup>1</sup>

<sup>1</sup>Nuclear Medicine Department, Faculty of Medicine, Kuwait University; <sup>2</sup>Pharmaceutical Chemistry Department, Faculty of Pharmacy, Kuwait University.

**Introduction:**

This study was to examine whether pentavalent dimercaptosuccinic acid labelled with technetium-99m ( $^{99m}\text{Tc}$ -(V)DMSA) (routinely used for tumour imaging) could be used as a non-invasive measure of cancer cell proliferation on the premise that rapidly proliferating tumours need to synthesize DNA and phospholipids to a greater extent than slower growing ones. As a simulation model we used cell monolayers at varying confluency and compared uptake with several proliferation parameters.

**Methods:**

Human breast cancer MCF-7, MDA-231 and pII, and prostate cancer PC-3 cell lines were grown to 30, 50 and 100% confluency and then pulsed with  $^{99m}\text{Tc}$ -(V)DMSA/ml DMEM containing 5% serum in 25 cm flasks for 60 min at 37°C. Incorporated radioactivity was determined following solubilisation of cells with 1% SDS. Uptake was correlated with intracellular fate of  $^{99m}\text{Tc}$ -(V)DMSA (phospholipid synthesis) in cell pellets, DNA synthesis reflected either by S phase using flow cytometry or [methyl-<sup>3</sup>H]thymidine incorporation, cell viability (MTT assay) and expression of proliferation markers PCNA and Ki-67 and sodium phosphate transporter (by realtime PCR). Appropriate t-test and ANOVA statistical methods were used to compare data.

**Results:**

In all cell lines rates of  $^{99m}\text{Tc}$ -(V)DMSA uptake, mean $\pm$ SD (p value) were inversely related to cell density. Normalised for 30% confluency relative uptake at 50 and 100% was  $0.94\pm 0.02$  and  $0.83\pm 0.07$  for MCF-7 ( $P=0.01$ ),  $0.67\pm 0.002$  and  $0.49\pm 0.001$  for MDA-231 ( $P<0.0001$ ),  $0.67\pm 0.002$  and  $0.41\pm 0.004$  for pII ( $P<0.0001$ ) and  $0.79\pm 0.009$  and  $0.74\pm 0.005$  for PC-3 ( $P=0.001$ ) cells. This was paralleled by similar trends in S phase proportions, [methyl-<sup>3</sup>H]thymidine incorporation, MTT assay and expression of proliferation markers PCNA and Ki-67 and sodium phosphate transporter.

**Conclusions:**

$^{99m}\text{Tc}$ -(V)DMSA uptake into different types of tumour cells correlates with cell density, and may be used as a convenient non-invasive tool to determine tumour cellular proliferation in vivo.

*Key Words: Tumor cell proliferation; MCF-7 cells*

*Funding Agency: MN03/07*



**Nuclear Medicine and Radiology**

Category: Clinical

119

**Magnetic resonance imaging of the lumbar spine in young Arabs with low back pain.**

Al-Saeed O<sup>1</sup>, Al-Jarallaha KF<sup>2</sup>, Dashti K<sup>3</sup>, \*Sheikh M<sup>1</sup>.

<sup>1</sup>Department of Radiology, Faculty of Medicine, Kuwait University; <sup>2</sup>Department of Medicine, Faculty of Medicine, Kuwait University; <sup>3</sup> Department of Radiology, Farwaniya Hospital, Kuwait.

**Introduction:**

The studies on the prevalence of magnetic resonance imaging (MRI) findings and their relationship with the low back pain (LBP) have mainly been conducted on the adult population in the developed countries. There are only a few such studies conducted mainly on the western young. The prevalence of MRI changes in the young Arab population with LBP is not known. We sought to investigate the prevalence of MRI features of the lumbar spine in LBP and the risk factors associated with it in young Arab population.

**Methods:**

Two hundred and fourteen patients of Arab origin in the 16-29 year age group with LBP symptoms were subjects to MRI examination using a 1.5T scanner. The prevalence of MRI changes in the lumbar spine and associated risk factors was determined and compared to age, race and gender matched controls.

**Results:**

Sixty four percent of the patients with LBP (138 out of 214) were found to have MRI evidence of degenerative disc disease (DD) compared to 10% ( 21 out of 214 ) in the control group . The majority (61%) of patients had multiple level disease, most commonly involving the lowest two disc levels (L4-5 and L5-S1). Reduced signal intensity of the disc followed by disc bulge were the most common MRI features seen in both the symptomatic as well as the controls. Obesity and activity correlated with the MRI prevalence of the disease.

**Conclusions:**

The prevalence of MRI features of DD disease among the young Arab presenting with LBP is high. Larger cross sectional studies is needed to further explore this high prevalence in the young Arab population.

*Key Words: Magnetic resonance Imaging; Low Back Pain; Young Arabs*

*Funding Agency: None*



***Nuclear Medicine and Radiology***

*Category: Clinical*

**120**

**Association of femoral intercondylar notch morphology, width index and the risk of ACL tear: A retrospective study on 560 knee MRIs.**

\*Al-Saeed O, Brown M, Reji A, Sheikh M

Department of Radiology, Faculty of Medicine, Kuwait University, Consultant Radiologist, Al Amiri Hospital, Kuwait.

**Introduction:**

To determine the relationship between femoral notch morphology and femoral notch width index (FNWI) with anterior cruciate ligament (ACL) tear in the Arab population using MRI.

**Methods:**

This study population consisted 560 consecutive patients who had MRI examination of the knee done between February 2010 and June 2011 to determine the relation between femoral notch morphology, FNWI and ACL tear. Depending upon the notch shape the femoral notch was classified into one of the 3 types. The type 'A' described as a narrow (Stenotic) notch which appears narrowed on visual appreciation from the base to the mid section as well as at the apex, type 'U' in which the mid section does not taper, allowing for a wider contour to the notch than shape 'A' and the type 'W' which has characteristics of the 'U' shape but with two apparent apices.

**Results:**

Of 560 patients (mean age 38 years, range 20 - 60) there were 280 cases each with and without ACL tear. The majority (73%) of the subjects with the 'A' shaped notch (176 out of 240) had ACL tear where as the majority (68%) of the subjects with type 'U' or type 'W' notch (216 out of 320) were normal. The type A notch correlated with ACL tear (p value <0.0001). Only 37% (88 out of 240) of the subjects with type 'A' notch had reduced FNWI while 72.5% of the subjects with 'U' or 'W' shaped notch (232 out of 320 cases) had normal FNWI. Of the subjects with reduced FNWI only 17% had ACL tear (48 out of 280).

**Conclusions:**

The A shaped notch appears to be a risk factor for ACL tear in the Arab population. There was no correlation between the reduced notch index and ACL tear in this study.

*Key Words: Magnetic resonance imaging; Anterior cruciate ligament tear; Femoral notch morphology.*

*Funding Agency: None*



**Nuclear Medicine and Radiology**

Category: Clinical

121

**Body mass index affects the doppler signal in the celiac artery**

\*Asbeutah AM

Department of Radiologic Sciences, Faculty of Allied Health Sciences, Kuwait University

**Introduction:**

Multiple factors might affect the peak systolic velocity (PSV) recording on the celiac artery (CA) causing a compression syndrome. Reports focused on the phase of respiration and patient position. They found that the CA is highly compressed during the phase of expiration but not inspiration and during supine position and not erect position. Little or no reports in the literature focused on the effect of the body mass index (BMI) on CA waveform during Doppler scanning of the CA. The aim of this study is to evaluate the effect of BMI on PSV recording in the CA.

**Methods:**

Forty male participants were entered prospectively into the study. Peak systolic velocity & vessel diameter at the origin of the celiac artery of participants with different BMI were recorded while the subject fasted for at least 4-6 hours using duplex ultrasound.

**Results:**

There were 40 participants males divided to two groups. Group A, their average age ( $\pm$ SD, year)  $24.6\pm 3.8$  and their average body mass index ( $\pm$ SD,  $\text{Kg/m}^2$ ) ( $23.1\pm 1.60$ ). Group B, their average age ( $\pm$ SD, year)  $31.35\pm 9.7$ , and their average body mass index ( $\pm$ SD,  $\text{Kg/m}^2$ ) ( $31\pm 5.1$ ). The average diameter ( $\pm$ SD, cm) of CA in group A was ( $0.66\pm 0.076$ ) and in group B was ( $0.80\pm 0.066$ ). However, the average peak systolic velocity ( $\pm$ SD, cm/s) was ( $116.97\pm 28.1$ ) in group A and ( $102.75\pm 12.4$ ) in group B. Paired student t-test for the effect of BMI on the peak systolic velocities and the diameter of the CA was performed and showed statistical significance between both groups ( $p < 0.05$ ).

**Conclusions:**

BMI is an important factor while performing Doppler for patients with celiac artery disease to avoid false positive results.

*Key Words: Celiac artery; Compression syndrome; Mesenteric vessels*

*Funding Agency: None*



***Nuclear Medicine and Radiology***

*Category: Clinical*

**122**

**MRI evaluation of non-traumatic painful heel in adults**

\*El-Sayed SB, Al-Kandary S, Galal A  
AlRazi Hospital

**Introduction:**

Heel pain is a common and frequently disabling clinical complaint in adults that may be caused by a broad spectrum of osseous or soft-tissue disorders. Our goal is to certain the value of Magnetic Resonance Imaging (MRI) as a primary imaging modality in cases of non-traumatic heel pain and highlight its accuracy as a diagnostic tool in these selected clinical problems.

**Methods:**

A retrospective study of the MRI examination of the ankle and foot of twenty patients referred from the outpatient clinic of Al-Razi specialized orthopedic hospital in Kuwait. Those patients complained of heel pain with no definite history of trauma. MRI was performed using 1.5T HDE - GE system and included T1-weighted, fat-suppressed proton density-weighted and/or short time inversion recovery (STIR) images at axial, sagittal and coronal planes. Post contrast fat-suppressed T1-weighted images was performed in selected cases.

**Results:**

The commonest non-traumatic causes of heel pain were plantar fasciitis in 7/20 cases (35%) followed by tendon & bursal lesions in 6/20 cases (30%), then osseous & compartmental lesions in 4/20 cases (20%) and finally musculoskeletal neoplasm in 3/20 cases (15%). The MRI diagnosis were confirmed in all cases either by the clinical follow up after treatment in 15/20 cases (75%) or the surgical& pathological results in 5/20 cases (25%).

**Conclusions:**

Although not routinely indicated in patients with heel pain, MRI provides a versatile tool for establishing the diagnosis & assessing the severity of the disease in ambiguous or clinically equivocal cases. In patients requiring surgery, MRI is useful in planning surgical treatment by showing the exact location and extent of the lesion.

*Key Words: Heel pain; Imaging; Diagnosis*

*Funding Agency: None*

**Nuclear Medicine and Radiology***Category: Clinical***123****Evaluation of bone mineral density in post-menopausal women in Kuwait**\*Gupta R<sup>1</sup>, Al-saeed O<sup>2</sup>, Azizieh F<sup>3</sup>, Albusairi A<sup>4</sup>, Mohammed A<sup>5</sup><sup>1,2</sup>Department of Radiology, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Mathematics and Biology, Gulf University for Science and Technology, Kuwait; <sup>4</sup>Mubarak Al Kabir Hospital; <sup>5</sup>Department of Medical Education, Kuwait University**Introduction:**

Menopause is the major risk factor for loss of bone mineral density (BMD) in women. Age-related decline in bone mass probably begins around the age of 40. In women, bone loss accelerates around the time of menopause due to oestrogen deficiency. As a result of increase in the average life expectancy, prevalence of osteoporosis and related morbidity has been increasing around the world. The purpose of this study was to determine the prevalence of osteoporosis in post-menopausal women in Kuwait and compared it to that reported in other studies from the Middle-east and the West.

**Methods:**

A cross-sectional study comprising of 2, 296 postmenopausal women in Kuwait was performed. Age ranged from 40 to 87 years and divided into four age groups by decade. Body weight and height was measured using an electronic beam scale and a stadiometer, respectively. BMC and BMD was measured at total lumbar spine (L1-L4) and/or left hip using a Dual Energy X-ray Absorptiometry (DXA – Hologic QDR 4500A). The diagnosis of osteoporosis was done using T-score values according to WHO criteria

**Results:**

Bone Mineral Content (BMC) and hip and spine BMD significantly decreased with age,  $p < 0.0001$ . Among the 2296 women, 444 (19.3%) showed osteoporosis, which is lower than in Saudi (40%) and Moroccan women (39.6%) and higher than in US/European (31%) and Lebanese women (11%). The number of osteoporosis cases significantly increased with age,  $p < 0.0001$ , and was highest among the normal BMI group (39.1%) ( $p < 0.0001$ ). 22.6% of those who found to be osteoporotic were overweight and only 15% were obese. Most of women with normal BMD (42%) were obese, 25.2% were overweight, and 19.5% had normal BMI category ( $p < 0.001$ ). Kuwaitis and non-Kuwaitis did not show any statistically significant difference in BMI, BMD or T-scores.

**Conclusions:**

Our study showed 19.3% of postmenopausal women in Kuwait to be osteoporotic and 45.6% with low bone mass. To assess the prevalence of osteoporosis in Kuwait, a national database is needed to develop national standardized reference curves in order to design the prevention and treatment of the osteoporosis.

*Key Words: Osteoporosis; Post-menopausal women; Kuwaiti women**Funding Agency: None*



**Nuclear Medicine and Radiology**

Category: Clinical

124

**Sonography of median nerve in a referred population of suspected CTS- Is it useful ?**

\*Ramachandran U, Dughbaj MI, Ramar S

Physical Medicine & Rehabilitation Hospital, Ministry of Health, Kuwait

**Introduction:**

Carpal Tunnel Syndrome (CTS) is the most common entrapment neuropathy seen in physiatric practice. Diagnosis of CTS is made by a combination of classical symptoms and positive provocative tests confirmed by electrodiagnosis. Ultrasound imaging of the carpal tunnel is increasingly gaining attention as a cheaper, less time consuming and less invasive modality for the diagnosis of CTS. The aim of the study is to assess the usefulness of sonographic measurements of median nerve cross sectional areas (CSA) in the diagnosis of CTS among a referred population of patients.

**Methods:**

The data of 47 patients (84 symptomatic hands) were collected and analysed from the electrodiagnostic and ultrasonographic labs of Physical Medicine and Rehabilitation hospital, Kuwait.

**Results:**

Symptomatic hands were grouped by electrodiagnosis as normal - 9 (10.7%), mild - 29 (34.5%), moderate - 26 (31.0%), and severe - 20 (23.8%). There were significant correlations between CTS grades by electrodiagnosis and sonographic measurements of CSA of median nerve at inlet ( $r_s=0.360$ ,  $p=0.001$ ), (tunnel  $r_s=0.439$ ,  $p<0.001$ ), outlet ( $r_s=0.405$ ,  $p<0.001$ ) and the mean of the three CSAs ( $r_s=0.430$ ,  $p<0.001$ ). Also, significant differences were observed between the four CTS groups in each CSAs. Using electrodiagnosis as the reference standard, the highest area under the curve was for outlet - 0.75 ( $p=0.013$ ); followed by mean - 74 ( $p=0.021$ ); inlet - 0.72 ( $p=0.030$ ); and tunnel - 0.71 ( $p=0.045$ ). A value of  $<8.5 \text{ mm}^2$  for the mean cross sectional area showed a negative LR of 0.09 and  $>12.3 \text{ mm}^2$  showed a positive LR of 4.08.

**Conclusions:**

Electrodiagnosis would be a more sensitive test than sonography in early mild cases whereas sonography would be more likely to diagnose moderate and severe cases when structural changes occur in median nerve. The findings need to be validated by further prospective studies including healthy controls.

*Key Words: Electrodiagnosis; Sonography*

*Funding Agency: None*



**Nuclear Medicine and Radiology**

Category: Clinical

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**Comparison of different techniques for assessment of thyroid functional status in patients with hyperthyroidism**

\*<sup>1,2</sup>Siraj QH, <sup>2</sup>Renilson S, <sup>2</sup>Masoomi M, <sup>1</sup>Afzal U, <sup>1</sup>Shammari I

<sup>1</sup>Department of Nuclear Medicine, Farwania Hospital, Kuwait; <sup>2</sup>Departments of Nuclear Medicine & Medical Physics, St. Mary's Hospital Portsmouth, UK

**Introduction:**

I-131 uptake is a established test for estimating thyroid activity diagnostically and prognostically prior to I-131 therapy. Tc-99m thyroid scan is performed in hyperthyroid patients to help diagnose the underlying pathology visually and through quantitation of thyroid activity by uptake parameters such as Tc-99m uptake index or by using a simple thyroid/background ratio. In this pilot study, the Tc-99m uptake parameters were compared with the 24-hr I-131 uptake in hyperthyroid patients to compare their relative sensitivity in the assessment of thyroid overactivity and also to investigate the potential relevance of thyroid uptake parameters for radioiodine therapy dose planning.

**Methods:**

The report includes retrospective data from a total of 192 patients investigated at the nuclear medicine departments of the Farwania Hospital Kuwait and the St. Mary's Hospital Portsmouth. The 3 radionuclide quantitative parameters were correlated with serum T4.

**Results:**

The correlation between serum T4 and the 24-hr I-131 uptake was statistically significant ( $r$  0.29,  $p$  0.007) but quite low ( $r^2$  0.08). There was good correlation between serum T4 and the thyroid/background ratio ( $r$  0.53,  $p < 0.0001$ ,  $r^2$  0.28). The correlation between serum T4 and the pertechnetate uptake was the highest ( $r$  0.63,  $p < 0.0001$ ,  $r^2$  0.40). There was good correlation between the 24-hour I-131 uptake and the pertechnetate uptake ( $r$  0.37,  $p$  0.0004,  $r^2$  0.13). However, a higher correlation was seen between the 24-hour I-131 uptake and the thyroid-to-background ratio ( $r$  0.63,  $p < 0.0001$ ,  $r^2$  0.40).

**Conclusions:**

Quantitative thyroid scintigraphic uptake parameters are superior to the 24-hour I-131 uptake test for the assessment of thyroid function. Technetium uptake is the most reliable quantitative parameter for the assessment of thyroid function and may be substituted for the radioiodine uptake test in the majority of patients for the pre-radioiodine therapy assessment of hyperthyroid patients.

*Key Words: I-131 uptake; Tc-99m thyroid scan; Technetium uptake*

*Funding Agency: None*

**Obstetrics and Gynecology***Category: Clinical***126****Diagnostic identification of ambiguous external genitalia before gender assignment.**\*Al-Jassar W<sup>1,3</sup>, Hammoud M<sup>2,4</sup>, Fouad M<sup>4</sup>, Al-Azemi MK<sup>1,3</sup>, Omu AE<sup>1,3</sup><sup>1</sup>Department of Obstetrics and Gynaecology; <sup>2</sup>Departments of Pediatrics, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Obstetrics and Gynaecology; <sup>4</sup>Departments of Neonatology, Maternity Hospital, Kuwait**Introduction:**

The neonate with disorder of sex development presents a difficult diagnostic and treatment to the clinician. Objective of the study: To evaluate a strict surveillance and clinical evaluation of ambiguous external genitalia before gender assignment.

**Methods:**

In this retrospective study all babies delivered at the Maternity Hospital during the study period (January 1, 2008 to December 3, 2011), were examined for disorders of sex development (DSD) in the form of ambiguous external genitalia, defined as external genitalia that are undifferentiated or discordant with the genotype. The abnormalities included penile and clitoral organs, absence of testes in the scrotal sac, pudendum, hypospadias and palpable testes in the inguinal canal. In addition to physical evaluation, investigations carried out included; Karyotype and determination of SRY gene, hormone profile, serum chemistry and electrolytes, androgen receptor levels, 5  $\alpha$  reductase type II levels and Ultrasonography.

**Results:**

During the four year study period, there were 32 neonates with ambiguous external genitalia out of 41, 676 deliveries, thus giving and incidence of 0.8 per a thousand births. Of the 32, 20 (62.5%) were 46 XY DSD, 10 (31.3%) were 46 XX DSD and 2 (6.2%) were mixed. Main locations of the testes in 46 XY DSD were inguinal canal in 90% and intra-abdominal 10%. Penoscrotal hypospadias occurred in 60% and chordee in 20 percent. One neonate had 46 XY genotype, SRY gene positive, enlarged clitoris, fused labia minora, presence of uterus by ultrasound but no ovaries and no testes and low androgens (probably pure gonadal dysgenesis (Swyer's Syndrome). 46 XY DSD was more commonly associated with renal anomaly such as hydroureter and hydronephrosis, urogenital sinus (2) and renal pelviectasia, than 46 XX DSD.

**Conclusions:**

Detailed clinical evaluation of neonates is mandatory before gender assignment as carried out in the present study.

*Key Words: Ambiguous External Genitalia; Evaluation; Gender Assignment**Funding Agency: None*



**Obstetrics and Gynecology**

Category: Clinical

127

**The role of intravenous immunoglobulin in the management of recurrent spontaneous miscarriage (RSM)**

Al-Jassar W<sup>1,2</sup>, Al-Shamali P<sup>2</sup>, \*Diejomaoh FME<sup>1,2</sup>, Al-Qenae M<sup>2</sup>, Bello Z<sup>2</sup>, Mohammed AT<sup>1</sup>.

<sup>1</sup>Dept of Obs and Gynae, Faculty of Medicine, Kuwait University; <sup>2</sup>Dept of Obse and Gynae, Maternity Hospital, Kuwait.

**Introduction:**

Previous trials with intravenous immunoglobulin [IVIG] in Recurrent Spontaneous Miscarriage [RSM] have yielded conflicting results: some trials reported improved pregnancy outcome in secondary RSM, others reported no benefits for IVIG therapy in RSM, while some authors have suggested a limited role for such therapy. The objective of our study was to evaluate the outcome of pregnancy in patients with RSM treated with IVIG.

**Methods:**

All the patients admitted for treatment with IVIG at Maternity hospital, January-December, 2010, were identified and their records were analyzed in detail. The social biodata, the past obstetric and gynaecological/medical/surgical histories were extracted and the diagnostic tests, indications and the dosage regimes for IVIG for the index pregnancy were recorded. The course/outcome of the pregnancies were established.

**Results:**

Forty seven patients received IVIG during the study period but only 36 case files were available for review and form the basis of this study. The mean age and parity of the study population were 33.28±5.311 and 1.60±1.958 respectively. 10 out of the 36 cases were diagnosed as Rhesus iso-immunization and 26, RSM; 65.4% of the RSM patients presented as secondary, and 34.6%, primary RSM. 76.9% of the miscarriages occurred in the first trimester. 92.3% of all patients received their initial IVIG dose in the first trimester. The pregnancies ended again in miscarriages in 34.6%, BUT progressed to preterm/term deliveries of living babies in 65.4%; the positive pregnancy outcome achieved using IVIG was double the rate of pregnancy loss, and significantly higher, P, <0.001. No significant adverse reactions were recorded in the patients treated with IVIG.

**Conclusions:**

The use of IVIG in RSM resulted in a favourable pregnancy outcome and has a positive role in RSM and it should be offered to selected patients with RSM.

*Key Words: Recurrent Spontaneous Miscarriage (RSM); Pregnancy Outcome; Intravenous Immunoglobulin[IVIG]*

*Funding Agency: None*



**Obstetrics and Gynecology**

Category: Clinical

128

**Does intra-uterine growth restriction have a pro-inflammatory cytokine bias?**

\*Azizieh F<sup>1</sup>, Al-Azemi M<sup>2</sup>, Raghupathy R<sup>3</sup>

<sup>1</sup>Department of Mathematics and Biology, Gulf University for Science and Technology, Kuwait; <sup>2</sup>Department of Obstetrics & Gynecology, Faculty of Medicine, Kuwait University;

<sup>3</sup>Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

Intrauterine growth restriction (IUGR) is an important perinatal syndrome that presents several serious short- and long-term problems for the fetus and neonate. A definite cause is still unknown in about 40% of cases of IUGR; in addition to known genetic and constitutional causes, it would be appropriate to investigate maternal immunologic reactivity that may lead to IUGR with and without placental insufficiency. With this objective in mind, we studied cytokine production by maternal peripheral blood lymphocytes stimulated by trophoblast antigens.

**Methods:**

36 women with a diagnosis of IUGR (19 women with placental insufficiency, 17 without placental insufficiency) and 22 healthy control pregnant women with normal fetal growth were included. Peripheral blood mononuclear cells were stimulated with trophoblast antigens and levels of the pro-inflammatory cytokines IL-6, IL-8, IL-12, IL-23, IFN- $\gamma$  and TNF- $\alpha$  and the anti-inflammatory cytokines IL-4, IL-10 and IL-13 were measured in culture supernatants by ELISA.

**Results:**

The pro-inflammatory cytokine IL-8 was produced at higher levels by peripheral blood cells of the IUGR group than normal pregnant women, while IL-13, an anti-inflammatory cytokine, is produced at lower levels. The pro-inflammatory cytokines IL-8, IFN- $\gamma$  and TNF- $\alpha$  were higher in IUGR with placental insufficiency than in normal pregnancy. IL-12 levels were higher and IL-10 levels were lower in IUGR with placental insufficiency than in IUGR without placental insufficiency.

**Conclusions:**

Our results are indicative of a stronger pro-inflammatory bias in IUGR as compared to normal pregnancy, and also in IUGR with placental insufficiency as compared to IUGR without placental insufficiency. The elucidation of possible immunological mechanisms underlying the pathogenesis of IUGR may lead to the development of regimens that improve fetal growth and development.

*Key Words: Cytokines; Placental insufficiency*

*Funding Agency: Kuwait University Research Grant No MI02/05.*



**Obstetrics and Gynecology**

Category: Clinical

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**Modern trend and determinants of multiple pregnancy in Kuwait**

\*Bello Z, Al-Jassar W, Al-Azemi MK, Rumaiah H, Omu AE

Departments of Obstetrics and Gynaecology, Maternity Hospital; Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

The rate of multiple pregnancy is increasing worldwide as a result of assisted reproductive technology (ART). In the Western countries, this surge seems to be slowing, but the situation in Kuwait is not known. Aim of the study: To evaluate the trends and determinants of multiple pregnancy at the Maternity Hospital of Kuwait.

**Methods:**

This is retrospective study evaluating all multiple pregnancies delivered at the Maternity Hospital, during a three year period from January 2009 and till December 2011. Patient files were scrutinised after delivery, and data extracted included biodata, whether pregnancy was spontaneous, induced or through ART, antenatal complications, mode of delivery and perinatal mortality. For statistical analysis Excel version 17 was used.

**Results:**

During the study period, there were 828 multiple pregnancies out of 29, 854 total deliveries; a multiple pregnancy rate of 27.7 per 1000 pregnancies. Spontaneous multiple pregnancies occurred in 384, at a rate of 12.9 per 1000, while ART included were 444 (58%) with a rate of 53.6 per 1000. There were 704 (85%) twin pregnancies, 109 (13.2%) triplets and 15 (1.8%) quadruplets. More ART pregnancies had prenatal complications like miscarriage, pregnancy induced hypertension, intrauterine death of one twin, triplet or quadruplet ( $P<0.01$ ,  $P<0.05$ ), preterm delivery ( $P<0.01$ ) and delivery by cesarean section ( $P<0.01$ ). Perinatal mortality and admission to NICU were more common with multiple pregnancy from ART than those from spontaneous pregnancy after adjusting for triplets and quadruplets.

**Conclusions:**

Multiple pregnancies following ART is common in Kuwait, with associated prenatal and fetal complications.

*Key Words: In-vitro fertilization; Multiple Pregnancy; Spontaneous*

*Funding Agency: None*



## ***Obstetrics and Gynecology***

Category: Clinical

130

### **Low-lying placenta to placenta praevia: Many rivers to cross.**

\*Omu AE<sup>1,2</sup>, Jassar W<sup>1,2</sup>, Jirous J<sup>1,2</sup>, Assem T<sup>1</sup>, Duwaisan W<sup>1</sup>, Mohammed AA<sup>1</sup>, Mohammed F<sup>1</sup>.

<sup>1</sup>Department of Obstetrics and Gynaecology, Maternity Hospital; <sup>2</sup>Faculty of Medicine, Kuwait University, Kuwait.

#### **Introduction:**

Placenta praevia is abnormal implantation of the placenta below the fetal presenting part. It is associated with maternal and perinatal mortality and morbidity. Given the increasing incidence of cesarean section along with assisted reproductive technology, there may be increase in the incidence of Placenta praevia.

#### **Methods:**

All women in whom the ultrasound scan at 18-22 weeks of gestation revealed the placenta lying low in the uterus below the fetus form the subjects of this study. The last ultrasound just before delivery whether preterm or at full term, now called placenta praevia. The risk factors of placenta praevia were identified. The obstetric outcome was documented. Statistical analysis: Data was analyzed with Excel version 17. Ultrasound scan at 18-22 was compared to that before delivery.

#### **Results:**

There were 1522 women with low-lying placenta at 18-22 weeks of gestation but 361 had placenta praevia at delivery. Risk factors identified included previous cesarean section, previous miscarriages, post-myomectomy, multiple pregnancy and In-vitro fertilization. About 24 percent of the women that had low-lying placenta had placenta praevia at delivery. Significantly more patients with previous cesarean section had placenta praevia, Placenta centralis and placenta accreta followed by post myomectomy compared to those without risk factors ( $P < 0.01$ ). Previous cesarean section was also associated with cesarean hysterectomy.

#### **Conclusions:**

Previous cesarean is significantly associated with severe placenta praevia and complications necessitating cesarean hysterectomy. This information should be used in pre-operative counseling of patients.

*Key Words: Cesarean section; Complications; Placenta praevia*

*Funding Agency: None*



## **Oncology**

Category: Clinical

131

### **Treatment of early stage classic Hodgkin's lymphoma outcome: A population based study: Kuwait experience.**

AlShemmari SH<sup>1</sup>, \*Elhagracy RS<sup>2</sup>, Elbassmy A<sup>3</sup>

<sup>1</sup>Department of Medicine, Kuwait University; <sup>2</sup>Medical Oncology Department, Lymphoma Division, Kuwait Cancer Control Center, <sup>3</sup>Cancer Statistics & Registry Department, Kuwait Cancer Control Center

#### **Introduction:**

Treatment of early stage classical Hodgkin's lymphoma (CHL) is changing targeting cure with minimal toxicity; ABVD is the mainstay chemotherapy (CT) with or without radiotherapy (RT).

#### **Methods:**

Retrospectively we evaluated treatment outcome and prognostic factors for early stage I&II CHL treated in KCCC 2001-2010. Data was analyzed using t-test and Chi2 test to test association between quantitative and qualitative variables respectively, survival analysis performed by Kaplan-Meier curve and Cox regression model for regression analysis. The study included 105 patients; divided to group A: 34 cases treated with 4 cycles and group B: 71 cases treated by 6 cycles ABVD with or without RT.

#### **Results:**

Nodular sclerosis accounted for 66.6% of cases. Group B had significant more stage II, B symptoms, higher platelets, ESR, total leukocyte count & lower albumin. RT offered to 60 cases (28 in A and 32 in B). Remission achieved in 84 (80%) cases, 82.2% vs 76.1% among group A vs B without significance difference. High dose chemotherapy and ASCT served to 13 patients, 7 with relapse and 6 with progressive/residual disease.

The 5-years survival rate was 86%; without significant difference between the two groups ( $p=0.51$ ). Cases with B symptoms had lower 5-years survival 73% compared to those without B symptoms 92% ( $p=0.02$ ). Lower 5-years survival noted in patients with bulky disease (77%) and  $ESR \geq 50$  mm/hr (82%) compared to those without bulky disease (89%) and  $ESR < 50$  mm/hr (89%); without statistical significance difference ( $p=0.1$  vs  $0.5$  respectively). There was no 5-years survival difference between treatment with combined modality or with CT only. On mean 5-years follow up (12-108 months), no cardiopulmonary toxicities were noted.

#### **Conclusions:**

Treatment outcome of early stage CHL is generally good; 4 vs 6 cycles had near same outcome. CT alone is equal to CT and RT outcome. Presence of B symptoms, high ESR and bulky disease can guide treatment as prognostic indicators.

*Key Words: Radiotherapy; ABVD*

*Funding Agency: None*



**Oncology**

*Category: Clinical*

132

**Profile of langerhans cell histiocytosis (LCH) cases in Kuwait: A study from pediatric oncology unit of KCCC**

\*Bedir R, Mittal R, Khalifa N, Khalifa S

Kuwait Cancer Control Centre

**Introduction:**

Langerhans Cell Histiocytosis (LCH) is due to clonal proliferation of abnormal cells from bone marrow derived langerhans cells. It is a rare disease with annual incidence ranging from 0.5-5.4 cases per million cases. It can affect children at any age group, including neonates and adolescents. Clinical presentation of LCH depends on the location and extent of dissemination of the disease. The course of the disease is unpredictable, varying from spontaneous regression and resolution to rapid progression and death, or recurrence.

**Methods:**

This is a retrospective study, in which we analyzed the data of all patients, who presented with diagnosis of LCH to pediatric oncology unit, over a 10 years period. During this period a total of 23 new cases of LCH were registered. They presented with a variety of symptoms and signs, and most of them received standard treatment.

**Results:**

The male- female ration was 3: 1. Median age was 7 years (range 2.5 months to 14 years). Nearly 60% patients had bony lesions (single or multiple), 17% had risk organ involvement, 13% with lymph nodes involvement and 9% had skin involvement. For treatment, 18 patients received chemotherapy alone, 3 were treated with curettage only and 2 were treated with curettage followed by chemotherapy. 74% of the treated patients achieved complete remission, 4.3% had partial remission, 4.3% had disease progression, 8.7% were lost to follow up, and 8.7% died. Disease reactivation occurred in 21.7% patients. Diabetes Insipidus occurred in 3 children, one at presentation and 2 after one year of treatment. At last follow up 18 patients were in complete remission & one patient is on treatment for relapse.

**Conclusions:**

LCH is a rare disease of childhood. It presents in variety of ways which can lead to delayed diagnosis. Although LCH is not strictly a cancer, it is usually treated with chemotherapy. If treated properly, overall prognosis is very good.

*Key Words: LCH; Histiocytosis; Childhood Cancer*

*Funding Agency: None*



**Oncology**

Category: *Clinical*

133

**Children with Down syndrome and leukemia in Kuwait**

\*Bourusly M<sup>1</sup>, Mourad<sup>1</sup>, Mustafa NY<sup>2</sup>, Al-Sharida S<sup>3</sup>, Mullah- Ali A<sup>1</sup>

<sup>1</sup>Department of Hematology, National Bank of Kuwait, Sabah Hospital, Kuwait; <sup>2</sup>Department of Pediatrics, Faculty of Medicine, Kuwait University; <sup>3</sup>Pediatric Hematology Unit, Mubarak Hospital

**Introduction:**

Children with Down syndrome are at a greater risk to develop leukemia. In this study we look at the morbidity and mortality of all children with Down syndrome and leukemia, since the establishment of the NBK hospital in Kuwait.

**Methods:**

This is a retrospective study of 20 children with Down syndrome leukemia who were seen at NBK pediatric hematology and oncology department, Sabah hospital, since it was open in 2001.

**Results:**

There was a total of 20 patients with Down syndrome, and diagnosed with leukemia during the last 10 years. Eleven were males and 9 were females. Eleven patients were Kuwaiti and the rest from different nationalities. Seven were suffering from congenital heart diseases, and 6 had bronchial asthma. There were 12 patients who had acute lymphoblastic leukemia ALL, and 8 had acute myloid leukemia AML. Most of the patients received the British chemotherapy protocols; however, 10 received half the required dose of chemotherapy. Most patients completed chemotherapy within 4 years, and went on remission after the initial induction. Most patients suffered from many complications during the course of treatment, such as pancytopenia and febrile neutropenia. Twelve patients remained cancer free up till now, however the rest had one or more relapses, majority of which were hematological. One patient underwent BMT and is doing well. Today 14 patients are alive, and 5 have passed away - all with ALL ( $p < 0.04$ ). Mortality was attributed to sepsis or pneumonias. There was a history of cancer in the family of 3 patients. Mortality was higher in patients with other medical problems ( $p < 0.014$ ). Cytogenetics played no role in the mortality ( $p < 0.495$ ).

**Conclusions:**

Children with Down syndrome are more at risk of leukemia. Down syndrome children with ALL carried worse prognosis than Down syndrome children with AML. Children with additional medical problems are at greater risk for complications and death.

*Key Words: Down syndrome; Acute lymphoblastic leukemia; Acute Myloid leukemia*

*Funding Agency: None*



**Oncology**

Category: Basic Sciences

134

**Differential effect of growth factors on invasion and proliferation of endocrine resistant breast cancer cells**

\*Khajah M<sup>1</sup>, Al Saleh S<sup>2</sup>, Luqmani Y<sup>3</sup>

<sup>1</sup>Department of Applied Therapeutics, Faculty of Pharmacy, Kuwait University; <sup>2</sup>Department of Pathology, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University

**Introduction:**

We have established several breast cancer cell lines that exhibit a permanent ER-depleted phenotype, induced by shRNA transfection of MCF7 cells, which afford a useful model system for studying acquired endocrine resistance. We previously showed that MDA231 and ER-silenced cells (pII) were able to invade through simulated extracellular matrix components. However, the contribution of individual serum components responsible for cell invasion was not determined.

**Methods:**

We used the under-agarose gel assay to quantitatively examine the invasive movement of two ER-silenced cell lines established in this laboratory (pII and YS2.5) in comparison to MDA231, the parental MCF7 and HBL100 cells, as well as a line that was ER-shRNA transfected but failed to exhibit ER down-regulation (YS1.2). In addition, we examined the effect of the growth factors EGF, IGF-1, TGF $\beta$  and RANTES on pII cell invasion and proliferation.

**Results:**

All breast cancer cell lines which had reduced ER expression exhibited a serum-dependent invasive ability that was related to the degree of induced ER loss. TGF $\beta$  treatment resulted in significant inhibition of pII cell proliferation and enhanced their invasive ability but at a relatively high dose. IGF-1 and EGF treatment resulted in similar effect on enhancing pII cell proliferation with the latter playing the major role in enhancing pII cell invasion. Targeting membrane receptor tyrosine kinase activity by imatinib resulted in significant inhibition of pII cell proliferation and invasion.

**Conclusions:**

Both de novo and siRNA induced reduction of ER expression is directly associated with enhanced cell invasion. TGF $\beta$  plays a major role in inhibiting cell proliferation, whereas IGF-1 and EGF, the latter plays a dominant role in cell invasion. Imatinib treatment significantly reduced the rate of pII cell proliferation and invasion suggesting its potential therapeutic usefulness for preventing spread of endocrine resistant breast cancer.

*Key Words: Breast Cancer; Endocrine Resistance; Growth Factors*

*Funding Agency: None*



**Pathology**

Category: Clinical

135

**Interleukin -18 upregulates serum matrix metalloproteinase -2 and tissue inhibitor of metalloproteinase -1 and is associated with fibrosis in patients with chronic hepatitis**

Abdeen S, \*Olusi SO, George S

Department of Pathology, Faculty of Medicine, Kuwait University

**Introduction:**

The exact mechanism by which activated hepatic stellate cells [HSCs] regulate the production of matrix metalloproteinases [MMPs] and their tissue inhibitors [TIMPs] in hepatic fibrosis is not fully known. In this study, we postulated that IL-18 may upregulate serum MMP-2 and TIMP-1 in different proportions in order to promote fibrogenesis in the liver.

**Methods:**

To test this hypothesis, we estimated the serum concentrations of IL-18, MMP-2, TIMP-1 in 56 patients with chronic hepatitis C [HCV], 28 with hepatitis B [HBV], 16 with non-alcoholic steatohepatitis [NASH] and 100 healthy controls using commercially available ELISA Kits. The METAVIR activity and fibrosis scores from the patients were determined histologically. Appropriate statistical methods were used to determine the relationships among these serum markers.

**Results:**

Serum IL-18 concentrations were significantly higher among HCV, HBV and NASH patients than in healthy controls. IL-18 increased in patients with no fibrosis [397.46 ±73.54 pg/ml] to [1384.11± 526.60 pg/ml] in patients with cirrhosis. IL-18 serum concentration was able to separate patients with cirrhosis from those with no fibrosis. Although IL-18 upregulated serum MMP-2 concentrations minimally throughout the period of fibrosis from 199.48±18.62 ng/ml at F0 to 225.25±14.75 ng/ml at F4, the upregulation of TIMP-1 was about double from 225.25±14.75 ng/ml at F0 to 500.77±30.500 ng/ml at F4. The relatively higher increase in TIMP-1 was necessary to promote fibrogenesis in the liver.

**Conclusions:**

IL-18 and TIMP-1 may be more important than MMP-2 in hepatic fibrogenesis.

*Key Words: Interleukin -18; Fibrosis; Hepatitis*

*Funding Agency: None*



**Pathology**

*Category: Clinical*

136

**Immunopositive aldosterone receptor hepatic stellate cell count: A novel method for assessing hepatic fibrosis in patients with chronic hepatitis**

\*Abdeen SM<sup>1</sup>, Olusi SO<sup>1</sup>, Askar HA<sup>2</sup>, Al-Azemi AE<sup>3</sup>, Saji T<sup>1</sup>, George S<sup>1</sup>

<sup>1</sup>Faculty of Medicine, Department of pathology, Kuwait University; <sup>2</sup>Ministry of Health Amiri Hospital; <sup>3</sup>Ministry of Health Mubarak Hospital.

**Introduction:**

Among the many mediators that take part in hepatic tissue remodeling during liver fibrosis, the components of the renin angiotensin system (RAS) are progressively assuming an important role. The objectives of this study were to find out if aldosterone receptors could be demonstrated immunohistochemically in liver biopsies from patients with chronic hepatitis and if immunopositive aldosterone receptor hepatic cell count correlated with METAVIR inflammatory and fibrosis scores.

**Methods:**

Ninety six liver biopsies were obtained from patients with chronic hepatitis. The METAVIR inflammatory and fibrosis scores were determined independently by two histopathologists unaware of the diagnosis. Immunohistochemical labeling for aldosterone receptor was performed on the biopsy specimens using monoclonal aldosterone receptor antibody from DAKO. The immunopositive aldosterone receptor cells were identified and counted. The serum concentration of aldosterone from the patients was measured by radioimmunoassay. Statistical methods were used to find out if there were any correlations among the different variables.

**Results:**

Immunopositive aldosterone receptors were identified only on hepatic stellate cells (HSC). Immunopositive aldosterone receptor HSC count was found to be positively associated with METAVIR inflammatory scores ( $r = 0.703$ ,  $p < 0.001$ ) and fibrosis scores ( $r = 0.446$ ,  $p < 0.001$ ). The count was able to distinguish among F0 (no fibrosis) and F3 and F4 fibrosis, but not among F0 and F1 and F2.

**Conclusions:**

We concluded that immunopositive aldosterone receptor HSC count could be a new additional tool for assessing hepatic fibrosis most especially cirrhosis.

*Key Words: Aldosterone receptors; Hepatic Stellate Cells; Chronic liver diseases*

*Funding Agency: None*



**Pathology**

Category: Clinical

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**Incidental parathyroidectomy during thyroid surgery: Incidence and risk factors**

\*Al-Ajmi S<sup>1</sup>, Al-Brahim N<sup>2</sup>, Sharma PN<sup>3</sup>

<sup>1</sup>Department of Surgery, Farwaniya Hospital; <sup>2</sup>Department of Pathology, Farwaniya Hospital; <sup>3</sup>Faculty of Medicine, Health Sciences Center, Kuwait University

**Introduction:**

Thyroid surgery is quite prevalent in Kuwait hospitals. Despite advances in surgical techniques, this surgery continues to be associated with complications, such as parathyroid resection and recurrent laryngeal nerve injury. This study aimed at (1) determining the incidence of incidental parathyroidectomy during thyroid surgery; and (2) identifying the predictive risk factors for incidental parathyroid resection.

**Methods:**

The electronic files of Department of Pathology, Farwaniya hospital, were screened for thyroidectomy procedures for the last eight years, from 2003 onwards to 2011. The pathology reports were reviewed for age, gender, underlying thyroid pathology, and type of thyroid surgery. In addition, the reports were also carefully examined for presence of incidental parathyroid resection, number of parathyroid and the presence of parathyroid pathology. The statistical analysis was carried out using SPSS V.19.0 computer software.

**Results:**

(n=314) thyroidectomy procedures were identified, which included 241 (76.8%) female patients. Of these, 61 (19.4%) procedures were Incidental parathyroid resections cases, with mean age as 38.6 ( $\pm$  10.1 SD) years, and M: F ratio as 1: 6.6. All resection parathyroids were normal except, one case of adenoma. Logistic regression analysis revealed females and underlying thyroid malignancy to be the statistically significant risk factors for parathyroidectomy ( $p=0.017$ , OR=2.7) and ( $p=0.001$ , OR=3.3), respectively. Age and type of thyroid surgery were not the risk factors for incidental parathyroidectomy, though higher proportion of total thyroidectomy were found (55.7% vs 42.1%) among incidental parathyroid than any other thyroidectomy cases.

**Conclusions:**

Incidental parathyroid resection during thyroid surgery is not uncommon (19.4%), and is comparable to published data in the literature. Females and underlying thyroid malignancy were found to be the risk factors associated with unintentional parathyroid resection.

*Key Words: Incidental parathyroidectomy; Thyroidectomy; Risk factors*

*Funding Agency: None*



**Pathology**

Category: Graduate (Resident)

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**Correlation of alanine aminotransferase with lipid profile and ultrasonographic findings in Kuwaiti lipid clinic patients**

\*AlAnjeri AKH<sup>1</sup>, Gupta R<sup>2</sup>, Mojiminiyi OA<sup>1</sup>, Chavan VNK<sup>2</sup>, Nampori P<sup>3</sup>

<sup>1</sup>Clinical Biochemistry Laboratory, Mubarak AlKabeer Hospital, Ministry of Health; <sup>2</sup>Department of Radiology, Mubarak AlKabeer Hospital, Ministry of Health; <sup>3</sup>Department of Pathology, Kuwait University, Faculty of Medicine

**Introduction:**

Nonalcoholic fatty liver disease (NAFLD) is the most common disease associated with abnormal liver test. Its diagnosis requires the demonstration of fat in liver by either imaging study or liver biopsy. We hypothesize that circulating alanine aminotransferase (ALT) concentration will increase as the degree of hepatic fat accumulation increases. This study aimed to identify the association of ALT with Ultrasonographic findings in Kuwaiti lipid clinic patients who are likely to have fatty liver change.

**Methods:**

78 Kuwaiti lipid clinic patients (42 men and 36 women) were enrolled. Their anthropometric parameters, chemistry profile and abdominal ultrasounds (US) were analyzed. Comparisons between males and females were performed with independent sample T test. Pearson correlation coefficient was used to describe the association between serum ALT and other variables of interest. A p-value < 0.05 was considered statistically significant.

**Results:**

ALT showed significant positive correlations with height, weight (WT), and triglyceride (TG) and an inverse correlation with high density lipoprotein cholesterol. TG showed significant correlations with all the variables, except the low density lipoprotein cholesterol. 55 (70.5%) patients showed US finding suggestive of fatty liver disease. Gender related differences were noticed in ALT and TG. The increase of severity of fatty infiltration detected by abdominal US was significantly associated with increased ALT in men (p= 0.046) and increased TG in women (p= 0.002).

**Conclusions:**

This study has found a relatively high prevalence of NAFLD in our lipid clinic patients. In general, TG was a better determinant of fatty liver change than ALT and could be a useful marker of the presence of NAFLD.

*Key Words: Alanine aminotransferase; Lipid profile; Liver ultrasound*

*Funding Agency: None*



**Pathology**

Category: Graduate (Resident)

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**An audit of 25-hydroxyvitamin D testing**

\*AlAnjeri AKH

Clinical Biochemistry Laboratory, Mubarak Hospital, Kuwait

**Introduction:**

Vitamin D plays an important role in skeletal system. Recently, nonskeletal actions of vitamin D have been suggested. 25-hydroxyvitamin D (25(OH) D) measured in serum or plasma is considered the most reliable indicator for assessment of vitamin D status. Due to the increasing awareness of potential effects of hypovitaminosis D on health, the number of requested analyses increased substantially. This audit aimed to identify the number of 25(OH) D requests received from Mubarak hospital and Hawalli governate's polyclinics.

**Methods:**

Results of measurement for serum 25(OH) D in patients following in Mubarak hospital and polyclinics within Hawalli governate were collected over a month period.

**Results:**

A total of 2120 requests for 25(OH) D were received. Females are the main participants in our audit (81%). Most of 25(OH) D requests were for Kuwaiti patients (80%). Most of requests were sent from Sabah AlSalim (11.4%), AlSalam (10.8%), and Mahmoud Haider (9.3%) polyclinics. Endocrinology clinic (5.4%) is main source of requests sent from Mubarak's clinics.

**Conclusions:**

The measurement of 25(OH) D is becoming increasingly important and clinical demand has risen substantially. High-throughput analytical methods for 25(OH) D became desirable.

*Key Words: 25-hydroxyvitamin D; Hawalli governate polyclinics; Mubarak hospital*

*Funding Agency: None*



**Pathology**

Category: Basic Sciences

140

**Raf kinase inhibitor protein (RKIP) expression in diabetes**

\*Al-Ali W<sup>1</sup>, Al-Mulla F<sup>1</sup>, Thomas M<sup>2</sup>, Jucy JG<sup>3</sup>, Fathima A, Linu V<sup>4</sup>, Sunitha P<sup>3</sup>, Betty T<sup>3</sup>, Bitar MS<sup>4</sup>

<sup>1</sup>Department of Pathology, Kuwait University, Faculty of Medicine; <sup>2</sup>Department of Biological Sciences, Kuwait University, Faculty of Sciences; <sup>3</sup>Research Core Facility, Kuwait University, Faculty of Medicine; <sup>4</sup>Department of Pharmacology and Toxicology, Kuwait University, Faculty of Medicine

**Introduction:**

Raf kinase inhibitor protein (RKIP) is a member of the phosphatidyl ethanolamine-binding protein (PEBP) family. It was originally described as an inhibitor of Ras/Raf/MEK/ERK pathway. Dysregulation of RKIP expression has the potential to contribute to pathophysiological processes including Alzheimer's disease and several types of cancer. It has been believed that oxidative stress plays a role in the pathogenesis in a variety of diseases including cancer and diabetes mellitus. Recently, one study found knocking down RKIP gene in immortalized cell line increased the oxidative stress. This study is aimed to investigate the expression of RKIP in diabetes mellitus.

**Methods:**

Diabetic Goto-Kakizaki (GK) rats were used as a model for type 2 diabetes and diabetic Streptozotocin (STZ) rats were used as model for type 1 diabetes. All experimental rats were wounded surgically and left to heal for 7 days. Different tissues (liver, kidney, heart and wounded skin) were removed from all experimental rats. Various oxidative damage markers (dihydroethidium, DNPH, lipid peroxidation) and antioxidant enzymes (catalase, SOD, GSH) were used to verify the status of oxidative stress. RKIP expression was determined by western blot and immunofluorescent assay.

**Results:**

The results showed significant increase in the level of oxidative stress ( $p < 0.05$ ) in all tissues derived from both types of diabetic rats compared to non-diabetic controls. RKIP expression was significantly decreased in all tissues derived from diabetic-GK rats ( $p < 0.05$ ) compared to those of non-diabetic control rats. Meanwhile, diabetic-STZ rats showed no change in the expression of RKIP

**Conclusions:**

RKIP expression is clearly decreased in type 2 diabetic model while it has no change in type 1 diabetic model. Oxidative stress appears to have no effect on the expression of RKIP indicating that RKIP in diabetes may not be associated with oxidative stress.

*Key Words:* RKIP; Diabetes; Oxidative Stress

*Funding Agency:* None



**Pathology**

Category: *Clinical*

141

**Diverticular disease of the appendix: A clinico-pathological study of 25 cases**

\*Al-Brahim N<sup>1</sup>, Al-Kandari I<sup>2</sup>, Manahi M<sup>2</sup>

<sup>1</sup>Department of Pathology, Farwaniya Hospital; <sup>2</sup>Department of Surgery, Farwaniya Hospital

**Introduction:**

Diverticular disease of the appendix is a rare disease and estimated to be 0.5-2 % of appendectomies. Due to this low incidence, this disease is not well described in the literature. However, some authors claim its association with appendiceal mucinous neoplasms and carcinoid tumors. This study was conducted to 1) further characterize the clinical and pathological features of this disease in our population and 2) to determine the association of appendiceal neoplasms with diverticular disease of the appendix.

**Methods:**

The electronic files of Department of Pathology, Farwaniya hospital were screened for diverticular disease of the appendix in appendectomy specimens from 2003 onward to 2011. The histological slides were reviewed for the underlying diagnosis, number of diverticulae and associated pathological findings. In addition, the clinical charts of the patients were reviewed for clinical presentation, radiological examination and operative findings.

**Results:**

Twenty five case were identified 24 (96%) were male. The patients' age ranged (20-59). The clinical presentations were: abdominal pain (25), fever in (17) patients. The most common associated symptoms were nausea, vomiting and anorexia that were seen in (12/25). No associated diseases were noted. Ultrasound were preformed in 7 patients, none of them were able to identify the diverticulae by U/S. Pathological examination revealed the following diagnoses: 1) diverticulosis in 4 patients, 2) diverticulitis in 5, 3) diverticulosis with acute appendicitis in 6 and 4) diverticulitis and acute appendicitis in 10 patients. No other pathology was identified.

**Conclusions:**

1) Diverticular disease of the appendix is a rare disease and only 25 cases were diagnosed over 10 years period. 2) This disease is more prevalent in male patients. 3) The clinical presentation is typical of acute appendicitis symptoms. 4) Diverticular disease of the appendix in our study was not associated with any appendiceal neoplasms.

*Key Words: Diverticulosis; Diverticulitis*

*Funding Agency: None*



**Pathology**

*Category: Clinical*

**142**

**Fine needle aspiration cytology of papillary lesions of the breast**

\*Alath P<sup>1</sup>, Kapila K<sup>1,2</sup>, Jassar A<sup>1</sup>, Francis IM<sup>1,2</sup>

<sup>1</sup>Department of Pathology, Hussain Makki Al Juma Centre for Specialized Surgery, Kuwait; <sup>2</sup>Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

Papillary lesions of the breast range from non-neoplastic proliferative lesions to duct papilloma and invasive papillary carcinoma occurring in pure papillary form or admixed with infiltrating duct carcinoma. The aim of this study is to analyze the cytologic features observed in Fine Needle Aspirates (FNA) reported as papillary lesions and to correlate them with histopathologic findings.

**Methods:**

Over a period of six years (2006 to 2011), 4090 breast FNA and 242 nipple discharge (ND) were examined. Of these 42 cases were reported as papillary lesions (19 FNA, 17ND and 6 with both FNA and ND). Histological material was available in 16 cases ( 13 /19 with FNA alone and 3/6 patients with both FNA and ND ) which comprised the study group.

**Results:**

The age ranged from 12-68 years (mean 46.81). The left breast was involved in 10 cases and the right in 6. The size ranged from 0.6 cm to 5x4 cm. The cytological diagnosis on review categorized 3/16 as papillary lesion (PL) with atypia; 7/16 as papillary lesion without atypia; 4/16 as benign proliferative lesions (BPL) and two as suspicious for papillary carcinoma.. Seven of the PL without atypia were diagnosed as BPL (2 cases), papilloma (3 cases) and epithelial hyperplasia (2 cases). The two cases with suspicious cytology were diagnosed as epithelial hyperplasia and papilloma on histology.

**Conclusions:**

Overlap of cytologic features in neoplastic and non-neoplastic papillary lesions makes it very difficult in differentiating benign from malignant tumors or making a precise diagnosis. In our opinion all cases diagnosed as papillary lesions on cytology necessitate a histological evaluation.

*Key Words: Breast; Papillary lesions; Fine needle aspirates*

*Funding Agency: None*



**Pathology**

Category: Graduate MSc (Basic Science)

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**Handling of infanticide cases reported to Forensic Medicine Department, General Department of Criminal Evidence, Kuwait; Retrospective study**

\*Al-Kandary NM, Ebrahim NK

Department of Forensic Medicine, General Department of Criminal Evidence, Ministry of Interior, Kuwait.

**Introduction:**

Filicide, neonaticide, and infanticide are terms that have been used interchangeably in the literature to describe child homicide. Infanticide emerges as an increasingly prominent issue for a society as a whole. According to Kuwait statistics; in 2009 infant mortality rate reached 8.1 deaths/1, 000 live births. A thorough investigation must be carried to investigate the cause of death and exclusion of the probability of the crime is a must. This retrospective study was designed to investigate the reported medico-legal infanticide cases to the Forensic Department in Kuwait from year 2003 to 2006 and its correlation to infant mortality cases as a whole.

**Methods:**

A total of 220 reported infant death cases were referred for Medico-legal examination out of 1760 infant death cases received in Kuwait health organization centers during the period January 2003 through December 2006. Full review of the following data has been made including: clinical background, scene examination, radiographic investigations, complete autopsy study including histo-pathological examination. Definitions employed in this study were those previously used by WHO.

**Results:**

The results of this study have clearly demonstrated that infant death cases due to infanticide are limited mainly to non-Kuwaiti nationalities especially in house-maids. Infanticide claimed 18.8 % of the total reported medico legal cases in Kuwait between 2003 and 2006 compared to the other causes. The reported cases of infanticide increased from 31.6% of reported medicolegal cases of infant deaths in 2003 to 32% in 2006. In 2004 the rate decreased to 19% but it went up to 31.8 % in 2005.

**Conclusions:**

This study has illustrated the importance of a coordinated effort between Ministry of Health and Ministry of Interior in the medico-legal investigation of infant deaths in Kuwait. Several urgent steps should be taken to solve the issue of infanticide of which the most important is adequate postmortem examination.

*Key Words: Infanticide; Infant Mortality; Medico-legal Examination*

*Funding Agency: None*



**Pathology**

*Category: Basic Sciences*

**144**

**Insulin effect on early liver pathohistological and functional changes in diabetic rats**

\*Al-Waheeb S<sup>1</sup>, Al-Saeedi FJ<sup>2</sup>, Pariyani S<sup>2</sup>

<sup>1</sup>Pathology Department, Faculty of Medicine, Kuwait University; <sup>2</sup>Nuclear Medicine Department, Faculty of Medicine, Kuwait University.

**Introduction:**

Diabetes is a disorder of metabolism. This study was undertaken to investigate effects of insulin-administrations on hepatic histology and reticuloendothelial function, in diabetic rats.

**Methods:**

Diabetes was induced by streptozotocin (STZ, 55 mg/kg, ip). We had 3 groups of rats. Untreated (DM), insulin-treated (IDM) rats that received insulin (3 IU/kg) daily and controls that received saline injections. Sections of 1 mm<sup>3</sup> of liver tissue from sacrificed rats from each group were placed on glass slides, stained and examined by one pathologist using light and electron microscopy. The hepatic function was investigated using non-invasive technetium-99m-sulfur colloid (99mTc-SC) tracer imaging. Ratios of heart, liver and spleen to whole body were obtained following 99mTc-SC imaging. Student's t-test and ANOVA were performed to determine statistical significance.

**Results:**

There were no liver morphologic changes seen in the DM rats and the IDM rats compared to the control rats. Electron microscopic films showed severe vacuolization of the hepatocytes of DM rats. IDM rats show complete resolution of the vacuolization. The 99mTc-SC uptake ratios (mean±standard deviation) showed a decreased uptake-ratio in liver (0.75±0.05) with increased uptake ratios in heart and spleen in the DM rats compared to both controls (0.81±0.06) and IDM (0.81±0.02) rats (P=0.026).

**Conclusions:**

Insulin-administration to diabetic rats resolved their severe hepatocyte vacuolization to complete resolution and restored their hepatic reticuloendothelial function to normal, preventing liver histological and functional changes at 2 weeks of diabetes.

*Key Words: Liver scan; Diabetes*

*Funding Agency: None.*



**Pathology**

Category: Undergraduate

145

**Polysomy of chromosome 17: Its clinicopathological significance in breast cancer female patients in Kuwait**

\*Bakhsh F, Francis I, Al-Mulla F

Department of Pathology, Kuwait University, Faculty of Medicine

**Introduction:**

Amplification of HER-2/neu gene is one of the established prognostic marker leading to protein overexpression in 20-30% of breast cancer cases. A subset of breast carcinoma showed polysomy of chromosome 17 which is frequently encountered during the assessment of HER-2/neu status.

Hypothesis: The hypothesis of this study is that polysomy 17, as compared to HER-2/neu positive and HER-2/neu negative tumors, had a distinct impact on clinicopathological features in breast cancer and can be considered as a prognostic marker. We also hypothesized that polysomy 17 is an indirect mechanism of increasing HER-2/neu gene copy number that results in protein overexpression.

**Methods:**

Archival formalin fixed paraffin embedded blocks of 271 breast cancer cases were collected. Expression of ER, PR, Ki-67 and HER-2/neu were studied using immunohistochemical (IHC) method. FISH assay was used to determine HER-2/neu gene amplification.

**Results:**

The frequency of polysomy 17 was 13.6%. In contrast to HER-2/neu negative, polysomy 17 was associated with late stage tumor. Right side of the breast was found to be the most frequent side of the breast tumor in polysomic patients. Moreover, polysomy 17 differed from HER-2/neu positive in ER and PR status, which is associated with hormone receptor positivity. Patients with polysomy 17 found to have the shortest overall survival (OS) ( $P = 0.001$ ) and a trend toward shorter disease free survival (DFS). A highly significant association has been observed between polysomy 17 and HER-2/neu protein overexpression ( $P = 0.000$ ) with majority of patients had a score of 2+ by IHC.

**Conclusions:**

These results suggest that clinicopathological features of patient with polysomy 17 differed from patients with HER-2/neu positive and HER-2/neu negative tumors. We also showed that polysomy 17 have a significant biological influence on HER-2/neu protein overexpression and can be considered as a prognostic marker in breast cancer.

*Key Words: Polysomy 17; Breast Cancer*

*Funding Agency: Research Administration (YM 17/09)*



**Pathology**

*Category: Clinical*

**146**

**Pattern of motor vehicle accident fatalities in Kuwait: 2007-2010**

\*Elfawal MA<sup>1</sup>, Mahfouz N<sup>2</sup>

<sup>1</sup>Department of Pathology, Faculty of Medicine, Kuwait University; <sup>2</sup>Department of Forensic Medicine, General Department of Criminal Evidence, Ministry of Interior

**Introduction:**

Motor vehicle accident fatalities (MVAF) are an important cause of death that affects millions of people worldwide. In the past few decades, Kuwait has been known to have a high incidence of road fatalities. MVAF in the Eastern Mediterranean Region, which includes the GCC, have been recorded as the joint highest in the world.

**Methods:**

This study investigated the pattern of MVAF at the Department of Forensic Medicine, Ministry of Interior, Kuwait, from 2007 to 2010. Examination entailed investigation of the circumstances of the accident, demographic data, medical records, and complete postmortem examination with drug screening. All the data thus collected were statistically analyzed.

**Results:**

An annual mean of 12.4 per 100,000 MVAF occurred during the study period. The overall MVAF mortality rate declined slightly from 2007 to 2010 (13.5 and 11.3 per 100,000 population, respectively). Kuwaitis comprised 45.4% of the fatalities. Most MVAF (93.8%) occurred in men, showing a risk 15 times higher than women. Drivers aged 20–30 years (127; 31.7%) had the highest risk of death. The majority of main fatal injuries (164; 63.3%) were described in the head and most of the injuries involved vascular and skeletal tissues (159; 39.6%).

**Conclusions:**

This study has demonstrated that the pattern of MVAF is by and large similar to that reported in other parts of the world. Nevertheless, the study has shown that incidence of MVAF in Kuwait is below the global average, with a slight decline over the study period. Further research may focus on the evaluation of the effectiveness of various interventions instituted during the past decade for road safety in Kuwait.

*Key Words: Motor vehicle accident; Fatalities; Kuwait*

*Funding Agency: None*



**Pathology**

Category: Clinical

147

**Ziehl-Neelsen staining of decolorized archival fine-needle aspiration (FNA) smears: Role in detection of acid-fast bacilli**

\*Das DK<sup>1,2</sup>, Al-Juwaiser AAA<sup>2</sup>, Sadek HM<sup>3</sup>

<sup>1</sup>Department of Pathology, Faculty of Medicine, Kuwait University; <sup>2</sup>Cytopathology Unit, Mubarak Al-Kabeer Hospital; <sup>3</sup>Microbiology Laboratory, Mubarak Al-Kabeer Hospital.

**Introduction:**

In absence of granulomatous reaction, fine-needle aspiration (FNA) cytodiagnosis of tuberculosis is difficult. When necrosis without granuloma is associated with suppuration, the lesion may be misdiagnosed as an acute inflammatory lesion till clinical follow up or histopathological diagnosis of tuberculosis leads to review of FNA smears. In these situations, Ziehl-Neelsen (ZN) staining of archival FNA smears may be necessary to demonstrate acid-fast bacilli (AFB). The present study is an attempt to find out the utility of ZN-staining on archival smears.

**Methods:**

Decolorized Papanicolaou-stained FNA smears from 31 patients diagnosed four years ago as granulomatous/ necrotizing/ tuberculous lesions, which were re-stained by ZN technique. 100 oil-immersion fields (OIF) were searched for detection and counting of AFB. If no AFB was found in 100 OIF, the count was extended to 200 OIF. Results of AFB positivity and their counts observed in original and archival smears were compared.

**Results:**

The routine smears showed epithelioid cells without granuloma in one case, necrotizing epithelioid granuloma in 27, and necrosis without granuloma in 3. In both the original and archival (re-stained by Z.N stain) smears, AFB was positive in 10 cases and negative in 14 cases each. AFB was positive in original smears but negative in archival smears in 4 cases. AFB was negative in original smears but positive in archival smears in 3 cases. Thus, the rate of AFB positivity was 45.2% in original smears and 41.9% in archival smears ( $P=1.0$ ). In 7 cases each, the count was more in original smear than archival smears and vice versa. The count was equal in 3 cases. The count was  $\geq 1$  per 100 OIF in 7 of 14 original smears and 10 of 13 archival smears ( $P=0.2365$ ).

**Conclusions:**

The rate of AFB positivity and AFB count was not significantly affected in 4 years old archival smears. Thus, the archival FNA smears can be used with equal efficacy for study of AFB.

*Key Words: Archival FNA smears; Ziehl-Neelsen staining*

*Funding Agency: None*



**Pathology**

*Category: Clinical*

**148**

**Fine needle aspiration cytology of salivary gland lesions: Six years experience in Mubarak Al-Kabeer hospital, Kuwait.**

\*Haji BE<sup>1</sup>, George SS<sup>2</sup>, Jaragh M<sup>1</sup>, Kapila K<sup>2</sup>

<sup>1</sup>Cytology Laboratory, Mubarak Al-Kabeer Hospital, Kuwait; <sup>2</sup>Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

FNAC is an inexpensive, rapid, well accepted, diagnostic modality for salivary gland lesions associated with low morbidity and high diagnostic accuracy. This study aims to evaluate the usefulness/accuracy of FNAC in the diagnosis of salivary gland lesions.

**Methods:**

From 2005-2011 the cytology reports of 464 salivary gland FNA (255 males and 209 females) performed in the clinic on palpable lesions at Mubarak Al-Kabeer Hospital (MAKH) were reviewed. In 44 aspirates the cytologic findings were correlated with the histological diagnosis.

**Results:**

Age ranged from 13-66 years (mean 41+1.9) with 24 males and 20 females. The sites involved were parotid (28 cases), submandibular (14 cases) and minor salivary glands (2 cases). Benign FNA were 32 (72.7%), 7 (15.9%) malignant, 2 (4.5%) suspicious and 3 (6.8%) unsatisfactory. Three of the four mucoepidermoid tumors on FNA were diagnosed as mucoepidermoid carcinoma and one as Warthin's. One case each of adenoid cystic carcinoma and acinic cell carcinoma were correctly diagnosed. One case considered as suspicious for malignancy was reported as sialadenitis. 21 of 32 benign tumors were reported as pleomorphic adenomas on FNA and 19 were confirmed on histology. One case each was reported as Warthin's and benign tumor NOS on histology. All 4 cases of Warthins were correctly typed. The 4 cystic lesions were reported as monomorphic adenoma and cystic lesions NOS. The 3 benign aspirates on FNA, were diagnosed as myoepithelioma and two as sialadenosis. The positive and negative predictive value of FNA was 89 and 100% respectively.

**Conclusions:**

FNAC is accurate and useful in the diagnosis of salivary gland lesions and helps plan an appropriate approach for treatment. Pleomorphic adenoma and mucoepidermoid tumors are the commonly occurring benign and malignant lesions seen in our study. They often create diagnostic problems and need experienced cytopathologists.

*Key Words: Fine needle aspirates; Salivary gland lesions; Mucoepidermoid tumors*

*Funding Agency: None*



**Pathology**

Category: *Clinical*

149

## **HER2/neu gastric cancer in Kuwait**

\*George SA<sup>1</sup>, John B<sup>2</sup>, Junaid TA<sup>2</sup>

<sup>1</sup>Department of Pathology, Mubarak Al-Kabeer Hospital, Ministry of Health, Kuwait; <sup>2</sup>Department of Pathology, Faculty of Medicine, Kuwait University.

**Introduction:**

Over-expression of the human epithelial growth factor receptor 2 protein arises from amplification of the HER2/c-erb2 gene, a key driver of tumorigenesis. Such amplification and protein overexpression have been observed in a number of solid tumours especially breast carcinoma where HER2 overexpression is observed in 15-25% and therapies that target HER2 are the standard of care. In Kuwait there is little information on the frequency or prevalence of HER2 expression in gastric cancers (GC) and this study was to determine this as 7-34% of GC worldwide have been reported to harbor HER2 overexpression.

**Methods:**

Archival surgical pathology materials of gastric lesions were retrieved and manually immunostained using a polyclonal rabbit anti-human c-erb2 oncoprotein Code A0485 (Dako Denmark A/S, Glostrup, Denmark) with microwave antigen retrieval and Dako Envision + Dual Link HRP detection system. Appropriate positive and negative controls were included. The HER2 status of each specimen was determined using the ASCO/CAP scoring criteria. Only lineal membranous stains were read as positive.

**Results:**

Seventy-three of the gastric lesions were carcinomas, 46 intestinal type and 27 diffuse. Eighteen were lymphomas while 2 were normal biopsies and 3 chronic gastritis. Four of the carcinomas (3 intestinal and 1 diffuse) had a score of 3+ while 9 were scored between 1+ and 2+. All other lesions (23) were negative.

**Conclusions:**

About 5% of GC in this small study showed HER2 over-expression, demonstrating that such tumors are encountered in Kuwait. There is a need for the study of a larger number of GC using optimized immunohistochemistry and FISH testing to ascertain HER2 status in equivocal cases.

*Key Words: Gastric Cancer; HER2; Kuwait*

*Funding Agency: None*



**Pathology**

*Category: Clinical*

150

**Correlation of cytological grading on fine needle aspirates of breast carcinoma with prognostic factors and tissue grading.**

\*Kapila K<sup>1</sup>, George SS<sup>1</sup>, Anim JT<sup>1</sup>, Francis IM<sup>1</sup>, Behbehani A<sup>2</sup>, Al-Mulla F<sup>1</sup>.

Department of Pathology, Faculty of Medicine, Kuwait University<sup>1</sup>; Department of Surgery, Faculty of Medicine, Kuwait University<sup>2</sup>

**Introduction:**

Carcinoma breast, is a heterogenous tumor with variable prognosis. The prognostic parameters histological grade, receptor status, Her-2 neu amplification and Ki-67 have been well studied on surgical specimens. Evaluation of these parameters is possible on Fine Needle Aspirates (FNA) which has been found to be extremely useful when establishing the best neoadjuvant therapy for advanced carcinoma or when surgical removal of the tumor is not the best option. This study aims to evaluate comparatively the cytological and histomorphological grade in infiltrating ductal carcinoma of the breast with specific reference to estrogen receptors[ER], progesterone receptors[PR], Her-2 neu expression and Ki-67.

**Methods:**

The cytological grade was correlated with the histological grade in 40 patients who underwent FNA and mastectomy for infiltrating ductal carcinoma and also with estrogen receptors alpha and beta; progesterone receptor isoforms PR and PRB; Her-2 neu and Ki-67 to assess the significance.

**Results:**

There was 75% concordance between the various grades of cytology and histology. FNA undergraded and overgraded 12.5% of the cases. ER  $\alpha$  and ER  $\beta$  positive tumors were seen in 23% and 42% cytological grade 1 tumors and 44% and 38% of grade 3 tumors. PR and PRB were demonstrable in 39% and 8% of Grade 1 tumors and 78% and 22% of Grade 3 tumors. Her-2 neu was seen in 50% of Grade 1 and 67% of Grade 3 tumors while ki-67 was seen in 11% of Grade 2 tumors and 22% of Grade 3 tumors. No significant correlation was observed.

**Conclusions:**

Apart from being non-invasive, cytological grading of invasive ductal carcinomas of the breast is fairly comparable to histological grading but not very consistent with the other prognostic parameters. Cytological grading could prove to be a useful parameter when selecting mode of therapy and predicting tumor behaviour.

*Key Words: Cytological grading; Breast carcinoma; Fine needle aspirates*

*Funding Agency: Kuwait University Research Grant MG01/04 and MG01/07*



**Pathology**

*Category: Clinical*

**151**

**Evidence for the involvement of protein citrullination in the pathogenesis of hepatic fibrosis in patients with chronic hepatitis**

Olusi SO, \*Abdeen S, George S  
Faculty of Medicine, Kuwait University

**Introduction:**

Protein citrullination is a known mechanism of fibrogenesis in the synovial joints of patients with rheumatoid arthritis. In this study, we postulated that protein citrullination may be partly involved in the pathogenesis of hepatic fibrosis in patients with chronic hepatitis.

**Methods:**

To test this hypothesis we measured the serum concentrations of anticyclic citrullinated peptide (anti-CCP) antibody in 46 patients with chronic hepatitis C (HCV), 20 with hepatitis B (HBV), 28 with non-alcoholic steatohepatitis (NASH) and 100 healthy controls using commercially available ELISA kits. The METAVIR fibrosis scores of liver biopsies from the patients were determined histologically. Appropriate statistical methods were used to compare these values between patients and controls and degrees of liver fibrosis.

**Results:**

The mean serum concentration of anti-CCP antibody in patients ( $1.21 \pm 0.075$  RU/ml) was significantly higher ( $P = 0.000$ ) than the mean in healthy controls ( $0.79 \pm 0.04$  RU/ml). Patients with cirrhosis had a mean anti-CCP antibody concentration that was significantly higher than that of healthy controls ( $1.61 \pm 0.27$  RU/ml vs.  $0.79 \pm 0.04$  RU/ml).

**Conclusions:**

We concluded that significant protein citrullination occurs in patients with cirrhosis of the liver

*Key Words: Anti-CCP; Fibrosis; Hepatitis*

*Funding Agency: None*

**Pathology***Category: Clinical*

152

**Receiver operating characteristic (ROC) curve analysis of a novel index for coronary heart disease risk prediction and diagnosis of the metabolic syndrome**\*Mojiminiyi OA<sup>1</sup>; Abdella NA<sup>2</sup>; Al-Mohammedi H<sup>3</sup>; Pinto C<sup>2</sup>; Al-Rammah T<sup>1</sup><sup>1</sup>Departments of Pathology; <sup>2</sup>Medicine, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Medicine, Mubarak Al-Kabeer Hospital, Kuwait**Introduction:**

There is a need to simplify screening tests for metabolic syndrome (MetS) and coronary heart disease (CHD) risk so that high risk patients can be identified early. In routine practice, components of MetS - increased waist circumference (WC), high fasting plasma glucose (FPG), low high-density lipoprotein cholesterol (HDL-C), high triglycerides (Tg) and hypertension are assessed separately with presence of three components being diagnostic. We hypothesized that an index (metabolic syndrome index – MSI), computed as  $WC \times Tg/HDL-C$  would offer a single diagnostic number with high sensitivity and specificity for CHD risk assessment and the diagnosis of MetS.

**Methods:**

Fasting insulin, FPG, adiponectin, high-sensitivity CRP (hs-CRP) and lipid profile were determined in 98 Type 2 diabetic (T2DM) subjects and 521 healthy first degree relatives. Clinical and anthropometric data were recorded; subjects were classified with the number of IDF criteria of the MetS. Insulin resistance was assessed with HOMA-IR. Linear and multivariate (with inclusion of age and gender as potential confounders) regression analyses were used to determine the associations of MSI with other risk factors, CHD and MetS.

**Results:**

MSI cut off values for MetS were 155 for males and 105 for females. MSI showed significant correlations  $\text{®}$  with age (0.2), WC (0.6), glucose (0.2), Tg (0.9), HDL-C (-0.6), Systolic BP (0.2), Diastolic BP (0.2), adiponectin (-0.4), HOMA-IR (0.4) and hs-CRP (0.4). MSI showed stepwise increase with increasing number of MetS criteria. Binary logistic regression showed that the odds ratio (OR) of MetS and CHD as predicted by MSI were 2.7 (95% CI: 2.1-3.55) and 3.6 (95% CI: 1.9 -5.3) respectively. ROC analysis showed that MSI had significantly higher area under the curve (0.986) compared with WC (0.682), HDL-C (0.790) and Tg (0.955) for detection of MetS.

**Conclusions:**

MSI offers a single, easily computable risk estimate for CHD and an excellent diagnostic test for MetS.

*Key Words: Metabolic Syndrome Index; Receiver Operating Characteristic Curve; Coronary Heart Disease Risk factors*

*Funding Agency: KFAS grant 2004-1302-03*



**Pathology**

Category: *Clinical*

153

**Putative mechanisms that link cystatin-C with development of coronary heart disease in patients with type 2 diabetes mellitus**

\*Mojiminiyi OA<sup>1</sup>; Abdella NA<sup>2</sup>; Al-Mohammedi H<sup>3</sup>; Pinto C<sup>2</sup>; Al-Rammah T<sup>1</sup>

<sup>1</sup>Department of Pathology, Faculty of Medicine, Kuwait University; <sup>2</sup> Department of Medicine, Faculty of Medicine, Kuwait University; <sup>3</sup> Department of Medicine, Mubarak Al-Kabeer Hospital, Kuwait

**Introduction:**

Recent evidence suggest that cystatin C (CC), a marker of GFR, may play a role in the pathogenesis of coronary heart disease (CHD). This study evaluates the associations of CC with CHD risk factors and incident CHD in patients with Type 2 diabetes (T2DM).

**Methods:**

CC, fasting insulin, glucose, homocysteine, high-sensitivity CRP (hs-CRP), adiponectin, leptin, leptin receptor, free leptin index (FLI), and lipid profile were determined in 250 T2DM patients with CHD (96) and without CHD (154) who were also classified as normo- or microalbuminuric. Clinical and anthropometric data were recorded and subjects were classified on the basis of the degree of insulin resistance (HOMA-IR) and serum CC levels ( $\leq 1.4$  mg/l was normal). Linear and multivariate regression analyses were used to determine the associations of CC with variables and risk factors.

**Results:**

CC correlated with age ( $r = 0.24$ ) and homocysteine ( $r = 0.35$ ) but not with the adipokines (adiponectin, leptin, FLI). Compared to those with normal levels, patients with high CC had significantly higher homocysteine (18 Vs 13  $\mu\text{mol/L}$ ), HOMA-IR (9.8 Vs 8.2), FLI (3.3 Vs 2.1 ng/U), Triglycerides (2.2 Vs 1.7mmol/L); hs-CRP (0.97 Vs 0.62 mg/L) and significantly lower HDL cholesterol (1.1 Vs 1.3). 62% of subjects with CHD had elevated CC. After adjustment for confounders, logistic regression analysis showed that elevated CC was significantly associated with hypertension (Odds Ratio (OR) = 1.2 ), HOMA-IR (OR = 1.3), hyperhomocysteinemia (OR = 2.8), microalbuminuria (OR =2.7), hs-CRP (OR = 8.9) and CHD (OR = 2.9).

**Conclusions:**

Local CC deficiency has been shown in atherosclerotic lesions where it is involved in the degradation of extracellular matrix. The associations of CC with several risk factors in this study suggests a multi-hit mechanism that goes beyond its local role in atherosclerotic lesions. We conclude that estimation of CC has potential as a predictive marker for CHD in patients with T2DM.

*Key Words: Coronary Heart Disease; Cystatin C; Risk factors*

*Funding Agency: KU Research Administration Grant MG-033*



**Pathology**

*Category: Graduate (Resident)*

**154**

**Analytical characteristics of the DAKO CgA enzyme linked immunoassay and its use in the evaluation of the CgA level in patients with high parathyroid hormone and patients with normal parathyroid hormone level**

\*May Al Rushood

KIMS Board clinical biochemistry

**Introduction:**

Chromogranin A (CgA) is a protein secreted from the parathyroid glands. Studies showed that CgA level is elevated in hyperparathyroidism. The DAKO ELISA kit for measurement of serum CgA was analytically evaluated and used in this study. This study has two parts: to evaluate the analytical performance of the CgA assay DAKO ELISA kit and to prove that patients with hyperparathyroidism have high CgA levels.

**Methods:**

Precision and dilution studies were performed using the standards provided by the manufacturer. CgA level was evaluated in three groups of patients with high PTH: patients with chronic renal failure (group two) sample number was seven, patients with primary hyperparathyroidism (group three) with only two subjects, and patients with vitamin D deficiency (group four) with nine subjects. The control group (group one) is composed of thirteen patients with normal PTH levels. Samples were retrieved from the hormonal laboratory in Mubarak Al Kabeer hospital. SPSS version 17.0 was used for data analysis.

**Results:**

Within- run and between- run Coefficient of variation for the high level standard was above the manufacturer recommendation. The recovery was less than 50% for the high level standard. Using Spearman correlations, there was significant correlation between CgA level and serum PTH, creatinine and urea levels ( $P < 0.0001$ ). CgA level in the control group was compared with CgA levels in the other groups of high PTH using Mann-Whitney U test: there was significant difference in CgA level between control and group 2 ( $P < 0.0001$ ) but this was not shown when comparing the control with group 3 or 4.

**Conclusions:**

Using Spearman correlations there was significant correlation between CgA and PTH levels. When I compared CgA level in the control group with the other groups, no difference in CgA level was noted between the control and group 3 or 4. This may be due to other factors that are different among the three groups.

*Key Words: Chromogranin A; Parathyroid gland; Enzyme immunoassays*

*Funding Agency: None*



**Pediatrics**

Category: Clinical

155

**Arginine/ornithine ratio in children with sickle cell disease**

\*Adekile AD<sup>1,2</sup>, Mustafa NY<sup>1</sup>, Al-Sherida S<sup>2</sup>, Azab AF<sup>2</sup>, Mojiminiyi O<sup>3</sup>

<sup>1</sup>Department of Pediatrics, Faculty of Medicine, Kuwait University, <sup>2</sup>Pediatric Hematology Unit, Mubarak Hospital, <sup>3</sup>Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait

**Introduction:**

Sickle cell disease (SCD) is characterized, in part, by chronic endothelial inflammation involving nitric oxide scavenging mediated via increased arginase activity, which converts arginine to ornithine, leading to a low arginine/ornithine ratio (AOR). However, Kuwaiti SCD patients have elevated HbF levels, lower levels of hemolysis and reduced steady-state inflammation. No previous AOR studies have been reported in this population of patients. The study was carried out to document any evidence of arginine consumption.

**Methods:**

We have studied consecutive SCD patients followed in the Pediatric Hematology clinics of Mubarak and Amiri Hospitals in Kuwait. The only selection criterion is no acute illness or crisis in the preceding 6 weeks. Controls were age-matched non-SCD siblings of the patients. Informed consent was obtained. Plasma arginine and ornithine levels were determined using high performance liquid chromatography. Mean values of arginine, ornithine and AOR were compared in the 2 groups and correlations computed with Hb, HbF and LDH levels.

**Results:**

There were 45 SCD (26 S $\beta$ , 16 SS and 3 SD) patients with a mean age of  $9.1 \pm 3.3$  years, while the number of controls was 14, mean age  $10.1 \pm 3.6$  years. The mean values of serum arginine were  $48.6 \pm 33.4$  and  $110.7 \pm 75.1$ ; ornithine of  $117.2 \pm 36.7$  and  $105.2 \pm 40.6$   $\mu\text{mol/l}$ , while AOR were  $0.46 \pm 0.35$  and  $1.0 \pm 0.47$  in the 2 groups respectively. The differences between arginine and AOR in both groups were highly significant ( $p=0.00$ ). There was no significant correlation between AOR and LDH, Hb or HbF ( $p>0.05$ ) in the control group but there was significant correlation against LDH among the patients ( $p=0.01$ ).

**Conclusions:**

Despite elevated Hb F level, our data suggests arginine depletion and on-going, steady-state inflammation in Kuwaiti children with SCD. Regular follow up with monitoring of AOR may be useful for surveillance and early identification of complications.

*Key Words: Sickle cell disease; Arginine; Ornithine*

*Funding Agency: Kuwait University Research MK01/08*

**Pediatrics***Category: Clinical***156****The comparison of the quality of life of pediatric sickle cell disease patients and their families, with other chronic hemolytic anemia patients.**\*Al-Sharida S<sup>1</sup>, Mustafa NY<sup>2</sup>, Azab A<sup>1</sup>, Bourusly M<sup>3</sup>, Adekile AD<sup>1,2</sup><sup>1</sup>Pediatric Hematology Unit, Mubarak Hospital; <sup>2</sup>Department of Pediatrics, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Hematology, National Bank of Kuwait Hospital, Sabah, Kuwait**Introduction:**

Sickle Cell Disease (SCD) is associated with poor quality of life, due to its morbidity and mortality. This study compares the quality of life of pediatric SCD patients and their families with other chronic hemolytic anemias in Kuwait.

**Methods:**

This was a cross sectional questionnaire study involving SCD patients seen in the pediatric hematology clinics in Mubarak, Amiri and Sabah hospitals in Kuwait. Their quality of life was compared to that of patients with some other chronic hemolytic anemias. Informed consent was obtained as appropriate. Patients' biodata, clinical course and effects of the disease on different aspects of the lives of the patients and their families were documented.

**Results:**

There were 62 SCD patients with (32 males and 30 females). The controls were 30 patients (20 Hb H disease and 9 hereditary spherocytosis and one with Hb E disease). Of the latter, 20 were males and 10 females. Most of the SCD patients are diagnosed between 1-3 years (37%) and the controls were mostly diagnosed at less than 1 year of age (57%). The initial symptom in the SCD patients was pallor and jaundice in 34%; among the controls pallor was the initial symptom in 80%. Forty eight (77%) of the SCD patients had been hospitalized usually (75.6%) for painful crisis. Only 12 (39%) of the control group had been hospitalized, usually for blood transfusion.

More common in the SCD patients were: school absences and learning difficulties; parental marital problems (conflict and divorce) and job issues (reprimands, early retirement and firing). However, most families are compliant (87% in the SCD and 83.3% in the controls) with medications and clinic attendance.

**Conclusions:**

SCD pediatric patients and their families suffer poor quality of life because of the severity of the illness, recurrence of admissions. The disease has negative impact on the patients' education and the family's social life compared to other forms of chronic hemolytic anemias.

*Key Words: SCD; Quality Of life; chronic hemolytic anemia**Funding Agency: None*



**Pediatrics**

Category: Clinical

157

**Kuwait national sickle cell disease registry**

\*Al-Sharida S<sup>1</sup>, Mustafa NY<sup>2</sup>, Marouf R<sup>3</sup>, Khamis A<sup>4</sup>, Bourusly M<sup>5</sup>, Al-Jaffar H<sup>4</sup>

<sup>1</sup>Pediatric Hematology Unit, Mubarak Hospital; <sup>2</sup>Department of Pediatrics, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Hematology, Mubarak hospital; <sup>4</sup>Department of Hematology, Amiri Hospital; <sup>5</sup>Department of Hematology, National Bank of Kuwait Hospital, Sabah; <sup>6</sup>Department of Pediatrics Jahra Hospital, Kuwait

**Introduction:**

Sickle cell disease (SCD) is a chronic inherited condition with different genetic backgrounds, distributed globally. The variant seen among Kuwaitis tends to have a mild phenotype. The Kuwait National Sickle Cell Disease Registry (KNSCDR) was recently established to document the distribution, Hb genotypes, severity, and complications among our patients.

**Methods:**

This is a multicenter study involving all the patients attending the clinics in Mubarak, Amiri, Sabah, Adan, and Jahra hospitals in Kuwait. Patients' demographics, investigations, clinical course, complications and management were documented and data entry was done using Microsoft Access program.

**Results:**

So far, 241 patients with (122 males and 119 female), have been registered; 216 were Kuwaitis. Twenty three (9.5%) were <5 years of age, 90 (37.3%) between 5-15 years, 30 (12.4%) between 15-20 years, 55 (22.8%) between 20-40 years and 43 (17.8%) were >40 years. Most of the patients had varying frequencies of hospitalization with vaso-occlusive crises; 156 (64.7%) had at 0-1/year (mild) and 53 (22.0%) had >3/year (severe). The common documented complications included: 70 (29.0%) had cholecystectomy for gallstones, 52 (21.6%) had a vascular necrosis of the femoral head. Overt stroke was documented in only 3 (1.2%) patients. The distribution of Hb F was: 10 - 30% in 153 (63.5%) patients while it was >30% in 32 (13.3%). Only 57 (23.7%) patients were on hydroxyurea treatment.

**Conclusions:**

SCD is well distributed in Kuwait, though we are still registering our patients. The disease is milder in our region hence severe complications are uncommon. The high HbF values are protective.

*Key Words: Sickle Cell; Registry; Kuwait*

*Funding Agency: None*

**Pediatrics***Category: Clinical***158****Neonatal sepsis in Asian Countries**

\*Al-Ta'iar A, Hammoud MS, Cuiqing L, Lee JKF, Lui K, Nakwan N, Isaacs D

<sup>1</sup>Department of Community Medicine and Behavioural Sciences, Faculty of Medicine, Kuwait University, Kuwait; <sup>2</sup>Departments of Pediatrics, Faculty of Medicine, Kuwait University, Kuwait; <sup>3</sup>Department of Neonatology, Children Hospital of Hebei Province, China; <sup>4</sup>Department of Paediatrics, Kuala Terengganu Hospital, Terengganu, Malaysia; <sup>5</sup>Department of Services of Paediatrics & Neonatology, Centro Hospitalar Conde Sao Januario, Macau, China; <sup>6</sup>Department of Paediatrics, Hat Yai Medical Educational Centre, Hat Yai, Songkhla, Thailand; <sup>7</sup>Department of Infectious Diseases and Microbiology; Children's Hospital at Westmead, Sydney, NSW, 2145, Australia.

**Introduction:**

Neonatal sepsis is a major cause of neonatal deaths in Asia but data remain scarce. We aimed to investigate the causative organisms and antibiotic resistance in neonatal care units in China, Malaysia, Hong Kong, and Thailand.

**Methods:**

Prospective four year study of neonatal sepsis defined as positive culture of a single potentially pathogenic organism from blood or cerebrospinal fluid differentiated into early-onset sepsis (EOS) occurring <3 days of birth and late-onset sepsis (LOS)  $\geq$  3 days after birth.

**Results:**

From 2006 to 2009, there were 963 episodes of neonatal sepsis. The incidence of EOS was 0.62 (95% CI: 0.45-0.82) per 1000 live births or 4.91 (95% CI: 4.22-5.68) per 1000 admissions while the incidence of LOS was 5.00 (95% CI: 4.51-5.53) per 1000 live births or 21.22 (95% CI: 19.79-22.77) per 1000 admissions.

The incidence of Group B Streptococcus (GBS) sepsis was low but remained the most common single pathogen for EOS among inborn babies. Klebsiella was the most common Gram-negative organism causing most deaths. The case-fatality was 7.0% (95% CI: 3.9-12.0%) for EOS and 16.0% (95% CI: 13.7-19.0%) for LOS, and was significantly different between participating units after adjusting for potential confounders. Of all Gram-negative organisms, 47%, 37%, and 32% were resistant to third-generation cephalosporins, gentamicin or both.

**Conclusions:**

The pattern of EOS is similar to that in industrialised countries, suggesting similar preventive approaches may be effective. The important features of neonatal sepsis in Asia are the burden of Klebsiella and high level of antibiotic resistance. These should be addressed while developing measures to reduce neonatal mortality due to infection.

*Key Words: Neonatal; Sepsis; Asia**Funding Agency: None*



**Pediatrics**

Category: *Clinical*

159

**Clinical and biochemical characteristics of congenital disorder of glycosylation patients in Kuwait**

\*Dhaunsi GS<sup>1</sup>, Makhseed N<sup>2</sup>, Al-Qabandi W<sup>1</sup>, Al-Tawari A<sup>3</sup>, Habib Y<sup>4</sup>, Jaeken J<sup>5</sup>

Departments of Pediatrics, Kuwait, Faculty of Medicine, Kuwait University<sup>1</sup>; Jahra Hospital<sup>2</sup>; Sabah Hospital<sup>3</sup>; Mubarak Al-Kabeer Hospital, Ministry of Health, Kuwait<sup>4</sup>; Center for Metabolic Disease (JJ), University Hospital Gasthuisberg, Leuven, Belgium<sup>5</sup>.

**Introduction:**

Congenital disorders of glycosylation (CDG) are a rapidly growing group of inherited metabolic diseases with impaired protein glycosylation. Clinical characteristics of CDG have been well described in reports from various parts of the world except Kuwait. This study was carried out to identify clinical and biochemical features of CDG patients in Kuwait.

**Methods:**

A total of 263 patients and 59 healthy age and gender matched controls were recruited from various hospitals in Kuwait. Clinical findings of each patient were recorded to identify distinct features associated with CDG in Kuwaiti or Arab patients. A blood sample was collected from patients and control subjects and used for isoelectric focusing of serum transferrin. Serum samples of patients suspected to have CDG were further analyzed by a carbohydrate specific staining and /or immunoblotting. CDG diagnosis was further confirmed by a capillary zone electrophoresis technique.

**Results:**

We confirmed diagnosis of 11 CDG patients. Based on clinical and biochemical characteristics, 7 of the diagnosed CDG patients were categorized as Type I CDG patients whereas other 4 were classified as Type II patients. Several distinct clinical features were observed in CDG patients from our study. Kidney stone and urinary tract infection, uncommon findings of CDG, were noted in 15% of our cases. Cardiomegaly in some of the CDGI and CDG II patients was another distinct finding. Inverted nipples and abnormal fat distribution, commonly reported features of CDG patients were notably rare or absent in our patients whereas 40% of CDG type I patients and 25% of CDG type II cases were consanguineous.

**Conclusions:**

This study concludes that occurrence of CDG is frequent in the Middle East and distinct features of our CDG patients highlight phenotype variation of CDG in the Middle East. These findings should help pediatricians with respect to correct diagnosis, management and treatment of the patients in Kuwait.

*Key Words: Glycosylation Disorders; Inherited; Children in Kuwait*

*Funding Agency: Kuwait University Research Administration Grant MK 01/05*

**Pediatrics***Category: Clinical***160****Persistent neonatal candidemia: A four-year retrospective study in a maternity hospital**\*Hammoud MS<sup>1</sup>, Al-Tayar A<sup>2</sup>, Fouad M<sup>3</sup>, Al-Sweih N<sup>4</sup>, Raina A<sup>3</sup>, Khan ZU<sup>4</sup><sup>1</sup>Departments of Pediatrics, Faculty of Medicine, Kuwait; <sup>2</sup>Departments of Community Medicine, Faculty of Medicine, Kuwait; <sup>3</sup>Department of Neonatology, AL-Sabah Maternity Hospital, Kuwait;<sup>4</sup>Departments of Microbiology, Faculty of Medicine, Kuwait**Introduction:**

Candida spp. are the third most common cause of bloodstream infection in preterm neonates with a case-fatality around 30%. This study aimed to describe how common is persistent candidemia among neonatal candida infections in Kuwait and compare between infants with persistent and non-persistent candidemia in terms of demographic characteristics and clinical outcome.

**Methods:**

A four-year retrospective study (2007 -2010) on infants with Candida species detected by blood culture was conducted in Maternity Hospital. Persistent candidemia was defined as continued isolation of the same Candida species from the blood of a candidemic patient 6 days after initiation of antifungal treatment. Data on demographic characteristics including gestational age, sex, birth weight, mode of delivery and other factors such as chemoprophylaxis, total parenteral nutrition, presence of central catheter or endotracheal tube and use of antibiotics were collected. Chi-square or Fisher's exact test, as appropriate, was used to compare between neonates with persistent candidemia and neonates with non-persistent candidemia.

**Results:**

During the study period, 92 cases of candidemia were identified of which three were excluded because they died before initiation of antifungal treatment. Of 89 candida infections, 54 (60.7%) had persistent candidemia. Infants with persistent candidemia were more likely to be females ( $p=0.04$ ), low birth weight ( $p=0.04$ ) and gestational age ( $p=0.04$ ), have more than one sterile site colonized with Candida species ( $p=0.05$ ) and develop meningitis ( $p=0.04$ ). Case-fatality was 29 (54%) and 1(3%) among persistent and non-persistent candidemia, respectively ( $p<0.001$ ).

**Conclusions:**

Persistent candidemia is common among neonatal candida infections in Kuwait. Neonates with persistent candidemia have certain characteristics that may help to identify them for intensive efforts of prevention and management.

*Key Words: Persistent candida; Preterm; Neonatal**Funding Agency: Kuwait university, Grant: MK 01/10*



**Pediatrics**

*Category: Clinical*

**161**

**Correlates of hypertension and obesity among adolescents in Jerusalem province, West Bank, Palestine**

\*Tayem Y<sup>1</sup>, Zaid B<sup>1</sup>, Herzallah M<sup>2</sup>

<sup>1</sup>Department of Physiology/Pharmacology, Al-Quds University, Faculty of Medicine;

<sup>2</sup>Center for Molecular and Behavioral Neuroscience Rutgers University

**Introduction:**

The prevalence of pediatric hypertension (HTN) and obesity in developing countries has increased over the last three decades. However, they have been largely under estimated, under diagnosed and undertreated. This study aimed to explore the prevalence of obesity and HTN among Palestinian adolescents in Jerusalem province schools, West Bank. Moreover, we sought to determine the correlation between HTN, obesity, family history of HTN, physical activity and sedentary lifestyle.

**Methods:**

Body mass index (BMI), blood pressure (BP), family history of HTN, total daily physical activity (school activities, sport out of school, walking) and the duration of sedentary lifestyle measures (daily time spent watching TV, playing video games and recreational computer use) were sought from 232 randomly selected adolescents (160 females, 72 males) aged 12-17 years from 6 schools in Bethany, Abu Dis, and Sawahra, West Bank. Age-, height- and gender-specific BP curves were used to determine pre-hypertension (90–95%) and HTN (>95%). Overweight (85-95%) and obesity (>95%) were assessed by growth charts adjusted for age and gender.

**Results:**

The prevalence of overweight was 14.2% (16.7% males, 13.1% females) and obesity 7.8% (15.3% males, 4.4% females). Pre-hypertension was detected in 9.5% (4.2% males, 5.6% females) and HTN in 12.1% (11.9% males, 15% females). A higher rate of obesity (10.7%) and positive family history (25%) were detected in hypertensive subjects but these correlations were not significant. Total physical activity was inversely associated with diastolic BP (DBP) whereas; no significant correlation was detected between sedentary lifestyle and BP.

**Conclusions:**

Our results have highlighted the high prevalence of overweight and obesity among adolescents in Jerusalem province. Given the correlation between anthropometric parameters and BP in overweight and obesity in adolescents in order to minimize the risk of HTN in adulthood

*Key Words: Hypertension; Adolescents*

*Funding Agency: Palestinian American Research Center, Washington D*



**Pharmacology and Toxicology**

Category: Graduate MSc (Basic Science)

162

**The effect of a novel enaminone derivative (CEE-1) on the release of pro-inflammatory prostanoids from human monocytes**

\*Al-Baghli HA, Edafigho IO, Ezeamuzie CI

Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University

**Introduction:**

CEE-1 is a novel enaminone derivative, synthesized in house. Previous studies revealed its capacity to inhibit the release of inflammatory cytokines from activated macrophages. Whether the compound can also inhibit the release of inflammatory prostanoids is unknown. The aim of this study is to determine (in vitro) whether CEE-1 also inhibits prostanoid release from activated monocytes.

**Methods:**

Human monocytic cells were either untreated or pre-treated with CEE-1, dexamethasone or indomethacin for 30 min before being stimulated by simultaneous addition of 50 nM PMA and 0.3 µg/ml LPS for 24 h. The release of PGE<sub>2</sub>, TXB<sub>2</sub> and TNF-α was determined by ELISA. COX mRNA expression was determined by ReT-PCR with the appropriate primers, whereas protein expression was determined by Western blotting.

**Results:**

CEE-1 produced a strong concentration dependent inhibition of PGE<sub>2</sub> and TXB<sub>2</sub> release. The efficacy of this inhibition was comparable to those of indomethacin and dexamethasone, even though it was less potent than both drugs. CEE-1 also inhibited TNF-α release with comparable efficacy and potency. The compound behaved like dexamethasone, producing no significant effect on COX enzyme function, in contrast to indomethacin that produced significant inhibition. ReT-PCR results showed significant inhibition by both CEE-1 and dexamethasone of COX-2 mRNA expression in activated cells. Such inhibition was also reflected in COX-2 protein expression.

**Conclusions:**

CEE-1 is the first enaminone derivative to exhibit a strong inhibitory effect on the release of both cytokines and prostanoids. The inhibitory mechanism of CEE-1 on prostanoid production involves suppressing COX-2 mRNA and therefore, protein expression, without affecting enzyme function. Mechanistically, CEE-1 behaves more like steroids than NSAIDs. These results suggest that CEE-1 is a potential alternative to steroids in the treatment of inflammation.

*Key Words: Cytokine; EnamiNone*

*Funding Agency: KU Grant YM 19/09*



**Pharmacology and Toxicology**

Category: Basic Sciences

163

**The effect of pomegranate extract of coronary artery atherosclerosis in SR-BI apoE double knockout mice**

\*Al-Jarallah A<sup>1</sup>, Igdoura F<sup>2</sup>, Tenedero CB<sup>2</sup>, White EJ<sup>3</sup>, Igdoura SA<sup>3</sup>, Trigatti BL<sup>2</sup>  
Kuwait University, McMaster University

**Introduction:**

To test the effect of pomegranate extract (POM) on inflammation and oxidative stress and the development of spontaneous occlusive coronary artery (CA) atherosclerosis in the SR-BI/apoE double knockout mouse model of coronary heart disease.

**Methods:**

SR-BI/apoE dKO mice were treated for 2 weeks with POM via drinking water. Plasma lipoproteins were analyzed by high performance liquid chromatography. Cryosections (10 µm) of hearts, or aortic sinus were stained for lipids with oil red-O, for oxidative stress markers with dihydroethidium or for myocardial fibrosis with Trichrome. Macrophage infiltration and myocardial inflammation were detected by immunofluorescence. The extent of atherosclerosis was determined by measuring the lipids area in Cas or aortic sinus and the degree of macrophage infiltration, inflammation and myocardial fibrosis were determined by measuring the staining intensity using Axiovision software.

**Results:**

Treatment with POM increased cholesterol ester content by about 2 folds thus reducing the abnormally high unesterified:esterified cholesterol ratio of VLDL sized lipoproteins. POM treatment resulted in ~40% reduction of atherosclerosis in the aortic sinus and reduced the proportion of CA with occlusive atherosclerotic plaques by 40%. MCP-1 and SAA levels in serum were at least 10 times higher in SR-BI/apoE dKO mice compared to age matched apoE KO control mice but were not reduced by POM treatment. Instead, POM substantially reduced the levels of oxidative stress (50-70%) and MCP-1 immunoreactivity (50-75%) in atherosclerotic aortic sinus and Cas. POM also reduced lipid accumulation, macrophage infiltration, levels of MCP-1 and fibrosis in the myocardium, and prevented cardiac enlargement in SR-BI/apoE dKO mice.

**Conclusions:**

POM reduced aortic sinus and occlusive CA atherosclerosis in the SR-BI/apoE dKO mice via mechanisms that involve reduced inflammation and oxidative stress and possibly alterations in lipoprotein composition.

*Key Words: Coronary Arteries; Atherosclerosis; Pomegranate*

*Funding Agency: MOP74753, PRG6502*



**Pharmacology and Toxicology**

Category: Basic Sciences

164

**Investigating basal activity of the incretin receptors**

\*Al-Sabah S, Al-Fulaij M, Ahmed HA

Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

The incretin effect is mediated by two gut hormones; glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). GLP-1 and GIP both potentiate insulin secretion in a glucose-dependent manner by binding to their respective receptors on pancreatic beta-cells. The GIP and GLP-1 receptors (GIPR and GLP-1R) are Family B (Secretin) G Protein-Coupled Receptors (GPCRs) and couple positively to adenylate cyclase via Gs. In type 2 diabetes mellitus (T2DM) an insensitivity to GIP develops so the focus has been on targeting GLP-1R to treat T2DM. The aim of this study is to investigate basal signaling via these two receptors in order to shed light on why type 2 diabetics remain responsive to GLP-1 but not GIP.

**Methods:**

GIPR and GLP-1R were transiently expressed in HEK-293 cells and receptor activity was assessed using a cAMP-responsive luciferase reporter gene assay. Dose-response curves were normalised to maximum forskolin response. Arrestin recruitment to either GLP-1R or GIPR was measured using enzyme fragment complementation and visualized on a confocal microscope using YFP-labelled arrestin.

**Results:**

GLP-1 and GIP stimulated cAMP-responsive luciferase activity with a pEC50 value of 10.3 ( $\pm 0.05$ ) and 10.7 ( $\pm 0.15$ ) respectively (n=3). Basal GIPR activity was significantly ( $P > 0.005$ ) higher than that of GLP-1R (77% compared to 28%). GLP-1 and GIP stimulated arrestin recruitment to their receptors with a pEC50 value of 8.2 ( $\pm 0.14$ ) and 8.1 ( $\pm 0.27$ ) respectively (n=3). Basal arrestin binding to GIPR was significantly higher ( $P < 0.05$ ) than GLP-1R (75% compared to 39%) and YFP-labelled arrestin displayed a robust translocation to agonist stimulated GLP-1R but not to GIPR.

**Conclusions:**

GIPR displays significantly higher basal activity and significantly higher basal arrestin binding than GLP-1R. This apparent constitutive activity may contribute to the loss of function of GIP in T2DM.

*Key Words: GPCR; Constitutive-Activity; Incretin*

*Funding Agency: KU Grant No. ZM01/10*



**Pharmacology and Toxicology**

Category: Graduate MSc (Basic Science)

165

**Combined inhibition of angiotensin converting enzyme and NADPH oxidase prevents diabetes-induced cardiac dysfunction**

\*Al-Sumairi A, Akhtar S, Benter IF

Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University

**Introduction:**

Cardiovascular disease continues to be the primary cause of morbidity and mortality in diabetic patients. Several pathological mechanisms have been postulated for the onset and progression of diabetic cardiac dysfunction, including activation of the rennin-angiotensin system, and production of reactive oxygen species (ROS) which cause oxidative stress. Angiotensin converting enzyme (ACE) inhibitors such as ramipril provide cardioprotective effects in diabetic patients. NADPH oxidase is one of the primary sources of ROS. This study aimed to test whether the combination of ramipril and apocynin, an NADPH oxidase inhibitor, would provide greater cardioprotection than ramipril alone in a model of type-1 diabetes.

**Methods:**

Diabetes was induced by intraperitoneal injection of 55 mg/kg of streptozotocin to Wistar rats. Hearts were isolated 30 days after induction of diabetes and perfused for 30 minutes and then exposed to 30 minutes of ischemia followed by 30 minutes of reperfusion. Hearts were perfused with vehicle, ramipril, apocynin or ramipril-apocynin combination. Post-ischemic left ventricular contractility and hemodynamics were detected.

**Results:**

Induction of diabetes resulted in significant attenuation of cardiac function. Perfusion of diabetic hearts with either ramipril or apocynin resulted in significant improvement in recovery after ischemia. However, perfusion of hearts with both ramipril and apocynin resulted in higher cardiac recovery in terms of left ventricular contractility and coronary flow than each drug alone.

**Conclusions:**

This observation suggests that treatment of diabetic patients with a drug that inhibits both ACE and NADPH oxidase would produce better cardioprotection than an ACE inhibitor alone.

*Key Words: Ramipril; Apocynin*

*Funding Agency: Collage of Graduate Studies*



**Pharmacology and Toxicology**

Category: Undergraduate

166

**Levosemindan improves cardiac recovery from ischemia in diabetic and/or hypertensive rat models**

Al-Turki A, Benter IF

Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University

**Introduction:**

Levosimendan is a calcium sensitizing drug that also has vasodilating properties through the opening of potassium-ATP channels. The aim of this study was to determine if Levosimendan given during perfusion before ischemia or during reperfusion would produce protection against ischemia-reperfusion (I/R) induced cardiac dysfunction in control, diabetic, hypertensive and diabetic-hypertensive rats.

**Methods:**

Diabetes was induced by intraperitoneal injection of 55 mg/kg of streptozotocin to WKY or SHR hypertensive rats. Hearts were removed from control, diabetic, hypertensive and diabetic-hypertensive rats, mounted on Langendorff apparatus and perfused at a constant pressure of 50mmHg with an oxygenated Krebs-Henseleit buffer. Left ventricular contractility and coronary flow were continuously monitored. The hearts were perfused for 30 min and then subjected to 40 min of no flow global ischemia (I) followed by a 30 min of reperfusion ®. Levosimendan was given either during perfusion before ischemia or during reperfusion.

**Results:**

Levosimendan significantly improved cardiac recovery after I/R in control, diabetic, hypertensive and diabetic-hypertensive rats in all parameters studied. Most improvement was observed in diabetic-hypertensive rats: 100% and 130% improvement in left ventricular developed pressure and dP/dtmax, respectively, and 700% improvement in coronary flow; improvement was more prominent when Levosimendan was given during reperfusion.

**Conclusions:**

Levosimendan significantly improved cardiac left ventricular contractility and hemodynamics after I/R especially in the diabetic-hypertensive and must be considered in the treatment of myocardial ischemic attacks

*Key Words: Levosimendan; Cardiac recovery from ischemia; Diabetic/hypertensive*

*Funding Agency: None*



**Pharmacology and Toxicology**

Category: *Clinical*

167

**Therapeutic drug monitoring services: 4 year experience in TDM-CT laboratory, Faculty of Medicine, Kuwait University, Kuwait**

\*Anwar AA<sup>1</sup>, Matar K<sup>2</sup>

<sup>1</sup>Department of Pharmacology & Toxicology, Kuwait University, Faculty of Medicine; <sup>2</sup>Department of Applied Therapeutics, Kuwait University, Faculty of Pharmacy

**Introduction:**

A retrospective study was conducted to observe the recent trend in the utilization of Therapeutic Drug Monitoring and Clinical Toxicology (TDM-CT) Service by the public hospitals in Kuwait over a period of four years. The aim of the study is to increase the awareness of the physicians about the existing TDM-CT services and their utilization provided by the TDM-CT Laboratory at the Faculty of Medicine. We also look forwards to get an input from the physicians so that we can increase the scope of the analyses offered by the TDM-CT laboratory in the future.

**Methods:**

Statistical analysis was conducted using the data collected in the TDM laboratory over the past four years. A total of 4200 samples were included in the study which were analyzed for Keppra, Lamictal, Trileptal, Topamax, Busivex, Sabril, Zorantin, Cordarone, Neurontin, Rivotril, and Myfortic. The samples were received from the following Hospitals: Mubarak Al-Kabir, Al-Sabah, Ibn-Sina, Amiri, Jahra, Infectious, Al-Razi, Farwaniya, Adan, Armed Forces, Psychological Medicine, Kuwait Cancer Control Center, Organ Transplantation Center, and Physical Medicine and Rehabilitation Center.

**Results:**

The analysis of the retrospective data demonstrates the relative preponderance of requests for different drugs, reasons of requests, problems encountered in the request forms and a study about the percentage of results found to be within, below or above the tentative therapeutic range for each drug being analyzed in the laboratory.

**Conclusions:**

The most requested drugs were Keppra and Trileptal followed by Lamictal and Topamax. We observed that the levels of the drugs in most of the samples were within the tentative therapeutic range with the exception of Topamax and Lamictal where the levels remained just above or below the lower limit of the desired value.

*Key Words: Kuwait; Experience*

*Funding Agency: None*



**Pharmacology and Toxicology**

*Category: Basic Sciences*

**168**

**Pamam dendrimer delivery system modulates epidermal growth factor receptor tyrosine kinase signaling via an oxidative stress-dependent pathway**

\*Chandrasekhar B, Akhtar S

Department of Pharmacology and Toxicology, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

Polyamidoamine (PAMAM) dendrimers are highly branched, cationic, macromolecules that are used as drug delivery systems. Ideally, they should only enhance drug delivery and exhibit no other adverse effects. Although we have previously shown that they can modulate global gene expression, little is known about their toxicological profiles in terms of their proteomic interactions at the level of signal transduction pathways. Here we investigated the impact of Superfect (SF), a commercially available PAMAM dendrimer, on epidermal growth factor receptor (EGFR) tyrosine kinase signaling in human embryonic kidney (HEK-293) cells.

**Methods:**

Different concentrations of SF were incubated with or without the antioxidants, apocynin and catalase, in HEK-293 cells for 4 or 24h. The levels of total and phosphorylated EGFR were determined by Western blotting.

**Results:**

At concentrations routinely used for transfection, SF increased total and phosphorylated forms of EGFR at 4h and 24h following treatment. Dendrimer-induced changes in EGFR signaling could be attenuated by apocynin and catalase for the 4 h but less so for the 24 h time point.

**Conclusions:**

The SF dendrimer delivery system can enhance EGFR expression and phosphorylation in HEK-293 cells. The acute activation of EGFR signaling appears to be mediated via an oxidative stress-dependent pathway as anti-oxidants were able to block dendrimer-induced changes in EGFR. These results suggest that dendrimers, aside from their ability to improve drug delivery, can modulate important cellular signal transduction pathways and thus, further understanding of their toxicology at the proteomic level will be important in their use clinically.

*Key Words: EGFR; Drug delivery*

*Funding Agency: None*



**Pharmacology and Toxicology**

Category: Graduate MSc (Basic Science)

169

**A chemically modified tetracycline (COL-3) inhibits lipopolysaccharide-induced microglia activation and inflammation in mice brains**

\*Edan R<sup>1</sup>, Luqmani YA<sup>1</sup>, Masocha W<sup>2</sup>

<sup>1</sup>Department of Pharmaceutical Chemistry, Faculty of Pharmacy Kuwait University; <sup>2</sup>Department of Applied Therapeutics, Faculty of Pharmacy, Kuwait University

**Introduction:**

Microglia activation, by tissue damage or exposure to pathogen molecules such as lipopolysaccharide (LPS), results in release of proinflammatory molecules including cytokines, which contribute to neuronal damage in the CNS if not controlled. Tetracyclines such as minocycline inhibit microglial activation and cytokine expression during CNS inflammation. In this study we investigated the potential of a chemically modified tetracycline COL-3, which is in clinical trials for treatment of malignant tumors, to inhibit LPS-induced glial cell activation and inflammation in the brain.

**Methods:**

BALB/c female mice (8-12 weeks old, n=48) were inoculated i.p. with LPS 1 mg/kg or its vehicle. The mice were treated for 3 days with minocycline (i.p.), COL-3 (orally) or their vehicles, commencing 2 days before LPS inoculation. Mice were sacrificed 24 h post LPS inoculation, brains dissected out and the expression of CD11b (a microglia/macrophage marker), GFAP (an astrocyte marker), cytokines, iNOS and p38 mitogen-activated protein kinase (p38 MAPK) quantified by realtime PCR and/or immunofluorescence.

**Results:**

COL-3 treatment significantly inhibited the LPS-induced increase in CD11b, TNF- $\alpha$ , IL-12 and IL-10 transcript levels, showed a tendency to decrease IFN-gama, GFAP, IL-1 $\beta$ , but did not alter the level of iNOS and IL-6 transcripts. On the other hand, minocycline treatment significantly reduced LPS-induced increase in GFAP transcripts and showed a tendency to decrease CD11b, TNF- $\alpha$ , IL-12, IFN-gama, IL-1 $\beta$  and iNOS but did not affect IL-10 and IL-6 transcript levels. Immunofluorescence imaging showed that both COL-3 and minocycline treatment reduced LPS-induced p38 MAPK, microglia and GFAP activation.

**Conclusions:**

Our results show that COL-3 inhibits LPS-induced microglia activation and cytokine up-regulation in the CNS, and displays potential as a therapeutic agent for treatment of conditions involving CNS inflammation

*Key Words: Microglia activation; Lipopolysaccharide*

*Funding Agency: KU Graduate Studies Grant # YM05/10*



**Pharmacology and Toxicology**

Category: Graduate MSc (Basic Science)

170

**The role of camp in the enhancement of vascular endothelial growth factor (VEGF) release from human macrophages by beta-2 adrenoceptor agonists**

\*El-Zohairy SN, Ezeamuzie CI, Oriowo MA

Department of Pharmacology and Toxicology, Faculty of Medicine, Kuwait University

**Introduction:**

Beta<sub>2</sub>-agonists are effective bronchodilators widely used in the treatment of asthma. However, their use in monotherapy may result in the progression of the disease over time. This is because they are able to enhance the release of pro-inflammatory mediators, especially VEGF, an angiogenic factor that has been implicated in the pathophysiology of asthma. The purpose of this study was to investigate the role of cAMP and its downstream pathways (PKA/EPAC) in the enhancement of VEGF release from human macrophages by beta<sub>2</sub>-agonists.

**Methods:**

Human U937 cells were differentiated into macrophages by culturing them in the presence of PMA. The enhancing effect of different beta<sub>2</sub>-agonists on LPS-induced release of VEGF from U937 cells was studied, and their ability to increase cAMP release was also investigated. The released VEGF and cAMP were measured by enzyme immunoassay. Finally, the involvement of the PKA and EPAC pathways was investigated using selective pathway agonists and antagonists.

**Results:**

The LPS-induced VEGF release was enhanced by all drugs in a concentration-dependent manner. Both the non-selective beta-antagonist propranolol and the beta<sub>2</sub>-selective antagonist, ICI 118551, inhibited isoprenaline-induced enhancement of VEGF release in a competitive manner. However, ICI 118551 was more effective than propranolol as confirmed by comparing their K<sub>b</sub> values. The results also established the involvement of cAMP as the second messenger mediating VEGF release by beta<sub>2</sub>-agonists.

**Conclusions:**

Beta<sub>2</sub>-agonists effectively enhance VEGF release from LPS-stimulated U937 cells. Their activity is mediated via an increase in intracellular cAMP levels where the use of several cAMP pathway agonists and antagonists has revealed that the PKA pathway, rather than EPAC pathway, is responsible for the cAMP-dependent VEGF release by beta<sub>2</sub>-agonists.

*Key Words: VEGF; Beta-2 agonists; Cyclic AMP*

*Funding Agency: (Grant # YM 14/09) Research Administration and College of Graduate Studies*



**Pharmacology and Toxicology**

Category: *Basic Sciences*

171

**Cultured human monocytes lose their sensitivity to beta-2 agonists as a result of a selective loss of their membrane beta-2 receptors**

\*Ezeamuzie CI, Shihab PK, Philip E

Department of Pharmacology, Faculty of Medicine, Kuwait University.

**Introduction:**

The short-acting beta-2 adrenoceptor agonists such as salbutamol, are effective bronchodilators used to treat asthma. They are ineffective as anti-inflammatory agents *in vivo*, and fail to inhibit the release of inflammatory mediators by isolated alveolar macrophages even though they exhibit this effect on freshly isolated monocytes. The purpose of this study was to determine if this observation is related to a change in the expression and/or function of surface beta-2 adrenoceptors during the differentiation of these cells from monocytes to macrophages.

**Methods:**

Monocytes were purified from fresh human blood using the CD14-dependent immunomagnetic method. Purified monocytes, cultured for 0 - 3 days were pre-treated with salbutamol or PGE<sub>2</sub> before being stimulated with bacterial lipopolysaccharide (LPS). After a further culture for 24h, the amount of released TNF- $\alpha$  and the intracellular level of cAMP were determined by enzyme immunoassay. Western blotting techniques were used to study the expression of the membrane beta-2 receptor protein.

**Results:**

In freshly isolated human monocytes, both salbutamol and PGE<sub>2</sub> significantly inhibited LPS-induced TNF- $\alpha$  release as well as increase intracellular cAMP. After culturing adherent monocytes for 24-72h, the ability of salbutamol to produce both effects was completely lost whereas that of PGE<sub>2</sub> remained essentially intact. Western blotting analysis of membrane receptor expression revealed a near complete loss of surface expression of beta-2 receptors, but not EP<sub>2</sub> receptors, in cells cultured for  $\geq$  24h.

**Conclusions:**

As cultured human monocytes differentiate into macrophages, they selectively lose their surface beta-2 receptors and hence become insensitive to the anti-inflammatory effect of beta-2 agonists. This may explain why beta-2 agonists lack significant anti-inflammatory effect on alveolar macrophages or in clinical asthma.

*Key Words: Anti-inflammatory; Beta-2 receptors*

*Funding Agency: Kuwait Foundation for the Advancement of Sciences*



**Pharmacology and Toxicology**

Category: Basic Sciences

172

**Angiotensin-(1-7) abrogates oxidative DNA damage in corpus cavernosum of type 1 diabetic rats**

\*Narayana K<sup>1</sup>, Yousif MHM<sup>2</sup>, Makki B<sup>2</sup>, Akhtar S<sup>2</sup>, Benter IF<sup>2</sup>

<sup>1</sup>Department of Anatomy, <sup>2</sup>Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University

**Introduction:**

Angiotensin- (1-7) [(Ang-(1-7)], a heptapeptide, is an ACE2 catalyzed breakdown product of angiotensin II and/or a product of neprilysin-mediated conversion of angiotensin I. The peptide acts via its receptor Mas to produce cellular effects such as nitric oxide release, Akt phosphorylation and vasodilation. The present study investigated the putative role of the peptide in alleviating type 1 diabetes mellitus (T1DM)-induced oxidative DNA damage in rat corpus cavernosum (CC).

**Methods:**

Adult male Wistar rats (N=3/group) were segregated into 4 groups and treated as follows. Group 1- treated with vehicle (citrate buffer), which served as control, group 2- Ang- (1-7) 576 µg/kg/day, group 3- T1DM induced by a single i.p., injection of 55 mg/kg streptozotocin, and group 4- similar to group 3 but also supplemented with Ang- (1-7) 576 µg/kg/day during last 3 weeks. The animals were sacrificed six weeks following the day of confirmation of hyperglycemia and the CC was separated from the penis and processed for Masson's staining, 8-oxo-dG immunohistochemistry and ELISA, and estimation of total antioxidant status (TAS) and total oxidant status (TOS). The data were analyzed by one way ANOVA followed by Fisher's least square difference test and P<0.05 was considered significant.

**Results:**

The CC from T1DM rats showed structural damage in terms of fibrous and muscular degeneration. Oxidative stress was induced in CC of T1DM rats as indicated by a decrease in TAS and a concomitant increase in TOS. The induced oxidative stress led to an increase in 8-oxo-dG activities in both cytoplasm and nuclei of the cells in CC of T1DM rats (P<0.05). Concomitant administration of Ang- (1-7) recovered the structure, mitigated the oxidative stress and ameliorated DNA damage in CC.

**Conclusions:**

Type 1 DM induces structural damage, oxidative stress and oxidative DNA damage and Ang- (1-7) abrogates diabetes-induced oxidative damage by neutralizing oxidative stress in CC.

*Key Words: Diabetes; Oxidative DNA damage; Oxidative stress*

*Funding Agency: This work was supported by KU grant #MR04/09*



**Pharmacology and Toxicology**

Category: Basic Sciences

173

**A chemically modified tetracycline (COL-3) prevents the development of paclitaxel-induced painful neuropathy in mice.**

\*Parvathy SS, Masocha W

Department of Applied Therapeutics, Faculty of Pharmacy, Kuwait University

**Introduction:**

This study was conducted to investigate the potential of a chemically modified tetracycline (COL-3), which has anti-inflammatory activities, to protect against development of paclitaxel-induced painful neuropathy. Paclitaxel is a chemotherapeutic agent used against solid tumors and COL-3 is in clinical trials for treatment of cancer.

**Methods:**

BALB/c mice (n = 150) were treated for 5 consecutive days with paclitaxel (2 mg/kg, i.p.) or paclitaxel + COL-3 (4, 20 or 40 mg/kg, orally). The reaction latency times to thermal stimuli (hot-plate test) were recorded before (baseline) and after treatment. Gene transcripts of 5 cytokines IFN- $\gamma$ , IL-1  $\beta$ , -6 and -10, and TNF- $\alpha$  were quantified by real time PCR in brains and spleens dissected out from mice sacrificed at 7 days post first dose administration of vehicle, paclitaxel or paclitaxel + COL-3 40 mg/kg.

**Results:**

Paclitaxel treatment reduced reaction latency time to thermal stimuli by 41%, 33% and 23% at 7, 10 and 14 days post-first drug administration, respectively, compared to baseline ( $p < 0.01$ , two-way ANOVA). Treatment with COL-3 40 mg/kg, but not lower doses 4 or 20 mg/kg, prevented paclitaxel-induced thermal hyperalgesia and produced reaction latencies significantly higher than paclitaxel only-treated mice ( $p < 0.01$ ). Paclitaxel did not significantly alter the transcript levels of cytokines in the brains or spleens of mice. Co-administration of COL-3 + paclitaxel significantly increased transcript levels of IL-6 in the spleen ( $p < 0.01$ ) compared with paclitaxel alone and showed a tendency of increasing IL-6 in the brain, but did not significantly alter expression of other cytokines.

**Conclusions:**

Our results indicate that COL-3 can prevent the development of paclitaxel-induced neuropathic hyperalgesia, possibly via its immunomodulatory activities including increasing the levels of the neuroprotective cytokine IL-6, thus, could be useful in the prevention of chemotherapy-induced painful neuropathy.

*Key Words: Chemically modified tetracycline; Paclitaxel*

*Funding Agency: Kuwait University Grant # PT01/11*



**Pharmacology and Toxicology**

Category: Basic Sciences

174

**Early postnatal lead exposure impairs learning and induces tau phosphorylation in the brain of young rats**

\*Rahman A<sup>1</sup>, Khan KM<sup>2</sup>, Khan I<sup>3</sup>, Attur S<sup>1</sup>

<sup>1</sup>Department of Family Sciences, College for Women; <sup>2</sup> Department of Anatomy; <sup>3</sup>Biochemistry, Faculty of Medicine, Kuwait University, Kuwait

**Introduction:**

Lead (Pb) is a known neurotoxic heavy metal with no known physiological functions in the body. Although, Pb affects several organ systems, the central nervous system is particularly sensitive to the insult of Pb, as it is affected by low doses of exposure. This work focuses on how the expression and phosphorylation state of the brain protein, tau, which is involved in learning and memory, is affected by Pb exposure.

**Methods:**

Wistar rat pups were exposed to 0.2% Pb-acetate via their dams' drinking water from postnatal day 1 to 21. Pb in blood and brain were measured by atomic absorption spectrophotometry and the expression of tau, phosphorylated tau and various serine/threonine protein phosphatases (PP1, PP2A, PP2B and PP5) in the brain was analyzed by Western blot.

**Results:**

Pb exposure resulted in significant impairment of learning and resulted in a significant reduction in the expression of tau but increased the phosphorylation of tau at serine 199/202, threonine 212/serine 214 and threonine 231. PP2A expression decreased, whereas, PP1 and PP5 expression increased in Pb-exposed rats.

**Conclusions:**

These results demonstrate that early postnatal exposure to Pb decreases PP2A expression and induces tau hyperphosphorylation at several serine and threonine residues. Hyperphosphorylation of tau may be involved in lead-induced deficits in learning and memory.

*Key Words: Lead; Learning and Memory; Tau Phosphorylation*

*Funding Agency: KU Grant # WF 01/07*



**Pharmacology and Toxicology**

Category: Graduate MSc (Basic Science)

175

**Lapatinib, a dual inhibitor of EGFR and erbB2 phosphorylation, prevents development of diabetes-induced vascular dysfunction.**

\*Sarkhouh F, Cherian A, Yousif MHM, Benter IF, Akhtar S

Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University

**Introduction:**

Cardiovascular complications are a major cause of morbidity and mortality in patients with diabetes. Diabetes induced elevation in epidermal growth factor (EGFR) signaling is an important early step in mediating vascular dysfunction. We propose that enhanced phosphorylation of both EGFR and erbB2 (a second member of the EGFR family) leads to diabetes-induced vascular dysfunction. The aim of this study was to examine the effect of Lapatinib (a dual inhibitor of EGFR & erbB2 phosphorylation) in preventing diabetes-induced vascular dysfunction in mesenteric bed of streptozocin-induced diabetic rats.

**Methods:**

Control and diabetic male Wistar rats were chronically treated with Lapatinib (100 mg/kg by oral gavage) for 4 weeks from onset of diabetes. The vascular responsiveness of the isolated perfused mesenteric bed to norepinephrine (NE) and carbachol were investigated.

**Results:**

Diabetes led to exaggerated responsiveness to NE and an attenuated response to carbachol that was associated with increased EGFR and erbB2 phosphorylation in the mesenteric bed. Lapatinib treatment led to significant correction of these vascular changes.

**Conclusions:**

Lapatinib prevented development of diabetes-induced vascular dysfunction by significantly inhibiting EGFR and erbB2 signaling. This may represent a novel strategy for the treatment of vascular complications associated with diabetes.

*Key Words: Mesenteric bed; Lapatinib*

*Funding Agency: College of Graduate studies, KU grant YM 07/10*



**Pharmacology and Toxicology**

Category: Basic Sciences

176

**Activation of epidermal growth factor receptor enhances the cardio-protective effects of Losartan in diabetes**

\*Varughese S, Chandrasekhar B, Attur S, Benter IF, Akhtar S

Department of Pharmacology and Toxicology, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

Signaling via the epidermal growth factor (EGF) receptor (EGFR) is a pro-survival, protective pathway in the heart. Losartan, an angiotensin II (type 1) receptor blocker (ARB), is a clinically established cardioprotective agent in diabetes that is also known to inhibit the beneficial EGFR signaling. We hypothesized that the cardioprotective effects of Losartan could be enhanced by activating EGFR signaling by co-administering its ligand, EGF, in a model of diabetes.

**Methods:**

Isolated hearts from streptozotocin-induced diabetic rats were mounted on a Langendorff perfusion assembly. Cardiac contractility and coronary flow parameters were measured following acute administration of EGF ( $10^{-8}$ M) and/or Losartan ( $2 \times 10^{-6}$ M) immediately after 40 min ischemia (I), during 30 min reperfusion (R). Western blotting was utilized to identify the levels of total and phosphorylated forms EGFR or actin.

**Results:**

EGF or Losartan treatment alone comparably improved cardiac recovery following I/R. Losartan and EGF combination treatment significantly improved cardiac recovery more than with each drug alone. Losartan reduced cardiac EGFR phosphorylation whereas co-administration with EGF, prevented the inhibitory effects of Losartan on EGFR as its phosphorylation levels were raised to similar levels to EGF alone.

**Conclusions:**

Activation of EGF/EGFR pro-survival pathway enhances the cardio-protective effects of Losartan in diabetes. Our data may have important clinical implications as they suggest for the first time that rescuing the EGFR inhibitory effect of ARBs by activators of the EGF/EGFR pathway may represent a novel clinical approach to improve cardiac function in diabetes.

*Key Words: EGFR; Ischemia-reperfusion*

*Funding Agency: None*



**Pharmacology and Toxicology**

Category: Basic Sciences

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**Chronic treatment with angiotensin-(1-7) corrects diabetes-induced erectile dysfunction**

Yousif MHM, Benter IF, \*Makki B, Cherian A, Akhtar S

Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University

**Introduction:**

Diabetes is a major risk factor for erectile dysfunction (ED). The pathophysiology of diabetic ED differs from nondiabetic ED and is more resistant to treatment. The objective of this study was to determine if treatment with angiotensin-(1-7) [Ang-(1-7)] can correct diabetes-induced abnormal changes in the rat corpus cavernosum.

**Methods:**

Experiments were done on control and diabetic male Wistar rats weighing about 250g (n=8/group). Diabetes was induced by a single ip injection (55mg/kg) of streptozotocin (STZ). Treatment with Ang-(1-7) (576µg/kg/day ip) was given daily during the last 3 weeks of diabetes induction. Animals were sacrificed at the end of 6 weeks. Strips of the corpus cavernosum were suspended in organ-bath chambers containing Krebs solution at pH 7.4. Reactivity of the corpus cavernosum was determined by measurement of changes in the isometric tension to vasoactive agonists. Cumulative concentration response curves were established to the constrictor agonists phenylephrine (PE) and endothelin-1 (ET-1), and to the relaxant agonist carbachol. Western blot analysis was used to detect the levels of endothelial nitric oxide synthase (e-NOS) and p38 mitogen activated protein (MAP) kinase.

**Results:**

Diabetes-induced increase in ET-1 and PE-mediated contraction and decrease in carbachol-mediated relaxation were corrected by Ang-(1-7) treatment ( $P < 0.05$ ). Similarly, diabetes-induced increase in p38 MAP kinase and decrease in e-NOS expression were corrected by Ang-(1-7) treatment.

**Conclusions:**

Chronic treatment with Ang-(1-7) can reverse diabetes-induced abnormal changes in the rat corpus cavernosum.

*Key Words: Diabetes; Erectile dysfunction; Relaxation*

*Funding Agency: Kuwait University, Research Administration, Project No. MR04/09*

**Pharmacy***Category: Clinical*

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**Population pharmacokinetics of amikacin in non-critical care pediatric Kuwaiti patients without cystic fibrosis.**\*AL-Lanqawi Y<sup>1</sup>, Buhamrah E<sup>2</sup>, Zeinab MD<sup>2</sup>, Al-Momen J<sup>2</sup><sup>1</sup>Drug and Poison Information & Research Unit, Pharmacy Department; <sup>2</sup>Pediatric Department, Al-Amiri Hospital, Ministry of Health, Kuwait.**Introduction:**

Amikacin (AMK) is commonly used to treat gram negative infections in pediatric patients. The AMK pharmacokinetic parameters such as volume of distribution (Vd) and clearance (Cl) in pediatrics displays an extensive interindividual variability. Age, body weight (bw), sex and creatinin clearance are the covariates of the interindividual variability in Vd and Cl. Published data on AMK pharmacokinetics are rare for Arab pediatric patients and there is none for the state of Kuwait. The aim of this study was to: (1) calculate the Vd and Cl in pediatric Kuwaiti patients and (2) investigate the effect of covariates on the individual Vd and Cl.

**Methods:**

62 (29 male and 33 female) non-critical care pediatric patients older than 0.3 of age without cystic fibrosis were identified for whom a confirmed steady-state AMK peak and trough levels were available. They received a multiple daily dosing regimen of AMK (4 to 15 mg/kg intravenously during 0.1, two to three times daily) between 2006 and 2009. The Vd and Cl were estimated using Sawchuck and Zaske method. Regression analysis was performed to assess the effect of age, body weight, sex and creatinin clearance on Vd and Cl.

**Results:**

The Mean+Sd (median, range) of the Vd and Cl were 6.52±5.67 (4.64, 0.73-21.07 l) and 1.77±1.38 (1.13, 0.19-7.18 l/h) respectively. The Vd and Cl were greater and smaller respectively, than those reported from western countries. The age and bw were found to have significant effects on Vd and Cl as indicated by the following equations:  $Cl=0.2291 \times Age + 0.4993$ , ( $R^2=0.7686$ );  $Cl=0.065 \times bw + 0.6013$ , ( $R^2=0.6106$ );  $Vd=0.9081 \times Age + 1.4938$ , ( $R^2=0.7129$ );  $Vd=0.3024 \times bw + 1.0924$ , ( $R^2=0.781$ ).

**Conclusions:**

In this population of pediatric Kuwaiti patients without cystic fibrosis we found that the age and bw are the primary covariates in explaining the variabilities in Vd and Cl. Initial dose regimen based on local age and bw models followed by measuring AMK levels are recommended.

*Key Words: Population Pharmacokinetics; Amikacin; Pediatric patients**Funding Agency: None*



**Pharmacy**

*Category: Clinical*

**179**

**A prospective study of acute medication misuse and abuse patterns admitted to Mubarak Al-Kabeer hospital**

Al-Mutawa A<sup>1</sup>, \*Abahussain E<sup>2</sup>, Hedaya M<sup>3</sup>

<sup>1</sup>Department of Medicine, Mubarak Al-Kabeer Hospital, Kuwait; <sup>2</sup> Department of Pharmacy Practice, Kuwait University, Faculty of Pharmacy; <sup>3</sup> Department of Pharmaceutics, Kuwait University, Faculty of Pharmacy

**Introduction:**

The identification and prevention of drug-related problems (DRPs) is one of the core components of pharmaceutical care. Any care activity for optimization of pharmacotherapy is usually designed to correct or prevent actual and potential DRPs. Documenting DRPs as part of the care process is essential and using the Accident and Emergency (AE) department to monitor ADRs could be useful. The primary aim of this study was to identify the proportion of DRPs caused by the patients intentionally (abuse) or unintentionally (misuse) and the possible demographic factors associated with these problems.

**Methods:**

A prospective study was conducted in AE department at Mubarak Al-Kabeer hospital. Data were gathered through a structured questionnaire on admission and follow up of the patients until their discharge from the hospital. Descriptive statistics, chi-square test were used for data analysis.

**Results:**

A total of 68 patients admitted through AE department due to DRPs participated in the study. The ages range from 12-85 years. 59% were due to medication abuse and 41% were due to medication misuse, mostly due to a wrong drug dose (25%). Paracetamol was the common drug involved in the intentional problems, while warfarin was the common drug involved with drug misuse. The intentional drug abuse was more prevalent among younger age, students and unmarried patients, while the unintentional drug misuse was more in the higher ages, married, non-working and patients with co-morbidity ( $p < 0.05$ ). Complications occurred more in patients with drug misuse and one case of death was reported in this group.

**Conclusions:**

DRPs are widespread and there is an urgent need for implementing strategies to reduce morbidity and mortality resulting from drug misuse and abuse in Kuwait especially among the youth. Also it is important to apply strict regulatory rules that can decrease the prevalence of DRPs.

*Key Words: Abuse; Misuse; Drug related problems*

*Funding Agency: None*



**Pharmacy**

Category: Graduate MSc (Basic Science)

180

**Effect of increased extracellular pH on morphological behavior of breast cancer cells**

\*Almohri IM, Luqmani YA

Kuwait University, Faculty of Pharmacy

**Introduction:**

De novo and acquired resistance to antiestrogens is a serious problem in therapy of estrogen receptor (ER)+ve breast cancer. To study endocrine insensitivity we have established several ER-depleted cell lines by shRNA transfection of MCF7 cells that have thereby acquired a mesenchymal phenotype. In this study we examined the motile behavior of these and ER expressing lines in response to a change in extracellular pH, as this is thought to be altered by tumor metabolism and may affect dispersion.

**Methods:**

Cells grown on several substrata were maintained at pH 7.4 in CO<sub>2</sub> buffered medium and then transferred to conditions of pH 8.3 and effects observed microscopically over 10-60 min. Time lapse photography was utilized to continuously monitor cell behavior and effect of returning cells to pH 7.4. Effect of drugs was assessed by addition at least 1h prior to pH shift. Photomicrographs were analysed using Adobe Photoshop measuring tool and differences assessed by student's t test.

**Results:**

ER down-regulated transfected cells exhibited reversible scattering/shrinking in response to increased extracellular pH; cell retraction from adhesion substratum (uncoated tissue culture dishes, fibronectin or collagen), shrinkage of cytoplasm and rounding-up were observed, with cell polarization and decreased clustering. Cells resumed normal appearance when returned to pH 7.4 for >70min. This shrinking/scattering effect was partially prevented by a Na<sup>+</sup> /H<sup>+</sup> antiport inhibitor but not by glucose uptake inhibitors. Change in pH had no effect on morphology of parental or transfected MCF7 cells that remained ER+ve, or of normal breast line HBL100 or the ER-ve tumor derived MDA-MB231.

**Conclusions:**

Loss of ER makes breast cancer cells susceptible to pH induced morphological changes that could play an important role in tumor metastasis. This suggests possibilities for novel drug targets.

*Key Words:* Breast cancer; Endocrine resistance; pH

*Funding Agency:* YM04/10



**Pharmacy**

*Category: Graduate MSc (Basic Science)*

**181**

**Information technology adaption in a community pharmacy**

\*Altmimy A

Institute of Leadership, Royal College of Surgeons in Ireland

**Introduction:**

Implementing a computerized inventory system within a community pharmacy, using a change management framework. Background: Increased workload through the use of manual documentary system led to supply shortages and insufficiencies in service delivery. Project rationale: The project was carried out to reduce labor, shortages, inventory and operating costs, in addition to human errors by improving stock management through information technology processing and adaption.

**Methods:**

Kotter's eight steps change framework was used as a guide for the adaption of the information technology within the pharmacy.

**Results:**

Implications for Pharmacy Inventory Management: Successful management of inventory system is related to the full understanding of information technologies and the system under consideration. Sufficient background on the bar-coding technology along with its risks and benefits are provided, and its impact on the pharmacy including profitability and productivity enhancement are discussed.

**Conclusions:**

The key component of project success is how to create a clear vision of the targeted goals and communicate it with the manpower involved in or affected by the change. Moreover, getting support from senior manager is essential for any project to be started and to allocate more resources. Sustainability of the change will depend on removing the obstacles and reducing resistance through proper communication and benefits utilization.

*Key Words: Community Pharmacy; Stock Management; Kotter's eight steps change framework  
Funding Agency: None*



**Pharmacy**

*Category: Basic Sciences*

**182**

**Effect of inhibition of the ubiquitin-proteasome-system and IkappaB kinase on airway inflammation and hyperresponsiveness in a murine model of asthma**

\*El-Hashim AZ<sup>1</sup>, Renno WM<sup>2</sup>, Abduo HT<sup>1</sup>, Jaffal SM<sup>1</sup>, Akhtar S<sup>3</sup>, Benter IF<sup>3</sup>.

<sup>1</sup>Department of Applied Therapeutics, Faculty of Pharmacy, Kuwait University, <sup>2</sup>Department of Anatomy; <sup>3</sup>Department of Pharmacology, Faculty of Medicine, Kuwait University

**Introduction:**

NF(K)B has recently been highlighted as an important pro-inflammatory transcriptional factor and its blockade is believed to represent a new therapeutic approach for asthma. The purpose of this study was to investigate the effects of blocking the actions of NF(k)B, through inhibition of the ubiquitin-proteasome system (UPS) or I(k)B kinase (IKK), in a murine model of asthma.

**Methods:**

The effects of the UPS inhibitor, MG-132 (0.1 and 0.3 mg/kg), and the IKK inhibitor, BAY 11-7085 were evaluated by assessing effects on lungs airway responsiveness, cytology, histologically and biochemical changes.

**Results:**

Treatment with the UPS inhibitor, MG-132 (0.03 and 0.1 mg/kg;i.p.), did not significantly affect the ovalbumin-induced increase in total and differential cell numbers, histological changes such as perivascular and peribronchial inflammatory cell infiltration, perivascular and peribronchial fibrosis or the airway hyperresponsiveness to methacholine. In contrast, treatment of mice with the IKK inhibitor, BAY 11-7085, (3 and 10 mg/kg;i.p.) dose-dependently inhibited the ovalbumin-induced increase in airway leukocyte influx and decreased the percentage of airway lymphocytes, neutrophils and eosinophils. Also, BAY 11-7085 (10 mg/kg) treated mice showed a significant decrease in the histologically assessed inflammatory indices as well as a significant reduction in the ovalbumin-induced increase in airway responsiveness to inhaled methacholine. Furthermore, BAY 11-7085 significantly inhibited the ovalbumin-induced increase in the level of phosphorylation of I(K)B $\alpha$  and extracellular regulated kinases (ERK) 1/2 whilst MG-132 significantly increased the phosphorylation of ERK1/2.

**Conclusions:**

These findings confirm the critical role that NF(k)B plays in airway inflammation, highlight the importance of IKK in regulating the pro-inflammatory activity of NF(k)B and also suggest that UPS may not be a useful drug target for asthma treatment.

*Key Words: Ubiquitin-proteasome-system; Inflammation*

*Funding Agency: None*

**Pharmacy***Category: Basic Sciences***183****In vitro/in vivo correlation of fast release mephenamic acid microspheres in humans**\*Etman MA<sup>1</sup>, Farid RM<sup>2</sup>, Nada AH<sup>3</sup>, Ebian AR<sup>1</sup><sup>1</sup>Department of Pharmaceutics, Faculty of Pharmacy, Alexandria University, Alexandria, Egypt;<sup>2</sup>Department of Pharmaceutics, Faculty of Pharmacy & Drug Manufacturing, Pharos University, Alexandria, Egypt; <sup>3</sup>Department of Pharmaceutics, Faculty of Pharmacy, Kuwait University, Kuwait**Introduction:**

The objectives of this study were to assess the bioavailability of an optimized mephenamic acid (MFA) microsphere (test) against Ponstan capsules (reference) in healthy volunteers, and to establish a correlation with in vitro parameters.

**Methods:**

Four subjects received the test and reference (250 mg MFA each) in a randomized crossover design, separated by a 1-week washout period. The drug was analyzed in plasma by a specific high performance liquid chromatographic method. The relevant pharmacokinetic parameters [maximum plasma concentration ( $C_{max}$ ), time of peak concentration ( $T_{max}$ ), area under plasma concentration-time curves from 0 to 12 h ( $AUC_{0-12}$ ) and area under plasma concentration-time curves from zero to infinity ( $AUC_{0-infinity}$ )] were calculated from the plasma drug concentration-time data.

**Results:**

The test product exhibited faster absorption ( $T_{max}$  of 1.87 ± 0.482 vs. 2.14 ± 0.20 h;  $C_{max}$  of 5.91 ± 0.604 vs. 3.58 ± 0.671 µg/ml) when compared to the reference. The relative bioavailability of the test compared to the reference capsule was 172%. Good correlations were established between the in vitro 90% dissolution (T90) and each of the  $AUC_{0-12}$  and  $T_{max}$ , as well as between the percentage of drug released and plasma concentrations.

**Conclusions:**

The formulation of MFA microsphere with polyethylene glycol improved the dissolution rate and bioavailability of MFA, as evidenced by a higher  $C_{max}$  and  $AUC_{0-12}$  and  $AUC_{0-infinity}$  and shorter  $T_{max}$  values. Good correlations between T90 and both  $AUC_{0-12}$  and  $T_{max}$  as well as between the percentage of drug released and plasma concentrations were achieved.

*Key Words: Microspheres; In vitro/in vivo correlation**Funding Agency: None*



**Pharmacy**

*Category: Clinical*

**184**

**Retrospective and prospective study on prescribing patterns of antimalarial drugs in KIMS Hospital and Research center Bangalore**

\*Jahurul HG, Priyanka N, Vanaja K

Visveswarapura institute of pharmaceutical sciences

**Introduction:**

Malaria is one of the major public health problems in India with 2 to 3 million cases of human malaria reported annually by NVBDCP. Irrational use of artemisinin and its derivatives as monotherapy can lead to drug resistance in malaria parasites which is one of the major obstacles to malaria control. Therefore, a need exists to study the correct use of antimalarial drugs.

**Methods:**

A retrospective observational study (January 2004 to December 2011) was conducted using a patient data collection form, by reviewing the patient's case record and medical record department. Mean  $\pm$  Standard deviation and Student t-tests were applied using SPSS 15.0.

**Results:**

The yearly trend of malaria occurrence data of retrospective study showed that the highest cases P.falciparum were reported in the year of 2004, 2005 & 2010 and that of P.vivax was more prevalent in 2006, 2009 & 2011. In the year of 2007 & 2008 the prevalence of both P.falciparum and P.vivax was found to be same. The prevalence of P.falciparum infection was more when compared to P.vivax infection in retrospective study. Among the total patient population (N=350), 75% received Artesunate, 15% received Primaquine and 10% received Chloroquine during monotherapy. In combination therapy, majority of the patient population (65%) received Artesunate + Primaquine, whereas, Artesunate with other combinations were prescribed to a lesser extent.

**Conclusions:**

The guidelines recommend combination therapy (ACTs) for P.falciparum infection and monotherapy for P.vivax infection. Although the guidelines recommended monotherapy for P.vivax infections, the hospital guidelines adopted Artemisinin Combination Therapy (ACTs). Even though the guidelines recommend combination therapy for P.falciparum infections, the hospital guidelines adopted monotherapy. Thus, a need exists for the health care professionals to adhere to the stipulated therapeutic options to ensure evidence based practice.

*Key Words: Retrospective & prospective study; Prescribing pattern; Antimalarial drugs*

*Funding Agency: None*



**Pharmacy**

*Category: Basic Sciences*

**185**

**Evaluation of a workshop on management of chronic asthma to the final year pharmacy students**

\*Katoue MG<sup>1</sup>, Al-Haqan A<sup>2</sup>, Abdel-Meguid S<sup>2</sup>

<sup>1</sup>Department of Applied Therapeutics, Kuwait University, Faculty of Pharmacy; <sup>2</sup>Department of Pharmacy Practice, Kuwait University, Faculty of Pharmacy.

**Introduction:**

Asthma is a common chronic disease in Kuwait. Pharmacists can have major contribution to the care of asthmatic patients. The workshop was conducted to enable future pharmacists to provide effective care for asthmatic patients. The objective was to apply various teaching activities and to assess their impact on students' acquisition of the knowledge and skills needed for asthma management.

**Methods:**

A workshop on asthma was organized to fourteen final year pharmacy students. It included interactive lecture, group discussion of case studies, tutorial on the use of inhalers and role-play to teach communication skills. An assessment that consisted of a quiz composed of multiple choice questions and an objective structured clinical examination (OSCE) was conducted. The workshop and the teaching activities were evaluated using pre-tested self-administered questionnaire.

**Results:**

The mean score in the quiz was: 70.5±18.1% (mean±SD). Students achieved overall good performance in the skills tested by OSCE. Eleven students (78.6%) strongly agreed that the workshop helped them understand management of asthma and that they will be able to provide better care to patients. Thirteen (92.9%) strongly agreed that they feel more confident in demonstrating the right inhaler technique and in employing effective communication skills. Most students strongly agreed that group discussion and role-play enhanced their understanding of the material (92.9%) and promoted their involvement (85.7%). The group discussion was the most preferred learning method by students (71.4%).

**Conclusions:**

The workshop was successful in providing students with confidence to manage asthmatic patients. The group discussion and role-play enhanced the learning experience of the students. By adapting the use of engaging methods in teaching pharmaceutical care, the subject becomes more understandable to students. This will help prepare qualified pharmacists who are able to provide optimal care for patients.

*Key Words: Pharmaceutical care; Teaching activities*

*Funding Agency: None*



**Pharmacy**

*Category: Basic Sciences*

**186**

**Self-medication among undergraduate medical students in Kuwait**

\*Maryam AH, Mustafa S

Department of Pharmaceutical Sciences, College of Health Sciences, The Public Authority of Applied Education & Training

**Introduction:**

Self-medication is associated with many problems as incorrect self-diagnosis, inadequate treatment of a disease and serious clinical effects with potential life-threatening complications. The aim of this study was to estimate the prevalence of self-medication among healthy undergraduate students and evaluate the factors associated with self-medication among them in Kuwait.

**Methods:**

A descriptive cross-sectional study was performed, using a pretested questionnaire on a sample of 841 students randomly selected from 4 health faculties in Kuwait. The prevalence of self-medication was estimated for twelve cases.

**Results:**

The prevalence of self-medication recommended by friend/family was significantly more than visiting a doctor in case of pain and headache (more than 50%), while it was equal in case of fever and drowsiness. However, the situation was the opposite in case of cough and abdominal pain seeking medical advice from a doctor was higher than friend/family. The previous differences were higher among university students than PAEET students. The role of the pharmacist was the least between all of them. The attitude of the students towards taking medication showed that they depend on their medical knowledge equally to that of the pharmacist.

**Conclusions:**

The prevalence of self-medication among undergraduate university students in Kuwait is high. The self-medication is alarming. Improved awareness for these substances in undergraduate students are critical for careful and cautious use of these drugs. The self-medication among university students is higher than among PAEET students. This difference may be due to their greater medical knowledge.

*Key Words: Self-medication; Medical student; Undergraduate*

*Funding Agency: None*

**Pharmacy***Category: Basic Sciences***187****Stability of Vitamin E in Selected Ingredients Commonly Used in Cosmetic Formulations**

\*Nada A, Zaghoul A, Khattab I, Hedaya M

Department of Pharmaceutics, Faculty of Pharmacy, Kuwait University, Kuwait

**Introduction:**

Vitamin E (Tocopherol, T) is one of the best established ingredients in the over the counter (OTC) products for delaying/treatment of skin ageing. Vitamin E is a lipid-soluble antioxidant which plays key roles in protecting cell membranes from lipid peroxidation by free radicals. Tocopherol acetate (TA) is more commonly included in cosmetic formulations. Previous evaluation of T/TA in commercial cosmetic preparations indicated low stability profiles, especially free T. The objective was to study stability of T and TA at different temperatures in presence of several common ingredients used in cosmetic formulations.

**Methods:**

T/TA were dissolved (1% w/w) in Ethanol, Polyethylene Glycol (PEG)-Ethanol mixture (4:1 w/w), Isopropyl Myristate (IPM), Propylene Glycol (PG)/ PEG-Ethanol mixture (1:1 w/w). Physical and chemical stability were evaluated after storage at 25° and 37°C over 9 months. T/TA were analyzed by HPLC using RP C-18 column.

**Results:**

The %-remaining of T in ethanol at 25°C was about 90% after 9 months, compared to 73% at 37° C. In PEG-Ethanol mixture and PG, the remaining concentrations were similar (80 and 60% after storage at 25 and 37°C, respectively). In IPM, T remained almost unchanged. The stability of TA was characterized by high profile, and vitamin content remained almost unchanged. Physically, the appearance of solutions remained unchanged, except separation of oily droplets with T at 37°C in presence of PG.

**Conclusions:**

Stability of the free vitamin (T) was less than its acetate ester (TA), due to blocking of the easily oxidizable free OH group by ester formation with acetic acid. Stability of T decreased at elevated temperature. The lipophilic vehicle IPM offered better stability for both T and TA, compared to the other polar solvents/solvent mixtures. Use of PG in vitamin E formulations carries degradation potential to free vitamin E.

*Key Words: Tocopherol acetate; Stability in Cosmetics**Funding Agency: Kuwait University, Research Administration, Project*



**Pharmacy**

Category: Basic Sciences

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**Monoamine oxidase inhibitory activity of novel oxazolidinones with antibacterial activity**

Phillips OA<sup>1</sup>, Benov L<sup>2</sup>, Udo EE<sup>3</sup>, \*Sharaf LH<sup>1</sup>, D'Silva R<sup>1</sup>

<sup>1</sup>Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University; <sup>2</sup>Department of Biochemistry, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Microbiology, Faculty of Medicine, Kuwait University

**Introduction:**

Oxazolidinones are potent antibacterial agents plagued with unwanted side effects, which include inhibition of monoamine oxidases (MAO) due to structural similarity to the MAO inhibitor, toloxatone. The aim of this study was to investigate the MAO inhibitory activities of selected antibacterial oxazolidinones.

**Methods:**

Oxazolidinones were synthesized by previously described methods. In vitro MAO-A or -B inhibition was determined by a continuous peroxidase-linked spectrophotometric assay in 96 well microtiter plates. Chromogenic solutions containing vanillic acid (1mM), 4-aminoantipyrine (500 $\mu$ M), and peroxidase (4.7 units/10 $\mu$ l) in phosphate buffer (0.2M, pH7.6), test compounds (50 and 200 $\mu$ M) and pure commercial MAO-A or -B were incubated. Tyramine was used as a mixed substrate for MAO-A and -B. Blanks containing buffer instead of tyramine, and controls containing distilled water instead of test compounds, were run simultaneously with the samples. Total volume in each well was adjusted to 300 $\mu$ l with phosphate buffer (pH7.6). Reactions were followed in Sunrise<sup>TM</sup> microplate absorbance reader. Absorbance measurements were taken at 498nm every minute for 10 minutes, then every 10 minutes for 20 minutes and every 20 minutes until 90 minutes. Results: A total of 22 oxazolidinone derivatives with antibacterial activity were tested.

**Results:**

Results showed that some of the compounds evaluated demonstrated noticeable degree of inhibitory activity against MAO-A and -B. The morpholino desmethyltriazolyl oxazolidinone, PH27 with potent antibacterial activity showed significant MAO-A and -B inhibition; while the inhibitory activities of the piperazinyl triazolyl oxazolidinones were dependent on the N4-piperazine substitutions.

**Conclusions:**

Inhibitory activities on pure MAO-A and -B are dependent on the substitution around the oxazolidinone pharmacophore. Further investigations are ongoing to determine the selectivity, potency and reversibility of MAO inhibition.

*Key Words: Oxazolidinone; Spectrophotometry*

*Funding Agency: Research Administration, Kuwait University Grant*



**Pharmacy**

Category: Basic Sciences

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**Synthesis and antibacterial activities of novel N-substitutedglycinyll containing 1H-1, 2, 3-triazolyl oxazolidinones**

Phillips OA<sup>1</sup>, Udo EE<sup>2</sup>, Abdel-Hamid ME<sup>1</sup>, \*Varghese R<sup>1</sup>

<sup>1</sup>Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University; <sup>2</sup>Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

**Introduction:**

The introduction of “Spacers” containing hydrogen bond donor and / or acceptor groups on the terminal substituent moiety at the C-4 position of the phenyloxazolidinone pharmacophore yielded potent antibacterial activity due to enhanced interactions at the bacterial 50S ribosomal binding sites. In this study we investigated the influence of varied N-substituted glycinyll on the antibacterial activity of piperazinyll-5-(4-methyl-1,2,3-triazolyl) oxazolidinones.

**Methods:**

Novel glycinyll oxazolidinones were synthesized and evaluated against antibiotic susceptible and resistant Gram-positive and -negative bacterial isolates including *Staphylococcus aureus*, coagulase-negative staphylococci, enterococci, *Streptococcus pneumoniae*, *Moraxella catarrhalis* and standard reference strains were tested. Minimum inhibitory concentrations (MIC's, ug/ml) was determined by agar dilution method on Mueller Hinton agar containing dilutions of antibacterial agents ranging from 0.06 - 64 ug/ml, with and without 50% human plasma.

**Results:**

Overall, derivatives with aroyll group substitution on the N-glycine were more potent (MIC: 0.06-4 ug/ml) than the substituted-acyll (2-8 ug/ml) derivatives against all Gram-positive bacteria tested. Nitro substitution on aryll and heteroaryll rings significantly enhanced activity against Gram-positive bacteria, as noted with the 5-nitrofuran-2-carbonyll and 3, 5-dinitrobenzoyll derivatives with MIC ranges of 0.06-0.5 and 0.25-0.5 ug/ml, respectively. Derivatives with water-soluble ammonium salts showed marginal activity, MIC 4->64 ug/ml. The 3, 5-dinitrobenzoyll and 5-nitrofuran-2-carbonyll derivatives showed extended activity against *M. catarrhalis*, MIC's of 0.25-1 ug/ml, compared to linezolid (MIC: 8ug/ml).

**Conclusions:**

The newly synthesized compounds exhibited moderate to strong antibacterial activity against all Gram-positive cocci tested with extension against *M. catarrhalis*.

*Key Words: N-Glycinyll spacer substitution; Triazolyl oxazolidinones*

*Funding Agency: Research Administration, Kuwait University Grant*



**Pharmacy**

*Category: Basic Sciences*

**190**

**Intravitreal injection of 20-HETE inhibitor protects against light-induced retinopathy in rats**

\*Qaddoumi MG<sup>1</sup>, Polosa A<sup>2</sup>, Lachapelle P<sup>2</sup>

<sup>1</sup>Department of Applied Therapeutics, Kuwait University, Faculty of Pharmacy; <sup>2</sup>Department of Ophthalmology, McGill University/Montreal Children's Hospital, Montreal, Canada.

**Introduction:**

20-HETE is well known to have pro-inflammatory and apoptotic properties. The purpose of this study was to evaluate if inhibition of 20-HETE can be beneficial in a model of retinopathy, namely light-induced retinopathy where photoreceptors are lost via apoptosis.

**Methods:**

Adult Sprague-Dawley rats were exposed to either cyclic normal light or bright light (2800 Lux, n = 6) for 3 consecutive days. All rat groups received an intravitreal injection of either DMSO or 2.5 mg/kg HET0016 (20-HETE inhibitor) 1 day prior to bright light exposure and continued for three days onwards. The effects of HET0016 on retinal function were evaluated via scotopic and photopic flash electroretinograms (ERG) recorded at day 1 and 7 following recovery from light exposure. In addition, whole retinal histology were performed.

**Results:**

At day 1 post intense light exposure, there was a significant reduction ( $P < 0.05$ ) in all ERG parameters (scotopic a- and b-waves) of control rats compared to their normal light group. However, HET0016-injected rats had a lower amplitude attenuation for both the a-wave (26% versus 52%) and b-wave (12% versus 38%) compared to DMSO-injected rats. Semi-complete recovery was noticed at day 7 for both light-exposed rat cohorts, but was more pronounced for the DMSO-injected rats. Photopic b-wave amplitudes of light-exposed rats at day 1 were not attenuated in HET0016-injected rats compared to the normal light-exposed rats.

**Conclusions:**

Our findings suggest that inhibition of 20-HETE may have protective effects on retinal damage from light exposure. However, the detailed protective mechanism to the retina by 20-HETE inhibition remains to be elucidated. It would be interesting to determine if this protective effect of 20-HETE can be sustained for longer periods.

*Key Words: 20-HETE; Electroretinography*

*Funding Agency: Reseau Vision of the FRSQ and NSERC*



**Pharmacy**

Category: Basic Sciences

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**Isolation of bioactive compounds from *Centaurea aegyptiaca* ethanol extract**

\*Sary HG<sup>1</sup>, Ayoub NA<sup>2</sup>, Singab AB<sup>2</sup>, Orabi KY<sup>1</sup>

<sup>1</sup>Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University; <sup>2</sup>Department of Pharmacognosy, Faculty of Pharmacy, Ain-Shams University, Egypt

**Introduction:**

In a previous work, *Centaurea aegyptiaca* ethanol extract has shown potential cytotoxic activity against liver and larynx carcinoma cell lines. The aim of this study is to isolate potential candidates responsible for this activity.

**Methods:**

Shade-dried aerial parts of *Centaurea aegyptiaca* were coarsely powdered and extracted with ethanol (96%). The ethanol extract was subjected to chromatographic separation on a flash silica gel column gradually eluted with increasing concentrations of methanol in chloroform. After successive purification, two compounds were isolated and identified using different spectroscopic methods. Moreover, the cytotoxic activities of these compounds were evaluated against liver and larynx carcinoma cell lines according to Skehan et al. method. IC<sub>50</sub> (µg/ml) of the isolated compounds were determined using doxorubicin as a positive control.

**Results:**

Two sesquiterpene lactones, desacylcynaropicrin (1) and chlorohyssopifolin B (2), were isolated and characterized from the ethanol extract of *Centaurea aegyptiaca*. Compound 1 exhibited cytotoxic activity against liver and larynx carcinoma cell lines with IC<sub>50</sub> values of 10.40 and 9.75 µg /ml, respectively. Additionally, compound 2 was more active against both cell lines with IC<sub>50</sub> values of 4.35 and 6.00 µg /ml, respectively.

**Conclusions:**

Chemical investigation of *Centaurea aegyptiaca* ethanol extract led to the isolation and identification of two sesquiterpene lactones. Moreover, these compounds may be responsible for the potential cytotoxic activity of the plant ethanol extract against liver and larynx carcinoma cell lines.

**Acknowledgements:**

Spectral analyses were done at Kuwait University, Faculty of Science, Science Analytical Facilities, (SAF) supported by Grant number GS01/03.

*Key Words: Centaurea aegyptiaca; Sesquiterpenes; Cytotoxicity*

*Funding Agency: Grant number GS01/03*



**Pharmacy**

Category: Basic Sciences

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**Development and characterization of controlled release naproxen microspheres and tablets**

\* Zaghoul A, Nada A, Khattab I, Hedaya M

Department of Pharmaceutics, Faculty of Pharmacy, Kuwait University, Kuwait.

**Introduction:**

Naproxen is a poorly water soluble NSAID with low bioavailability and GIT adverse effects. Naproxen microspheres (MS) compressed to produce controlled release (CR) tablets may help to solve these problems especially for long term disease management.

**Methods:**

Naproxen-Eudragit L100-55 microspheres were prepared by coprecipitation technique. The MS were characterized using DSC and XRD. Tablets were prepared by compressing MS containing 500 mg drug. Dissolution of MS and physical mixture tablets was performed according to USP specifications. A 3-factor 3-level Box-Behnken experimental design was employed to evaluate the main and interaction effects of deaggregating agent concentration (X1), compression pressure (X2) and amount of precipitating water (X3) on naproxen release. The optimization was conducted to obtain a formulation with a predictable CR behavior. The dependent variables (Y1-Y5) were dissolution at different time points. The dissolution constraints were placed such that naproxen is released for 12 hours. Tablets were characterized for surface roughness measurements.

**Results:**

The DSC showed no interaction between the polymer and the drug, XRD showed a change in crystalline form of the drug. The mathematical relationship obtained between X1-X3 and (Y5) was  $Y5 = 92.39 - 1.13X1 - 4.84 X2 - 2.12 X3 - 2.26 X1X2 - 0.5X1X3 - 0.4X2X3 + 2.4X21 - 0.4 X22$  ( $R^2 = 0.9$ ).

The equation shows that X1, X2, and X3 affected the release inversely and the most significant interaction was between X1 and X2. A good correlation between the observed and the predicted values was obtained. Topographic surface roughness measurements showed increase in porosity of tablet surface indicating diffusion mechanism of drug release

**Conclusions:**

MS of naproxen with optimum matrix properties were prepared and successfully compressed to obtain CR tablets with predictable drug release characteristics compared to the physical mixture.

*Key Words: Naproxen; Formulation; Experimental Design*

*Funding Agency: None*

**Physiology***Category: Basic Sciences***193****Molecular mechanisms underlying glucocorticoid-induced intrauterine growth restriction (IUGR)**\*Al-Bader M<sup>1</sup>, Narayana K<sup>2</sup>, El-Farra A<sup>1</sup>, Mouihate A<sup>1</sup>, Khan K<sup>2</sup>, Omu AE<sup>3</sup>, Al-Abdullah A<sup>4</sup><sup>1</sup>Department of Physiology; <sup>2</sup>Department of Anatomy; <sup>3</sup>Department of Obstetrics and Gynecology, Faculty of Medicine, Kuwait University; <sup>4</sup>American University of Middle East, Kuwait.**Introduction:**

Passage of glucocorticoid from maternal to fetal circulation is regulated by placental 11 beta hydroxysteroid dehydrogenase (11 $\beta$ -HSD) activity. We hypothesize that carbenexolone mediated 11 $\beta$ -HSD inhibition-induced IUGR may be due to alterations in expressions of estrogen receptors (ER),  $\beta$ -catenin, cyclin D1, p21, p27, p53, Bcl-2 and Bax in the placenta.

**Methods:**

Pregnant SD rats (240 g) received vehicle (control) or 20 mg carbenoxolone (EG) once daily (s.c.) from gestational day (dg) 1-21. Placentae were collected on 16, 19 and 21dg. Gene expressions of Eralpha, Erbeta, p53, p27, p21, beta-catenin, cyclin D1, Bax and Bcl2 were studied by ReT-PCR in basal (BZ) and labyrinth (LZ) zones. Data were analysed by one way ANOVA followed by LSD ( $p < 0.05$  was considered significant).

**Results:**

Compared to CG, maternal body weight decreased (at 19 and 21 dg), placental weights increased (at 19 and 21 dg) and fetal body weights decreased (at 21 dg) in EG. In EG, the expression of Eralpha was decreased in BZ (at 16 dg and 21 dg) and in LZ (at 21dg), that of Erbeta was decreased on all dg in both BZ and LZ, that of p53 was decreased in BZ (at 19 dg) and increased (at 21 dg) and decreased in LZ (at 19 dg and 21 dg). The expression of p27 in BZ and LZ was decreased (at 19 dg and 21 dg, respectively), that of p21 was decreased at all dg in BZ and increased in LZ (at 16 dg). The expression of beta-catenin was decreased in BZ (at 19 dg) and in LZ (at 21 dg), that of cyclin D1 was decreased in BZ (at 21 dg) and in LZ (at 19 dg). The expression of Bax was decreased in BZ (at 16 and 19 dg) and that of Bcl-2 was decreased in BZ (at 16 dg) and increased in BZ (at 19 and 21 dg).

**Conclusions:**

Carbenoxolone induces IUGR along with concomitant compensatory increase in placental weight. Inhibition of 11 $\beta$ -HSD and subsequent IUGR is due to alterations and complex cross talks between cell cycle regulatory molecules that control cell survival and death in the placenta

*Key Words: Intrauterine Growth Restriction; Estrogen receptors; Cell cycle regulatory molecules*

*Funding Agency: Kuwait University, Research Administration, Grant #MY02/08*



**Physiology**

*Category: Basic Sciences*

**194**

**The energetic and functional impact of stairs and elevators**

\*Alkandari JR<sup>1</sup>, Mohammad SH<sup>2</sup>, Al Hashem RA<sup>1</sup>, Telahoun G<sup>1</sup>

<sup>1</sup>Department of Physiology, Faculty of Medicine, Kuwait University; <sup>2</sup>Department of Physical Education, College of Basic Education, The Public Authority of Applied Education and Training.

**Introduction:**

As the chronic diseases increased globally and even more in the Gulf Cooperation Council Countries (GCC) specially diabetes and obesity that reached to a pandemic level, so has sedentariness. Progressive sedentariness has been attributed to labor saving devices such as washing machines, cars and elevators. In this study, we investigated the energetic cost and functional benefits of ascending and descending of stairs compared with elevators.

**Methods:**

Energy expenditure was measured in 23 female and male subjects using indirect calorimetry while the subjects climbed stairs or used the elevator up and down five floors in the Faculty of Medicine at Kuwait University. Heart rates (HR) and blood pressures (BP) were monitored at each floor for HR and at ground floor and the fifth floor for BP.

**Results:**

Heart rate response during ascending the stairs from ground floor to the 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> were 51.1%, 66.5%, 75.2%, and 82.7% higher than the ground floor respectively. In descending the stairs, the HR response were 31%, 33.3%, 35.7%, and 36.9% from the fifth to the ground floors respectively. A significant HR differences between floors has occurred between ascending and descending stairs, and between stairs compared with elevator.

The energy cost of climbing the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup>, 4<sup>th</sup>, and 5<sup>th</sup> floors were 1.95, 4.21, 5.53, 6.10 and 6.11 Kcal/kg.hour-1 respectively and descending the five floors were 1.52, 2.18, 2.6, 2.84 and 2.70 Kcal/kg.hour-1 respectively. Systolic BP increased by 22.2% above the resting level in ascending from 1<sup>st</sup> to 5<sup>th</sup> floor while no change in the diastolic BP.

**Conclusions:**

Stairs have great impact on the energy expenditure in both ascending and descending steps. If an 80 kg individual use the stairs for one hour, he would have spent approximately 700 Kcal. Ascending stairs HR responses resembled vigorous activity, while descending the stairs reflected mild to moderate level activity.

*Key Words: Heart Rate; Stairs*

*Funding Agency: None*

**Physiology***Category: Basic Sciences***195****Pacing postconditioning protects the heart by a pathway involving modulation of mitochondria permeability transition pore and reactive oxygen species production.**\*Babiker FA<sup>1</sup>, Joseph S<sup>1</sup>, Juggi JS<sup>2</sup>, Prinzen F<sup>3</sup><sup>1</sup>Department of Physiology, Kuwait University, Faculty of Medicine; <sup>2</sup>Emeritus professor, Department of Physiology, Kuwait University, Faculty of Medicine; <sup>3</sup>Department of Physiology, Maastricht University, Faculty of Medicine.**Introduction:**

Intermittent dyssynchrony, induced by left ventricular (LV) pacing (pacing postconditioning (PPC) immediately upon reperfusion induces cardioprotection. We tested the role of mitochondrial permeability transition pore (mPTP), reactive oxygen species (ROS), nitric oxide (NO) and peroxynitrite (ONOO<sup>-</sup>) in PPC protection. We also investigated the suitable time and location for PPC application.

**Methods:**

Isolated perfused rat hearts (Langendorff) (n=8) were used for this study. The protocol of PPC was 3 cycles of 30 seconds LV pacing alternated with 30 seconds right atrial (RA) pacing. PPC was applied at different time points during ischemia and reperfusion or at different locations on the heart. Selective blockers of mPTP, ROS and ONOO<sup>-</sup> or exogenous hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) were added to investigate the pathways of PPC. All groups were allowed a period of 30 minutes reperfusion. Hemodynamics were computed by a data acquisition program. Infarct size was determined by triphenyltetrazolium chloride (TTC) staining.

**Results:**

Ischemia reperfusion (I/R) resulted in poor recovery of heart hemodynamics. PPC significantly (p<0.03) improved heart hemodynamics and decreased the infarct size (p<0.05) only when pacing was done at the middle of LV or the RV. Pacing during ischemic period significantly (p<0.05) improved hemodynamics and decreased the infarct size. This protection was abrogated when pacing was delayed 5 or 15 min after the start of reperfusion. Blockade of mPTP normalized the hemodynamics (p<0.04) and significantly (p<0.05) decreased the infarct size. This protection was antagonized by the blockers of ROS and ONOO<sup>-</sup> and exogenous H<sub>2</sub>O<sub>2</sub>.

**Conclusions:**

Pacing postconditioning provides myocardial protection when applied during ischemia or early reperfusion at the middle of left or right ventricles. In its protection PPC uses a pathway involving mPTP, nitric oxide and reactive oxygen species.

*Key Words: Ischemia; Postconditioning; Pacing**Funding Agency: Kuwait University MY2/10*



**Physiology**

*Category: Basic Sciences*

**196**

**Effect of acute cold exposure on lung perfusion and tracheal smooth muscle contraction in rabbit**

Elgazzar A<sup>1</sup>, \*Mustafa S<sup>2</sup>, Khadadah M<sup>3</sup>

<sup>1</sup>Department of Nuclear Medicine; <sup>3</sup>Department of Medicine, Faculty of Medicine, Kuwait University; <sup>2</sup>Department of Pharmaceutical Sciences, College of Health Sciences, Public authority for applied education & training, Kuwait

**Introduction:**

Acute exposure to cold temperature can affect the respiratory system of those exposed to extreme weather and induces asthma in asthmatic patients. However, the effect on lung perfusion and the pulmonary circulation was not addressed in any previous study. The present study investigates the effects of acute cold exposure on tracheal smooth muscle and lung perfusion.

**Methods:**

Twelve adult male New Zealand White rabbits of the same age (10 weeks) weighing 3–3.5 kg were studied. For in vitro experiments, isolated tracheal segments were suspended in organ baths containing Krebs' solution for isometric tension recording. Tissue response to cooling from 37 to 4°C was examined. For in vivo experiments, the rabbits were kept in a cold room (4°C) for 1 h. Lung perfusion scintigraphy was performed at the end of this period. Each rabbit was injected with 74 MBq (2 mCi) technetium-99m macroaggregated (99mTc MAA). Perfusion studies were done by using Gamma camera equipped with a low-energy, highresolution, parallel-hole collimator interfaced with a computer. Static images were acquired 5 min after administration of the radiotracer.

**Results:**

Cooling induced a rapid and reproducible contraction in the tracheal smooth muscle Rabbits exposed to cold temperature had lesser lung perfusion than controls using radionuclide perfusion study. Our results highlight the response of tracheal muscle and pulmonary circulation to cold exposure.

**Conclusions:**

These results indicate that cooling induced contraction of the trachea and decreased pulmonary circulation and lung perfusion. This summation of acute cooling for tracheal smooth muscle and pulmonary circulation seems to be the reason for the severe cooling-induced contraction.

*Key Words: Radionuclide; Respiratory system*

*Funding Agency: None*



**Physiology**

Category: Basic Sciences

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**Maternal glucocorticoids alter gene expression of p53 family in fetal brains: A gender specific impact.**

\*Mouihate A, Al-Bader MD

Department of Physiology, Faculty of Medicine, Health Sciences Centre, Kuwait University

**Introduction:**

Immune and psychological stresses in pregnant mothers negatively impact fetal brain development. Both stresses induce increased maternal plasma levels of glucocorticoids (GC). GC hamper fetal brain development. The molecular mechanism (s) underlying GC effects on fetal brain development are not well understood. P53 gene family (namely p53, p63 and the dominant negative  $\Delta N$  p63) has been recently shown to be involved in brain cell death during embryonic development. Whether GC impact fetal brain development by modulating the expression and action of the genes of p53 family in utero is not yet known.

**Methods:**

Feto-placental enzyme 11 $\beta$ -hydroxysteroid dehydrogenase 2 (11 $\beta$ -HSD-2; an enzyme that converts maternal GC into an inert form) was inhibited by daily administration of carbenoxolone throughout pregnancy. The expression of p53 gene family was monitored in fetal rat brains on gestation days (GD) 16, 19 and 21 using RT-PCR. The impact of carbenoxolone on body and brain weights of rat fetuses was assessed.

**Results:**

In the absence of carbenoxolone, the expression of p53 mRNA was reduced on GD21 in the brain of male fetuses but was increased in the brain of female fetuses. Carbenoxolone reduced p53 gene expression in the male brains but potentiated its expression in female brains. In contrast to p53, p63 gene expression progressively increased during pregnancy in brains of male but not female fetuses. Carbenoxolone reduced p63 gene expression in both male and female brains.  $\Delta N$ p63 was significantly reduced in the brains of both male and female fetuses and was further decreased by 11 $\beta$ -HSD-2 inactivation. Finally, exposure to excess GC reduced fetal body and brain weights on GD21.

**Conclusions:**

Our results suggest that GC induced female brain weight reduction is likely mediated by the enhanced gene expression and the pro-apoptotic effect of p53. p63 gene does not appear to play a role in the negative impact of GC on fetal brain development.

*Key Words: Prenatal stress; 11 $\beta$ -hydroxysteroid dehydrogenase 2; Fetal brain*

*Funding Agency: KU Grant #MY02/08 and GM01/01-GM 01/05 (RCF)*



**Psychology**

*Category: Basic Sciences*

**198**

**Working memory capacity in Arabic monolingual and English/Arabic Bilingual Kuwaiti learners**

\*Alansari BM, Soliman AM

<sup>1</sup>Department of Psychology, College of Social Sciences, Kuwait University, Kuwait; <sup>2</sup>Department of Psychology, University College, Umm Al-qura University, KSA

**Introduction:**

Research in the field of psycholinguistics focusing on cognitive processing in bilinguals and the role played by working memory about cognitive processing indicated that Working Memory (WM) was instrumental in cognitive processing in bilinguals but that its role was different and generally more complex than it was in monolinguals. However, the specific manner in which the use of WM differed between monolinguals and bilinguals was not always clear and yet this might affect the way in which bilingual learners acquire new knowledge or use existing knowledge and the way bilingual learners perform on assessments gauging their scholastic progress. This research explored the capacity of WM and the role of gender in two Kuwaiti populations: a monolingual Arabic group (L1) and a bilingual English/Arabic group (L2).

**Methods:**

The participants were 396 Kuwaiti pupils representing the six Kuwaiti governorates (Asimah, Hawally, Ahmadi, Mubarak Alkabeer, Farwaniyah, and Jahra). The participants mean age  $8.01 \pm 1.94$  years (198 monolingual aged  $7.99 \pm 1.97$  years and 198 bilingual aged  $8.03 \pm 1.92$ ) with no significant age differences ( $t=0.23$ ,  $p>.05$ ). Learners in the two groups were compared on how they performed in the Automated Working Memory Assessment (AWMA), a computerized instrument developed by Alloway (2007). Although the AWMA has been used extensively in the UK, where it was developed, its use in Kuwait is limited. In addition, AWMA is well documented on monolingual populations but not in bilingual populations. Independent Sample t Test was used to examine group differences in WM performance and 2- Way ANOVA to test the interaction effect of language and gender.

**Results:**

( $t=3.04$ ,  $p<.001$ ) in visuo-spatial WM. Moreover, the interaction effect of language and gender was non-significant ( $f=3.72$ ,  $p>.05$ ) with verbal WM and ( $f=2.48$ ,  $p>.05$ ) with visuo-spatial WM tasks.

**Conclusions:**

Group differences in working memory capacity exist. This warrants further investigation.

*Key Words: Bilingualism; Working memory; Kuwait*

*Funding Agency: Kuwait University Research Administration through research grant # (OP02/07).*



**Psychology**

*Category: Graduate PhD (Basic Science)*

**199**

**Evaluating the reliability, validity of the Arabic version of the Diabetes treatment satisfaction questionnaire (DTSQs) in a Kuwaiti population.**

\*Alshatti TS

Department of Psychology, Kuwait University, Faculty of Social Sciences

**Introduction:**

The Diabetes Treatment Satisfaction Questionnaire (DTSQs) was first developed in the early 1980s. It is now widely used, particularly in clinical trials, but also for routine clinical monitoring. It is available in more than 90 languages. Four Arabic versions were developed for Egypt, KSA, UAE and Qatar. There is a need to adapt a new version to be used in Kuwait. This study aims at examining psychometric properties of a The Diabetes Treatment Satisfaction Questionnaire (DTSQ) in Arabic language for type 1&2 diabetes patients in Kuwait.

**Methods:**

Data were collected from (223) Kuwaiti subjects, including (107) males and (116) females of whom were identified as having type 2 diabetes in Mubarak Al-Kabeer hospital. The mean age of the sample was 47 years. The DTSQs, consists of 8 items (7-point likert scale): 6 Treatment Satisfaction items: Qs.1 and 4-8: 2 perceived blood glucose control items (Perceived Frequency of Hyper- and Hypoglycemia): Qs.2 and 3 respectively.

**Results:**

As expected, unforced factor analysis for the DTSQs showed the six Satisfaction items to load together  $>0.46$ . Reliability was confirmed ( $\alpha$  coefficients: 0.72), and (test-retest correlation coefficients = 0.84). The DTSQs showed satisfactory discriminative ability in which DTSQs scores were negatively correlated with the Diabetes Quality of Life measure DQOL ( $r=-0.41$ ), Beck Depression Inventory-II BDI-II ( $r=-0.27$ ) and the Diabetes Symptom Checklist DSC-R ( $r=-0.25$ ). Moreover, the Diabetes treatment satisfaction score ranging from 0 to 36 with mean  $21.72 \pm 6.75$ . Furthermore, no significant gender difference in the DTSQs was found ( $f=1.53$ ,  $p>.05$ ).

**Conclusions:**

This study provides evidence for the reliability and validity of the in DTSQs Arabic language for diabetes patients in Kuwait. We recommend that you use the DTSQs at baseline and endpoint (and at one or two interim points in a 12-month trial).

*Key Words: DTSQs; Type 2 diabetes; Kuwait*

*Funding Agency: None*

**Surgery***Category: Graduate (Resident)***200****Bioenterics intragastric balloon and weight reduction: A Kuwaiti experience**

\*Al-Ajeel F, Al-Sabah S, Patty S, Al-Najjar F, Al-Azmi W, Abduljaleel M, Suresh A

<sup>1</sup>Department of Surgery, Amiri Hospital, Kuwait; <sup>2</sup>Department of Gastroenterology, Amiri Hospital, Kuwait**Introduction:**

Obesity has reached the epidemic proportion worldwide with serious implications on morbidity, mortality, and quality of life of affected individuals. Currently, Kuwait has been ranked as the 8th fattest population worldwide with almost 80% of its people classified as overweight and 47.5% considered obese. Although the popularity of BioEnterics Intragastric Balloon (BIB) application as a temporary method to lose weight is increasing worldwide, there is no current study that focuses on Kuwait's population regarding this matter. The objective of this study is to evaluate the safety, efficiency and effectiveness of the BIB as a method for treating obesity in Kuwait.

**Methods:**

A prospective study was conducted on 70 overweight/obese patients who had undergone the BIB procedure at Amiri Hospital performed from 2010-2011, of which 51 completed follow-up in the surgical out-patient department; 11 were males, 40 were females; relative information including age, weight, height and endoscopy results pre and post BIB insertion was collected. BIB was inserted for an average duration of six months. Patients were called one month after removal to evaluate for satisfaction, weight gain, and bariatric surgery consideration.

**Results:**

Mean age, mean weight, and mean BMI of the patients were: 34.83 ±10.72 years (range 16-67 years), 102.36±28.04 kg (range 68-230 kg), and 38.27±7.94 kg/m<sup>2</sup> (range 30.5-73kg/m<sup>2</sup>) respectively. The mean weight and mean BMI after an average of 6 months (range 4-6 months) were 89.47±25.90 kg (range 64-195 kg), 32.90±8.16 kg/m<sup>2</sup> (range 24-65kg/m<sup>2</sup>) respectively. There was a statistically significant reduction in weight and BMI at an average of 6 months post BIB (p<0.001). Excess weight loss (EWL) ranged between 0 to 35 kg with a mean value of 12.64±7.66 kg. The subjects had 0 to 114% %EWL (mean 44.72±27.33); reduction in BMI ranged between 0-10.2 kg/m<sup>2</sup> with a mean value of 4.49±2.75 kg/m<sup>2</sup>. The percent excess of body mass index loss (%EBMIL) was 44.22±27.51%, range 0-113%. Of the 51 subjects, 64% were not satisfied with the BIB outcome and 41% of them were considering surgery as an alternative option, however, the effect of weight lost on satisfaction was statistically significant (p =0.04). Although 67% of the patients were dieting with the balloon, 46% gained all of the weight reduced one month after removal. From the 70 patients, two developed acute pancreatitis, one of which required immediate removal.

**Conclusions:**

The BIB has been effective to temporarily treat obesity with a 45% loss of excess body weight after an average of 6 months; however only 40% of the patients were satisfied with the BIB results. It was not associated with mortality and showed minimal risk of major complications.

*Key Words: Intragastric Balloon; Weight reduction; Kuwait**Funding Agency: None*



**Surgery**

Category: Graduate (Resident)

201

**Appendiceal Phlegmon; A Laproscopically defeated FOE**

\*Al-Aradi DF, Haider HH, Juma RT, Al-Herz W, Juma T

Amiri Hospital

**Introduction:**

It is not clear in the literature whether laparoscopic appendectomy for phlegmons is destined to a high rate of conversion to open surgery or not. The aim of this study is to concentrate on the rate of conversion, and the factors that contributes to it.

**Methods:**

A retrospective analysis of a prospectively collected data in Amiri hospital from year 2000 till April 2011. We identified 125 cases of appendiceal masses out of 2358 laparoscopic appendectomies performed during the study period. One patient was excluded because of concurrent pregnancy. Statistical analysis used included Pearson's chi-square and student's t-test.

**Results:**

We identified 76 males and 48 females with an average age of 34 years (9-78 years). Twenty three percent of the patients had pre-existing medical comorbidities. Average onset of pain at presentation was 2.3 days (1-10 days), while surgery was performed on an average 2.7 days (1-11 days) from onset of pain. When onset of pain was 3 days or more, senior surgeons were more involved in the surgery than junior surgeons (65% Vs 28%,  $P=0.001$ ). Average surgery time was 72 minutes (20-150 min.). 19 patients needed conversion out of 124 (15%). Conversion was highest when onset of pain was 3 days or more (32% Vs 5%,  $P=0.001$ ). Post-operative complications developed in 8% of patients after laparoscopy and 29% after open surgery ( $P=0.02$ ), and developed more in patients with pre-existing medical comorbidities (28% Vs 6%,  $P=0.003$ ). Post-op diet was started later when patients developed complications (4 days Vs 2 days  $P=0.00$ ). Average hospital stay after laparoscopy was 4 days while that after open was 6 days ( $P=0.02$ ).

**Conclusions:**

Laparoscopic appendectomy can be successfully performed in 85% of the cases of appendiceal phlegmons. There was a higher chance of conversion to open when onset of pain was 3 days or more. Laparoscopy significantly decreased post-operative complications and hospital stay.

*Key Words: Appendiceal mass; Laparoscopic appendectomy; Appendiceal phlegmon*

*Funding Agency: None*



**Surgery**

*Category: Graduate (Resident)*

**202**

**Gastric histopathologies in patients undergoing laparoscopic sleeve  
gastrectomies**

\*Almazeedi S, Al-Sabah S

Al-Amiri Hospital, Kuwait

**Introduction:**

With almost 80% of its people classified as overweight, Kuwait has a serious obesity problem. This has led to wide-spread practice of bariatric surgery, with little or no studies regarding operative findings and patient follow-up. In addition, H. Pylori testing pre-op has been widely regarded as a compulsory step in preparing the patients undergoing sleeve-gastrectomies, with few studies confirming its importance. The objectives of the study were to study the prevalent gastric histology of obese patients and to review the significance of H. Pylori eradication pre-op.

**Methods:**

In collaboration with the histopathology department at the hospital, we gathered the pathology specimen results of the sleeve gastrectomies performed from 2009-2011 at our facility. The patients' medical files were then retrieved to look up pre-op H. Pylori investigation.

**Results:**

The histopathologies of 340 cases of sleeve gastrectomies carried out at Al-Amiri from 2009 to 2011 were retrieved. The results of the patients showed 285 cases with chronic gastritis, and 51 cases of follicular gastritis. There were 11 cases that showed other findings including 3 cases of atrophic gastritis, 3 cases of granulomatous disease, 1 gastric polyp, and 1 case of Gastro-Intestinal Stromal Tumor. H. Pylori was discovered in 26 of the patients, most of which were found with chronic or follicular gastritis, 6 and 18 cases respectively. 90 cases had documented pre-op H. Pylori tests, and of those 16 were positive and received treatment. However, 6 of those patients remained positive at the time of the operation.

**Conclusions:**

The histopathologies of most patients involved in this study had an element of chronic gastritis, which has previously been shown to be very prevalent in the obese population. There were however a few cases that required special attention and possibly careful follow-up. In addition, almost one-third of the patients who underwent H. Pylori eradication pre-op had recurrence.

*Key Words: Sleeve Gastrectomy; Histopathology; H. Pylori*

*Funding Agency: None*



**Surgery**

*Category: Graduate (Resident)*

**203**

**Laparoscopic sleeve gastrectomy for the treatment of type 2 DM: Experience from Kuwait**

\*Al-Mulla A, Al-Sabah S, Juma T, Mousa M, Al-Sharhan A, Al-Haifi M, Al-Enizy K, Bastaki W, Murad A, Buhaimed W, Al-Mossawi A, Al-Manfohi H, Parakash B  
Department of Surgery, Amiri Hospital, Kuwait

**Introduction:**

Type 2 Diabetes Mellitus (T2DM) comprises 90% of diabetics and is largely the result of excess body weight. Prevalence of T2DM in the Kuwaiti adult population is increasing. There is enough evidence in the literature to suggest that laparoscopic sleeve gastrectomy (LSG) produces effective weight loss and cure or improvement of co-morbidities such as T2DM. LSG is now gaining popularity as a treatment of T2DM associated with obesity due to the low morbidity and mortality associated with it; however, this type of treatment modality is best achieved through a multidisciplinary team approach to predict the beneficial effects and risks of this procedure on the patient. The objective of this study is to assess the treatment outcomes of LSG on patients with T2DM associated with obesity.

**Methods:**

A retrospective study on 736 obese patients who underwent LSG at Al-Amiri Hospital from October 2008 to November 2011 was conducted. Eleven percent (N=81) were found to have T2DM preoperatively. Data was analyzed using SPSS program.

**Results:**

The mean age of the patients was 41 years (18-66); female to male ratio was 60:40; Mean preoperative BMI was 46.7kg/m<sup>2</sup> (34.3-88.5) and mean postoperative follow up period was 14.5 months. Pre and postoperative fasting blood glucose and HbA1C were measured. Resolution and improvement of T2DM was 73.2%(n=30) and 26.8%(n=11) respectively. Mean %EWL was 68.5%(n=57). Gender based treatment analysis showed that most of the resolved patients were males (51.6%) and most of the improved patients were females (77%). Duration based analysis showed that most of the resolved patients had diabetes for less than 5 years. Preoperative treatment based analysis showed that most of the resolved cases were on diet control or taking OHA compared to the improved cases who were on OHA or OHA and insulin. Age based treatment analysis showed a trend towards resolution of T2DM in younger patients.

**Conclusions:**

LSG resulted in a 73.2% remission of T2DM which is consistent with the international literature. LSG is more effective for the treatment of patients with a short term duration of T2DM. There is a trend of higher resolution of T2DM in younger patients after LSG.

*Key Words: Sleeve Gastrectomy; Diabetes; Kuwait*

*Funding Agency: None*



## **Surgery**

*Category: Graduate (Resident)*

**204**

### **Al-Amiri obesity surgery outcome**

\*Al-Sabah S, Al-Mulla A, Juma T, Mousa M, Al-Sharhan A, Al-Haifi M, Al-Enizy K, Bastaki W, Murad A, Buhaimed W, Al-Mossawi A, Al-Manfohi H, Parakash B  
Department of Surgery, Amiri Hospital, Kuwait

#### **Introduction:**

Kuwait with a population of 3 million has one of the highest level of obesity in the world. 75% of the population is obese and childhood obesity is rising. In addition, Kuwait has the highest percentage of obesity among the Gulf countries with an average of 66% in males and 36% in females. Estimated cost of obesity to Kuwait, is a minimum of \$2.8 billion annually in direct and indirect costs. The objective of this study is to determine the efficiency and effectiveness of the Laparoscopic Sleeve Gastrectomy (LSG) procedure as a method for treating obesity in Kuwait.

#### **Methods:**

A retrospective study was conducted on 736 consecutive sleeve gastrectomy cases operated in Amiri Hospital from October 2008 to November 2011; 172 were males, 563 were females. Data was collected from bariatric cases database at Amiri Hospital. Patient's demographics, operative and post-operative outcomes were analyzed utilizing SPSS program.

#### **Results:**

The mean age of the patients was  $35.1 \pm 10.7$  years. The initial median BMI was  $45 \text{ kg/m}^2$  with a range between  $31\text{-}82 \text{ kg/m}^2$ , which was higher in males ( $p = 0.016$ ). There was a significant amount of weight lost at different follow-up points among both males and females ( $p < 0.001$ ). Percent excess weight loss (%EWL) was 74% at 18 months post-operative. The median length of hospital stay was 3 days, median operative time was 90 min (30-270) and median follow up time was 12 months (1-36). One case of mortality occurred during the first 30 days and 31 intensive care admissions. Eight patients had leak (1.1 %), 3 patients had pulmonary embolism (0.4%), 9 had bleeding (1.2%), and 7 had mesenteric thrombosis (1%). Late complications were lower limb weakness/neuropathy (1%), pancreatitis and port site hernia (0.27%) and gallstones (2.3%).

#### **Conclusions:**

Preliminary analysis of our experience with LSG indicates that this is an effective and safe procedure for the treatment of obesity in Kuwait with a mean EWL% at one year of 85% and 74% at 18 months. Surgeons performing LSG are encouraged to collect and report outcome data in the peer-reviewed scientific literature. Multi-disciplinary team approach is important to encourage patients for follow up in Kuwait.

*Key Words: Obesity; Surgery; Al-Amiri*

*Funding Agency: None*



**Surgery**

*Category: Basic Sciences*

**205**

**Hormonal response to a meal in a rat model of sleeve gastrectomy with diet-induced obesity.**

\*Al-Sabah S<sup>1</sup>, Al-Asfar F<sup>2</sup>, Al-Khaledi GM<sup>1</sup>, Dinesh R<sup>1</sup>, Al-Saleh M<sup>2</sup> Abul H<sup>1</sup>

<sup>1</sup>Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University, Kuwait; <sup>2</sup>Department of Surgery, Faculty of Medicine, Kuwait University, Kuwait.

**Introduction:**

Morbid obesity has reached epidemic proportions in Kuwait. Bariatric surgery (BS) is considered to be the “standard of care” option that provides significant and sustained weight loss in morbidly obese patients. In addition BS can dramatically improve glycemic control and co-existing type II diabetes. Increasing evidence points to changes in gut hormone secretion following BS. Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP) are incretin hormones which potentiate insulin secretion in a glucose-dependent manner. The aim of this project is to measure the changes in incretin hormone (GIP & GLP-1) and ghrelin (an orexigenic hormone) in response to a standard test meal in rat a model of sleeve gastrectomy with diet induced obesity in order to better understand the mechanisms that mediate the beneficial effects of this surgery and to identify potential drug targets.

**Methods:**

Blood sampling was performed in free moving rat at various time points through chronic vascular access of the jugular vein in 2 groups (n=6) of male Sprague Dawley rats, lean controls and diet induced obese (DIO) rats. GLP-1, GIP & ghrelin were measured by ELISA.

**Results:**

DIO rats were significantly ( $P<0.05$ ) heavier than lean controls and there was a significant ( $P<0.05$ ) increase in the area under the curve (AUC) following an oral glucose tolerance test. Although the level of blood glucose at the 2 hour point was higher for the DIO animals it did not reach significance. There was no significant difference between the AUC for the GIP response in lean controls and DIO rats. GIP concentration were  $192.2\pm 29.66$  pg/ml and  $225.9\pm 13.42$  pg/ml ( $\pm$ SEM) at 2 hours for controls and DIO respectively.

**Conclusions:**

The animal model and hormonal assays are appropriate tools to investigate the changes in gut hormone response to a meal that occur following sleeve gastrectomy.

*Key Words: Incretin; Sleeve Gastrectomy; Blood Sampling*

*Funding Agency: MR 01/10*



## **Surgery**

*Category: Graduate (Resident)*

**206**

### **Factors influencing the practice of breast cancer screening in Kuwait**

\*Bushehri A<sup>1</sup>, O'Sullivan M<sup>2</sup>

<sup>1</sup>Department of Surgery, Al Sabah Hospital, Kuwait; <sup>2</sup>Department of Surgery, University College Cork, Cork University Hospital, Ireland

#### **Introduction:**

There is good evidence that screening mammography can reduce mortality in breast cancer. This study aims to evaluate the prevalence of breast cancer screening and factors associated with it among working females in Kuwait.

#### **Methods:**

A cross-sectional study was carried on working women aged 40 years in Kuwait. A survey consisting of 28 questions on demographic information, history of breast cancer among contacts and other related aspects of breast cancer screening including mammographic screening history was administered in summer 2009. Binary logistic regression was used for statistical analysis.

#### **Results:**

1124 working females aged 40 years were analyzed. The prevalence of breast cancer screening was 273 (24.3%). 102 (9.1%) had undergone mammography, whereas breast clinical examination was the commonest type of screening (n=127; 11.3%). Women were more likely to undergo screening if they were 50 years (OR=1.88; CI 1.42-2.47), if their mother had breast cancer (OR=8.25; CI 4.44-15.34), if they had a personal history of breast cancer (OR=14.67; CI 6.98-30.82), or if they had heard of screening modalities for breast cancer. Area of residence, nationality, marital status, education and income had no impact on the likelihood of women undergoing screening. 783 (69.7%) agreed that screening helps to detect early stage breast cancer, but only 259 (23.1%) felt that mammography was the best screening tool.

#### **Conclusions:**

The overall prevalence of breast cancer mammographic screening is very low. Awareness about the benefits of screening mammography needs to be highlighted, and education campaigns need to be launched to encourage a higher uptake of mammographic screening.

*Key Words: Breast cancer; Screening; Mammography*

*Funding Agency: None*



**Surgery**

Category: Clinical

207

**The efficacy of combined amikacin and ciprofloxacin prophylaxis in the prevention of septicemia after transrectal ultrasound guided biopsy of the prostate gland is maintained for a minimum of 5 years.**

\*Kehinde EO<sup>1</sup>, Hussein S<sup>2</sup>, Al-Maghrebi M<sup>2</sup>, Hussein AYT<sup>2</sup>, Abdulla H<sup>3</sup>, Sheikh M<sup>3</sup>.

<sup>1</sup>Department of Surgery (Division of Urology), Faculty of Medicine, Kuwait University, Kuwait;

<sup>2</sup>Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait; <sup>3</sup>Department of Radiology, Faculty of Medicine, Kuwait University, Kuwait

**Introduction:**

We observed a significant rise in the occurrence of septicemia following transrectal ultrasound guided biopsy (TRUSB) of the prostate gland in our unit between 2001 and 2005. This prompted us to review our prophylactic antibiotic regimen in patients undergoing such procedures. This study compares septicemia rates in these patients between 2001 and 2005 when only oral ciprofloxacin was used prophylactically with those in patients between 2006 to 2010 when a single dose of intravenous (IV) amikacin was added to ciprofloxacin.

**Methods:**

Between 2001 and 2005, 300 consecutive patients (Group 1) undergoing TRUSB of the prostate were given oral ciprofloxacin 500 mg BD one day before and for 2 days after the biopsy. From 2006 to 2010, 897 patients (Group 2) in addition to ciprofloxacin as above, also received IV amikacin 500 mg 30 minutes before the biopsy. All patients had standard 6-12 core prostate biopsies taken. Patients were required to report: high fever ( $T > 39^{\circ}\text{C}$ ), chills or malaise with a low grade pyrexia within 7 days of the procedure. Culture and sensitivity of blood and urine samples were done for patients who developed septicemia post biopsy.

**Results:**

Septicemia requiring parenteral antibiotic treatment was seen in 24/300 (8%) and 15/897 (1.7%) patients in groups 1 and 2 respectively ( $p < 0.001$ ). In group 1 patients, the occurrence of septicemia after TRUSB of the prostate rose from 2.1% in 2001 to 13% in 2005 ( $p < 0.001$ ). In group 2 patients, the occurrence of septicemia was 1.5% in 2006 and 1.6% in 2010 ( $p < 0.25$ ). *Escherichia coli* resistant to quinolones was responsible for 34/39 (87.2%) septicemic cases, while 2 (5%) cases each were due to *Enterococcus faecalis* and *Klebsiella spp* resistant to quinolones.

**Conclusions:**

The addition of IV amikacin to quinolone prophylaxis significantly reduces infectious complications of TRUSB of the prostate. The effectiveness of the combination appears to be maintained continuously for a minimum of 5 years.

*Key Words: Prostate Biopsy; Antibiotics; Septicaemia*

*Funding Agency: Kuwait University Research Grant MS 01/05*



## **Surgery**

*Category: Undergraduate*

**208**

### **Prevalence and risk factors associated with self-reported carpal tunnel syndrome among office workers in Kuwait.**

Raman S<sup>1</sup>, \*Al-Halabi B<sup>2</sup>, Landry M<sup>3</sup>, Hamdan E<sup>4</sup>

<sup>1</sup>University of North Carolina at Chapel Hill, Epidemiology, Chapel Hill, United States of America; <sup>2</sup>Faculty of Medicine, Kuwait University, Kuwait; <sup>3</sup>University of Toronto, Physical Therapy, Toronto, Canada; <sup>4</sup>Fawsia Sultan Rehabilitation Institute, Kuwait City, Kuwait,

#### **Introduction:**

To investigate the prevalence and factors associated with self-reported carpal tunnel syndrome (CTS) in Kuwait due to lack of basic epidemiological data about common musculoskeletal conditions in countries such as Kuwait.

#### **Methods:**

A cross-sectional, self-administered survey of CTS-related symptoms surveying adult office workers (n = 470, 55.6% males) in public and private sector companies in Kuwait City employing more than 50 people. Prevalence of self-reported CTS, prevalence of CTS symptoms and odds ratios (OR) for factors of interest such as gender, body mass index, comorbidities, smoking status, computer use and exercise level were measured. Multivariate logistic regression was used to estimate adjusted odds ratios for factors of interest.

#### **Results:**

Self-reported CTS was reported in 18.7% of the group (88/470). CTS was significantly associated with the following demographic factors: female gender, obesity and number of comorbid conditions. Self-identification of CTS was associated with key symptoms and impairment in daily activities (e.g., wrist pain, numbness, weakness, night pain, difficulty carrying bags, difficulty grasping [Chi-Square Test for Association:  $P < 0.05$  for all symptoms/activities]). Symptoms such as wrist pain, weakness, and functional disabilities were reported frequently among those who do not self report CTS (range: 12.1% – 38.2%).

#### **Conclusions:**

The symptoms and functional impairments experienced by those who self report CTS are consistent with the clinical profile of CTS. Risk factors for CTS in this population included female gender, obesity and number of related comorbidities. Although the estimated prevalence is high compared with other studies utilizing self-report of CTS, the prevalence of symptoms in the population of people who do not self report CTS suggest that CTS may be still be under-recognized in the general population.

*Key Words: Carpal Tunnel Syndrome; Cumulative trauma disorders; Occupational exposure*

*Funding Agency: None*



***Surgery and Transplantation***

*Category: Undergraduate*

**209**

**Prevalence of and experience with bariatric surgery among government employees in Kuwait**

\*Masters YD, Al-Haqan DM, Jeraq MW, Al-Eidan AW, Al-Shaiji R, Oudah H  
Community Medicine Department, Faculty of Medicine, Kuwait University

**Introduction:**

The frequency of bariatric surgery in the treatment of severe obesity has increased dramatically in the past two decades worldwide. This cross sectional study measured the prevalence of a history of bariatric surgery among Kuwait government ministry employees, the factors associated with it, and the self-reported effectiveness of the procedures.

**Methods:**

The data collection method for this cross-sectional study comprised a questionnaire containing four sections (sociodemographic, weight loss history, bariatric surgery history and future plans for weight loss) and was distributed in March 2011 among 920 ministry workers. Six randomly chosen ministries included justice, finance, commerce and industry, housing, social affairs, and public works. The overall participation rate was 96.2%. Multivariate logistic regression with bariatric surgery as the dependent variable was used to adjust for confounding.

**Results:**

Out of 920 participants, the prevalence of bariatric surgery was 7.0% [95% C.I. 5.4 – 8.8], and was 5.0% and 8.0% among men and women respectively. Of the 124 (13.5%) of participants eligible to have the surgery, 34.7% underwent bariatric surgery. This study also showed that 2.8% are currently on the waiting list for the surgery. After adjustment, use of bariatric surgery was associated with income level >1500KD (OR, 2.1, p=0.046), and morbid obesity (OR, 77.0, p<0.0001), and with female gender (OR, 2.1, p=0.055), with marginal statistical significance.

**Conclusions:**

Bariatric surgery among eligible ministry employees in Kuwait was common. Moreover, the self-reported effectiveness of the procedure compared favorably with that seen in other studies. These data can be used by health planners in the development of multi-faceted programs to address the growing problem of obesity in Kuwait.

*Key Words: BMI; Bariatric surgery; Multi-faceted programs*

*Funding Agency: None*



# **Original Research Case Report By Subject Area**



**Allied Health**

*Category: Clinical*

**210**

**Intramuscular injection- Induced sciatic nerve injury: A new physical therapy approach**

\*Alshammari M

Physiotherapy Department, Ibn Sina Hospital, MOH

**CASE REPORT**

**Background:**

The physical therapy rehabilitation of a patient with sciatic nerve injury is quite complicated unless real reason elicited. Although post gluteal intramuscular (IM) injection sciatic nerve injury is rare, no definite physical therapy program is agreed in literatures. In our case complete management of sciatic nerve injury induced by IM injection was successfully achieved by a new physical therapy approach.

**Case summary:**

A 16-year-old medically free female patient presented with severe right gluteal pain, and inability to walk after IM injection with non steroidal anti-inflammatory drug (NSAID) to relieve menstrual symptoms. Physical therapy examination showed a clear trigger point in right buttock, and severe constant shooting pain (NRS 9/10) which was aggravated by sitting, standing, and walking. She was using elbow crutches for non-weight bearing ambulation. Gait speed was 0.21 m/s. No sensory deficit elicited. Five days later after pain control manual muscle testing showed muscle weakness of right hip extensors and abductors (3/5), bilateral ankle dorsiflexors (3/5), and all other muscles were good (4/5). Patient received 12 sessions of physical therapy program divided in to two stages; pain control stage, then gait training. Pain control included decompressive, de-tensile methods, use of ultrasound and cold packs. After pain control, gradual weight bearing, muscle strengthening and gait training exercises were applied. Results: (1) pain was completely relieved (NRS 0/10) on the 4th session. (2) Independent and safe walking with speed of 1.21 m/s. on the 9th session. (3) Full regain of all lower limb muscles' power. (NRS: numerical rating scale)

**Conclusion:**

It's proved in our case that a patient with sciatic nerve injury due to gluteal IM injection was totally recovered within a relatively short time period. A well, individualized physical therapy program was used to manage her post-injection sciatic nerve injury.

*Key Words: Pain Control; Physical Therapy; Intramuscular injection*



**Biochemistry**

Category: Clinical

212

**Citrullinemia in a young Kuwaiti boy**

\*Alrashed H

Department of Clinical Biochemistry and Metabolic Medicine

**CASE REPORT**

**Background:**

A Kuwaiti boy presented with hyperammonemia few days after birth. By quantitative amino acid analysis, he was diagnosed as a case of citrullinemia. He is being followed regularly by metabolic specialist and nutritionist for controlling disease activity and preventing complications.

**Case summary:**

The patient is a product of full term normal vaginal delivery. His parents were first degree cousins. He presented on the second day of life with vomiting, and dehydration then became lethargic with weak cry, grunting, and distress. Soon he developed convulsions and his sensorium deteriorated. He was admitted to the hospital, vitally unstable, with high blood pressure, tachycardia and tachypnea. He was immediately transferred to the Pediatric Intensive Care Units due to respiratory failure, cardiac failure and metabolic encephalopathy. Extensive metabolic and radiological work up had been done to rule out other causes. Echocardiogram was done showing hyper echoic cardiac musculature and depressed biventricular function suggesting metabolic cardiomyopathy. Investigations revealed high blood ammonia level and high blood lactate. Metabolic screen on blood spot specimen collected onto filter paper analysed by Tandem MS showed raised citrulline. The result was confirmed by quantitative amino acid analysis of blood specimen by HPLC in which citrulline was found to be very high. The patient was intubated and ventilated to support his respiratory status. Then aggressive management with arginine, sodium benzoate and exchange transfusion through umbilical cord were done. During the hospital stay he became better and regained his consciousness after 48 hours. Close follow up with the metabolic specialist and nutritionist was arranged in order to keep the patient on protein free diet.

**Conclusion:**

I have presented a case of infantile citrullinemia successfully diagnosed and managed with good practice, nutritional supports and multidisciplinary approach.

*Key Words: Citrullinemia; Hyperammonemia; Protein free diet*



**Dentistry**

*Category: Clinical*

**213**

**Complication of improper management of Sodium Hypochlorite accident during root canal treatment**

Abo Alhassan F<sup>1</sup>, \*Sadeq A<sup>2</sup>, Burezq H<sup>3</sup>

<sup>1</sup>Surgical Department, Al Adan Hospital; <sup>2</sup>Department of Endodontics, Al Farwaniya Hospital; <sup>3</sup>Department of Plastic Surgery, Ibn Sina Hospital (Al Babtain)

**CASE REPORT**

**Background:**

Sodium Hypochlorite is a very common detergent used in dentistry during root canal treatment, because of its strong antibacterial, lubricating, and tissue dissolving properties. Nevertheless, it has some serious complications, some of which are life-threatening. Sodium hypochlorite accident occurs when the solution extravagates beyond the apex of the root canal into the surrounding tissue

**Case summary:**

A 24 year old male presented to Al-Babtain Center with a severe chemical burn of the right infraorbital area and necrosis of part of the hard palate. This all started during root canal treatment of the upper right first molar tooth, when the patient felt immediate severe pain after injection of sodium hypochlorite into the tooth canal. There was no intervention taken for half an hour until the patient was sent by ambulance to the emergency department, where only sedation and analgesia were given. The patient ended up having a scar on his face secondary to the deep chemical burn. Mucosal damage has healed nearly completely, and no information regarding the root canal treatment is available.

**Conclusion:**

There are several precautions that must be taken during sodium hypochlorite use, to prevent the spread of the solution into the surrounding tissue. In case of sodium hypochlorite accident, early recognition of sign and symptoms and proper immediate management is important to achieve the best possible outcome.

*Key Words: Sodium hypochlorite; Root canal; Endodontics*

**Dentistry***Category: Clinical*

214

**Central odontogenic fibroma of maxilla: A case report**Al-Harkan A<sup>1</sup>, \*Al-shamali W<sup>2</sup>, Brazda A<sup>3</sup>Oral & Maxillofacial department of Farwaniya Dental Center<sup>1,3</sup>; Medical laboratory services of Farwaniya Hospital- Histopatology Department<sup>2</sup>**CASE REPORT****Background:**

Central odontogenic fibroma (COF) is a rare benign neoplasm of mesenchymal tissue of dental origin. It represents less than 0.1% of all odontogenic tumors. Clinical and radiological features of COF often open the door to a broad differential diagnosis. On the other hand, microscopic diagnosis, in most occasions, can be relied upon.

**Case summary:**

We report a case of 45-years-old Philippino female, who presented with a 3 cm painless swelling of left maxillary edentulous alveolar ridge with unremarkable overlying mucosa in April 2010. The lesion had been growing slowly over the past three years. Panoramic radiography showed radiolucent-to-radiopaque unilocular lesion associated with impacted third molar and its border was diffusely sclerotic. Histopathologically, the initial biopsy revealed cellular plump fibroblasts in loose fibrous stroma with heterotonous hard tissues formation ranged from cementoid-like bodies to dysplastic bone tissue. Such histomorphological features were consistent with benign fibro-osseous lesion preferably central cemento-ossifying fibroma, for which resection with 0.5cm margin was carried out. Macroscopically, a 4.0cm excised tumor had relatively demarcated, non-capsulated, firm to hard mass with the lesion which was focally infiltrating the palatal margin. Unexpectedly, it showed presence of numerous inactive-looking epithelium components within the cellular fibrous tissue. Hence, the final diagnosis was central odontogenic fibroma. The healing process was uneventful. Despite the infiltrative nature of the present lesion, there was no evidence of recurrence for one year of follow up.

**Conclusion:**

It is essential that oral surgeons, radiologists and pathologists integrate all relevant and available information to come up with a correct diagnosis of COF which leads to appropriate disease management.

*Key Words: Central odontogenic fibroma; Maxilla; Fibro-osseus lesion*



WITHDRAWN



**Dentistry**

*Category: Clinical*

216

**Trigeminal neuralgia associated with multiple sclerosis: Case report**

\*Al-shamali WA

Dental Center, Farwaniya Hospital

**CASE REPORT**

**Background:**

Trigeminal neuralgia (TN) is an idiopathic episodic neuropathic condition and characterized by an extremely severe lancinating pain limited to one or more branches of the trigeminal nerve. Occasionally, secondary TN involves TN-like pain that develops owing to multiple sclerosis (MS), which represents approximately 4% of affected patients.

**Case summary:**

A 55-year-old Syrian woman presented, with recurrent episodes of mild to severe, sharp, steady, burning pain in the distribution of left maxillary and mandibular dermatomes.

The patient attended the dental clinic, in September 2009, complaining of oral discomfort that started two years earlier as a vague dull, aching, and burning pain of left maxillary gingiva. The pain was mild to moderate intensity. Comprehensive dental investigation failed to reveal any dental disease. Percutaneous injection with lidocaine (2%) of trigeminal trunk resulted in instantaneous resolution of her symptom. The provisional diagnosis was neuropathic pain favoring TN. Carbamazepine (200 mg thrice daily) was prescribed to be increased every third day to reach up to 1800mg. Unfortunately, she was lost to follow-up. In October 2010 she returned presenting a well-defined pain pattern and distribution. The discomfort recurred in irregular episodes of several weeks or months separated by pain-free remissions. The discomfort was of low intensity except when maxillary gingiva was triggered by chewing, light touch and inhaling of cold air causing a sudden volley of paroxysmal pain in the distribution of left maxillary and mandibular dermatomes. Infrequently, the right maxillary dermatome exhibited similar symptoms. She found carbamazepine ineffective in controlling her symptoms and denied instability while walking or vision disturbances, but complained of increasing fatigue. Magnetic resonance image (MRI) confirmed of the presence of demyelinating lesions affecting periventricular areas bilaterally.

Patient referred to neurological department of a specialized hospital where she was managed for MS in addition to MS-associated TN.

**Conclusion:**

TN, even though infrequent, can precede multiple sclerosis. Risk of delay in diagnosing a debilitating condition such as MS is not uncommon. The dental practitioner should be familiar with TN to avoid unnecessary dental interventions and ensure prompt initiation of appropriate treatment.

*Key Words: Trigeminal Neuralgia; Multiple Sclerosis*



**Dentistry**

Category: Clinical

217

**Eruption of oral lichen planus after interferon therapy for Hepatitis C Infection**

\*Al-Shamali WA<sup>1</sup>, El-Khalawany<sup>2</sup>, AL-Serayee S<sup>3</sup>

<sup>1</sup>Department of Pathology, Farwaniya Hospital <sup>2</sup>Department of Dermatology, Farwaniya Hospital. <sup>3</sup>Department of Medicine, Farwaniya Hospital.

**CASE REPORT**

**Background:**

Oral lichen planus (LP) is a relatively common chronic inflammatory condition that affects the oral mucous membrane with variable clinical traits. The association between LP and hepatitis C virus (HCV) infection has been well documented, although the exact pathogenesis remains uncertain. The role of alpha-interferon (INF), being used for treatment of HCV-positive patients, has been highlighted in the causation or exacerbation of oral LP.

**Case summary:**

We present a case of 44-year-old Egyptian male, who presented with painful, swollen and ulcerated lower lip. He had been diagnosed with HCV infection (genotype 4) in 2008 for which he received combined therapy of INF and ribavirin for 48 weeks. However, during therapy he reported oral soreness for brief period, of which no details are available. This therapeutic intervention was terminated as it failed to hold the progression of viral activity. The oral symptoms reappeared five months following discontinuation of anti-hepatitis therapy with severe pain, difficulty in eating, swallowing and speaking. At the present visit peri-oral examination revealed swollen lower lip with central erosive areas and there were white fine and coarse lace-like mucosal changes abutting the eroded lesions. Oral examination showed bilateral white and red lesions on posterior part of the buccal mucosa. The lesion on right buccal mucosa was found rubbing against heavily restored molar tooth with amalgam. No other oral lesions were seen. The clinical presentation of the lip and oral cavity lesions were consistent with LP, which was confirmed by the histopathology report of the incision biopsy of lower lip lesion. The patient was treated with topical cream 0.1% three-four times daily for 2 weeks. The lower lip status improved dramatically.

**Conclusion:**

In presented case, altered immunogenicity of HCV appears to be the likely explanation for eruption of oral LP, underscoring the importance of follow-up of the patient post anti-HCV therapy.

*Key Words: Oral lichen planus; Hepatitis C infection; Interferon*



**Medicine**

*Category: Clinical*

**218**

**Endoscopic stent placement as a therapeutic option for post bariatric surgery leaks: The Kuwait Experience**

\*Al-Ali J<sup>1</sup>, Ahmed A<sup>2</sup>, Al-Asfar F<sup>3</sup>, Alsumait B<sup>4</sup>, Hasan F<sup>1</sup>

The Departments of Medicine<sup>1</sup>, Radiology<sup>2</sup>, Surgery<sup>3</sup>, University of Kuwait, Faculty of Medicine; Department of Surgery, Mubarak Al-Kabeer Hospital, Kuwait.

**CASE REPORT**

**Background:**

Gastric leak after different types of bariatric surgeries is one of the most serious complications that can lead to death if not managed promptly. Revisional surgery for leaks is time consuming and associated with considerable morbidity. We report a series of cases with post sleeve gastrectomy and gastric bypass leaks that were successfully managed endoscopically by endoluminal stenting.

**Case summary:**

Twenty-six patients (19 females and 5 males) with a post sleeve gastrectomy leaks and two (female) cases of leaks after gastro-jejunal bypass surgery were treated at Mubarak Al Kabeer Hospital, Kuwait with self- expandable partially covered metal stent (SEPCMS) (Ultraflex esophageal NG stent system, Boston Scientific.) to seal the leaks and CT-guided percutaneous drainage of intra-abdominal fluid collections . Fever and abdominal pain were the most common symptoms at the time of the presentation. Gastric leak was confirmed by fluoroscopic single-contrast (Visipaque 270) upper gastrointestinal study and/or CT-abdomen with oral contrast. Under fluoroscopic guidance the SEPCMS was inserted and kept in place for 6-8 weeks. All patients showed dramatic improvement of their symptoms with a decrease of draining amount. Oral feeding started 3-5 days after stenting. At week six, fully covered esophageal plastic stents (Polyflex esophageal stent, Boston Scientific) were deployed inside the SEPCMS to decrease the amount of granulation tissue. Both stents were removed successfully in all patients. One patient had esophageal mucosal tear that was treated endoscopically and four failed the endoscopic treatment and required surgical intervention. Twenty-two patients had a totally sealed leak.

**Conclusion:**

Gastric leak after bariatric surgery is one of the most serious complication that need to be diagnosed and managed promptly. Endoluminal stenting to seal the leaking site is a viable, safe and minimally invasive therapeutic option in selected patients presenting with

*Key Words: leak; Endoluminal stents*



**Medicine**

Category: Clinical

219

**Giant cell tumor of tendon sheath mimicking Nodal Osteoarthritis**

\*Al-Jarallah K<sup>1</sup>, Al-Waheeb S<sup>2</sup>, Attiya Youssef<sup>2</sup>, Abraham Mini<sup>1</sup>

<sup>1</sup>Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait; <sup>2</sup>Department of Medicine, Ministry of Health, Kuwait.

**CASE REPORT**

**Background:**

Giant cell tumors of tendon sheath (GCTTS) are the second most common benign tumors of hand, simple ganglion cysts being the commonest. Symptoms of the disease are nonspecific. Peak age of occurrence is 30-50 years, often seen in women. There is a 50% association with trauma. GCTTS could be a reactive or regenerative hyperplasia associated with inflammatory process. Our objective is to report an unusual presentation of GCTTS of the distal interphalangeal (DIP) joints of the hand.

**Case summary:**

A 51-year old Indian driver was referred to rheumatology clinic with history of painless swellings of DIP joints of both hands with a referral diagnosis of nodal osteoarthritis (OA). Examination of hand revealed 3x4 mm lobulated, nodular swellings located on dorsal aspect of all digits, adjacent to DIP joints. There was no trans-illumination through the swelling. Plain radiography of hands showed no erosion or calcification and with preserved joint space. A diagnosis of GCTTS was made based on histopathological findings. Patient was followed up for a period of three years. There was no recurrence of excised tumor.

**Conclusion:**

Presentation of GCTTS involving all the DIP joints of both hands simulating nodal OA is unusual. Treatment of choice is surgical excision if patient is symptomatic. Clinicians should include GCTTS among differential diagnosis of DIP joint swellings of hand.

*Key Words: Giant Cell Tumor; Nodular tenosynovitis; Osteoarthritis*



**Medicine**

Category: Graduate (Resident)

220

**Unusual cause of myocardial infarction.**

\*Alkharaza A

Medical Department, Al-Adan Hospital, Ministry of Health, Kuwait

**CASE REPORT**

**Background:**

Adult Still's disease is an autoimmune disease of unknown etiology presenting usually with fever, arthritis/arthralgia and a characteristic skin rash. It is diagnosed by exclusion of other infective, autoimmune and malignant disorders.

**Case summary:**

We present a 25-year young man who presented 2 hours after arrival from a trip to the Far East with severe chest pain, ECG changes and raised cardiac enzymes suggested acute antero-lateral myocardial infarction, for which, he was thrombolysed. Two days later, he was transferred to the medical ward where detailed history showed that he was feeling sick 2 weeks before presentation with hectic fever, body aches, and arthritis. Investigation of PUO was commenced, 3 days later he developed bilateral pleural effusion and pericardial effusion associated with ascites and hepatosplenomegaly. These findings were confirmed by CT scan of chest, abdomen and pelvis which also revealed para-aortic lymphadenopathy. All investigations did not reveal any infective agent and also autoimmune screening was negative. In spite of the fact that, the patient did not develop a Salomon rash, he fulfilled Yamaguchi Criteria for diagnosing Adult-Still's disease. The patient was started on steroids with favourable response of fever, effusion, and hepatosplenomegaly.

**Conclusion:**

Acute myocardial infarction possibly due to coronary vasculitis, despite rare, is to be considered as a feature of Adult Still's disease.

*Key Words: Hepatosplenomegaly; Yamaguchi; Ascites, Pleural effusion*



**Medicine**

*Category: Clinical*

**221**

**Nail psoriasis treated with pulse dye laser**

\*Al-Mutairi A, Elkashlan M

Ahmadi Hospital, Kuwait

**CASE REPORT**

**Background:**

Nail affection is a common feature of psoriasis resulting in psychological and functional impairment for the affected patients. Pulse dye laser has proved effective for plaque-type psoriasis, but it has not been evaluated in nail psoriasis.

**Case summary:**

Our patient is 40 years old female suffering from nail psoriasis for the past two years. She received three pulse dye laser sessions on monthly basis. The nails were evaluated before treatment and one month after the last session using NAPSI score. NAPSI score showed marked reduction following pulse dye laser treatment.

**Conclusion:**

We believe that PDL would be an effective convenient treatment option of nail psoriasis. However, more studies are needed to objectively judge its effect.

*Key Words: Psoriasis; Nail; Pulse dye laser*



**Medicine**

Category: Clinical

222

**Impact of superior vena cava on patient and graft survival in renal transplant recipients: Case report and review of literature**

\*Al-Otaibi T, Gheith O, Halim M, Said T, Prasad N, Nampoory MNR

OTC

**CASE REPORT**

**Background:**

The superior vena cava (SVC) syndrome is due to obstruction of the SVC and may present by dyspnea, chest pain, cough, headache, dysphasia, and symptoms of increased intracranial pressure; however, the affected patients can be asymptomatic. Double lumen subclavian and internal jugular dialysis catheters are commonly used as immediate vascular access for patients requiring urgent hemodialysis. Thrombosis and stenosis are frequent complications with infrequently reported SVC syndrome in these patients. Herein, we describe the impact of SVC syndrome-related to long-term use of hemodialysis indwelling catheters – in renal transplant recipient.

**Case summary:**

A 22-year-old man, who developed end stage renal disease (ESRD) secondary to renal dysplasia, had received his 1st renal allograft from his mother on 1993. However, he developed chronic graft failure after 14 years due to chronic transplant glomerulopathy. After a period of hemodialysis, he developed benign intracranial hypertension possibly due to superior vena cava stenosis with repeated central vein catheterization and difficult vascular access. Following desensitization with immunoabsorption- due to high anti-HLA antibodies- he underwent 2nd renal allotransplant on 2009 with slow graft function. Few months later, he developed bilateral pleural effusion that was proven to be chylothorax. Magnetic resonant venography revealed stenosis of both subclavian veins and also superior vena cava. Tube drainage was performed and he was managed successfully with anticoagulation for two years without relapse.

**Conclusion:**

In renal transplant patients, conservative management by anticoagulation can be applied successfully in cases of chylothorax secondary to superior vena cava stenosis.

*Key Words: Sup vena cava; Thrombosis; Renal transplant*



**Medicine**

*Category: Clinical*

**223**

**Unusual presentation of Lyme disease.**

\*Al Otaibi M<sup>1</sup>, Al-Hashel J<sup>2</sup>

<sup>1</sup>Department of Medicine, Faculty of Medicine; <sup>2</sup>Department of Medicine, Mubarak Al-Kabeer Hospital

**CASE REPORT**

**Background:**

Lyme disease is uncommon in Kuwait due to the lack of host and vector required for the spirochete, *Borrelia burgdorferi*, to be transmitted. In this case we are describing uncommon hypothalamic manifestation of the disease which has not been reported before.

**Case summary:**

A 37 year old Bulgarian female, previously healthy started to complain of polyuria, polydipsia and fatigability of 3-4 weeks duration in addition to a generalized non specific rash. Her physical exam was unremarkable.

Endocrinological workup was totally normal. MRI brain revealed multiple hyperintense lesions in the deep subcortical and periventricular white matter in addition to a small lesion seen in the hypothalamic area. A possible diagnosis of multiple sclerosis (MS) was suspected. Six months later, the patient was hospitalized again with severe fatigue, unsteady gait, weakness and polyarthralgia. She was treated with methylprednisolone presuming a possibility of a relapsing attack of MS. A year later, the patient developed severe fatigability, polyuria, polydipsia, bradycardia and hypothermia. Full immunological screening and skin biopsy looking for vasculitis were done and found to be normal. Three years later the patient went to Bulgaria for a second opinion since her symptoms of chronic fatigability and arthralgia did not resolve completely. She was seen by a rheumatologist for that. Based on her ethnicity and the chronicity of her symptoms, Lyme disease was investigated. ELISA test was positive for IgM. Western blot was done and it was positive as well. The diagnosis of Lyme disease was confirmed and the patient improved after treatment with antibiotics and IVIG.

**Conclusion:**

Lyme disease should be suspected in patients coming from endemic areas like Europe and North America. It can mimic MS in terms of symptoms and radiological findings. It can be also misdiagnosed with chronic fatigue syndrome. IVIG is a possible treatment for Lyme disease but further studies are needed

*Key Words: Hypothalamic dysfunction; Western blot*



**Medicine**

Category: Graduate (Resident)

224

**Kikuchi-Fujimoto disease: A case report**

\*Al-Taweel A, Al-Jassim A, Zaki MY

Mubarak Al-Kabeer Hospital, Department of Medicine.

**CASE REPORT**

**Background:**

Kikuchi-Fujimoto Disease is a very rare benign condition that is self-limiting in nature. The disease has a worldwide distribution with higher prevalence among Japanese and other Asian individuals. It is characterized by cervical lymphadenopathy and fever and is clinically a diagnosis of exclusion. Recognition of the disease is crucial, as its symptoms may be mistaken for systemic lupus erythematosus, malignant lymphoma and rarely adenocarcinoma. Histopathology of the involved lymph nodes is the method used to differentiate Kikuchi's disease from more serious conditions it may mimic.

**Case summary:**

This case report describes recurrent cervical lymphadenitis for 6 months in an 18 year old Kuwaiti girl at Mubarak Al-Kabeer Hospital. Moreover, the patient was complaining of fever, night sweats and tenderness over her left aspect of the neck. She also mentioned a loss of 5 kg over one month.

**Conclusion:**

Histopathology sections of her lymphnodes showed extensive foci of eosinophilic necrosis, sprinkled with karyorrhectic debris. These areas are rimmed by signet ring type and foamy histiocytes, epithelioid cells and plasma cells which are typical of necrotising lymphadenitis consistent with KFD. The patient received a 2 week trial of a non-steroidal anti inflammatory, but the cervical lymphadenopathy had finally resolved after treatment with corticosteroids, and the patient is currently being followed up regularly as an outpatient.

*Key Words: Kikuchi-Fujimoto; Lymphadenopathy; Fever*



**Medicine**

*Category: Clinical*

**225**

**Acute rectal ischemia: Case report**

\*AlTourah L, Owayed S, Al-Ali J

<sup>1,3</sup>Department of Medicine, Kuwait University, Faculty of Medicine; <sup>2</sup>Department of Medicine, Al-Adan Hospital.

**CASE REPORT**

**Background:**

Because of its extensive collateral circulation, involvement of the rectum is distinctly rare in ischemic disorders of the large intestine. Occasional cases reported in the literature have occurred in elderly patients with atherosclerotic disease.

**Case summary:**

A 70 yr-old gentleman, a known case of coronary artery disease and atrial fibrillation on multiple treatments, presented with acute fresh lower Gastro-intestinal bleeding. The complaint started after admission to Cardiology service for episodes of irregular heartbeats and lightheadedness; he was started on heparin, and as he complained of constipation, was treated with Senna and lactulose. Subsequently, the patient had six to eight bowel movements with reddish blood, accompanied by urgency with no abdominal pain or previous history of weight loss. On examination, patient was vitally stable with irregular heart beat; abdominal examination was unremarkable. Patient had a hemorrhoidal tag and rectal examination showed obvious blood. His hemoglobin was 172, platelets 143, INR 1.6, PTT 34.3. He was blood grouped and cross matched.

**Conclusion:**

After obtaining the patient's consent, colonoscopy was done and showed immediate striking evidence of acute colitis, extending from lower rectum to sigmoid colon, with the proximal level at approximately 20 cm from the anal verge. Considerable whitish mucus exudate was present and the mucosa was intensely hyperemic, edematous, and friable with no ulceration. At 20cm, a quite abrupt demarcation between abnormal mucosa distally and normal mucosa proximally was noticed. The rest of colon was normal. Biopsies were obtained at 20cm, 15cm and from rectum. The biopsies showed necrosis of superficial aspect of the colonic crypts associated with an eruptive volcano-like lesion of fibrin with acute surface inflammatory exudates; this was highly suggestive of ischemic colitis. The patient was managed conservatively; the precipitating cardiovascular factor was effectively treated.

*Key Words: Rectal; Ischemia*



**Medicine**

*Category: Clinical*

**226**

**A case report of acute kidney injury following the abuse of anabolic androgenic steroids**

Al-Turki M, \*Esmail A, Alansari Y, Altaiar A

<sup>1</sup>Mubarak Al-Kabeer Hospital; <sup>2</sup>Department of Community Medicine, Kuwait University, Faculty of Medicine

**CASE REPORT**

**Background:**

Body satisfaction and body mass index (BMI) have been demonstrated as key factors affecting self-esteem. People who are dissatisfied with their body image tend to misuse drugs and exhibit an unhealthy behavior to enhance their body image. Anabolic Androgenic steroids (AAS) is one of these drugs and have been abused by general public to enhance body image and thus became a public health problem. AAS have an adverse effect on mental, physical, and sexual wellbeing but more seriously an acute kidney injury. The case we report here describes an acute kidney injury due to AAS abuse as a result of hypercalcemia.

**Case summary:**

A 32 year-old white male complaining of body aches, malaise and weakness concomitant with abdominal pain, nausea and vomiting. Initial laboratory investigations showed severe hypercalcemia and renal impairment.

**Conclusion:**

Although acute kidney injury is a rare side effect of AAS it is likely to increase with increasing number of people using AAS. This case in addition to other renal, cardiovascular, reproductive, endocrine, hepatic, dermatological and psychiatric side effects of AAS, highlight the importance of increasing awareness about AAS side effect among general public.

*Key Words: Body satisfaction; Hypercalcemia*



**Medicine**

Category: Clinical

227

**Foot drop, atypical presentation for ADEM**

\*Hamdy G<sup>1</sup>, Helal R<sup>2</sup>, Hassino L<sup>2</sup>, Al-Anzi AA<sup>2</sup>, Hamed I<sup>3</sup>, Solomon TD<sup>4</sup>, Youssef AS<sup>2</sup>, Ahmed M<sup>2</sup>, Amin M<sup>2</sup>.

<sup>1</sup>Department of Internal Medicine, University of Cairo Faculty of Medicine; <sup>2</sup>Department of Internal Medicine, Al-Jahra hospital, Kuwait; <sup>3</sup>Department of Clinical Radiology, Al-Jahra hospital, Kuwait;

<sup>4</sup>Department of Neurology, Ibn Sina hospital, Kuwait

**CASE REPORT**

**Background:**

Acute disseminated encephalomyelitis (ADEM) is an immune mediated acute inflammatory demyelinating disease of the central nervous system. It is a monophasic polysymptomatic disease that usually occurs following a viral infection but may appear following bacterial or parasitic infection, vaccination or even appear spontaneously.

**Case Summary:**

42 years Kuwaiti gentleman was admitted with inability to walk appropriately for 10 days, he described having left foot drop with a steppage gait on walking associated with parasthesia in the left leg up to the left nipple. He didn't report any associated fever, headache, disturbed consciousness or seizures. His three young children had developed chickenpox a few weeks earlier; from them he caught the infection 20 days prior to his recent complaint. On examination he had a diffuse fading skin rash on his upper body. His intellectual function and cranial nerves were normal. He had left steppage gait with foot drop, grade 2 weakness of the left ankle and toe dorsiflexors with equivocal left planter response. He had grade 4+ motor power in the rest of the left lower limb. All DTR were normal. There was subjective diminution of sensations over the left lower limb. The initial differential diagnosis was multilevel radiculopathy and left common peroneal neuropathy however urgent CT brain was done to rule out central causes and it showed faint hypodense area affecting white matter of left parietal lobe. MRI of the brain and the spinal cord showed multiple areas of hypo/hyperintense pattern on both T1/T2. NCV and EMG were normal. The diagnosis was made as post-chickenpox ADEM. He responded dramatically to IV methylprednisolone with complete recovery on the 5th day of treatment.

**Conclusions:**

Focus must be given for adults who are susceptible to rare serious complications of chickenpox. MRI should be considered early in patients with acute onset of focal neurological deficit.

*Key Words: ADEM; Chickenpox; Foot drop*

**Medicine***Category: Clinical***228****CNS Tuberculosis in a young lady: A case report**

Helal R, \*Hamdy G, Arafa EM, Tawakol M, Abdelhami A, Youssef AS, Marwa AS, Al-Anzi AA, Hassino L, Al-Sawy AM, Attia Y, Kharafi S  
Department of Medicine, Al-Jahra Hospital

**CASE REPORT****Background:**

Cerebral tuberculosis continues to be a serious problem with significant morbidity and mortality. Cerebral tuberculosis is diagnosed based on clinical features, cerebrospinal fluid studies combined with radiological images. Early diagnosis, prompt institution of anti-tubercular treatment, and the clinical stage at which the patient presents are important and deciding factors for final outcome.

**Case summary:**

23-year old Ethiopian lady, housemaid in Kuwait since 4 months, presented with headache, fever, occasional vomiting, confusion, behavioural changes and blurring of vision. On examination she was confused, afebrile, blood pressure was 110/70 and pulse was 82/minute. Her chest showed bilateral crackles. Heart and abdominal examinations were unremarkable. Neurological examination showed neck rigidity, patient was irritable. Chest X ray showed bilateral miliary shadows. CT brain showed multiple ring enhancing lesions in both cerebral hemispheres, brain stem and both cerebellar hemispheres with focal areas of oedema at the left and right parietal regions and also the left frontal region. Lumbar puncture done and showed clear CSF with cells less than 5, high protein 1.25 g/l and glucose 2.4 mmol/l Serum glucose was 4.7 mmol/l. CSF and blood culture were negative. Her liver and renal functions were normal. Full blood count was normal and ESR was 29. Sputum for AFB was negative. Quantiferon-TB gold result was positive. Serology for toxoplasmosis and cysticercosis were negative. HIV was negative. The patient received anti TB treatment and steroids with dramatic improvement in her conscious level within 24 hours.

**Conclusion:**

The prompt treatment of anti TB is important for the prevention of neurological and respiratory complications. Steroids have an important role in the management of brain oedema in brain tuberculomatae.

*Key Words: Headache; Confusion; Miliary*



**Medicine**

Category: Clinical

229

**Progressive multifocal leukoencephalopathy (PML) in kidney transplantation, case series and review of literature.**

\*Said T, Al-Otaibi T, Nampoory MRN, Nair P, Gheith O, Halim MA, Balaha M, Elsayed Z  
Hamed Al-Essa Organ Transplant Center, Ibn Sina Hospital, Kuwait

**CASE REPORT**

**Background:**

PML is a serious neurological disease that has to be considered in the differential diagnosis of any central nervous system (CNS) dysfunction-affecting patients receiving potent immunosuppressive medications. Kidney transplant recipients are a vulnerable group with heavy immunosuppression who can develop such complication. Despite the late presentation of PML in reported kidney transplant cases, outcome is generally fatal. However, regression has been reported in some cases especially after reduction or withdrawal of mycophenolate.

**Case Summary:**

We report here three cases that had been diagnosed as PML and treated by immunosuppression reduction in two and discontinuation in a third. Patients were two males and one female aged 69, 28 and 63 years respectively at the time of diagnosis. They manifested 4, 9 and 3 years post transplantation. Presentation was acute with hypertension and loss of consciousness in the first and subacute with persistent headache in the second and slow deterioration of consciousness in the third patient. The three patients were diagnosed by brain magnetic resonance imaging. Cerebrospinal fluid (CSF) was nearly normal in the three patients. JC virus was detected by polymerase chain reaction in the CSF in the first and third cases but it was not detected in the second one. The first patient recovered completely clinically and maintained on low immunosuppression with normal renal function. The second one has discontinued his immunosuppression recently except for steroids and still under follow up with functioning kidney. The third one had a slow progression of CNS dysfunction with normal renal function on very low immunosuppression and died after five years of diagnosis.

**Conclusion:**

Despite the fatal outcome of PML in the literature, kidney transplant recipients may have better prognosis with reduction/discontinuation of immunosuppression.

*Key Words: Progressive Multifocal Leukoencephalopathy; Kidney Transplantation; JC virus*



**Medicine**

*Category: Clinical*

**230**

**Posterior reversible encephalopathy syndrome**

\*Sherif AH, Ibrahim H, Mohsen N

Medical Department, Al Jahra Hospital; Radiology Department, Al Jahra Hospital

**CASE REPORT**

**Background:**

Posterior Reversible Encephalopathy Syndrome (PRES) is a syndrome characterized by headache, confusion, seizures and visual loss. The clinical manifestations of PRES in the setting of acute blood pressure elevation is characterized by the subacute development of neurologic signs and symptoms and may include headache, altered mental status, seizures, and visual disturbances. The characteristic clinical features and imaging findings, notably MRI led to the description of PRES. The posterior predominance of PRES is reflected by the frequent occurrence of unilateral or bilateral visual disturbances.

**Case Summary:**

A 34 years old woman presented by sudden onset of headache, vomiting and diminished visual acuity, 20 days after vaginal delivery. Past history of pregnancy-induced hypertension was elicited for which she refused antihypertensive treatment. Clinical examination revealed disoriented patient with her Blood Pressure was 220/120 mmHg; visual acuity was diminished to counting fingers on the right side and hand movement on the left side, with no evidence of papilledema on fundus examination, as well as left lower limb weakness, left extensor planter response. CT brain initially showed no significant abnormality. MRI brain showed bilateral parieto-occipital altered signal intensity areas in terms of hypo/hyperintense signal on both T1/T2WIs and Flair series respectively with associated brain edema, picture was suggestive of PRES.

**Conclusion:**

The key of diagnosis of PRES depends up on correlation of the clinical data with imaging findings, notably MRI, yet suspicion must be raised by the clinician based on the patient's condition. The diagnosis has important implications because the reversibility of the clinico-radiological findings depends up on the prompt control of blood pressure and/or withdrawing of the offending drug.

*Key Words: Encephalopathy; Hypertensive; Reversible*



**Medicine**

*Category: Clinical*

**231**

**Rate of incidence of transfusion reaction in the Medical Department of Al- Jahra Hospital Year 2010**

\*Youssef AS, Thouweni A, Fakeir A, Hamid R, Hamdy G

Department of Medicine, Al-Jahra Hospital; Department of Haematology, Al Jahra Hospital

**CASE REPORT**

**Background:**

In 1840, Samuel Armstrong Lane, aided by Dr. Blundell, performed the first successful whole blood transfusion to treat hemophilia. It was not until 1901, when the Austrian Karl Landsteiner discovered human blood groups, that blood transfusions became safer. Each unit contains approximately 42.5-80 g of hemoglobin or 128-240 mL of pure red cells, depending on the hemoglobin level of the donor.

**Case summary:**

Data collection was retrospective from the Blood Bank Unit in Al Jahra Hospital for packed RBCs transfusion in the Medical Department in the year 2010. Packed Red Blood Cells is commonly used in Al Jahra Hospital. All data were collected from the registry of the hospital blood bank. These data were compared with the medical record of each case developed any transfusion reaction. Febrile non-hemolytic reaction is typically manifested by a temperature elevation of  $\geq 1$  C occurring during or shortly after a transfusion and in the absence of any other pyrexia stimulus. This may reflect the action of antibodies against white cells or the action of cytokines, either present in the transfused component or generated by the recipient in response to transfused elements. Allergic reactions usually occur as urticaria, but may also include wheezing or angioedematous reactions. The total number of blood transfusion in the medical department of Al Jahra hospital in 2010 was 646. Three developed allergic reaction and five developed febrile reaction. No haemolytic reaction recorded. Rate of blood transfusion reaction was 1.2% and is calculated as: Total number of transfusion reaction / Total number of blood transfusion during 2010 X 100 = 8 Cases / 646 Cases X 100 = 1.2%

**Conclusion:**

The febrile non-haemolytic transfusion reactions that occurred in the Medical Department constitutes a very small percentage. No haemolytic reaction occurred at all. Strict adherence to the international guidelines regarding the protocol of blood transfusion is strongly recommended.

*Key Words: Transfusion; Nonhaemolytic; Febrile*



**Medicine**

Category: Clinical

232

**Polyuria in an adult female**

\*Youssef AS, Al-Anzi FM, Al-Anzi AA, Hamdy G, Helal R, Enas EA, Hassino L, Al-Sawy AM  
Department of Medicine, Al-Jahra Hospital

**CASE REPORT**

**Background:**

Central diabetes insipidus is characterized by decreased release of antidiuretic hormone, resulting in a variable degree of polyuria. Lack of antidiuretic hormone can be caused by disorders that act at one or more of the sites involved in antidiuretic hormone secretion: the hypothalamic osmoreceptors; the supraoptic or paraventricular nuclei; or the superior portion of the supraopticohypophysal tract.

**Case summary:**

28-year old lady, married with 2 kids, delivered by caesarian section without any residual complications and had normal lactation. She started to notice polyuria associated with thirst and polydipsia of 3 months duration and denied any visual disturbance or chest symptoms. On examination she was of normal built, weight was 83 kg, not dehydrated. BP was 127/86 without postural drop, afebrile, pulse was 88/minute. Her electrolytes were normal as well as her renal and liver functions. Complete blood count was normal. Serum prolactin, cortisol and thyroid function were normal. MRI brain and sella showed loss of the normal T1 hyperintense signal of the posterior pituitary. Normal brain parenchyma. Water deprivation test done and showed loss of 3 kg in 5 hours, and a total amount of 3 litres of urine were collected during that period. The urine osmolarity was less than 30% in all the samples and the serum osmolarity raised from 292 to 310.8 mosmol/L. The serum sodium raised from 139 to 146 mmol/l. Then desmopressin 4 microgram was given subcutaneous and within 3 hours the urine osmolarity raised to 411 mosmol and the serum osmolarity diminished to 300.2 mosmol. The patient responds well to desmopressin and was discharged on dDAVP nasal spray 2 buffs daily.

**Conclusion:**

In central diabetes insipidus the urine osmolarity after water deprivation test rises to more than 100%, while in nephrogenic diabetes insipidus or psychogenic polydipsia, the urine osmolarity rarely exceeds 50%.

*Key Words: Diabetes; Polyuria; Desmopressin*



**Microbiology, Virology and Immunology**

Category: Clinical

233

**A rare case of submandibular abscess due to *Nocardia Otitidiscaviarum***

\*Abdullah AA, Shetty SA, Mokaddas E.

Department of Laboratory Medicine, Ibn Sina Hospital

**CASE REPORT**

**Background:**

Infections caused by *Nocardia* species are uncommon and have a wide variety of clinical manifestations in immunocompetent and immunocompromised patients. In contrast to invasive pulmonary and disseminated nocardioses, which affects predominantly severely immunocompromised patients, cutaneous nocardiosis is usually a primary infection affecting apparently immunocompetent individuals.

**Case summary:**

A 48 day old Bedouin female baby presented with a swelling on the right side of the neck of two days duration. Birth weight was 3.1 kgs. with no congenital anomalies. On examination, the baby was febrile (38.4°C). Swelling was tender, erythematous and localized to the submandibular region. Skin over the region was indurated. Submandibular lymph nodes were enlarged. Routine blood investigation showed leucocytosis (29.8) and a CRP of 56. Ultrasound examination of the right submandibular swelling revealed a well defined cystic inflammatory lesion measuring 15×12×15 mm. with volume of 3.6 ml. On incision and drainage, 5 ml of thick yellow pus was collected and sent to the microbiology lab. Gram- stain of the pus revealed slender Gram-positive beaded branching filaments. Modified Ziehl-Neelson stain showed weakly acid-fast bacilli. Culture of the pus on blood agar grew cream coloured colonies with a dry chalky appearance. Gram-stain of those colonies revealed the same morphology. The bacteria was susceptible to co-trimoxazole, amikacin, gentamicin, kanamycin and ciprofloxacin. Patient was started on amikacin IV and oral co-trimoxazole.

**Conclusion:**

This case highlights the fact that *Nocardia* can be responsible for submandibular abscess, and should be considered as one of the differential diagnosis for such abscesses.

*Key Words: Submandibular; Abscess; Nocardia asteroides*



**Microbiology, Virology and Immunology**

Category: Graduate (Resident)

234

**Complicated Panton-Valentine leukocidin associated Staphylococcal disease: A case report**

\*Almerdasi N, Aldousari T, Alramezi Y, Jamal W, Udo EE, Rotimi VO

Department of Microbiology, Mubarak Alkabeer Hospital

**CASE REPORT**

**Background:**

Methicillin-resistant *Staphylococcus aureus* (MRSA) is a known cause of nosocomial infections worldwide. However, the prevalence of community-acquired MRSA infections is on the rise in previously healthy young individuals. The severity of CA-MRSA is associated with the production of the Panton-Valentine leukocidin (PVL), a toxin that destroys white blood cells and induces the release of inflammatory markers, which cause widespread tissue necrosis.

**Case summary:**

We report a case of 14-year-old female, a known case of IDDM, who presented with diabetic ketoacidosis and acute febrile illness. She had history of left shoulder pain, fever and productive cough. On admission, her temperature was 37.8 and left arm was tender and erythematous. White blood cell count was  $5.9 \times 10^9 /L$  and X-ray chest showed right-sided consolidation. Empirical therapy with piperacillin/tazobactam 4.5g q 8 h IV and clarithromycin 500 mg q 12 h IV was initiated. Blood culture showed Gram-positive cocci in clusters, so cloxacillin 2 g q 6 h IV was added. Once the isolate was finally identified as PVL-positive MRSA the previous antibiotics were discontinued as also vancomycin, which was started following MRSA report of blood culture, although clindamycin was retained and linezolid 600 mg q 12 h IV and rifampicin 300 mg q 12 h IV were added. MRI showed bone marrow infection of the left humeral metaphysis and diaphysis with joint effusion. Despite receiving appropriate therapy her clinical condition worsened, with repeat chest X-ray showing bilateral pleural effusion. The culture of fluid drained grew MRSA. After receiving a combination therapy for 4 weeks, she improved and was discharged after 5-week stay in the hospital.

**Conclusion:**

CA-MRSA infections differ from hospital acquired MRSA by presenting as minor skin & soft tissue infections in healthy hosts. However, our patient presented with “PVL syndrome” requiring aggressive combination therapy with linezolid, rifampicin & clindamycin.

*Key Words: Methicillin-resistant Staphylococcus aureus (MRSA); Panton-Valentine leukocidin (PVL); Tissue necrosis*



**Microbiology, Virology and Immunology**

Category: Clinical

235

**A case of Pyomyositis in immunocompetent child**

\*Bafna R, Emara M, Purohit P, Obaid IA

Al-Sabah Hospital, Kuwait

**CASE REPORT**

**Background:**

Pyomyositis, a rare primary acute bacterial infection of the skeletal muscles is usually caused by *Staphylococcus aureus* (50-90%). Endemic in tropical areas, it is often overlooked in the clinical settings in the other parts of the world.

**Case summary:**

A 2 year old previously healthy girl was admitted to Orthopedic Casualty with pain and limitation of movement, swelling of left upper arm and fever with features of toxic shock syndrome. She had a past history of pulling of upper left arm three days earlier, for which she was given analgesics at the polyclinic and was sent back home. Repeated X-rays and ultrasounds of the part were inconclusive except for soft tissue swelling. Being haemodynamically unstable, she was shifted to the pediatric ICU of Sabah Hospital and empirical broad spectrum antibiotics were started. Community-associated methicillin resistant penton-valentine-leukocidin (PVL)-producing *Staphylococcus aureus* was isolated from blood and from the aspirated pus of left upper arm. The MRI done after two weeks of presentation revealed massive pyomyositis involving all the muscles of the left upper arm with reactionary changes in humerus and septic arthritis of the left shoulder and elbow joints. Surgical debridement was done after three weeks of admission, two days after which the patient expired.

**Conclusion:**

Diagnosis of pyomyositis is often overlooked. It should be considered in the differential diagnosis of immediate onset of musculoskeletal pain with a history of trauma and fever, particularly in children. High degree of clinical suspicion and early radiological (MRI) evaluation leading to appropriate antibiotic therapy and/or surgical intervention in time, are the mainstay of pyomyositis management. Neglected cases may result in overwhelming sepsis, which might prove fatal especially in cases caused by PVL producer CA MRSA.

*Key Words: Pyomyositis; Staphylococcus aureus; CA MRSA*



*Neuroscience*

*Category: Graduate (Resident)*

236

**Acute clinical and radiological deterioration in MS following chronic cerebrospinal venous insufficiency treatment- Two case reports**

\*Al-Shammri S, Chadha G, Abu Quora A, Girgis M

Faculty of Medicine, Kuwait

**CASE REPORT**

**Background:**

Chronic cerebrospinal venous insufficiency has been hypothesized to play a role in the pathophysiology of Multiple Sclerosis, and an endovascular intervention for the syndrome has been attempted ever since Paolo Zamboni put forth the hypothesis in 2008. The procedure has generated both optimism (in patients of MS) and scepticism (in scientific fraternities across the globe), and has caused a lot of concern for Zamboni's research, which was neither blinded nor controlled, and further studies have all had variable results.

**Case summary:**

We report two cases of progressive MS, who were on Natalizumab, which was discontinued after few doses, before undergoing the endovascular interventional procedure. One of these cases developed iatrogenic internal jugular vein thrombosis during the procedure, requiring anticoagulants. Both cases developed a clinical worsening, prompting investigations to search for progressive multifocal leukoencephalopathy. MRI showed a remarkable increase in number and severity of white matter lesions, with multiple ring enhancing lesions seen in both instances. They were both treated with pulse steroids, followed by oral steroids. Both developed a septicemia during this fulminant period, requiring intravenous antibiotics. A follow up MRI at the time of discharge for one case showed improvement, with no enhancing lesions. The other case progressively deteriorated, coming in with repeated relapses over the next few months, with worsening disability.

**Conclusion:**

While alerting fellow physicians of the possible serious consequences of this procedure, we express our concern about the treatment being offered to an unsuspecting, desperate population of patients suffering from a debilitating progressive illness, without adequate research to ascertain the benefits versus risks of this procedure.

*Key Words: CCSVI; Multiple Sclerosis; Endovascular intervention*



**Neuroscience**

Category: Graduate (Resident)

237

**Treatment responsive autoimmune limbic encephalitis- Two case reports.**

\*Chadha G, Zeyada A, Fathy O, Al-Shammri S.  
Faculty of Medicine, Kuwait

**CASE REPORT**

**Background:**

Limbic encephalitis as initially reported as part of a paraneoplastic manifestation of cancer. it was thought to be extremely rare and unresponsive to treatment. the discovery of antineuronal antibodies (Hu, Cv2, CRMP5) reinforced these concepts, identifying a subgroup of encephalitides which were difficult to treat.

**Case summary:**

we report two cases of encephalitis admitted to our unit in the last 8 months. Both cases presented with seizures, behavioral changes and memory deficits. MRI showed abnormalities in the limbic areas of the temporal lobes, CSF showed a lymphocytic pleocytosis with increased proteins, EEG was abnormal. A paraneoplastic work up searching for a tumor was negative in both cases. Anti GAD antibodies were positive in one case. Both cases responded well to treatment with plasmapheresis, Intravenous immunoglobulins, and pulse methylprednisolone.

**Conclusion:**

The importance of a high index of suspicion, early identification and treatment of this subgroup of encephalitides, which are potentially fatal, is emphasized. A search for an underlying neoplasm may be negative, the importance of studying these disorders with antibodies to other cell surface antigens is discussed.

*Key Words: Limbic; Encephalitis; Anti gad antibodies*



***Nuclear Medicine and Radiology***

*Category: Clinical*

**238**

**A case of dupable duple duplicity and duplexity**

\*Afzal U, Siraj QH, Hebbar S

<sup>1</sup>Department of Nuclear Medicine, Farwania Hospital Kuwait; <sup>2</sup> Department of Radiology, Farwania Hospital Kuwait

**CASE REPORT**

**Background:**

Horseshoe kidney is the most common congenital renal as well as the most common renal fusion anomaly. The combination of horseshoe kidney and bilateral ureteral duplication is a very rare entity. We present a case of a horseshoe kidney with bilateral duplication of their collecting systems, ureters and arterial supply together with most of the possible associated sequelae. This appears to be quite a unique combination of congenital renal anomalies and abnormalities.

**Case summary:**

A 30-year-old lady was incidentally discovered with a horseshoe kidney. The patient presented with a 3-month history of breakthrough recurrent UTI whilst on prophylactic antibiotics. Blood cultures were positive for infection. Her renal function was preserved. Structural imaging included abdominal ultrasonography and a CT urogram, which revealed a horseshoe kidney with bilateral duplex collecting system, bilateral duplication of the ureters and bilateral renal calculi. On the right the ureters were bifid and on the left there was moderate hydronephrosis of the upper moiety and a significant hydroureter. In addition, there was bilateral duplication of arterial supply to the two kidneys. MCUG showed left-sided grade IV vesicoureteric reflux. Dynamic renal scintigraphy was performed to investigate renal drainage and divided renal function. A MAG3 renogram with Lasix washout and indirect cystography revealed normal functioning right kidney with no evidence of obstruction or vesicoureteric reflux; however on the left both moieties had relatively reduced function without any evidence of obstruction although there was significant vesicorenal reflux in the upper moiety of this kidney.

**Conclusion:**

To our knowledge, a case of a horseshoe kidney with bilateral double collecting systems, bilateral ureteral duplication and bilateral duplication of vascular supply has not been previously reported.

*Key Words: Horseshoe kidney; Duplex kidney; Ureteric duplication*



***Nuclear Medicine and Radiology***

*Category: Clinical*

**239**

**Iliac artery aneurysm in Behcet's disease patient treated by endovascular stent grafting**

\*Al-Muzaini A<sup>1</sup>, Al-Ali A<sup>1,3</sup>, Makram H<sup>1</sup>, Kamal E<sup>1</sup>, Al-Bader M<sup>1</sup>, Asfar S<sup>1,2</sup>

<sup>1</sup>Department of Surgery, Mubarak Al Kabeer Hospital; <sup>2</sup>Departments of Surgery; <sup>3</sup>Radiology, Faculty of Medicine, Kuwait University, Kuwait

**CASE REPORT**

**Background:**

Isolated iliac artery aneurysms (IIAAs) are rare, but have a high risk of rupture which can be fatal. Most lesions are discovered incidentally. Traditionally these aneurysms were treated by open surgery, but now endovascular treatment has been shown to be safe and effective as an alternative procedure. Patient suffering from Behcet's disease are known to be prone to development of arterial aneurysms.

**Case summary:**

A 33-years old man presented to emergency unit with right iliac fossa pain radiating to his back of 7 days duration. The patient is a smoker, a known case of Behcet's disease complicated by ilio-femoral deep venous thrombosis (DVT) in his left lower limb and he is on oral anticoagulation since 2009 and enucleation of his right eye because of severe uveitis. Computed tomography scan (CT) of the abdomen showed a leaking right common iliac artery (CIA) aneurysm measuring about 5 cm in diameter. Aneurysmal dilatation also involved the right internal iliac artery (IIA). Endovascular repair was done using coil embolization for IIA and stent graft for CIA. Computed tomography angiography (CTA) was done post endovascular procedure demonstrated endoleak adjacent to the proximal attachment site of the stent graft (Type 1 endoleak). Similar findings were detected by Duplex scan (DS). One week later a second DS follow-up revealed increased endoleak amount; however, aneurysmal sac did not increase in size. Third follow-up, a week later, DS demonstrated patent stent graft with total occlusion (Thrombosis) of aneurysmal sac and absence of endoleak.

**Conclusion:**

Endovascular repair for IIAAs is safe and effective even if the patient is on oral anticoagulants. Endoleaks including type 1 are not uncommon, however, can subside and close spontaneously with conservative treatment if aneurysmal sac did not increase in size which can be followed up successfully and reliably by Duplex scan.

*Key Words: Iliac Artery Aneurysms; Endovascular repair; Endoleak*



***Nuclear Medicine and Radiology***

*Category: Clinical*

**240**

**Computed tomography appearance of methanol intoxication. A case report and review of imaging findings.**

\*Alsarraf L<sup>1</sup>, Shaker M<sup>2</sup>, Almousawi M<sup>3</sup>

<sup>1,2</sup>Diagnostic Imaging dept, MKH, Kuwait; <sup>3</sup>Internal Medicine Dept, MKH, Kuwait

**CASE REPORT**

**Background:**

Methanol, which is an industrial solvent, is sometimes used as an alternative to beverage alcohols, especially in countries where consuming alcohol is illegal. We present a case of a young gentleman who was suspected to have methanol intoxication with CT findings to prove that.

**Case summary:**

A 33 year old gentleman was brought to the casualty department in a comatosed state. He was found unconscious at home by his brother, who stated that he had been complaining of blurred vision and behavioural changes during the past day. He also gave an additional past history of epilepsy, of doubtful medication compliance, and regular alcohol intake. No history of trauma or witnessed epileptic fit was noted. After the initial clinical examination and blood workup, an urgent CT scan was done. It showed bilateral Putamen hypodensities. In view of the clinical history provided, acute Methanol toxicity was suggested as the most likely cause for the non-hemorrhagic putamenal necrosis. Further evaluation with MRI was advised, however the patient's deteriorating condition precluded further radiological workup.

**Conclusion:**

Our aim is to describe the radiological findings associated with acute methanol toxicity, especially the role of CT in emergency diagnosis when the clinical history is not clear.

*Key Words: Methanol intoxication; Computed tomography; Putamen hypodensities*



***Nuclear Medicine and Radiology***

*Category: Clinical*

**241**

**Demonstration of the uncommon antibiotic induced Achilles' tendon rupture by three phase bone scan and PET/CT**

\*Alshammari A, Asa'ad S, Saud Alenezi

Nuclear Medicine Department, Faculty of Medicine, Kuwait University

**CASE REPORT**

**Background:**

One of the uncommon adverse effects of antibiotic administration in clinical practice is Achilles tendonitis and Achilles tendon rupture. This is a well recognized and rare adverse effect of antibiotics like fluoroquinolones.

**Case summary:**

52 year old patient received a long term course of antibiotics to treat severe episodes of pneumonia. Weeks later, he was referred to our department to confirm the MRI finding of Achilles' tendon rupture and other remote complication. In this case report we demonstrate Achilles' tendon rupture by three phase bone scan and PET/CT images.

**Conclusion:**

Three phase bone scintigraphy as well as FDG PET-CT can be used to diagnose and demonstrate the extent and local complication of Achille's tendon rupture. It may also play a role in confirming the resolution of this abnormality.

*Key Words: PET/CT; Acilles rupture; Antibiotics*



***Nuclear Medicine and Radiology***

*Category: Clinical*

**242**

**Precise localization of the uncommon transverse process fracture with SPECT/CT**

Asaad S, \*Alenezi S

Nuclear Medicine Department, Mubarak Al-Kabeer Hospital, Kuwait University

**CASE REPORT**

**Background:**

Fractures of the lumbar spinal vertebrae could occur whenever forces applied to the lower spinal column exceed the strength and stability of the vertebral column. Common injuries resulting in fractures of the lumbar spine include fall from a height, sports activities and that resulting from traffic accidents. Fractures of the transverse process is uncommon, and may result from direct blunt trauma (as in motor vehicle accidents), violent lateral flexion-extension forces or extreme sideways (lateral) bending (as in sports), avulsion of the psoas muscle or Malgaigne fractures of the pelvis.

**Case summary:**

This case study report portrays the significance of combined SPECT/CT image to evaluate transverse process fractures which can be easily overlooked. This is a case of a 36 year old of horse rider woman presented to us with a history of chronic back pain since she fell off her horse six months previously. Conventional radiograph and MRI failed to demonstrate the isolated and subtle injury at the transverse process of lumbar vertebra. Combined SPECT/CT scan clearly delineated the active lesion with fractures and sclerotic changes over both L3 & L4 transverse processes.

**Conclusion:**

SPECT/CT play a great role in the anatomical delineation of isolated active bone lesion resulting from transverse process fracture which can easily be overlooked by other conventional imaging modalities.

*Key Words: SPECT-CT; Bone Scan; Transverse process fracture*



***Nuclear Medicine and Radiology***

*Category: Clinical*

**243**

**Symptomatic vertebral artery loop: A case report and review of literature.**

\*Doweidar AA, Elsayed SB, Al-Kandery SR  
Department of Clinical Radiology, Al-Razi hospital

**CASE REPORT**

**Background:**

Vertebral artery loop formation (VALF) is a rare anatomical variant capable of causing bony erosion, widening of cervical neural canal, encroachment on cervical neural foramen, neurovascular compression, or vertebrobasilar insufficiency. This case report aims at increasing the awareness of both clinicians and radiologists of this entity as a known rare cause of cervical radiculopathy. In suspected cases, magnetic resonance angiography (MRA) is very helpful in visualization and diagnosis of VALF.

**Case summary:**

70-year-old woman presented with neck pain radiating to her left upper limb, and numbness for 1 year, was referred to our hospital with the diagnosis of cervical neural sheath tumor for possible resection, based on computed tomography (CT) scan. No neurologic deficit was revealed on clinical examination. CT showed widening of the left C5-6 intervertebral foramen and erosion of the adjacent bony structures. T1 and T2-weighted axial and sagittal magnetic resonance (MR) images showed that the previously reported suspected neural sheath tumor was nothing but a signal-void vascular structure in the left C5-6 neural canal compressing the left C6 nerve root. Another smaller vascular structure was also seen within right C4-5 neural canal. MR angiography (MRA) confirmed that both structures were representing VALF migrated into neural canals at both levels. Patient's symptoms were resolved after conservative treatment.

**Conclusion:**

Although it is a rare cause of cervical radiculopathy, clinicians should keep VALF in mind, especially when the plain radiograph of the cervical spine shows enlargement of the intervertebral foramen. If overlooked, serious complications like vertebral artery (VA) injury may occur during surgery or vertebrobasilar angiography, as well as cerebrovascular stroke during transforaminal cervical epidural steroid injections.

*Key Words: Cervical radiculopathy; Magnetic resonance angiography*



***Nuclear Medicine and Radiology***

*Category: Graduate (Resident)*

**244**

**An uncommon case of cystic mediastinal parathyroid adenoma**

\*Javaid A, Siraj QH, Al-Awadi I, Afzal U, Al-Salem Reem, Shammeri I

Department of Farwania Hospital, Kuwait

**CASE REPORT**

**Background:**

Parathyroid adenoma is the most common cause of primary hyperparathyroidism. We present a case of a functional parathyroid cyst, which is a rare entity that can also cause primary hyperparathyroidism. These cysts can be found anywhere between neck to mediastinum and hence pre-surgical localization of the functional parathyroid cysts by dual-phase MIBI scan can be extremely helpful to the surgeon. Complete surgical removal of the cyst is the treatment of choice.

**Case summary:**

A 46-year-old lady presented in the emergency department with severe abdominal pain associated with vomiting and fever. She was diagnosed as acute pancreatitis and managed conservatively. Her routine laboratory results in addition to raised WBC counts and raised CRP, also showed serum calcium raised at 4.14 (normal range: 2.2-2.6 mmol/L) and a high parathormone (PTH) level of 25.1 (normal range: 1-7.5 pmol/L). Chest x-ray demonstrated a mass in the right mediastinum and contrast-enhanced CT showed a fairly well defined mediastinal cystic lesion in right paratracheal region, measuring 5.5x4.0x3.7 cm, with marginal enhancement and fine internal septations. Bilateral pleural effusions were also visible. The patient's MIBI parathyroid scan showed a large doughnut shaped lesion in the right upper mediastinum characterized by increased uptake at the periphery, seen to be corresponding to the lesion seen on CT. Presurgical serial PTH levels showed a rising pattern with the highest value of 125.40 pmol/L. A diagnosis of bronchogenic cyst was made and video-assisted thoracoscopic surgery (VATS) performed. Excision biopsy of the lesion confirmed parathyroid adenoma. PTH level fell to 38.3 following surgery. A repeat dual-phase MIBI scan was negative.

**Conclusion:**

The functional mediastinal parathyroid cysts can be located successfully by dual-phase MIBI scan and is not only valuable in pre-surgical localization but also helps in the differential diagnosis.

*Key Words: Cystic parathyroid adenoma; Ectopic parathyroid; Mediastinal mass*



***Nuclear Medicine and Radiology***

*Category: Clinical*

**245**

**Chondroblastoma of the humerus: A unusual imaging presentation.**

\*Nouh MR, Abu Shady H, Al-Kandri SR.

El-Razi Hospital, MOH.

**CASE REPORT**

**Background:**

Chondroblastoma (CB) is an uncommon primary benign cartilage-producing neoplasm arising most often in the epiphysis of long bones. Local aggressive behavior and metaphyseal extension disfavor imaging diagnosis in adolescence in face of round cell neoplasms and atypical osteosarcomas.

**Case summary:**

A 15-year-old girl presented with limited motion of her right shoulder and insidious onset of dull aching pain dating back to more than 6 month followed by recent fullness of her right shoulder posteriorly. Imaging workup showed a sizable right humeral epi-metaphyseal lesion with fine lamellar periosteal reaction on X-ray, rarified posterior humeral cortex on CT with non-visualized chondroid matrix on either examination. MRI showed considerable adjacent glenohumeral joint effusion with undetermined curve pattern on dynamic contrast MRI study. Core-biopsy and histopathologic evaluation revealed chondroblastoma.

**Conclusion:**

This case proves that absence of chondroid matrix calcifications and metaphyseal location has not to preclude chondroblastoma diagnosis in the immature skeleton.

*Key Words: Chondroblastoma; Humeral; Metaphyseal*



***Nuclear Medicine and Radiology***

*Category: Clinical*

246

**Thoracic ectopic kidney with diaphragmatic hernia**

<sup>1</sup>Ragab O, \*<sup>1</sup>Siraj QH, <sup>2</sup>Hassan A

<sup>1</sup>Department of Nuclear Medicine, Farwania Hospital, Kuwait; <sup>2</sup>Department of Radiology, Farwania Hospital, Kuwait

**CASE REPORT**

**Background:**

Intrathoracic renal ectopia denotes either a partial or a complete protrusion of kidney above the level of the diaphragm into the posterior mediastinum. Thoracic kidney is a very rare form of renal ectopia representing less than five percent of all ectopic kidneys. Early evaluation through functional radionuclide imaging, both pre- and post surgery, helps in assessing function and location of the organs involved.

**Case summary:**

A 7-months-old boy with prenatal diagnosis of congenital diaphragmatic hernia was operated 35 days after delivery for surgical closure of left-sided congenital diaphragmatic hernia. Five months after the surgery our patient still complained of shortness of breath and repeated chest infection, then patient was referred to the nuclear medicine department for a perfusion lung scan to assess relative lung function and renal cortical scintigraphy to localize the kidney and to estimate the split renal function. The Tc-99m MAA perfusion lung scan showed severe diffuse reduction of uptake affecting the left lung with the right lung showing normal uptake. The Tc-99m DMSA confirmed the presence of the left kidney in the left hemi-thorax cavity compressing the left lung but both kidneys were seen to contribute equally to the total renal function.

**Conclusion:**

This findings reflecting the failure of the surgery to close the left diaphragmatic hernia after delivery, with persistent the ectopic left kidney in the chest, it demonstrates the physiological sequelae of the diaphragmatic hernia on the pulmonary vasculature and function, the physical location of the kidney pre- and post-surgery and the functional integrity of the ectopic kidney.

*Key Words: Intrathoracic kidney; Renal Cortical Scan; Diaphragmatic hernia*



**Obstetrics and Gynecology**

Category: Clinical

247

**Triplet pregnancy in a diabetic mother with kidney transplantation, case report and review of literature.**

\*Said T<sup>1</sup>, Mujaibel Kh<sup>2</sup>, Al-Otaibi T<sup>1</sup>, Attia H<sup>3</sup>, Halim MA<sup>1</sup>, Abo-Atiyah H<sup>1</sup>, Nair P<sup>1</sup>

<sup>1</sup>Nephrology Department, Hamed Al-Essa Organ Transplant Center, Kuwait; <sup>2</sup>Obstetric and Gynecology Department, Royal Hayat Hospital, Kuwait; <sup>3</sup> Radiology Department, Ibn Sina Hospital, Kuwait.

**CASE REPORT**

**Background:**

Triplet pregnancy carries an increased risk of both maternal and fetal complications. Reported cases of triplet pregnancy with kidney transplantation are few. Despite showing fare outcomes, they were associated with perinatal complications. Presence of diabetes in such cases worsens both fetal and maternal outcomes.

**Case summary:**

We report here a case of 31-years female patient with kidney transplantation who had her first pregnancy 5 years post transplant. Pregnancy was complicated by gestational diabetes, miscarriage and post-partum impaired glucose tolerance. She developed frank diabetes mellitus during her second pregnancy one year later and it was ended in a premature live singleton birth. Two years later, she had a triplet pregnancy after ovulation induction with clomiphene. Glycemic control was maintained using intensive insulin therapy guided by frequent home blood glucose monitoring (HbA1c was 5.8% at 22 weeks). Both gynecological and nephrological care was carried out through close outpatient follow up. Pregnancy was complicated by hypertension and mild renal dysfunction without proteinuria and ended in elective premature abdominal delivery at 32 weeks gestation. She had 3 male babies with very low birth weight (1300, 1200 and 950 g), the largest one developed sepsis and required ICU then incubator for 50 days. The other two required incubator only for 35 days. Their weights after 11 months were 10, 11 and 8 kg respectively. The mother is now normotensive with normal renal function and impaired glucose tolerance.

**Conclusion:**

Care of diabetic kidney recipients with triplet pregnancy constitutes a special challenge requiring multispecialty skilled team to insure best outcome.

*Key Words: Triplet pregnancy; Diabetes; Kidney transplantation*



**Obstetrics and Gynecology**

Category: Clinical

248

**Bilateral Luteoma of Pregnancy: Ambiguous External Genitalia**

Shalkany ZS<sup>1</sup>, Al-Sheyji W<sup>1</sup>, Al-Kandari F<sup>1</sup>, Omu A<sup>1,2</sup>

<sup>1</sup>Departments of Obstetrics and Gynaecology, Maternity Hospital; <sup>2</sup>Faculty of Medicine, Kuwait University

**CASE REPORT**

**Background:**

Ambiguous External Genitalia caused by luteoma of pregnancy is very rare. This condition was first described by Steinberg in 1962, This lesion is usually found unexpectedly at Cesarean section and regresses after parturition. The tumour develops from the ovarian stroma or its derivatives (stroma-lutein cells, theca of atresic follicles under the influence of chorionic gonadotrophins.

**Case summary:**

Mrs. T. C is a 33 years old P1+0+0+1, admitted to Maternity Hospital with Antepartum Haemorrhage and Ultrasound scan confirmed singleton, cephalic presentation, gestational age of 34 weeks and placenta praevia almost covering but 1.3cm from internal OS. Elective LSCS was done at 38 wks of gestation to deliver alive baby girl weighing 3.5 kg at birth, with apgar scores 9 at 1minute and 9 at 5 minutes, with features of ambiguous external genitalia, enlarged clitoris, fused rugose external genitalia with one opening below the clitoris. Bilateral ovarian masses highly vascular, bluish about 6x7x8 cms were observed. Fresh frozen biopsies revealed circumscribed encapsulated lesion formed by cells, cohesive with abundant eosinophilic granular cytoplasm and uniform nuclei, immuno reactive to inhibin and negative to CK and S100, features consistent with luteoma of pregnancy. Serum testosterone and 17 hydroxy progesterone were elevated. Karyotype was XX and baby was referred to the ambiguous external genitalia committee. U/S at 2 months after delivery revealed normal ovarian size and normal levels of androgens.

**Conclusion:**

We have reported bilateral luteoma of pregnancy, a rare cause of ambiguous external genitalia.

*Key Words: Ambiguous Genitalia; Luteoma; Pregnancy*



**Oncology**

Category: Clinical

249

**Intra thyroidal metastasis from breast carcinoma**

\*Bushehri A<sup>1</sup>, George T<sup>1</sup>, Abuzallouf S<sup>1</sup>, Fayaz S<sup>1</sup>, Mehany GA<sup>1</sup>, Amanguno H<sup>2</sup>

<sup>1</sup>Department of Radiation Oncology, Kuwait Cancer Control Center; <sup>2</sup>Department of Pathology, Kuwait Cancer Control Center

**CASE REPORT**

**Background:**

Metastasis to the thyroid gland is not as rare as previously believed. In both clinical and autopsy series, renal cell, breast, stomach and lung carcinomas are the most frequent sources of metastases to the thyroid. The purpose of this report is to describe a case of metastatic disease to the thyroid gland in a patient known to have breast carcinoma.

**Case summary:**

A previously healthy 55-year old woman known smoker presented with locally advanced left invasive lobular breast carcinoma, stage T4b N1 M0. Family history was non significant. Following her negative metastatic work up, she received neoadjuvant chemotherapy with partial response. She underwent left mastectomy and axillary clearance. Post-operatively, she received further 2 courses of adjuvant chemotherapy and completed a course of external beam radiotherapy. She was then placed on Tamoxifen for 5 years. Her follow ups have been regular. Five years later, she started to complain of neck pain. MRI showed a nodule in the thyroid with multiple neck nodes. Cytology confirmed the diagnosis of metastatic carcinoma in the thyroid and cervical lymph nodes.

**Conclusion:**

Thyroid gland metastasis can present many years after treatment of a distant primary tumor. The appearance of metastatic disease in the thyroid gland is a sign of poor survival because it indicates disseminated disease. FNA could confirm a clinical suspicion of metastasis to the thyroid gland accurately with low morbidity. Management of thyroid metastasis should depend on the individual situation. There is no clear consensus regarding the role of surgery in metastatic disease to the thyroid. In the absence of a randomized, prospective trial comparing surgical and nonsurgical therapies for treatment of isolated metastases to the thyroid, the true benefit of thyroidectomy is unclear.

*Key Words: Intra Thyroid; Metastasis; Breast Carcinoma*



**Pathology**

Category: Graduate (Resident)

250

**Acute abdomen and Schistosomiasis**

\*Alkandari M<sup>1</sup>, Hamza A<sup>2</sup>, Zayed M<sup>3</sup>, Junaid TA<sup>1</sup>

Department of Pathology, Mubarak Al-Kabeer Hospital<sup>1</sup>, Department of Surgery, Mubarak Al-Kabeer Hospital<sup>2</sup>; Department of Radiology, Mubarak Al-Kabeer Hospital<sup>3</sup>

**CASE REPORT**

**Background:**

Schistosomiasis is one of the most common and widespread parasitic infections worldwide particularly among certain geographical areas and populations. *Schistosoma mansoni* is one of many trematode parasites of Schistosomiasis. The majority of infected patients do not present as acute emergency but usually as a consequence of chronic infestation and the effect of inflammatory reaction to the *Schistosoma ova* in tissues and organs. We present what we believe to be a very unusual case of acute mesenteric ischaemia leading to gangrenous jejunum caused by *Schistosoma mansoni* infection.

**Case summary:**

A 27-years old Egyptian male, not known to have any previous medical history, presented to the emergency department with acute abdomen. He gave a history of 4 days deteriorating persistent abdominal pain which was associated with vomiting, constipation, and passing black stool. CT scan showed totally acutely thrombosed superior mesenteric vein. Exploration laparoscopy revealed a gangrenous small bowel loop. The procedure converted to laparotomy with resection of the diseased bowel segment. Many *Schistosoma ova* were seen within the excised ischaemic jejunum as well as thrombosis within the mesenteric vessels with adult *Schistosoma mansoni* worms nearby in the veins.

**Conclusion:**

This is a very unusual case of Schistosomiasis presenting as an acute abdomen with acute mesenteric ischaemia and gangrenous jejunum. The exact pathogenesis of *Schistosoma mansoni* worm triggering intravascular thrombosis is not fully understood. This case leaves us with a greater perception of the variety of ways that Schistosomiasis may present especially in patients from areas where *Schistosoma* is prevalent.

*Key Words: Acute abdomen; Schistosoma mansoni; Mesenteric vein thrombosis*



**Pathology**

Category: Graduate (Resident)

251

**Adenocarcinoma arising from terminal ileal duplication cyst with metastasis to liver: A case report**

\*Alrefae N<sup>1</sup>, Alsabbagh A<sup>2</sup>, Alhindal A<sup>2</sup>, Katchy K<sup>1</sup>

<sup>1</sup>Department of Pathology, Alsabab Hospital; <sup>2</sup>Department of Surgery, Alsabab Hospital

**CASE REPORT**

**Back ground:**

Duplication cysts of the gastrointestinal tract are rare congenital anomalies. Carcinoma arising within a duplication cyst and metastasis to other organs is extremely uncommon.

**Case summary:**

A 35-year-old male patient presented as an emergency case of abdominal pain and vomiting for one day duration. The abdominal pain started 25 days earlier. Otherwise, the patient has no prior medical or surgical history. CT abdomen with oral contrast showed a bilobed wall cystic mass at the terminal ileal mesentery with multiple liver nodules. A segmental ileal resection including the mesenteric mass and liver biopsy was performed. The resected small bowel measured 10.5 cm in length and 4.0 cm in diameter with a 9.0x3.5x2.8cm cystic mesenteric mass which was filled with dark brown bloody fluid.

**Conclusion:**

Histopathologic examination showed a duplication cyst with a poorly differentiated adenocarcinoma going through the wall of the mesentery. The liver biopsy had a metastatic adenocarcinoma.

*Key Words: Adenocarcinoma; Duplication cyst; Metastasis*

**Pathology***Category: Clinical***252****Epithelioid placental site trophoblastic tumor presented as postmenopausal bleeding.**\*Al-Safi R<sup>1</sup>, Al-Jassar W<sup>2</sup><sup>1</sup>Department of Laboratory Medicine, Histopathology Unit, Maternity Hospital, Kuwait; <sup>2</sup>Department of Obstetric & Gynecology, Faculty of Medicine, Kuwait University**CASE REPORT****Back ground:**

Epithelioid trophoblastic tumor represents the most recent addition to the gestational trophoblastic tumors category. Most of the patients reported in the literatures were of reproductive age group and its occurrence after menopause is extremely rare.

**Case summary:**

A 51-year-old woman presented with postmenopausal bleeding for which an endometrial tissue was obtained through dilatation and curettage. It was reported histologically as poorly differentiated endometrial carcinoma. A subsequent total abdominal hysterectomy and bilateral salpingo-oophorectomy along with pelvic lymph nodes dissection were performed. Macroscopic examination of the uterus revealed a 5x4x2cm polypoid mass filling the endometrial cavity and infiltrating the myometrium with circumscribed pushing margins. Histologically, features of epithelioid trophoblastic tumor were noted and seen as a well-circumscribed growth formed by sheets of epithelioid intermediate trophoblasts with areas of geographic necrosis. The tumor cells were immunoreactive to human placental lactogen, human chorionic gonadotropin, cytokeratin, alpha inhibin, placental alkaline phosphatase and Ki67 receptors. The immunohistochemical results confirm the trophoblastic nature of these cells and excluded other differential diagnoses such as endometrial adenocarcinoma and squamous cell carcinoma.

**Conclusion:**

Epithelioid trophoblastic tumor is an extremely rare neoplasm in postmenopausal women, which can create a diagnostic dilemma in its diagnosis on endometrial curettage material. Relevant clinical history and careful microscopic examination of the endometrial tissue along with the adjuvant use of proper and relevant immunohistochemical stains are crucial in establishing the diagnosis.

*Key Words: Postmenopausal bleeding; Epithelioid; Trophoblastic tumor*



**Pathology**

Category: Graduate (Resident)

253

**Diffuse colonic ganglioneuromatosis - A case report**

\*Al Taleb AF, Parayil SM, Madda JP

Department of Histopathology, Amiri Hospital, Kuwait

**CASE REPORT**

**Back ground:**

Intestinal ganglioneuromatosis is a rare condition that features proliferation of ganglion cells, Schwann cells and nerve fibers in the wall of the bowel. The pathogenesis remains unclear. Three forms have been recognized namely: polyploid, diffuse, and ganglioneuromatosis polyposis . It can occur as an isolated disorder or can be associated with other syndromes including MEN Iib and neurofibromatosis 1.

**Case summary:**

A 71 year-old lady presented with chronic diarrhea for few years despite medical treatment. She also reported recent onset of weight loss. CT scan showed zonal thickening of the large bowel wall, and colonoscopy revealed mild edema, diffuse erythema and focal tiny erosions. These findings were considered as suspicious for Inflammatory bowel disease. However histopathologic examination of the biopsies revealed typical features of diffuse colonic ganglioneuromatosis.

**Conclusion:**

This rare case represents a pure histopathologic diagnosis which can be missed by both imaging studies and endoscopic investigations. Such clinical presentations should warrant a meticulous histopathologic assessment for neuronal abnormalities within the bowel wall and endocrine investigations.

*Key Words: Ganglioneuromatosis; Chronic diarrhea; Colonic wall*



**Pathology**

*Category: Clinical*

**254**

**Uterine leiomyoma with peculiar skeletal muscle like and rhabdoid cells**

\*Arora R, Abou-Bakr AA, Al Bannai R  
Farwaniya hospital

**CASE REPORT**

**Background:**

Tumors with skeletal muscle differentiation (rhabdomyoma, rhabdomyosarcoma) and extra-renal rhabdoid tumors have been reported in uterus but cases of uterine leiomyoma with skeletal muscle like cells or cells resembling those of extra-renal rhabdoid tumors are rare. We describe one such case.

**Case summary:**

A total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed in a 45 year old lady for endometrial hyperplasia which revealed an incidental intramural leiomyoma on gross examination. Histopathology showed presence of rounded, polygonal, and strap cells having abundant eosinophilic cytoplasm with round to oval nuclei, some of which were eccentric in position. Intra and extracytoplasmic hyaline globules were observed, however no cross striations were seen. Immunohistochemistry confirmed smooth muscle origin (positive for desmin and h-caldesmon while negative for cytokeratin, myogenin, myoglobin, and myoD1).

**Conclusion:**

We describe clinical and pathological features of a rare phenomenon of presence of skeletal muscle like and rhabdoid cells in a uterine leiomyoma. The presence of such cells may lead to problems in differential diagnosis and appropriate recognition is important so that overly aggressive management of a benign tumor is avoided.

*Key Words: Uterus; Leiomyoma; Skeletal muscle like cells*



**Pathology**

*Category: Clinical*

**255**

**Desmoid fibromatosis with chondro-osseous metaplasia: a rare entity**

\*Arora R, Abou-Bakr AA, Ahmad MS  
Farwaniya hospital

**CASE REPORT**

**Background:**

Extra-abdominal fibromatosis is an infiltrating fibroproliferative process of deep soft tissue. Microscopically it is composed of fibrocytes, fibroblasts and myofibroblasts in a collagenous to myxoid stroma with bland nuclear morphology. Presence of metaplastic bone and cartilage is rarely seen. We describe one unique case which showed mainly myofibroblastic proliferation and extensive chondro-osseous metaplasia.

**Case summary:**

A 55 year old Indian lady presented with a large soft tissue swelling on back which was progressively increasing for the last three years. A wide local excision was performed with a clinical diagnosis of mesenchymal tumor. Grossly, hard bony areas were felt. Microscopy showed proliferating spindle to stellate cells in a fibromyxoid background with extensive chondro-osseous metaplasia. There was no significant pleomorphism, mitosis, or necrosis.

**Conclusion:**

Presence of chondro-osseous metaplasia in extra-abdominal fibromatosis is rare. It is of paramount importance to recognize this phenomenon since it can be erroneously misdiagnosed leading to serious therapeutic implications.

*Key Words: Fibromatosis; Desmoid; Metaplasia*



**Pathology**

*Category: Clinical*

**256**

**The morphological and histological pulmonary parenchymal manifestations observed in mitral annular calcification complicated with pulmonary hypertension and right atrium mural thrombus**

\*Ebrahim NK, Satar SA, Badran DS

Forensic Medicine (MOI)

**CASE REPORT**

**Background:**

Pulmonary parenchymal manifestations of mitral valve disease are the result of either pulmonary venous hypertension in mitral stenosis or abnormal regurgitant flow into pulmonary veins in mitral insufficiency.

**Case summary:**

A non Kuwaiti female, 34 years, suddenly died, beside her bed with a group of Bronchodilator drugs found beside her. On autopsy, the heart weighed: 338gms with apparently normal coronaries and dilated chambers. The mitral valve cusps were markedly thickened and deformed, with prominent fibrosis and calcification; mostly nodular. The chordae tendinae were short and thick, with hypertrophied papillary muscles. The pulmonary artery wall was markedly thickened. Both lungs were congested, with patchy firm whitish gritty areas. Microscopic examination revealed, markedly thickened mitral cusps with myxomatous changes, calcifications, mononuclear cells, including plasma cells, giant cells with neo-vascularization foci. The pulmonary artery wall showed marked thickening, myxomatous changes and marked adventitial extravasations. The right atrial wall showed: adherent mural thrombus. The lungs showed marked congestion, focal acute intraalveolar edema, foci of fibrinous matching deposits on alveolar walls, thickened interalveolar septa, with sequestered intravascular megakaryocytes, increased polymorphs and interalveolar edema, occasional mononuclear cell aggregates, thickened vasculature, with chronic congestive features (hemosiderin matching laden macrophages, plexogenic pulmonary arteriopathy, fibrous bodies, giant cells), pleural thickening with mononuclear cells reaction.

**Conclusion:**

Lung parenchymal changes are frequently seen in patients with mitral valve disease.

*Key Words: Mitral valve; Lung disease; Atrial mural thrombi*



**Pathology**

Category: Clinical

257

**Solid pseudopapillary tumor of the pancreas: An unusual presentation**

\*Mannan AASR, Waheeb SA, Amre AA, Singh NG, Nur AM

Departments of Pathology and Surgery, Al Jahra Hospital

**CASE REPORT**

**Background:**

Solid pseudopapillary tumor (SPT) is an uncommon pancreatic neoplasm that typically affects young women. Extra pancreatic SPT is extremely rare. We present a case of SPT which presented as an anterior abdominal mass.

**Case summary:**

A 32-year-old lady presented with vague upper abdominal pain for three months. On examination there was a nontender mass in the periumbilical region. CT scan revealed a well-defined solid cystic mass lesion abutting duodenum and just adherent to the anterior surface of the pancreas. There was no involvement of the pancreatic gland parenchyma. The mass was excised under general anesthesia. On macroscopy the tumor was composed of a well circumscribed globular mass measuring 10 cm in diameter. Cut surface was solid and grayish brown with areas of hemorrhage. On microscopy, the tumor showed large areas of hemorrhage and necrosis. Cellular areas exhibited both solid and pseudopapillary pattern with prominent myxoid change in the stroma. Individual cells were polygonal with abundant eosinophilic to clear cytoplasm, round to oval nuclei with fine nuclear chromatin. Immunohistochemistry showed strong expression of vimentin, CD10, CD56 and alpha 1 antitrypsin. Beta catenin immunostain showed both nuclear and cytoplasmic positivity. Stains for cytokeratin, EMA, chromogranin, calretinin, CEA and S-100 protein were negative. Based on the morphologic and immunophenotypic characteristics a diagnosis of solid pseudopapillary tumor was entertained.

**Conclusion:**

Extra pancreatic SPT is a very rare occurrence. Differentiation from neuroendocrine tumor is often difficult. A high index of suspicion and a judicious utilization of immunohistochemical markers help in establishing the diagnosis. The current case highlights the importance of recognizing SPT at unusual location considering its excellent prognosis after excision.

*Key Words: solid pseudopapillary tumor of pancreas; pancreatic endocrine tumor; beta catenin*

**Pathology***Category: Clinical***258****Fine needle aspiration cytodagnosis of a soft tissue primitive neuroectodermal tumor with preaspiration clinical and sonological diagnosis of inflammatory lymph node pathology.**\*Pathan SK<sup>1</sup>, Jaragh M<sup>1,2</sup>, Dashti HAH<sup>1</sup>, Said SS<sup>3</sup>, Agarwal L<sup>4</sup>, Das DK<sup>1,2</sup>.<sup>1</sup>Department of Cytopathology, Mubarak Al-Kabeer Hospital; <sup>2</sup>Department of Pathology, Faculty of Medicine, Kuwait University; <sup>3</sup>Department of Surgery, Jahra Hospital; <sup>4</sup>Department of Histopathology, Hussein Makki Juma Centre for Specialized Surgery, Kuwait.**CASE REPORT****Background:**

The Ewing's sarcoma (ES) family of tumors including primitive neuroectodermal tumor (PNET) involving soft tissue is extremely rare accounting for 1% of all soft tissue sarcomas. It is a heterogeneous group of malignancies thought to be derived from neural crest. It is the second most common soft tissue tumor in adolescents.

**Case summary:**

A 23 year old man was admitted to Jahra hospital with a soft tissue mass in the left axilla of 3 weeks duration. Ultrasound examination showed a soft tissue mass likely to be lymph node approximately 4X6 cm, with central area of degeneration suggestive of an inflammatory lesion. Smears showed two populations of cells, arranged in loose cohesive clusters as well as dispersed singly. The large pale cells had round to oval bland nuclei, prominent nucleoli and moderate amount of vacuolated cytoplasm. The small dark cells with scanty cytoplasm were seen intermixed with these cells. At places rosette-like structures were seen. Immunocytochemistry results showed that the tumor cells were positive for CD-99, chromogranin, vimentin and S-100 protein. These cells were negative for LCA and pan-cytokeratin. Cytological diagnosis was a malignant small round cell tumor likely to be Ewing's sarcoma/PNET. Excisional biopsy taken from the left axilla was also diagnosed as Ewing's sarcoma/ PNET.

**Conclusion:**

Fine needle aspiration cytology with immunocytological aid was of help in the diagnosis of this rare tumor, which was thought to be an inflammatory lesion by clinical and imaging studies.

*Key Words: Soft Tissue; PNET; Fine Needle Aspiration Cytology*



**Pathology**

Category: Clinical

259

**Occult Papillary Thyroid Carcinoma (PTC) with disseminated metastasis: Solution to the dilemma of multiple organs as possible primary site by Fine Needle Aspiration Cytology(FNAC) and immunocytochemistry.**

\*Sheikh ZA<sup>1</sup>, Ibrahim B<sup>1</sup>, El-Refaei N<sup>2</sup>, Al-Mousawi FA<sup>1</sup>, Behbehani N<sup>3</sup>, Das DK<sup>1,4</sup>

<sup>1</sup>Cytology Unit, Mubarak Al-Kabeer Hospital, Kuwait; <sup>2</sup>Department of Radiology, Mubarak Al Kabeer Hospital; <sup>3</sup>Department of Medicine, Faculty of Medicine, Kuwait University; <sup>4</sup>Department of Pathology, Faculty of Medicine, Kuwait University

**CASE REPORT**

**Background:**

Patients presenting with an occult primary and multiple organs metastatic disease coupled with equivocal radiological findings pose a serious challenge to the physician.

**Case summary:**

A 69- years-old non-Kuwaiti male presented in the surgical casualty of Mubarak Al Kabeer Hospital with retention of urine and shortness of breath. CT scans show bilateral multiple shadows in lungs, sclerotic lesions in lumbar vertebrae and multiple small nodular lesions in liver suggesting possible sites of primary in prostate, colon or liver. Upper and lower GIT endoscopic examination was unremarkable. Ultrasonography showed a mass at the base of the bladder. However, TRUS biopsy of prostate showed benign nodular hyperplasia. On clinical examination a swelling measuring 2X2 cm was palpable in the right cervical region. FNA revealed a metastatic poorly differentiated malignant tumor. Immunocytochemistry done on cell block preparation showed positivity for Pan CK, CK7, Vimentin, TTF1 & thyroglobulin. Whereas CK10, CK20 & calcitonin were negative. PSA was non contributory. A report of metastatic carcinoma with thyroid as most likely primary site was suggested. Later US examination of the neck showed bilateral thyroid nodules each measuring about 1-1.2 cm. FNA performed under US guidance on these nodules showed an epithelial malignancy with nuclear grooves and inclusions, which was positive for thyroglobulin. Cytodiagnosis was bilateral papillary thyroid carcinoma.

**Conclusion:**

FNA cytology aided by immunocytochemistry was of enormous help in solving the diagnostic dilemma in this interesting case with multiple suspected primary sites.

*Key Words: Papillary Carcinoma; Metastasis; Fine Needle Aspiration Cytology(FNAC)*

**Pathology***Category: Clinical***260****Twin pregnancy with a complete hydatidiform mole and surviving co-existent fetus: Report of a case**\*Singh NG<sup>1</sup>, Rifaat AA<sup>1</sup>, Mannan AASR<sup>1</sup>, Al Waheeb S<sup>1</sup>, Shahed SR<sup>2</sup><sup>1</sup>Department of Pathology, Al Jahra Hospital; <sup>2</sup> Department of Obstetrics & Gynecology, Al Jahra Hospital**CASE REPORT****Background:**

Hydatidiform mole co-existing with a fetus is an extremely rare phenomenon. Frequency rates have been reported to be between 1 in 22,000 to 100,000 pregnancies. Traditionally when a placenta displaying a live fetus and molar degeneration is seen, three possible conditions may be considered: (1) Partial molar pregnancy with triploid fetus (2) Dichorionic twin pregnancy with normal fetus and complete molar pregnancy, that is, complete hydatidiform mole and co-existent live fetus (CHMCF) and (3) Twin pregnancies, partial molar with normal fetus (46 chromosomes, 23 maternal and 23 paternal) combination, which is extremely rare. Most cases suffer severe complications such as spontaneous abortion, preterm delivery, intrauterine fetal death, bleeding, preeclampsia, persistent trophoblastic disease. Delivery of a viable normal infant from this combination is even rarer. Here we present a case of CHMCF because of its rarity.

**Case summary:**

A 27-year-old woman conceived following six cycles of ovulation induction with clomiphene citrate. Successive ultrasound examinations documented a normally growing live fetus with a normal placenta and an additional intrauterine echogenic mass with features of molar pregnancy. Follow-up serum  $\beta$ -hCG estimation and genetic amniocentesis was done. Fetus revealed normal female 46XX karyotype. The pregnancy was continued till 28th weeks. Labor was induced at 28 week gestation due to vaginal bleeding, which resulted in the delivery of a live normal female infant and two adjoining placentas. One placenta was normal and the other placenta was composed of vesicles of various sizes. Microscopic examination of the abnormal placenta documented complete hydatidiform mole.

**Conclusion:**

The prenatal diagnosis of twin pregnancy with CHMCF was based on ultrasound findings, abnormally elevated  $\beta$ -hCG levels and normal fetal karyotype (46XX). The pregnancy should be continued with close follow up to detect potential maternal and fetal complications.

*Key Words: Hydatidiform mole; Twin pregnancy; Serum  $\beta$ -hCG*



**Pediatrics**

Category: Clinical

261

**Persistent acidosis in a child with type 1 diabetes at presentation: Concomitant diagnosis of distal renal tubular acidosis**

\*Abdul-Rasoul<sup>1</sup>, Alterkait A<sup>2</sup>, Merza J<sup>2</sup>

<sup>1</sup>Faculty of Medicine, Department of Pediatrics, Kuwait University, <sup>2</sup>Department of Pediatrics, Mubarak Hospital

**CASE REPORT**

**Background:**

We present a rare case of a 7-year-old boy who was diagnosed with type 1 diabetes mellitus and type 1 distal renal tubular acidosis concomitantly.

**Case summary:**

The patient presented with history of polyuria, polydipsia and lethargy. He was found to be severely dehydrated. Initial pH value was 7.025 with bicarbonate level of 5.3 mmol/L, and serum glucose of 23 mmol/L. Despite adequate rehydration and insulin therapy (0.1U/kg/hr), he continued to have persistent metabolic acidosis with normal bicarbonate and negative urine ketones.

Other causes for acidosis were thought of, and with further inquiry, the parents revealed that the father and two other siblings are treated for renal tubular acidosis.

Our patient had urine pH of 8, serum potassium 2.9-3.7 (3.5-5.4 mmol/L), chloride 110-116 (98-110mmol/L).

The diagnosis of type 1 renal tubular acidosis was made, and the acidosis was corrected with oral sodium bicarbonate and potassium chloride. The patient was discharged on subcutaneous multiple daily insulin injections.

**Conclusion:**

This case demonstrate that not all acidosis in diabetes is due to ketoacidosis. Other causes should be considered in cases of persistent acidosis despite adequate rehydration and insulin therapy.

*Key Words: Type 1 Diabetes; Renal tubular acidosis; Ketoacidosis*



**Surgery**

Category: Graduate (Resident)

262

**Iliacus Abscess: Case report**

\*Lari A, Alkanderi I, Almuhanna Y

Farwaniya Hospital, Department of General Surgery

**CASE REPORT**

**Background:**

Iliacus abscess is a rare condition, with very few numbers of reported cases in the literature, and to be the first reported case in Kuwait. The problem is that there is little evidence in the management, and the appropriate managing team (e.g. orthopedic or general surgery).

**Case summary:**

A 58 years Indian lady, with multiple medical problems, was found to complain of right hip pain, while being in the medical side for toxic epidermal necrolysis. A decision to do magnetic resonance imaging was carried out, to rule out avascular necrosis of the femoral head, yet it showed a right-sided iliacus abscess. Incision and drainage was conducted by the general surgeon to evacuate the abscess.

**Conclusion:**

Iliacus abscess, despite being rare, is a separate entity from the other local abscesses (e.g. psoas or ilio-psoas). But like any other type of abscess, early recognition and intervention is highly crucial in this deep seated abscess, which can present with vague clinical signs and/or symptoms. In this case, we believe that the patient being immunocompromized (diabetic, on corticosteroid therapy) predisposed her to the aforementioned condition.

*Key Words: Iliacus abscess; Hip pain; Iliacus muscle*

**Surgery***Category: Clinical***263****T-cell non hodgkin lymphoma of the urinary bladder: Report of a rare case.**

\*Zahir M<sup>1</sup>, <sup>2</sup>Rifat Mannan AAS, <sup>2</sup>Al Tawheed A, <sup>3</sup>Al Adwani M, <sup>3</sup>Hagazy RM, <sup>3</sup>Al Muttairi H, <sup>2</sup>Wadah C, <sup>2</sup>Sayeh A

<sup>1</sup>Departments of Urology, Al-Jahra Hospital, Kuwait; <sup>2</sup>Pathology, Al-Jahra Hospital, Kuwait; <sup>3</sup>Radiology, Al-Jahra Hospital, Kuwait .

**CASE REPORT****Background:**

Malignant lymphoma of the urinary bladder is very rare entity. Majority of them are B-cell lymphomas. T-cell NHL of the urinary bladder is extremely rare. Here we report a case of T-cell lymphoma of the urinary bladder.

**Case summary:**

A 42-year-old man was admitted to our hospital because of intermittent painful gross haematuria /bilateral loin pain lasting for seven days. Results of his analytical studies including serum chemistry were normal except creatinine (161.0mmol/L), prostate specific antigen (PSA), and coagulation studies. A mild anaemia (haemoglobin = 11.3g/L) with a normal mean corpuscular volume was reported. An ultrasonographic study of his abdomen revealed bilateral gross hydro-uretericnephrosis with a much thickened urinary bladder wall. CT scans of abdomen and pelvis showed large circumferential growth involving the entire bladder and both ureteric orifices with internal calcification, peri-vesical infiltrations and bilateral gross hydro-uretericnephrosis. He also had enlarged iliac and para-aortic nodes with normal liver and spleen. CT Chest revealed multiple small pulmonary nodules. Bone scan reported as evidence of a photopenic defect at L1 body. Cystoscopy was performed and an irregular mass affecting his left antero-lateral wall was found. A TURBT was performed. Histopathological exam revealed a tumour composed of diffuse population of medium to large cells with high nuclear cytoplasmic ratio and a hyperchromatic nuclear chromatin. Immunohistochemistry showed strong expression of CD3 in the tumour cells and negativity for CD20 and cytokeratin. A diagnosis of T-cell non Hodgkin Lymphoma was entertained.

**Conclusion:**

The indexed case has been highlighted for its rarity and unusual histologic appearance. An ancillary technique, Immunohistochemistry was essential to arrive at the correct diagnosis with subsequent institution of appropriate management.

*Key Words: Non Hodgkin lymphoma; Urinary bladder; T cell*

***Surgery and Transplantation****Category: Clinical***264****Scrotal abscess as a rare complication of perforated appendicitis in patient with patent processus vaginalis: A case report**

\*AlOsaimi S, Eshra A, Moussa L

Department of General Surgery &amp; Urology, Al-Sabah Hospital, Kuwait

**CASE REPORT****Background:**

Abscess formation following appendectomy for perforated appendicitis is well known, it commonly occurs in potential spaces of the peritoneal cavity, such as pelvis, subphrenic and subhepatic spaces. Drainage is the ultimate treatment. Scrotum as an extension of the peritoneal cavity via patent processus vaginalis is very rarely considered as a site of abscess formation following appendectomy.

**Case summary:**

A 15 year old boy, not known to have any medical problems presented with three days history of right lower quadrant pain, repeated vomiting and fever. Abdominal examination showed tender rebound right iliac fossa, temperature was 38.2, with elevated white cell count. He was diagnosed as acute appendicitis, an open appendectomy done for perforated appendicitis. There was moderate amount of peritoneal reaction noted during the operation, mopping was done till clean before closing up. Postoperatively, antibiotics was started and the patient was gradually improving, except for a hectic high grade fever. On the third post-op day, patient developed redness, swelling and pain in his right hemiscrotum with indurated erythematous area along the right inguinal region. Doppler US examination revealed a normal testis with turbid fluid-filled right scrotum. The fluid could not be aspirated under ultrasound guidance due to thick nature. Scrotal abscess incised and drained, a patent processus vaginalis discovered and ligated. Antibiotics was continued and adjusted according to culture. The patient made uneventful recovery.

**Conclusion:**

Patients with patent processus vaginalis at initial presentation of peritonitis due to perforated appendicitis must be carefully followed in the postoperative period, if scrotal pain and swelling becomes manifest, scrotal abscess should be suspected and managed accordingly as early as possible. We present this case as a rare complication of perforated appendicitis.

Key words: Scrotal Abscess, Processus Vaginalis, Appendectomy.

*Key Words: Processus Vaginalis; Appendectomy*



***Surgery and Transplantation***

*Category: Clinical*

**265**

**Small bowel gangrene caused by looping of Meckel's diverticulum in an adult: Case report**

\*Elshafey W, Fahmy HG, Mohamed M, Al amin A, Hussein N  
Department of Surgery, Royal Commission Medical Center, YANBU

**CASE REPORT**

**Background:**

Meckel's diverticulum is the most common congenital anomaly of the small intestine. It is a result of the failed obliteration of the omphalomesenteric duct. It arises from the antimesenteric border of the terminal ileum, and typically appears as a finger like pouch about 3-6 cm long. Meckel's diverticulum is mostly a symptomatic and usually discovered as an incidental finding during laparotomy or autopsy. Painless gastrointestinal bleeding is the most common presentation in children, whereas painful inflammation or obstruction is more common in adults.

**Case summary:**

A 28 year's old male presented with sudden onset of abdominal pain for 12 hours duration associated with twice vomiting. He had no other gastrointestinal symptoms. On examination, the patient was in pain, dehydrated, tachycardic, afebrile and his blood pressure was normal. Abdomen was mildly distension with marked tenderness and rigidity mostly in its upper quadrants and his bowel sounds were sluggish, P.R. examination did not detect any bleeding. The white blood cell count was 16.7/l with left shift. The chemistry panel results were within normal limit. Plain X-ray abdomen showed prominent small bowel loop in the epigastric area and chest x-ray showed no air under diaphragm. The patient was admitted as a case acute abdomen with differential diagnosis of perforated duodenal ulcer versus acute cholecystitis. During laparotomy, long segment of small bowel was found to be gangrenous we found an eleven centimeter Meckel's diverticulum encircling the mesentery of the gangrenous bowel loops and compromising its vascular supply. About 135cm of the ileum including the Meckel's diverticulum was resected with end to end anastomosis performed.

**Conclusion:**

Meckel's diverticulum should be kept in mind as one of the differential diagnosis of an acute abdomen and surgical intervention should be done early to prevent strangulation and gangrene of the bowel

*Key Words: Gangrenous bowel; Adult; Meckel's diverticulum*



***Surgery and Transplantation***

*Category: Clinical*

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**Bizarre presentation of colonic perforation following un-noticed toothpick ingestion: Case Report**

\*Eshra A, AlOsaimi S

Department of General Surgery, AlSabah Hospital, Kuwait

**CASE REPORT**

**Background:**

An ingested foreign body often passes the gastrointestinal tract without any complications. Toothpick perforation of the gastrointestinal tract is infrequently reported, but the consequences are often serious. Toothpick injury to the gastrointestinal tract is often suspected only at the time of operation because patients rarely relate a history of swallowing toothpicks and most toothpicks are not radiopaque.

**Case summary:**

A 65 year old female known multi medical problems presented with gangrenous skin at the perianal area. This was associated with fever (38.5°C) and leucocytosis, this was diagnosed as Necrotizing Fasciitis of the perianal region and septicemia. Extensive debridement done and IV antibiotics started. Another two settings of debridement were done under general anesthesia, where more necrotic tissues excised and pus was drained, a foreign body was found deeply embedded in the wound (Toothpick). She was improving except of low grade fever. CT abdomen with contrast revealed multiple retroperitoneal pockets of fluid collection extending from subhepatic level down into the pelvis, the largest collection measuring 3.6x7.7 cm, At the same area, the collection appears to indent on the right colon with associated colonic wall thickening, however there is no evidence of fistulous tracts. Percutaneous drainage of these collections was done under CT guidance, Culture of the aspirated pus revealed ESBL producer E. Coli (the same organism which was isolated from perianal region). The follow up CT abdomen showed complete resolution of the collection, the drain was removed subsequently. TPN, adjustment of antibiotics and wound care were initiated earlier in the course of treatment, she was referred to plastic surgeon for reconstructing the raw area in perineum.

**Conclusion:**

We present this case of colonic perforation due to foreign body ingestion (Toothpick) with bizarre presentation in form of extensive necrotizing fasciitis and intraabdominal infection.

*Key Words: Colonic perforation; Toothpick ingestion; Gastrointestinal tract*



***Surgery and Transplantation***

*Category: Clinical*

267

**Laparoscopic resection of a hypoglycemia-inducing retroperitoneal fibrosarcoma.**

\*Fahmy HM, Al-Amin AT, Jallad FA

Royal Commission Medical Center, Yanbu industrial city, Kingdom of Saudi Arabia.

**CASE REPORT**

**Background:**

Retroperitoneal sarcoma represents approximately 12-15% of all sarcomas. Complete surgical resection is the only potential curative treatment modality for retroperitoneal sarcomas. The ability to completely resect a retroperitoneal sarcoma and tumour grade remain the most important predictors of local recurrence and disease-specific survival. The most likely mechanism of hypoglycemia appears to be production of an insulin like substance and increased utilization of glucose by the tumor. Laparoscopic surgery represents an alternative technique for radical resection of such tumours as a minimally invasive rather than traditional surgery. Few cases of retroperitoneal tumours resected laparoscopically were reported in the literature.

**Case Summary:**

We report a case of 53 year old Filipino gentleman presented to ER unconscious due to hypoglycemia. The patient was resuscitated with 10% dextrose, recovered and admitted for further investigations. Initial serum glucose value was 35mg% (2.0 mmol/L). We found hypokalemia (serum potassium, 2.3 mEq/L). His abdominal ultrasound and his CT scan showed the presence of a large retroperitoneal tumour (15cm×15cm×10cm). A glucose supplement was required during laparoscopic resection of the tumour. The pathological diagnosis of retroperitoneal solitary fibrous tumour was confirmed.

**Conclusion:**

Non-islet cell tumour hypoglycemia (NICTH) is one of the major causes of fasting hypoglycemia. Solitary fibrous tumours are typically benign in nature, with corresponding pathological findings, but malignant solitary fibrous tumours have frequently been reported. In summary, we report a rare case of hypoglycemia associated with retroperitoneal solitary fibrous tumour which was completely resected with minimally invasive technique. Based on the findings in this report, we think that the production of the high molecular weight form of insulin like growth factor by the tumour caused the hypoglycemia.

*Key Words: Hypoglycemia- inducing; Retroperitoneal fibrosarcoma.*



***Surgery and Transplantation***

*Category: Clinical*

**268**

**Persistent absolute neutropenia after renal transplant- Case report and review of Literature**

\*Halim MA

Hamed Alessa Organ Transplant Center

**CASE REPORT**

**Background:**

Chronic persistent neutropenia (CPN) can be congenital, cyclic or idiopathic. In renal transplant recipients CPN is almost always idiopathic. Such patients receive many bone marrow (BM) suppressant drugs (immunosuppressive drugs, antibiotics, antivirals or other drugs) and exposed to life threatening infections causing BM depression.

**Case Summary:**

A 51 years old Yemeni patient has CKD due to ADPKD, received the second unrelated renal transplant on 16/6/2010 with thymoglobulin induction and steroid avoidance protocol (mycophenolate mofetil and tacrolimus) due to history of bilateral femoral head avascular necrosis. He developed chronic diarrhea and CPN ( $\pm 500$ ) with total leucocytic count  $\pm 1500$  requiring high doses of granulocyte-colony stimulating factor ( $\pm 140$  megaunits/week). A trial of shifting MMF to sirolimus failed to improve CPN and diarrhea. BM biopsy was done on 26/8/2010 showed hypercellularity with myeloid hyperplasia due to G-CSF injections. Colonoscopy was normal but clostridium difficile toxin was positive in stool. Virology studies were negative for CMV, EBV, parvovirus B19, BKV, HHV-6, adenovirus and enterovirus. Serology was negative for ANA, anti-DNA, RF and ANCA P&C. Serum B12 and folate were normal. Diarrhea improved with metronidazole treatment, stopping MMF, shifting sirolimus back to tacrolimus and starting small dose of steroid (5mg daily) (12/1/2011). He responded well and leucocytic count improved to  $\pm 3000$  with stable graft function (12/1/2011). Repeat BM biopsy is done on 1/2/2011 after stopping G-CSF for 2weeks was normal. Slowly G-CSF injections were tapered and leucocytic count stabilized and mycophenolic could be added slowly up to a dose of 540mg BID.

**Conclusion:**

We conclude that CPN after renal transplant is a serious problem which requires high doses of G-CSF and responds to careful drug manipulations and maintenance steroid.

*Key Words: Neutropenia; Renal transplant; Bone marrow*



***Surgery and Transplantation***

*Category: Clinical*

**269**

**Rapamycin induced cast nephropathy in a renal transplant recipient: A case report**

\*Nair MP, Gheith O, Awadain WH, Al- Waheeb S, Halim M, Balaha MA, Elsayed A, Abd-el-tawab K

Department of Nephrology, Hamed Al Essa, Organ Transplant Center, Kuwait

**CASE REPORT**

**Background:**

Rapamycin is an immunosuppressive drug used to prevent rejection in organ transplantation, especially in renal transplantation. Rapamycin related cast nephropathy has been reported in the setting of delayed graft function in the early postoperative period in renal transplant recipients and in animal models with protein overload nephropathies. We report an unusual case of rapamycin induced cast nephropathy in a patient, 45 months post renal transplant.

**Case summary:**

A 13 year old Kuwaiti girl with infantile polycystic kidney disease and stage V chronic kidney disease underwent a preemptive live renal transplant in October 2006. Her immunosuppression included induction with two doses of Basiliximab and maintenance with steroids, cyclosporine and rapamycin. She had good initial graft function and continued to have stable renal function with creatinine around 120umol/L and no proteinuria. In July 2010 she presented with graft dysfunction with a rise in serum creatinine to 200umol/L. After routine investigations a renal biopsy was performed which revealed cast nephropathy with extensive intratubular casts which were negative for light chain staining. Evaluation for myeloma including serum and urine electrophoresis, urine light chains and skeletal survey failed to demonstrate any abnormalities. Rapamycin induced cast nephropathy was considered as the cause of cast nephropathy and the drug was discontinued. Her renal function steadily improved over the next few weeks and a repeat renal biopsy performed six weeks after discontinuing rapamycin revealed a much improved cast nephropathy. Her serum creatinine reached baseline value of 115umol/L and she continues to have excellent renal function till date.

**Conclusion:**

Rapamycin can induce tubular toxicity with a unique form of cast nephropathy and withdrawal of the offending drug leads to clinical and histological resolution.

*Key Words: Cast nephropathy; Renal transplantation*



***Surgery and Transplantation***

*Category: Clinical*

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**Gastric carcinoid and obesity: Association or coincidence**

\*Shakir M<sup>1</sup>, Al-Harbi O<sup>1</sup>, Al-Brahim N<sup>2</sup>

<sup>1</sup>Department of Surgery; <sup>2</sup>Department of Pathology, Farwaniya Hospital

**CASE REPORT**

**Background:**

Bariatric surgery is a prevalent procedure in Kuwait due to high incidence of obesity and co-morbidities. Upper gastrointestinal endoscopy is one of the procedures used to evaluate the patient before surgery. However, its role is questionable. The incidental findings during endoscopy are variable including inflammatory diseases, ulcers, epithelial and stromal tumors. Here in a report of two obese sisters with incidental finding of gastric carcinoids were diagnosed during pre-bariatric surgery endoscopy.

**Case summary:**

35 and 41 year old female patients presented with obesity and BMI of 40 and 46 kg/m<sup>2</sup> respectively. Both patients underwent upper gastrointestinal endoscopy as part of pre-surgical evaluation. Multiple polyps were indentified in both patients and biopsy was taken. Histological examination revealed tumors that were formed by nests of epithelial cells. The cells have eosinophilic cytoplasm and monomorphic nuclei, typical morphology of neuroendocrine tumors. Immunohistochemical stains showed strong expression of chromogranin and synaptophysin.

**Conclusions:**

1) Upper gastrointestinal endoscopy is an important procedure for pre-bariatric surgery evaluation. 2) Gastric carcinoid is a rare tumor with higher incidence among obese patients. 3) The evidence showed an association between obesity and gastric carcinoid due to abnormal feeding behavior.

*Key Words: Endoscopy; Obesity*



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