



16th HEALTH SCIENCES CENTRE POSTER CONFERENCE

HEALTH SCIENCES CENTRE
KUWAIT UNIVERSITY



May 3-5, 2011



ABSTRACT BOOK



**SIXTEENTH HEALTH SCIENCES CENTRE
POSTER CONFERENCE 2011**



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Organizing Committee

- Prof. Widad Al-Nakib, *Vice Dean for Research & Postgraduate Studies*
- Prof. Ludmil Benov, *Chairman & Coordinator, Scientific*
- Prof. Suhail Ahmad
- Prof. Yunus Luqmani
- Dr. Joseph Longenecker, *Coordinator, Printing & Information Technology*
- Dr. Maie Al-Bader
- Dr. Laila Qadan
- Dr. Ebaa Al-Ozairi
- Dr. Gursev Dhaunsi, *Coordinator, Logistics, Social & Public Relations*
- Dr. Maamoun Al-Aynati, *Coordinator, Finance*
- Dr. Arjuna Ellepola
- Dr. Mashaal Al-Mutairi
- Mr. Jassim Al-Khorafi
- Mr. Dheya HA Al-Hasan
- Ms. Amna Safar

Special Acknowledgements

- Prof. Adel K Ayad, *Dean, Faculty of Medicine*
- Prof. Fuad AM Hasan, *Former 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. Ludmil Benov, *Chairman*



Prof. Suhail Ahmad



Prof. Yunus Luqmani



Dr. Joseph Longenecker, *Coordinator, Printing & Information Technology*



Dr. Maie Al-Bader



Dr. Laila Qadan



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Dr. Maamoun Al-Aynati ,
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Dr. Arjuna Ellepola



Mr. Jassim Al-Khorafi



Mr. Dheya HA Al-Hasan



16th HSC Poster Conference 2011 Message from the Former Dean, Faculty of Medicine

Since its establishment more than 30 years ago, the Faculty of Medicine has been keen on fostering high quality biomedical research in order to meet the health needs of people in Kuwait and beyond. To celebrate the research activities of our staff, students and practicing healthcare workers, the Faculty holds the Annual Poster Conference which has become a landmark event in Kuwait University academic calendar.



With a deep sense of pride and appreciation, I would like to note that this year 218 abstracts have been accepted. It is heartening to see how closely clinicians and basic scientists are working to address, key questions regarding the epidemiology, diagnosis and treatment of common disease conditions. I am certain that this year's Poster Conference will serve as a forum for exchange of ideas and expertise leading to further collaboration of academics and practitioners in Kuwait.

We are also honoured to have Prof. Rury Holman, the Director of the University of Oxford Diabetes Trials Unit as our *keynote speaker* this year. Prof. Holman will talk about his main field of expertise: Cardiovascular outcome trials in diabetes.

I am certain that you will enjoy this year's Conference and I take this opportunity to thank Prof. Widad Al-Nakib, Vice-Dean for Research and Postgraduate Studies and Prof. Ludmil Benov, the Chairman of the Organizing Committee and their colleagues for their commitment and outstanding efforts. The Faculty is also indebted to the Kuwait University whose support has been crucial for the success of this event.

Prof. Fuad A.M. Hasan
Former Dean, Faculty of Medicine



Message from the Acting Dean Faculty of Medicine

Research activities is essential for academic excellence and future development. This forum provides a great opportunity for the advancement in knowledge, searching the literature and improving the skills of doing research.



Events like a Poster Day has become a great stimulus for staff and students to work out a high quality research presentation. This yearly scientific gathering of all contributors provides an excellent feedback and further development in research. It encourages scientific discussions and collaboration of all scientists and health care physicians in Kuwait. This reflects the high number of submitted abstracts and it is growing yearly.

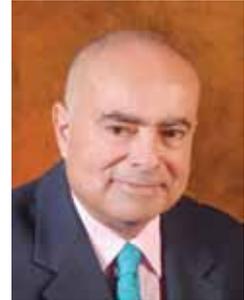
The Annual Health Sciences Poster Day is organized through the Office of the Vice-Dean for Research and Postgraduate studies. I take the opportunity to thank the Vice Dean for Research and Post graduate studies for his support of this activity. I also thank all the Organizing Committee and the Abstract Review Committee members for their great effort and commitment. This event would not have been possible without their support . A word of thanks is also for the support from Kuwait University.

Prof. Adel K. Ayed
Acting Dean, Faculty of Medicine



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

Strong research is a prerequisite for academic excellence, and this concept was clearly understood when the First Poster Day was held sixteen years ago, in April 1996, in the Faculty of Medicine. The founders of Poster Day started with a premise that scientific knowledge and therefore progress depends on investigation and critical analysis, and that exchange of ideas and information is an essential part of this continuous process. Poster Day started with an aim to stimulate communication between scientists in various health-related specialties and has grown progressively to involve diverse scientific fields in all the faculties of the Health Sciences Center (HSC).



A tradition that has received enthusiastic support is to invite internationally recognized scientists, whose work has great impact upon the Health Sciences, to give a keynote lecture. Following this tradition, we welcome Professor Rury Holman, a world renowned expert in diabetes-related mega trials who will present a lecture on “Cardiovascular Outcome Trials in Diabetes”.

I have no doubt that the 16th HSC Poster Conference will be a success and a continuation of the quest towards excellence. I am grateful to Kuwait University for continuing support and sponsorship, to Professor Rury Holman for accepting our invitation to participate as the keynote speaker in the Poster Conference and share his vast knowledge with us, and to all those who are presenting their research at this meeting. I would like to express my appreciation to the Vice President of HSC and Dean of the Faculty of Medicine, for their encouragement and support, to all HSC technical and support staff who assisted in the organization and implementation of this meeting. Success does not come without hard work and I would like to thank all members of the Organizing Committee for their commitment and efforts which have made this event possible.

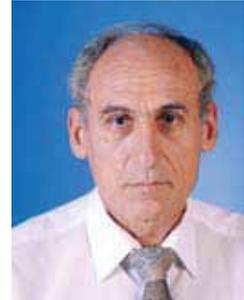
Professor Widad Al-Nakib

Vice Dean for Research and Postgraduate Studies



Message from the Chairman, 16th HSC Poster Conference Organizing Committee

On behalf of the Organizing Committee of the 16th HSC Poster Conference I would like to welcome all participants to this scientific forum. From its inception the Poster Conference became a forum for exchanging ideas, establishing collaborations and communicating scientific advancement. Started as a Poster Day, to meet the need for sharing information among basic and clinical scientists, residents, and graduate and undergraduate students, the Poster Conference progressed to become an important venue for presentation of health-related research. The Conference has received international recognition by attracting world-renowned Keynote speakers. This year we are honored to have Professor Rury Holman, Director of the Diabetes Trials Unit, University of Oxford, UK, to deliver the keynote address. I believe that the 16th HSC Poster Conference will build upon the success of the previous meetings. This year the main goal of the Organizing Committee was to raise the quality of the presentations by application of international standards, with stress on originality and scientific feasibility. To further broaden communication, winners of poster awards will have the opportunity to give a short oral presentation after the completion of the meeting.



I would like to thank the previous Dean of the Faculty of Medicine, Prof. Fuad Hasan, the current Dean, Prof. Adel Ayed, and the Vice Dean for Research and Postgraduate Studies, Prof. Widad Al-Nakib, for their confidence in the Organizing Committee and for their ongoing support and encouragement. Staging the conference is a result of close collaboration among the faculties of the Health Sciences Center and Kuwait University Administration. We are especially grateful to Kuwait University for sponsoring the meeting, and to the Administration Staff, HSC Computer Department, Photography Unit, Public Relations Office, and the members of the Judging Committee. Finally, I would like to express my gratitude to all members of the Organizing Committee of the 16th HSC Poster Conference, who worked tirelessly towards the achievement of our goals.

I am confident that 16th HSC Poster Conference will stimulate further research, will establish new collaborations, and will fuel enthusiasm for further scientific endeavor. On behalf of the Organizing Committee I wish all participants a successful, productive, and enjoyable meeting.

Prof. Ludmil Benov
Chairman, 16th HSC Poster Conference



16th Annual HSC Poster Conference 2011

Professor Rury Holman



Rury Holman is the Director of the University of Oxford Diabetes Trials Unit and the first Professor of Diabetic Medicine to be appointed at the University of Oxford. He is Honorary Consultant Physician to the Oxford Radcliffe Hospitals NHS Trust and immediate past Academic Chairman of the Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM).

Professor Holman was a joint recipient of the 1999 ADA Charles H. Best Award, the Pfizer Visiting Professor at the University of Washington in 2002, gave the 2003 Royal College of Physicians Lord Rayner Memorial Lecture, was awarded the 2006 Helmutt Mehnert/Unesco/German Diabetes UNION Award, received the 2007 Outstanding Foreign Investigator Award from the Japan Society of Diabetic Complications, gave the 2008 Ricardo Fernando Professorial Lecture, the 2008 Diabetes UK Banting Memorial Lecture and the 2009 Toronto Diabetes Association Charles H. Best Lecture.

Professor Holman divides his time between clinical care of patients, teaching and his many research interests. He has designed and run many multicentre studies that focus primarily on the prevention, appropriate treatment and cardiovascular risk reduction in type 2 diabetes, and has published over 200 peer-reviewed manuscripts. Currently he is Co-chair of NAVIGATOR, Joint Chair of TECOS and EXSCEL, and Chief Investigator of the 4-T, ACE and UKPDS trials.



Best Poster Award Winners -2010

Dr. Nael Al-Naqeeb Award for Best Undergraduate Research

- Aboqrais NA, Abahussain EA, Qaddoumi MG; Role of Pharmacists as Health Educators in Early Detection and Prevention of Breast Cancer in Kuwait.

Graduate Research in Basic Sciences (Masters)

- Nashawi H, Oriowo MA, Kombian SB; The potential of TH-9, a Theophylline Derivative, as a Memory Enhancer in Dementia.

Graduate Research for Resident Doctors

- Safar FH, Mojiminiyi OA, Al Rumaih H, Al Rammah T., Diejomaoh FME; Associations of Leptin, Leptin Receptor and Free Leptin Index with Metabolic Phenotypes of PCOS

Basic Sciences

- Renno WM, Al-Maghrebi M, George P, Mathur A; (-)-Epigallocatechin-3-Gallate (EGCG) Promotes Functional and Sensory Recovery in Crushed Rat Sciatic Nerve.
- Mustafa AS, Shaban F; Propred Analysis for Prediction of HLA-DR-Promiscuous Regions and Epitopes of Mycobacterium tuberculosis Protein Rv1980c, and their Recognition by Human T Cell Lines

Clinical Sciences

- Zahid MA, Ohaeri JU; Schizophrenia Psychopathology in a Kuwaiti Arab Sample.
- Mokaddas E, Ahmad S; Large Scale Evaluation of Multiplex PCR and DNA Sequencing of Internal Transcribed Spacer Region for Rapid Differentiation and Identification of Mycobacterium Species Isolates in Kuwait
- Akanji AO, Thalib L, Al-Isa AN; Folate, Vitamin B12 and Homocysteine Levels in Kuwait Adolescent Subjects: Potential Implications for Cardiovascular Disease Risk in Later Life.

Case Report

- AlHarbi O, AlOsaimi S, AlKandari I; Scoliosis as a Rare Risk Factor for Colon Perforation During Colonoscopy: A Case Report



Past Poster day Keynote Speakers and Lectures

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 McSMaster 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.

2005

How Corticosteroids Work in inflammatory Diseases: New Molecular Insights



Past Poster Day Keynote Speakers and Lectures, Cont.

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

1999

Nutrition, Immunity and Infection: Basic Considerations and Public Health Significance

Dr. Ranjit Kumar Chandra, Professor & Director, Allergy, Asthma and Immunology Centre, Gurgaon, India



Past Poster day Keynote Speakers and Lectures

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

*Aljazaf K, Al-Mohammed S, Al-Ajmi R, Al-Khaldi A: Energy drinks consumption and bone mineral density measurements of young healthy males in Kuwait.

2

Al-Obaidi S, *Hassan N, Nadar MS: The association of smoking with reduced grip strength: implications to hand therapy practice.

3

*Alotaibi N: The adaptation process of clients with hand injury in Kuwait: Reflections and implications.

4

*Dashti AA, Vali L, Jadaon MM, El-Shazly S, Jose B: The emergence of a multidrug-resistant Escherichia coli isolate harboring a novel SHV-122 enzyme is a serious threat for hospitalised patients.

5

*Qasem M, Khudada S, Popov C: Changes in muscle power in patients following coronary artery bypass grafting.

6

*Nadar M, Dashti M, Cherian J: Fingers position can alter the Median nerve within the Carpal Tunnel: An MRI study.

7

*Vali L, Dashti AA, Jadaon MM, El-Shazly S, Jose B: First report on the infiltration of mobile fluoroquinolone resistance genes in Kuwait.

8

*Zafar T: Sweetened whey protein beverages attenuate plasma glucose, hunger and calorie intake in young women.

Anatomy

9

*Al-Mujaibel LM, Kilarkaje N: Lead stimulates mitogen activated protein kinases in an oxidative stress-independent manner but in correlation with pathological changes.

10

*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.



Behavioral Sciences

11

*Renno WM, Al-Khalidi G, Abul H, Karam S, Mousa A, Asfar S: Systemic intravenous infusion of (-)-epigallocatechin-3-gallate (EGCG) mitigates motor and sensory deficits and attenuates central pain behavior in experimental traumatic spinal cord injury rat model.

12

Al-Sahhaf A, Abdullah J, *Al-Awadhi M, Habib M, Al-Sayed S, Jafar Y, Tadros N, Longenecker JC: Prevalence, awareness, and sources of antibiotics among ministry employees in Kuwait.

13

Rahman A, Khan KM, Al-Khaledi G, Khan I: Lead exposure during early life affects synaptogenesis in hippocampus and impairs water maze performance in young rats.

14

*Shah NM, Badr HE, Yount K, Shah M: Foreign live-in domestic workers as caretakers of older Kuwaiti men and women: Socio-demographic and health correlates.

Bioanalysis & Therapeutic Drug Monitoring

15

*Matar KM, Aziz AH, Anwar AA, Kurian S: A simple and rapid UPLC-MS/MS assay for the quantification of levetiracetam in human plasma.

Biochemistry

16

*Al-Ansari M, Benov L, Jadon MM, Craik JD: Decreased erythrocyte expression of hENT1 nucleoside transporter in G6PD deficiency.

17

*Al-Rashidi B, Narayana K, Cheng B: Adrenal Retinoid-X-receptor Beta expression and aldosterone synthesis in the rat are both sensitive to KCl-fortified drinking water.

18

*Dhaunsi GS, Dashti HM, Mathew TC, Al-Zaid NS: Induction of PPAR- γ and Catalase activities in kidneys of low-carbohydrate ketogenic diet-fed rats.

19

*Madhu D, Zamoon J: Revealing the Mechanism of RAGE action in diabetic vascular lesions.

20

*Mubarak M, Craik J, Benov L: Cellular uptake and photophysical properties of Zn (II) N-alkylpyridylporphyrins.



21

*Odeh A, Ezzidene R, Craik J, Benov L: The role of molecular charge and structure on the efficacy of photosensitizers.

22

*Thomas M, Batinic-Haberle I, Benov L: A combination of two antioxidants produces a prooxidant effect.

Community Medicine

23

*Abbas AB, Wafaa Y Al-Johar, Ali H Abu- Abbas, Seham A Al-Muftay, Fatma D El-Saidy: Energy drinks analysis at Kuwait market, scientifically safe with some cautions.

24

*Al-Awadhi N, Al-Kandari N, Al-Hassan T, Al-Murjan D, Al-Foudery S, Al-Taiar A: Age at menarche and its relationship to body mass index among adolescent girls in Kuwait.

25

Al-Basri A, AlHamoud H, *Abo Al-Hassan F, Al-Daithan A, Bouhamrah M, Al-Sabah R: Knowledge and practices of barbers in Kuwait regarding blood-borne infections.

26

Al-Halabi B, Al-Jadaa B, Yaiesh R, Bushehri S, *Mustafa Z, Bouhaimed M: Clinical guidelines and costs of diagnostic investigations: A Survey among secondary health care physicians in Kuwait.

27

Al-Hashemi AA, Jumaa AI, *Jaafar AM, Al-Khadhari A, Al-Jassar MA, Al-Taiar A: Internet use among high school students in Kuwait.

28

Al-Kandari AA, *Anbar ME, Al-Hajji FJ, Al-Qenaee AA, Alaj KF, Al-Sahhaf ZM, Bouhaimed M: Attitudes towards mental illness in Kuwait and the associated stigma.

29

*AlQaderi A, Ibrahim N, Almutairi F, AlMusabhy A, AlQadeeri A, Moussa M: Prevalence, associated factors, and disability assessment of musculoskeletal symptoms among dentists in Kuwait.

30

Al-Jazzaf L, Salem F, Mohammed F, Al-Bader S, Al-Mutairi M, Longenecker J: Self-medication with over-the-counter analgesics among Kuwait University students.

31

Al-Rayes J, Al-Dhammer S, *Askar D, Al-Mejalhem A, Shah N: Dissatisfaction with body shape and depression among working women in Kuwait.



32

Dashti A, Al-Sarraf H, *Al-Fouzan R, Al-Hassan R, Al-Ajlan S, Bouhaimed M: Knowledge and practice of road safety among Kuwait university students.

33

*Elsori D, Al-Saleh M, Al-Bader D, Al-Howell F, Abu-Albanat H, Moussa M: Knowledge and risk assessment of osteoporosis among female employees in Kuwait.

34

*Maha RA, Tasneem JA, Fatma MA, Sarah AA, Sara MA, Akhtar S: Prevalence and factors associated with sleep deprivation among nurses working in Kuwait public hospitals.

35

*Marwan Y, Behbehani A, Al-Mousawi A, Mulla-Juma'a A, Sadeq H, Shah N: Sports injuries among male athletes in Kuwait: Prevalence and associated factors.

36

*Mohammad J, Al-Saraji M, Al-Musawi F, Al-Haddad Z, Al-Sharaf D, Akhtar S: Knowledge and practice of universal precautions among Kuwait University medical students in their clinical years.

37

*Qadoura F, Baqer M, Al-Azmei K, Al-Hendi A, Al-Shammari A, Al-Sabah R: Aggression and general well-being: A comparison between Kuwait police academy cadets and Kuwait University students.

Dentistry

38

*Akpata ES, Mojiminiyi AO, Behbehani J, Akbar J, Thalib L: Urinary fluoride excretion among children in Kuwait, a non-fluoridated community.

39

*Al-Mutawa SA, Shyama M, Al-Nafisi M, Soparkar P: Prevalence of malocclusions in Kuwaiti schoolchildren.

40

*Al-Sendi M, Yousef A, Al-Khabbaz: Periodontal health attitude and knowledge among school children in Kuwait.

41

*Behbehani JM, Honkala S, Honkala E: Toothache and the other perceived symptoms by Kuwaiti adolescents.

42

*Elsalhy M, Barrieshi K, Azieh F, Raghupathy R: Immunological analysis of dental pulp inflammation.



43

*Honkala E, Runnel R, Honkala S, Olak J, Saag M, Makinen K: The changes in ICDAS codes of the schoolchildren in 2008-2009

44

*Honkala S, Behbehani MJ, Honkala E: Associations between sugar consumption and other health habits in Kuwait.

45

*Qudeimat MA, Al-Saiegh FA, AlOmari Q, Omar R: Treatment recommendations for primary molars with pulp degeneration.

46

*Shyama M, Al-Mutawa SA, Al-Nafisi M, Soparkar P: Prevalence of dental fluorosis in Kuwaiti schoolchildren in different governorates.

47

*Thomas A: Attitudes of dentists, dental hygienists and patients about dental professionals' role in smoking cessation and prevention.

Ethics

48

Al-Hader S, *Ghadanfari K, Al-Amir H, Bouhaimed M: A one day informed consent and surgical check lists audit at a secondary care hospital in Kuwait.

49

*Al-Khalifa J, Al-Abduljaleel A, Al-Eidan S, Al-Juaidi F, Al-Kandary A, Al-Safi A, Sadeq H, Jakob S, Bouhaimed M: Prevalence of child abuse among grade nine students in governmental schools in Kuwait.

50

*Haider HH, Haider R, Samhan M: Free donors are not really free.

Forensic Science

51

Al-Kandary MN, Muhammad JA, Varghese R: Patterns of accidental death in Kuwait, 2003-2009.

52

*Al-Kandary MN, Al-Mousawy A, Elfawal M, Varghese R: The value of virtual autopsy in gunshot injuries.

53

*Elfawal MA, Al-Qattan SI, Ghallab NA : Racemization of aspartic acid as a tool for age estimation.



Genetics

54

*AlEnezi KS, Nair S, Akbar A, Behbahani H, Almomin S: Optimization of DNA extraction protocol for Hamour (*Epinephelus coioides*).

55

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

56

*AlFadhli S, Nizam R: Expression of CTLA-4 splice variants in autoimmune diseases.

57

*Al-Haddad A, Al-Mulla F, Al-Ayadhy B, Francis I: The ESR1 gene amplification in breast cancer.

Medical Education

58

*Kullman L, Joseph B: The relationship between medical disorders and oral diseases.

Medicine

59

Al Otaibi T, *Gheith O, Halim M, Zakareya Z, Said T, Nampoory MRN: Impact of positive BK virus-kidney donors on renal transplant recipient outcome.

60

Al Otaibi T, *Gheith O, Nampoory MRN, Halim M, Said T, Nair MP, Balaha MA, Abd-el-tawab K, Zakareya Z, Hosni W, Mokadas E, Sawey M, Magdolina M: Legionella infection: An outbreak in organ transplant center.

61

Al Otaibi T, *Gheith O, Nampoory MRN, Halim M, Said T, Nair MP, Balaha MA, Abd-el-tawab K, Zakareya Z, Hosni w: Acute Antibody Mediated Rejection: Kuwait experience with Bortezomib.

62

*Al-Adsani AMS, Abdulla KA: Reasons for elderly patient hospitalization: The impact of diabetes and other comorbidities.

63

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



64

*Alawadhi SA, Ohaeri JU: Validity and reliability of the European Organization for Research and Treatment in Cancer Quality of Life Questionnaire (EORTC QLQ): Experience from Kuwait using a sample of women with breast cancer.

65

*Al-Hasan Y, Mathew J, Rahimi R, Al-Awadi F, Al-Dabbous T, Al-Isa A: Spirometric assessment of lung function and evaluation of respiratory symptoms among the oil industry workers of Kuwait: A comparative study.

66

Awadain W, *Alsayed Z, Osama G, Ahmed H, Nabil H, El-Deeb S, El-Agroudy A, Ashraf, Mohamed G: Steroid resistant T-cell mediated acute cellular rejection: risk factors and impact on graft and patient survival.

67

*Awadain WH, Nair MP, Nampoory MRN, Said T, Halim MA, Moneim MA, Vareed B, Geith O, Elsayed A, Al-Otaibi T: Zero-HLA mismatched renal transplants – A Single Centre Experience.

68

*Al-Shoumer KAS, Nair VS, Ali AH: Vitamin D level in Kuwaiti subjects with type 2 diabetes.

69

*Al-Shammri S, Akanji AO, Bhattacharya A, Girgis M, Singh S, Mathew R: Preliminary observations on relationship of Vit D and clinical phenotypes in Kuwaiti patients with multiple sclerosis.

70

*Abdella NA, Mojiminiyi OA, Ozairi ES, Al-Mohammed H, Pinto C, Al-Rammah T: Paradigm shift - fasting Glucose, HbA1c and estimated average glucose as screening and diagnostic tests in a high risk population.

71

*Ayman ElSayed: Plasma Leptin in kidney transplanted patients during the early post transplanted period.

72

*Elsayed A, Nampoory MRN, Nair P, Al-Otaibi T, Said T: Kidney transplantation in the elderly.

73

*Bouhaimed MM: Community eye health initiative in Kuwait: A strength, weakness, opportunities and threats (SWOT) qualitative analysis.



74

El Ghamry F, *Alboraie M, Goda M: Detection of transfusion transmitted virus (tt virus) in body fluids and secretions of Egyptian volunteer blood donors.

75

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

76

*Manee FS: Relationships between occupational roles and quality of life among Kuwaiti women living with chronic neuromuscular conditions.

77

*Hassan S, Hippolito CH, Al-Ali M: Detection of cold reactive antibodies in pregnant women and in patients who are going for surgery.

78

*Mansour HA, Akl AI, Wafa EW, Adul ELReheem M, Salem ME, El-Shahawy EE, Ghoneim MA: Post-Transplant glomerulonephritis in live-donor renal transplant recipients: Clinical course and risk factors.

79

*Nair MP, Al-Otaibi T, Nampoory MRN, Said T, Halim MA, Moneim MA, Elsayed A, Nawas KM, Vareed B, Geith O: Chronic active antibody mediated rejection (CAMR) in renal transplant recipients: Is intervention justified?

80

*Nair MP, Al-Otaibi T, Nampoory MRN, Said T, Halim MA, Vareed B, Moneim MA, Nawas KM, Elsayed A, Geith O: Renal transplantation in nephropathic cystinosis.

81

*Shehab D, Al-Jarallah K, Mugeemini S, Mohamadi H, Abdellah N: Does Vitamin D deficiency play a role in type 2 diabetic peripheral neuropathy?

Microbiology and Immunology

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Original Research Abstracts By Subject Area



Allied Health

Category: *Clinical*

1

Energy drinks consumption and bone mineral density measurements of young healthy males in Kuwait.

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Introduction:

The practice of drinking energy drinks is wide spread, especially among male college students. Previous studies have investigated a variety of physiological and psychological effects associated with energy drinks and their ingredients. Although it has been reported that various components of energy drinks could cause reduction in bone mineral density (BMD), direct studies of the effect of energy drinks on BMD are lacking. The purpose of this study is to investigate the effect of energy drinks on bone mineral density.

Methods:

44 healthy male volunteers from the Health Science centre Faculties (HSC) participated in the study. They were divided into two groups, energy drink consumers (22) and non-consumers (control group) (22). Ultrasound Bone Densitometer (Sonost) was used to measure the bone density on both heels of each participant. T-score was divided into three categories; ≥ -0.1 (normal), $-0.1 \geq T\text{-score} \geq -2.5$ (osteopenia) and < -2.5 (osteoporosis). T-score $p < 0.05$ was accepted as statistically significant.

Results:

Although the final outcome demonstrates that energy drinks have no significant effect on bone density, 4 out of 22 energy drink consumers showed low bone density according to T-score (2 osteopenia, 2 osteoporosis). Slight different was noticed in the T-score between the non-consumers and the energy drink consumers. T-score of the control group was 0.31 against 0.05 for the energy drink consumers. Otherwise, there was no statistical significant difference between the T-score of consumers and non-consumers (control group).

Conclusions:

There was no significant difference in bone mineral density between non-consumers and consumers.

Key Words: (BMD) Bone mineral density; Energy drinks; Osteoporosis

Funding Agency: None



Allied Health

Category: Clinical

2

The association of smoking with reduced grip strength: implications to hand therapy practice.

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Introduction:

Purpose: To examine whether grip strength and fatigue resistance are impaired in smokers, and to determine if smoking related impairments can be predicted by years of smoking, number of packets smoked per day, and physical activity.

Design: Nonequivalent quasi-experimental groups design

Participants: Male smokers (n=111) and non-smokers (n=66).

Methods:

Maximum isometric grip strength (MIGS) was measured before and after the fatigue challenge test with a Jamar dynamometer. The fatigue index was calculated based on the percentage change in MIGS from initial and final fatigue induced test.

Results:

Smokers demonstrated less MIGS prior to and after induced fatigue at all 5 hand positions (5HP) ($P < 0.001$) and had a higher fatigue index. The MIGS deficit was greater among smokers and peaked at positions I, IV and V. Plotting the MIGS obtained from the 5HPs displayed a bell shaped curve with its peak always at position III even after fatigue. Packets of cigarettes smoked per day and age emerged as strong predictors of MIGS ($p < 0.05$ -0.1).

Conclusions:

Smokers may be more susceptible to hand injuries specifically as a result of repetitive contractions.

Key Words: Grip Strength in smokers; Jamar Dynamometer; Fatigue

Funding Agency: None



Allied Health

Category: Clinical

3

The adaptation process of clients with hand injury in Kuwait: Reflections and implications.

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Introduction:

Hands offer us competence and independence, and a sense of autonomy (Meyer, 2003). However, injury to the hand may cause functional loss; the amount of loss will depend on the extent and severity of the injury (Gustafsson & Ahlstrom, 2004). The purposes of the study were to determine the extent to which the Arabic clients with hand injuries experienced the adaptation process and provide study implications to practice and research.

Methods:

Ten Arabic clients diagnosed with various hand conditions acted as key informants and were face to face interviewed. The transcribed semi-structured interviews were thematically analyzed using the phenomenological approach. The setting was Alrazi Orthopedic Hospital in Kuwait-Hand Unit. The inclusion criteria for the clients were Arabic clients diagnosed with only hand conditions, male and female included, and onset within three months and the age of the clients was beyond the age of 21.

Results:

The themes that emerged were: faced challenges and limitations, psychosocial manifestations, adaptive responses and facilitators of adaptive responses. The results of this study suggest that active involvement of the occupational therapist in the therapeutic process, particularly in the early stages of the diagnosis is essential for improving the client's adaptation process. The findings of the present study illuminated the process of adaptation with clients of upper extremity conditions and identified the dimensions for adaptation so that competence in occupational performance can be achieved.

Conclusions:

To the author's knowledge, this study was the first of its kind to gain a deeper understanding of the hand injury phenomenon with Arabic clients suffering from various hand conditions. The use of qualitative research studies to obtain evidence regarding clients with hand injuries was employed. Implications to occupational therapy education, practice and research were presented.

Key Words: Hand therapy; Qualitative research; Adaptation

Funding Agency: None



Allied Health

Category: Basic Sciences

4

The emergence of a multidrug-resistant *Escherichia coli* isolate harboring a novel SHV-122 enzyme is a serious threat for hospitalised patients.

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Introduction:

Recently the antibiotic resistance has increased significantly in the Middle Eastern communities and hospitals. This study was conducted to characterize a multi-drug resistant *E. coli* recovered from ascetic fluid of a haemodialysis patient who was admitted to Amiri hospital, Kuwait, suffering from advanced liver disease with portal hypertension and multiple current inter-abdominal abscesses.

Methods:

Antimicrobial susceptibility testing was determined by Vitek 2, Microscan systems and disc diffusion against a panel of 26 antimicrobial agents. The isolate was screened by PCR for the presence of: blaSHV, blaTEM, blaCTX-M, gyrA, parC, plasmid mediated qnrA, qnrB, qnrS, & class 1 integrons. Conjugation experiments were performed using our clinical isolate as a donor and *E. coli* HB101 strain as a recipient.

Results:

Phenotypic and genotypic studies confirmed the isolate identity as *E. coli*. Susceptibility testing showed the isolate was resistant to all antibiotics tested except sulfamethoxazole, trimethoprim and nitrofurantoin. E-test showed the isolate was resistant to meropenim, imipenim, ciprofloxacin, cefotaxime and ceftazidime with MIC >16 mg/l, 32 mg/l, >64 mg/l, 32 mg/l and > 32mg/l, respectively. PCR conferred the expected sizes of the amplified ESBL-genes. DNA sequencing showed that the isolate harboured TEM-1, CTX-M-15 & had a new point-mutation at amino acid 248 of the SHV gene reflecting a novel SHV-122 (GeneBank GQ290211).

Conclusions:

The detection of an *E. coli* strain highly resistant to a wide range of antimicrobial agents in Kuwait is of considerable importance. In particular, when the evidence suggests that the resistance genes are located on a transferable plasmid indicating the risk of the spread of these genes to other bacteria. Therefore, it will be to the benefit of the clinical practice and epidemiological studies if resistance genes especially the rapidly evolving β -lactamases should be identified and sequenced promptly in Kuwait.

Key Words: Multi-Drug resistant; ESBL- E.coli; Novel SHV-122

Funding Agency: GM 01/01 and GM 01/05



Allied Health

Category: Clinical

5

Changes in muscle power in patients following coronary artery bypass grafting.

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Introduction:

Coronary Artery Disease (CAD) causes a significant decline in physical capacity. Coronary Artery Bypass Grafting (CABG) is one of the major procedures utilized to alleviate the effects of cardiovascular disease. This study examines the muscle power of patients with CAD before and after CABG, and compares both readings. The objective is to determine if there is any difference in muscle power after CABG, and what kind of Physical Therapy (PT) program may be suggested to overcome the deficit in muscle power.

Methods:

The study included 10 participants: 7 right hand and leg dominant and 3 left hand and leg dominant volunteers with Ischemic Heart Disease scheduled for CABG with mean Age fifty years old, average eighty kilogram, Body mass index average twenty eight. Hand Grip and Leg Strength of the participants were measured prospectively by using a Jamar dynamometer and Martin Vigorimeter preoperatively, third day post, and seventh day post surgery. Physical Therapy Program follows ICU Protocol. Vital signs are monitored.

Results:

Data show that muscle power decreases in patients post CABG especially on third Post Operated Day (POD). It was recorded that the biggest loss in muscle power for upper limbs and lower limbs was: Right Hand= -7.66 % in third P.O.D and Left hand muscle power decreased to -6.3 %. The lower limbs showed higher loss in muscle power also on third POD in which the Right Leg was dominant & affected, the Right Leg= -12.3% while the loss in muscle power for Left leg= -9.4.00%. Oxygen saturation shows no changes, but on third POD all patients have support 3-5 Liter O₂.

Conclusions:

The results has shown reduced muscle power after CABG especially in the lower limbs. Standard PT Program is sufficient to improve Muscle Power. The study need to be repeated on larger sample.

Key Words: CABG; Muscle Power; Physical therapy

Funding Agency: None



Allied Health

Category: Graduate PhD (Basic Science)

6

**Fingers position can alter the Median nerve within the Carpal Tunnel:
An MRI study.**

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²Radiography Department, AlSabah Hospital, Kuwait

Introduction:

Fingers position has been suggested to contribute to the etiology of Carpal Tunnel Syndrome. The purpose of this study was to measure the immediate effects of fingers position on the properties of the carpal tunnel area and the median nerve.

Methods:

34 volunteers participated in the study. The measurements were taken at the level of hook of hamate using A 2D axial section on a 3T MRI scanner. The boundaries of the median nerve were manually traced by using the tools available within the MRI system software. The flexor retinaculum displacement was measured by calculating the perpendicular distance from the linear line between the hook of hamate and trapezium tubercle to the highest point of the median nerve transverse carpal ligament junction. The pressure angle of the median nerve within the carpal tunnel was measured by connecting the end of the perpendicular line (which measures the flexor retinaculum displacement) and the beginning of the trapezium tubercle - hook of hamate strait line.

Results:

When compared to full finger extension, forceful finger flexion resulted in significant alterations within the carpal tunnel and the median nerve. The analyses revealed a significant decrease in Median Nerve Area ($p < .001$), an increase in flexor retinaculum displacement toward the volar aspect of the wrist ($p < .001$), and a flattening ration of the median nerve ($p < .002$). The shift in the pressure angle of the median nerve was not significant ($p > .05$).

Conclusions:

Finger flexion altered the shape and properties of the carpal tunnel area and the median nerve, indicating contribute to median nerve compression. Hand therapists are recommended to immobilize the whole hand and prevent fingers from flexion to allow better healing of median nerve in Carpal Tunnel Syndrome patients

Key Words: Median nerve; Carpal Tunnel Syndrome; MRI

Funding Agency: None



Allied Health

Category: Basic Sciences

7

First report on the infiltration of mobile fluoroquinolone resistance genes in Kuwait.

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Introduction:

Therapeutic options for the Extended Spectrum Beta-Lactamase (ESBL)-mediated multiple antibiotic resistant Enterobacteriaceae are limited. Preserving the efficacy of fluoroquinolones (FQ) is essential to reduce the dependence on carbapenem therapy. The purpose of the present study is to determine the prevalence of plasmid-mediated FQ resistance in ESBL-producing Enterobacteriaceae from urinary tract infections in Kuwait.

Methods:

50 quinolone and cephalosporin resistant strains of Enterobacteriaceae were selected from UTI patients from Ahmadi hospital from August to November 2010; consisting of 31 *Escherichia coli*, 11 *Klebsiella pneumoniae*, 5 *Proteus mirabilis* and 3 *Enterobacter cloacae*. Antimicrobial susceptibility testing was determined by Vitek 2, Microscan, disc diffusion and E-test. Isolates resistant to ciprofloxacin and for which the ceftaxidime or cefotaxime MICs were $>8\text{mg/L}$ were screened for ESBLs and *qnr* genes. The isolates were screened by PCR for the presence of *bla*SHV, *bla*TEM, *bla*CTX-M, *gyrA*, *parC*, *qnrA*, *qnrB* & *qnrS*. Pulsed-field gel electrophoresis was used for phylogenetic typing.

Results:

All 50 isolates were resistant to ciprofloxacin MIC >2 , tazobactam MIC >8 , Cefotaxime MIC >8 & ceftazidime MIC >8 . All *E.coli* isolates contained one or more *bla*-genes, but plasmid mediated *qnr* was not detected. The 3 *E. cloacae* isolates harboured minimum one *bla* gene. One isolate carried *bla*SHV, *bla*TEM & *qnrA*. Four *P.mirabilis* harboured minimum one *bla* gene and one isolate also contained *qnrA*. All *K.pneumoniae* contained *gyrA* with at least one ESBL gene. One isolate harboured *bla*SHV, TEM, CTX-M & *gyrA* & *qnrA*. PFGE revealed clonality among profiles of *E.coli* and among *K. pneumoniae* isolates harbouring similar ESBL genes.

Conclusions:

In this study, we have demonstrated the infiltration of mobile FQ resistance genes in Kuwait. The dissemination of *qnrA* gene among ESBL producing UTI isolates raises concern and should be monitored closely to control infections.

Key Words: ESBL; Quinolone and cephalosporin resistant; gyrA & qnrA genes

Funding Agency: GM 01/01 and GM 01/05



Allied Health

Category: Clinical

8

Sweetened whey protein beverages attenuate plasma glucose, hunger and calorie intake in young women.

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Introduction:

The high prevalence of diabetes and obesity calls for food-based prevention. As a functional food component, whey protein has a potential to reduce the blood glucose spike and regulate body weight by providing satiety signals. Sweetened beverages are popular and may prove an effective vehicle for delivering whey protein for consumption. However, whey protein is insulinotropic and when mixed with sugars may excessively reduce blood glucose. Aims: The current study was designed to investigate the effect of whey-glucose mixed drinks relative to glucose or whey alone on a) glycemic response, b) appetite response and c) calorie intake.

Methods:

Test beverages were given randomly once a week after an overnight fast as 50g or 75g glucose, 25g whey protein or 25g whey protein mixed with 50g glucose. Blood glucose and appetite were measured simultaneously at 0, 15, 30, 45, 60, 90, 120, 150 and 180 min by a portable glucometer and visual analogue questionnaires. Pizza was served at 180 min. Calories consumed from the pizza were calculated.

Results:

The blood glucose incremental area under the curve showed almost 50% reduction after the whey-glucose mixed drink compared to pure glucose drinks. Calorie intake was reduced after both whey protein drinks with or without glucose. The change from baseline blood glucose was associated with reduced appetite and calorie intake.

Conclusions:

In young women, whey protein drinks prevented excessive fluctuation in blood glucose response and suppressed appetite and calorie intake.

Key Words: Whey protein; Body weight; Appetite

Funding Agency: Kuwait University research grant WF02/09.



Anatomy

Category: Graduate MSc (Basic Science)

9

Lead stimulates mitogen activated protein kinases in an oxidative stress-independent manner but in correlation with pathological changes

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Introduction:

Lead, an environmental toxicant, is known to affect several organ systems. The present study was designed to investigate the effects of lead on oxidative stress, structural changes, cell death and mitogen activated protein kinases (MAPKs) in the liver.

Methods:

Adult Wistar rats (13-15-week-old; N=8/group) were exposed to 0.5% and 1% lead acetate and the livers were collected on day 36. The oxidative stress was assessed by total antioxidant status (TAS) and lipid peroxidation. The structural changes were evaluated by light and electron microscopy; cell death was quantified by the TUNEL assay and p38 α / β , JNK and ERK α / β were evaluated by Western blotting and immunofluorescence. Data were analyzed by one way ANOVA and Dunnett's T3 test.

Results:

Five week-long exposure to lead did not alter TAS and lipid peroxidation ($p > 0.05$). However, lead induced structural changes and affected the organelles. In addition, lead also induced DNA damage characteristic of both apoptosis and necrosis. The proteins- ERK α / β and JNK were down-regulated whereas p38 was up-regulated at 0.5% dose-level and all three proteins were up-regulated in 1% dose-level ($p < 0.05$). All the proteins were localized to cytoplasm of hepatocytes.

Conclusions:

Lead does not induce oxidative stress but initiates DNA damage and structural changes, and enhances MAPKs activities in the liver. Lead-induced hepatotoxicity is mediated by altered MAPKs indicating the coexistence of cell proliferation and death.

Key Words: Hepatocytes; Oxidative stress; Kinases

Funding Agency: College of Graduate Studies & Research Administration YS05/09 and GM01/01 & GM01/05



Anatomy

Category: Basic Sciences

10

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

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Introduction:

(-)-Epigallocatechin gallate (EGCG) has been reported to have neuroprotective and neuroregenerative role in the nervous system. Previously, we have shown functional and neurobehavioral improvements after chronic constrictive and sciatic nerve crush injuries. This study was designed to examine whether EGCG could improve survival of spinal neurons and restore the subcellular morphology of the sciatic nerve in sciatic nerve crush model.

Methods:

Adult male Wistar rats (n=8) were randomly assigned to: (i) Sham control (SC), (ii) Sciatic nerve crush+Saline (SNC+S) and (iii) Sciatic nerve crush+EGCG (SNC+EGCG) groups. In SNC+S and SNC+EGCG groups, sciatic nerve was exposed and crushed with forceps for 60s and treated with saline (i.p) or EGCG (50mg/kg) respectively for two weeks. Lumbosacral spinal cord (LSC) and nerve segments distal to crush were harvested, processed for light and electron microscopy (EM).

Results:

Ventral grey horn (VGH) of LSC showed irregular, darkly stained neurons and substantial reduction in number of neurons ipsilateral to the crush injury in SNC+S group. Such degenerative changes were not seen in SNC+EGCG group. Contralateral side of SNC+EGCG group was comparable to contralateral side of SNC+S and SC groups. Morphometric analysis of sciatic nerve in SNC+S group showed significant increase in the number of myelinated fibers compared to SC group. EGCG treatment significantly decreased the number of myelinated axons compared to SNC+S. EM revealed normal appearance of regenerated fibers, normal thickness of myelin sheaths and axons in SNC+EGCG group. The axons in EGCG treated group also had normal Schmidt-Lantermann clefts. The extracellular matrix was comparable to normal collagen fibers with well-organized distribution and absence of disintegrated myelin figures.

Conclusions:

EGCG protects spinal neurons and enhances subcellular recovery subsequent to peripheral nerve injury and thus improves nerve regeneration.

Key Words: EGCG; sciatic crush injury; spinal cord

Funding Agency: Department of Anatomy, Faculty of Medicine, Kuwait University



Behavioral Sciences

Category: Basic Sciences

11

Systemic intravenous infusion of (-)-epigallocatechin-3-gallate (EGCG) mitigates motor and sensory deficits and attenuates central pain behavior in experimental traumatic spinal cord injury rat model

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Introduction:

Spinal cord injury (SCI) causes severe and long lasting morbidity in humans. Up-to-date, there is no successful treatment for any of the main types of dysfunction following SCI, including motor and sensory deficits, chronic pain, and autonomic dysreflexia. This double blind study designed with the aim of assessing behavioral outcomes following intravenous (i.v.) infusion of EGCG in acute and chronic SCI rats.

Methods:

48 SD F rats grouped as follows: (I) Sham: T9 -T10 laminectomy, preserving intact dura with no injury to the SC, n=12. (II) Drug infusion, initiated within the first 4 hours post SCI, n=24, subdivided further to: n=12 continuous i.v. infusion for 36 h, and n=12 i.v. infusion 1h/day for 3 days. (III) Infusion initiated at 1 year post SCI, n=12. Flow rate 20 mg/kg/h delivered by a Harvard twin Syringe Pump. 1wk prior to drug infusion, animals were cannulated through the jugular vein. The label of the drugs EGCG and vehicle were cloaked from the surgeon and coded. A very well characterized, standard mid-thoracic T9 moderate SCI was inflicted using the MASCIS Impactor. Two SCI animals were picked for either A or B drug by flipping a coin. Two independent investigators blind to the animal groups conducted the behavioral tests. Standard battery of Motor function tests: BBB open field scale and the Louisville swim test. Sensory tests: Von Frey, paw pressure, hot plate, and tail flick. Tests commenced 1 wk after infusion cessation, every week for 6 weeks, one test a day.

Results:

EGCG 36 h infusion significantly improved motor function, in both acute and chronic SCI: BBB 17 ± 0.23 $p < 0.001$, Swim test 12 ± 1.212 , $p < 0.005$. Central pain concomitant with chronic SCI tactile allodynia and mechanical hyperalgesia were significantly attenuated by EGCG infusion after 1 year of SCI onset.

Conclusions:

Our results provide evidence that EGCG i.v. infusion for 36 h, depicts substantial beneficial behavioral outcomes compared to vehicle treated SCI rats.

Key Words: SCI; EGCG i.v. infusion; double blind study

Funding Agency: This work was supported by Kuwait University, Research Grant No. [MA01/08].



Behavioral Sciences

Category: Undergraduate

12

Prevalence, awareness, and sources of antibiotics among ministry employees in Kuwait

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Introduction:

Antibiotic misuse has become a significant problem in Kuwait. This research aims to measure the prevalence and the associated factors of antibiotic use among Kuwaiti government workers during the most recent common cold and the past 3 months. Also, the knowledge, attitudes and perceptions regarding antibiotic are investigated, as well as the source of acquiring them.

Methods:

This cross-sectional study enrolled 477 employees at the Kuwait government ministry complexes, using a stratified random cluster sampling method. Three ministries were selected: The Ministry of Energy, Ministry of Industry, and the northern Ministry Complex building. The response rate was 85.2%. Data collection was done by a self-administered, standardized questionnaire comprising of 45 questions.

Results:

Over half of respondents used antibiotics in their last common cold and during the past three months. The most common reason for using antibiotics in the last three month was common cold (60.4%). Among those who used antibiotics to treat their last common cold, 53.3% stopped the antibiotics when symptoms subsided, and 93.1% considered them effective as treatment for their cold symptoms. More than half thought antibiotics are overused in Kuwait and answered that misuse of antibiotics can render them ineffective in the future. Antibiotic use was not associated with sociodemographic characteristics, but was associated with cough, fever, believing that antibiotics are required for cold symptoms or body aches, and willingness to pay for antibiotics for a common cold.

Conclusions:

Although most participants responded that antibiotics are overused in Kuwait, a large percentage takes antibiotics inappropriately for the common cold. Education and enforcement of current laws and guidelines should be directed at doctors and pharmacists. Health promotion efforts to reduce inappropriate antibiotic use should be implemented among the general population.

Key Words: Antibiotics; Misuse; Kuwait

Funding Agency: None



Behavioral Sciences

Category: Basic Sciences

13

Lead exposure during early life affects synaptogenesis in hippocampus and impairs water maze performance in young rats

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Introduction:

Lead is a persistent environmental toxin that affects developing brain and lead toxicity is linked with impairment of cognitive and behavioral development. Lead preferentially accumulates in hippocampus, an area associated with learning and memory. We tested the hypothesis that chronic exposure to low level of lead (Pb) during early life alters synaptogenesis in the CA3 region of hippocampus of young rats that leads to impaired learning and memory.

Methods:

Wistar rats pups (n=10) were exposed to 0.2% Pb-acetate via their dams' drinking water from postnatal day (PND) 1 to 21 and directly via drinking water from weaning until PND 30. The control group (n=10) was given regular water. Pb in blood and brain tissues of was measured by atomic absorption spectrophotometer. Synapses were counted in electron micrographs of the CA3 region of hippocampus. Spatial learning and memory was tested by Morris water maze test.

Results:

Mean values of Pb in blood, brain and hippocampus in Pb-exposed group were significantly ($p < 0.05$) higher than in control animals at PND21 and PND30. Hippocampus had significantly higher levels of Pb compared to the brain. Pb-exposed rats had significantly lower number of synapses in the molecular layer of hippocampus compared to control animals ($p < 0.01$). Pb-exposed rats learned slower than controls. Short term memory was largely unaffected by Pb, whereas, it significantly affected long-term memory.

Conclusions:

These data suggest that Pb preferentially accumulates in hippocampus that leads to a significant reduction in the number of synapses in the molecular layer of CA3 region. Higher accumulation of Pb and decreased number of synapses in the hippocampus appears to be the cause of the observed impairment of learning and memory in the Pb-exposed rats.

Key Words: Hippocampus; Synaptogenesis; Lead toxicity

Funding Agency: Kuwait University Grant No. WF01/07



Behavioral Sciences

Category: Basic Sciences

14

Foreign live-in domestic workers as caretakers of older Kuwaiti men and women: socio-demographic and health correlates

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Introduction:

Aging of the population is posing new challenges for caretakers, with live-in domestic workers playing an increasing role worldwide, and in Kuwait. This paper aims to: (I) examine the age and gender differences in care provided by domestic workers vs. various family members in the performance of activities of daily living (ADL), and during illness; (ii) assess the socio-demographic correlates of care during illness by a domestic worker vs. a family member; (iii) examine self-reported physical, functional, and psychological health status in relation to care by a domestic worker rather than a family member.

Methods:

A cross-sectional survey of Kuwaiti households was conducted during April 2005 to December 2006, in which 2487 Kuwaiti nationals aged 50 years or older were interviewed. This paper focuses primarily on persons aged 70 or more.

Results:

We found that among respondents needing assistance with ADL, 28 % men and 58 % women received such care from a domestic worker. During illness, 14 % men and 51 % women were usually looked after by a domestic worker. Logistic regression indicated that care by a domestic worker was about 7 times more likely for women than men, about 10.8 times more likely for those with no co-resident children compared with ones who had 3 or more co-resident children, and 44% less likely for the poorest compared with the richest persons.

Conclusions:

Respondents who were looked after during illness by a domestic worker ranked poorer on several health indicators and reported higher depressive symptoms score than ones looked after by a family member. It appears that reliance on domestic workers will increase with continued aging particularly among older women, as well as those suffering from relatively poorer self-reported and psychological health. Such reliance will be necessary in the absence of alternative institutional arrangements that may be culturally acceptable.

Key Words: Live-in domestic helpers; Older population; Caretaker

Funding Agency: (Grant No. KFAS 2003-1302-02)



Bioanalysis & Therapeutic Drug Monitoring

Category: Clinical

15

A simple and rapid UPLC-MS/MS assay for the quantification of levetiracetam in human plasma

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Introduction:

Levetiracetam (LEV) is a novel antiepileptic drug that is structurally unrelated to any of the existing antiepileptic drugs (AEDs). It is indicated as adjunctive therapy in the treatment of partial seizures, with or without secondary generalization refractory to other established first line AEDs.

The objective of this report was to describe a simple, rapid, and validated method for the quantification of LEV in human plasma using ultra performance liquid chromatography with tandem mass spectrometric detection (UPLC-MS/MS).

Methods:

Liquid liquid extraction (LLE) with dichloromethane was used to extract LEV and the internal standard (2,4-Diamino-6-(4-methoxyphenyl)-1,3,5-triazine, IS) from human plasma samples. Chromatographic separation was achieved using Acquity UPLC BEH C18 column with Vanguard precolumn. The mobile phase consisted of methanol:ammonium acetate:acetic acid (97:3:0.1 v/v/v) at a flow rate of 0.3 ml/min. The method used ESI+ ion mode and multiple reaction monitoring (MRM) for quantification. The quantification was achieved using linear regression of peak area ratio using Masslynx V4.1 software.

Results:

Calibration curve was linear over a range of 0.5 – 100 µg/ml ($r > 0.99$) with 0.5 µg/ml as lower limit of quantification (LLOQ). Intra- and inter-run accuracy and precision were both < 15%. Stability tests demonstrated that LEV is stable under various storage conditions. This method showed satisfactory results for all validation parameters and proved to be specific, sensitive, selective, reproducible and cost effective.

Conclusions:

The described method is validated and standardized to measure LEV in plasma of patients receiving this drug. It is being assessed on monthly basis by an external quality control (EQC) scheme and found to compare well with the consensus mean of different participating centers. This method is suitable and is being used for the therapeutic drug monitoring (TDM) of LEV in our TDM laboratory.

Key Words: UPLC-MS/MS; Levetiracetam; Plasma

Funding Agency: None



Biochemistry

Category: Graduate MSc: Basic Science

16

Decreased erythrocyte expression of hENT1 nucleoside transporter in G6PD deficiency

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Introduction:

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked disorder that can cause hemolytic anemia. It is the most prevalent inherited enzyme deficiency worldwide and is one of the most common hematologic disorders in Kuwait and the Middle East. G6PD catalyses the first rate-limiting step in the pentose phosphate pathway (PPP) that produces NADPH, which acts by reducing glutathione, an important component that protect RBCs from oxidative damage. Deficiency of G6PDH puts patients at risk of haemolytic episodes in response to certain foods, pharmaceuticals and infections. Pathologies associated with G6PD are variable, suggesting that additional factors may contribute to clinical responses.

The project aim was to investigate membrane changes that might contribute to red cell pathology in G6PD deficiency.

Methods:

SDS-PAGE and immunoblotting techniques were applied to samples from G6PD deficient individuals and normal controls; statistical analysis was undertaken using SPSS.

Results:

SDS-PAGE demonstrated no major differences in membrane protein profile. However, immunoblot analysis showed marked decrease in hENT-1 nucleoside transporter expression (mean 51.5%, 95%CI 41.2-61.9%, n=14 p<0.001 vs controls n=8) while expression of glucose transporter (GLUT-1) and anion exchanger AE-1 ('Band III') polypeptides showed no significant changes (mean 106.9%, 95%CI 96.7-117.1%, p=0.308, mean 100.1%, 95%CI 97.2-102.8%, p=0.329 respectively) .

Conclusions:

We believe that this is the first demonstration of reduced expression of a membrane nutrient transporter in G6PDH deficiency. The discovery that many G6PD deficient patients have substantially lower hENT1 expression suggests that this could be an additional factor that should be considered in the assessment and treatment of G6PD deficient patients.

Key Words: G6PD deficiency; Membrane transporters; Erythrocytes

Funding Agency: Kuwait University, YM15/09



Biochemistry

Category: Graduate MSc (Basic Science)

17

Adrenal Retinoid-X-receptor Beta expression and aldosterone synthesis in the rat are both sensitive to KCl-fortified drinking water

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Introduction:

Retinoid X receptor (RXR) is a nuclear receptor expressed in three isoforms, alpha, beta, and gamma. RXR-beta plays a role in controlling expression of ATP-binding cassette transporter that regulates cholesterol homeostasis of the cell. Immunohistochemical studies revealed that in the adrenal gland, RXR-beta is specifically expressed in the aldosterone-producing zona glomerulosa (ZG). This study was aimed to correlate adrenal expression of RXR-beta with aldosterone synthesis in the rat maintained with KCl-fortified drinking water.

Methods:

Adult Wistar rats were divided into four groups provided with drinking water containing 0 (control), 4, 8 or 12% KCl (w/v) for four days. Plasma potassium (K) was determined by atomic absorption spectroscopy. Urinary aldosterone was measured by immunoassay. Adrenal glands were harvested for immunolabeling of RXR-beta, and a ZG marker aldosterone synthase (AS). RXR-beta protein levels were analyzed by Western blotting. Student's t-test was used for statistical analysis.

Results:

Immunohistochemical studies confirmed that both adrenal AS and RXR-beta were localized in the ZG. Increased KCl to 4% caused elevations in plasma K content ($P < 0.02$), urinary aldosterone content ($P < 0.02$) and adrenal RXR-beta protein level (1.7 fold). In parallel, ZG showed hypertrophy with markedly increased immunolabeling of AS and RXR-beta. However, further increases of KCl to 8% and 12% resulted in reductions of RXR-beta protein levels, urinary aldosterone contents, and immunolabeling of both RXR-beta and AS.

Conclusions:

Both aldosterone synthesis and adrenal expression of RXR-beta and AS are sensitive to altered K concentrations in the circulation, suggesting that RXR-beta is involved in regulation of mineralocorticoid synthesis in the rat. Since RXR agonists are currently contemplated as therapeutic agents to treat type-II diabetes, the present finding may serve as an important reference for the strategy.

Key Words: RXR; Aldosterone; Type-II diabetes

Funding Agency: College of Graduate Studies



Biochemistry

Category: Basic Sciences

18

Induction of PPAR- γ and Catalase activities in kidneys of low-carbohydrate ketogenic diet-fed rats

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Introduction:

Peroxisome proliferator activated receptor (PPAR)- γ and catalase are now known to play a significant role in pathophysiology of various diseases such as diabetes, cancer and atherosclerosis. Besides its use for treatment of seizures and epilepsy, ketogenic diet has also been shown to exert beneficial effects in conditions such as obesity and diabetes. In this study, we have examined the long-term effects of ketogenic diet on key peroxisomal enzyme activities and PPAR- γ in rat kidney.

Methods:

Following treatment of rats with ketogenic diet for 12-18months, kidneys were removed. A portion of the renal tissue was frozen for molecular studies whereas the remaining tissue was homogenized in isotonic sucrose buffer for assay of peroxisomal enzymes, catalase and Acyl CoA oxidase. Levels of PPAR- γ were measured using Western blot analysis and Polymerase Chain Reaction (PCR).

Results:

Activity of key peroxisomal enzyme, catalase was significantly increased ($p < 0.01$) in kidneys of rats treated with ketogenic diet for 12 months or 18 months. Western blot analysis revealed that levels of catalase protein were also markedly elevated in kidneys following treatment with ketogenic diet. However ketogenic diet did not have any significant effect on the activity of renal acyl-CoA oxidase, another key peroxisomal enzyme. PCR studies as well as Western blot analysis revealed that ketogenic diet treatment for 12 months or 18 months markedly induced the gene expression of PPAR- γ in rat kidneys as levels of both PPAR-mRNA as well as PPAR-protein were significantly ($p < 0.01$) increased.

Conclusions:

An activation in the activity of catalase, an antioxidant enzyme and induction in the gene expression of PPAR- γ , a nuclear transcription factor associated with anti-inflammatory effects, by low carbohydrate ketogenic diet as observed in this study provide a new insight into the molecular mechanisms of the beneficial effects of ketogenic diet.

Key Words: PPAR- γ ; Catalase; Ketogenic Diet

Funding Agency: None



Biochemistry

Category: Basic Sciences

19

Revealing the Mechanism of RAGE action in diabetic vascular lesions

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Introduction:

RAGE (Receptor for Advanced Glycation End products) is a transmembrane protein belonging to the Ig superfamily. It plays a central role in inflammatory diseases, and its malfunction has been directly linked to vascular injury in diabetes. Our long-term objective is to decipher the three dimensional structure of RAGE at atomic resolution using nuclear magnetic resonance spectroscopy (NMR). This should facilitate understanding its biological mechanism of action.

Methods:

We have used molecular biology tools, such as LIC (ligation independent cloning), to construct various expression plasmids for two isoforms of RAGE in the vector pmcsg9. We focused on the transmembrane domain and the cytosolic signalling portions of the RAGE molecule, as they have not been previously characterized. We made fourteen different constructs of RAGE, each of which we confirmed by restriction digestions and DNA sequencing. We also have completed test expressions of these constructs in various E.coli strains, in order to produce recombinant forms of RAGE for biophysical analysis. Lastly, we have performed small scale purification trials of the recombinant RAGE constructs. We analyzed the pure proteins by mass spectrometry and NMR.

Results:

For each construct, the optimum E.coli strain giving the highest yield of recombinantly expressed RAGE was determined. Then, protein purification trials were optimized using affinity purification (IMAC), followed by cleavage with TEV protease, and finally FPLC size exclusion chromatography. The RAGE constructs showing the expected mass, as determined by MALDI TOF/TOF were selected and further screened for optimum NMR conditions.

Conclusions:

Our efforts at the level of molecular biology, protein chemistry and NMR screening have revealed which of our RAGE constructs to be most amenable for further structure determination. Our next goal will be to carry out these atomic resolution studies by 3-D NMR.

Key Words: RAGE; Diabetes; NMR

Funding Agency: RS01/09



Biochemistry

Category: Graduate MSc (Basic Science)

20

**Cellular uptake and photophysical properties of Zn (II)
N-alkylpyridylporphyrins**

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Introduction:

In photodynamic therapy, the presence of molecular oxygen and light activation of the photosensitizer leads to the local production of singlet oxygen (1O_2) and other reactive oxygen species (ROS) that damage and kill the target cells. The aim of this study was to clarify the relationship between cellular uptake of Zn (II) N-alkylpyridylporphyrins (ZnPs) and their efficiency in cell killing.

Methods:

Cellular photodamage was determined by measuring ATP leakage due to membrane damage and cellular respiration (O_2 consumption). Photophysical efficiency was assessed based on the ability of ZnPs to generate singlet oxygen. Cellular uptake of ZnPs was measured spectrophotometrically.

Results:

No differences in the generation of singlet oxygen were observed among isomeric ZnPs. Cellular photodamage was related to cellular uptake and intracellular distribution of the ZnPs.

Conclusions:

Since all ZnPs studied were equally efficient in generating 1O_2 , the differences in their biological efficiency must be due to their cellular uptake and intracellular distribution.

Key Words: Membrane damage; Photosensitizer; Photophysical efficiency

Funding Agency: Grant YM18/09 from Kuwait University



Biochemistry

Category: Graduate MSc (Basic Science)

21

The role of molecular charge and structure on the efficacy of photosensitizers

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Introduction:

Photodynamic therapy (PDT) is emerging as a promising medical treatment for both neoplastic and non-neoplastic disorders. Cell destruction is achieved by a combination of visible light and light-sensitive compounds called photosensitizers (PSs). Upon illumination, photo-excited PSs produce cytotoxic reactive species, mainly singlet oxygen. Therefore, singlet oxygen quantum yield determines the efficiency of a PS. The aim of this project is to investigate how changes in lipophilicity and charges of the PS will influence the quantum yield and the efficacy of the PS in cell killing.

Methods:

Nine different N-alkylpyridylporphyrin derivatives and a hematoporphyrin derivative (HpD) were tested. Singlet oxygen quantum yield was followed by the decomposition of 1,3-diphenylisobenzofuran (DPBF). NAD(P)H oxidation was assessed at 340nm. Student's t-test was applied for data analysis with $p < 0.05$ accepted as statistically significant; each experiment was repeated 3-6 times.

Results:

Assessment of singlet oxygen generation showed that ZnTBAP is the least efficient PS followed by HpD. The para isomers give the highest singlet oxygen generation. It was found that the ortho Zn(II) isomers are the most efficient in causing photo-oxidation of NADH, followed by the para isomers then the meta. All the tested porphyrins were more efficient in NADH photo-oxidation than the hematoporphyrin derivative. ZnTBAP and HpD had a negligible effect on NADH oxidation even at higher concentrations. NADPH oxidation showed the same pattern as NADH oxidation except that the longer chain derivative, ZnHx2, had a stronger effect than the shorter derivative (ZnTM2).

Conclusions:

The efficiency of the PS depends on the chemical character of the molecule which is in turn controlled by the type and number of charges and the lipophilicity. Anionic PSs showed lower singlet oxygen generation and NAD(P)H photo-oxidation.

Key Words: Photodynamic therapy; Singlet oxygen; Photosensitizer

Funding Agency: College of Graduate Studies



Biochemistry

Category: Basic Sciences

22

A combination of two antioxidants produces a prooxidant effect

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Introduction:

Cationic Mn(III) N-alkylpyridylporphyrins (MnPs) are among the most powerful catalytic antioxidants (AO). When administered *in vivo* they can interact with natural AOs, including the most abundant, ascorbate (vit C) and glutathione (GSH). They could be readily reduced from Mn^{III}P to Mn^{II}P by ascorbate and glutathione, and in a subsequent step reduce either O₂⁻ (acting as superoxide reductase) or O₂ (exerting pro-oxidative action). In the latter case, O₂⁻ and H₂O₂ would be formed. Thus, a combination of two AOs can produce a prooxidant effect, which might explain why very often administration of exogenous AOs does not bring about the expected beneficial effects. The aim of this study was to test this hypothesis.

Methods:

Wild *E. coli* and mutants carrying deletions of superoxide dismutases (SOD), and of the *soxRS* and *oxyR* regulons were used as a test system. The antioxidant/prooxidant action of MnPs alone or in combination with ascorbate were determined by assessing their effects on cell division and on induction of antioxidant enzymes. All experiments were repeated at least 3 - 5 times with 3 replicates. Results are expressed as means ± S.E.

Results:

When added to SOD-deficient cells, MnPs acted as powerful SOD mimics/antioxidants. In the presence of ascorbate, however, MnPs caused oxidative damage, suppressed cell growth and induced *oxyR*-dependent antioxidant enzymes. Catalase prevented the effect indicating H₂O₂ as the major damaging species.

Conclusions:

The *in vivo* action (anti- or pro-oxidative) of exogenous AOs is determined by their redox properties and cellular localization, and depends on cellular redox status.

Key Words: Antioxidant; Ascorbate; Superoxide dismutase

Funding Agency: Kuwait University; Grant MB01/09



Community Medicine

Category: Basic Sciences

23

Energy drinks analysis at Kuwait market, scientifically safe with some cautions

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Introduction:

Energy drinks are designed to increase stamina and improve physical performance. The producers make many claims about health effects. Scientists and physicians have written to FDA asking for more regulation of increasingly popular energy drinks because their high caffeine content puts young drinkers at possible risk for caffeine intoxication and higher rates of alcohol-related injuries. Main constituents are caffeine, taurine, and glucuronolacton which occur naturally in the body but present much higher doses in energy drinks may cause concern. Alcoholic energy drinks faced a ban in the US after a series of binge deaths. Kuwait Food specification does not permit concentrations of caffeine and ethanol that exceed specification levels which is 320 ppm and 0.05%, respectively in the final products. Our work determines the prevalence of both above the threshold level in all samples by different techniques. Determination of ethanol, caffeine content and public awareness to read the label instructions are the aims of this study.

Methods:

A total of 167 of marketed samples from eighteen countries origin, collected during a period of January 2010 to January 2011 and evaluated by modified methods using Head space FID gas chromatography for Ethanol (OVI-G43 capillary column), and High performance liquid chromatography for Caffeine(260 nm detector,C18 column, flow 2 ml/min, 20% acetic acid pH 3 mobile phas) were used to analysis.

Results:

Screening of ethanol revealed that 100% of samples were within the allowed limit and ranged from 0.008 to 0.05 with average recovery of $90\% \pm 4$. Caffeine analysis ranged between 30 – 320 mg/l with average recovery of $93\% \pm 2\%$.

Conclusions:

Energy drinks at Kuwait market are safe regarding to caffeine and alcohol content but we ask consumers to look for label instructions where drinks is not recommended for children, pregnant women, caffeine sensitivity people, diabetics, and consume moderately.

Key Words: Energy drinks; Caffein analysis; Ethanol analysis

Funding Agency: NO



Community Medicine

Category: Undergraduate

24

Age at menarche and its relationship to body mass index among adolescent girls in Kuwait

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Introduction:

Early age at menarche has several implications on health by increasing the risk of diseases such as breast cancer. It has also been linked to obesity, but this relationship is not evident across racial or ethnic groups. In Kuwait, age at menarche remains mostly unknown, and it is not clear if it is associated with obesity among adolescent girls. This study aimed to estimate age at menarche and explore the association between menarcheal age and obesity or overweight among adolescent girls in Kuwait.

Methods:

A cross-sectional study was conducted on 1,273 randomly selected female high school students from all governorates in Kuwait. Height was measured with a portable stadiometer, and weight was measured using a portable digital weight scale. Overweight and obesity were defined as higher than or equal to the 85th percentile and 95th percentile, respectively. Data on menarche, socio-demographic status, physical activity and diet were collected using confidential self-administered questionnaire.

Results:

Out of 1,273 students, 23 (1.8%) were absent or refused to participate. The mean \pm SD of age at menarche was 12.40 ± 1.25 years (95% CI: 12.33-12.47). The prevalence of early menarche, defined as less than 11 years of age, was 8.6% (95% CI: 7.1-10.3). The prevalence of obesity and overweight was 18.3% (95% CI: 16.2-20.6) and 25.8% (95% CI: 23.4-28.3), respectively. Early age at menarche was significantly associated with overweight and obesity before and after adjusting for dietary intake and physical activity.

Conclusions:

This study estimated age at menarche among adolescent girls in Kuwait and showed a significant inverse association between age at menarche and obesity or overweight. Trends in menarcheal age should be monitored and taken into account in strategies that aim to combat obesity.

Key Words: Menarcheal Age; Obesity; Overweight

Funding Agency: None



Community Medicine

Category: Undergraduate

25

Knowledge and practices of barbers in Kuwait regarding blood-borne infections

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Introduction:

A barbershop is a place that is regularly visited by most people. It is, however, a place that can silently transmit blood-borne infections in the community as the use of sharp objects is frequently carried out. This cross-sectional study in Kuwait assessed the knowledge and practices of barbers regarding blood-borne infections (HIV, HCV, and HBV).

Methods:

This study consisted of two parts, an observation and a questionnaire. In the first part, 83 randomly selected barbers were observed to see if certain practices, that would alter the risk of disease transmission, were carried out. In the second part, a questionnaire was answered by 179 randomly selected barbers in 6 governorates. The median knowledge score was used as a cut-off point.

Results:

The percentages of participants who reported that they have heard about HIV, HCV, and HBV were 91.1%, 69.3%, and 60.3%, respectively. All respondents mentioned that a new razor blade should be used for every customer. Moreover, the majority (88.5%) reported that Dettol (a chloroxylenol based compound) is the detergent of choice for cleaning razors. In addition, more than 65% of the participants mentioned that barbers are at risk of being infected by HIV, HCV, or HBV. Logistic regression analysis showed that attaining high school degree or above was significantly associated with knowledge about HCV and HBV ($p \leq 0.001$) but not with knowledge about HIV.

Conclusions:

Barbers with different sociodemographic variables have different levels of knowledge. In addition, variations exist between knowledge scores about HIV, HBV, and HCV infections. Moreover, there were misconceptions and deficiencies in the knowledge about modes of transmission and ways of prevention of these blood-borne infections. Health education and promotion campaigns are recommended to target barbers to increase their knowledge and improve their practices regarding blood-borne diseases.

Key Words: Blood-borne infections; Kuwait; Barbers

Funding Agency: None



Community Medicine

Category: Undergraduate

26

**Clinical guidelines and costs of diagnostic investigations: A Survey
among secondary health care physicians in Kuwait**

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Introduction:

To explore physicians' use, knowledge, and acceptance to guidelines, to assess knowledge about cost of investigations, and to test the association between the previous factors and doctors' response through a given Irritable Bowel Syndrome (IBS) clinical case scenario.

Methods:

We conducted a cross-sectional survey on 312 doctors in 6 secondary hospitals in Kuwait from General Surgery, General Medicine, and Gastro-enterology Departments who routinely see patients presenting with symptoms of IBS, a relatively common condition in Kuwait, through a self-administered questionnaire via convenient sampling.

Results:

Out of the total participants, the majority were Kuwaitis, males, and aged 22-35. About 68% of the total indicated that they use guidelines in their practice. After developing a score of poor, fair, and good for guideline acceptance, only 22.3% scored good. Physicians' knowledge about cost of investigations ranged from 3.8% for barium study to 42.3% for colonoscopy. A score of no, fair, and good knowledge of cost of investigations was developed on which only 17.9% scored good. Only 25 doctors based their clinical decision regarding ordering tests for the case scenario on guidelines. After adjusting for potential confounders, trainees and assistant registrars were 2.45 times more likely to follow guidelines than registrars and senior registrars with regard to exclusion of other differentials. Furthermore, those whose cost knowledge score was good were 2.67 times more likely to base their confirmation of IBS on guidelines than those who scored poor.

Conclusions:

It is necessary to introduce clinical guidelines to secondary healthcare in Kuwait. In response to the hypothetical case scenario, there was high prevalence of non evidence-based use of diagnostic investigations, although a high number of self-reported use of guidelines was shown.

Key Words: Knowledge; Guidelines; Costs

Funding Agency: None



Community Medicine

Category: Undergraduate

27

Internet use among high school students in Kuwait

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Introduction:

Internet addiction is a new behavioural disorder which is increasing among adolescents affecting their daily life and academic performance. Although this disorder has been investigated in other settings, the prevalence of internet addiction among adolescents remains mostly unknown in Kuwait or in other countries in the Gulf region. This study aimed to investigate the prevalence of internet addiction among public high school students in Kuwait, and explore the association between internet addiction and student's academic performance or obesity.

Methods:

This is a cross-sectional study on randomly selected students from public high schools in all governorates in Kuwait. Data on internet use and internet addiction were collected by a self-administered questionnaire. Internet addiction was measured using the modified version of the Diagnostic Questionnaire for Internet Addiction (YDQ). Weight and height of the students were measured using standardized protocols, while student's performance was extracted from schools' records.

Results:

Out of 1000 students selected, 909 (90.9%) students responded. The prevalence of internet addiction was 99 (10.9%, 95% CI: 8.9% - 13.1%), slightly higher among females 70 (12.3%, 95 CI: 9.7% - 15.2%) than males 29 (8.6%, 95% CI: 5.8% - 12%) ($p=0.081$). Internet addiction was not significantly associated with obesity or overweight ($p= 0.634$). There was a significant inverse association between internet addiction and student's academic performance before and after adjusting for potential confounders.

Conclusions:

The study reported high prevalence of internet addiction among high school students in Kuwait and showed that it may interfere with their academic performance. Efforts should be made to increase the awareness on this newly existed health problem, and focus the research on developing a reliable tool to measure this problem and its trends in the future.

Key Words: Internet Addiction; Student's nonacademic performance; Obesity

Funding Agency: None



Community Medicine

Category: Undergraduate

28

Attitudes towards mental illness in Kuwait and the associated stigma.

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Introduction:

The aim was to assess the level of awareness and attitudes about mental illness and to explore any associated stigma through generating a culturally-sensitive quantitative tool using qualitative research methodology.

Methods:

Six focus group discussions were conducted using a structured guide. These were analyzed by the research team and eight main themes about mental illness were generated (types, descriptions, attitudes, beliefs, stigma, current relationships, future relationships and personal experiences). A total of 130 statements were integrated into an anonymous, self-administered questionnaire in Arabic, which was distributed to Kuwaiti employees in the Ministry of Public Works.

Results:

Approached were 423 employees who met the inclusion criteria, with a response rate of 94.6%. Gender showed the most significant differences in response. About 65% of the participants in the quantitative stage correctly identified at least half of the mental diseases listed, and their attitudes, beliefs and related stigma were subsequently described. The majority of our participants agreed to a more scientific explanation to mental illness, like the role of psychological trauma (91.5%) and mental illness curability (84.5%). Even though most participants (65%) agreed that a person with mental illness cannot be judged by external appearance only, they all agreed to a certain extent with the variable descriptions generated by the focus groups. Interestingly, while more women were sympathetic with the mentally ill, more males were willing to accept future relationships with such individuals.

Conclusions:

Contrary to popular belief that people in this area of the world are less aware about mental illness, our data reflected a relatively good awareness level, as well as a more positive and tolerant attitude among the studied population. However, a substantial deficit in knowledge about some mental illnesses and a certain level of associated stigma were also detected.

Key Words: Qualitative study; Mental illness; Awareness and attitude

Funding Agency: None



Community Medicine

Category: Undergraduate

29

Prevalence, associated factors, and disability assessment of musculoskeletal symptoms among dentists in Kuwait

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Introduction:

To evaluate the prevalence and identify the associated factors and level of disability of musculoskeletal symptoms among dentists in Kuwait.

Methods:

A cross-sectional sample survey was conducted on 306 dentists in primary and specialized dental care facilities in Kuwait. The data were collected using a valid and reliable self-administered questionnaire. Standardized Nordic Instrument was used after modification to assess the musculoskeletal pain. To evaluate the extent of pain disability, Modified Oswestry Musculoskeletal Pain Disability Assessment Scale was employed. The short form of the International Physical Activity Questionnaire was utilized to measure the level of physical activity. The questionnaire consisted of 4 sections: sociodemographic characteristics, work-related aspects, musculoskeletal pain assessment, and disability assessment.

Results:

The response rate was 87.4%. The prevalence of musculoskeletal pain among dentists in Kuwait was found to be 84.6%. Musculoskeletal symptoms were more prevalent among female, single, and Kuwaiti responding dentists. Shoulders pain was highest among general practitioners. The median pain disability score was higher in respondents with history of related diseases or injuries as well as among female dentists. The logistic regression analysis showed that musculoskeletal pain at neck (adjusted odds ratio= 4.33, $p= 0.009$), upper back (adjusted odds ratio= 3.26, $p= 0.002$), and ankles/feet (adjusted odds ratio= 4.04, $p= 0.002$), and related diseases (adjusted odds ratio= 3.42, $p= 0.005$) were independently associated with disability score level after adjusting for sociodemographic and work-related variables.

Conclusions:

High prevalence of musculoskeletal symptoms was reported among dentists in Kuwait. These findings invite health authorities to increase the awareness of dentists about preventive measures to alleviate the burden of musculoskeletal symptoms through modifying some of the contributing factors.

Key Words: Musculoskeletal; Dentists; Kuwait

Funding Agency: None



Community Medicine

Category: Undergraduate

30

Self-medication with over-the-counter analgesics among Kuwait University students

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Introduction:

Over the counter (OTC) analgesics are among the most commonly used medications worldwide, yet inappropriate or prolonged use may lead to toxicity. This study aimed at measuring the prevalence of OTC analgesic use, including acetaminophen, NSAIDs, and aspirin, among Kuwait University students, to identify the reasons and factors pertaining to their use, and to assess the level of awareness regarding their adverse effects.

Methods:

A questionnaire was distributed to 753 Kuwait University students, from the Faculty of Medicine and 5 other randomly selected faculties. Data were entered, coded, and recoded using SPSS. Multivariate logistic regression was used to adjust for age, gender, nationality, and faculty, using one month prevalence of OTC use and of overuse (defined as >10 days/month, >4 doses/day, or >2 pills/dose) as the two main binary outcome variables.

Results:

The one and 12-month period prevalence's of OTC use were 84% [95%CI, 81-87%] and 97% [95%CI, 96-98%], respectively. The one-month prevalence of overuse was 23% [95%CI, 20-27%] of which 40-50% said they used OTC analgesics at this level for a year or more. The major reasons for use were headache and flu-like symptoms. Around 22% of participants reported using these drugs for non-medical reasons. Factors significantly associated with the one month prevalence of OTC analgesic use included non-medical faculty, headache, and inappropriate reason for use. Factors significantly associated with the one month prevalence of OTC analgesic overuse included male gender, non-medical faculty, bone pain and toothache, not reading the information leaflet, and inappropriate reason for use. Between 23% and 40% were not aware of the presence of dangerous side-effects.

Conclusions:

This study revealed that the majority of Kuwait University students were using OTC analgesics, among which many reported overuse and long-term use. This should be addressed by public health research, policies, and programs.

Key Words: over-the-counter analgesics; pain medications; None

Funding Agency: None



Community Medicine

Category: Graduate MSc (Basic Science)

31

Dissatisfaction with body shape and depression among working women in Kuwait

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Introduction:

To assess the association between perceived body shape and depression, as well as to examine their relationship with different socio-demographic variables, and the use of weight reduction strategies.

Methods:

A cross-sectional study was conducted among adult working women in the Ministries Complex of Kuwait. A total of 1064 working women were approached, of whom 1006 (94.5%) agreed to participate. Data was collected using a self-administered questionnaire. Beck Depression Inventory (BDI-II) and the Body Shape questionnaire (BSQ-16) were used to assess depression and body shape perception, respectively. Univariate and multivariate logistic regression were used to determine the association between depression, body shape satisfaction and other variables.

Results:

The Spearman correlation coefficient between the total body shape score and the total Beck depression score was 0.324 ($p < .001$). The odds of depression in those extremely dissatisfied with their body image was 6.5 times the odds in those who were satisfied (95% CI: 4.02-10.7; p -value < 0.001) after adjusting for age, nationality, marital status, monthly salary and BMI. The odds of moderate/severe depression in the divorced/widowed were 2.3 times greater than in single women. Those earning more than a 1000 KD monthly were 60% less likely to be depressed than those earning less than 500 KD. BMI was positively associated with body shape dissatisfaction.

Conclusions:

A positive association between body shape dissatisfaction and level of depression existed; therefore, public health interventions should be directed towards dissatisfied women in order to reduce the prevalence of depression among them.

Key Words: body Dissatisfaction; depression; females

Funding Agency: None



Community Medicine

Category: Undergraduate

32

Knowledge and practice of road safety among Kuwait university students

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Introduction:

Road traffic accidents in Kuwait are a public health threat, being the third cause of death in general and the first among the young population. The main objective of this study is to evaluate the knowledge of road traffic signs and laws among Kuwait University students and its association with their driving behavior.

Methods:

A cross sectional study was conducted involving 1200 students between the ages of 18–25 from 6 different Kuwait University faculties, using a self-administered questionnaire. Chi-square test was used to assess the associations between the independent variables with knowledge and practice scores. Then, a multivariate logistic regression was used to adjust for potential confounders.

Results:

Poor knowledge of traffic signs and regulations was statistically ($p < 0.001$) associated with risky driving behaviors, $OR = 1.654$ [95%CI 1.253–2.183]. Males had higher unsafe driving practices than females (adjusted $OR = 5.725$, [CI 4.320–7.587]; $p = 0.001$). Three years or more of driving experience was also associated (adjusted $OR = 2.053$ [CI 1.420 – 2.968]; $p < 0.001$) with risky driving behavior compared with less than three years of driving experience. Art students had significantly ($p = 0.002$) higher unsafe driving practices - $OR = 2.078$, [CI 1.300–3.323] compared to other faculties. Another significant ($p = 0.032$) association was living in Al Jahra governorate as they had higher unsafe driving practices -adjusted $OR = 1.918$ [CI 1.058–3.477] compared to other participants.

Conclusions:

The prevalence of traffic violations and car accidents is high among Kuwait University students. Older age, male gender, faculty of study, residential governorate, driving experience, and poor knowledge of traffic signs and laws were found to be statistically associated with risky driving behavior. Educational interventions, public awareness campaigns, reinforcement of existing laws and introduction of new laws could greatly reduce this hazard in Kuwait.

Key Words: Traffic; Accident; Road

Funding Agency: None



Community Medicine

Category: Undergraduate

33

Knowledge and risk assessment of osteoporosis among female employees in Kuwait

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Introduction:

To evaluate the level of knowledge about osteoporosis among female employees in Kuwait and assess its association with sociodemographic characteristics and the risk for developing osteoporosis.

Methods:

A cross-sectional study was carried out including 613 female employees from 3 governmental institutions. Data was collected through a self-administered questionnaire, including 3 sections: sociodemographic characteristics, knowledge, and risk assessment. A knowledge score was based on 20 items (13 predisposing factors, 6 signs, and 1 for diagnostic test). The risk assessment score was adopted from the International Osteoporosis Foundation and was based on 18 items. Different weights from 1 to 3 were assigned to various items according to the magnitude of risk attached to each item. A logistic regression model was used to assess the association between the diagnosis of osteoporosis as a binary dependent variable (0 for not diagnosed with osteoporosis, 1 for diagnosed with osteoporosis) and independent variables about sociodemographic characteristics, knowledge and risk scores.

Results:

There was a significant association between osteoporosis knowledge score and nationality, level of education, marital status, and menopausal status. Level of education was positively associated with knowledge score. There was a negative association between the level of education and the risk to develop osteoporosis, while there was no association between the level of knowledge about osteoporosis and the risk for developing the disease. The majority of participants (81.6%) reported that their source of information about osteoporosis was from their relatives or friends. Fewer participants (37.6%) reported health staff such as doctors or nurses, school (17.4%) or university (14.9%) as their sources of information. The logistic regression analysis showed that age (adjusted odds ratio= 3.042, $p= 0.003$), level of education (adjusted odds ratio= 2.153, $p= 0.027$), menopause (adjusted odds ratio= 3.141, $p= 0.021$), and risk score (adjusted odds ratio= 4.227, $p= 0.001$) were independently associated with osteoporosis, after adjusting for potential confounders.

Conclusions:

Although the participants in the study had sufficient knowledge it did not reduce their risk for developing the disease, which may be due to lack of practice of preventive measures. Women at the pre-menopausal stage were more knowledgeable about predisposing factors and signs of osteoporosis than those at the post-menopausal stage.

Key Words: Osteoporosis; Knowledge; Risk Assessment

Funding Agency: None



Community Medicine

Category: Undergraduate

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Prevalence and factors associated with sleep deprivation among nurses working in Kuwait public hospitals

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Introduction:

Objectives: This study aimed to assess the prevalence of poor sleep quality and to identify the factors associated with poor sleep among nurses working in Kuwait public hospitals.

Methods:

A cross-sectional study was conducted on nurses currently working in three tertiary-care public hospitals in Kuwait, including Amiri, Mubarak Al-Kabeer, and Farwaniya Hospital. A self-administered questionnaire was used to collect data on socio-demographic, life-style and work-related factors. Pittsburgh Sleep Quality Index (PSQI) was used to assess the sleep quality during past one month.

Results:

Of 362 nurses who completed most of part of the questionnaire including all questions on PSQI, 195 (51.1%) were classified to have had poor sleep (PSQI score > 5) during the past one month. Multivariate logistic regression model showed that self-percieved stress of undefined source during past one month (adjusted OR = 2.9; 95% CI: 1.8-4.7) and time of last meal before going to bed (last meal < 2 hours: adjusted OR = 0.6; 95% CI: 0.4-0.9) were significantly associated with poor sleep among the nurses in this study.

Conclusions:

This study revealed high prevalence of poor sleep among nurses and identified the time of last meal before going to bed and self-reported stress of undefined source during the past one month as the independent factors associated with poor sleep in this population. Further studies are needed to examine the sources of self-perceived stress among nurses working in public hospitals to subsequently improve the patient-care in Kuwait.

Key Words: Sleep deprivation; Nurses; Public hospitals

Funding Agency: None



Community Medicine

Category: Undergraduate

35

Sports injuries among male athletes in Kuwait: Prevalence and associated factors

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Introduction:

To assess the lifetime and 12 months period prevalence of sports injuries among male athletes according to type of sport, type of injury and its seriousness, and examine the association of injuries with sociodemographic, lifestyle and preventive factors.

Methods:

In this cross-sectional study we approached 475 ball games professional athletes, aged 15 years and older, from 5 sports clubs in Kuwait. Of them, 452 (95.2%) responded. Four ball games, soccer, basketball, handball and volleyball, were included. Data were collected through a self-administered questionnaire. Bivariate and multivariate relationships between associated factors and experience of injury were tested by using chi-square and logistic regression.

Category: Undergraduate

Results:

The overall 12 months and lifetime prevalence of sports injuries was 73.8% and 89.8%, respectively. Prevalence was highest among volleyball athletes, and lowest among soccer athletes. Lower limbs were the most common site of injuries (73.1%), and joints injuries were the most common type (43.6%). 48.8% of athletes took more than 10 days off practice for their most recent injury. Compared to volleyball, soccer and handball athletes were 2.9 times (95% CI: 1.3 – 6.3) and 3.4 times (95% CI: 1.5 – 7.8) more likely to take more than 10 days off practice. Athletes who sometimes wore protective gears were 3.1 times (95% CI: 1.7 – 5.8) more likely to report an injury compared with those who never wore protective gears (p-value <0.001).

Conclusions:

Sports injuries are highly prevalent among professional athletes in Kuwait. Future studies are needed to provide guidelines for interventions that may reduce such injuries.

Key Words: Sport injuries; Prevalence; Male athletes

Funding Agency: None



Community Medicine

Category: Undergraduate

36

Knowledge and practice of universal precautions among Kuwait University medical students in their clinical years

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Introduction:

This cross-sectional study aimed to assess the knowledge and practice of universal precautions among the Faculty of Medicine, Kuwait University (FOM, KU) medical students in their clinical years.

Methods:

We used a self-administered questionnaire to assess the level of awareness and application of universal precautions among medical students of the 5th, 6th and 7th years. This sample included students of the old and new curriculums in the FOM, KU.

Results:

The frequency of correct answers for 7 of 9 knowledge questions about universal precautions ranged from 65% to 90% among the students. All the questions regarding the practice of universal precautions were answered correctly by over 62% (range: 62% - 96%) of the students. The prevalence of poor knowledge (< median score equals six of nine total) was 38.4% (84/ 220) and poor practice (< median score equals seven of nine total) was 27.7% (61/ 220). GPA was significantly ($P = 0.008$) associated with the knowledge status of the respondents. However, there was a non-significant ($P = 0.397$) relationship of GPA with the practice of universal precautions. Furthermore, neither the knowledge status nor any of the socio-demographic variables were significantly associated with the practice of universal precautions.

Conclusions:

Students in the clinical years appear to have poor level of both knowledge and practice of universal precautions, perhaps due to the lack of introduction of universal precautions as a part of the curriculum in the FOM, KU. Efforts are needed to optimize the level of knowledge and practice among students to minimize the risk of preventable infections.

Key Words: Universal precautions; Medical students; Infection control

Funding Agency: None



Community Medicine

Category: Undergraduate

37

Aggression and general well-being: A comparison between Kuwait police academy cadets and Kuwait University students

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Introduction:

To compare aggression levels and General Well-being among Police Academy cadets and Kuwait University students, as well as to assess the possible confounding effects of various socio-demographic and lifestyle variables.

Methods:

Cross-sectional study conducted on 1052 students; 581 Police Academy cadets and 471 Kuwait University students, that used a five-part questionnaire, socio-demographic questions, health-related questions, life-style questions, the General Well-being Schedule and the Buss & Perry Aggression questionnaire.

Results:

The overall response rate was 88.3%. The median age of the respondents was 20 years with an interquartile range of 1.88 years, all were males and the majority were Kuwaiti. T-test analyses showed no statistically significant difference ($p=0.094$) between Police Academy cadets and KU students in term of their aggression scores. Physical activity was significantly associated with the General Well-being of Kuwait University students ($p<0.001$) but not that of Police Academy students ($p=0.33$). Smoking was significantly associated with General Well-being (i.e. smokers and ex-smokers had lower well-being) among Police Academy students ($p<0.001$) and Kuwait University students ($p=0.037$). There was a statistically significant association between aggression and smoking status for Police Academy ($p<0.001$) and Kuwait University ($p=0.002$). Multiple linear regression analyses showed a significant association between institutional enrollment and aggression scores as well as between General Well-being and aggression scores (i.e. the more aggressive, the lower the well-being), after adjusting for the effects of possible confounding variables.

Conclusions:

Life-style factors (e.g. smoking, physical inactivity) were associated with poor well-being and increases in aggression. Health promotion regarding these factors should be considered in order to improve the outcomes. Future studies to further evaluate other dimensions that might affect aggression and well-being must be considered.

Key Words: Aggression; Police cadets; University students

Funding Agency: None



Dentistry

Category: *Clinical*

38

Urinary fluoride excretion among children in Kuwait, a non-fluoridated community

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Introduction:

Objective: To determine urinary fluoride excretion by children aged 1-9 years in Kuwait, a non-fluoridated community.

Methods:

Spot early morning urine samples were collected in polyethylene bottles from 317 children, randomly selected from households in the six governorates in Kuwait. The fluoride content of the samples was measured, using fluoride-ion specific electrode. Similarly, fluoride concentrations in drinking water samples, collected from the same households, were determined. The urinary creatinine content of the spot urine samples was then measured by the kinetic Jaffe reaction, using Beckman Synchron LX 20 automated analyzer.

Results:

The mean fluoride level in the drinking water was low, being 0.065 (+ 0.086) ppm. The mean fluoride concentrations in the spot urine samples was also low, being 0.37 (\pm 0.33) ppm, while the mean creatinine concentration was 7.1 (\pm 5.7) mmol/L. The fluoride/creatinine ratios at ages 1-3, 4-6 and 7-9 years were 0.69 (\pm 1.13), 0.47 (\pm 0.44), and 0.48 (\pm 0.58), respectively. These ratios were low when compared to values (1.49+0.63) obtained from an English community with 0.81 (+0.09) ppm fluoride in drinking water (Zohouri et al., Community Dent Oral Epidemiol 2006; 34:130-138)

Conclusions:

Urinary fluoride excretion among children in Kuwait is low, and the results from this work would be useful in monitoring fluoride intake, should fluoridation of public water supplies in Kuwait be re-introduced.

Key Words: Fluoride; Urine; Excretion

Funding Agency: Kuwait Foundation for the Advancement of Sciences, Project No. 2007-1302-06.



Dentistry

Category: *Clinical*

39

Prevalence of malocclusions in Kuwaiti schoolchildren

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Introduction:

Information on prevalence of malocclusion in the children of Middle-East countries is limited. National surveys of children's oral health were carried out in Kuwait in 1982 and in 1993. The purpose of this national dental survey was to determine the prevalence of malocclusions in Kuwaiti schoolchildren.

Methods:

A national epidemiologic survey of the 5-14 year old children (n = 4,338) was conducted in the 5 governorates of Kuwait. The mean age of the children was 9.3 years. Malocclusion was identified in accordance with WHO criteria. Eight trained and calibrated dentists examined the children. Chi-square tests were used for testing the associations of the variables with the prevalence of malocclusion. Multivariate analysis (logistic regression) was used to assess the risk factors for the occurrence of malocclusion.

Results:

The prevalence of severe malocclusion was 5.3% and that of slight malocclusion was 62.3%. There was a significant difference in the occurrence of malocclusions between governorates ($p < 0.001$) and in age ($p = 0.001$), but no difference by gender. Children in Ahmadi governorate (OR = 6.8; $p < 0.0001$) and increasing age (OR = 1.1; $p = 0.001$) had a higher risk for the occurrence of severe malocclusion.

Conclusions:

Severe malocclusion was less prevalent among these children than had been reported by the previous national oral health surveys in Kuwait.

Key Words: Malocclusions; Schoolchildren; Kuwait

Funding Agency: Ministry of Health, Kuwait and the Forsyth Institute



Dentistry

Category: Undergraduate

40

Periodontal health attitude and knowledge among school children in Kuwait

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Introduction:

Objectives: To assess the knowledge and attitude of school children towards oral and periodontal health.

Methods:

Children with an average age of 13, attending public schools in three districts in Kuwait, were recruited into this study. The participants completed a self-administered, anonymous, structured questionnaire.

Results:

A total of 1539 school children (836 males and 703 females) participated in the study. There was no significant difference between the two groups regarding the mean age and gender distribution. Around 50% of the participants never flossed, visited the dentists only when in pain, and had never had scaling. Females were significantly more aware of the importance of dental visits ($p=0.008$), the presence of gum disease ($p=0.019$) and the importance of treating gum disease ($p=0.001$), with higher brushing frequency per day ($p=0.001$) compared to males. Almost 75% reported bleeding gums during brushing. Participants were considered as having a positive attitude towards oral health if they brushed twice a day, visited a dentist at least once a year, and believed that regular dental visits were important. Only 215 of all participants (14%) scored a positive attitude. Receiving brushing advice from the parents was the only factor significantly associated with having a positive attitude towards oral health in logistic regression analysis (OR=4.6; CI: 1.4-14.6; $P=0.01$).

Conclusions:

Awareness of the importance of periodontal health was generally low. In order to stress the importance of oral and periodontal health, educational programs are essential for school children. Parents must play a major role in their children's oral health education.

Key Words: Periodontal; Knowledge; Attitude

Funding Agency: None



Dentistry

Category: Basic Sciences

41

Toothache and the other perceived symptoms by Kuwaiti adolescents

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Introduction:

The aim of this study was to find out the prevalence of perceived toothache among Kuwaiti adolescents and its associations with the other subjective health complaints.

Methods:

Nationally representative sample of the adolescents from the government schools were drawn into this study. Altogether 2,312 schoolchildren at the ages of 11 and 13 years (grades 5 and 7) participated in this study by filling a structured questionnaire anonymously in the school classrooms in 2002–2003. The questionnaire of the WHO Collaborative (HBSC) study was modified to the Kuwaiti situation. The Ethical Committee of the Faculty of Dentistry, Kuwait University approved the study. Chi-square tests, logistic regression models and Pearson correlation coefficients were used in the analyses.

Results:

Response rate of the study was 93%. Daily experience of toothache during the last six months was very common, 10.4% by the 11-year-olds and 5.4% by the 13-year-olds. Less than half (47.8%) of the 11-year-olds and 65% of the 13-year-olds had not experienced toothache in the past six months. There were high correlations between toothache and earache ($r=0.43$), stomachache (0.37) and backache (0.34). Also asthmatic and allergic symptoms were associated with the toothache experience. Some subjective complaints like feeling sad, nervous or dizzy, irritability or bad temper, having difficulties in getting to sleep were associated with perceived toothache.

Conclusions:

The prevalence of perceived toothache was high among Kuwaiti adolescents. The perceived toothache, other pain symptoms and subjective complaints were all inter-correlated.

Key Words: Toothache; Dental pain; Adolescents

Funding Agency: Kuwait University [DD1/02]



Dentistry

Category: Graduate MSc (Basic Science)

42

Immunological analysis of dental pulp inflammation

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Introduction:

Assessing the degree of inflammation in the dental pulp poses a diagnostic dilemma as it influences the decision on conservative versus invasive dental treatment. However, there are no objective, quantitative and clinically-practical methods for evaluating pulpal inflammation. Cytokines have been suggested to be markers of pulpal inflammation, but estimation of cytokine levels has been possible only after extraction of inflamed teeth. We set out to develop a method to measure cytokines from the dental pulp prior to decision making.

Methods:

108 dental pulp blood samples were obtained with cotton pellets from pulp sites exposed on pulpectomy. 25 samples were from normal teeth, 40 from asymptomatic pulps with caries exposure and 43 from symptomatic pulps clinically diagnosed as irreversible pulpitis. The levels of inflammatory cytokines IL-2, IL-6, IL-8, IL-17, TNF alpha and IFN gamma and anti-inflammatory cytokine IL-10 were quantified using high-sensitivity ELISA. Levels of cytokines and ratios of inflammatory cytokines to IL-10 were compared using Kruskal–Wallis and Mann–Whitney tests.

Results:

Significantly higher levels of IL-6, IL-8, IL-10, TNF alpha and IFN gamma were detected in caries exposed and irreversible pulpitis as compared to normal teeth. IL-2 levels were higher in caries exposed as compared to normal teeth. IL-2 and IL-10 levels were higher in caries exposed pulps as compared to irreversible pulpitis, while IL-8 was higher in irreversible pulpitis as compared to caries exposed. Most interestingly, IL-6/IL-10 and IL-8/IL-10 ratios were significantly higher in irreversible pulpitis compared to both caries exposed and normal teeth.

Conclusions:

The IL-8/IL-10 ratio promises to be a good indicator of irreversible pulpitis. An important and potentially very useful outcome of this study is the demonstration that cytokine estimation in pulpal blood obtained easily using cotton pellets may help in the diagnosis of pulpal inflammation.

Key Words: Dental pulp; Cytokines; Inflammation

Funding Agency: None



Dentistry

Category: Clinical

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The changes in ICDAS codes of the schoolchildren in 2008-2009

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Introduction:

This study aimed to describe the changes of the ICDAS (International Caries Detection and Assessment System) codes between the examinations in 2008 and in 2009 among the Estonian primary schoolchildren.

Methods:

The sample of 10 schools with 1st and 2nd grade pupils (n=438) were drawn in 2008, in South-East Estonia. The mean age was 7.8 years in the 1st and 8.8 years in the 2nd grade. The clinical examinations with ICDAS criteria were completed in January 2008 and in 2009 by four calibrated examiners. The Ethical Committee of the University of Tartu approved the study. The inter- and intra-examiner consistency was high (kappa>0.9).

Results:

The distribution of the ICDAS codes were similar in 2008 and in 2009. The mean numbers of the surface-based codes in 2008 were: 0.8 (code 1), 1.4 (2), 0.4 (3), 0.1 (4), 0.1 (5), and 0.1 (6). There were on the average 2.3 surfaces with the higher ICDAS code and 2.5 surfaces with the lower one in 2009 than in 2008. There were 43% children without any higher codes and 45% without any lower codes in 2009 than in 2008. The distribution of the ICDAS codes of the occlusal surfaces of 16/26 were 64% (0), 12% (1), 17% (2), 5% (3), 1% (4), 1% (5), 0% (6).

Conclusions:

The distributions of the ICDAS codes were similar in both years. The changes of the ICDAS codes were small and appeared on the average less than 3 surfaces/child.

Key Words: Dental caries; ICDAS; Schoolchildren

Funding Agency: Cargill R&D Centre Europe



Dentistry

Category: Basic Sciences

44

**Associations between sugar consumption and other health habits in
Kuwait**

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Introduction:

This study was aimed to find out if daily consumption of soft drinks, sweets and caked/pastries had associations with the other health-related habits among schoolchildren in Kuwait.

Methods:

Nationally representative sample of the children from the government schools were drawn into this study. Altogether 1,292 schoolchildren at the aged 13 years (SD \pm 1.04) participated in this study by filling a structured questionnaire anonymously in the school classrooms during 2002 and 2003. The questionnaire of the WHO Collaborative (HBSC) study was used after modifying it for the Kuwaiti situation. The Ethical Committee of the Faculty of Dentistry, Kuwait University approved the study. Chi-square tests, logistic regression models, Pearson correlation coefficients and Cronbach's alphas were used in the analyses.

Results:

Daily consumption of soft drinks, sweets and caked/pastries was very high, especially among the Kuwaiti schoolchildren. Very strong inter-correlations were found between the daily consumption of sweets and cakes/pastries ($r=0.60$), soft drinks and sweets ($r=0.50$), and soft drinks and cakes/pastries ($r=0.42$). Unfavorable health habits such as late bedtime, frequent watching of TV and early onset of smoking had a strong correlation with the daily use of these sugar products. Socio-demographic and socio-economic factors had a weak associations with the daily consumption of these foods.

Conclusions:

Daily consumption of the common sugar products was alarmingly high in Kuwait. Other unhealthy habits seemed to be associated with the daily consumption of these sugar products.

Acknowledgements: This study was supported by Kuwait University Research Grant No. [DD1/02].

Key Words: Sugar consumption; Health habits; Adolescents

Funding Agency: Kuwait University Research Grant No. [DD1/02].



Dentistry

Category: *Clinical*

45

Treatment recommendations for primary molars with pulp degeneration

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Introduction:

Objectives: To evaluate dentist-related factors that might influence decision-making for the management of extensively decayed primary molars with pulp degeneration

Methods:

A pre-coded questionnaire that sought dentists' management choices for a deeply carious second mandibular primary molar teeth with pulp and periapical involvement, as depicted in a simulated periapical radiograph, along with a specific clinical scenario, was distributed among a random sample of 167 dentists. Dentists were instructed to answer all questions. A binary dependant variable was constructed for dentists who chose to extract the tooth and those who decided to preserve it through pulp therapy. Logistic regression of the ratio of the participants who would extract or pulpally treat the tooth in question was run.

Results:

A total of 152 dentists (115 males and 37 females) completed the survey, giving a response rate of 91 %. Fifty-five per cent of participants recommended pulp therapy followed by definitive restoration and 40% recommended extraction of the tooth in question. In the logistic regression model, graduates of dental schools from Europe and the Middle East ($P < 0.01$ and $P < 0.008$, respectively), and dentists with work experience of less than 10 years ($P < 0.02$) had higher probabilities of extracting the tooth. Dentists who treated an average of 0-5 child patients during a week had a smaller probability of extracting the tooth than those who treated 17 or more children during a week ($P < 0.006$). Specialty training, language of undergraduate dental education, work place and area of practice had no significant effect on the decision making.

Conclusions:

It is possible that a lack of specific guidelines for the management of decayed 2nd primary mandibular molars with pulp degeneration may account for the difference in opinion among dentists in this study regarding their optimal treatment recommendations. This disagreement appears to be due mainly to inter-individual, educational, training and practice characteristic factors.

Key Words: Children; Decision Making; Pulp Therapy

Funding Agency: None



Dentistry

Category: *Clinical*

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Prevalence of dental fluorosis in Kuwaiti schoolchildren in different governorates

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Introduction:

Dental fluorosis is a specific fluoride-induced disturbance of tooth formation in which enamel development is disrupted and hypomineralised. The premolars and second molars are most frequently affected, followed by the maxillary incisors, while mandibular incisors are least affected. The most important risk factor in determining the occurrence of fluorosis occurrence and severity is the total amount of fluoride consumed from all sources during the critical period of tooth development. National surveys of children's oral health were carried out in Kuwait in 1982 and in 1993. The prevalence of dental fluorosis was found to be quite high although rarely severe. The aim of this study was to determine the prevalence of dental fluorosis in Kuwaiti schoolchildren in five different governorates.

Methods:

A national epidemiologic survey of the 5-14 year old children (n = 3,653) was conducted in the 5 governorates of Kuwait. Dental fluorosis was scored according to Dean's Index. Eight trained and calibrated dentists examined the children. Chi-square tests were used for testing the associations of the variables with the prevalence of fluorosis. Multivariate analysis (logistic regression) was used to assess the risk factors for the occurrence of fluorosis.

Results:

Less than 0.1% of the children had severe and moderate fluorosis; 0.3% had mild fluorosis; 2.3% had very mild fluorosis and 7.8% had questionable fluorosis. Considerable variation was observed between the governorates. Dental fluorosis was highest in Jahra (5.5%) and lowest in Ahmadi (0.2%) (p<0.001). There was also difference in the occurrence of dental fluorosis between genders (p=0.002) and age (p<0.001). Male (OR=1.8), children in Jahra governorate (OR=22.9) and increasing age (OR=2.4) had a higher risk for the occurrence of dental fluorosis.

Conclusions:

There are variations in the prevalence of dental fluorosis between the governorates. Dental fluorosis was less prevalent than had been reported among the previous national oral health surveys in Kuwait.

Key Words: Dental fluorosis; Schoolchildren; Kuwait

Funding Agency: Ministry of Health, Kuwait and the Forsyth Institute



Dentistry

Category: Basic Sciences

47

Attitudes of dentists, dental hygienists and patients about dental professionals' role in smoking cessation and prevention

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Introduction:

Use of tobacco can cause harmful effects on oral health. Dentists and dental hygienists can play an important role in promoting smoking cessation and prevention. Patient attitude is an influencing factor in health professional's decision to provide preventive health services. Therefore the objective of this study was to determine the attitude of the dental professionals and patients about dental professionals' role in smoking cessation and prevention.

Methods:

The data were collected from 24 dental professionals (21 dentists and 3 dental hygienists) of Dental Centre, Ahmadi Hospital and 71 patients from Kuwait Oil Sector seeking treatment at the Dental Centre through separate self-administered questionnaires.

Results:

Seventy five percent of dental professionals believed that it was part of their responsibility to prevent smoking and majority of them (62.5%) also believed it was their responsibility to help patients in smoking cessation. They were more optimistic about the effectiveness of their smoking prevention and cessation efforts, as 66.7% thought they could be effective; 62.5% of them were confident in their ability in counseling patients in smoking prevention and cessation. More than eighty percent of the patients agreed that dentists or dental hygienists should ask patients about their tobacco use (83.3%), tell patients about how tobacco use can affect their oral health (87.2%), and advice patients who use tobacco to quit. Majority of patients believed that their dentists or dental hygienists can help in smoking cessation and prevention.

Conclusions:

Dentists and dental hygienists can play an important role in promoting smoking cessation and prevention. Effective training and continuing education need to be introduced and implemented to allow the dental team to engage in smoking cessation and prevention.

Key Words: Smoking cessation and prevention; Dental professionals; Kuwait oil sector

Funding Agency: None



Ethics

Category: Undergraduate

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A one day informed consent and surgical check lists audit at a secondary care hospital in Kuwait

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Introduction:

The objective of this study is to audit the informed consent and the surgical check list appropriateness and completeness in a secondary care hospital in Kuwait.

Methods:

All the identified consent forms in a one day worth of discharges in addition to all entries in a surgical list of elective procedures were assessed to evaluate adherence to standard safety policies of data recording and entry.

Results:

The audit showed that all 18 patients requiring a written informed consent during their admission had correctly a form included in their medical record. There were however significant missed elements from many with potential risk to patients' correct identification and safety. The surgical procedure name was abbreviated in 39% of the consent forms, 33% of forms didn't include patients full name, 28% didn't specify site or side of procedure, and 17% didn't include a medical record number. Not a single consent had the date of birth of patient included but had patients' age entered instead. All the forms included physician's name and signature. In the same day, the surgical list of scheduled elective procedures was reviewed to identify deviation from safety standards in data entry. A total of eighteen procedures were included in the list (16 surgical and 2 nephrology cases). Half the entries included an abbreviated name of the procedure. Around one third didn't have the patient's full name, only one of the five cases needing clear remarks on laterality before the procedure name to specify side and site had this mentioned. The age of the patients in years was included and None specified date of birth. The physician's name was not identified in any entry; however the medical or surgical unit was specified.

Conclusions:

Many significant gaps in the documentation of informed consents and surgical lists were demonstrated in this one day audit. There is an urgent need to abide by patients' safety policies and standards to reduce potential adverse events and errors.

Key Words: Informed Consent; Surgical Check List; Patient Safety

Funding Agency: None



Ethics

Category: Undergraduate

49

Prevalence of child abuse among grade nine students in governmental schools in Kuwait

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Introduction:

Every child has the right to a life free from violence. At schools, there should be zero tolerance to all forms of physical, emotional and sexual abuse by adults or other children.

Methods:

The International Society for Prevention of Child Abuse and Neglect (ISPCAN) validated child abuse screening translated tool was used in an interview-based survey enrolling 339 Middle School students (141 boys and 198 girls) in Grade 9 from three randomly selected governorates in Kuwait in 2010.

Results:

Among male students, 77% reported being sworn at and 47% been humiliated by shouting at during the last year. This was less among female students at 64% and 58% reporting similar abuse respectively. Physical abuse was reported by 48% of male students being hit by an object, 35% being cut purposefully with a sharp object, and 36% being slapped on face or head as punishment. Fingers or hands crushing were reported by 18.4% of students. Physical abuse among female students was less reported at 19% for being hit by an an object, 13% being slapped on face or head as punishment, 7% reported to be cut purposefully with a sharp object and 12% experienced twisting their ears. Five male students reported that they were made to have sex in school, 11% reported that their private parts or breast were touched and 40% were shown pictures, magazines or movie of people or children doing sexual things. Sexual abuse among female students was higher. Fourteen students reported being made to have sex with someone in school (50% with another adolescent or child and 28% with adults). Around 13 % reported that their private parts or breast were touched at school when they didn't want them to. One quarter of the female students reported that they were made to see pictures, magazines or movies of people or children doing sexual things at school.

Conclusions:

One case of abuse in our schools is a one case too many which should be studied and prevented from affecting another child in the future.

Key Words: Physical Abuse; Emotional Abuse; Sexual Abuse

Funding Agency: None



Ethics

Category: Clinical

50

Free donors are not really free

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Introduction:

Balancing the escalating demand for organs against the supply remains one of the big issues facing the transplant community. In Kuwait, a controlled living unrelated committee was initiated in 1999 allowing unrelated donors to donate kidneys according to Kuwait transplant law of 1987, which prohibits organ sale but allows altruistic donation. To further boost the availability of organs from live donors, incompatible directed living unrelated kidney donors are offered the option of being placed in the list of free non-directed donors. Previous work at our center revealed that around 48% of the donors that agreed to be free donors eventually proceeded to kidney donation. The aim of this study is to assess the patterns, amounts, and circumstances of any cash payments made by recipients to their free donors.

Methods:

Data from the living unrelated ethics committee at Hamed Al-Essa Organ Transplant Center from 22/7/08 till 2/2/10 was reviewed. Recipients that received organs from free donors were contacted to enquire about whether they paid the donors any money for the donation.

Results:

18 committees were held during the study period. Out of 207 potential donors interviewed, 125 (60%) were accepted to be donors. 40 of them were later found to be medically unfit for donation and another 40 (32%) were found to be incompatible for the designated recipient (incompatible ABO, positive crossmatch, and recipient death or medical unfitness for surgery). These donors were offered the option of being a free donor matched to the most compatible patient in the waiting list. Initially 5 refused to be free donors and another 7 (total 12, 30%) later changed their mind and were excluded. With additional investigations, 9 (22.5%) were found to be medically unfit for donation (Proteinuria, HTN, high GTT, abnormal anatomy on CT). Of the remaining 19 potential free donors (47.5%), 16 already underwent surgery and 3 are scheduled and awaiting. The recipients from those 16 free donors were contacted to verify that donors were not paid. Only one donor from the 16 did not ask and refused to take money. Nine did not ask, but did not refuse honorary money award when given, and the remaining 6 donors actually negotiated the price with the recipient before donation. Average money paid was \$21,000 (\$14,000 - \$28,000). This alarming data has lead us to contact the medical authorities in Kuwait to re-evaluate the whole process of living-unrelated donation and to come up with new recommendations and selection criteria.

Conclusions:

Living Unrelated Donation, even if non-directed can still be abused into commercialism. One way to avoid this problem might be to not allow free donors to meet recipients before or after donation.

Key Words: Kidney donation; Living unrelated; Commercialism

Funding Agency: self fund



Forensic Science

Category: Graduate MSc (Basic Science)

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Patterns of accidental death in Kuwait, 2003-2009

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Introduction:

This study addresses patterns of accidental deaths in Kuwait, 2003-2009. Reviews of data that the Department of Forensic Medicine (DFM) has collected can be used to improve the public's health.

Objective The objectives of this study include: 1) to compile and review medico-legal cases of accidental deaths in Kuwait from 2003-2009; 2) to compare manner of death to locality, sex, and age; and 3) to facilitate a discussion on preventative measures to reduce unnatural deaths.

Methods:

Data was compiled from cases referred to the DFM for medico-legal examination, 2003-2009. A total of 4,886 accidental death cases were sorted accordingly: by the governorate in which the death occurred, sex, age, ethnicity, and the type of accidental death.

Results:

This study determined that accidental deaths are the major cause of unnatural deaths in Kuwait, constituting 86.7% of unnatural deaths. RTA was the major cause (64.6%) of death in accidental deaths followed by other unnatural deaths: falls from height (13.1%), drug over dose (6.2%), burns (5%), asphyxia (2.8%), occupational injury (2.5%), drowning (2.2%), electric shock (1.4%), mine explosions (1.2%), and poison (1%). According to sex, males outnumber females in all categories; also non-Kuwaitis outnumber Kuwaitis in all categories of death except drug overdose.

Conclusions:

There is highly significant difference in various death categories when the governorates, gender, ethnicity, and marital status are considered. This study demonstrates the need for the strengthening of public health education campaigns that target unsafe practices in the private and public sector alike.

Key Words: Accidental Death; asphyxia; RTA

Funding Agency: None



Forensic Science

Category: Graduate MSc (Basic Science)

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The value of virtual Autopsy in gunshot injuries

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Introduction:

Virtual autopsy is a new, non-intrusive form of performing post-mortem examination in forensic investigations. This technology can utilize post-mortem multi-slice computed tomography (MSCT) and magnetic resonance imaging (MRI) with the purpose of achieving a detailed scrutiny of the body. Radiological examination is invaluable in the forensic investigation of gunshot injuries and is universally used to locate the missile, identify the type of ammunition, document the pathway of the missile, and assist in its retrieval.

Objective

The objective of this study is to evaluate the effectiveness of CT and MRI as diagnostic procedures, in comparison with conventional autopsy, in the forensic investigation of gunshot wound victims.

Methods:

Data was collected in Detroit Medical Examiner Office, Michigan, United States. Thirty bodies of gunshot wound victims were studied using post-mortem pre-autopsy imaging (18 male, 12 female, mean age 40.6 years). Data were interpreted at a three-dimensional workstation by radiologists using CT scanning and MRI. The radiologists did not have access to the autopsy findings. Images were evaluated and compared with autopsy findings.

Results:

MSCT aided in the accurate identification of all lethal injuries, and metallic fragments were precisely located in every case. In eight subjects sustaining chest wounds, MSCT assisted in confirming that the chest was the site of the lethal injury. However, in two of the cases, it failed to recognize the specific site of thoracic hemorrhage. In sixteen cases, MSCT helped in the precise identification of the injured organs, lethal wounds, and the number of wounds. Yet, in four cases of craniofacial injury, the pathway of the wound was not clear.

Conclusions:

In consideration of the above mentioned facts, MRI and MSCT have the ability to play an important role to assist in the prediction of site and number of lethal wounds as well as the location of metallic fragments.

Key Words: MRI; MSCT; Virtual Auopsy

Funding Agency: None



Forensic Science

Category: Basic Sciences

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Racemization of Aspartic Acid as a Tool for Age Estimation

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Introduction:

Age estimation in living subjects, cadavers, and human remains may elucidate matters with considerable legal and social consequences. Amino acid racemization (AAR) is one of the most reliable methods of age estimation. The present study investigated the application of racemization of aspartic acid in dentin root in a Kuwaiti population. The objective of this work is to establish a reliable method of age estimation based on the conversion of D-L aspartic acid using root dentine.

Methods:

A total of 89 upper first premolar teeth were divided into 2 groups, a test group (50), and a validation group (39). Analysis of the D/L ratio for aspartic acid in dentin was conducted by an HPLC system. The estimated age was assessed from the D/L ratio employing the formula: $\ln [(1+D/L) / (1-D/L)] = 2kt + A$.

Results:

A linear regression line was established between AAR and age. The racemization age "t" of each subject was calculated by applying the formula: $\ln [(1+D/L)/(1-D/L)] = 0.003181 t + (-0.01591)$ and correlation coefficient R was 0.9647. Standard error (SE) was ± 1.26 years. Among the test group, estimated age was equal to chronological age in 26/50 cases. Age was calculated in the validation group as follows: Estimated age "t" = $\{\ln[(1+D/L)/(1-D/L)] + 0.01591\} / 0.003181$, the range of error was less than one year in 82.1% of the cases, and between 3 and 4 years in 5.1%.

Conclusions:

The current work is the first to investigate the correlation of AAR and age estimation in the Middle East in a fairly large series of 89 first premolars. It has established a reasonably significant correlation of the D/L ratio with age, and proposed an apparently reliable formula for calculating the age through AAR. Our findings have demonstrated that HPLC technique can be able to provide reliable results. Further research is required to find out whether similar findings are applicable to other populations.

Key Words: Aspartic acid; Racemization; Age estimation

Funding Agency: None



Genetics

Category: Basic Sciences

54

Optimization of DNA extraction protocol for Hamour (*Epinephelus coioides*)

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Introduction:

Molecular techniques have been applied in stock assessment and identification of many species. DNA quality is an essential prerequisite for molecular studies. However, Extraction techniques may differ depending on tissue type and period of sample preservation. In this study, Hamour (*Epinephelus coioides*) was the target species. Several genomic DNA extraction techniques were optimized for different tissues (liver, muscle, scales and fins). Extraction technique optimization was also conducted on fresh or preserved tissues.

Methods:

DNA was extracted from 28 Hamour samples (Kuwaiti, Iranian and Pakistani). Samples were dissected and tissues (liver, muscles, scales and fins) were preserved at -80C, absolute ethanol or 95% ethanol-100 μ M EDTA pH 8.0. Four different extraction protocols (Wizard gDNA purification kit, Proteinase K conventional method, Urea protocol and CTAB method) were used and optimized.

Results:

DNA yield and quality was evaluated using spectrophotometer and electrophoresis. As low as 30 mg was optimum for good DNA yield. The highest yield was obtained from liver followed by fins, scales and muscles. All the conventional extraction techniques were very effective with respect to DNA yield, time and Cost. Yet, they include a hazardous phenol:chloroform:isoamylalcohol step. Preserving the samples up to 8 months did not show any effect on the DNA integrity, however, preservation for two years showed a total degradation of gDNA.

Conclusions:

All the used methods and tissues were effective for DNA extraction but varied in the DNA yield. The highest gDNA yield was obtained from liver and the lowest from muscles. Good yield was obtained from non-invasive tissues (fins and scales). Total gDNA extraction is recommended to be from fresh or short term preserved tissues. Long term preservation is not idealistic for DNA isolation

Key Words: Epinephelus coioides; DNA extraction; fish

Funding Agency: this work was part of general activity No. FB062G



Genetics

Category: Graduate MSc (Basic Science)

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Autosomal dominant congenital cataract of a consanguineous Kuwaiti family revealed genetic and clinical heterogeneity discovered to have novel mutations in CRYGB gene

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Introduction:

Congenital cataract is a clinically-genetically heterogeneous lens disorder. Members of a Kuwaiti family diagnosed with autosomal dominant congenital cataract (ADCC) across three generations were clinically characterized by complete eye examination and screened for causative mutation in CRYGB gene. Three phenotypes were identified; lamellar, anterior polar & complete cataract.

Methods:

DNA was extracted for all family members and subjected to Whole genome linkage analysis (WGLA) using Affymetrix 250K Chip. WGLA of both healthy and patients was compared. The locus with the highest LOD score was thoroughly screened for potential gene related to lens development. The candidate gene was amplified using PCR, cloned, and sequenced to screen for the causative mutation.

Results:

WGLA showed that locus 2q34-36.1 harbours CRYBA2 gene, with the highest LOD score of 1.5. Sequencing CRYBA2 gene showed no alteration in the coding region or the exon-intron boundaries in patients. Therefore, locus 2q33-q37 with LOD score (1.49), harbouring γ -crystallin gene clusters CRYGA,B,C and D, was considered. All γ -crystallin genes were screened for mutation. Two novel heterozygous deletions were detected in CRYGB; intron1(58delG) and exon2(72delC) and a novel tri-nucleotide polymorphism in intron1 (11-13GGT>AAA). Heterozygous intron1(58delG) was detected in 4 affected members with lamellar cataract. Heterozygous 72delC was detected in 2 affected members, with either anterior polar or extreme cataract phenotype. One patient had a complete cataract found to be a compound heterozygote with 72delC and intron1(58delG) mutations. The novel, tri-nucleotide polymorphism in intron1(11-13GGT>AAA) was found to be maternally inherited to 2 affected daughters while the mother showed no clear eye abnormality. Therefore, the involvement of this polymorphism in ADCC is not clear. The 72delC mutation results in a truncated protein of 43 aa which preserved the first 24aa of wild type protein, a frame shift generating 19 random amino acids.

Conclusions:

We demonstrate the first complex mutation in CRYGB gene in ADCC. The genetic heterogeneity resulted in clear clinical presentation of the disease. This case will advance our understanding of the genotypic-phenotypic correlation of ADCC.

Key Words: Cataract; CRYBA2; Whole genome linkage analysis

Funding Agency: Kuwait University, Grants: YM10/09, GM01/01 & GM 01/05



Genetics

Category: Basic Sciences

56

Expression of CTLA-4 splice variants in autoimmune diseases

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Introduction:

Cytotoxic T lymphocyte associated antigen 4 (CTLA4) is a candidate susceptibility gene for the study of autoimmune diseases. Preliminary studies were carried out to explore the expression pattern of CTLA4 gene in autoimmune patients with Hashimoto thyroiditis (HPOT), Rheumatoid arthritis (RA) and Systemic lupus erythematosus (SLE), compared to healthy controls (HC).

Methods:

A total of 88 age, gender and ethnically matched individuals were recruited in this study. Hypersensitive capillary electrophoresis was employed to detect CTLA4 spliced forms. PCR amplification of patient cDNA was performed using CTLA4 specific primers followed by cloning and sequencing to distinguish various CTLA4 splice variants.

Results:

Six alternatively spliced variants of CTLA4 gene were detected in this study: 672bp, 562bp, 292bp, 277bp and 143bp. The 143bp and 292bp represent two novel splice variants. The shortest splice variant, 143bp, was found at higher frequency in both patients and healthy subjects. However, a decreased expression of the 292bp splice variant was observed in HPOT patients (4.5%) compared to HC (31.8%) and it was not detected in RA or SLE cases. The very rare 277 splice variant (Gene Bank: AY792514) was detected in 4.5% of both HPOT patients and HC. The 214bp variant was predominantly expressed in all 4 tested cohorts. While the full length, membrane bound, variant 672bp and soluble variant 562bp was detected in HPOT and HC but not SLE or RA.

Conclusions:

Our study highlights the occurrence of CTLA4 splice variants in pathogenesis of autoimmune diseases. SLE and RA seems to have the same pattern of expression of the CTLA4 variants while HPOT showed a similar pattern to the HC.

Key Words: SLE; RA; HPOT

Funding Agency: KURA Grant NM 01/07 and partially by HSC Shared facilities Grants GM 01/01 & GM01/05



Genetics

Category: Graduate MSc (Basic Science)

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The ESR1 gene amplification in breast cancer

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Introduction:

Around two thirds of Kuwaiti women with breast cancer are estrogen receptor positive. The reason behind this selection is not known. Estrogen receptor has two types; estrogen receptor alpha ($Er\alpha$) and beta ($Er\beta$), which may be involved in the resistance and aggressiveness of carcinomas. Recent finding demonstrated that amplification of ESR1 gene that encodes for estrogen receptor alpha ($Er\alpha$) at q25 of chromosome 6 was driving the expression of $Er\alpha$ in Caucasian breast cancer patients. This study was initiated to find out whether breast cancer in Kuwaiti citizens that largely express estrogen receptors could be driven by the same type of gene amplification.

Methods:

Eighty eight Kuwaiti breast cancer cases collected from Kuwait cancer control center (KCCC) were used in this study. Hematoxylin and eosin sections used to determine tumor type. $Er\alpha$ protein production was determined using immune reaction score (IRS) immunohistochemistry (IHC). While ESR1 gene copy number was investigated using chromogenic in situ hybridization (CISH) and quantitative RT-PCR (q RT-PCR).

Results:

We found that most (65.91 %) of the histological tumor types collected were invasive ductal carcinoma. $Er\alpha$ protein expressed in (69.32%) of samples. There was no ESR1 gene increase copy number or amplification using CISH in the eighty eight breast cancer samples. Only two samples were on the border line. While qRT-PCR result showed one ESR1 gene amplification and one gain.

Conclusions:

We concluded over-expression of $Er\alpha$ protein in our study is not driven by ESR1 gene increase copy number or amplification but other molecular pathways may be involved. More investigation is required to determine the definite prevalence of ESR1 gene amplification and ER α expression on transcription and translation levels.

Key Words: Estrogen receptor alpha (ER α); Breast cancer; Chromogenic in Situ Hyberdization (CISH)

Funding Agency: Research Administration



Medical Education

Category: Basic Sciences

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The relationship between medical disorders and oral diseases

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Introduction:

It is evident from earlier research that many chronic medical diseases and the majority of oral disease share common risk factors. Periodontal disease, caries, apical periodontitis are some of the oral diseases related to general health. Since many patients see their dentists on a regular basis the dentists also have a role in advising patients to visit a physician. Hence the main objective of this project was to examine the association between oral disease and general health based on panoramic radiographs and general health in a population admitted to Kuwait University Dental Centre. The hypothesis to be tested was, whether individuals exhibiting good oral health have fewer systemic diseases.

Methods:

General health was assessed from the medical history given by each patient when they were admitted. The number of reported diseases and serious symptoms were used to create a medical disorder index. One hundred patients was used for this pilot-study. The following parameters were assessed in the panoramic radiographs to create an oral index: periapical radiolucencies, caries, pericoronitis or other signs of longstanding infection, number of remaining teeth, root remains, amount of horizontal and vertical marginal bone loss and calculus deposits.

Results:

A significant positive correlation was found between the used oral index and medical disorder index (Spearman $r = 0.219$, $p < 0.05$). When the studied sample was divided into two groups based upon their number of oral diseases, the low oral disease group was affected by fewer medical disorders.

Conclusions:

The oral index used in this study appears to be suitable to give an indication of medical disorders in patients.

Key Words: Oral index; Medical disorder; Panoramic radiograph

Funding Agency: DP01/10



Medicine

Category: Clinical

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Impact of positive BK virus-kidney donors on renal transplant recipient outcome

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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 kidney donors with positive BK virus in blood and urine-both qualitative and quantitative PCR-, 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 ± 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 ± 4.2 years; mean body weight 68.2 ± 4 kgm and mean follow up duration 21.6 ± 4 months. The original kidney disease was diagnosed in 4 cases as APCKD, chronic interstitial nephritis, 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 .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. The mean basal creatinine was 108.8 vs. 116.4 mmol/L at the last follow up. 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. Further longer term and larger randomized studies are needed to evaluate this issue.

Key Words: Renal transplant; BK virus; kidney donor

Funding Agency: None



Medicine

Category: *Clinical*

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Legionella infection: An outbreak in organ transplant center

Al Otaibi T, Gheith O, Nampoory MRN, Halim M, Nair MP, Balaha MA, Abd-el-tawab K, Zakareya Z, Hosni W, Mokaddas E, Sawey M, Magdolina M
Hamed alessa OTC

Introduction:

Renal transplant recipients are particularly susceptible to legionella infections due to abnormalities in cell-mediated immunity. A causative relationship has been found between cases of hospital acquired legionellosis and isolation of the bacteria from the hospital water supply. Here, we describe an outbreak of nosocomial legionella pneumonia in renal transplant center during the last 6 months of 2009.

Methods:

Between July 2009 and January 2010 an outbreak of legionella pneumonia occurred among patients hospitalized in Hamed Al-Essa organ transplant Center of Kuwait. Patients were diagnosed by respiratory secretion culture obtained by bronchoscopy and/ or by its antigen in urine. Water sampling from different sites of the hospital water supply were positive regarding such organism. After the diagnosis of 1st few cases of legionella we adopted the policy of empirical anti-legionella drugs .

Results:

Out of 250 patients treated in our center during the same period, 40 patients developed respiratory symptoms with bilateral pulmonary infiltrates and 19 patients underwent bronchoscopy for their evaluation. Legionella pneumonia was proven in 20(50%). Most of patients developed respiratory symptoms within 11 days of coming to casualty; hence, the infection was hospital acquired. The incidence of legionella infection during that period was 20/250(8%) among all transplant patients. Three sub-clinical cases were diagnosed by antigen in urine. We observed significantly lower white blood count (especially natural killer cells among Kuwaiti patients ($p < 0.05$)).

Conclusions:

However, the type of immunosuppressive protocol had no significant impact on the prevalence .Conclusion Longer casualty stay, lower white cell count increase the risk of legionella infection. Early diagnostic, preventive and treatment measures, for patients and environment, led to successful termination of the outbreak.

Key Words: Legionella; Renal transplant; Infection

Funding Agency: None



Medicine

Category: *Clinical*

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Acute Antibody Mediated Rejection: Kuwait experience with Bortezomib

Al Otaibi T, Gheith O, Halim M, Said T, Nair MP, Balaha MA, Abd-el-tawab K, Zakareya Z, Hosni W
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Introduction:

The most vexing clinical condition caused by antibodies in organ transplants is antibody-mediated rejection (AMR), which can be found in 20% to 30% of episodes of acute rejection. The current antihumoral therapies (plasmapheresis, intravenous immune globulin, and polyclonal antilymphocyte antibodies, including rabbit anti-thymocyte globulin [rATG]) lack direct effects on the major antibody producing cell (the mature plasma cell). A growing dissatisfaction with the results of standard (AMR) therapies led to a search for antihumoral agents with activity against plasma cells. This search led to the identification of bortezomib- which was approved by FDA for the treatment of multiple myeloma -as an antiplasma cell agent. In addition to anti-plasma cell properties, it suppresses T-cell function. And therefore they also have potential for treatment or prevention of cell-mediated allograft rejection. Aim of the study was to assess the efficacy and safety of bortezomib therapy in the management of resistant AMR to the standard therapies.

Methods:

We had managed two kidney transplant recipients who developed resistant antibody mediated rejection after 2 years of transplantation. After completing the standard conventional protocol of therapy of AMR followed by conversion to more potent maintenance immunosuppression- without satisfactory response- each patient received one cycle of bortezomib (special protocol). The patient who had AMR with underlying chronic changes responded less than the other case with AMR alone.

Results:

The two patients were tolerating the drug without significant adverse effects till now -6months -with stabilized graft function and acceptable levels of anti-HLA antibodies.

Conclusions:

Bortezomib represents the first effective antihumoral therapy targeting plasma cells, provides effective treatment of AMR with minimal toxicity. Randomized controlled trial is needed to validate these findings.

Key Words: bortezomib; renal transplant; rejection

Funding Agency: None



Medicine

Category: *Clinical*

62

Reasons for elderly patient hospitalization: The impact of diabetes and other comorbidities

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Introduction:

Studies have shown that hospitalizations in elderly patients aged 65 and above are preventable. This study aimed to determine the main reasons for elderly patient hospitalization in Kuwait, and to analyze the impact of diabetes and other comorbidities on these hospitalizations.

Methods:

Data related to patients admitted to the Department of Internal Medicine in Al-Sabah hospital, from 1st January to 29th February 2008, were abstracted manually from the medical records.

Results:

Of all hospital eligible admissions during the study period (n=552), elderly patients accounted for 31.0% of patients. Among elderly patients, 52.6% were male and 80.1% were Kuwaiti. The most frequent reasons for hospitalization were cardiovascular diseases (47.4%) and respiratory tract diseases (29.2%). The most frequent specific diagnoses for hospitalization were pneumonia (19.9%), acute coronary syndrome (ACS) (18.7%), stroke (14.0%), heart failure (10.5%), and chronic obstructive airway disease (5.8%). Among elderly patients, prevalence of history of hypertension, diabetes, and dyslipidemia was 80.1%, 63.7%, and 53.2%, respectively, which is twice as high as patients aged <65 years. However, prevalence of smoking was lower in elderly patients compared to patients aged <65 years (23.2% vs. 36.7%; $p < 0.005$). Hospital stay was longer in elderly patients compared to patients aged <65 years (10.6 days vs. 7.7 days, respectively; $p < 0.005$).

Conclusions:

Elderly patients accounted for approximately one-third of admissions in the Department of Internal Medicine in Kuwait, with longer stay during hospitalization. The most frequent diagnoses of elderly patients were pneumonia and ACS. These findings support efforts to improve care for elderly patients, especially those with hypertension, diabetes, and dyslipidemia, and they highlight the need for primary and secondary preventive and therapeutic outpatient care strategies, particularly influenza and pneumococcal vaccinations.

Key Words: Diabetes; Elderly; Hospitalization

Funding Agency: None



Medicine

Category: Graduate (Resident)

63

Patients presenting to secondary emergency services: a comparison study between Kuwait and Ireland

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Introduction:

Many patients attending accident and emergency (A&E) in secondary care hospitals could be managed appropriately by general practitioners (GP). Inappropriate attendance of non urgent patients to A&E results in reduced efficiency of A&E departments. This study attempts to compare patients attending to two hospitals in two different countries

Methods:

A questionnaire aided by interview was conducted between August 2006 and July 2007 including a total of 500 patients presented to A&E departments of Al-Amiri (Kuwait) and Cork University hospital (CUH) in Ireland after excluding patients younger than 15 years old. Sampling was by convenience and the data were analyzed using Statistical Package for the Social Sciences.

Results:

Majority of patients were between 25-64 yrs old. 63.6% of patients presented to Al-Amiri hospital were non-GP referred compared to 58% of patients presented to CUH ($P=0.2$). 3.6% and 10% of patients came by ambulance in Kuwait and Ireland respectively ($P=0.004$). 39.6% of patients presented to CUH had both hematological and radiological investigations while 10% had no investigations compared to 24% and 23.2% in Kuwait. In Kuwait, 48.8% presented to A&E didn't require follow up compared to 19.6% in Ireland ($P<0.001$), and only 14.8% were admitted in Kuwait compared to 30.8% in Ireland. There was also significant difference in patients detained for observation in the two groups (Kuwait: 1.6%, Ireland: 17.2%, $P<0.001$).

Conclusions:

Regardless of GP referral rate, data showed that the majority of Irish patients needed further follow up, observation and admission maybe suggesting more appropriate self and GP referral. In conclusion, primary health services need to be audited to assure the important role of general practitioners as gate-keepers of the health system in Kuwait.

Key Words: primary care; gp referral; accident and emergency

Funding Agency: non



Medicine

Category: *Clinical*

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Validity and reliability of the European Organization for Research and Treatment in Cancer Quality of Life Questionnaire (EORTC QLQ): Experience from Kuwait using a sample of women with breast cancer

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Introduction:

Although the EORTC QLQ-C30 and its breast-specific module (BR-23) are widely used instruments, the few reports on their psychometric characteristics from Arab and neighboring countries involved limited analyses. Our objective was to assess the psychometric characteristics of both questionnaires using the responses of a larger sample of Arab women.

Methods:

Participants were consecutive clinic attendees at the Kuwait Cancer Control Center in stable clinical condition in 2007/8. The indices assessed were alpha coefficients, item- internal consistency (IIC), item - discriminant validity (IDV), and known-groups validity.

Results:

The 348 women were aged 48.3(10.3) years (range: 20 – 81). Majority (58.7%) were being treated for advanced disease (i.e., stages III and IV). They were predominantly married (89.9%), and in gainful occupation (87.9%). The comparison general population sample consisted of 95 women, age range: 23 -55, who were all married and in gainful occupation. The intra-class correlation for the test – retest statistic and the internal consistency values for the multi-item scales were > 0.7 alpha. With the exception of the pain subscale, all items met the IIC criterion of >0.4 correlation with the corresponding scale. For IDV, the BR - 23 performed better than the QLQ – C30. The scale scores discriminated significantly ($P < 0.001$) between patients at different disease stages, and between sick and well populations.

Conclusions:

With the exception of the pain subscale, the Arabic version of the questionnaires is psychometrically sound. We encourage their use in cancer QOL studies in the Arab world, in order to make for international comparability of data.

Key Words: EORTC QLQ - C30; Psychometrics; Arab

Funding Agency: None



Medicine

Category: Undergraduate

65

Spirometric assessment of lung function and evaluation of respiratory symptoms among the oil industry workers of Kuwait: A comparative study

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Introduction:

In the oil industry airborne pollutants are emitted into the workplace atmosphere during the refining process. Our aim in this study was to investigate the relationship between working in the oil industry, prevalence of respiratory symptoms and lung function among the employees.

Methods:

This comparative cross-sectional study was conducted using a supervised self administered questionnaire, spirometry, and height and weight measurements. It was performed on 287 male employees. The employees were classified into two groups: oil industry workers and office workers. For statistical analysis, Chi-square test, Fisher's exact test, and the student t-test were used. In addition, to adjust for certain confounders, multiple logistic regression, was used.

Results:

In general, the study found that history of respiratory diseases was more common in office workers. Of the respiratory diseases studied, pneumonia and asthma were statistically significant. Office workers also reported more respiratory symptoms than the oil industry workers. However, of the reported symptoms, only wheeze and shortness of breath were statistically significant. After re-categorization of symptoms, further analysis confirmed that 21% of the workers in the oil industry reported having at least one symptom, in comparison to 40.7% of the office workers. Analysis of symptoms in relation to smoking status demonstrated a significant association between having ever smoked and the presence of at least one symptom. It was found that 28.7% of the industry workers and 39.2% of the office workers had some form of pulmonary impairment.

Conclusions:

This study found that respiratory diseases and symptoms were higher among office workers than oil workers. Smoking was significantly associated with reporting respiratory symptoms in oil workers. Mean FEV-1 and median FEV-1/FVC ratio were normal in both groups but significantly lower in office workers.

Key Words: Oil Industry; Spirometry; Respiratory Symptoms

Funding Agency: None



Medicine

Category: Clinical

66

Steroid resistant T-cell mediated acute cellular rejection: risk factors and impact on graft and patient survival

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Introduction:

Acute rejection in renal transplantation was 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 were 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 it did not affect either patient

Key Words: -; -; -

Funding Agency: None



Medicine

Category: Clinical

67

Zero-HLA mismatched renal transplants – A Single Centre Experience

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Introduction:

Background: The evidence that antigens of the HLA system provide the major barrier to acceptance of renal transplants was first obtained with living-related donor transplants. Graft survival was superior in sibling pairs having both the same serologically defined HLA antigens. However, an intermediate level of graft survival was reported in haploidentical parent to child or sibling to sibling transplants. Therefore the compatibility at all three HLA loci is desirable for optimal graft outcome.

Aim: - To assess the long-term outcome of HLA zero-mismatched renal transplant recipients in Kuwait.

Methods:

From 1993 to 2010, 1050 renal transplants were performed in Hamed Al-Essa Organ transplant center, including 40 (3.8%) kidney transplant recipients with zero-HLA mismatches. All of them received their initial transplants. There were 21 (52.5%) males, 19 (47.5%) females with their mean age 28.8 ±7.1 years (range 7-53 yrs). The primary renal disease was chronic glomerulonephritis (GN) in 17 (42.5%), chronic tubule-interstitial nephritis in 12 (30%), diabetes mellitus in 2 (5%) and idiopathic in 9 (22.5%). All recipients had negative B and T cell lymphocytotoxicity cross match prior to the time of transplantation. Without induction, they were maintained on triple immunosuppressive protocol based on steroid, antiproliferative agent (azathioprine or mycophenolate mofetil) and calcineurin inhibitor (cyclosporine or tacrolimus).

Results:

Mean follow up period was 8.76±2.1 years and the mean serum creatinine on last follow-up was 112 umol/L (range 51 to 186 umol/L). Graft survival was 100%, 97.2%, 93.9% and 84% at 1, 3, 5 and 10 years respectively with 100% patient survival during the whole follow up period. Four grafts were lost during the follow up period due to chronic rejection. Biopsy proven acute rejection represented 5% (2 episodes) during the 1st year after transplantation with complete response to pulse steroid. There were in total, 3 (7.5%) cases of post transplant GN, 2 being recurrent diseases (lupus nephritis and IgA nephropathy) and the third, a case of denovo membranous GN. Post transplant diabetes and hypertension were reported in 6 and 2 patients respectively .There were no cases of post transplant malignancy.

Conclusions:

Favorable patient and graft outcome was observed in zero-mismatched renal transplant recipients possibly related to less post-transplant co-morbidities.

Key Words: -; -; -

Funding Agency: None



Medicine

Category: *Clinical*

68

Vitamin D level in Kuwaiti subjects with type 2 diabetes

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Introduction:

In the past several years, vitamin D has received an enormous renewal of attention, at various health levels. Recent literature suggests a link between vitamin D deficiency and several disorders including diabetes mellitus. Insulin resistance and impaired insulin action have also been found to be prevalent in vitamin D deficiency. Data on vitamin D status in Kuwaiti subjects with insulin resistant type 2 diabetes are not known.

Methods:

We studied 69 Kuwaiti subjects with type 2 diabetes and 60 normal control Kuwaitis. Patients and controls were matched for age and sex. Patients were included in the study if they are either treated with diet or oral antidiabetic agents. After overnight fasting, blood was collected for the measurement of parameters of glycemia (glucose, insulin and HbA1c), parameters of calcium homeostasis (corrected serum calcium, phosphate, alkaline phosphatase (ALP)), serum 25-hydroxyvitamin D (25OHD) and parathyroid hormone (PTH) level.

Results:

Patients had significantly elevated fasting glucose ($P=0.001$), insulin ($P=0.0003$) and HbA1c (0.005) than controls. Patients and controls had similar levels of serum calcium and ALP, whereas serum phosphate was significantly lower in the patients (patients versus controls, mean \pm SEM, 1.1 ± 0.02 vs. 1.23 ± 0.02 mmol/l, $P=0.0001$). Patients and controls had similar 25OHD levels (25.4 ± 2.1 vs. 21.6 ± 2.0 nmol/l, $P=0.09$) but levels of 25OHD in all were in the deficiency range (WHO reference of normal concentrations). PTH levels were similar in patients and controls. 25OHD correlated negatively with PTH ($r=-0.4$, $P=0.02$), but did not demonstrate any relation with fasting glucose, insulin, BMI, HbA1c, corrected ca, phosphate or ALP.

Conclusions:

Although the studied subjects had vitamin D concentrations in the deficiency range, levels of vitamin D did not differ in the diabetic insulin resistant subjects compared with controls. Insulin resistance in Kuwaiti diabetic do not seem to have an influence on vitamin D levels.

Key Words: Vitamin D; Diabetes; Type 2

Funding Agency: None



Medicine

Category: *Clinical*

69

Preliminary observations on relationship of Vit D and clinical phenotypes in Kuwaiti patients with multiple sclerosis.

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Introduction:

Vitamin D deficiency is endemic in Arabian Gulf countries, including Kuwait; reports are suggestive of important associations between vitamin D deficiency and prevalence multiple sclerosis (MS). This cross-sectional, retrospective study attempts to evaluate vitamin D levels, effects of its deficiency on biochemical & radiological markers of bone metabolism in MS patients; extent of influence of vitamin D deficiency on the clinical presentation & phenotypes of MS patients.

Methods:

Medical records of 45 patients fulfilling Mc Donald criteria and followed up in a national MS clinic in Kuwait were reviewed. Different biochemical indices including indices of calcium homeostasis, total 25-OH-Vitamin D (VitD2 and D3) (VitD) status, blood marker of bone osteoblastic activity (osteocalcin) & urinary markers of bone osteoclastic activity [total & free pyridinoline crosslinks–pyridinoline (PYD) & deoxypyridinoline(DPD); type 1 collagen N-terminal telopeptides(NTx) were assessed.

Results:

Mean age and age at presentation of the cohort was 35.58±11.84 and 29.33±12.27, respectively. Female vs male ratio was 2:1. Median duration of the disease was 5years (range = 1-19years). Relapsing–remitting (RR) disease course was most common (82.2%) followed by relapsing progressive (RP;17.8%). Most of the patients (62.2%) had an Expanded Disability Status Scale<3. Level of VitD was found below normal in 82.2% of patients. No correlation was found between VitD level & osteocalcin and/or PYD, DPD, and NTx in this cohort. No significant difference in VitD level was found between RR & RP patients. However, Ntx level was significantly ($p<0.01$) higher in RP vs RR patients (median:range=90.75:25.57-116.51 nm BCE/Mm vs 34.49:10-122.28 nm BCE/Mm, respectively).

Conclusions:

This study suggests VitD deficiency is prevalent in MS patients irrespective of disease course. No correlation was found between VitD level & EDSS; however number of patient with advanced disability is small. Higher Ntx level in RP patients suggests more bone resorption.

Key Words: 25-OH-Vitamin D; Bone osteoblastic activity; Expanded Disability Status Scale

Funding Agency: Kuwait University #mm 03/09



Medicine

Category: *Clinical*

70

Paradigm shift - fasting Glucose, HbA1c and Estimated Average Glucose as Screening and Diagnostic tests in a high risk population

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Introduction:

Recently HbA1c was included in the criteria for diagnosis of diabetes - HbA1c of $\geq 6.5\%$ is diagnostic, HbA1c of 5.7% to 6.4% identifies prediabetes. Converting HbA1c to estimated average glucose values (eAG) might help understanding and interpretation of HbA1c. This study evaluates and compares the utility of fasting Glucose, HbA1c and eAG as screening tests for undiagnosed diabetes and the metabolic syndrome (MS) in healthy first degree relatives (FDR) of patients with Type 2 diabetes.

Methods:

We measured fasting glucose, HbA1c and calculated eAG in 575 (232M, 343F) in the FDR classified by the IDF criteria for the MS. Receiver operating characteristic curve (ROC) analysis was used to examine the diagnostic performance characteristics for DM and MS.

Results:

At standard cut offs for glucose, HbA1c and eAG, the relative prevalence of undiagnosed diabetes in the FDR were 16/575 (2.8 %) for glucose, 66/575 (11.5%) for HbA1c and 62/575 (10.8%) for eAG. At standard cut-offs, the prevalence of impaired fasting glucose (IFG) was 55/575 (9.6%), 195/575 (33.7%) and 437/575 (76%) for glucose, HbA1c and eAG respectively. Using the ADA glucose diagnostic criteria as reference, the areas under the ROC (0.989; 95% CI (0.874 – 0.982)) for diagnosis of DM were the same for HbA1c and eAG. HbA1c and eAG also had the same ROC areas for the diagnosis of IFG (0.719; 95% CI = 0.647 – 0.791, respectively) and the MS (0.678 (95% CI = 0.600 – 0.756)). The ideal cut-off points with the highest sensitivity (100%) and specificity (65%) for diagnosis of DM in our cohort were HbA1c = 5.9% and eAG = 6.7 mmol/L. These values are different from recommendations in international guidelines.

Conclusions:

We conclude that there are significant differences in the number of undiagnosed diabetic subjects identified by screening with glucose, HbA1c and eAG. HbA1c and eAG are potentially useful tools for diagnosing subjects who are unaware of their glucose tolerance status.

Key Words: Fasting Glucose; HbA1c; Estimated Average Glucose

Funding Agency: KFAS grant 2004-1302-03



Medicine

Category: Clinical

71

Plasma Leptin in kidney transplanted patients during the early post transplanted period

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Introduction:

Leptin is a 16 KD protein that is encoded by the ob gene and secreted by adipocytes. Leptin is primarily cleared from the circulation by the kidney and elevated plasma leptin are reported in uremic patients. The present study aimed to assess plasma leptin concentrations in patients with kidney transplant during the early post renal transplant period.

Methods:

Serum leptin were measured in 30 ESRD patients undergoing renal transplant (22 males and 8 females), 20 subjects as a control (17 males and 3 females).

Results:

This study showed hemodialysis patients (pre-transplant patients) had significantly lower mean BMI than the control subjects. The study showed the mean serum leptin concentration in hemodialysis patients (pre-transplant patients) was higher than the control subjects. Our study showed that post-transplant patients had mean serum leptin concentration similar to the control subjects and significantly lower than the hemodialysis patients (pre-transplant patients). This study showed serum leptin levels are correlated positively with BMI in all groups and significantly decreased in post-transplant than pre-transplant. There was correlation between serum leptin and age in pre-transplant group while no correlation in post-transplant group. This work showed that there were no correlation between serum leptin and parameters commonly used to assess the extent of renal function. Our data revealed higher serum leptin levels in females than males' inspite of similar BMI.

Conclusions:

leptin may play an important role in improvement of anorexia, weight gain after normalization of renal function after renal transplantation.

- i Factors other than excretory capacity of the transplanted kidney are apparently in the post transplant decrease of leptin concentrations.

Key Words: Leptin; Renal; Transplant

Funding Agency: None



Medicine

Category: *Clinical*

72

Kidney transplantation in the elderly

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Introduction:

The number of elderly patients accepted in renal replacement programmes is increasing. There is a general agreement that age per se does not constitute a contraindication to transplantation. Yet many centres are still reluctant to accept patients >60 years old, as they are frail, have more comorbid conditions and their overall life expectancy is lower.

Methods:

This study is a retrospective case control analysis study in elderly patients (Group I; >60 years). Data were collected from 11/1993 till 5/2005. Data were compared to those obtained in patients (Group II) who were matched for HLA mismatches and time of follow up but not with recipients' age (20-50). Primary end points are graft loss and/or patient death, while secondary end point are cerebrocardiovascular events, malignancies or rejection.

Results:

Thirty-two patients with mean age (\pm SD) 63.4 (\pm 3.2), ranged from 60 to 73 years old (11 females and 21 males) were compared with 32 patients with mean age (\pm SD) 33.5 (\pm 7.46) ranged from 21 to 50 (11 females and 21 males). There is no statistically significant difference between the 2 groups in the result of mean s.creatinine after 1 year while mean s.creatinine after 3 years in Gr II is significantly higher than Gr I ($p < 0.003$) and prevalence of malignancy was similar in both groups (one patient in each group). Seven graft were lost in Gr I (6 due to patient deaths and 1 from trauma) while only 1 was lost in Gr II (due to renal vein thrombosis) ($p < 0.01$).

Conclusions:

Elderly age was associated with lower number of graft losses due to rejection, while they had higher death rate result in significantly worse overall renal transplant survival.

Key Words: Kidney; Transplant; Elderly

Funding Agency: None



Medicine

Category: Clinical

73

Community eye health initiative in Kuwait: A strength, weakness, opportunities and threats (SWOT) qualitative analysis

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Introduction:

Recently, we introduced the Kuwait University Community Eye Health Initiative (CEHI) projects after the strategic review of eye care services in the country. The primary aim of the initiative is to join the national, regional and international efforts in preventing avoidable blindness as part of the educational responsibility of the university, its vested interest in research and its contribution to community service in an evidence based approach.

Methods:

The objective of this work is to present a SWOT analysis of the newly introduced CEHI. Interviews of 30 key-informants (clinicians, nurses, administration staff, patients, and carers) were completed in Kuwait focusing on the CEHI in October 2010. The SWOT framework (strengths, weaknesses, opportunities, and threats) was applied to categorize the emerging themes and provide a strategic direction for the profession.

Results:

Informants reported that strengths included motivation of the ophthalmic care providers, collaboration with the primary health care providers, establishment of national Non Governmental Organization (NGO), and the international partnership with International Agency for the Prevention of Blindness IAPB. Weaknesses included lack of education and professional resources especially in areas of primary eye care, low vision, and rehabilitation. Quality of Care Assessment is completely missing and would affect having measurable outcomes of the initiative and its impact. Opportunities discussed were the potential role of the Kuwaiti board of ophthalmology curriculum and the ophthalmology society activities focusing on community eye health, prevention, and early screening schemes. Threats addressed were possible public misperception of risk factors and creating a panic element, in addition to the inter professional communication gaps.

Conclusions:

Our research indicates that many unique opportunities exist to introduce community eye health programs in Kuwait and that genuine efforts to identify standards for these programs can benefit from international evidence-based support to achieve the right to sight for all.

Key Words: Community Eye Health; SWOT analysis; Prevention of Blindness

Funding Agency: Fawzia Al-Sultan Rehabilitation Institute (FSRI)



Medicine

Category: *Clinical*

74

Detection of transfusion transmitted virus (tt virus) in body fluids and secretions of Egyptian volunteer blood donors

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Introduction:

Transfusion transmitted virus (TT virus) was identified in patients with post transfusion hepatitis in Japan. It shares several characteristics with parvovirus. Several genotypes and subtypes of TT virus have been isolated, also it replicates in a manner that generates extensive sequence heterogeneity so it is a chronic virus that can persist for years and can mutate inside the body. TT viraemia is frequent in blood donor populations and high prevalence of TT virus has been found in patients exposed to blood.

Objective:

Detection of TT virus in serum, some body fluids and secretions of Egyptian volunteer blood donors.

Methods:

Serum samples were collected from 65 apparently healthy blood donors without clinical or biochemical (normal transaminases) evidence of hepatitis (45 males and 20 females with mean age $32 \pm SD 10$ years). Serum samples from all subjects were tested by PCR (polymerase chain reaction) to detect TT virus pure gene DNA. Positive subjects were further studied for detecting TT virus DNA in urine, saliva, breast milk (from lactating mothers) and semen (from adult males).

Results:

The results showed that 12 out of 65 (18.4%) serum samples were positive for TT virus (8 males 12.3% and 4 females 6.1%). Saliva and urine (from 12 positive patients) were positive for TT virus DNA in 50% and 58.3% respectively. All tested breast milk and semen samples were negative for TT virus.

Conclusions:

TT virus was common in a group of Egyptian volunteer blood donors and TT virus might be transmitted by urine and saliva.

Key Words: Transfusion transmitted virus (TT virus); Post transfusion hepatitis; TTV

Funding Agency: None



Medicine

Category: *Clinical*

75

Critical illness polyneuromyopathy in renal transplant recipients

Gheith O, Al Otaibi T, Abdelhalim M, Said T, Nair MP, Balaha MA, Abd-el-tawab K, Zakareya Z, Hosni w, Nampoory MRN
OTC hamed al-essa

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 in other prospective studies included: 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, vasopressor and 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.

Aim: 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- during the period between August 2009 and March 2010 – 22 of them necessitated mechanical ventilation following diagnostic broncho-scopic aspiration and lavage. All patients presented by cough, dyspnea, hypoxia, and low grade fever. Of them seven cases developed acute onset of flaccid tetra paresis with deep hyporeflexia and failure to wean from mechanical ventilator. We managed sepsis aggressively in all cases and this was in agreement with most authors who agree that it is the most important measure to reduce the incidence of CIP/CIM.

Results:

Nutritional interventions were started earlier with supportive albumin infusion and Intravenous immunoglobulins (IVIG) for all patients. We tried to avoid hyperglycemia using insulin therapy to maintain strict glycemic control. Our lines of management were supportive, initially consisted of aggressive pulmonary hygiene in addition to prevent secondary complications of immobility such as bed sores, deep venous thrombosis and superimposed compressive neuropathies and finally all cases survive in good humor .

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.

Key Words: *Critical illness myopathy; Renal transplant; Management*

Funding Agency: *None*



Medicine

Category: Basic Sciences

76

Relationships between occupational roles and quality of life among Kuwaiti women living with chronic neuromuscular conditions

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Introduction:

Neuromuscular injuries are among the leading causes of disability among adults. The impact of these injuries on an individual is unanticipated. A disability can leave a person with residual impairment of physical, psychological and social functions. The purpose of this study is to investigate the quality of life of Kuwaiti women living with chronic disabilities.

Methods:

A cross-sectional design was used to determine the relative impact of functional impairment and occupational roles on the quality of life of Kuwaiti females living with chronic conditions. The study included 50 community living Kuwaiti females with chronic disabilities who are at least one year post injury. Standardized assessment were used. The data analyzed with SPSS version 15.

Results:

The mean overall Quality of Life score was (17.3), indicating moderate quality of life, and was lower than those of other stroke studies. The mean score for the health and functioning subscale of the QLI was the lowest of the four subscales (13.4). Psychological and Spiritual subscale of the QLI was (16.88). Whereas, the family subscale had the highest mean (25.4). The mean Barthel Index score was (75) indicated mild disability. Occupational role checklist showed that most Kuwaiti stroke had limited participation in various occupational roles.

Conclusions:

Health care practitioners in non western Islamic countries such as Kuwait have special needs with respect to women with chronic disabilities and that their needs with respect to optimizing QOL may be distinct to other groups. Studies related to the relationship between QOL and disability, are mostly based on western people. The experiences and needs of people with disabilities in Arab Muslim countries may be more pronounced than in western countries given gender roles in Muslim countries. Our results may help elucidate ways in which QOL may be enhanced in Kuwaiti women beyond a singular focus on impairment level.

Key Words: Quality of Life; Neuromuscular injuries; Occupation

Funding Agency: None



Medicine

Category: Graduate MSc (Basic Science)

77

Detection of cold reactive antibodies in pregnant women and in patients who are going for surgery

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Introduction:

Antibodies that react below 37°C are considered clinically insignificant because they do not affect the clearance of antigen-positive red cells in vivo. However, they can cause considerable frustration in routine testing. Antibodies that maybe expected in the colder range of temperature include A1, H, I, IH, Lea, Leb, P1, M and N. Although identification of the cold reactive antibody is not of clinical significance, recognition of its presence will aid in selection of procedures to avoid interference of cold antibody with antibodies screening and cross match. Cold antibodies maybe detected in the serum of many normal persons if they are tested under the right condition. However, most of this antibody is benign cold agglutination that shows optimal reactivity at 4°C and little or no reactivity at 37°C. Some studies show that cold antibodies are found in patients for surgery and pregnant women for delivery
Objective: To investigate if there is an association between cold reactive antibodies in pregnant women for delivery and in patients for surgery.

Methods:

The data that had been collected last year of 2010 in Kuwait Central Blood Bank, RBC Serology Lab. Section showed that cold reactive antibodies was investigated by using Pre-Warm Technique and Rabbit Erythrocyte Stroma (REST) Adsorption Technique.

Results:

There were 2100 patients that are positive for antibodies and out of this number, 250 patients were found to be reactive to cold antibodies. Statistics showed that 40% were patients who are going for surgery with different cases, 42% were pregnant women for delivery and the remaining 18% were found to be from other cases.

Conclusions:

Cold antibodies are mainly found in patients who are going for a surgery such as Coronary Artery Bypass Graft and pregnant women. When cold agglutinins are detected, one or more cold reactive antibodies or even significant antibodies can often be identified.

Key Words: Cold antibody; Cardio by pass; Cold agglutination

Funding Agency: None



Medicine

Category: *Clinical*

78

Post-Transplant glomerulonephritis in live-donor renal transplant recipients: clinical course and risk factors

*Mansour HA, Akl AI, Wafa EW, Adul ELReheem M, Salem ME, El-Shahawy EE, Ghoneim MA
Mansoura UNC

Introduction:

Glomerulonephritis (GN) post transplantation can be either De novo or recurrence of original disease. The graft outcome among recipient with post transplant GN is not well identified.

Methods:

Out of 2000 transplant recipients who were transplanted between 1976 to 2007, 250 patients (157 males, 93 females) suffered from pre-transplant end stage GN (35 mesangial, 22 membranous, 71 FSGS, mesangio-proliferative, 16 crescentic, 48 hereditary, 33 amyloidosis). Donors were 77% related and 23% unrelated. Those patients were compared with the remaining recipients. Patients suffered post transplant GN were classified into 2 groups according to their graft biopsy histopathological findings. Graft survival was calculated using Kaplan Meier and Multivariate risk factors analysis was done using Cox ph.

Results:

22 patients suffered recurrent GN, 8 De-Novo GN and 33 transplant glomerulopathy. De-Novo GN suffered from hypertension compared to recurrent GN. 50% of DeNovo suffered from diabetes, while only 5% among recurrent GN. There was a significant difference in graft survival among the different post-transplant GN groups. Recurrent GN displayed a worse graft survival compared to De-Novo and transplant glomerulopathy GN. Middle aged donor, different recipient/donor blood group and sirolimus based regimen were among risk factors for post transplant.

Conclusions:

Unfortunate GN does not end by renal failure but it may continue after transplantation. Early identification of De novo & recurrent GN post-transplantation and consequent management are critical issues for graft survival.

Key Words: Glomerulonephritis; Transplantation; Liverelated

Funding Agency: None



Medicine

Category: *Clinical*

79

Chronic active antibody mediated rejection (CAMR) in renal transplant recipients: Is intervention justified?

Nair MP, Al-Otaibi T, Nampoory MRN, Said T, Halim MA, Moneim MA, Elsayed A, Nawas KM, Vareed B, Geith O.

Hamed Al-Essa, Organ Transplant Center, Kuwait.

Introduction:

Recent data showing the association of circulating antiHLA antibodies and C4d deposits in peritubular capillaries (PTC) in chronically failing renal allografts indicate a pathogenic role of humoral mechanisms leading to CAMR in a subset of patients with chronic allograft dysfunction. Therapeutic strategies for acute antibody mediated rejection have been fairly established but the treatment of CAMR is generally unknown. Our aim was to conduct a pilot study on 5 patients with CAMR by treating them with a new protocol and to see the effectiveness of the treatment

Methods:

5 renal transplant recipients fulfilling the diagnostic criteria of CAMR (Banff 07) were recruited for the study and were given the following treatment- a) maximise immunosuppression, b) daily plasma exchange (PE) for 5 days, c) intravenous immunoglobulin 25 gms per day for 5 days and d) Rituximab 1gm IV for 2 doses at 14 days interval. These patients were followed up prospectively for a period of 1 year from the time of starting treatment by monitoring renal function.

Results:

All the five patients on follow up were found to have stable or no significant deterioration of their graft function in terms of serum creatinine and estimated GFR. The mean pretreatment serum creatinine and estimated GFR were 208.8 $\mu\text{mol/L}$ and 42.3 ml/mnt and mean posttreatment serum creatinine and estimated GFR were 221.8 $\mu\text{mol/L}$ and 41.8 ml/mnt respectively.

Conclusions:

We conclude that our pilot study was found to be effective in treating CAMR and to stabilize renal function. Larger studies are needed to establish the effectiveness of our study

Key Words: Chronic active antibody mediated rejection; Renal transplant; Immunosuppression

Funding Agency: None



Medicine

Category: *Clinical*

80

Renal transplantation in nephropathic cystinosis

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Introduction:

Nephropathic cystinosis is a rare autosomal recessive storage disease with abnormal cystine accumulation within lysosomes, primarily manifesting as progressive renal failure. Renal transplantation corrects renal failure and prolongs survival but the disease may develop in the allograft and continue to progress in nonrenal organs in those who have not received the cystine depleting agent cysteamine.

Methods:

We present 4 patients with nephropathic cystinosis, 3 males and 1 female who received 5 renal transplants during the period from 1977 to 2006.

Results:

Patient number 1 underwent a live related renal transplant at the age of 9 years and lost his graft due to chronic rejection. He had a second live related renal transplant and currently has normal graft function with creatinine around 80umol/L. He received cysteamine therapy years after his second renal transplant and has most of the complications of cystinosis. Patient number 2 underwent a cadaver renal transplant at the age of 12 years and underwent graft nephrectomy 2 months after transplant due to bleeding from a mycotic aneurysm of transplant renal artery. He was on cysteamine therapy and had short stature and photophobia. Patient number 3 was on cysteamine therapy since diagnosing cystinosis and underwent a preemptive cadaver renal transplant at age 12 and is doing well with a creatinine of 118umol/L, 49 months post transplant. Patient number 4 was also on cysteamine therapy from the time of diagnosis of cystinosis and was on hemodialysis for 2 months prior to receiving a kidney transplant from his mother at the age of 9 years. He has normal growth and normal renal function with creatinine around 50umol/L, 40 months post transplant and so far has no cystinosis related complications.

Conclusions:

Renal transplantation is a successful treatment for patients with nephropathic cystinosis. Complications related to cystinosis are much less in those patients receiving cysteamine.

Key Words: Nephropathic Cystinosis; Renal Transplant; Immunosuppression
Funding Agency: None



Medicine

Category: Clinical

81

Does Vitamin D deficiency play a role in type 2 diabetic peripheral neuropathy?

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Introduction:

Despite recent reports linking Vitamin D deficiency with increased risk of diabetes mellitus and complications, there is limited data on patients with diabetic peripheral neuropathy (DPN). We aimed to evaluate the prevalence and associations of Vitamin D deficiency in 210 patients with Type 2 diabetes with and without DPN.

Methods:

Renal, liver, lipid profile and HbA1c were measured. Vitamin D status was determined by measuring 25-dihydroxyvitamin D. Presence or absence of coronary heart disease (CHD) was determined and early-morning urine microalbumin:creatinine ratio was measured. All patients were assessed clinically using neuropathy symptom score (NSS), neuropathy disability score (NDS) and nerve conduction study (NCS).

Results:

87 patients had DPN and these patients had significantly longer duration of diabetes and higher HbA1c. Age, gender, incidence of retinopathy and CHD were not significantly different from those without DPN. Mean (SD) Vitamin D was significantly lower in those with DPN (36.9 (39.9) nmol/L), compared to those without (58.32 (58.9) nmol/L). 81.5% of patients with DPN had vitamin D deficiency compared to 60.4% of those without. Vitamin D showed significant ($p < 0.05$) correlations with Total cholesterol, LDL-Cholesterol and urine microalbumin:creatinine ratio. Binary logistic regression analysis showed that DPN was significantly associated with Vitamin D deficiency (Odds ratio = 3.47; $p = 0.043$) after inclusion of potential confounders such as duration of diabetes, HbA1c and LDL- cholesterol.

Conclusions:

Vitamin D deficiency is an independent risk factor for DPN. Further studies are required to confirm if Vitamin D supplementation could prevent or delay the onset of DPN.

Key Words: Vitamin D; Type 2 Diabetes; Peripheral Neuropathy

Funding Agency: None



Microbiology and Immunology

Category: Clinical

82

In vitro susceptibility of *Campylobacter jejuni* isolated from diarrhoeal patients in Kuwait to tigecycline and other antimicrobial agents.

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Introduction:

Campylobacter jejuni is a major foodborne diarrhoeal pathogen. Serious *C. jejuni* infections are treated with antibiotics. Increasing resistance to clinically useful antimicrobials has been reported from different parts of the world. Tigecycline, a member of new group of antibiotics, glycylcyclines is a broad spectrum antibiotic. There are only two studies in the world on the in vitro activity of tigecycline against *C. jejuni*. We studied the activity of this agent and those of other agents against *C. jejuni* cultured from diarrhoeal patients in Kuwait.

Methods:

A total of 105 *C. jejuni* strains isolated from patients treated at Mubarak Al-Kabir Hospital, Kuwait during 2002-'10 were studied by E test on Mueller-Hinton blood agar inoculated with test bacterium and incubated microaerobically at 37°C for 48 h. The antibiotic strips used (with MIC break points indicated in parentheses) were: tigecycline (≥ 0.5 µg/ml), amoxicillin-clavulanic acid (≥ 32 µg/ml), ciprofloxacin (≥ 4 µg/ml), cefotaxime and ceftriaxone (both ≥ 64 µg/ml) and imipenem, meropenem, gentamicin, erythromycin and tetracycline (all ≥ 16 µg/ml).

Results:

All isolates were uniformly susceptible to tigecycline as well as to amoxicillin-clavulanic acid, cefotaxime, gentamicin, imipenem and meropenem. Resistance was found against ceftriaxone (7.6%), erythromycin (7.6%), tetracycline (48.6%), and ciprofloxacin (60.0%). The resistant rates in recent isolates were higher than the rates in older isolates.

Conclusions:

As all tested *C. jejuni* isolates were uniformly susceptible to tigecycline, it is a useful alternative drug to treat resistant infections. There were high prevalences of resistances to ciprofloxacin and tetracycline with recent isolates showing higher rates.

Key Words: Campylobacter; Tigecycline; Susceptibility

Funding Agency: None



Microbiology and Immunology

Category: Graduate MSc (Basic Science)

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Recombinant Mycobacterium smegmatis vaccine constructs express M. tuberculosis RD1 proteins and induce antigen-specific cellular immunity in mice and guinea-pigs

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Introduction:

Tuberculosis (TB) is among the top ten causes of death worldwide. With the rapid increase in drug-resistant TB and poor efficacy of BCG vaccines, there is an urgent need to develop new vaccines against TB. BCG vaccines lack 11 genomic regions that are conserved in the virulent strains of *M. tuberculosis*. One of these regions is RD1 that contains four open reading frames (ORFs) important for protective immunity, i.e. ORF3 (Rv3872), ORF5 (Rv3873), ORF6 (CFP10), and ORF7 (ESAT6). The aim of this work was to express these ORFs in the fast-growing *M. smegmatis* and evaluate their immunogenicity in mice and guinea-pigs model of TB in order to develop non-pathogenic mycobacterial-vector based recombinant vaccines against TB.

Methods:

RD1 orf3, orf5, orf6, and orf7 genes were cloned in three types of shuttle plasmids, and wild-type *E. coli* and *M. smegmatis* were transformed with the recombinant plasmids. The transformed bacteria were grown on a selective medium containing hygromycin. The presence of cloned DNA in hygromycin-resistant bacteria was determined by polymerase chain reaction and the expression of the proteins was studied by sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) and Western immunoblotting. Immunogenicity of the proteins was determined in cell mediated immunity (CMI) assays in mice and guinea-pigs after immunization with recombinant *M. smegmatis*.

Results:

E. coli and *M. smegmatis* were successfully transformed with recombinant plasmids containing RD1 genes. The expression of the recombinant proteins in transformed cells was successfully detected by SDS-PAGE and/or Western immunoblotting. The RD1 proteins expressed by recombinant bacteria were immunogenic in mice and guinea-pigs as shown by positive CMI responses using peptide pools and individual peptides of RD1 proteins.

Conclusions:

The recombinant *M. smegmatis* constructs available through this work are ready for evaluation as candidate vaccines against TB.

Key Words: Tuberculosis; *M. smegmatis*; Recombinant Vaccine

Funding Agency: Funded by the College of Graduate Studies and Kuwait University Research Administration Project No. YM12/07



Microbiology and Immunology

Category: Graduate MSc (Basic Science)

85

Identification, diagnostic potential and natural expression of immunodominant seroreactive peptides encoded by five Mycobacterium tuberculosis-specific genomic regions

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Introduction:

Comparative genomic studies have identified several Mycobacterium tuberculosis-specific genomic regions of differences (RDs), which are absent in the vaccine strains of BCG, and may be useful in the specific diagnosis of tuberculosis (TB).

Methods:

A total of 775 overlapping synthetic peptides (25-mers) covering the sequence of 39 open reading frame (ORF) proteins encoded by genes predicted in five RDs of M. tuberculosis, i.e. RD1, RD4, RD5, RD6 and RD7, were tested to identify immunodominant peptides by enzyme-linked immunosorbent assays (ELISA) using sera from HIV-ve pulmonary TB patients (n = 100) and BCG-vaccinated healthy subjects (n=100). Anti-peptide antibodies were raised in rabbits after immunization with pools of 11 peptides corresponding to each protein of immunodominant peptides. These antibodies were used as probes to detect the natural expression of the proteins in M. tuberculosis.

Results:

Ninety of the 775 peptides, belonging to 28 of the 39 ORFs of RDs, were recognized by antibodies present in TB patients' sera, but only four peptides were immunodominant and reacted with >50% TB sera. Three of these peptides, i.e. aa 346-370 of Rv3876, aa 241-265 of Rv1508c and aa 325-336 of Rv1516c had significantly strong antibody reactivity with sera from TB patients than healthy subjects ($P < 0.001$), and significantly higher positivity with TB sera (% positives = 66 to 93%) than sera from healthy subjects (% positives = 10 to 28%). Anti-peptide antibodies were successfully raised in rabbits after immunization with pooled peptides, and the peptides immunodominant in humans were also immunodominant in rabbits. Probing of culture filtrate and whole cell lysates of M. tuberculosis with anti-peptide antibodies suggested the natural expression of Rv3876, Rv1508c and Rv1516c in whole cell lysates of M. tuberculosis.

Conclusions:

The immunodominant RD peptides with serodiagnostic potential are naturally expressed in M. tuberculosis.

Key Words: Tuberculosis; Serodiagnosis; RD peptides

Funding Agency: The College of Graduate Studies and Research Administration (Grant No. YM08/07).



Microbiology and Immunology

Category: Graduate MSc (Basic Science)

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First detection and genotyping of camel rotavirus in the Gulf region

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Introduction:

Rotaviruses are the major cause of acute viral gastroenteritis in neonates and young children worldwide, and in the young animals of a large variety of species. Globally, rotavirus infections had been reported to account 17 to 28% of childhood hospitalizations with diarrhea, and were associated with about 600,000 deaths annually among children under 5 years of age. Animal rotaviruses have a huge economic burden and impact. In Kuwait only bovine rotavirus has been detected in addition to human rotaviruses so far. Camels which have economic importance in the Middle East have never been screened for rotavirus in Kuwait. The aim of this study was to investigate rotavirus in camels.

Methods:

Fecal samples (405) were collected from camels from different farms in Abdali, Sulaibia, Kabd, Al-Jahra and Al-Wafra areas in Kuwait. Blood samples were also collected from camels of different ages for study of rotavirus seroprevalence. Rotavirus was detected by commercial ELISA kits and genomic RNA was amplified by VP6-specific RT-PCR. Genotyping was undertaken with VP4 and VP7 specific primers and amplicons were sequenced. RotaC and BLAST programs were used for sequence analysis.

Results:

Maternal antibodies against rotavirus gradually decrease with time and their lowest prevalence was found in 3 and 4 month-old camel calves. After 5 months of age rotavirus infections frequently occur and seroprevalence reaches 100% by two years of age. Rotavirus was detected in only six stool specimens by RT-PCR but not by ELISA. One strain was genotyped as G10P.

Conclusions:

This study demonstrates for the first time in Kuwait (and in the Gulf region) that camel rotaviruses are circulating in the country and one calf rotavirus strain was G and P genotyped. This is the first successful P genotype determination of camel rotavirus in the Middle East. To determine the impact and burden of camel rotavirus infection, further investigations are needed.

Key Words: Camel rotavirus; Camel rotavirus seroprevalence; Camel rotavirus genotyping

Funding Agency: YM16/08



Microbiology and Immunology

Category: Basic Sciences

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Kinetics of spontaneous and mycobacterial antigen-induced secretion of Th1, Th2 and proinflammatory cytokines by peripheral blood mononuclear cells of tuberculosis patients

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Introduction:

The cytokines produced by T helper (Th)1 cells, i.e. IFN-g, IL-2 and TNF-b correlate with protection, whereas the cytokines released by Th2 cells, i.e. IL-4, IL-5 and IL-10 correlate with pathogenesis and the proinflammatory cytokines IL-1-b, IL-6, IL-8 and TNF-a are responsible for both protection and pathogenesis of tuberculosis (TB). The in vitro release of these cytokines by peripheral blood mononuclear cells (PBMCs) has been studied previously in cultures on day 6. However, this time point may not be optimal because some cytokines, being growth factors for the activated cells in PBMCs, are consumed by the cells. The aim of this work was to determine the kinetics of cytokine release by quantifying the amount of cytokines present in early (day 2) and late (day 6) cultures of PBMCs.

Methods:

PBMCs were isolated from the peripheral blood of TB patients and cultured in vitro in the absence and presence of exogenously added complex mycobacterial antigens and RD1 peptides. The supernatants were collected on day 2 and day 6 of culture and assayed for Th1, Th2 and proinflammatory cytokines using FlowCytomix kits by flow cytometry. The results were analyzed for significant differences in cytokine concentrations on day 2 vs. day 6 using Mann-Whitney U-test.

Results:

All of the cytokines were spontaneously secreted by PBMCs of TB patients, but only TNF-a concentration was significantly higher on day 2 than on day 6 ($P < 0.05$). In response to the complex mycobacterial antigens and RD1 peptides, only IFN-gamma and IL-5 were detected at significantly higher concentrations on day 6 ($P < 0.05$), whereas significantly higher concentrations of IL-8 and IL-10 were detected to some complex mycobacterial antigens on day 2.

Conclusions:

The significant increase in concentrations of IFN-gamma and IL-5 to all antigens on day 6 suggests that this is the optimal time point to study antigen-induced in vitro cytokine release by PBMCs of TB patients.

Key Words: Tuberculosis; Cytokines; Kinetics

Funding Agency: Supported by KFAS grant no. 2002-1302-04



Microbiology and Immunology

Category: Graduate PhD (Basic Science)

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Role of Human Metapneumovirus in Respiratory Tract Infections in Kuwait

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Introduction:

Human metapneumovirus (hMPV) has been recognized as an important cause of respiratory tract infections (RTIs) in all age groups and in all geographical areas. The role of hMPV in causing RTIs in Kuwait was not yet been investigated. The aim of the current study was to determine the prevalence of hMPV infection in Kuwait among patients with RTIs with respect to the other respiratory viruses, and to identify the hMPV genotypes.

Methods:

During January to December 2009, 460 respiratory samples from 388 patients with RTIs were collected from different hospitals. They were tested for hMPV RNA by real-time PCR, and other respiratory viruses by conventional PCR. The type of detected hMPV RNA was identified by direct sequencing. Samples positive for H1N1 have been excluded from this study.

Results:

Out of 388 patients, 110 (28%) were positive for viral respiratory infections; 21 (5.4%) of them were positive for hMPV, 29 (7.5%) were positive for rhinovirus, 13 (4%) were positive for respiratory syncytial virus, and 10 (3%) were positive for adenovirus. Most (n=19, 90.5%) of hMPV-positive patients were admitted to the ICU, 76% of them were of age 2 years and below, and 24% of age 59 and above. All hMPV-positive elderly patients have been diagnosed as having pneumonia while most 50% of hMPV-positive infants had bronchopneumonia. Children with hMPV and rhinovirus co-infection (n=3, 1%) had recurrent chest infection and frequent ICU admission. Genotype B2 was more prevalent than genotype A, and the hMPV infection was mostly detected between December and May.

Conclusions:

This is the first study demonstrating the prevalence of hMPV infection in Kuwait (5.4%) and suggests that hMPV infection is prevalent in winter and spring months, and usually targets young children and aged individuals with lower RTI. The hMPV B2 is the predominate genotype in Kuwait.

Key Words: Human metapneumovirus (hMPV); Prevalence; Viral load

Funding Agency: Supported by College of Graduate Studies and Research Administration, Grant # YM 05/09, Kuwait University



Microbiology and Immunology

Category: Graduate MSc (Basic Science)

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Prevalence of carbapenem-resistant *Acinetobacter baumannii* isolated from patients in two hospitals in Kuwait

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Introduction:

Objectives: This study was conducted to evaluate the antimicrobial susceptibility of *Acinetobacter baumannii* isolated from patients in two Kuwait teaching hospitals and investigate the mechanism of carbapenem resistance and clonal relatedness of the isolates.

Methods:

A total of 94 isolates, 36 from Mubarak hospital and 58 from Al-Adan hospital, were genetically identified by PCR as *A. baumannii* using the primers for blaOXA-69 gene. Antimicrobial susceptibility testing of all isolates was performed using Etest method and resistance determinants of metallo-β-lactamase (MBL) were characterized by PCR. Pulsed-field gel electrophoresis genotyping was used to determine their clonality.

Results:

Of the 94 isolates, 80 (85.1%) were multidrug-resistant, and 40 (42.6%) were resistant to the carbapenems; 17 (42.5%) and 23 (57.5%) of these were from Mubarak and Al-Adan hospitals, respectively. Of these, blaIMP-1 was found in 8 (27.8%), blaVIM-2 in 18 (62%), blaOXA-23 in two isolates and blaVIM-1 in one isolate. No gene was detected in 5 out of 17 (29.4%) and 6 out of 23 (26.1%) carbapenem-resistant *A. baumannii* isolated from Mubarak and Al-Adan hospitals, respectively. Sixteen (94.1%) out of the 17 bla gene carrying strains from Al-Adan hospital belonged to genotype A but only 5 (41.7%) of 12 from Mubarak hospital belonged to genotype A.

Conclusions:

In this study, a high prevalence of carbapenem-resistant *A. baumannii* was encountered in the two Kuwaiti hospitals, and blaVIM-2 and blaIMP-1, more than blaVIM-1, were the predominant genes encoding MBL production. There appeared to be an inter-hospital clonal spread of carbapenem-resistant *A. baumannii*.

Key Words: Acinetobacter baumannii; Carbapenem-resistance; Kuwait

Funding Agency: This study was supported by Kuwait University Research Administration Grant No. YM 01/08.



Microbiology and Immunology

Category: Clinical

90

First report of molecular detection of fluoroquinolone resistance-associated gyrA mutations in multidrug-resistant clinical Mycobacterium tuberculosis isolates in Kuwait

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Introduction:

Extensively drug-resistant Mycobacterium tuberculosis (XDR-TB) strains are defined as multidrug-resistant M. tuberculosis (MDR-TB) strains additionally resistant to a fluoroquinolone (FQ) and an injectable agent and have been detected in >55 countries. Infections with XDR-TB strains are extremely difficult to treat in developing countries. This study detected gyrA mutations associated with FQ resistance among MDR-TB strains in Kuwait.

Methods:

A total of 85 MDR-TB strains isolated from 55 TB patients and 25 susceptible M. tuberculosis strains were tested. The gyrA mutations were detected by DNA sequencing of quinolone resistance-determining region. For isolates with gyrA mutations, 3'-end of rrs, three regions of rpoB, katG codon 315 (katG315) and inhA-regulatory region were also sequenced. Double-repetitive-element PCR and genetic group analysis based on polymorphisms at gyrA95 and katG463 was done for further fingerprinting of isolates.

Results:

None of susceptible but six of 85 MDR-TB strains contained gyrA mutations. Only gyrA94 was mutated in all six (D94A in one and D94G in five) strains. Three of 6 mutant strains were recovered from 1 patient while 3 other strains represented individual patient isolates. Fingerprinting studies identified all individual patient isolates as genotypically distinct strains. All 6 strains with a gyrA mutation contained wild-type rrs sequence.

Conclusions:

Although FQs are not generally used for chemotherapy of TB and drug susceptibility testing for second-line drugs is not routinely carried out in Kuwait, four of 55 (7%) individual patient MDR-TB strains contained FQ resistance-associated mutations in gyrA gene. The data advocate routine drug susceptibility testing for this important second-line drug for proper management of MDR-TB in Kuwait. Lack of mutations in 3'-end of rrs gene that confer resistance to injectable agents reduce the likelihood of occurrence, at least for now, of XDR-TB in Kuwait.

Key Words: Mycobacterium tuberculosis; Multidrug-resistant strains; gyrA mutations

Funding Agency: KURA grant YM 03/06.



Microbiology and Immunology

Category: Clinical

91

Antimicrobial susceptibility of Gram-positive isolates to Daptomycin, Glycopeptides and Linezolid in a tertiary care hospital in Kuwait.

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Introduction:

Increase in infections caused by methicillin resistant *Staphylococcus aureus*, (MRSA) vancomycin resistant *Enterococcus* (VRE) and penicillin resistant *Streptococcus pneumoniae* have created the need for newer and novel antibiotics with activity against these organisms.

Objective: This prospective study was done to determine the type of Gram-positive organisms isolated from various clinical specimens. The in vitro activity of daptomycin was assessed in comparison with that of vancomycin, teicoplanin and linezolid against Gram-positive isolates. The minimum inhibitory concentration MIC₅₀ and MIC₉₀ and susceptibility range were evaluated.

Methods:

This study was done at Ibn Sina Microbiology Laboratory on all Gram-positive isolates from various clinical specimens from September 2010 to November 2010. They were identified by Vitek 2 (bioMérieux, France). Their antimicrobial susceptibility pattern to daptomycin, vancomycin, teicoplanin and linezolid was determined using E-test method (AB Biodisk, Solna, Sweden) and their MIC₅₀, MIC₉₀ and Range was calculated.

Results:

A total of 144 Gram-positive isolates were evaluated, out of which 56 (39%) were *Staphylococcus aureus*, 38 (27%) were MRSA, 42 (29%) were coagulase-negative *Staphylococcus*, 5 (3%) were *Enterococcus faecalis* and 3 (2%) were *Streptococcus agalactiae*. Daptomycin MIC for *Staphylococcus aureus*, MRSA, coagulase negative *Staphylococcus* were in the range of 0.06 – 0.5. A slight trend towards higher Daptomycin MIC values ranging from 0.12-1.0 was observed for *Enterococcus faecalis*. Vancomycin and Linezolid showed higher MIC values ranging from 0.5-4.0 and 0.5-2.0 respectively against coagulase-negative *Staphylococcus* and MRSA.

Conclusions:

Daptomycin is a rapidly bactericidal antibiotic that showed excellent in vitro activity against all the Gram-positive bacteria tested. It is a good therapeutic option for serious infections caused by MRSA and VRE.

Key Words: Daptomycin; Gram positive; Susceptibility pattern

Funding Agency: None



Microbiology and Immunology

Category: Basic Sciences

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Genotype-specific nucleotide signatures in rDNA and molecular genetic basis of 5-flucytosine resistance among clinical *Candida dubliniensis* isolates in Kuwait

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Introduction:

Clinical *Candida dubliniensis* isolates are classified into 4 genotypes based on internal transcribed spacer (ITS)1 and ITS2 region sequences of rDNA. All genotype 3 and genotype 4 isolates from Middle East were reported as resistant to 5-flucytosine (5FC). This study determined genotype-defining signature nucleotides within rDNA and their association with 5FC resistance among *C. dubliniensis* isolates in Kuwait. The 5FC-resistant status of selected isolates was explored by sequencing of DNA region including codon 29 of cytosine deaminase.

Methods:

Genotype assignment of 103 *C. dubliniensis* isolates was done by PCR amplification with genotype-specific primers. DNA sequencing of rDNA was performed to determine genotype-specific signature nucleotides and their association with resistance to 5FC. Susceptibility of isolates to anti-fungal agents was performed by Etest. Direct DNA sequencing of cytosine deaminase codon 29 region was done to confirm 5FC-resistant status of selected isolates.

Results:

Only 94 isolates yielded amplicons with a genotype-specific primer pair. DNA sequencing of rDNA identified 7 *C. dubliniensis* genotypes including 4 new genotypes. Majority (68 of 103, 66%) of isolates belonged to genotype 1 while 1, 25, 6, 1, 1 and 1 strains belonged to genotype 3, 4, 5, 6, 7 and 8, respectively. No genotype 2 strains were detected. All genotype 4 isolates but None of other genotypes were resistant to 5FC and contained a 'T' signature residue at ITS1 position 82. All genotype 4 isolates also contained S29L mutation while 30 selected genotype 1 and all other isolates contained wild-type codon 29 (S29) in cytosine deaminase.

Conclusions:

Seven different genotypes were detected among *C. dubliniensis* isolates in Kuwait with most of the isolates belonging to genotype 1 (66%) followed by genotype 4 (24%). All 5FC-resistant strains belonged to genotype 4 and contained a unique signature at ITS1 position 82 and S29L mutation in cytosine deaminase.

Key Words: Candida dubliniensis; rDNA signature sequences; Genotypes and 5-flucytosine resistance

Funding Agency: KURA grant MI 01/08.



Microbiology and Immunology

Category: Basic Sciences

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**Redirection of Cytokine Profiles by the Dydrogesterone metabolite
Dihydrodydrogesterone**

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Introduction:

Evidence from our laboratory and others indicates that successful pregnancy is associated with an anti-inflammatory cytokine profile, while pregnancy loss is associated with a pro-inflammatory profile. Research has shown that pro-inflammatory cytokines may lead to pregnancy loss or complications. This association between miscarriage and pro-inflammatory cytokines has led us to explore ways of suppressing pro-inflammatory cytokine production to create a milieu favorable to pregnancy. We have demonstrated that dydrogesterone (an orally-administered progestogen, similar to progesterone, used for treating luteal phase defects and habitual and threatened abortion) downregulates the production of the pro-inflammatory cytokines and upregulates the production of anti-inflammatory cytokines. However, in circulation, dydrogesterone is rapidly metabolized to dihydrodydrogesterone (DHD) which has not been studied for immunomodulation; it is critical that we ascertain whether this metabolite possesses immunomodulatory activities.

Methods:

Mitogen-stimulated blood mononuclear cells from 25 women with recurrent miscarriage were exposed to dydrogesterone and DHD after which culture supernatants were analyzed for levels of selected pro- and anti-inflammatory cytokines by ELISA.

Results:

DHD was as effective as dydrogesterone in inducing blood lymphocytes to produce significantly lower levels of the pro-inflammatory cytokines IFN gamma and TNF alpha, and higher levels of the anti-inflammatory cytokine IL-10.

Conclusions:

Pro-inflammatory cytokines are downregulated by DHD and the anti-inflammatory cytokine IL-10 is upregulated, confirming that dihydrodydrogesterone retains the ability to modulate cytokine profiles towards one that is conducive to successful pregnancy. If dydrogesterone is to be considered seriously as a potential immunomodulator, it is important that its metabolite DHD is also a potent immunomodulator; our results indicate that this is indeed the case.

Key Words: Immunomodulation; Cytokines; Recurrent miscarriage

Funding Agency: Kuwait University, MI04/08



Microbiology and Immunology

Category: *Clinical*

94

Correlation between inoculum size, positivity rates and types of organisms isolated from blood cultures in adult patients

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Introduction:

Adequate volume & proper collection of blood sample are fundamental requirements for reliable diagnosis of sepsis, which in turn is important for appropriate antimicrobial therapy. The inadequate volume questions the value of blood cultures because of lack of optimal organism recovery. We performed the current study to determine how the inoculum size affects time & rate of positive cultures & the isolation rates of different organisms.

Methods:

During six months, 3006 sets of blood culture samples were received. Of these 2919 aerobic & 2901 anaerobic vials were analyzed. Each inoculated vial was weighed using an electric balance. All the inoculated vials were incubated at 35°C on the BACTEC 9240 system (BD Diagnostics) & monitored for positive signal over a five-day period. The time taken to signal a positive culture was recorded. The isolated organisms were identified by Phoenix (BD Diagnostics).

Results:

Of 2919 aerobic blood cultures 297 (10.2%) yielded microbial growth. Of these 75% signaled positive within 24 h. Among samples with adequate (> 8.0 ml) blood volume the rate of positivity was 56.2%, isolation rates of Gram-negative bacilli (GNB), S.aureus, Candida spp., & contaminating organisms (CO) were 63.5%, 10.2%, 2.4% & 17.4%, respectively & overall time to positivity (TOP) was < 24 h in 77.2% samples. In comparison, samples with inadequate (< 8.0 ml) blood volume showed positivity rate of 43.8%, yield of GNB, S.aureus, Candida spp. & CO was 63.0%, 15.4%, 3.0% & 26.1%, respectively & TOP was < 24 h in 73.0% samples. Results obtained in 2901 anaerobic culture vials showed an overall positive rate of 8.2% with adequate blood volume in only 40.5% vials. The yield of anaerobes was 3.0%.

Conclusions:

Although our data indicate the contamination rates to be higher in the inadequate-volume blood culture, isolation of significant pathogens was similar in adequate & inadequate blood volume groups.

Key Words: Blood culture; Sample volume; Positive rates

Funding Agency: None



Microbiology and Immunology

Category: Graduate MSc (Basic Science)

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Molecular characterization and species-specific identification of clinical *Candida glabrata*-complex isolates in Kuwait

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Introduction:

Mucosal and systemic infections due to *Candida glabrata* have increased in recent years. Molecular studies have shown that phenotypically identified *C. glabrata* isolates represent a complex of three species, i.e., *C. glabrata*, *C. nivariensis* and *C. bracarensis*. The three species exhibit varying susceptibility to azoles warranting species-specific identification. This study determined the frequency of *C. nivariensis* and *C. bracarensis* among phenotypically regions identified *C. glabrata* isolates in Kuwait.

Methods:

Type strains of *C. glabrata*, *C. nivariensis* and *C. bracarensis* were used as reference. A total of 120 *C. glabrata* isolates identified by Vitek2 yeast identification system were tested by a multiplex PCR that is designed to yield species-specific amplicons from *C. glabrata* (360 bp), *C. nivariensis* (250 bp) and *C. bracarensis* (180 bp). The identification of all clinical isolates was also performed by uniplex PCR amplification of internally transcribed spacer (ITS) regions of rDNA using species-specific primers. Identity of selected isolates was further confirmed by DNA sequencing of ITS regions of rDNA.

Results:

Amplicons of expected size were obtained with DNA from type strains of *C. glabrata*, *C. nivariensis* and *C. bracarensis* in multiplex PCR and species-specific uniplex PCR. All 120 clinical *C. glabrata*-complex isolates yielded an amplicon of ~360 bp in multiplex PCR and also yielded an amplicon of expected size in PCR with *C. glabrata*-specific primer pair but not with *C. nivariensis*-specific or *C. bracarensis*-specific primer pair. The DNA sequencing of ITS region of rDNA confirmed the identification of 10 selected isolates as *C. glabrata*.

Conclusions:

All 120 clinical *C. glabrata*-complex isolates in Kuwait were identified as *C. glabrata* by a multiplex PCR and a uniplex species-specific PCR. The data show that recently recognized *C. nivariensis* and *C. bracarensis* are clinically not significant species among patients with *Candida* infections in Kuwait.

Key Words: Candida glabrata-complex; Species-specific identification; Clinical isolates

Funding Agency: Supported by KURA grant YM 24/09



Microbiology and Immunology

Category: Clinical

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**The value of ProbeTec ET Mycobacterium tuberculosis Complex assay
in the early diagnosis of tuberculosis**

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Introduction:

The slow growth of *M. tuberculosis* organism delays clinical diagnosis and treatment, contributing to the spread of the disease. The use of strand displacement amplification (SDA) technique allows the rapid detection and identification of *M. tuberculosis* in clinical specimen thereby promoting faster medical intervention. ProbeTec ET *M. tuberculosis* Complex Direct Detection (DTB) assay is based on the amplification and detection of target DNA. This study was done to over view the value of this system in the direct detection of tuberculosis from clinical specimens both pulmonary and extra pulmonary.

Methods:

A total of 805 specimens were included in the study. Pulmonary samples comprised 511 specimens (Sputum 395, BAL 83, ETT 33). Extra pulmonary samples comprised 294 specimens (fluids 99, FNA 49, pus 31, biopsy 26, urine 24, CSF 28, blood 20, gastric lavage 11, swab 4, stool 2). All the specimens were subjected to direct smear microscopy by Ziehl–Neelsen stain, culture by MGIT960, Bactec 460 and direct detection by ProbeTec ET system.

Results:

Out of 511 pulmonary specimens, 445 were smear negative while out of 294 extra pulmonary specimens, 276 were smear negative. The sensitivity, specificity, positive predictive value PPV and negative predictive value NPV for smear-negative pulmonary samples were 82%, 100%, 100% and 99%, respectively. While for smear positive the sensitivity and specificity were 100%. For smear-negative extra pulmonary specimens, sensitivity was 95%, the specificity; PPV and NPV were 100%, 100% and 99%, respectively. Where as for smear positive the sensitivity and specificity were 100%. One NTM sputum sample was smear positive, culture grown but PCR negative. Where as one *M. leprosy* FNA sample was smear positive, culture and PCR negative.

Conclusions:

ProbeTech ET *M. tuberculosis* system showed high specificity for both pulmonary and extra-pulmonary samples. It is a reliable technique for the early diagnosis of tuberculosis.

Key Words: Evaluation, Diagnosis; ProbeTec; Mycobacterium tuberculosis

Funding Agency: None



Microbiology and Immunology

Category: Basic Sciences

97

Immune responses induced by DNA vaccine constructs expressing Mycobacterium tuberculosis-specific genes

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Introduction:

RD1 PE35, PPE68, EsxA, EsxB and RD9 EsxV genes are specific for Mycobacterium tuberculosis genome. The aim of this study was to clone these genes into DNA vaccine vectors capable of expressing them in eukaryotic cells as fusion proteins, fused with immunostimulatory signal peptides of human interleukin-2 (hIL-2) and tissue plasminogen activator (tPA), and evaluate the recombinant DNA vaccine constructs for induction of antigen specific cellular immune responses in mice.

Methods:

DNA corresponding to the above RD1 and RD9 genes were cloned into DNA vaccine plasmid vectors pUMVC6 and pUMVC7 (with hIL-2 and tPA signal peptides, respectively), and a total of 10 recombinant DNA vaccine constructs were obtained. BALB/c mice were immunized with the parent and recombinant plasmids and their spleen cells were tested for antigen-induced proliferation with antigens of M. tuberculosis and pure proteins corresponding to the cloned genes.

Results:

The results showed that antigen-specific proliferation responses were observed for a given antigen only with spleen cells of mice immunized with the homologous recombinant DNA vaccine construct. The mice immunized with the parent plasmids did not show positive immune responses to any of the antigens of the cloned genes.

Conclusions:

The ability of the DNA vaccine constructs to elicit cellular immune responses makes them an attractive weapon as a safer vaccine candidate for preventive and therapeutic applications against TB.

Key Words: Tuberculosis; DNA vaccines; RD1, RD9, Proteins

Funding Agency: Research Administration grant YM01/03



Microbiology and Immunology

Category: *Clinical*

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Cryptosporidiosis in Kuwaiti children: Association of clinical characteristics with *Cryptosporidium* species and subtypes

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Introduction:

Cryptosporidiosis is a major cause of diarrhea in developing countries which generally causes self-limited watery diarrhea in immunocompetent patients or chronic severe diarrhea in immunocompromized individuals. The objective of this was to determine the association of clinical characteristics with *Cryptosporidium* types and subtypes.

Methods:

Fecal specimens from 2548 children with diarrhea were screened by microscopy for *Cryptosporidium* spp. And the positive specimens were genotyped and subtyped by PCR-restriction fragment length polymorphism. Socio-demographic data and information on clinical characteristics were also collected from each of the patients.

Results:

Eighty seven of 2548 (3.4%) children had cryptosporidial diarrhea by microscopy and the majority (41.4%) of the infected children were between 4-8 year-old age group. Molecular characterization showed that *C. parvum* was the most commonly identified species (72.5%) and consisted of 3 subtypes, Iia, Iid were the commonest (80.2%) followed by Iic. Twenty-two (26.5%) of the children had *C. hominis* and showed three subtypes, Id was the most common (54.5%) followed by Ia (36.4%) and Ie. Associated clinical manifestations varied between *C. parvum* and *C. hominis*. Diarrhea associated with subtype Id, the most commonly identified *C. hominis* subtype, was more severe than that associated with other subtypes.

Conclusions:

This is the first study from the Gulf countries that has documented correlation of clinical characteristics in *Cryptosporidium* infection with its types and subtypes. Our study confirms a very different *Cryptosporidium* genotype and subtype distribution, with a predominance of *C. parvum* Iia and Iid among the Kuwaiti children with diarrhea. In addition, subtype Id of *C. hominis* was associated with more diverse and severe clinical manifestations in infected children suggesting that parasite genetics may play an important role in the clinical manifestations of human cryptosporidiosis.

Key Words: Clinical characteristics; *Cryptosporidium* types and subtypes; mode of transmission

Funding Agency: Kuwait University Research Administration grant MI 03/03.



Microbiology and Immunology

Category: Clinical

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Molecular identification and characterization of clinical isolates of filamentous fungi by direct DNA sequencing of species-specific regions of rDNA

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Introduction:

Objective: Species-specific identification of filamentous fungi is highly desirable due to differences in susceptibility to antifungal agents. Phenotypic identification of filamentous fungi is challenging due to non-specific morphological characteristics. This study evaluated the usefulness of direct DNA sequencing of species-specific internal transcribed spacer (ITS) region of rDNA for accurate identification of clinical isolates of filamentous fungi.

Methods:

A total of 39 clinical isolates were tested. The ITS region (including ITS1-5.8S rRNA-ITS2) was amplified by panfungal primers and both strands were sequenced by using amplification and internal primers. Species-specific identification was achieved by sequence comparisons with type/reference strains of various fungal species by BLAST. Identification of some selected isolates was further confirmed by direct DNA sequencing of the highly conserved D1-D2 domains of 28S rRNA.

Results:

All isolates were speciated with >99.1% sequence identity with type/reference strains of various filamentous fungi. The method identified 6, 2, 4, 2, 3, 2 and 2 strains as *Rhizopus microsporus*, *R. oryzae*, *Fusarium solani*, *F. equiseti*, and *Pseudoallescheria boydii*, *Paecilomyces lilacinus* and *Emericella nidulans*, respectively, and one each as *Aspergillus oryzae*, *A. nivea*, *A. flavus*, *Cladosporium cladosporioides*, *Alternaria alternata*, *Lasioidiplodia parva*, *Exophiala spinifera*, *E. jeanselmei*, *Mucor circinelloides*, *Scytalidium dimidiatum*, *Pyrenochaeta romeroi*, *Acremonium kiliense*, *Bullera dendrophila*, *Arthroderma benhamiae*, *Achaetomium globosum*, *Conidiobolus coronatus*, *Colletotrichum gloeosporioides* and *Exserophilum rostratum*. The D1-D2-based identification was completely concordant with ITS-based data.

Conclusions:

Sequencing of rDNA is an excellent approach for correct identification of clinical isolates of filamentous fungi and may help in proper management of patients with infections by known or novel emerging fungal pathogens.

Key Words: Filamentous fungi; Identification; rDNA sequencing

Funding Agency: KURA grant MI 04/02



Microbiology and Immunology

Category: Clinical

100

Distribution and In-Vitro Antimicrobial Susceptibility of *Kluyvera* spp. isolated from clinical specimens.

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Introduction:

Kluyvera is a relatively newly described bacterial genus of family Enterobacteriaceae. Though frequently regarded as saprophytic and contaminant in clinical specimens it has recently been well documented as a causative agent of urinary tract, gastrointestinal, meningeal and soft tissue infections in humans. Antimicrobial susceptibility of *Kluyvera* spp. is variable and multidrug resistant strains are described in literature. We present 5 years data of our isolates.

Methods:

The clinical details of patients were recorded. The identification and susceptibility testing was done in MicroScan using NUC 35 and NBPC 34. Whenever required imipenem susceptibility was also checked by disc diffusion. *E. coli* 25922 was used as control.

Results:

Of 96 isolates, 73(76.04%) were recovered from adults and 23(23.96%) from pediatric patients. While 70.83% isolates were recovered from urine, 29.17% were from wound swabs/aspirated pus and other body site swabs/specimens. 92.71% isolates were *K. ascorbata* and only 7.29% were *K. cryocrescens*. All specimens had pure growth of *Kluyvera* spp. except 15(15.63%) which had mixed growth with another bacterial spp. Multidrug resistant strains (resistant to 3 or more major groups of antimicrobials) were seen in 68.75% isolates. Whereas 95.83%, 93.75% and 76.04% strains were susceptible to imipenem, meropenem and amikacin respectively, more than two thirds strains were resistant to ampicillin, cephazolin, tetracycline, piperacillin, trimethoprim/sulfamethoxazole and ampicillin/sulbactam.

Conclusions:

Kluyvera spp may be either contaminants in clinical specimens or a cause of well recognized clinical infections. Multidrug resistant *Kluyvera* spp. is a serious concern.

Key Words: Antimicrobial susceptibility; *Kluyvera* spp.

Funding Agency: None



Microbiology and Immunology

Category: Clinical

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Arrival of *Klebsiella pneumoniae* producing carbapenemases (KPCs) and New Delhi metallo-beta-lactamases (NDM-1) in Kuwait – A preliminary report.

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Introduction:

Reports of carbapenemases and metallo-beta-lactamases are on the increase, particularly the plasmid-mediated enzymes *Klebsiella pneumoniae* carbapenemases (KPC) and in the last one year, the so-called New Delhi metallo-beta-lactamase-1 (NDM-1). Both enzyme-types inactivate the carbapenems and a host of other classes of antibiotics. Our objective is to report the arrival of both KPC- and NDM-1 -producing members of the family Enterobacteriaceae, hitherto rare, in Kuwait.

Methods:

Isolates belonging to the family Enterobacteriaceae with reduced susceptibility to the carbapenems were collected over the last 6 months from infected patients in Mubarak Al-Kabir Hospital. Cultures from rectal and tracheal aspirations grown on MacConkey agar supplemented with 4ug/ml meropenem were conducted on positive patients. Isolates were identified by VITEK-2 ID System. Susceptibility was performed using the E test method. Results were interpreted according to the CLSI guidelines. The presence of KPC and NDM-1 were detected by PCR.

Results:

A total of 11 isolates (9 *K. pneumoniae*, 1 *Escherichia coli*, and 1 *Enterobacter cloacae*) were obtained. All isolates exhibited resistance to all antibiotics tested, except colistin and tigecycline. Ertapenem, imipenem and meropenem resistances were observed in a range of 8->32mg/L. Seven isolates were positive for metallo-beta-lactamase (MBL). One NDM-1 positive *K. pneumoniae* was isolated from the wound of a 52-year old SE Asian man in the ICU. Bla_{VIM-1} -harboring *K. pneumoniae* and *E. coli* were isolated from blood and urine samples of 6 patients in the ICU/ wards. Infection control procedures were implemented when the index case was detected.

Conclusions:

This study presents the first report of KPC and NDM-1 in Kuwait. The possibility of spread across all Kuwait hospitals is worrisome. Thus, stringent infection control strategies are required to prevent clonal spread.

Key Words: Klebsiella pneumoniae; KPC and NDM-1; Kuwait

Funding Agency: None



Microbiology and Immunology

Category: *Clinical*

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Is premarital screening for syphilis in Kuwait justified?

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Introduction:

As do most GCC countries, Kuwait requires Premarital Serological Screening Tests (PMSTs) for syphilis starting from August 2009. The aim of this study was to determine the seroprevalence and cost effectiveness of premarital screening for syphilis in Kuwait.

Methods:

RPR and TPHA test results during the period April - November 2010 from four premarital clinics in Kuwait were retrospectively undertaken.

Results:

During this period, sera from 13165 persons attending the premarital clinics were screened for syphilis. Out of 13165 screened persons 11841 were Kuwaitis and 1324 were non Kuwaitis. 52.7% of persons were from the age group of 15-24 years and 11.44% were ≥ 35 years. Only 15 were found to be infected with syphilis (incidence=0.11%). Serologic tests identified only 3 (0.02%) new cases of asymptomatic infectious syphilis. Five (0.04%) were biological false-positive. The peak age-specific incidence was ≥ 35 (86%) years old. Of these 75% were males and 25% were females.

Conclusions:

An analysis of the figures obtained from this study indicates that the effectiveness of the PMSTs is minimal in terms of new cases of infectious syphilis located and treated as a result of this type of screening. Kuwait requires that all persons applying for a marriage license have a "standard serologic test, as may be necessary for the discovery of syphilis. The cost-effectiveness of routine premarital screening for syphilis is a concern of many. Despite the fact that the cost is borne by government, it still represents a cost to society whose efficacy should be proved. Future work has to be done on the cost of syphilis screening and the benefits of the program.

Key Words: Kuwait; Syphilis; Premarital Screening

Funding Agency: None



Microbiology and Immunology

Category: Basic Sciences

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Is candida dubliniensis an emerging bloodstream pathogen in Kuwait?

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Introduction:

Candida dubliniensis, a newly recognized species, shares close genetic and phenotypic relationship with *Candida albicans*. It forms only a minor component of normal yeast microbiota and its role is mainly restricted to oral colonization, particularly among HIV-infected patients. This study determined the prevalence and clinical significance of *C. dubliniensis* in Kuwait.

Methods:

Yeast isolates grown in Mycology Reference Laboratory or received from other hospitals and producing germ tubes were included. The identity of *C. dubliniensis* was determined by Vitek2 yeast identification system and by its ability to form rough colonies and chlamyospore on sunflower seed agar. Identity of 100 selected isolates was confirmed by sequencing of rDNA. Antifungal susceptibility was determined by Etest. The prevalence of *C. dubliniensis* was determined retrospectively for 9-year period (2002-2010).

Results:

During the period, 367 *C. dubliniensis* isolates from 315 patients were recovered. Their distribution according to specimens/sites was as follows: respiratory, 240 (65%); oral, 41 (11%); urine, 34 (9.2%); blood, 13 (3.5%); vagina 10 (2.7%) and others, 27 (7.3%). The isolation proportion of *C. dubliniensis* for 2002-2004, 2005-2007, and 2008-2010 was 15%, 41% and 44%, respectively. Interestingly, increasing rates of isolation of *C. dubliniensis* from blood cultures were noted. Of 1153 bloodstream yeast isolates characterized, the % prevalence of *C. dubliniensis* was: 2002 to 2004, (1 of 244, 0.4%); 2005 to 2007, (2 of 356, 0.6%) and 2008 to 2010, (10 out of 553, 1.8%). Mean inhibitory concentration (MIC) values (in µg/ml) of 0.224 during 2002-2004, 0.307 during 2005-2007 and 0.338 during 2008-2010 for fluconazole suggest an increasing trend in MIC for this commonly used antifungal agent.

Conclusions:

Data suggest that *C. dubliniensis* is increasing in occurrence in clinical specimens. This species may now be emerging as a significant bloodstream pathogen in Kuwait.

Key Words: Candida dubliniensis; Emerging bloodstream pathogen; Kuwait

Funding Agency: KURA grant MI 118



Microbiology and Immunology

Category: Basic Sciences

104

Granulocyte-Macrophage colony stimulating factor (GM-CSF): A dominant chemotactic agent for neutrophils?

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Introduction:

GM-CSF is well recognized as an important proliferative and priming agent for neutrophils. In addition, we showed that GM-CSF can act as a chemotactic agent for neutrophils *in vitro* and *in vivo*. Our Aim was to determine the significance of GM-CSF's chemotactic ability compared with classical potent chemoattractants.

Methods:

Bone marrow derived neutrophil chemotaxis was studied using the *in vitro* under agarose assay. Neutrophil chemotaxis towards an intermediate target KC, an end target, WKYMVm, or GM-CSF was quantified. In separate experiments, competition assays were performed where neutrophils were given the choice between two chemoattractants (KC vs. WKYMVm, KC vs. GM-CSF, or WKYMVm vs. GM-CSF).

Results:

The optimal doses of WKYMVm and GM-CSF -induced neutrophil chemotaxis were 1 μ M (48.8 \pm 8.3 cells) and 67nM (31.9 \pm 7.2 cells) respectively. The optimal dose for KC was 1.25 μ M which induced fewer cells to chemotax (13.5 \pm 2.5 cells). In competition assays, neutrophils choose to move toward an end target attractant WKYMVm (37 \pm 5.5) over an intermediate attractant, KC (5.2 \pm 0.96) when they are given the choice. Surprisingly, when given the choice neutrophils move in greater numbers towards GM-CSF (82 \pm 9.2) over WKYMVm (37 \pm 6.4) suggesting GM-CSF is the dominant attractant. Furthermore, neutrophils will move away from a WKYMVm-containing well towards GM-CSF well. We hypothesized that GM-CSF acts as a dominant attractant to recruit neutrophils to be 'primed' and that once primed they will regain the ability to move towards end target chemoattractants. Using GMCSF-primed neutrophils we demonstrated that a) chemotaxis is enhanced towards WKYMVm and KC and b) neutrophils maintain their ability to distinguish between WKYMVm and KC.

Conclusions:

These data suggest that neutrophils will divert towards GM-CSF en route to their ultimate target (e.g. bacterial antigens), demonstrating an important prerequisite for priming prior to arriving at their destination.

Key Words: GM-CSF; Neutrophil; Chemotaxis

Funding Agency: Canadian Institute of Health and Research (CIHR).



Microbiology and Immunology

Category: Clinical

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Value of (1-3)- β -D-glucan, Candida mannan and Candida DNA detection in the diagnosis of candidemia and invasive candidiasis

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Introduction:

Background and Objective: Diagnosis of candidemia and invasive candidiasis poses a major diagnostic and therapeutic challenge in seriously ill patients. The study determined the value of β -D-glucan, Candida mannan, and Candida species-specific DNA as surrogates for the diagnosis of candidemia or invasive candidiasis.

Methods:

Thirty-nine clinically suspected patients who with Candida species in blood cultures were investigated. The Candida species isolates were identified by germ tube test, and by Vitek2 yeast identification system. The serum levels of Beta-D-Glucan (BDG) and Candida mannan (MN) were determined by Fungitell (Associates of Cape Cod, USA) and Platelia Candida Ag Plus (Bio-Rad, France), using positive cut-off values of 80 pg/ml and 125 pg/ml, respectively. Candida species-specific DNA was detected by PCR using species-specific primers designed from the internally transcribed region of rDNA.

Results:

The distribution of Candida spp. Isolated in blood cultures showed: *C. albicans* (n=16), *C. tropicalis* (n=10), *C. parapsilosis* (n=7), *C. glabrata* (n=3) and *C. dubliniensis* (n=3). All 39 serum samples were positive for Candida DNA for the corresponding Candida species isolated in blood. The BDG levels ranged from 43 pg/ml to 979 pg/ml (mean = 339 pg/ml) and MN levels from 15 pg/ml to 845 pg/ml (mean = 262 pg/ml). Three patients yielded BDG values in the intermediate range, that is, 60, 72, and 77 pg/ml with corresponding MN values of 40, 135 and 30 pg/ml, respectively. Two patients who yielded BDG levels lower than the positive cut-off value (43 and 52 pg/ml) had the corresponding MN value of 165 and 270 pg/ml, respectively.

Conclusions:

In culture proven cases of candidemia, detection of Candida spp. DNA was found to be 100% specific and sensitive, whereas the positivity of BDG and MN tests was 87% and 59%, respectively. The data suggest that concomitant detection of these markers provide a useful strategy in the diagnosis of candidemia and invasive candidiasis.

Key Words: (1-3)- β -D-glucan; Candida mannan; Invasive Candidiasis

Funding Agency: KFAS grant no. 2005-130-205



Microbiology and Immunology

Category: Clinical

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Evaluation of automated BACTEC MGIT 960 system for testing susceptibility of Mycobacterium tuberculosis strains to first-line drugs: Comparison with the radiometric BACTEC 460TB system

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Introduction:

The reliability of nonradiometric, BACTEC MGIT 960 system for drug susceptibility testing (DST) of Mycobacterium tuberculosis to first-line drugs isoniazid (INH), rifampin (RMP), streptomycin (STR) and ethambutol (EMB) was compared to that of radiometric BACTEC 460TB system. Detection of resistance conferring mutations in appropriate regions of M. tuberculosis genome by DNA sequencing was used to resolve discrepant results.

Methods:

M. tuberculosis strains (n=38) with various susceptibilities to first-line drugs were tested. DST by BACTEC 460TB and MGIT 960 systems were performed according to protocols supplied by the manufacturer (Becton Dickinson). DNA sequencing of three regions of rpoB, katG codon 315 and inhA regulatory region, embB codons 306, 406 and 497, rpsL codons 43 and 88 and 500 and 1400 regions of rrs gene was performed to resolve discrepant results. False resistance and false susceptibility results were defined as major errors (ME) and very major errors (VME), respectively.

Results:

Overall level of agreement between BACTEC 460TB results and those of BACTEC MGIT 960 method was 93.4%. All strains yielded identical results by both methods for INH and STR. Rifampin results agreed for 36 strains (95% agreement) while EMB results agreed for 30 strains (79% agreement). Ten strains yielded discrepant results of which 8 and 2 strains were resistant to EMB and RMP, respectively, by BACTEC 460TB but susceptible by MGIT 960 system. DNA sequencing studies resolved all discrepant results in favor of BACTEC 460TB system.

Conclusions:

Our data demonstrate that MGIT 960 system is an accurate method for rapid DST of M. tuberculosis against INH and STR while two VME for RMP were caused due to a very rare (I572F) rpoB mutation. However, 8 VME associated with DST to EMB by MGIT 960 system are in line with previous reports showing EMB with least concordant results. More studies are needed to solve the problem of DST for EMB by MGIT 960 system.

Key Words: Mycobacterium tuberculosis; Drug susceptibility testing; MGIT 960 system

Funding Agency: KURA grant MI 02/04.



Microbiology and Immunology

Category: Basic Sciences

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Bioinformatics analysis for identification of promiscuous Th1-cell antigens and peptides encoded by Mycobacterium tuberculosis region of difference 1

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Introduction:

Comparative genomics have identified 16 regions of differences (RDs) specific for *M. tuberculosis*. Among these, RD1 is the most important region that encodes several immunogenic proteins of *M. tuberculosis*. However, an important requirement for RD1 proteins to be useful in diagnosis or vaccination against tuberculosis (TB) is their HLA-non-restricted presentation to protective Th1 cells. In this study, HLA- non-restricted proteins and peptides of RD1 were identified by using a virtual matrix-based prediction program (ProPred) for binding to 51 HLA-DR alleles and the results were confirmed by experimental evaluation in humans.

Methods:

The ProPred analysis of RD1 proteins (n=12) and their peptides (n=220, 25-mers) was performed using the server (<http://www.imtech.res.in/raghava/propred/>). The proteins and peptides predicted to bind >50% HLA-DR alleles were considered HLA-non-restricted and thus promiscuous. Peripheral blood mononuclear cells (PBMCs) were obtained from PPD +ve healthy subjects (n=30) and TB patients (n=40) to determine HLA-DR types by genomic typing and test with RD1 proteins and peptides in Th1-cell assays, i.e. Antigen-induced proliferation and IFN- γ secretion assays.

Results:

The ProPred analysis suggested that all of the RD1-encoded proteins were promiscuous HLA-DR binders. Furthermore, each of these proteins had peptides/epitope regions (9 aa in length) that qualified to be HLA-promiscuous. Testing of PBMCs from HLA-heterogeneous healthy subjects and TB patients showed HLA-DR-non-restricted presentation of several full-length proteins and peptides to Th1 cells, which were identified as HLA-promiscuous by ProPred.

Conclusions:

Bioinformatics-based identification of promiscuous antigens and peptides of *M. tuberculosis* is a time and cost-saving approach to identify HLA-non-restricted antigens and peptides of *M. tuberculosis*, and possibly other infections, with potentials in diagnosis and vaccine applications.

Key Words: Bioinformatics; M. tuberculosis RD1; Diagnosis and Vaccine

Funding Agency: Kuwait University Research Administration Project MI06/08



Microbiology and Immunology

Category: *Clinical*

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ESAT6-like proteins of *Mycobacterium tuberculosis* for diagnosis and vaccine applications

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Introduction:

Previous studies have shown the immunodominance of two small-sized proteins of *Mycobacterium tuberculosis*, i.e. ESAT6 and CFP10. However, more recently, the genome analysis has predicted 21 other proteins with similar size and gene organization. These proteins have been grouped as ESAT6-like proteins with four subfamilies. To identify the proteins useful in the diagnosis and/or developing new vaccines against tuberculosis (TB), the study aimed to determine the immunological reactivity of all ESAT6-like proteins,

Methods:

A total of 141 peptides covering the sequence of all ESAT6-like proteins were synthesized chemically. Peptide pools of each protein were evaluated for protective T helper (Th)1-cell reactivity by testing peripheral blood mononuclear cells (PBMCs) from TB patients (n=30) and PPD+ healthy subjects (n=108) in antigen-induced proliferation and IFN- γ assays. The immunodominant peptides of the reactive proteins were identified by testing individual peptides in the same assays. Furthermore, PBMCs were typed for HLA-DR molecules using genomic methods.

Results:

All ESAT6-like proteins were recognized by PBMCs of TB patients and healthy subjects in the both Th1-cell assays, although, to a varying degree, with the major recognition of Rv1198 and Rv3905 in TB patients and Rv0288 and the proteins of subfamily-1 and subfamily-2 in PPD+ healthy subjects. Further testing of individual peptides showed immunodominance of P1 of Rv1198 and P4 of Rv3905 in TB patients, but the reactivity in healthy subject was scattered throughout the sequence of the recognized proteins. HLA-DR typing showed that the responding donors were HLA-heterogeneous, suggesting that the recognized proteins and peptides were presented promiscuously to Th1 cells in association with many HLA class II molecules.

Conclusions:

Rv1198 and Rv3905 could be suited best in the diagnosis of active TB, and Rv0288 and proteins of subfamilies-1 and 2 for use as candidate vaccines against TB.

Key Words: ESAT-like proteins; Synthetic peptides; Diagnosis and Vaccines

Funding Agency: Kuwait University Research Administration Grant MI05/08



Microbiology and Immunology

Category: Basic Sciences

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Evaluation of Bichro-Dubli latex agglutination test for differentiation of candida dubliniensis from candida albicans

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Introduction:

Candida dubliniensis has several morphological similarities with *Candida albicans* including formation of germ tubes and chlamydo spores, the two key characteristics which differentiate them from other *Candida* species. Since both the species share common phenotypic characteristics, *C. dubliniensis* is often under identified. Traditionally, *C. dubliniensis* is considered to be an opportunistic oral colonizer/pathogen. In recent years, the species has assumed greater clinical significance including its propensity to acquire resistance to azoles. In this study, we have evaluated the specificity of Bichro-Dubli Test for accurately differentiating *C. dubliniensis* from *C. albicans*.

Methods:

One hundred ten clinical isolates, 65 of *C. dubliniensis* and 55 of *C. albicans* were included in the study. *Candida dubliniensis* isolates were differentiated from *C. albicans* by their ability to form rough colonies and chlamydo spores on sunflower seed agar and by assimilation profiles obtained by Vitek2 yeast identification system. The identity of *C. dubliniensis* isolates was confirmed by sequencing of the internally transcribed regions of rDNA. Bichro-Dubli test (Fumouze Diagnostics, Levallois-Perret, France) was performed according to manufacturer's recommendations. Reference strains of *C. dubliniensis* (CBS 7987) and *C. albicans* (ATCC90028) were included in the study.

Results:

All isolates of *C. dubliniensis* showed rapid agglutination when mixed with Bichro-Dubli test reagent, whereas None of *C. albicans* isolates did so. Thus, the test was 100% specific for accurately differentiating *C. dubliniensis* from *C. albicans*.

Conclusions:

Bichro-Dubli test provides a simple, easy-to-use tool for rapidly identifying *C. dubliniensis* isolates with 100% specificity. A wider use of this test is recommended to determine occurrence of this species in different clinical specimens and to assess its emerging role as an opportunistic pathogen.

Key Words: Candida dubliniensis; Candida albicans; Bichro-Dubli test

Funding Agency: KURA grant # MI01/08



Microbiology and Immunology

Category: Clinical

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Nosocomial outbreak of bloodstream infection in an ICU setting caused by CTX-M-15- producing *Klebsiella pneumoniae* associated with high mortality.

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Introduction:

Klebsiella pneumoniae is a well-described healthcare associated pathogen and hospital outbreaks of multiresistant (MDR) strains are posing increasing threat of great dimension to healthcare providers. The objective of this study is to report an outbreak of MDR *K. pneumoniae* bloodstream infections in our ICU and the associated high mortality rate.

Methods:

The isolates were identified using automated VITEK 11 ID System. Susceptibility testing was performed with the E-test method. Extended-spectrum beta-lactamase (ESBL) production was assessed using ESBL E-test and confirmed by PCR. Carriage of *bla* genes and gene-types was determined by PCR and sequence analysis. Isolates were typed by pulsed-field gel electrophoresis (PFGE). Patients, healthcare providers and the environments were screened. Disease severity between MDR infected and non- MDR infected patients was measured by APACHE scores. Patients infected by susceptible isolates were used as controls.

Results:

MDR *K. pneumoniae* isolated from 9 patients with bloodstream infections within a period of 2 months were studied. They were susceptible only to imipenem, meropenem, colistin and tigecycline and all were ESBL producers of CTX-M-15 variety which could be demonstrated in transconjugants created in mating experiments with *Escherichia coli* J53^r strain. One environmental isolate harboring *bla*_{CTX-M-15} was recovered from a suction machine in the ICU. PFGE revealed a cluster of the same strain. Although no significant association was demonstrated between individual risk factors and infection by MDR organism, 3 (33.3%) of the outbreak patients died compared to None in the 11 controls. Outbreak was curtailed by aggressive infection control measures.

Conclusions:

We report an outbreak of CTX-M-15 producing *K. pneumoniae* infections in an ICU setting associated with high mortality. Strict adherence to infection control strategies are indicated in all patients at risk in ICU.

Key Words: Outbreak; Klebsiella pneumoniae; CTX-M-15

Funding Agency: None



Microbiology and Immunology

Category: Basic Sciences

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Molecular characterization and species-specific identification of phenotypically characterized clinical *Candida tropicalis* isolates in Kuwait

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Introduction:

Infections due to non-albicans *Candida* species have increased in recent years. Molecular studies have shown that *Candida* spp. Isolates identified by conventional methods represent a complex of two or more species that exhibit common phenotypic characteristics but differ in their susceptibility to antifungal agents in few instances. Epidemiological data on the occurrence of two closely related *Candida* spp. (*C. tropicalis* and *C. viswanathii*) in clinical settings is lacking. This study determined the frequency of *C. tropicalis* and *C. viswanathii* among phenotypically identified *C. tropicalis* isolates in Kuwait.

Methods:

Type strains of *C. tropicalis* and *C. viswanathii* were used as reference. A multiplex PCR (mPCR) was developed by targeting species-specific sequences in internal transcribed spacer (ITS)1 and ITS2 regions of rDNA that yielded amplicons of 321 bp from *C. tropicalis* and 262 bp from *C. viswanathii*. A total of 82 *C. tropicalis* isolates identified by Vitek2 yeast identification system were tested by mPCR. Species-specific identification of selected isolates was confirmed by PCR amplification of ITS region (including ITS1-5.8S rRNA-ITS2) of rDNA by panfungal primers followed by sequencing of both strands with internal primers.

Results:

DNA from type strains of *C. tropicalis* and *C. viswanathii* yielded amplicons of expected size in mPCR. All 82 phenotypically identified *C. tropicalis* isolates yielded an amplicon of ~321 bp in mPCR that is characteristic of *C. tropicalis* isolates. The DNA sequencing of ITS region of rDNA confirmed the identification of 10 selected isolates as *C. tropicalis*.

Conclusions:

Our limited data on 82 phenotypically identified *C. tropicalis* isolates show that *C. viswanathii* is not a clinically significant pathogen among patients with *Candida* infections in Kuwait. Further studies with larger number of clinical isolates from patients representing different geographical regions are warranted to confirm these findings.

Key Words: Candida glabrata; C. viswanathii; Species-specific identification

Funding Agency: KURA grant MI 01/08



Microbiology and Immunology

Category: Basic Sciences

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Molecular cloning, expression and purification of recombinant ESAT6-like proteins of Mycobacterium tuberculosis

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Introduction:

ESAT6-like proteins (n=23) are among the major antigenic proteins of Mycobacterium tuberculosis, and are useful in the diagnosis and/or developing new subunit vaccines against tuberculosis (TB). However, for both applications, it is required that these proteins are obtained in pure form. The aim of this study was to obtain these proteins by gene cloning, protein expression and purification.

Methods:

Molecular cloning and expression of all ESAT6-like proteins in Escherichia coli was attempted by amplifying their genes using genomic DNA from M. tuberculosis and gene-specific primers in PCR. The amplified DNA were cloned in a cloning vector (pGEMT-Easy) and subcloned in the expression vector pGEST-TH1 for high level expression using glutathione-S-transferase as the fusion partner. The expression of recombinant fusion proteins in E. coli was detected by SDS-PAGE and Western immunoblotting. Some of the proteins were expressed in the soluble fraction and others in the pellet fraction of E. coli sonicates. The pellets were solubilized in urea and the ESAT6-like proteins were purified by loading the soluble or solubilized fusion proteins on Glutathione affinity columns and treatment of the column-bound proteins with thrombin protease. The purified proteins were eluted from the columns and analyzed for purity by SDS-PAGE. If still found contaminated with E. coli proteins, a second affinity column (Ni:NTA column) was used to remove the impurities.

Results:

The successful cloning and expression as recombinant fusion proteins was achieved for 11 of 23 ESAT6-like proteins in E. coli. The affinity purification strategy of soluble and solubilized recombinant proteins lead to the purification of six ESAT6-like proteins (ESAT6, CFP10, Rv2346, Rv2347, Rv1038 and Rv3905) to homogeneity.

Conclusions:

Molecular cloning and expression in E. coli is useful to obtain some of the immunogenic ESAT6-like proteins of M. tuberculosis for diagnostic and vaccine applications.

Key Words: ESAT-like proteins; Molecular cloning; Expression and purification

Funding Agency: Supported by Kuwait University Research Administration Grant MI05/08



Microbiology and Immunology

Category: Clinical

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A comparison of microscopy and rapid diagnostic test for the diagnosis and identification of malaria parasites in Kuwait

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Introduction:

Malaria remains endemic in 106 countries and half of the world's population are at risk of malaria, with 225 million people developed clinical malaria last year (86% in Africa), with nearly 781, 000 deaths (89% in Africa, mostly children). The parasite based diagnosis is increasing, most suspected cases of malaria are still not properly identified, resulting in over-use of anti-malarial drugs and poor disease monitoring.

Methods:

Rapid diagnostic tests (RDT) are promoted for the diagnosis of malaria in many countries. Our aim is to find the suitability and superiority of RDT (Immunoquick Malaria +4, Pf/Pv/Pm/Po) over microscopy, a method known as gold standard, for malaria diagnosis.

Results:

238, 136 new immigrants were screened by Giemsa stained microscopy for the diagnosis of malaria in 2010 and 94 (0.039%) were found positive. All the four species of malaria were detected and their distribution was; *P. vivax* 48.00%; *P. falciparum* 29.00%; *P. ovale* 1.00%, *P. malariae* 2.00% and mixed infection of *P. vivax* and *P. falciparum* 23.00%. Infection with *P. vivax* was found in 46.00% and *P. falciparum* in 12.00% in ICT. A high number of false positive results were found in immunochromatographic technique (ICT) at lower parasitemia and it cannot differentiate the four species.

Conclusions:

ICT has limitations in its routine use under resource-limited conditions. At present, based on these results, microscopy remains the best option for routine diagnosis of malaria in Kuwait.

Key Words: Malaria; ICT; Microscopy

Funding Agency: Ministry of Health, Kuwait



Microbiology and Immunology

Category: Basic Sciences

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Return of High-Level Mupirocin resistance in Methicillin-resistant Staphylococcus aureus in Kuwait hospitals

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Introduction:

The proportion of methicillin-resistant Staphylococcus aureus (MRSA) expressing high-level mupirocin resistance (mupH) in Kuwait hospitals declined from 28% in 1999 to 5.5% in 2009. However, in 2010, the proportion of mupH among MRSA increased to 12.0%. This study was conducted to characterize mupH - MRSA isolated in 2010 to ascertain whether they represent new clones or the reemergence of old clones.

Methods:

A total of 69 single patients mupH MRSA isolates were obtained between January and November 2010. They were characterized using antibiogram, plasmid analysis, pulsed-field gel electrophoresis (PFGE) and staphylococcal Cassette chromosome mec (SCCmec) typing using standard techniques. PCR was used to screen for the presence of mupA, that codes for mupH.

Results:

All 69 isolates contained mupA. They were resistant to ciprofloxacin (98.5%), erythromycin (98.5%), clindamycin (98.5%), gentamicin (95.6%), streptomycin (95.6%), fusidic acid (91.3%), tetracycline (82.6%) and trimethoprim (31.9%). They had three different plasmid profiles: (i) 26 and 2.0 kb; (ii) 40 and 20 kb; and (iii) 28 and 26 kb. PFGE defined seven genotypes designated types A-G. However, 88.3% of the isolates belonged genotypes A (60.5%) and B (27.5%) and were isolated in one hospital. The other genotypes were isolated sporadically in seven hospitals. SCCmec typing showed that 68 of the isolates contained SCCmec III. One isolate contained SCCmec IV.

Conclusions:

The study revealed that the high proportion of high-level mupirocin-resistant MRSA detected in Kuwait hospitals in 2010 was due to the transmission of two clones in one hospital. Whereas the dominant mupH MRSA clones in Kuwait in the 1990s contained 38 or 32 kb plasmids, the current clones lack these plasmids indicating the emergence of new mupH clones.

Key Words: MRSA; Mupirocin resistance; SCCmec typing

Funding Agency: KU Grant MI 01/05



Microbiology and Immunology

Category: Basic Sciences

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Characterization of ampicillin- and vancomycin -resistant enterococcus isolated in a tertiary hospital in Kuwait

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Introduction:

Vancomycin-resistant Enterococci (VRE) is isolated sporadically in Kuwait hospitals. However, a cluster of seven VRE were isolated from patients residing in four wards in a tertiary hospital in Kuwait between 1 and 30 March 2010. This study was conducted to determine the mechanism of vancomycin resistance in these isolates and to determine their genetic relatedness.

Methods:

All 7 Enterococcus isolates were identified using the Vitek GP card and tested for susceptibility to antibiotics by disk diffusion. Minimum inhibitory concentration (MIC) was determined with Etest. Beta-lactamase production was detected using nitrocefin. All isolates were typed using pulsed-field gel electrophoresis (PFGE). PCR assays were used to determine the vancomycin resistance determinant (vanA, vanB or vanC).

Results:

All seven isolates were identified as *E. faecium*. They were isolated from urines (4 isolates), blood (1 isolate), wound (1 isolate) and fluid (1 isolate) from patients in ICU (2 patients), ward 8 (1 patient), ward 12 (2 patients) and ward 11 (1 patient). All were resistant to vancomycin (MIC >256 mg/L), teicoplanin (MIC: 32-64 mg/L), penicillin (MIC: > 32 mg/L), ampicillin (MIC: >256 mg/L), tetracycline, ciprofloxacin and rifampicin but susceptible to linezolid. All contained vanA. None of them produced beta-lactamase. PFGE revealed that all seven isolates were closely related. Five isolates from patients in the ICU, Ward 8 and Ward 11 had identical PFGE patterns.

Conclusions:

The results suggest the transmission of ampicillin –resistant vancomycin –resistant *E. faecium* among patients residing in different wards in a tertiary hospital in Kuwait.

Key Words: Ampicillin resistance; Vancomycin resistant Enterococcus; PFGE

Funding Agency: MI 01/05



Nephrology

Category: *Clinical*

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Impact of swine flu (H1N1) infection in renal transplant recipients

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Introduction:

Swine influenza is a highly contagious respiratory disease in pigs caused by one of several swine influenza A viruses.

Methods:

A retrospective study carried out in Organ Transplant Centre in Kuwait over 69 patients who were infected with swine flu (H1N1). The mean age group of those patients was 38 with a range of (5 -71 year). 19 of them had live related kidney transplant (LRTx), 35 have live unrelated kidney transplant and 15 had cadaveric kidney transplant. All of them have co-morbid conditions. 18 of them have diabetes mellitus, 61 have hypertension, 13 have ischemic heart disease and 13 have pulmonary disease. All are on regular immunosuppression and under regular follow up. All patients underwent history taking about symptoms of the disease and its possible complication, physical examination. Laboratory detection of the virus by polymerase chain reaction from the nasopharyngeal and throat swab and assessment of renal functions before, during, and after recovery of infection. All patients received oseltamivir.

Results:

There is no signification change in renal functions before and after getting the infection. There is no mortality over the period of infection and 6 months follow up post recovery. 4 cases were complicated with pneumonia and was treated in the hospital. 43 cases were treated as outpatient and 22 required admission for observation in infectious disease hospital.

Conclusions:

The course and prognosis of swine flu is benign in renal transplant patients.

Key Words: H1N1; Good prognosis; Not superseeding

Funding Agency: None



Nephrology

Category: Clinical

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Spectrum of glomerulonephritis in Kuwait

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Introduction:

Renal biopsy was first introduced into regular clinical practice by Iverson and Brun in 1951 and since that time it is considered as a useful diagnostic tool in assessing diagnosis, prognosis, and guiding the treatment plans of various renal diseases. Little is known about the pattern of glomerulonephritis (GN) in Arab countries. The aim of this study was to describe the spectrum of GN in Kuwait.

Methods:

All adult native renal biopsies performed in Mubarak Al Kabeer Hospital from January 1995 to December 2009 were retrospectively reviewed. Patients' clinical records were reviewed for demographic data as well as the indications for biopsy.

Results:

Thousand three hundred ninety one adult native renal biopsies were performed during the study period, 47 biopsies were insufficient and were excluded from the study, and 1344 patients with adequate biopsy specimens were enrolled in the study. Three hundred seventy nine (55%) were males and 605 (45%) were females. The mean age was 35.81 12.65 (range 16-77 years). Indications for renal biopsy was; nephrotic syndrome in 810 (60.3%) cases, nephritic syndrome in 221 (16.4 %) cases; and unexplained renal failure in 313 (23.3%) cases. Biopsy results showed glomerular diseases in (86.8%) cases, tubular diseases in 135 (10.2%) cases, and end stage renal disease in 32 (2.4% cases), 21 cases (1.6%) showed normal renal tissue. The commonest primary GN was focal segmental glomerulosclerosis (FSGS) detected in 199 (14.8%) cases, followed by membranous GN detected in 163 (12.1%) cases. Secondary GN was seen in 290 (21.6%) cases. Lupus nephritis was the commonest cause of secondary GN seen in 178 (13.2%) of cases.

Conclusions:

The commonest primary GN in Kuwait was focal segmental glomerulosclerosis (FSGS) (14.8%) cases. Secondary GN was seen in (21.6%) cases. Lupus nephritis was the commonest cause of secondary GN.

Key Words: Renal Biopsy; Primary glomerulonephritis; Secondary glomerulonephritis

Funding Agency: None



Nuclear Medicine and Radiology

Category: *Clinical*

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Differential Regional Lung (DRL) Perfusion Analysis of the Lung Scan as an Adjunct Interpretation Parameter for Pulmonary Embolism

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Introduction:

Pulmonary embolism (PE) causes blockage of branches of the pulmonary artery by clots, manifested as defects on the standard lung perfusion scan. Another effect, which has not been well studied, is the diversion of blood and the blood-borne radiolabeled particles injected for the lung scan, from the blocked areas to the adjacent territories. Hence, a pattern of increased uptake would be seen in those areas on the lung scan that would show normal uptake if no such diversion exists. The aim of this study is to evaluate a semiquantitative analysis method, differential regional lung uptake (DRL) of Tc-99m MAA lung perfusion scan to check for areas of increased uptake as a parameter that shows this phenomenon.

Methods:

The posterior view of the standard lung perfusion scan was divided by 6 regions of interest for each lung to approximate the segmental anatomy in that projection. The DRL uptake was calculated as the deviation from the average count in a selected ROI segment to the average count in the adjacent segment and was obtained for 30 scans of each normal, low, intermediate and high probability scan, diagnosed using the conventional PIOPED criteria used in the department.

Results:

The results showed a significantly higher DRL in an average of 8.3 ± 2.2 lung segments per study in high probability scan compared to the normals ($p > 0.001$). An average of 3.1 ± 0.9 and 5 ± 2.7 lung segments per study was found in low and intermediate probability respectively. In intermediate scans, higher number of segments with an increase of DRL was found to have positive spiral lung CT, whereas lower values had negative CT.

Conclusions:

Cutoff values for the ratio in each region were defined using the data from normal and high probability scans. These values could be used as basis for comparison in cases with intermediate or low probability scans for PE to provide a more objective confirmation of the pathophysiological phenomenon of regional blood flow diversion.

Key Words: PE; Lung scan; DRL

Funding Agency: None



Nuclear Medicine and Radiology

Category: Clinical

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Evaluation of parathyroid lesions with Tc-99m MIBI in patients with end stage renal disease

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Introduction:

Technetium-99m MIBI scintigraphy nowadays is a useful technique in the diagnosis of parathyroid gland disease. The diagnosis of parathyroid lesions with Tc-99m MIBI scintigraphy is based on the difference in clearance rates between the thyroid gland and diseased parathyroid glands. The characteristic retention of Tc-99m MIBI within the diseased parathyroid has been attributed to the high metabolic activity and mitochondria-rich oxyphil cell content of the lesion.

Methods:

This study included 30 patients with end stage renal disease. PTH level was assayed. Planar and sometimes SPECT parathyroid scintigraphy was performed 15–30 minutes and 2–3 hours after intravenous administration of 20–25 mCi (740–925 MBq) of Tc-99m MIBI. The field of view encompasses the neck and thorax. For planar imaging, anterior, sometimes lateral, and oblique views are obtained with a low-energy, high-resolution collimator. An additional pinhole image was used to evaluate some cases.

Results:

PTH level was ranged from 25-143 pg/mL.

In the Tc 99m MIBI scintigraphy we found:

- ı 17 patients had no abnormalities in spite of some had high PTH level.
- ı 13 patients had parathyroid abnormalities in spite of normal PTH level in some of of them; in this category:
 - ı 8 patients had parathyroid adenoma.
 - ı 5 patients had hyper parathyroid.

Conclusions:

From this small number of patients we found:

- Not all cases with end stage renal disease had high PTH level, or abnormal parathyroid Tc99m MIBI scintigraphy.
- No correlation between PTH level and the abnormalities in the parathyroid scintigraphy as some parathyroid lesions may be below the camera resolution.

Key Words: Parathyroid lesions; Tc99m MIBI; End stage renal disease

Funding Agency: None



Nuclear Medicine and Radiology

Category: Clinical

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The role of radionuclide guided sentinel lymph node biopsy in high risk ductal carcinoma in situ of the breast

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Introduction:

Ductal carcinoma in situ (DCIS) currently represents about 15-25% of all breast cancers detected. Although inherently a non-invasive disease, occult invasive disease could be found at definitive histology. The role of Sentinel Lymph Node (SLN) biopsy in DCIS is still unclear. The aim of the present study is to evaluate the clinical usefulness of sentinel lymph node biopsy and the incidence of sentinel lymph node metastases in a selected high-risk ductal carcinoma in situ who are at highest risk for being upstaged to invasive carcinoma.

Methods:

Twenty three high risk patients with DCIS proven on core biopsy (mean age, 50yrs; median age 48yrs; age range, 37-78 yrs) were included in the study. SLN scintigraphy was performed 2-4 hour before surgery by injecting Tc-99m labeled nanocolloid intra-dermally in the periareolar region. First lymph node (LN) to appear on the scan was labeled as SLN and marked on the skin by using gamma probe. LN was explored in the axilla using a gamma probe.

Results:

The SLN was identified in all patients (100% success rate). Out of 23 cases of DCIS on core biopsy, seven patients (30%) turned out to have ductal carcinoma on final histological specimen. Among these seven patient, three had minimal invasive carcinoma (<1cm) and None of these patients has positive SLN for metastases. Among 23 cases only one (4%) SLN was positive for metastasis despite histopathological diagnosis of pure DCIS.

Conclusions:

Although the study population is small our findings suggests that high risk DCIS patients have an increased risk of invasive disease as approximately one-third of these patients had invasive component at the time of definitive operative procedure. Further the study also suggest that SLNB appear to be reliable in identifying axillary lymph nodes status of these patients

Key Words: Sentinel lymph node biopsy; Lymphoscintigraphy; Ductal carcinoma-in-situ

Funding Agency: None



Obstetrics and Gynecology

Category: *Clinical*

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Maternal obesity and pregnancy in Kuwait: A major problem

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Introduction:

Obesity in women can cause serious pregnancy-related complications, but it is a risk factor that can be modified to improve birth outcomes. The aim of the study is to investigate the incidence of obesity among Kuwaiti pregnant and explore consequences of obesity on pregnancy in Kuwaiti mothers.

Methods:

A comparative study that included 550 pregnant women (367 Kuwaitis and 174 Non-Kuwaitis) who were registered for antenatal care between April and June of 2010. Body weight (Kg) was measured in light clothing and height (cm) was measured using a stadiometer. Comparison between mean values of BMI in the 2 groups (Kuwaitis and non-Kuwaitis) mothers was evaluated using students t test. The association between BMI and gestational diabetes risk was determined by calculating the odds ratio (OR) using binary logistic regression.

Results:

394 (71%) were obese (defined as those BMI >30 Kg/m²) and 124(22.5%) were overweight (defined as those BMI 25-30 Kg/m²) whereas the BMI of 32(5.8%) of cases were in the desirable BMI range (≤ 25 Kg/m²). Of 367 Kuwaiti mothers, 72.34% were obese according to WHO guidelines, 23.4% were overweight while 4.26% of Kuwaiti mothers had desirable BMI (defined as BMI ≤ 25 Kg/m²). There was a significant ($p=0.024$) difference in BMI between Kuwaitis (BMI =35.5 Kg/m²) and Non-Kuwaitis mothers (BMI = 29.5 Kg/m²). We also found that there is a significant association between BMI and mode of delivery ($p=0.007$). Obese women were more likely to have delivery by caesarean section than non-obese pregnant women [OR=2, 95%CI (1.5-3)]. Obese women were more likely to have gestational diabetes than non obese women [OR=1.5, 95%CI (1-2.5)].

Conclusions:

Obesity is a major problem among pregnant women in Kuwait. Labour is more likely to be slow and prolonged, increasing the likelihood of cesarean section. Thus, there is need for immediate mass media to increase the pregnant women awareness on obesity and related health problems.

Key Words: Obesity; Pregnancy; Kuwait

Funding Agency: None



Obstetrics and Gynecology

Category: *Clinical*

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Features of Polycystic Ovarian Syndrome in Adolescent Women and management with Metformin.

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Introduction:

Polycystic ovary syndrome (PCOS) is characterized by anovulation, in form of irregular or absent menstrual periods and hyperandrogenism manifesting as elevated androgens with hirsutism, acne and deepening voice. Adolescent PCOS presents a serious treatment challenge because the features are like those of pubertal changes.

Objective: To investigate the clinical features of PCOS in adolescent women and the role of Metformin and exercise in the management.

Methods:

Twenty-seven adolescent women, between 10 and 20 years of age with anovulation and hyperandrogenism, were recruited from the outpatient clinic. All had clinical (history and physical examination) and biochemical (Hormone and lipids profiles and SHBG) evaluation and randomized into 3 treatment groups: Metformin only, Metformin and Exercise and Exercise only and followed up for 3 months.

Results:

The features of PCOS included oligomenorrhea, high BMI and acne like in other parts of the world. All the three options resulted in weight reduction and regular menstrual periods in about 34 % respectively. Metformin with exercise had a more significant effect in decreasing total testosterone 50 % as compared to 28% with metformin only 14 % with exercise only. Similarly, there was increase in HDL (44 % to 20 % and 12%) and SHBG, but no effect on hormone profile.

Conclusions:

Metformin and exercise individually resulted in significant weight reduction and regular periods, but combined metformin and exercise was better at reducing total testosterone and increasing HDL.

Key Words: Adolescence; Polycystic ovaries; Metformin

Funding Agency: None



Obstetrics and Gynecology

Category: Graduate MSc (Basic Science)

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Chlamydia trachomatis, Mycoplasma hominis, Mycoplasma genitalium and Ureaplasma urealyticum infections and seminal quality in infertile men

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Introduction:

Objective: The aim of this study was to compare the occurrence of genital Chlamydia trachomatis, genital mycoplasmas and ureaplasmas in semen samples of fertile and infertile men in Kuwait

Methods:

A total of non-duplicated 315 semen samples collected from 127 infertile and 188 control men seen at the infertility clinics in Maternity hospital were studied after informed consent. Semen analysis was performed according to the guidelines of World Health Organization. The specimens were examined for the presence of Ureaplasma urealyticum, Mycoplasma hominis, Mycoplasma genitalium and Chlamydia trachomatis by PCR using published specific primers. Biodata, such as age, nationalities, and marital status were carefully recorded.

Results:

The frequency of genital U. urealyticum, M. hominis, M. genitalium and C. trachomatis in all semen samples was respectively 26% (82/315), 27% (86/315), 5.4% (17/315) and 8.3% (26/315). Mixed infections were detected in 14% (44/315). The infertile participants positive for U. urealyticum and M. hominis, respectively had semen samples that showed statistically significant difference in the mean of sperm concentration, vitality percentage, total progressive and rapid progressive motility in comparison to control fertile participants ($P < 0.001$). Similar statistical significance difference was noted for those infertile and fertile men positive for M. genitalium and C. trachomatis ($P < 0.001$). Infections in infertile men who had been married for less than 5 years were significantly higher than in infected fertile men of the same length of marriage.

Conclusions:

Infections caused by these urogenital pathogens were more common among infertile men than fertile men and may possibly play a role, in part, in the etiology of male infertility in this part of the world. Genital mycoplasmas and chlamydial infections may negatively influence semen quality.

Key Words: Genital infections; Semen Quality; Kuwait

Funding Agency: Kuwait University Research Administration Grant No. YM 03/09.



Obstetrics and Gynecology

Category: Clinical

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The prevalence and Predictors of Gestational Diabetes Mellitus in Kuwait and its relationship with Butyrylcholinesterase.

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Introduction:

Gestational diabetes mellitus (GDM) is commonly defined as glucose intolerance first recognized during pregnancy. The underlying aetiology is insulin resistance and its association with oxidative stress. The relationship between butyrylcholinesterase (BuChE) and GDM is of clinical interest

Objective of Study: To evaluate the Prevalence and Predictors of GDM and its relationship with BuChE.

Methods:

The study is in three parts. The first part involves all patients who delivered at the Maternity Hospital with diagnosis of Diabetes Mellitus in Pregnancy, the pregnancy course and neonatal outcome. Diagnosis is made using a sequential model of universal screening with fasting blood glucose, followed by a diagnostic 75-g three-hour oral glucose tolerance test for women with a positive screening test. The second part is to attempt to evaluate the predictors of GDM through detail history 50 randomly selected patients. The third part will investigate the role of BuChE in the pathogenesis of GDM.

Results:

The prevalence of diabetes mellitus in Maternity Hospital in 2010 was 4.5 percent (544/12100) made up of 409 (75.2%) patients with GDM, 120 (21.1%) Type 2 diabetes and 15 (2.7%) with Type 1 diabetes mellitus. Pregnancy induced hypertension was a common antenatal complication in 17.5% of the patients. Predictors of GDM included Obesity, family history of type 2 diabetes mellitus, macrosomic baby and GDM in a previous pregnancy. Butyrylcholinesterase activity was reduced in the serum of patients with GDM compared to controls.

Conclusions:

GDM and its maternal and perinatal complications are common in Kuwait. Understanding the pathogenesis and predictors and implementing an effective management strategy of GDM should be an issue of priority.

Key Words: Gestational; Diabetes; Butyrylcholinesterase

Funding Agency: None



Obstetrics and Gynecology

Category: *Clinical*

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Pregnancy outcome in the fifth decade and beyond a concern?

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Introduction:

To study maternal and perinatal outcomes in healthy women aged 50 years and older.

Methods:

This study was of 59 clinical pregnancies, of which 10 ended in the first trimester spontaneous miscarriage (and were excluded from further studies) and 58 live births. This retrospective review of 58 live births in 49 essentially healthy women (mean [SE] age, [52±2.4] years; range 50-55 years), with no chronic medical conditions (of which 28 were primigravidas). Pregnancy outcomes were ascertained by chart review and telephone follow-up.

Results:

Of the 58 live births, 41 were singletons, and 7 were twins and 1 triplet, for which the mean ±SE gestational age at delivery were 38.09 weeks ±0.39, 36.19 weeks ±0.09 and 34.09 weeks respectively. Birth weights (mean ± SE) were 3, 201 g±09, 2, 252 g±39 and 1, 998±94 g respectively. Mean Apgar score ± SE at 1 and 5 min were 9.2±0.79 and 8.8±0.59 respectively. Total cesarean deliveries were 73% (36/49). Of singleton 68% (28) were delivered by cesarean section as were all multiples. The incidence of pre-eclampsia was 30.6% mild pre-eclampsia 20.4% (10/49), severe pre-eclampsia 10.2% (5/49). Gestational diabetes required insulin in all 19.5% of women. Anemia was noted in 6.5%.

Conclusions:

Appropriately screened women, aged 50 years or older, can deliver successfully. During pregnancy, they appear to be at increased risk of pre-eclampsia and gestational diabetes. A significant majority can expect to deliver via cesarean.

Key Words: Fifth decade; Maternal outcome; Perinatal outcome

Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

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Emergency peripartum hysterectomy in a Kuwait Teaching Hospital: A preliminary 26 year review

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Introduction:

To identify the risk factors and study the incidence, indications and complications of emergency peripartum hysterectomy (EPH) from January 1983 till Jan 2011

Methods:

A retrospective case control study. Controls were women who delivered immediately before and after the indexed case. Index cases were identified from the delivery register. Demographic, pregnancy, intrapartum, and postpartum data were collected, as were medical and surgical records.

Results:

There were 59 Cases of EPH in 150, 993 deliveries, giving a rate of 0.390 per 1000. Analysis was made for 56 Cases, as 3 files were unavailable. These women were significantly older (mean age 35 years vs 21 years, $P<0.01$) and multiparous ($P=0.02$). 68% of Cases had previous caesarean section (CS) and this was significantly greater than the controls (22%, $P<0.01$). Significantly more index cases had a history of atonic postpartum haemorrhage (PPH) (46% vs 4%, $P<0.001$) and placenta praevia (34% vs 4%, $P<0.01$). Significantly more Cases than controls delivered by CS (66% vs 23% ; $P=0.003$). Repeat CS with placenta praevia were increased in index Cases ($P<0.01$). All hysterectomies were done by senior Obstetricians. Leading indications for emergency peripartum hysterectomy were haemorrhage due to uterine atony and placenta praevia. Independent risk factors were older age, multiparity, history of one or more CS and placenta praevia. There were 2 maternal deaths from coagulopathy following massive haemorrhage due to difficult instrumental delivery and atonic postpartum haemorrhage. The main complications of EPH were febrile morbidity(21%), wound infection (14%) and bladder/ureteric injury (14%).

Conclusions:

Caesarean deliveries, especially repeat CS in women with placenta praevia and persistent uterine atony significantly increase the risks of peripartum hysterectomy. Anticipation, prompt resuscitation and early surgical intervention by skilled operators will reduce maternal morbidity/mortality.

Key Words: Peripartum Hysterectomy; Risk factors; Haemorrhage

Funding Agency: None



Obstetrics and Gynecology

Category: *Clinical*

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Sickle Cell Disease in pregnancy in a tertiary care centre in Kuwait.

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Introduction:

Sickle cell disease in pregnancy may be complicated by increased incidence of miscarriages, preterm delivery, fetal growth restriction and sickle cell pain crises and complications. Low maternal/perinatal morbidity/mortality are attainable with multidisciplinary management. The aim of this study was to assess the performance of patients with sickle cell disease in pregnancy.

Methods:

A retrospective study of 28 patients admitted with sickle cell disease in pregnancy, June 2007-September 2010, at Maternity hospital, Kuwait, was undertaken. The social bio-data, the past medical/surgical/haematological/obstetric records of the patients were retrieved. The antenatal/intrapartum/postpartum performance of the patients were extracted from the records and the maternal/ perinatal morbidity/mortality documented.

Results:

85.7% were Kuwaitis and 14.3% non-Kuwaitis. 53.6% of the patients presented with sickle cell anaemia[SS], 25.6% with SC and 21.4%, S beta thalassaemia. The patients had previous history of bone pain crises[25%], haemolytic crises[32.1%], previous blood transfusion[60.7%] and cholecystectomy[10.7%]. The mean age and parity of the patients were 29.25±6.547 years and 2.44±2.577. The incidence of preterm delivery was 35.7%, sepsis, 14.3% and fetal growth restriction, 7.1%. 39.2% of the patients were admitted in the intensive care unit of the hospital with severe bone pain crises/haemolytic crises, suspected acute chest syndrome[14.3%], and severe anaemia[10.7%]. 28.6% of the patients required blood transfusion and 10.7% exchange blood transfusion. Caesarean section was performed in 28.6%. The mean gestational age at delivery was 33.79±3.965 weeks, and the mean birth weight, 2.862±0.574kg. 68% babies had Apgar score of ≥7. There were no maternal/perinatal deaths.

Conclusions:

Sickle cell disease in pregnancy was associated with a high incidence of maternal morbidity. The incidence of preterm delivery and the rate of caesarean section were high.

Key Words: Sickle cell disease; Miscarriages; Preterm delivery

Funding Agency: None



Obstetrics and Gynecology

Category: Basic Sciences

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Placental transport kinetics of 3-O-methyl glucose in vitro in obese gestational diabetic pregnancies

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Introduction:

Previous reports from our laboratory had shown that maternal-fetal transport kinetics of D-glucose were altered in insulin-dependent diabetic pregnancies. This study was meant to explore whether transport kinetics of a non-metabolisable glucose analogue, 3O-methyl glucose were altered in non-insulin dependent obese diabetic pregnancies.

Methods:

Human placentae from obese gestational diabetic pregnancies and from control pregnancies were collected post-partum. ¹⁴C labelled 3-O-methyl 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 and perfusate samples collected from maternal and fetal circulations over a period of 5 minutes. National Culture and Tissue Collection medium, diluted with Earle's buffered salt solution was used as the perfusate. Concentration of labelled substances in perfusate samples was assessed by scintillation spectrometry (LKB Wallac Scintillation Spectrometer, Denmark) using pre-adjusted double window counting. Transport kinetics of substances studied were computed using established permeation parameters.

Results:

Differential transport rates of methyl glucose and tritiated water in 8 perfusions differed significantly (Student's t-test ; $p < 0.05$) for all transport fractions studied in control and experimental perfusions. TR50 indices of 3-0-methyl glucose, compared to reference marker averaged 0.79 and 0.81 in control perfusions (n=8) and diabetic perfusions (n=8) respectively. The difference observed in TR 50 indices of the methyl glucose in control and study groups was not statistically significant (Student's t-test, $p > 0.05$) Indices of transport fraction and certain pharmacokinetic parameters such as area under the curve, absorption rate, elimination rate of methyl glucose compared to reference marker were significantly different ($p < 0.05$) between the two groups. Absorption rate: elimination rate indices of methyl glucose differed significantly between control and study groups (Student's t-test ; $p < 0.05$).

Conclusions:

Our studies show for the first time that transport behaviour of a non-metabolizable glucose is altered in obese gestational diabetic pregnancies and that the altered behaviour of placental membrane in hexose transport in such pregnancies, has the potential to cause undesirable consequences for the mother as well as the fetus and neonate.

Key Words: Maternal-Fetal Exchange; O-Methyl Glucose; Human Diabetic Pregnancies

Funding Agency: Kuwait University Research Grant#M0032



Obstetrics and Gynecology

Category: *Clinical*

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Management of midtrimester premature Rupture of Membranes: Do not abort Destiny.

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Introduction:

Background: Midtrimester preterm premature rupture of membranes (PROM) confronts both clinicians and patients with a difficult management dilemma

Objective: To evaluate the maternal and neonatal outcomes in expectant management of PROM between 14- 23 weeks of gestation.

Methods:

Patients with spontaneous PROM from 14 to 23 weeks' of gestation between January 1, 2006 and December 31, 2010 form the subjects of the present study. A total of 88 pregnancies were managed during the period. The diagnosis of PROM was made with nitrazine pH meter, ferning test or direct visualization drainage of liquor through the external os. Digital examination and tocolysis were avoided.. Antibiotic therapy included Gentamycin, Metronidazole and Ampicillin and modified according to the sensitivity after culture of high vaginal swab. Dexamethasone was administered when the patient reached 24 weeks of gestation.

Results:

Out of the 88 patients, 72 (81.8%) were singleton pregnancies, 12 (13.6%) twins, 3 (3.4) Triplets and 1 (1.2%) quadruplets. Median latency period was 9 days (1-56 days). Indications for delivery included spontaneous labour (72.7%), chorioamnionitis (33%), cord prolapse (12.5%), Abruption placenta (11.4) and elective induction (2.3%). 19 babies (21.6%) survived and were discharged home with their mothers, 16 (18.2%) early neonatal deaths, intrauterine fetal deaths (IUFD) 14 (15.9%) and miscarriage (44.3%). Perinatal outcome Singletons was 20.8%, Twins 12.5% and Triplets 11.1%, and gestation at PROM:14-16 weeks 8.3%, 17-19 weeks 13.0% and 20-23 weeks 29.7%. Maternal postpartum infection occurred in 25 % of the women.

Conclusions:

Neonatal survival in spontaneous midtrimester PROM is low, especially PROM below 20 weeks of gestation. Survival improves with increasing gestational age at ROM and at delivery.

Key Words: Midtrimester; Premature rupture of membranes; Perinatal outcome

Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

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The consequences of cesarean section by demand in Kuwait.

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Introduction:

Introduction: In responding to patient requests for Cesarean Section(CS), the physician must consider ethical principles and the effect on the service.

Objective of the study: To investigate the determinants of demands of patients for CS and possible consequences.

Methods:

This is a prospective evaluation of requests for CS by patients who delivered at the Maternity Hospital, Kuwait between January 2008 and December 2010. During the study period, all patients that requested for CS and mentioned at the hand-over morning meetings, were interviewed before their discharge from hospital.

Results:

During the study period, there were 33, 966 total deliveries, out of which 9, 647 were by CS, thus giving an incidence rate for CS to be 32.8 percent (From 3.9% in 1973 and 12.6% in 1989). Patients demand for CS during the study period was 1351 (14.0%). The main indications for request for CS were prior 1 CS, Multiple pregnancy and Breech presentation. CS on demand is presently the third commonest indication for CS behind 2 previous CS or more and failure to progress in labour.

Conclusions:

Demands for CS by patient have contributed to the increase in the CS rates. Lack or poor education of the patients by doctors.

Key Words: Demand; Caesarean Section; Consequences

Funding Agency: None



Obstetrics and Gynecology

Category: *Clinical*

131

The problem of Primary Ovarian Insufficiency: Biochemical and thematic analysis of emotional reaction.

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Introduction:

Primary ovarian insufficiency is cessation of ovarian function before the age of 40 years with consequent permanent cessation of menstruation

Objective of study: To evaluate the clinical features and biochemical and thematic analysis of the emotional reactions of the women.

Methods:

Forty-one women seen at the outpatient clinic of Maternity Hospital fulfilled the study criteria and were recruited into the study. At the first clinical consultation, clinical evaluation with history, physical examination and investigation was carried out. The investigations included blood samples were taken for determination of autoimmune antibodies, hormone profile –FSH, LH, prolactin, testosterone and thyroid function test and lipid profile. Bone density evaluation using QCT Scan was carried out in 17 of the patients. In order to have an idea of ovarian reserve, serum levels of Anti-Mullerian hormone were estimated using sandwich ELISA. Thematic analysis of emotional reaction was done providing relevant themes of the adaptation of the Chronic Disease Self-Efficacy Scale.

Results:

All patients had high FSH and LH levels in the menopausal age (> 40 iu/L). However only 20 (48.8%) had climacteric symptoms. Unpredictable ovarian function occurred in about 35 % of cases with spontaneous menstruation. Evidence of autoimmunity was observed in 41.5% of the women including anti-thyroid and antiovarian antibodies. About 15 % had elevated total cholesterol and LDL. Anti-Mullerian hormone was extremely low in all the patients. Learning of the diagnosis of ovarian insufficiency is a traumatic life event similar to bereavement, with high level of depression, lower life satisfaction and impaired self esteem. Fertility is usually of profound concern.

Conclusions:

Primary ovarian insufficiency is associated with health issues such as cardiovascular disorders, osteoporosis and fracture and severe emotional distress.

Key Words: Primary Ovarian insufficiency; Emotional distress; Health issues

Funding Agency: None



Oncology

Category: Graduate MSc (Basic Science)

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Effect of growth factors and Tyrosine Kinase Inhibitors on invasion of endocrine dependent and resistant breast cancer cell lines using an Under-Agarose Assay

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Introduction:

Endocrine therapy is the basis of treatment of women with estrogen receptor (ER) +ve breast cancer, but is seriously hampered by de novo and acquired loss of responsiveness and high relapse rate. To study mechanisms of resistance we examined the effect of loss of cellular ER function on in vitro invasive ability.

Methods:

Using an under-agarose gel assay as a partial simulation of the extracellular matrix, we compared the ability of ER+ve (MCF7), ER-ve (MDA231) and ER-siRNA silenced (pII) cell lines (seeded into wells) to invade into surrounding agarose either randomly or directionally towards growth factors (added into separate wells) acting as chemoattractants. Movement of cells was monitored 24h after treatments by visual microscopic counting and data statistically compared by Student's t test.

Results:

MCF7 were unable to penetrate into the agarose under any condition. Both MDA231 and, to a significantly greater extent, pII exhibited specific invasion towards wells containing TGF β , RANTES, EGF and IGF-1 in a dose dependent manner. Random invasion of pII cells could be reduced by the prior addition of Imatinib, a receptor tyrosine kinase inhibitor, at concentrations (85nM) that were previously shown to block cell proliferation. Competitive effects were also observed on the specific movement of pII towards a source of TGF β , with 87% inhibition of invasion towards 1 ng/ml TGF β and 66% with 1 ug/ml.

Conclusions:

The loss of ER confers propensity for invasion on breast cancer cells. This activity is accentuated by induced loss of ER compared with cells exhibiting a de novo low level expression. Chemotactic movement towards several growth factors confirms their increased role in promoting cellular invasion permitting subsequent metastasis of endocrine resistant cells, which could be blocked by inhibiting tyrosine kinase activity of particularly epidermal growth factor receptor.

Key Words: Breast cancer; Endocrine resistance; Invasion

Funding Agency: Kuwait University, ZP01/10



Oncology

Category: Graduate MSc (Basic Science)

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Ki-ras proto-oncogene mutation and p53 expression in colorectal cancer in Kuwait: demographic, clinicopathological characteristics and clinical significance

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Introduction:

Genetic alterations in p53 and Ki-ras genes have a pivotal role in colorectal cancer (CRC) tumorigenesis. Purpose: To estimate the frequency of Ki-ras mutation and p53 tumor expression in CRC in Kuwait, and evaluate their clinical usefulness as prognostic factors.

Methods:

185 available paraffin-preserved CRC samples were collected from patients who were treated surgically from 1999 through 2008 in Kuwait Cancer Control Center (HMJ). Ki-ras proto-oncogene mutations were determined using dideoxysequencing. The expression of p53 protein and apoptotic index (AI) was studied using specific monoclonal antibody and TUNEL assay, respectively. The correlation between studied factors and each of the clinicopathologic variables was evaluated using the appropriate statistical analysis.

Results:

Ki-ras mutations were detected in 18.3% of cases in which 16.7 % showed codon 12 mutations, while 1.6% had mutations in codon 13. Out of 179 analyzed samples, p53 protein expression was negative in 35.1% tumor tissues. The median apoptotic index (AI) was 12 % (range 5-20%). Using Chi-square test, there was no significant correlation between p53 expression, Ki-ras mutations and clinicopathologic features. In contrast, AI was found to be significantly high in early Dukes' stages ($p=.042$) and well/moderate tumor differentiation ($p=.042$). Using multivariate Cox-regression analysis, Dukes' stage classification showed to be the only factor affecting the progression-free survival (PFS), in which tumors with early Dukes' stage showed reduce risk of disease recurrence(hazard ratio, .289; 95% CI, .122- .684; $p=.005$).

Conclusions:

Ki-ras mutation and p53 stability appear to be common events in CRC in Kuwait. While Dukes' stage remains the best criterion to estimate PFS, AI appears to differentiate between early and late Dukes' stages, a data that may have significant clinical relevance in the future.

Key Words: Colorectal cancer (CRC); Ki-ras; p53 protein

Funding Agency: College of Graduate Studies and Research administration facility- project number 16/09



Pathology

Category: *Clinical*

134

Utility of fine needle aspiration cytology in the follow-up of patients with breast carcinoma

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Introduction:

Core Needle Biopsy (CNB) is gradually replacing fine needle aspiration cytology (FNAC) in many major breast clinics in the West due to its ability to definitively diagnose invasion and provide tissue for valuable markers for management of the patient. However, FNAC is still effective for women with fluid filled cysts, in preoperative staging of screen detected invasive breast carcinoma and in the post operative management. The aim of this study was to document the utility of FNAC in the follow-up of patient with breast carcinoma.

Methods:

Over a three year period (2008 – 2010), 535 breast cancer patients had undergone a FNAC during their routine follow up in Hussain Makki Al Juma Centre for Specialized Surgery. Their age ranged from 28 to 86 years with a mean of 51.48 years.

Results:

The recurrence/ metastatic sites aspirated were 224 breast, 209 lymph nodes, 53 scar nodules, 35 others and in 14 patients multiple sites were aspirated. Of the 535 aspirates, 101 were reported as unsatisfactory. Of the 434 satisfactory aspirates, 236 were benign, 18 atypical cytology, 19 suspicious cytology, 160 carcinoma and 1 Non-Hodgkins Lymphoma.

In 250 aspirates, the same side as the primary breast carcinoma had a recurrence (left 114 and right 136) while in 132 the contralateral side was involved. The lymphnodes involved were 180 (contralateral 51, ipsilateral 129). The other sites with metastasis were bone (9), liver(6), soft tissues(13), lung(3), mediastinum(1), pleural fluid (1) and neck(2).

Conclusions:

FNAC is used less frequently in centres where CNB is routinely performed for breast carcinoma. However, it is found to be of great value in documenting recurrence/ metastasis in the follow of patients.

Key Words: Recurrence, metastasis; Fine Needle Aspirates; Breast carcinoma.

Funding Agency: None



Pathology

Category: Undergraduate

135

Determinants of blood uric acid levels in a dyslipidemic Arab population

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Introduction:

Hyperuricemia is associated with coronary artery disease (CAD) in some populations, for reasons yet unknown. This study therefore explored relationships between circulating uric acid (UA) and lipids' levels and components of the metabolic syndrome (MetS), in Arab dyslipidemic subjects, a group already at high CAD risk.

Methods:

The medical records of 1229 subjects (632 men & 597 women) referred for treatment of dyslipidemia and followed up for at least 12 months were reviewed. Serum levels of UA and lipids (total cholesterol, triglycerides, LDL, HDL) and other variables in the National Cholesterol Education Program (NCEP) ATP III criteria definition of MetS were assessed at initial presentation and every 4-6mo, on specific treatment, in each of the subjects. Their respective associations were explored by appropriate logistic regression techniques with control for confounding.

Results:

About 24% of the study population was hyperuricemic; the latter were more likely to be men, obese and diabetic. Also serum UA was greater in men with MetS compared with men without, an observation not reproduced in women. UA levels had significant associations with presence of fasting hyperglycemia, hypertension, and large waist circumference (WC) in men, but only with large WC in women. With statin treatment, UA levels decreased by 10% by 1 yr of treatment; with fibrates, UA levels remained unchanged or slightly increased.

Conclusions:

Hyperuricemia is common in dyslipidemic patients in Kuwait, where its important determinants are male sex, obesity, diabetes and statin treatment.

Key Words: Urate; Metabolic syndrome; Dyslipidemia

Funding Agency: None



Pathology

Category: *Clinical*

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Castleman disease: A clinico-pathological study of four cases in Farwaniya hospital

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Introduction:

Castleman disease (CD) is a rare lymphoproliferative disorder characterized by wide spectrum of clinical presentations. Histologically, (CD) is classified into hyaline vascular disease and plasma cell variant which carries worse prognosis. In this report we are presenting clinico-pathological review of four cases diagnosed in Farwaniya hospital .

Methods:

The pathology files of Farwaniya hospital were searched for (CD). The clinical history, follow-up data were retrieved from patients charts.

Results:

Four cases were retrieved from files. The patients were one male and three females. Age ranges (27-56). The clinical presentations were variable from asymptomatic solitary mass to multi-systemic disease. Pathological findings revealed two cases of hyaline vascular type and two plasma cell variant.

Conclusions:

(CD) is a rare systemic disease. Clinicians and pathologists should be aware of it. To the best of our knowledge. This is the largest series of cases to be presented in Kuwait

Key Words: Castelmann disease; Lymph node; Lymphoproliferative disorder
Funding Agency: None



Pathology

Category: Clinical

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Fine-Needle Aspiration (FNA) Cytodiagnosis of anaplastic large cell lymphoma (ALCL): value and limitations

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Introduction:

Anaplastic large cell lymphoma (ALCL) is a rare subtype of non-Hodgkin's lymphoma that is difficult to diagnose on fine needle aspiration cytology (FNAC) because of their resemblance with other neoplasms. There are only a few studies on ALCL involving a series of cytologically diagnosed cases.

Methods:

In the present report, the clinico-cytomorphological features of six histologically diagnosed ALCL cases are described and compared with those of 14 Hodgkin's lymphoma (HL) cases in which ALCL was a possibility in cytology. These cases were diagnosed by during a 5-year period (1998-2002). Immunocytochemical staining on FNA smears and immunohistochemical staining on paraffin sections were performed in 11 and 17 cases, respectively.

Results:

There were 6 histologically diagnosed and immunohistochemically confirmed ALCL cases with initial FNA cytologic diagnosis of ALCL and/or NHL other than ALCL. In 14 histologically diagnosed as HL cases, the possibility of ALCL was considered during initial FNA cytodiagnosis (9 cases) or following review of smears (5 cases). When the clinical features were compared, significantly higher number of ALCL cases were above the age of 50 years (83.3% versus 7.2%, $p=0.0022$) and had inguinal lymphadenopathy (66.7% versus None, $p=0.0031$). Comparison of cytomorphological features between these two groups revealed significantly higher number of ALCL cases with hall-mark cells (83.3% versus 14.3%, $p=0.0072$), non-descript small round neoplastic cells (66.7% versus None, $p=0.0031$) and prominent elongated nucleoli in the neoplastic cells (66.7% versus 14.3%, $p=0.0374$).

Conclusions:

There is considerable overlap in clinicocytologic features between ALCL and HL. However, significant difference was observed in features such as >50 years of age and inguinal lymphadenopathy as well as cytologic features like hall-mark cells, non-descript small round neoplastic cells, and prominent elongated nucleoli in the neoplastic cells.

Key Words: Anaplastic large cell lymphoma; Hodgkin's lymphoma; Fine needle aspiration cytology
Funding Agency: None



Pathology

Category: *Clinical*

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Clinico-Cytologic study of 76 Cases of Kikuchi's Disease versus 684 cases of reactive hyperplasia of lymph node

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Introduction:

Kikuchi's disease (KD) is a benign and self-limiting disease that typically involves cervical lymph nodes and commonly affects young Asian women. A polymorphous lymphoid cell population with abundant karyorrhectic debris and histiocytes, many of which are crescentic, are characteristic cytologic features of KD. In absence of typical cytologic features, these cases may be confused with reactive hyperplasia (RH) of lymph nodes. In this report we attempt to differentiate Kikuchi's disease from reactive hyperplasia of lymph node.

Methods:

During a period of 5 years (2005-2009) 21 cases were diagnosed as KD by fine needle aspiration (FNA) cytology and 55 additional cases were detected following review of 815 RH cases. The clinico-cytologic features of these 76 KD cases were compared with 684 RH cases of lymph nodes to find out the differentiating features.

Results:

63.2% of KD were in 3rd and 4th decades of life as compared to 40.2% of RH (p= 0.0002). Male to female ratio was 1: 2.45 for KD and 1: 1.09 for RH (p= 0.0022). Kuwaity: non-Kuwaity ratio was 1: 2.04 for KD and 1.31: 1 for RH (p< 0.0001). Capillary networks was present in 71.1% of KD smears and 52.6% of RH (p= 0.0023). Tingible body macrophages and dendritic reticulum cells were detected in 17.1% and 22.4%, respectively, in KD cases as opposed to 50.1% and 58.8%, respectively, in RH cases (p<0.0001). Rare Kikuchi cells were detected in 16 (2.3%) cases diagnosed as RH but in None of them the count exceeded 1%, whereas in all cases of KD their count was >1% (p< 0.0001).

Conclusions:

Kikuchi disease cases differed significantly from nonspecific reactive hyperplasia of lymph node in respect of age and sex distribution, Kuwaity: non-Kuwaity ratio and cytomorphologic features such as capillary networks, Kikuchi cells count, tingible body macrophages, and dendritic reticulum cells.

Key Words: Kikuchi's disease; Reactive hyperplasia; Fine needle aspiration cytology

Funding Agency: None



Pathology

Category: *Clinical*

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Significance of the cytologic report of atypical cytology in fine needle lymphnode aspirates

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Introduction:

Fine needle aspiration(FNA) has become an integral part of the initial diagnosis and management of patients presenting with lymphadenopathy. Its diagnostic ability may be limited in patients with an atypical cytology report. The purpose of this study was to correlate atypical cytology report of lymphnodes on FNA with the histological diagnosis.

Methods:

Of 1659 lymphnode aspirates performed in the cytology laboratory, MAKH between 2004 to 2009, 149 were reported as atypical cytology preoperatively. A histological correlation was available in 50 cases. The mean age was 36.38 years, ranging from 13 to 77 years. The study group consisted of 34 (68 %) males and 16 (32%) females. The medical records of these patients were assessed retrospectively.

Results:

In 34 cases with atypical cytology, the suggestion of a Non Hodgkins Lymphoma (NHL), Hodgkins Disease (HD) and Lymphoreticular malignancy (LRM) was made in 7, 18 and 9 cases respectively. All 7 cases suspected as NHL were histologically documented as Follicular lymphoma (2 cases), Diffuse large B cell lymphoma (3 cases) and one case each of T cell rich B cell lymphoma and Mantle cell lymphoma. Ten of the 18 cases suspected HD were histologically documented as HD while 4, 2 and one each were reported as NHL, atypical lymphoid hyperplasia (ALH), reactive lymphnode (RLN) and metastatic papillary carcinoma (MPC). Of the 9 suspected LRM on aspirates, 5, 2 and one each were histologically reported as HD, NHL, RLN and Castleman's disease. The remaining 16 cases with atypical cytology were reported as RLN (8 cases), HD (2 cases), NHL (2 cases) and 1 case each of Castleman's disease, ALH and MPC.

Conclusions:

FNA is a feasible, rapid and inexpensive first-approach method in the evaluation of enlarged lymphnodes. Immunocytochemical studies help in reducing the margin of error in lymphoproliferative disorders. Aspirates reported as atypical cytology warrant a histological examination especially if the node persists.

Key Words: Atypical cytology; Lymphnode aspirates; Lymphoreticular malignancy

Funding Agency: None



Pathology

Category: Basic Sciences

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Determination of the prevalence of Factor V Leiden in Kuwaitis: A molecular/epidemiological/anthropological approach

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Introduction:

Factor V Leiden mutation (FVL), a point mutation (G1691A) in the human clotting factor V, was found to be the most common risk factor for venous thrombosis with high mortality and morbidity rates. FVL was present in high prevalence in Caucasians patients (15-65%) and healthy controls (1-15%) but was rare or absent in non-Caucasians. FVL was found in 5-27% of populations living in countries northern to the Arabian Peninsula, including Kuwait, but was almost absent in the Arabian Peninsula itself like in Saudi Arabia. Kuwaitis originally are from Saudi Arabia or from Iran and Iraq (northern to Kuwait and the Arabian Peninsula). This study was conducted to determine the prevalence of FVL in Kuwaitis and determine any differences based on the origin of the cases studied.

Methods:

Real-time PCR was used to determine FVL in 400 healthy Kuwaiti cases: 141 were of Iranian origin, 121 of Iraqi origin and 138 of Saudi origin.

Results:

In these cases, FVL was found in 9 (6.4%), 8 (6.6%) and 0 (0%), respectively. No statistical difference was present between prevalence in cases of Iranian and Iraqi origin, but both were statistically different from the prevalence in cases of Saudi origin. No difference was found between females and males in all groups.

Conclusions:

This study shows that epidemiological distribution of FVL in Kuwait is determined by the origin of the Kuwaitis, being present only in those of Iranian and Iraqi origin. Consequently, clinical approach towards FVL in Kuwait should consider the origin of the cases being managed.

Key Words: Factor V Leiden; Kuwaitis; Real-time PCR

Funding Agency: Kuwait University



Pathology

Category: *Clinical*

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Expression of progesterone receptor (PR) and its isoforms PRAB and PRB in fine needle aspirates from breast carcinoma

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Introduction:

Progesterone Receptor (PR) is a surrogate member of a functional Estrogen Receptor (ER) and is mediated by two functionally different isoforms PRAB and PRB. The relative levels of PRAB and PRB within target cells may determine the functional response of PR. Little is known regarding the expression of PRAB and PRB in breast carcinomas. The aim of this study is to evaluate the expression of PR, PRAB and PRB in fine needle aspirates (FNA) from breast carcinoma and correlate with its expression in tissue sections and other prognostic parameters namely cytologic grading, ER, C-erb B2 and Ki -67.

Methods:

In 40 cases of breast carcinoma with available material for cytohistologic correlation, PR, PRAB and PRB were studied by immunocytochemical methods. Their expression in aspirates and tissue sections were correlated with cytologic grading, ER, C-erb B2 and Ki-67.

Results:

PR and its isoforms PRAB and PRB were demonstrated by immunocytochemistry on FNA smears in 43, 69 and 7% of grade 1 carcinomas and 78, 33 and 22% of grade 3 carcinomas respectively. In tissue sections PR, PRAB and PRB were demonstrable in 88, 38 and 19% of grade 1 carcinomas in contrast to 40, 0 and 20% of grade 3 carcinomas respectively. No significant correlation was observed between the grade of the tumor and PR expression. PR positive breast carcinoma cases were positive for PRAB [63%] and PRB [19%]. This corroborated with tissue section findings. PR, PRAB and PRB were positive in 55, 45 and 15% of ER α negative cases respectively. In tissue sections there was marginal PR (25%) and PRAB (12%) positivity in ER α negative tumors. No statistical correlation between Ki-67 and C-erb B-2 with ER and PR status of the tumor was observed in the cases studied.

Conclusions:

The expression of PR and its isoforms PRAB, PRB was concordant with their expression in tissue sections in majority of the cases. No statistical correlation was found with C-erb B2 and Ki-67.

Key Words: Progesterone receptor PR; Isoforms PRAB and PRB; Breast Carcinoma Aspirates

Funding Agency: Kuwait University Research Grant MG01/04.



Pathology

Category: *Clinical*

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**Prospective longitudinal study of factors associated with progression/
regression of microalbuminuria in patients with Type 2 diabetes
mellitus**

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Introduction:

Microalbuminuria (MA) is a predictor of the progression of diabetic nephropathy and an independent risk factor for coronary heart disease (CHD). Regression of MA is desirable in diabetic subjects but the factors associated with regression or progression of MA have not been studied in the Kuwaiti population. The aims of this study were to estimate the frequency and factors associated with progression of MA.

Methods:

123 (72F, 51M) patients were followed up for median of 5.5 years. During the follow-up period, MA was assessed three times a year on separate visits. We evaluated whether MA had progressed (mean $\geq 50\%$ of baseline mean), had remained unchanged, or had regressed (mean $\leq 50\%$ of baseline mean). Multiple regression analysis was used to determine the predictive values of sex, age, duration of diabetes, CHD, baseline Cystatin C (CC), baseline high-sensitivity C-reactive protein (hs-CRP), leptin, adiponectin, mean HbA1c, diastolic blood pressure, systolic blood pressure and the insertion/deletion polymorphism of the Angiotensin Converting Enzyme (ACE) gene for the progression of MA.

Results:

At baseline, 49.5% were normoalbuminuric and 50.5% were microalbuminuric; at the end of follow-up, 64% had no change; 10% regressed and 26% progressed. Mean hs-CRP, leptin, HbA1c and CC were higher and mean adiponectin lower in patients with progression compared to those who regressed or had no change. Odds ratios (OR) for significant factors in progression are: CHD (1.2); CC (10.4); hs-CRP (1.5); mean HbA1c (1.2) and ACE I/D DD genotype (11.5). All MA patients with CC > 1.4 mg/L had progression of MA with OR of 26.1; whereas patients with CC < 1.1 mg/L had regression with OR of 2.0.

Conclusions:

ACE I/D genotype and CC at baseline are the most significant of the multiple determinants of the progression/regression of MA. These findings have significant implications for clinical practice as prevention of MA is an important therapeutic target.

Key Words: Microalbuminuria; Microalbuminuria Progression; Microalbuminuria regression

Funding Agency: KU research admin grant MG 033



Pediatrics

Category: *Clinical*

143

Quality of life in children with type 1 diabetes in Kuwait

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Introduction:

Recent research has shown that health-related quality of life (HRQOL) in children and adolescents with type 1 diabetes is markedly affected, resembling that of children with other chronic diseases, like malignancies. The objective of the study was to investigate the HRQOL in children and adolescents with diabetes in Kuwait.

Methods:

A total of 341 children and adolescents aged 5-18 years and 408 parents of children aged 2-18 years participated in the study. They were recruited from diabetes out-patient clinics in the 6 governorate hospitals. The paediatric quality of life inventory (PedsQL) questionnaire was used.

Results:

The mean (\pm SD) age of participants was 9 ± 1.2 years, and the duration of diabetes was 4.9 ± 2 years. The Cronbach α coefficient of child and parent report generally approached 0.825, indicating their internal consistency and reliability. There was a statistically significant difference in the total scores among children and their parents in all 3 age groups ($p < 0.001$), however, to a lower degree in the adolescent group, where the main difference was in the "worry" section where parents reported worse QOL. The total scores showed good psychological adjustment of children and adolescents with diabetes, mean score (\pm SD) was 85.7 (12.45), with slightly worse QOL in the 8-12 year old (71.2 ± 13.1) $p > 0.05$. Growing age, HbA1c, mode of insulin therapy, SES did not influence QOL of children with diabetes.

Conclusions:

Children and adolescents with type 1 diabetes and their parents in Kuwait showed good psychological adjustment and QOL. Parents appeared to be more worried than their adolescents about the effectiveness of the treatment and the long term complications.

Key Words: Type 1 diabetes; QOL; Children

Funding Agency: Kuwait University ZM03/10



Pediatrics

Category: Clinical

144

Response to hydroxyurea in children with sickle cell disease and high baseline Hb F levels

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Introduction:

Hydroxyurea (HU) is the only currently-approved medicine for sickle cell disease (SCD). It induces Hb F production and reduces the adhesion of blood cells to the vascular endothelium, thus reducing the frequency of painful crisis, acute chest syndrome and requirements for blood transfusion. The aim of this study was to investigate HU effects on the frequency of pain crisis and Hb F levels in SCD patients with high baseline Hb F levels (>10%).

Methods:

HU (20 mg/kg per day) was given to a selected group of SCD children with frequent, severe painful crisis (>3 hospital admissions in a year) in spite of elevated Hb F levels. Informed parental consent was obtained. The children were followed in the Pediatric Hematology clinic of Mubarak Al-Kabeer or Amiri Hospital for at least 1 year. Hematological and other data (drug side effects, pain crisis and other clinical events) were obtained. The baseline data were compared to those at the end of the first year of therapy.

Results:

10 HbSS and 6 Hb Sbeta⁰-thal patients aged 4 – 17 years were studied. There was dramatic reduction in pain crises in 13 while 2 remained about the same and 1 was worse than before starting the medicine. No significant side effects were noticed. There was a significant ($p<0.05$) increase in the mean MCV (74.9 ± 9.1 vs 85.2 ± 17.4 fl) and the Hb F (14.9 ± 7.4 vs $21.3 \pm 10.6\%$) in the pre and post-HU levels. Other parameters did not show significant differences. Ten patients (62.5%) increased their Hb F levels by at least 50% and 4 of these more than doubled their values. However, 5 i.e. 31.3% (3 of whom were HbSbeta-thal) did not show any increased F values.

Conclusions:

Kuwaiti SCD patients respond very well to HU; with almost uniform reduction in pain crisis. The Hb F response is more profound in HbSS than in Hb Sbeta-thal patients. The genetic basis for the marked differences in Hb F induction with HU in our patients deserves further studies.

Key Words: Hydroxyurea; Sickle cell disease; Hb F

Funding Agency: None



Pediatrics

Category: Clinical

145

Rate and management pattern of congenital diaphragmatic hernia at Maternity Hospital, Kuwait

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Introduction:

Congenital diaphragmatic hernia (CDH) occurs in around 1 in 2000 live births and associated with high mortality rate reaching up to 50%, even with prenatal diagnosis and recently advanced and extensive neonatal intensive care management. The objectives of this study are to document the incidence, clinical experience and outcomes of congenital diaphragmatic hernia (CDH) in newborn infants admitted to the neonatal unit at Maternity Hospital, Kuwait.

Methods:

A retrospective chart review of all newborn infants admitted to the neonatal unit at Maternity Hospital in Kuwait from January 2007 till December 2010. Demographic data of the babies were collected along with variables involving the levels of sickness and therapeutic interventions.

Results:

A total of 21 cases of CDH were admitted to the unit over the four years period. The gestational age ranged from 33 to 40 weeks. 13 cases died giving a mortality rate of 65%. All the cases received mechanical ventilation, and 16 of them was high frequency ventilation (HFO), while almost half of the cases received nitric oxide gas treatment. Almost all the cases were on 100% oxygen.

Conclusions:

Our results showed a little higher mortality than other centers worldwide, in spite our management pattern was not different. More cases from the neonatal units in the other hospitals in Kuwait are to be collected to compare the mortality rates and patterns of management.

Key Words: CDH; Mortality; HFO

Funding Agency: None



Pediatrics

Category: *Clinical*

146

The quality of life of pediatric sickle cell disease patients and their families.

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Introduction:

Sickle Cell Disease (SCD) is a leading genetic condition and chronic disease associated with significant morbidity and mortality. This study investigated the effect of the disease on the quality of life of Kuwaiti pediatric SCD patients and their families.

Methods:

This was a questionnaire study involving patients seen in the pediatric hematology clinics in Mubarak, Amiri and Sabah hospitals in Kuwait. Informed consent was obtained and the patients' identities were kept anonymous. Personal information such as age of the child, sex, occupation of parents and the clinical course of the disease and its effects on different aspects of the lives of the patients and their families were documented. The data were coded and processed using SPSS version 17.0.

Results:

There were 51 children (28 males and 23 females) in the study and the response rate was 100%. Forty nine (96%) were Kuwaitis, 16 (31.4%) were diagnosed <1 year of age and 28 (54%) between 1-5 years. The initial symptoms (usually pallor and jaundice) started at the age of <1-3 years in 64.6%. Pain crisis is the commonest cause of admission and 33 (64.7%) were admitted > 3 times per year. Twenty four (47.05%) had recurrent absences from school and 5 (9.8%) had learning difficulties. The marital life of the parents suffered in 19 (37.2%) families. The parent's job was affected in 21 (38.4%) with reprimands from superiors, early retirement or loss of jobs. However, most (80.4%) families are compliant with medications and clinic attendance.

Conclusions:

SCD pediatric patients and their families experience significant health-related deficiencies in quality of life. Health practitioners should bear this in mind in planning appropriate interventions in these patients. It is mandatory to consider improvements in their quality of life to improve their outcomes.

Key Words: Sickle cell disease; Quality of life; Pediatric

Funding Agency: None



Pediatrics

Category: *Clinical*

147

Pattern and etiology of proven early onset neonatal sepsis in neonatal care units in Kuwait

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Introduction:

Further reduction in neonatal mortality requires knowledge on the patterns and trends of neonatal infections which remain mostly unknown in Kuwait and other countries in the Gulf region. This study aimed to investigate the incidence of early-onset neonatal sepsis and identify the main pathogens over a 5-year period in Kuwait.

Methods:

Blood samples were collected from all infants with any clinical or laboratory feature suggestive of sepsis, from 1st January 2005 to 31st December 2009, in Maternity Hospital in Kuwait where more than one third of all child births occur. Cases of early-onset neonatal infections were defined as an isolation of a single potentially pathogenic organism cultured from blood and/or Cerebrospinal Fluid (CSF) from infants who were younger than 7 days of age in combination with clinical or laboratory findings consistent with infection.

Results:

A total of 153 early-onset neonatal infections occurred among 56, 134 live births with an overall incidence of 2.7 (95%CI:2.3-3.2) episodes per 1000 live births. Case-fatality was 13.1% (95%CI:8.6%-18.9%). Group B Streptococcus (GBS) accounted for 17.6% of infections among infants younger than 7 days but 38.1% of infections in the first two days of life. Neither the incidence of early-onset infection by GBS nor by E. coli changed significantly over the study period.

Conclusions:

Over a five-year period, although the incidence of early-onset neonatal infections due to GBS was low, GBS accounted for most early-onset infections. Intrapartum antibiotic prophylaxis against GBS should be strengthened in Kuwait. There was no evidence to suggest that early-onset infection due to non-GBS organisms such E coli has increased in the last five years.

Key Words: Neonate; Infections; Prematurity

Funding Agency: None



Pediatrics

Category: Graduate MSc (Basic Science)

148

The effect of maternal anemia on neonatal outcome

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Introduction:

Anemia is the commonest medical disorder in pregnancy and has a varied prevalence, etiology and degree of severity in different population, being more common in non-industrialized countries. According to the world health organization, anemia contributes to 40% of maternal death in third world countries. The etiology of the more common anemias encountered in pregnancy are iron-deficiency, anemia caused by acute blood loss and folate deficiency anemia.

The aim of this study is to assess the relationship between the maternal anemia and neonatal outcome.

Methods:

Study design: Analytic prospective case control study. This study included randomly selected 150 pregnant women and their newborns to evaluate the effect of maternal anemia on neonatal outcome.

They were divided into two groups:

Group I: included 100 anemic pregnant women.

Group II: included 50 non anemic pregnant women as a control group.

Results:

Maternal anemia is associated with preterm delivery, low birth weight and decrease level of neonatal hemoglobin. Apgar score in 1st minute decrease with maternal anemia while in 5th minute Apgar score did not affected. Other anthropometric measures-as body length and head circumference- did not affected by maternal anemia. Iron and folic acid intake can improve anemia with pregnancy but have no effect on birth outcome.

Conclusions:

Recommendations: As the maternal anemia can increase the incidence of pre term and low birth weight deliveries, so it's recommended to improve level of maternal hemoglobin before and during the pregnancy. Also, maternal anemia decreases the Apgar score in the 1st minute after birth so; the resuscitation team should be present at delivery room. Further studies are recommended to explain the decrease in gestational age despite regular iron supplementation.

Key Words: maternal anemia; neonat; pragnancy

Funding Agency: None



Pediatrics

Category: Clinical

149

Pattern and etiology of proven late onset neonatal sepsis in neonatal care units in Kuwait

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Introduction:

Late-onset neonatal infections are nosocomial and represent a major cause of death and morbidity among premature infants. This study aimed to investigate incidence, etiological pattern and antimicrobial resistance of late-onset neonatal infections over a period of five-year.

Methods:

Data were collected prospectively from January 2005 to December 2009. Blood samples were collected from all infants with any clinical or laboratory feature suggestive of sepsis in the Maternity Hospital. Late-onset neonatal infection was defined as an isolation of a single potentially pathogenic organism cultured from blood or cerebrospinal fluid among infants older than 6 days in combination with clinical or laboratory findings consistent with infection.

Results:

Over five-year period, 949 late-onset neonatal infections were detected among 56, 134 live births. The overall incidence was 16.9 (95%CI:15.8-18.0) episodes per 1000 live births. The main pathogens were Coagulase-negative staphylococci 339(35.7%), while E coli, Enterococcus, and Enterobacter each was responsible for about 6% of all infections. Candida spp. and Pseudomonas spp. accounted for 38(4%) and 104(11%), respectively, while Klebsiella spp. was the most common gram-negative infection 178(18.8%). This pattern of infection remained unchanged over the study period. Case-fatality was 11.7%(95%CI:9.7%-13.9%) and was particularly high among infections caused by Pseudomonas spp. and Candida spp. Approximately, 24% and 20% of Klebsiella spp. Infections were resistant to cefotaxime and gentamicin, respectively while 28% and 24% of E coli infections were resistant to cefotaxime and gentamicin, respectively.

Conclusions:

The incidence of late-onset neonatal infections in Kuwait is high resembling that in resource-poor countries. Preventive measures against hospital-acquired infections should be strengthened to further reduce neonatal mortality in Kuwait.

Key Words: Neonates; Infection; Preterm

Funding Agency: None



Pediatrics

Category: *Clinical*

150

2009 pandemic influenza A (H1N1) in infants less than one year

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Introduction:

Infants (children ≤ 1 year) represent an important risk group for influenza infection because of the immaturity of the immune system and the absence of prior immunity to the virus. They represent high risk group for morbidity and hospitalization. The objective of this study was to evaluate the clinical presentation and outcome in infants hospitalized with pandemic influenza A H1N1.

Methods:

A retrospective chart review of infants with laboratory evidence of H1N1 infection in two hospitals in Kuwait. The following data were collected; demographic characteristics, underlying health conditions, clinical features at presentation, complications, hematologic and radiologic findings, therapeutic measures and outcome.

Results:

There were 62 infants comprising 32% of all admissions with influenza A H1N1. The median age \pm SD was 6 \pm 4 months. There were 29 (47%) infants with an age 0-6 months. There were 31% of children with an underlying health condition. Mean hospitalization duration was 5.6 \pm 4.6 days. The most common clinical presentations were: fever (95%), cough (77%), and rhinorhea (60%). There were 4 infants (6.5%) who were required admission to the Intensive care unit. There was one mortality.

Conclusions:

Despite the large proportion of hospitalization; influenza A H1N1 had a mild course in infants. According to the latest ACIP recommendations, annual immunization with influenza vaccine is recommended for any child 6 months of age and older, particularly those with underlying medical condition.

Key Words: Influenza H1N1; Infants; Influenza vaccine

Funding Agency: None



Pediatrics

Category: Clinical

151

Epidemiology and clinical presentation of Pandemic influenza A (H1N1) among hospitalized children in Kuwait

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Introduction:

In 2009, pandemic H1N1 influenza caused significant morbidity and mortality worldwide. We describe the epidemiological and clinical characteristics of children hospitalized for 2009 H1N1 infections in Kuwait

Methods:

We conducted a retrospective chart review of hospitalized children with laboratory-confirmed H1N1 infections in two hospitals in Kuwait. Epidemiological characteristics, clinical features, risk factors for severe disease, complications and mortality were analyzed.

Results:

A total of 255 children were hospitalized for 2009 pandemic H1N1 infection from August 2009-January 2010. Majority of children (52.8%) were admitted during the month of October. The median age was 2 years. Majority of admitted children were in two age categories: infants (32%) and school children (31%). The most common presentations were: fever (98.25%), cough (76%) and runny nose (53.5%). Majority of admitted children (57%) had an underlying medical condition. All children had received an antiviral agent (oseltamivir) and antibiotics were administered to 147 (75%). Bacterial infections occurred in 3 children. Six children (3%) were admitted to the intensive care unit (ICU), of which 4 (66%) required artificial ventilation. There was only one death.

Conclusions:

The pandemic H1N1 infection is associated with a wide spectrum of clinical manifestations. The majority of hospitalized children had an underlying health condition. Majority of admitted children had an uncomplicated course.

Key Words: Influenza A H1 N1; children; Kuwait

Funding Agency: None



Pharmacology and Toxicology

Category: Basic Sciences

152

Characterization of the interaction between arrestin and the incretin receptors.

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Introduction:

The incretin effect is mediated by two gut hormones; glucose-dependent insulintropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). Both GIP and GLP-1 potentiate insulin secretion in a glucose dependent manner by binding to their respective receptors on the pancreatic beta-cell. The GIP and GLP-1 receptors are both Family B G protein-coupled receptors (GPCRs). In type 2 diabetes mellitus (T2DM) GIP no longer has the ability to potentiate insulin secretion so focus has shifted to GLP-1 to treat T2DM. In this study the interaction between arrestin (an important protein involved in the homologous desensitization of GPCRs) and both the GIP and GLP-1 receptors is investigated with the aim to shed light on why type 2 diabetics remain responsive to GLP-1 but not GIP.

Methods:

Arrestin recruitment to either GLP-1R or GIPR was investigated using the PathHunter™ eXpress kit (DiscoverX Corporation Ltd., UK). Briefly, the kit detects the interaction of arrestin with the activated receptor using enzyme fragment complementation.

Results:

GLP-1 and GIP stimulated arrestin recruitment to their receptors with a pEC₅₀ value of 8.2(± 0.14) and 8.1(±0.27) respectively (n=3), which translates to EC₅₀ values of 5.7 nM and 7.6 nM. However the most striking finding was that GIPR displayed significantly (P < 0.05) higher basal binding to arrestin than the GLP-1R (75% compared to 39%)

Conclusions:

The GIP receptor displays significantly higher basal binding to arrestin than the GLP-1 receptor. This may be a result of a combination of the GIP receptor's constitutive activity and an increase in phosphorylation events with hyperglycemic conditions (10 mM), as arrestin binding to receptor requires both phosphorylation and an active conformation. This high level of basal arrestin binding may contribute to the loss of function of GIP in T2DM.

Key Words: Incretin; GPCR; Arrestin

Funding Agency: KU Grant No. ZM01/10



Pharmacology and Toxicology

Category: Graduate MSc (Basic Science)

153

Superfect and polyfect polyamidoamine dendrimers differentially affect the epidermal growth factor receptor signaling pathway in diabetic rat kidneys

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Introduction:

Polyamidoamine (PAMAM) dendrimers are highly branched macromolecules that are being explored as delivery vectors for nucleic acid-based therapeutics. However, little is known about their toxicological profiles in terms of their proteomic interactions at the level of signal transduction pathways. We previously showed that Polyfect (PF) and Superfect (SF), same monomer chemistry but differing in structural architectures, elicited multiple gene expression changes in cultured cells including opposing effects on epidermal growth factor receptor (EGFR) gene expression. Here, we investigated the effects of PF and SF on EGFR signaling via ERK1/2 and p38 MAPK in the kidneys of diabetic rats.

Methods:

Diabetes was induced by intraperitoneal(i.p) injection of 55 mg/kg of streptozotocin. Dendrimer formulations were administered i.p. at three different doses 1, 5, and 10 mg/kg 24 hours prior to sacrifice after 4 weeks of diabetes. Western blotting was utilized to identify the levels of EGFR, phosphorylated EGFR, ERK 1/2 and p38MAPK.

Results:

PF reduced whereas SF increased EGFR and p-EGFR levels in a dose dependent manner in the kidneys of diabetic rats. However, the impact of PF and SF on the potential downstream effectors of EGFR signaling, ERK1/2 and p38MAPK were similar whereby both dendrimers increased phosphorylation of ERK1/2 and p38 MAPK in a dose-dependent manner.

Conclusions:

These findings suggest that PF and SF have opposing effects on EGFR phosphorylation in an animal model of disease. Activation of the EGFR signaling in the diabetic kidney was associated with increased activation of ERK1/2 and p38 MAPK for SF. However, in the case of PF, inhibition of EGFR phosphorylation also led to elevated levels of the downstream effectors implying that other pathways converging at the level of ERK1/2 and p38MAPK may be differentially affected. These results will be important in defining the toxicology of these delivery systems prior to clinical use.

Key Words: Dendrimer; EGFR; Diabetes

Funding Agency: KU Grant (YM 21/09)



Pharmacology and Toxicology

Category: Graduate MSc (Basic Science)

154

Inhibition of soluble Epoxide Hydrolase by CDU attenuates vascular dysfunction in the perfused mesenteric vascular bed of diabetic SD rats

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Introduction:

Epoxyeicosatrienoic acids (EETs) are endogenous ligands derived from arachidonic acid by CYP epoxygenases through the monooxygenase pathway. Once EETs formed, they undergo hydrolysis by soluble epoxide hydrolase (she) to the corresponding dihydroxyeicosatrienoic acids (DHETs), whereby the biological effects of EETs are diminished. The objective of this study is to investigate the effect of inhibition of soluble epoxide hydrolase on the vascular responsiveness of the perfused mesenteric beds of diabetic SD rats to some vasoactive agonists.

Methods:

Male Sprague Dawley rats weighing about 250 g were used in this study (n=40). Diabetes was induced in 20 animals by a single intraperitoneal (ip) injection of 55 mg/kg of STZ. Animals were sacrificed after four weeks of diabetes induction. The mesenteric beds were isolated from control and diabetic animals and were perfused with Krebs' solution using a multichannel masterflex peristaltic pump. Dose-response curves were established for 11, 12-EET (10^{-13} – 10^{-8} mole), carbachol (10^{-13} – 10^{-7} mole) and sodium nitroprusside (SNP) (10^{-13} – 10^{-7} mole) before and after incubating the mesenteric beds with (10^6 M) 1-cyclohexyl-3-dodecylurea (CDU, an inhibitor of soluble epoxide hydrolase). Changes in perfusion pressure were measured via a pressure transducer connected to a Lectromed.

Results:

The vasodilator responses to 11, 12-EET and carbachol were significantly reduced in the mesenteric beds isolated from diabetic animals compared to the non-diabetic ($P < 0.05$). Incubation of the mesenteric beds isolated from diabetic animals with CDU resulted in a significant increase in the vasodilator responses to 11, 12-EET and carbachol in the perfused mesenteric beds.

Conclusions:

Results from this study suggest that inhibition of the hydrolysis of EETs play a role in reducing diabetes-induced abnormal vascular reactivity and therefore may lead to the development of novel therapies.

Key Words: Carbachol; CDU; Diabetes

Funding Agency: None



Pharmacology and Toxicology

Category: Graduate MSc (Basic Science)

155

Characterization of the signaling pathways involved in mediating the vasodilator responses to 11, 12-Epoxyeicosatrienoic Acid (11, 12-EET) in the rat perfused mesenteric vascular bed

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Introduction:

Arachidonic acid is metabolized by cytochrome P450 enzymes to 20- hydroxyeicosatetraenoic acid (20-HETE) and epoxyeicosatrienoic acids (EETs). 20-HETE is a vasoconstrictor whereas EETs are potent vasodilators that have been proposed to function as an endothelium-derived hyperpolarizing factor in some tissues. The objective of this study is to examine the role of K[±]ATP potassium channel, guanylyl cyclase, and vanilloid receptors in mediating the vasodilator response of 11, 12-EET in the mesenteric vasculature.

Methods:

Male Sprague Dawley rats weighing about 250 g were used in this study (n=40). Animals were sacrificed and the vascular responsiveness of isolated perfused mesenteric beds to 11, 12-EET was investigated. The mesenteric beds were perfused with Krebs' solution at 37°C, oxygenated with 95% oxygen and 5% carbon dioxide. A dose-response curve was established for 11, 12-EET (10⁻¹³ -10⁻⁸ mole) before and after incubation with glibenclamide (10⁻⁵M), an inhibitor of K[±]ATP channel, ODQ (10⁻⁵M) a soluble guanylyl cyclase inhibitor, or ruthenium red (10⁻⁶M), an inhibitor of vanilloid receptor. Changes in perfusion pressure were measured.

Results:

Incubation with glibenclamide or ODQ did not inhibit the vasodilator response to 11, 12-EET in the mesenteric vascular bed. However, incubation with ruthenium red significantly reduced the vasodilator response to 11, 12 EET (P < 0.05).

Conclusions:

These results suggest that vanilloid receptors but not K[±]ATP channels or cGMP may have an essential role in mediating the vasodilator responses of 11, 12-EET in the rat perfused mesenteric bed.

Key Words: Glibenclamide; 11, 12-EET; Mesenteric bed

Funding Agency: None



Pharmacology and Toxicology

Category: Basic Sciences

156

Potentially useful interactions between Theophylline and Salbutamol on cytokine release in human monocytes

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Introduction:

Beta-2-adrenoceptor agonists and theophylline are widely-used bronchodilators. Unlike beta-2-agonists, theophylline has additional anti-inflammatory effect. While beta-2-agonists are commonly combined with inhaled steroids in the treatment of asthma, the effect of combining theophylline with beta-2-agonists has not been studied. This study investigated the effect of theophylline and salbutamol, as well as their combination, on the release of TNF-alpha and IL-6 from stimulated monocytes, and to compare such effect with that of dexamethasone and its combination with salbutamol.

Methods:

Highly purified human blood monocytes were, pre-treated with the drugs (alone or in combination) for 30 min before being stimulated in culture with 250 ng/ml LPS for 24h. Released TNF-alpha and IL-6 were determined by ELISA. The corresponding mRNA expression for the two cytokines were also determined by RT-PCR using appropriate primers.

Results:

Salbutamol and procaterol (≥ 0.1 microM) significantly inhibited the release of TNF-alpha, but also enhanced that of IL-6. In contrast, theophylline (30 – 100 microM) strongly inhibited the release of both cytokines. Interestingly, the combination of theophylline and salbutamol was additive in inhibiting TNF-alpha release but theophylline blocked the IL-6-enhancing effect of salbutamol. A similar effect was seen when dexamethasone was combined with salbutamol. These effects were also reflected in the mRNA expression of the cytokines, suggesting that the effects were genomic.

Conclusions:

Beta-2-agonists have opposing effects on the generation of TNF-alpha and IL-6, but when combined with theophylline, the latter, like dexamethasone, was capable of augmenting the anti-inflammatory effects of the beta-2-agonists while preventing their pro-inflammatory effect. Thus, theophylline may have a potentially useful steroid-sparing effect.

Key Words: Asthma; Theophylline; Beta-2 agonists

Funding Agency: Grant # 2005-130-203, Kuwait Foundation for the Advancement of Sciences (KFAS).



Pharmacology and Toxicology

Category: Graduate MSc (Basic Science)

157

Effect of experimentally-induced colitis on the function of muscarinic receptor subtypes in the rat colon

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Introduction:

Muscarinic receptors belong to the superfamily of G-protein coupled receptors comprising of seven transmembrane domains. They are located prejunctionally modulating the release of acetylcholine from cholinergic nerves, and postjunctionally where they mediate the effects of endogenous and exogenous Ach. The objective of this study was to examine the effect of colitis on the function of muscarinic receptor subtypes in the rat colon.

Methods:

Female Sprague-Dawley rats weighing 150-250g were used in this study. Colitis was induced by intra-rectal administration of 2, 4, 6-trinitrobenzene sulfonic acid (TNBS) and the animals were sacrificed on day 5 post-TNBS. Colonic segments were removed and set up in Krebs' solution (37°C) for tension recording. The Krebs' solution was oxygenated with 95% O₂/ 5% CO₂ mixture. Contractions were recorded on a four channel lectromed polygraph.

Results:

Carbachol produced concentration-dependent contractions of colon segments from control and TNBS-treated rats. Pirenzepine (M1-), methoctramine (M2-) and 4-diphenylacetoxy-N-methyl piperidinmethiodide (4-DAMP, M3-) produced rightward shifts of carbachol concentration response curves in colon segments from both groups. There was no significant difference in the potency of 4-DAMP and pirenzepine between the groups indicating no change in the affinities of M3- and M1-receptor subtypes in inflamed tissues. However, methoctramine (M2-) was significantly more potent in colon segments from TNBS-treated rats.

Conclusions:

These results would suggest that TNBS-induced colitis in rats was associated with increased activity of M2-receptors in the rat colon.

This study was funded by the College of Graduate Studies.

Key Words: Muscarinic receptors; TNBS; Colon segments

Funding Agency: None



Pharmacology and Toxicology

Category: Basic Sciences

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In vitro testing of PH084 as a potential anticonvulsant agent.

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Introduction:

Currently, about 30-40% of seizures are either not adequately controlled or are resistant to available antiepileptic drugs (AEDs). Most of these AEDs also have side effects that make patients non-adherent. Hence the need for newer, more effective anticonvulsants that may cover these resistant cases with few side effects is paramount. Here we tested PH084, a novel oxazolidinone, for anticonvulsant activity using in vitro seizure models.

Methods:

Whole-cell and extracellular field recordings were done in coronal slices of rat hippocampus. The effect of PH084, a prototype oxazolidinone, was tested on excitatory postsynaptic currents (EPSCs), action potentials and chemically- and electrically-induced seizures.

Results:

Bath application of PH084 caused suppression in EPSC amplitude in a concentration-dependent manner, with 10 μ M suppressing EPSC by $-25.4 \pm 10.4\%$ (n=6). PH084 (10 μ M) also suppressed action potential firing frequency by $-42.2 \pm 13.5\%$ (n=6) and population spike (PS) by $-38.2 \pm 8.9\%$ (n=4). Perfusion with buffer containing zero Mg²⁺ converted evoked PS to multiple PS (mPS: 5.0 ± 0.3 spikes; n=7) accompanied by spontaneous bursting (SB) activity ($9.0 \pm 1.6/\text{min}$; n=5). PH084 (10 μ M) suppressed the number of spikes mPS by $-38.7 \pm 8.3\%$ (n=7) and the frequency of SBs by $-47. \pm 8.9\%$ (n=5). It also depressed picrotoxin-induced mPS by $-44.7 \pm 7.0\%$ (n=5). However, pretreatment of slices with PH084 (10 μ M) did not block or attenuate the zero Mg²⁺-induced mPS (3.9 ± 0.6 spikes, n=5) and SBs ($11.0 \pm 1.8/\text{min}$, n=4). Furthermore, PH084 (10 μ M) did not also alter stimulus train induced bursts elicited by high frequency electrical stimulation of excitatory afferents.

Conclusions:

Our data suggest that, while PH084 has potential for use as an anticonvulsant in chemically-induced seizures, it may not have potential for use in electrical seizures or as an antiepileptogenic agent.

Key Words: Anticonvulsants; Population spikes; Spontaneous bursts

Funding Agency: PT 01/10



Pharmacology and Toxicology

Category: *Clinical*

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Development and validation of a simple and rapid Ultra Performance Liquid Chromatography Mass Spectrometry (UPLC-MS-MS) method for the quantitation of Busulfan in human plasma for Therapeutic Drug Monitoring

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Introduction:

Busulfan (BSN), 1, 4-butanediol dimethanesulfonate has been used as a part of many high dose conditioning regimens before hematopoietic stem cell transplantation and for some genetic diseases e.g. sickle cell disease. Similar to most alkylating agents, it has narrow therapeutic window and variable inter and intra-patient pharmacokinetics. We describe a simple, fast, reliable, and accurate UPLC-MS-MS method for therapeutic drug monitoring of BSM in plasma.

Methods:

After addition of the internal standard Buslfan-d8, BSN is extracted from the plasma samples by liquid-liquid extraction using diethyl ether preceded by salting out with saturated sodium chloride solution. The Acquity UPLC system consists of a binary solvent and sample managers coupled to a triple quadrupole mass detector from Waters Corp., Milford, MA, USA. The chromatographic separation is carried out using Acquity UPLC BEH C18, 2.1 x 50 mm, 1.7 μm column accompanied by a Vanguard pre-column. Mobile phase composed of 90:10 % (v/v) methanol: 20 mM ammonium acetate buffer is used in isocratic mode at a flow rate of 0.3 ml/min and the run time is 1.5 minutes. Data acquisition and quantitation is achieved by linear regression analysis using MassLynx V4.1.

Results:

Calibration is linear to 2000 microg/ml ($r > 0.99$) with limit of quantitation of 25 microg/ml. The intra and inter-day precision at four levels (50, 500, 1250 and 1750 microg/ml) is <3.5 and $<7\%$ respectively and the recovery remained above 77% for BSN at the above mentioned concentrations and 81% for the internal standard. No ion suppression is observed and the samples spiked with BSN remained stable for four weeks when stored at -70°C .

Conclusions:

This simple and rapid, time and cost effective UPLC method for measuring BSN levels in human plasma is suitable for optimizing individual dosing based on area under the curve (AUC) to avoid engraft failure and relapse in case of low dosage and increased risk of hepatic veno-occlusive disease and liver toxicity in susceptible patients in case of over dose.

Key Words: Busulfan; UPLC; Therapeutic Drug Monitoring

Funding Agency: None



Pharmacology and Toxicology

Category: Basic Sciences

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Alteration of metastasis-associated protein 1 transcription and translation: A novel mode of action of chemotherapeutic drugs and antioxidants?

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Introduction:

Metastasis-associated protein 1 (MTA1), a component of nucleosome remodeling deacetylase complex, seems to be associated with DNA damage and response pathway. The present study investigates the effects of anticancer drugs and an antioxidant cocktail on MTA1 in the testis.

Methods:

Adult male Sprague-Dawley rats (13-15-week-old; N=7/group [G]) were treated with bleomycin, etoposide and cisplatin (BEP) at the human dose-levels of 1.5 mg/kg, 15 mg/kg and 3 mg/kg, respectively as follows: G1- control; G2- antioxidant cocktail [AO; α -tocopherol, 100 mg/kg; L-ascorbic acid, 50 mg/kg; Zn, 40 mg/l and Se, 100 μ g/l]; G3- EP; G4- EP+BEP; G5- EP+BEP+EP; G6- EP+BEP+EP+EP and G7-G10 were similar to G3-G6, but also treated with the AO. The transcription of MTA1 and its short form (MTA1s) was evaluated by ReT-PCR and the protein expression was estimated by Western blotting, immunohistochemistry and confocal microscopy. Data were analyzed by One way ANOVA followed by Dunnett T3 and LSD (ReT-PCR) post hoc tests. The p value <0.05 was considered significant.

Results:

The transcription of MTA1 was decreased in G2 and G6-G10 and that of MTA1s in G2, G6, and G8-G10. This effect was exacerbated in BEP+AO groups ($p < 0.05$). On the other hand, the protein level increased in G2, G4-G10 with the maximum effect in G4 and G8 ($p < 0.05$). The protein was localized to both nuclei and cytoplasm of germ cells.

Conclusions:

We report for the first time that the BEP and AO reduce the transcription but maintain an elevated protein level in the organ indicating a new mode of action. Elevated MTA1 activities may have a role in DNA damage and eventual cell death in chemotherapy and AO exposed testis.

Key Words: DNA damage; Chromatin remodeling; Apoptosis

Funding Agency: Kuwait University grant # MA02/08 and GM01/01 & GM01/05



Pharmacology and Toxicology

Category: Basic Sciences

161

Lead toxicity during post weaning and young adult age - Golgi and Electron microscopic study

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Introduction:

Exposure to chemical agents at critical periods of development may cause some permanent changes in the functioning of the nervous system. Lead is a widespread environmental contaminant worldwide and is associated with adverse outcomes in children, including impaired neurobehavioral development and learning difficulties. The objective of the present study was to investigate dendritic pattern and ultra structure of hippocampus in rats exposed to lead during early post weaning period and during young adult age.

Methods:

Wistar rats, 21 days old (n=18) and young adult (4 months, n=18), were allowed to drink water containing 0.2% lead acetate for 90 days. Lead treated rats were sacrificed along with age matched normal control rats (n=18), hippocampus was processed for Golgi staining, light and electron microscopic study.

Results:

Blood lead was a significantly increased in lead treated rats compared to age matched control rats. There was a marked stippling of RBC in lead treated groups, which indicates lead toxicity in these rats. There was large number of degenerating neurons in sub region regions of the hippocampus, in both age groups. Dendritic analysis of Golgi stained neurons showed a significant decrease in the dendritic length and spines in hippocampal neurons in both groups; however effect was more severe in post weaned group compared to young adult group. Ultra structure showed degenerative features which was very prominent in post weaned group.

Conclusions:

Lead affects hippocampus of very young and adult age groups, both at light and electron microscopic level. Effect is more severe if rats were exposed to lead during early age than later age. This may be the basis for pronounced neurological deficits in children exposed to lead during child hood.

Key Words: Hippocampus; Lead; Electron microscopy

Funding Agency: None



Pharmacology and Toxicology

Category: Basic Sciences

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Lead effects on aging brain

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Introduction:

Lead is a ubiquitous environmental toxin that is capable of causing numerous acute and chronic neurological pathologies. The primary target of lead toxicity is the central nervous system. The objective of the present study was to investigate the lead toxicity on the hippocampus during the aging process.

Methods:

Wistar rats, young aged (4 months, n=18), middle aged(12 months, n=18) and old aged(20 months, n=18) were allowed to drink water containing 0.2% lead acetate for 90 days. Lead treated rats were sacrificed along with age matched normal control rats(n=18 in all age groups), brain with hippocampus was processed for Golgi staining, light and electron microscopic study.

Results:

There was a significant increase in blood lead content in all the treated rats compared to age matched control rats. Red blood cells showed marked stippling as an indication of lead toxicity. Cresyl violet stained sections of the hippocampus clearly revealed lead toxicity effect (neurodegeneration) in all age groups (in CA1, CA3, and dentate hilus region), with significant inter group difference among young, middle aged and aged group of rats. Dendritic analysis of Golgi stained neurons showed a significant decrease in the dendritic length, and spines in hippocampal neurons (CA1, CA3 and dentate hilus region) in all lead treated groups, which also varied significantly among the different age groups. Electron microscopy of the lead treated rats in all age groups, demonstrated several abnormal features in the neurons and in the neuropil in all age groups.

Conclusions:

Lead affects hippocampus of all the age groups, both at light and electron microscopic level, but for variable extent. This may be the basis of differential neurological consequences of lead toxicity during ageing process.

Key Words: Lead; Hippocampus; Golgi stain

Funding Agency: None



Pharmacology and Toxicology

Category: Basic Sciences

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Arrhythmogenic effect of central sympatholytics

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Introduction:

Survival prolongation with beta-blockers supports the notion that dysfunction of the autonomic nervous system plays an important role in the pathogenesis of heart failure. It was therefore surprising that central sympatholysis with moxonidine was associated with increased mortality of heart failure patients. Reasons for this excessive mortality are not clear, but sympatho-vagal imbalance causing malignant arrhythmias is a possible option. The aim of this study was to compare the effect of central sympatholytic drug moxonidine with the beta-adrenergic blocker metoprolol on autonomic regulation of heart rate variability.

Methods:

Wistar-Kyoto male rats (n=8) were implanted with telemetric transmitters to monitor ECG and blood pressure. Time-frequency analysis was used to calculate power spectra of RR-intervals (RRI). Detrending fluctuation analysis was used to calculate fractal scaling exponents (FSE). 2-way ANOVA by time and dose for repeated measures was used for multiple comparisons of changes induced by the different moxonidine and metoprolol doses.

Results:

Moxonidine and metoprolol caused comparable reduction in heart rate. Moxonidine but not metoprolol bradycardia was strongly associated with increased vagal activity. Higher moxonidine doses reduced RRI FSE to values that characterize white noise, but metoprolol did not change it significantly. Bradycardia produced by metoprolol was associated with the “smoother” variability characterized by the rising FSE that tended to reach the value of Brownian noise. Bradycardia after moxonidine was associated with more “rough” fluctuations with frequent supraventricular ectopic beats characterized by FSE moving toward white noise value of 0.5.

Conclusions:

Central sympatholytics but not metoprolol broke down the fractal organization of RRI. This was associated with increased vagal drive to the heart, sinus bradycardia, sinus

Key Words: Heart failure; Central sympatholysis; Arrhythmia

Funding Agency: Kuwait University Research Grant No. [MY02/04]



Pharmacy

Category: Basic Sciences

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Identification of communication apprehension among pharmacy students using the personal report of communication apprehension (PRCA-24) instrument

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Introduction:

Communication apprehension (CA) is an individual's level of fear or anxiety associated with either real or anticipated communication with others. Effective communication is important for student's academic success and is a principle for provide a pharmaceutical care. The rationale of this study was to explore the oral CA levels of second and fifth year faculty of pharmacy students and compare them.

Methods:

Three hundred and three (140 second year and 163 fifth year) pharmacy students were included in the study from 2007 to 2010. The 24-item, Likert-type PRCA-24 instrument was completed in 15 minutes by second and fifth year students at the beginning and at the end of their academic year. The overall CA scores and sub scores for four communication contexts-groups (discussions, meetings, interpersonal conversations, and public speaking) were computed. Descriptive statistics, chi-square test and t-test were used for data analysis.

Results:

The surveyed students at the fifth year had significantly lower overall score in CA than the students at year two (61.6 ± 16.3 vs 67.9 ± 17.6 , $p=0.001$). Also, the proportion of high level of CA (overall score ≥ 80) was higher among year two students compared to year five (25.0% vs 12.9%, $p=0.013$). The mean CA contexts-group scores were significantly high among year two students compared to year five students, except for the group discussion there was no difference found.

Conclusions:

This study showed that year two pharmacy students have a high level of CA than year five. Ongoing evaluation for CA is needed and more planed strategies should be followed to improve communication skills among pharmacy students from the beginning of the learning process.

Key Words: Communication Apprehension; Personal Report of Communication Apprehension (PRCA); Pharmacy Students

Funding Agency: None



Pharmacy

Category: Basic Sciences

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Study of the effects of formulation and route of administration on in-vitro and in-vivo availability and ulcerogenicity of Ibuprofen

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Introduction:

Solubility and dissolution are essential factors for therapeutic effectiveness of poorly water soluble drugs. In this study, evaluation of the effects of beta-cyclodextrin (beta-CD) and hydroxypropyl beta-cyclodextrin (HP-beta-CD) on the solubility, dissolution and oral and rectal bioavailability of ibuprofen (IB) was performed. Some formulations were assessed for IB ulcerogenicity on GIT mucosa.

Methods:

The IB-polymer complexes were prepared. The resulted formulations (IB-beta-CD and IB-HP-beta-CD) side by side with physical mixture and pure drug, in oral capsule or rectal Witepsol H15 suppository were evaluated for IB solubility and dissolution. Formulations showing good results were subjected to bioavailability studies using rabbits. For ulcerogenic effects, adult male rabbits were divided into 5 groups, each group was given one formulation once daily for 30 days and the fifth as control. At the end, animals were sacrificed and the rectum and stomach were isolated, cut into slices and stained with H&E stain and observed under light microscope.

Results:

The solubility and dissolution of IB increased linearly as a function of concentration of polymer. The dissolution profiles of oral IB were found to be higher for IB-CDs complexes compared to rectal, physical mixture and pure drug. The bioavailability of IB from capsule is better than from suppository regarding the AUC and C_{max}. The ulcerogenic effects revealed that animals received drug alone showed marked ulceration while little changes with mild edema in between the epithelial cells were observed in groups received formulations containing CD.

Conclusions:

Inclusion of IB in CD polymers resulted in improving the solubility, dissolution and bioavailability compared to the drug alone and the drug-polymer physical mixture. These formulations also showed lower damage on the GI tract. The rectal formulations showed lower bioavailability and lesser mucosal damage compared to the oral ones.

Key Words: NSAIDS; Cyclodextrin; Formulation

Funding Agency: None



Pharmacy

Category: *Clinical*

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Determination of amikacin population pharmacokinetic parameters in Kuwaiti hospitalized patients using Nonparametric Adaptive Grid (NPAG) bayesian algorithm

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Introduction:

Amikacin (AMK) is commonly used to treat gram-negative infected patients such as those hospitalized in intensive care unit (ICU), medical wards (MW) and surgical wards (SW). AMK has a narrow therapeutic index and exhibits large variabilities in its pharmacokinetic parameters (PKP). The NPAG has been shown to be a suitable tool to determine the AMK PKP. Recently, the ward was found to affect the AMK PKP. The study aim was to estimate AMK PKP using NPAG and to investigate the effect of ward on AMK PKP.

Methods:

394 patients hospitalized in ICU (n=42), MW (n=177) and SW (n=175) were given AMK for the management of various infections. Peak and trough were measured after a multiple dose. Using NPAG (USC*PACK software), the PKP were estimated by fitting 1 and 2-compartment models first only to the ICU data; second, only to MW data; third, only to SW data; and fourth to all data. The PKP were: V (volume of the central compartment, l.kg-1); K₁₂ and K₂₁ (rate constants for the two compartment model, h-1); and K_i (h-1) and K_s (min.ml-1.h-1) are the intercept and slope of the following equation: elimination rate=K_i+K_s.creatinin clearance. We assessed the effect of ward on the PKP.

Results:

A 2-compartment model was best fitted the data. PKP estimated were (mean±SD): ICU: K_i=0.337±0.281; K_s=0.010±0.001; K₁₂=10.810±4.801; K₂₁=1.401±0.982; V=0.038±0.009; MW: K_i=0.111±0.210; K_s=0.004±0.002; K₁₂=5.460±5.100; K₂₁=3.210±3.200; V=0.110±0.001; SW: K_i=0.384±0.271; K_s=0.002±0.002; K₁₂=3.720±5.520; K₂₁=3.600±3.980; V=0.123±0.021; ICU+MW+SW: K_i=0.213±0.244; K_s=0.004±0.002; K₁₂=6.170±5.686; K₂₁=3.645±3.259; V=0.114±0.011. The K_s for ICU was greater than that for MW and SW, reflecting the greater elimination taking place in ICU patients. The V for MW and SW were greater than that for ICU, this may have reflected an increase in extracellular fluid in MW and SW patients.

Conclusions:

This study demonstrated a significant influence of the patient's hospitalization on AMK PKP.

Key Words: Amikacin; Population Pharmacokinetics; Patients Hospitalization.

Funding Agency: None



Pharmacy

Category: Basic Sciences

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Formulation and evaluation of gellan gum-based intranasal in situ gel of salbutamol sulfate

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Introduction:

Nasal delivery protects drugs from hepatic first-pass metabolism. Mucoadhesive in situ gel for salbutamol sulfate (SS) with gellan gum (GG) and additional mucoadhesives; sodium alginate (SA) or xanthan gum (XG) were formulated and tested in rats.

Methods:

SS in situ gels (2% w/v) were prepared at concentration of 0.4% w/v GG or in-combination with SA or XG in 0.1 and 0.3% w/v with Me-paraben preservative. Formulations were evaluated for hydrogel formation, invitro release, content uniformity, rheological behavior, in vivo mucoadhesiveness, nasal deposition, histopathology of nasal tissues and for aging at refrigeration condition.

Results:

SS showed relatively fast release in simulate dnasal fluid;100% release was achieved after 2 hours. Incorporation of SA or XG with GG resulted in slower release rate during the first hour. Release kinetics followed diffusion model and in situ gels exhibited pseudoplastic behavior. Gels were safe and did not show any mucosal changes after repeated doses for 14 days. In vivo mucoadhesiveness test, showed that GG gel prolonged mucociliary transport time (MTT) 3.3 fold than control solution. Incorporation of SA or XG to GG prolonged this time. Significant difference in % drug deposited from in situ gel and control was observed (t-test, p<0.05). The in situ gels remained liquid for 6 months without turbidity or gelation. Statistical analysis revealed non-significant difference in content uniformity, rheological behavior and release after storage compared to the fresh ones (t-test, p<0.05).

Conclusions:

In situ gel is a promising approach for intranasal delivery of SS. It has demonstrated prolonged deposition at the site of absorption in vivo with adequate safety to nasal mucosa. This gel combines the advantage of a solution, administration convenience with favorable residence time and expected improved drug absorption.

Key Words: Salbutamol sulphate; Nasal delivery; Gellan gum

Funding Agency: None



Pharmacy

Category: Basic Sciences

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Influence of beverages and meals on the oral bioavailability of ciprofloxacin

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Introduction:

Ciprofloxacin is a class III drug according to the Biopharmaceutics Classification System (BCS). The objective of the study was to investigate the effect of beverages and meal composition on the bioavailability of ciprofloxacin.

Methods:

Ten healthy volunteers received 500 mg ciprofloxacin with 200 mL water, acidic, and alkaline beverages in three-way crossover study. Another group of ten volunteers received 500 mg ciprofloxacin with water while fasting, after standardized, fat-rich, and protein-rich meals in four-way crossover study. After each drug administration, serial plasma samples were obtained and were analyzed for ciprofloxacin by HPLC.

Results:

The average ciprofloxacin AUC were 9.26, 10.6, and 6.99 mg-hr/L when taken with water, alkaline beverage and acidic beverage, respectively. This indicates that the acidic beverage significantly decreased the bioavailability of ciprofloxacin by 25% and 34% compared to water and alkaline beverage. This can be explained by reduction in the dissolution rate of ciprofloxacin due to decreased gastric pH. All types of meals delayed the absorption of ciprofloxacin as indicated by the significantly prolonged time to maximum concentration. The average ciprofloxacin AUC were 9.46, 10.3, 8.50, and 5.76 mg-hr/L for the fasting, standardized, protein-rich, and fat-rich meals, respectively. The fat-rich meal significantly reduced ciprofloxacin bioavailability by 38% compared to the fasting state.

Conclusions:

These results can be attributed to delay gastric emptying, reduced ciprofloxacin dissolution, and possibly inhibition of the absorptive transporters. These findings agree with the expected food effect on class III drugs on BCS and the proposed Biopharmaceutical Drug Disposition Classification System.

Key Words: Food drug interaction; Bioavailability; Ciprofloxacin

Funding Agency: None



Pharmacy

Category: Clinical

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Role of community pharmacists in the prevention and management of the metabolic syndrome in Kuwait

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Introduction:

The metabolic syndrome is a cluster of cardiovascular risk factors and its prevalence is alarmingly high in Kuwait. This study was conducted to assess the awareness of community pharmacists about the metabolic syndrome and identify the services they provide to the public for identification, monitoring and management of patients with this syndrome.

Methods:

A descriptive, cross-sectional study was performed on a randomly selected sample of 225 community pharmacists. Data were collected via face-to-face structured interview of the pharmacists using a pre-tested questionnaire.

Results:

The response rate was 97.8%. Nine pharmacists claimed to know about the metabolic syndrome but only one could correctly identify the condition. After being introduced to its definition, the majority of respondents strongly agreed that the metabolic syndrome has a rising prevalence in Kuwait (67.7%). Nearly two thirds of the pharmacists reported to provide height and weight measurement service. Blood pressure measurement was available in 182 pharmacies (82.7%) with the wrist automated device being most commonly used. Blood glucose measurement was available in 131 pharmacies (59.5%) while waist circumference and lipid profile measurements were the least provided services (1.8%). Respondents claimed to be very involved in counseling patients on lifestyle modifications including weight reduction through diet (71.4%), increased physical activity (69.5%), salt restriction (62.3%) and smoking cessation (52.3%). Most of the pharmacists were very involved in encouraging patient adherence with prescribed treatments and 58.2% were involved in advising patients about nonprescription treatments. Documentation of patient care services was not available in most of the pharmacies (93.2%).

Conclusions:

This study revealed a low level of awareness among community pharmacists about the metabolic syndrome. Interventions are needed to improve their knowledge and practice to provide efficient pharmaceutical services to control this emerging epidemic in Kuwait.

Key Words: Metabolic Syndrome; Community Pharmacists; Kuwait

Funding Agency: None



Pharmacy

Category: Basic Sciences

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Comparative Stability of Tocopherol/Acetate in Commercial and Experimental Cosmetic Formulations

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Introduction:

Vitami E (alpha tocopherol) is one of the best established ingredients in OTC products of skin ageing. Vitamin E is a lipid-soluble antioxidant which plays key roles in protecting cell membranes from lipid peroxidation by free radicals and reducing photocarcinogenesis. The vitamin is prone to oxidation, especially under frequent opening of the container by the user, at elevated temperature of storage. Therefore, the stability of T/TA in four marketed products (A, B, C and D) and two experimental cosmetic formulations (F1 and F2) were investigated.

Methods:

F1 and F2 are cream-emulsion formulations, containing T and TA respectively. The commercial products contained only TA, without declaration of quantity. Sets of each formulation were stored at 2-8°C, 22-25°C, and 37°C and investigated for physical changes. Chemical stability was monitored by HPLC method (mobile phase of 3%v/v water/methanol at 1.5 ml/ min). The eluents were monitored at 290 nm and 283 nm for T and TA, respectively (Nada et al. 2010). Statistical analysis of the data was performed by t-test at p< 0.05.

Results:

Product-A stored at 37°C showed loss of consistency and color change. Product-C showed leakage after 5 months at 37°C with loss of content. Product-D was no longer homogenous in appearance after 5 months at 37°C. Experimental preparations maintained the initial consistency, homogeneity, color and appearance. The initial concentrations of commercial products A, B, C and D were 0.12, 0.68, 0.53, and 0.49%, respectively. The experimental formulations contained 0.57 and 0.58%w/w of T and TA, respectively. The stability progressively decreased upon storage at higher temperatures. TA-containing formulations showed higher stability compared to T. After storage for 20 weeks at 37 °C, F1 lost about 80%, while F2 lost only 10% of the initial concentration.

Conclusions:

Stability of T and TA is questionable during use and storage of cosmetic products. Storage of vitamin-E products at 37 °C for 1-2 months results in appreciable loss of vitamin.

Key Words: Vitamin E; Commercial Cosmetics; Experimental preparations

Funding Agency: This work was supported by Kuwait University, Research



Pharmacy

Category: Basic Sciences

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Evaluation of new 5-(1H-1, 2, 3-triazolyl) methyl oxazolidinones as anti-tubercular agents

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Introduction:

Tuberculosis caused by *Mycobacterium tuberculosis* (M.tb.) accounted for ~1.3 m deaths in 2008, with potentials for spread of resistance. Linezolid, an oxazolidinone antibacterial agent is active against Gram-positive bacteria and M. tb strains. We evaluated the anti-*Mycobacterium* activity of a series of 5-triazolylmethyl oxazolidinones.

Methods:

The compounds were synthesized and were evaluated (100 to 0.19 µg/mL) against M. tb. H37Rv in BACTEC 12B medium using Microplate Alamar Blue Assay (MABA) to give 90% inhibitory concentration (IC₉₀, µg/mL) values. Mammalian Vero cell cytotoxicity using Promage's Cell Titer Glo Luminescent Cell Viability assay gave CC₅₀ (µg/ml) values, which allowed calculation of selectivity index (SI: ratio of CC₅₀ / IC₉₀); and preliminary bioavailability assays were performed. Bioassays were performed by the Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF, USA).

Results:

From the data, concise structure-activity relationships (SARs) were established. Analogs with alkylcarbonyl and arylcarbonyl groups at the piperazine 4-N-position displayed best activities with IC₉₀ value ranges of <0.2 to 2.095 and <0.2 to 2.103 µg/ml, respectively. This is comparable to methanesulfonyl analog and linezolid. These compounds gave acceptable SI value ranges of >13.76 to >257.3. Among the heteroaryl analogs, furanylcarbonyl derivative was most active (IC₉₀: <0.2 µg/ml, SI: >220.2), while others showed IC₉₀: 0.209 to 1.389 µg/ml and SI: >34.98 to >217.3. However, the arylsulfonyl derivatives were inactive (IC₉₀: 5.469 to >100 µg/ml, SI: >8.896). Nicotinoyl, isobutryl and morpholino analogs showed low to medium bioavailability and were selected for further testing in vivo.

Conclusions:

Triazolyl oxazolidinones showed potent activity against M. tb H37Rv with exciting SARs, and acceptable therapeutic index.

Key Words: Anti-tubercular agents; Mycobacterium tuberculosis; Oxazolidinones

Funding Agency: None

Pharmacy

Category: Basic Sciences

172

Isolation of a Bioactive Compound from *Centaurea aegyptiaca* Ethyl Acetate Extract*Sary HG¹, Ayoub NA², Singab AB², Orabi KY¹¹Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University; ²Department of Pharmacognosy, Faculty of Pharmacy, Ain-Shams University, Egypt**Introduction:**

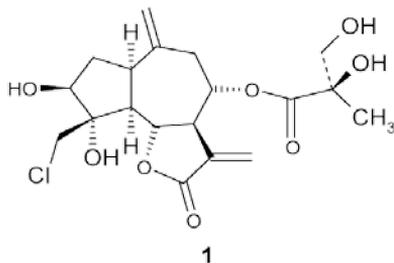
In a previous work, the ethyl acetate extract of *Centaurea aegyptiaca* has shown potential cytotoxic activity against liver and larynx carcinoma cell lines. The aim of this study is to continue the isolation of the compound(s) that may be responsible for the potent biological activity of *Centaurea aegyptiaca* extract.

Methods:

The shade-dried aerial parts of *Centaurea aegyptiaca* were coarsely powdered and extracted with ethanol (96%). The ethanolic extract was partitioned successively with five solvents to afford; petroleum ether, CHCl₃, EtOAc, n-BuOH, and H₂O fractions. The ethyl acetate extract was subjected to chromatographic separation on a flash silica gel column gradually eluted with an increasing strength of methanol in methylene chloride. After successive purification, one compound was isolated and analyzed using different spectroscopic methods. Moreover, the cytotoxic activity of this compound was evaluated against liver and larynx carcinoma cell lines. IC₅₀ (µgram/well) of the compound was determined using doxorubicin as a positive control.

Results:

A sesquiterpene lactone (1) was isolated and characterized from the ethyl acetate extract of *Centaurea aegyptiaca*. It exhibited potential cytotoxic activity against larynx carcinoma cell line with IC₅₀ of 2.72 µgram/well.

**Conclusions:**

Chemical investigation of *Centaurea aegyptiaca* ethyl acetate extract led to the isolation and identification of a sesquiterpene lactone (1). Moreover, this compound may be responsible for the potential cytotoxic activity of *Centaurea aegyptiaca* ethyl acetate extract against larynx carcinoma cell line.

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*; Cytotoxicity; Sesquiterpene

Funding Agency: None



Physiology

Category: Basic Sciences

173

Effect of Three Months of Aerobic and Resistance Training on Diabetic and obese subjects.

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Introduction:

Exercise is effective in glucose control because exercise has an insulin-like effect that enhances the uptake of glucose even in the presence of insulin deficiency. An exercise prescription emphasizing low intensity, long duration aerobic activity as well as resistance training decreases resting glucose and insulin level in diabetic patients. Purpose: the aim of this study was to show the effect of a combination of resistance training and aerobic conditioning on patients with diabetes and obesity.

Methods:

21 diabetic and obese subjects, 11 females, and 10 males (age = 47.71 ± 13.13) participated in 12 weeks of aerobic and resistance training. Maximum oxygen consumption (VO_{2max}), grip strength, flexibility, vertical jump, push up, sit up, and body composition were measured twice, before and after the training program.

Results:

There were significant improvements ($P < 0.05$) between pre and post training program in weight (84.34 ± 20.83 vs. 82.32 ± 20.66), VO_{2max} (17.61 ± 5.32 vs. 19.97 ± 6.36), resting heart rate (84.47 ± 14.90 vs. 79.04 ± 12.78), flexibility (19.35 ± 11.11 vs. 24.04 ± 9.53), pushup (3.29 ± 8.74 vs. 7.62 ± 8.35), and grip strength (59.35 ± 22.31 vs. 64.02 ± 23.35).

Conclusions:

It is concluded that a combination of regular aerobic and resistance training programs appeared lead to significant improvements of the fitness and fatness of diabetic and obese patients.

Key Words: Aerobic; Resistance; Diseases

Funding Agency: None



Physiology

Category: Basic Sciences

174

Pacing postconditioning protects the heart against ischemia reperfusion injury without gender discrimination

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Introduction:

We previously showed a protective role for the intermittent dyssynchrony (pacing postconditioning (PPC)), induced by ventricular pacing immediately at the beginning of reperfusion. The aim of this study was to determine the suitable protective dose of PPC in rats and gender differences in PPC.

Methods:

Isolated perfused rat hearts (Langendorff) (n=3-7) were used for this study. Controls were subjected to 30 minutes unprotected ischemia. PPC protocol was varied between 10 cycles of 30 seconds and 3 cycles of 30 seconds left ventricular (LV) pacing alternated with 30 seconds right atrial (RA) pacing at the beginning of reperfusion to determine the effective PPC dose. For gender differences study, separate male and female groups underwent 3 cycles of 30 seconds PPC alternated with 30 seconds RA pacing at the beginning of reperfusion. 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:

Unprotected ischemia reperfusion (I/R) resulted in poor recovery of hemodynamics (left ventricular end-diastolic pressure (LVEDP), left ventricular developed pressure (Pmax), Maximal derivative of left ventricular pressure (dP/dtmax), coronary flow (CF), and coronary vascular resistance (CVR)) compared to baseline data ($p < 0.02$). At least 3 PPC cycles of 30 seconds on/off were required to significantly ($P < 0.006$) decrease infarct size and improve the deteriorated hemodynamics compared to control. PPC resulted in a significant decrease ($P < 0.05$) in the infarct size and significantly improved hemodynamics in the male and female hearts compared to baseline and control.

Conclusions:

PPC provides myocardial protection when at least 3 cycles of 30 seconds periods of pacing are used. PPC protects both male and female hearts showing the lack of gender differences in this treatment.

Key Words: Ischemia; Postconditioning; Gender

Funding Agency: Kuwait University, grant number MY03/10



Physiology

Category: Graduate PhD (Basic Science)

175

Effect of (H_2O_2) on the delayed rectifier potassium current in dissociated Hippocampal CA1 Neurons

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Introduction:

Hydrogen peroxide (H_2O_2) is generated in the body as part of normal cellular metabolism. When in excess, H_2O_2 is known to cause damage to various biomolecules. Direct application of membrane permeable H_2O_2 has been frequently used in previous studies to induce oxidative stress conditions. The present study examined the effect of H_2O_2 on the delayed rectifier potassium current (IKDR), a voltage – dependent current of paramount importance for neuronal excitability.

Methods:

Whole cell voltage-clamp experiments were performed on freshly dissociated hippocampal CA1 neurons of young adult SD rats before and after treatment with H_2O_2 . To reveal the mechanism behind H_2O_2 -induced changes in IKDR different antioxidants and reagents were used.

Results:

The external application of membrane permeable H_2O_2 inhibited IKDR in a concentration dependent manner. H_2O_2 reduced IKDR's amplitude and voltage-dependence. Desferoxamine (DFO), an iron-chelator that prevents hydroxyl radical (.OH) generation, prevented H_2O_2 -induced reduction in IKDR. Application of the cysteine-SH oxidizing agent, 5, 5 dithio-bis-nitrobenzoic acid (DTNB) mimicked the effect of H_2O_2 , whereas SH-reducing agents dithiothreitol (DTT) and glutathione (GSH) reversed and prevented the inhibition in IKDR respectively. Addition of reducing agents DTT and GSH alone did not affect IKDR. Membrane impermeable oxidative and reducing agents had effects only when added intracellularly.

Conclusions:

This study provides evidence for the redox modulation of IKDR. H_2O_2 reduced IKDR, and this reduction was prevented by DFO thus identifying .OH as the intermediate oxidant responsible for the decrease in current amplitude. The reversal of H_2O_2 -induced reduction of IKDR by SH-reducing agents identified SH groups as an oxidative target. The oxidative modulation of IKDR by H_2O_2 was via .OH which targeted free SH groups of cysteine residues found in the intracellular aspect of the KDR channel protein.

Key Words: Delayed Rectifier; Hydrogen peroxide; Patch-clamping

Funding Agency: The College of Graduate Studies



Physiology

Category: Basic Sciences

176

Early life activation of toll-like receptor 4 reprograms neural anti-inflammatory pathways

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Introduction:

A single postnatal exposure to the bacterial endotoxin, lipopolysaccharide (LPS), reduces the neuroimmune response to a subsequent LPS exposure in the adult rat. The attenuated fever and proinflammatory response is caused by a paradoxical, amplified, early corticosterone response to LPS. The mechanisms underlying this heightened corticosterone response is not yet known.

Methods:

Rats were given LPS at postnatal day 14 and different component of the adult hypothalamic pituitary adrenal axis (HPA) were assessed using real-time PCR, Western blotting and ELISA. Signaling pathways leading to the heightened adult HPA axis activity were monitored both in central and peripheral compartments. These signaling pathways include the vagus nerve activity and humoral signaling pathways via peripherally born prostaglandins.

Results:

Hypothalamic corticotrophin-releasing hormone mRNA, pituitary proopiomelanocortin mRNA, and circulating adrenocorticotrophic hormone were all increased after adult exposure to LPS without significant modification to hippocampal or hypothalamic glucocorticoid receptor mRNA or protein or vagally mediated afferent signaling to the brain. Postnatal LPS administration did cause a persistent upregulation of the LPS Toll-like receptor-4 (TLR4) mRNA in liver and spleen, but not in brain, pituitary, or adrenal gland. Cyclooxygenase-2 (COX-2) was constitutively expressed in the liver. Adult immune activation of the upregulated TLR4 and COX-2 caused a rapid, amplified rise in circulating, but not brain, prostaglandin E₂ that induced an early, enhanced activation of the hypothalamic-pituitary-adrenal (HPA) axis.

Conclusions:

Postnatal LPS reprograms the neuroimmune axis by priming peripheral tissues to create a novel, prostaglandin-mediated activation of the HPA axis brought about by increased constitutive expression of TLR4 and COX-2.

Key Words: Neuroimmunology; Toll-Like Receptors; Hypothalamic Pituitary Adrenal Axis

Funding Agency: Canadian Institutes of Health Research, Robertson Fund for Cerebral Palsy (Canada), Alberta Heritage Foundation for Medical Research (Canada), Heart and Stroke Foundation (Canada)



Psychiatry/Psychology

Category: Basic Sciences

177

Gender and governorates differences in working memory performance among children in Kuwaiti

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Introduction:

The term 'working memory' WM refers to the capacity to store and manipulate information for a brief period. There is now extensive evidence that working memory predicts current and subsequent scholastic attainments of children across the school years in both literacy and numeracy. This study was intended to explore gender and governorates differences in WM performance among Kuwaiti children.

Methods:

The participants were 1180 Kuwaiti pupils representing the six Kuwaiti governorates (Asimah, Hawally, Ahmadi, Mubarak Alkabeer, Farwaniyah, and Jahra). The participants mean age 109.05 ± 28.57 months (536 girls aged 109 ± 28.64 months and 644 boys aged 112.39 ± 27.54). All participants completed a computerized WM battery (Alloway, 2007) to measure a verbal and visual-spatial WM tasks.

Results:

A significant gender differences were found in which females significantly lower ($t=4.65$, $p<.001$) in verbal WM and ($t=5.83$, $p<.001$) in visuo-spatial WM. Moreover, the Bonferroni test results showed a significant difference among all governorates in verbal WM ($f=8.84$, $p<.001$) and visual-spatial WM ($f=27.36$, $p<.001$) in which indicated that, students living in Ahmadi governorate outperformed their counterparts in almost all the other governorates in both verbal and visuo-spatial WM tasks. Moreover, the interaction effect of gender and governorates was found to be significant ($f=7.93$, $p<.001$) with verbal WM and ($f=6.43$, $p<.001$) with visuo-spatial WM tasks.

Conclusions:

Gender differences in working memory exist. Furthermore, the significant differences in WM in six governorates may be attributable to cultural background of the children, parents' levels of education, number of siblings, children's birth order. This warrants further investigation.

Key Words: Working memory; Gender differences; Children in Kuwaiti

Funding Agency: Research Administration, grant # OP02/07.



Psychiatry/Psychology

Category: Clinical

178

Gender and age differences in quality of life in a nation-wide sample of Kuwaiti high school students are associated with perceived quality of parental emotional relationship.

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Introduction:

Interest in the quality of life (QOL) of children is in line with the 1989 Convention on the Rights of the Child, which stressed the child's right to adequate development. The study's objectives were to: (i) highlight how satisfied Kuwaiti students were with life circumstances as in the WHO Quality of Life Instrument (WHOQOL-Bref); (ii) assess the prevalence of those at risk for impaired QOL, establish QOL normative values; and (iii) examine the relationship of QOL with socio-demographic, parental and environmental factors.

Methods:

A nation-wide sample of students in senior classes in government high schools (N = 4437, 48.6% boys; aged 14 -23 years) completed the questionnaires in 2007/8.

Results:

Using Cummins' norm of 70% - 80%, we found that, as a group, they barely achieved the threshold score for physical health (70%), social relations (72.8%), environment (70.8%) and general facet (70.2%), but not for psychological health (61.9%). These scores were lower than values from other countries. Using the recommended cut-off of < 1SD of population mean, the prevalence of at risk status for impaired QOL was 12.9% - 18.8%. Boys had significantly higher QOL than girls, mediated by anxiety/depression; while the younger ones had significantly higher QOL (P < 0.001), mediated by difficulty with studies and social relations. Although poorer QOL was significantly associated with parental divorce, the most important predictors of poorer QOL were perception of poor emotional relationship between the parents, poor self-esteem and difficulty with studies.

Conclusions:

Poorer QOL seemed to reflect a circumstance of social disadvantage and poor psychological well-being in which girls fared worse than boys. Programs that address parental harmony and promote study-friendly atmospheres could help to improve QOL. The application of QOL as a school population health measure may facilitate the tracking of health status.

Key Words: Quality of life; Kuwait -high school; Students

Funding Agency: The Kuwait Society for the Advancement of Arab Children (KSAAC).



Psychiatry/Psychology

Category: Graduate PhD (Basic Science)

179

Evaluating the reliability, validity of the arabic version of the diabetes quality of life measure (DQOL) in a Kuwaiti population.

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Introduction:

Non diabetes HRQOL instruments are available in Arabic language. While the DQOL, DSQOLS and WED have clear emphases on concerns of individuals with type 1&2 diabetes. This study aims at examining psychometric properties of a Diabetes Quality of Life –DQOL (Jacobson, de Groot, & Samson, 1994) in Arabic language for type 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 and in Kuwait Diabetes Society clinics. Mean age of the sample was 47 years. Exploratory factor analysis identified factor structure of the DQOL, Cronbach's alpha assessed internal consistencies, test-retest reliability was assessed, and Pearson's correlations among scores of the DQOL, the Diabetes Symptom Checklist (DSC-R) and the Arabic version of Beck Depression Inventory-II (BDI-II), were estimated to determine discriminant validity of the DQOL.

Results:

A one-factor solution of the three specific domain scores of the DQOL (impact .87, satisfaction .81, and Social worry .74), showed all domain items to load%.65.27, Reliability was acceptable for the DQOL (internal consistency =0.93; test-retest correlation coefficients = 0.72). The DQOL showed satisfactory discriminative ability in which DQOL scores were more strongly correlated with the depression ($r=.56$) and the Diabetes Symptom Checklist ($r=.53$). Moreover, no significant gender difference in the DQOL was found ($f=0.52$, $p>.05$).

Conclusions:

This study provides evidence for the reliability and validity of the DQOL in Arabic language for diabetes patients in Kuwait.

Key Words: DQOL; Type 2 diabetes; Kuwait

Funding Agency: None



Psychiatry/Psychology

Category: Undergraduate

180

Primary caregiver and child's perception, attitude and coping in paediatric cancer.

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Introduction:

Background: Cancer is a disease that affects the body as well as the life of patients and families. The word "cancer", especially in children, strikes fear in the minds of many people in Kuwait, which makes them avoid open and honest discussions on this topic. Our study attempted to shed some light on the quality of life, perception, and attitude of primary caregivers and children with cancer in Kuwait.

Methods:

This cross-sectional study enrolled paediatric cancer patients ages 4-18 years and their primary caregivers from three specialized cancer centers in Kuwait. Children were interviewed using the (PedsQL), while their caregivers completed a self-report questionnaire which included among other questions the PedsQL- parent version and the Beck Depression Inventory-II.

Results:

Upon knowing their child's diagnosis most caregivers were either upset or afraid. The majority of children were not informed about their diagnosis and the most common reasons were that the child was young or it was better for the child not to know. The older the child, the more he or she was likely to be informed ($p < 0.001$). Although most of the support received was from family members, the majority of caregivers needed support from medical staff. Female caregivers reported a decrease in their social duties and ability for self-care and reported more depressive symptoms. A slight agreement was found between child and caregiver evaluations of the PedsQL.

Conclusions:

Child and caregiver quality of life was greatly affected after the diagnosis of cancer. Many children were not informed of their cancer diagnosis or treatment plan. More support was needed from the medical staff.

Key Words: Perception; Attitude; Coping

Funding Agency: None



Psychiatry/Psychology

Category: Clinical

181

How do we classify anxiety and depression in the forthcoming WHO ICD-11 and American DSM-V?: A contribution from the Arab world using a nation-wide Kuwaiti general population sample and based on diagnostic - criteria instruments

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Introduction:

Our study was prompted by the need to contribute data from the Arab world for resolving the difficult problem of how to classify major depressive disorder (MDD) and generalized anxiety disorder (GAD) in the planned WHO's ICD-11 and the American DSM-V. At issue is how to account for the relationship between these disorders, in view of their noted high frequency of co-morbidity. We examined two research questions: First, using a data-driven approach (exploratory factor analysis - EFA), will the symptoms that define MDD and GAD appear together in one factor?. Second, using a theory-driven approach (confirmatory factor analysis - CFA) how will the structural integrity of the resulting factors compare with those of alternative models?.

Methods:

Participants (N = 3303, 44.8% men, aged 16-87yrs) were a general population sample of Kuwaitis who self-completed DSM-IV criteria - based questionnaires in 2007. EFA was by principal axis factoring. Models were compared in CFA using AMOS-16 software.

Results:

In EFA, while the core symptoms of depression formed an empiric cluster separate from the core symptoms of anxiety, there was an overlap of some symptoms which the two disorders share. In confirmatory factor analysis, the model that best explained the relationship between the symptoms (Goodness of Fit Index >0.9, RMSEA < 0.08) was the hierarchical bifactor model. This indicates that the symptoms are related at more than one (dimensional) level. At one level, which supports the noted co-morbidity, there is a general (second-order) factor that represents a depression-anxiety psychopathology. At another level, the empiric clusters indicate individual tendency to endorse either specific symptoms.

Conclusions:

Our findings support the view that, while MDD and GAD can be classified as distinct disorders, they should belong to the same group of "overarching superclass" of emotional disorders.

Key Words: Depression; Anxiety; WHO ICD - DSM

Funding Agency: Kuwait Foundation for the Advancement of Sciences (KFAS): 2006-1302-02.



Psychiatry/Psychology

Category: *Clinical*

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Family caregivers of subjects with schizophrenia are burdened by patients' disruptive behavior, sedentary life style and poor quality of hospital care

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Introduction:

Although the burden experienced by families of people with schizophrenia has long been recognized as one of the most important consequences of the disorder, there are no reports from the Arab world. We explored the following research question: In a conservative culture, how is the family experience of caregiving (as in the Involvement Evaluation Questionnaire - IEQ-EU) affected by caregivers'/ patients' socio-demographics, clinical features and indices of quality of care; and how does this compare with the pattern in the literature?

Methods:

Consecutive family caregivers of outpatients with schizophrenia at Psychological Medicine Hospital, Kuwait, were interviewed with the IEQ-EU in 2006/8. Patients were interviewed with measures of needs for care, service satisfaction, quality of life (QOL) and psychopathology.

Results:

There were 121 caregivers (66.1% men, aged 39.8). The IEQ domain scores (total: 46.9; tension: 13.4; supervision: 7.9; worrying: 12.9; and urging: 16.4) were in the middle of the range for the European data. In regression analyses, higher burden scores were associated with caregiver lower level of education, patient's female gender and younger age, as well as patient's lower subjective QOL, needs for hospital care, and not involved in outdoor activities. Disruptive behavior was the greatest determinant of global rating of burden.

Conclusions:

Despite generous national social welfare provisions in Kuwait, experience of family burden was the norm and was significantly associated with patient's disruptive behavior and sedentary life style. The results underscore the need for adequate drug and psychological treatment, provision of community - based rehabilitation programs and continued interaction with the families in order to improve their caregiving ability and prevent relapse. Differences with the international data reflect peculiarities of culture and type of service.

Key Words: Schizophrenia; family caregiver; burden

Funding Agency: Kuwait University: MQ01/05



Surgery

Category: Clinical

183

Ten Years of ATV (Buggy) injuries in ICU.

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Introduction:

Riding on an ATV (Buggy) has become a recreational activity despite of increasing mortality and morbidity since its use as a recreational sport in the State of Kuwait about 10 years ago. It was introduced in the America in 1970, its use among children less than 16 years was banned in 1988 due to mortality and morbidity.

Methods:

To assess the mortality and morbidity associated with ATV related injuries, a retrospective analysis of 62 cases admitted in ICU from January 2001 to December 2010 in Adan Hospital of Kuwait.

Results:

There were 62 cases, male 52 (84%) and female 10 (16%). Age ranges from 5 to 43 years with the average of 16.5 years. The mortality rate was 10 out of 62 cases (16%) that died within 24 hours of admission. The duration ICU stay was from 1 to 45 days with the average of 6.76 days. The commonest cause was head injury followed by multiple fractures of bones, chest and abdominal injuries. There were 2 cases of paralysis. It is interesting point that February being the shortest month of the year shows the highest number of admissions 15/62 (24 %). Due to large number of admission of ATV related injuries, we excluded those cases admitted to other department. Riding without safety gears and improper supervision continues to be a major cause especially among children. This study shows ATV injuries have become a serious issue to the state of Kuwait.

Conclusions:

The seriousness of head injury related to ATV continues which warns about strict supervision and requirement of safety gears. We suggest introduction of ATV driving school especially for young children.

Key Words: ATV(Buggy); Ten Years experience; ICU

Funding Agency: None



Surgery

Category: Clinical

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**Role of intrapleural tissue plasminogen activator in management
complicated pleural effusions**

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Introduction:

Intrapleural fibrinolysis remains a controversial therapy for complicated pleural effusions. Our aim was to evaluate safety and efficacy of intrapleural fibrinolysis in a single institution experience.

Methods:

Over a 1-year period (2009-2010), 23 consecutive patients (age 7months–58 years; 16 [69.6%] male, 7 [30.4%] female) received intrapleural fibrinolysis for complicated pleural effusions related to infection (n = 20 secondary to bacterial pneumonia: 4 tuberculosis), malignancy (n = 1: lung cancer), hemothorax all related to trauma (n = 3) .Pediatric patients n=8 (34.8%); 5 [62.5] male, 3 [37.5] female. Indications for intrapleural fibrinolysis were persistent radiological evidence of loculations after failing drainage by tube thoracostomy, and included intrapleural tissue plasminogen activator (ACTYLASE; n = 11, 47.8%) or (RAPILASE n = 12, 52.2%) as a daily dose of 16 mg in 100 mL normal saline via pleural tube.pediatric dose is 4 mg of TPA in 20 ml of normal saline. Patients were treated for 1–6 days (mean 3, standard deviation [SD] 1.4); 2 patients (8.7%) received 2 cycles (6 d) of fibrinolytics. Once clinical and radiological reevaluation confirmed minimal drainage (< 150 mL/24 h), and resolving empyema and effusion, the chest tube or pigtail was removed. Failure of treatment (i.e., inadequate lung re-expansion) or clinical deterioration (i.e., sepsis syndrome) mandated surgical intervention.

Results:

Following intrapleural fibrinolysis, clinical and radiological improvement occurred in all patients (100%) and no failure requiring surgical intervention. The avarage length of stay was 3-5 days± 1.8days. There was no complication and no mortality related to TPA.

Conclusions:

Intrapleural administration of tissue plasminogen activator is an effective and safe mode of treatment for complicated pleural effusions and may decrease the need for operative intervention.

Key Words: Complicated pleural effusion; Tube thoracostomy; Tissue Plasminogen Activator (TPA)

Funding Agency: None



Surgery

Category: *Clinical*

185

Sirolimus rescue therapy after acute rejection in renal transplant recipients: One year follow up

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Introduction:

Conversion from calcineurine inhibitors (CNIs) to sirolimus (SRL) is proved to be effective in improving long-term graft outcome. SRL treatment of high risk renal transplant recipient (RTR) is still under investigation.

Aim: We studied the long-term effects of conversion from CNI to SRL as rescue therapy on RTR after treatment of biopsy proven acute rejections (BPAR).

Methods:

RTR converted from CNI, mycophenolate mofetil (MMF) as 2gm daily and steroid to SRL, MMF and steroid after treatment of BPAR were studied.

Results:

Thirty candidates were maintained on CNIs (24 were on cyclosporine-A and 6 on tacrolimus) after receiving ATG (80%) or basiliximab (13.3%) induction therapy. The overall mean age was 35.1±13.5 years, including pediatric and geriatric age groups and patients with multiple co-morbid conditions. Black patients were 63.3%. Mean body mass index (BMI) was 27.8±8 and 33.3% had a BMI >30. Pre-conversion steroid-resistant rejection incidence was 16.7%. Mean time to convert to SRL was 10±18.8 months post-transplantation. Post-SRL rejection episodes were reported in 16.6% with 10% resistance to steroid treatment. Leucopenia, hypercholesterolemia and hypertriglyceridemia increased significantly post-SRL (p 0.031, 0.0001 and 0.007 respectively). Graft and patient survival were 100 % each. There were significant improvements in estimated creatinine clearance from 58±22.1 to 69.6±22.2 ml/min/1.72 (MDRD formula) at one year (p 0.001). SRL had to be discontinued in 6.6% of candidates mainly due to its side effects.

Conclusions:

SRL rescue therapy after treatment of BPAR is proved to be effective as a CNI free regimen for high risk RTR after one year of follow up.

Key Words: Sirolimus; Rejection; Renal Transplant

Funding Agency: None



Surgery

Category: *Clinical*

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Abdominoplasty in kidney transplant recipients: Safe or crazy?

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Introduction:

There is a lack of literature on the outcome of abdominoplasty surgery in kidney transplant (Tx) recipients. The aim of this study is to determine whether kidney Tx recipients have any additional risk when undergoing this kind of surgery.

Methods:

All cases of abdominoplasty that involved kidney Tx patients from 1/1/2004 till 30/4/2010, were collected for review. There were 12 patients (8 females & 4 males) who underwent abdominoplasty during the study period. A control group of 26 non-Tx patients were selected randomly to compare outcome. Statistical analysis included student T-test and Chi-square.

Results:

There was a statistically significant difference between the two groups with regards to sex (P=0.044, more males in Tx group), Age (P=0.0001, older patients in Tx group), BMI (P=0.005, higher BMI in Tx group), and DM (P=0.001, more patients with DM in Tx group). There was no difference in overall post-operative complications rate, especially those that are wound related, among the Tx and non-Tx groups (42% Vs 31% respectively, P=NS). Overall the operative time was shorter and the hospital-stay longer in Tx patients (P=0.01, and P=0.054 respectively). When patients were grouped into those that developed complications against those who didn't, the factor that was statistically significant for developing complications was the operative time (P=0.02, longer time in patients with complications).

Conclusions:

Immunosuppression is not a risk factor for developing overall complications, especially those that are related to the surgical wound. And that is despite the fact that the transplant patients in our study were older, had higher BMI, included more males, and had higher rate of DM. Reducing time of surgery, on the other hand, leads to reduction in post-operative complications rate.

Key Words: Abdominoplasty; Kidney transplantation; Immunosuppression

Funding Agency: None



Surgery

Category: Clinical

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Gallstones and kidney transplantation; prophylactic or expectant laparoscopic cholecystectomy?

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Introduction:

Laparoscopic cholecystectomy (LC) is a relatively safe procedure in the modern era. Whether there is advantage in performing this surgery prophylactically in asymptomatic kidney transplant recipients is still controversial. The aim of this study is to compare outcome of kidney transplant recipients who underwent prophylactic LC with those who had it because of gallstone (GS) disease complications.

Methods:

Retrospective chart review of all kidney transplant recipients who underwent LC at Hamid Al-Essa organ transplant center from 1/1/2003 till 1/5/2010. Data was analyzed using student t-test and chi-square.

Results:

38 patients were identified that met the criteria; 12 asymptomatic (Group 1), and 26 symptomatic (Group 2). Group 1 patients were relatively older than group 2 (average 57, and 48 respectively, $P=0.01$). 10 patients (38.5%) in Group 2 required admission to manage GS symptoms before surgery ($P=0.01$), and 5 (19%) required ERCP intervention. 3 patients in Group 1 underwent simultaneous LC and kidney transplantation. LC time from transplant was 0-17.5 years, median 1 year in group 1, and 6 months-19.8 years, median 4.9 years in group 2, $P=0.04$). There was no statistical significance in hospital stay, operation time, complication to kidney graft, and intra or post-operative surgical complications between the two groups. Despite that, 5 patients in Group 2 (19%) required post-operative re-admission to manage complications, while None in Group 1 did.

Conclusions:

In addition to suffering from GS disease complications, symptomatic patients required more admissions to manage these complications before surgery, needed more ERCP intervention and more post-operative re-admission than asymptomatic patients. LC in asymptomatic GS disease patients resulted in minimal morbidity and no graft loss. Our observations favor LC at asymptomatic stage. A randomized multi-center study is needed to answer this question accurately.

Key Words: Kidney Transplantation; Gallstones; Prophylactic cholecystectomy

Funding Agency: Self fund



Surgery

Category: Clinical

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Temporomandibular joint disc pathology; correlation between clinical, surgical findings and outcome

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Introduction:

Temporomandibular joint dysfunction is a heterogeneous collection of signs and symptoms characterized by the presence of pain, TMJ noise, and disruption of normal function of the joint. It includes clinical problems that involve masticatory musculature, joint, or both. It can be caused by many etiological factors, which may overlap and/or exacerbated by each other as trauma, irregularities in occlusion and myofascial pain.

Methods:

30 patients aged between 19-52 years; 11 males and 19 females. The main complains were pain and tenderness in TMJ region, clicking, with/without limited mouth opening. Clinical assessment included history taking, and clinical examination as range of motion, TMJ palpation, & joint auscultation. Radiologic assessment included Panorama, Magnetic resonance imaging. Management of disc pathology initiated with conservative management, then intervention procedures by disc plication with repositioning, disc suspension with/without high condylar head shave, or discectomy.

Results:

Clinical examination alone is a poor predictive value for diagnosing disc displacement with reduction but acceptable for disc displacement without reduction. MRI proved superiority over other radiologic modalities. Management needs collaboration between dentist, physical therapist, and psychiatrist before surgical intervention. Disc suspension and disc plication procedures were useful tools to manage difficult advanced disc pathologies.

Conclusions:

Disc pathology disorders including disc displacement with/without reduction and disc deformation are of the most common causes of temporomandibular joint dysfunction. Trauma and anxiety are the main etiologic initiating and perpetuating factors. MRI is the radiologic image of choice for disc pathology diagnosis. Surgery is the only choice of management of advanced disc pathology disorders.

Key Words: Temporomandibular joint dysfunctions; Clicking; Magnetic resonance image

Funding Agency: None



**Original Research Case Report
By Subject Area**



Allied Health

Category: *Clinical*

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Infected facial tissue fillers: new epidemic in Kuwait. Case series.

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CASE REPORT

Background:

Injectable soft tissue fillers provide an attractive option in facial rejuvenation. The apparent relative simplicity of the procedure can lead to a frivolous attitude toward the use of fillers, but serious complications can and do occur. These complications may be related to the filler material itself yet more often are attributed to poor patient or region selection and injection technique.

Case summary:

Since 2007 we treated 11 female patients aged between 25 and 44 who presented with signs of facial cellulitis or abscess, which either did not have obvious infectious focus, or did not readily respond to standard therapy of odontogenic infection. All these patients admitted, some of them after considerable prevarications, previous application of injectable tissue fillers done either in private plastic surgery practices or cosmetic saloons. The time period between injection and infection varied between 2 weeks and 4 years. The injected substance remained in most cases unknown. None of our patients received any warning about possible complications. In 7 cases hospital admission and surgical treatment under GA was necessary. Remaining 4 cases were managed on outpatient basis. Dental source of infection was discovered in 5 cases, no obvious infectious focus was identified in 6 cases.

Conclusion:

Infectious complications of injectable tissue fillers were previously unknown in Kuwait. With their increasing use the prevalence of complications is also expected to increase. While these products are primarily meant for treatment of aging face, the age structure of our patients suggests their misuse and spurious indications. Especially worrisome is recently observed application of fillers in cosmetic saloons. We believe that use of injectable tissue fillers should be regulated and their administration in non-medical facilities prohibited. Female patients with atypical course of facial infection should be questioned about previous history of cosmetic procedures.

Key Words: Injectable tissue fillers; Facial rejuvenation; Orofacial infection



Medicine

Category: *Clinical*

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Unusual cause of vague abdominal pain

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CASE REPORT

Background:

Adrenal cyst is very rare and it affects only one or two people in 10, 000. Most adrenal cysts are found incidentally. The majority of people who are diagnosed with adrenal cysts are female, and although it can occur at any age, most of them are found in patients between 30 and 60 years of age. Adrenal cyst usually causes no symptoms, although if it becomes large in size, it can cause pain in the abdomen or back.

Case summary:

37-year old lady admitted because of vague abdominal pain, around the umbilical region not radiated and not associated with vomiting. Abdominal ultrasound was normal. CT abdomen done and showed accidental finding of left adrenal cyst 6 by 5. 5 cm arising and splaying the lateral limb of the adrenal gland with a definite line of cleavage between it and the ipsilateral kidney. No wall calcification. The rest of the study was normal. Complete blood count: WBC = 6. 5 haemoglobin = 9. 9 normocytic normochromic anaemia, platelet = 286 Her liver and renal functions were normal. Hormonal profiles were within normal ranges. Serum testosterone = 0. 15 pmol/l, serum andostenedione = 3. 1 nmol/l. Dihydroepiandrostedione = 1. 32 umol/l, serum prolactin = 472. 83 mU/l, serum cortisol = 692. 86 nmol/l. 24-hour urine for cortisol = 999. 5 nmol/24 hours. 24-hour urine for catecholamines were normal. The patient received symptomatic treatment and improved. She refused surgical removal of the cyst and was advised for regular follow up.

Conclusion:

Adrenal cyst is one of the rare causes of vague abdominal pain. It is rarely symptomatic, but if its size increases it will cause abdominal discomfort and may necessitate surgical removal. Surgical removal is recommended for all lesions larger than 5 cm. Symptomatic adrenal cysts should be operated, but small, asymptomatic, non-functional cysts with benign characteristics may be treated conservatively with regular follow-up by sonography or computed tomography and hormonal evaluation.

Key Words: Adrenal; Cyst; Catecholamines



Medicine

Category: *Clinical*

191

Drug-induced lupus caused by contraceptive pills

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CASE REPORT

Background:

Objective: We report a case of SLE induced by contraceptive pills.

Clinical presentation: Mrs R is a 35-year-old lady presented with one year history of progressive pleuritic chest pain, joint pain, fatigue and excessive hair fall. The patient gave history of being on a regular dose of Diane-35 (a combination of cyproterone acetate and ethinylestradiol) which was used as a contraceptive method for three years prior to admission. Hemoglobin was 96 g/L (normocytic normochromic with normal reticulocyte count), ESR 120, ANA 1:640, Anti-ds-DNA negative, anti-histones antibodies positive, anti-Ro and anti-La antibodies positive. Complements were normal and ANCA was negative. A work up for antiphospholipid syndrome was negative. Echocardiogram showed 7 millimeters of pericardial effusion and CT chest showed a minimal pleural effusion and pleural thickening. Viral screen including parvovirus serology was negative. All bacterial cultures were negative and ASOT titer was negative. There was no evidence of any other organ involvement including the kidneys. Diane-35 was discontinued. Methylprednisolone pulse therapy was initiated for three days followed by 30 mg of daily prednisolone.

Case summary:

The patient markedly improved after starting steroid therapy. Chest pain, joint pain, pericardial effusion and pleural effusion improved. Both ESR and Hgb improved. ANA became weakly positive and anti-histones, anti-Ro and anti-La antibodies became negative. Prednisolone was gradually tapered down and successfully discontinued after a total of six months. The patient has been followed up since then and she has been completely disease free and off medications for about four years.

Conclusion:

Contraceptive pills should be considered as one of the drugs that can induce SLE. Symptoms of SLE should be carefully looked for and diagnosed in patients on contraceptive pills. The disease is completely irreversible and treatable in our case.

Key Words: contraceptive pills; lupus; Diane



Medicine

Category: *Clinical*

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A case of active SLE treated with vitamin D

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CASE REPORT

Background:

Our case emphasizes the need to consider the role of vitamin D in the treatment of SLE.

Clinical presentation: Mrs S is a 33-year-old lady who is known to have SLE for eight years, manifested as a butterfly rash, polyarthritis, pleural effusion, tonic-clonic seizures, leucopenia, neutropenia, lymphopenia, positive ANA, positive anti-ds-DNA antibodies and positive anti-Ro and anti-La antibodies. Her disease was controlled on azathioprine and an average daily dose of 7.5 mg prednisolone. Upon reducing the dose of prednisolone one year ago the disease flared with mainly cytopenia, joint pain and fatigue. Because of persistent generalized bony ache 25-hydroxy vitamin D was measured which showed a level below 10 nmol/L (ideal > 125) and parathyroid hormone was 24.1 pmol/L (normal 1.0-7.5). Serum calcium, alkaline phosphatase, liver and renal functions were normal. She was already receiving 600 mg calcium and 200 IU of vitamin D daily. Treatment with vitamin D was initiated which included three intramuscular injections of 600,000 IU each, given one month apart.

Case summary:

After starting treatment with vitamin D the patient improved gradually. Fatigue, joint pain and bony ache disappeared, leucocyte count raised from 1.6 to 4.6 X10⁹/L after completing vitamin D treatment, absolute neutrophil count from 0.8 to 3.2, absolute lymphocyte count from 0.4 to 1.1 and hemoglobin from 107 to 12 g/L. She continued to be seizure free. A repeat MRI brain and EEG remained normal. Prednisolone was tapered down and successfully discontinued. Azathioprine was also discontinued. She remained disease free and off treatment except for calcium and vitamin D for six months.

Conclusion:

Vitamin D deficiency should be screened and treated in all patients with SLE. Our case suggests a crucial role for vitamin D in the pathogenesis and treatment of SLE which should be further studied.

Key Words: SLE; Vitamin D; Treatment



Medicine

Category: *Clinical*

193

Unusual cause of biphasic jaundice in a patient with sickle thalassemia disease

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CASE REPORT

Background:

Sickle beta plus thalassemia (sickle B+ thalassemia) is a “mild” form of sickle cell disease when the red blood cells contain an abnormal hemoglobin called hemoglobin S or sickle hemoglobin, in addition to a small amount of the normal hemoglobin called hemoglobin A. The red blood cells have a defect called beta plus thalassemia, which results in red cells that are somewhat small, pale and misshapen

Case summary:

13-year old male admitted because of right hypochondrial pain, yellow discoloration of the skin and the eyes, no vomiting. He was afebrile, jaundiced with normal pulse and blood pressure. Abdominal examination revealed splenomegaly and tender right hypochondrium. Haemoglobin was 88 g/l hypochromic microcytic, retics 4%, WBC 5100 and platelet 181000 Total bilirubin was 385 umol/l raised to 807 umol/l and direct bilirubin 142 umol/l raised to 409 umol/l, ALT = 199 U/L raised to 242 U/L, AST = 181 U/L raised to 249 U/L Haemoglobin electrophoresis showed a picture of sickle cell-B thalassemia. Sickling test was positive. Coagulation profile was normal. Abdominal ultrasound showed normal liver, minimal intrahepatic biliary radicle dilatation, multiple gall stones, splenomegaly and no ascites. Magnetic resonance cholangio-pancreatography done and showed multiple gall bladder stones with no evidence of biliary obstruction. The patient received one unit of packed RBCs, intravenous fluids and oxygen. Whole blood exchange procedure has been done and the liver function started to improve slightly. Hepatitis A, B and C were negative. Parvo virus IgM was negative. Cytomegalovirus IgM and IgG were both positive. The patient started on gancyclovir for 2 weeks and discharged with the plan of surgical removal of the gall bladder after complete recovery of the liver function.

Conclusion:

The patient presented with abdominal pain and jaundice with cholestatic derangement of liver enzymes although gall bladder stone was present. The cause of cholestasis was assumed to be due to both intrahepatic sickling and recent CMV hepatitis. Cytomegalovirus is one of the rare complication in sickle cell disorder and active treatment of the virus is required before sending the patient to operation.

Key Words: Sickle; Crisis; Cytomegalovirus



Medicine

Category: *Clinical*

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Unexpected cause of meningitis

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CASE REPORT

Background:

Meningitis has several underlying causes as viral, bacterial, mycoplasma, mycobacteria, brucellosis and collagen diseases. Additional etiologies include other infections as fungi, spirochetes, parameningeal infections, medications, and malignancy. Parameningeal sources, such as an epidural or subdural abscess, sinus, or ear infection, can occasionally extend to involve the central nervous system. ENT opinion should be considered in such cases.

Case summary:

31-year old lady admitted because of fever, headache of 3 days duration associated with nausea, vomiting and diplopia on looking to the right side. She got one attack of generalized seizure. No skin rash. Neurological examination showed neck rigidity, right sided nystagmus, normal motor and sensory systems. Fundus examination showed no papilloedema. WBC was 13.4 and the blood culture showed no growth. Cold agglutination and brucella agglutination tests were negative. Collagen profile was negative. CT brain on admission without contrast showed normal cerebral hemispheres but revealed expansion of the frontal sinuses filled with fluid with marked thinning out of the posterior boundary. Lumbar puncture done and showed clear colourless fluid with cells less than 5, high protein 1.79 g/l, normal glucose and LDH. No micro-organism was detected. MRI brain showed frontal sinus abscess complicated with bony outline interruption and intracranial extension in the form of right frontal cerebritis, left epidural empyema. The patient received ceftriaxone and vancomycin and she improved markedly after drainage with no subsequent seizure.

Conclusion:

This is a unique case of epidural empyema secondary to frontal sinus abscess and treatment should be aggressive with drainage and parenteral use of extended spectrum antibiotics. A thorough history and physical examination can lead to appropriate imaging and the correct diagnosis.

Key Words: Meningitis; Frontal; Seizure



Microbiology and Immunology

Category: *Clinical*

195

Abdominal lymphadenopathy and multiple splenic microabscesses in an immunocompetent child with cat scratch disease

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CASE REPORT

Background:

Cat-scratch disease (CSD), caused by *Bartonella henselae*, is a self-limiting disease in immunocompetent children with history of contact with cats. Classic presentation is tender and swollen regional lymph nodes and a papule at the site of initial infection. Diagnosis is usually possible by serology and or histopathology.

Case summary:

An 14-year-old healthy Kuwaiti girl, was admitted with fever, abdominal pain, nausea and generalized weakness. She had arrived from a trip to Egypt five days earlier. On Examination the patient looked ill with a temperature of 40 C and abdominal tenderness. Blood investigations showed a WBC of 14.1×10^9 , ESR 44 mm/h and CRP 150 mg/l. A diagnosis of appendicitis was made and appendicectomy was performed. The patient, however, continued to have fever. Therapy with piperacillin-tazobactam and metronidazole was initiated with no response. A suspicion of enteric fever prompted changing of therapy to ceftriaxone. Blood culture, brucella agglutination, T spot test, Widal test were all negative. Anti-tuberculous treatment was added later when patient failed to improve. CT of the abdomen showed mesenteric and para-aortic lymphadenopathy and multiple splenic lesions. After 10 days of treatment & no signs of defervescence voriconazole was added. Patient remained symptomatic so, antibiotics changed to meropenem and fluconazole. Pet-CT scan showed similar finding to CT and raised the possibility of myeloproliferative/ myelodysplastic disorder. Finally splenectomy and lymph node biopsy was done and a pathology report concluded a multiple splenic granulomas with a picture suggestive of CSD. Serology, however, proved negative. There was dramatic improvement in her condition after splenectomy.

Conclusion:

To the best of our knowledge this is the first case of CSD being reported from Kuwait. We recommend to consider CSD in the differential diagnosis in children presenting with PUO, lymphadenopathy and splenic involvement.

Key Words: Cat-Scratch Disease; Lymphadenopathy and Splenic abscesses; PUO



Microbiology and Immunology

Category: *Clinical*

196

An unusual case of left-sided thoraco-abdominal abscess due to actinomyces spp.

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CASE REPORT

Background:

Actinomycosis is a subacute/chronic bacterial infection which may affect different parts of the body especially mouth, gastrointestinal tract, & vagina where it is a part of normal flora. Isolated involvement of abdominal wall is extremely rare.

Case summary:

A 30-year-old Bedouin male presented with history of blunt trauma to left lower chest two months earlier. He complained of abdominal swelling, pain & fever. On examination patient had a temperature of 37.5 C, chest movement on left side was diminished & a hard tender 10 x 12 cm mass was palpable in the left hypochondrium. Blood investigation revealed haemoglobin of 131 g/L, total WBC count of 12.8 X 10⁹/L, C-reactive protein 113 mg/L & platelet count of 473 x 10⁹/L. Blood biochemical profile was normal. CT abdomen revealed fluid attenuation with peripheral contrast enhancement at the lower anterior chest wall extending to anterior abdominal wall. Ultrasound-guided FNAC of the mass showed features consistent with inflammatory process. Few aggregates of bacterial colonies (filamentous) were noticed. The acid fast stain was negative for AFB. However, aspirated material grew Actinomyces spp. Incision & drainage was performed. Treatment with amoxicillin/clavulanic acid was initiated. Patient had an unremarkable recovery.

Conclusion:

Isolated actinomycosis of the abdominal wall is an extremely rare entity. The exact pathogenesis remains to be elucidated. It is usually mistaken for malignancy. It is, therefore, important for clinicians to be aware of such presentation so that appropriate antimicrobial therapy can be initiated.

Key Words: Abdominal wall; Abscess; Actinomyces spp.



Microbiology and Immunology

Category: Clinical

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A case of bacterial endocarditis: The lessons learnt

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CASE REPORT

Background:

Several issues are related to vancomycin therapy—reduced susceptibility, penetration and dosage-schedule. Albeit a drug of choice for treatment of staphylococcal endocarditis, its nephrotoxic potential warrants monitoring of the serum trough levels for select cases. Presently in Kuwait, the therapeutic trough levels for vancomycin are considered to be 3. 5-6. 9 μ mol/ml (5-10mg/ml). Several studies and guidelines have now raised this bar to 6. 9-10. 35 μ mol/ml (15-20mg/ml) after the advent of new, more purified vancomycin salt. The possible reasons of vancomycin-failure and present recommendations are discussed in this case-report.

Case summary:

A case of bacterial endocarditis with methicillin-susceptible, penton-valentine-leukocidin (PVL) toxin-producing *Staphylococcus aureus* is presented here. A vegetation on mitral valve was missed by transthoracic echocardiography, but was seen with transoesophageal echocardiography. Patient was treated with intravenous vancomycin, as the strain was PVL-producer and no other non-beta-lactam bactericidal agent approved for bacterial endocarditis was available in Kuwait. Vancomycin was administered along with trough level-monitoring with erratic timings. Reference values for vancomycin trough levels used were 3. 5-6. 9 μ mol/ml. Patient expired.

Conclusion:

This case shows the importance of testing methicillin-susceptible *S. aureus* for PVL-production in serious infections. The correct time to draw sample for checking the serum vancomycin-level is just before the scheduled dose. Trough-monitoring should start after administering at least three doses. By that time vancomycin levels get stabilised. Transoesophageal echocardiography is recommended as the diagnostic technique of choice. The therapeutic serum vancomycin trough-levels need to be changed to 6. 9-10. 35 μ mol/ml. To achieve these levels, 25-30 mg/kg body-weight as loading dose followed by 15-20 mg/kg q8-12h dose-schedule is recommended for the seriously ill patients.

Key Words: Bacterial endocarditis; Vancomycin; Staphylococcus aureus



Nuclear Medicine and Radiology

Category: Graduate (Resident)

198

**Femoral fracture non-union in a young female: role of the bone scan
for elucidating the cause**

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CASE REPORT

Background:

In certain clinical presentations, such as trauma, involving the musculoskeletal system, an apparently isolated finding by plain film may not provide an accurate diagnosis of an underlying condition, which is more generalized and more serious. Therefore, detailed evaluation of the skeleton for possible multifocal or diffuse involvement is required especially where atypical presentation, or deviation from the expected pattern of healing is encountered. This role can be aptly fulfilled by the radionuclide bone scan which provides functional evaluation of the whole skeleton. Other nuclear medicine studies could add diagnostic information that would help in the management of the condition as illustrated in this presentation.

Case summary:

A 22-y old female was diagnosed with a fissure fracture in the distal Rt femur. The plain x-ray showed a large lucency in that area. Conventional treatment with a cast was not successful prompting further investigation of the cause. Bone scan showed a superscan appearance with foci of increased uptake leading to the diagnosis of metabolic bone disease caused, as further lab tests showed, by primary hyperparathyroidism. A parathyroid scan confirmed presence of adenoma in Rt lower neck.

Conclusion:

Bone scintigraphy is an important adjunct to investigation of atypical presentation of seemingly isolated abnormalities by the plain film thus enabling the evaluation of the whole skeleton and elucidating the underlying pathology in the case under study.

Key Words: Bone Scan; Fracture; Hyperparathyroidism



Nuclear Medicine and Radiology

Category: Clinical

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Ultrasound guided non surgical closure of post angiographic femoral pseudoaneurysm: A case report

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CASE REPORT

Background:

Iatrogenic femoral arterial injuries are a common occurrence due to the large number of angiographic studies. Colour Doppler is a sensitive technique for the diagnosis of femoral pseudoaneurysms [PSA] and arteriovenous fistulas [AVF]. It can also be used to guide external compression in an attempt to obliterate the PSA and AVF, with good results.

Case summary:

We report a 68-year-old male patient who developed a PSA and AVF of the right femoral vessels as diagnosed by duplex ultrasound. The diagnosis was confirmed by computed tomography angiography (CTA). The patient was receiving multiple medications including anticoagulants which could not be interrupted because of atrial fibrillation. His International Normalized Ratio [INR] was maintained between [2.5-3]. An ultrasound guided compression technique was used successfully to close both the PSA and the AVF.

Conclusion:

Ultrasound guided compression of the post-angiographic femoral arterial injuries is a technically simple and relatively safe method.

Key Words: Femoral pseudoaneurysm; Arteriovenous fistula; Ultrasound guided compression



Nuclear Medicine and Radiology

Category: Clinical

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Duplication of the ascending colon presenting as lower gastrointestinal bleeding. A Case Report.

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CASE REPORT

Background:

Common causes of lower GI bleeding include angiodysplasia, diverticular diseases, neoplasm, and benign anorectal diseases (polyps) that have a focal bleeding site. Diagnosis and location of the bleeding site is necessary to obtain haemostasis of the bleeding site.

Case summary:

We present a young 25 year old patient who presented with acute lower gastrointestinal bleeding. Radiological workup of the patient suggested diagnosis of sub hepatic malpositioned iliocecal angiodysplasia. Patient underwent surgery which revealed large bowel duplication with the angiodysplasia in the duplicated segment.

Conclusion:

To our knowledge no such case has been reported before. We report this case because of its rare nature.

Key Words: Gastrointestinal tract, ; Hemorrhage; Diagnosis.



Nuclear Medicine and Radiology

Category: Clinical

201

Brain and Spinal tuberculomas; A rare form of central nervous system tuberculosis

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CASE REPORT

Background:

Central nervous system tuberculosis is still uncommon compared with the involvement of other systems. Spinal intramedullary tuberculomas are rare and constitute only 0.2 to 0.5% of all central nervous system (CNS) tuberculomas. Among patients with spinal tuberculosis, only 7% presented with intramedullary lesions. The combination of intramedullary and intracranial tuberculomas is extremely rare and only five cases have been reported in the literature since 1988 when Rhoton, et al published the first MRI documented description of the spinal intramedullary tuberculoma.

Case summary:

A 50-year-old male presented to Razi hospital with increasing lower dorsal pain and developed paraparesis. Evaluation including plain x-ray, CT with reformat, MRI with intravenous contrast revealed tuberculous spondylodiscitis associated with disseminated tuberculomas involving brain and spinal cord. The MRI features of spinal intramedullary and intracranial tuberculomas have been described as low-intensity lesions with or without central hyperintensity (because of varying amount of caseous necrosis) on T2-weighted images and as hypo- to isointense lesions on T1-weighted images with homogenous or ring enhancement.

Conclusion:

We report a rare case of tuberculous spondylodiscitis associated with disseminated tuberculomas involving the spinal cord and brain.

Key Words: Tuberculomas; Brain and spinal cord; Magnetic Resonance Imaging



Obstetrics and Gynecology

Category: *Clinical*

202

Dizygotic, dichorionic diamniotic triplet pregnancy with conjoint twins with multiple anomalies associated with a normal singleton: A very rare entity

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CASE REPORT

Background:

Congenital malformations occur more frequently in high order gestation with the percentage of at least one fetus affected by anomalies approaching 30-70%. We present a case of dizygotic dichroionic-diamniotic triplet pregnancy in which the monoamniotic twin pair had concordant anomalies: thoracopagus, omphalocele, cystic hygroma. The other sac contained an apparently normal male fetus. To the best of our knowledge, this is the first report to describe such an entity.

Case summary:

Conjoint twins in a triplet pregnancy was diagnosed in a 27 year old women at 16 weeks of gestation. This pregnancy was spontaneous after 2 years of infertility, after discontinuation of drugs used for induction of ovulation. Two and 3D ultrasonography revealed 2 amniotic sacs and 2 separate placentae, with female twins in one sac and a male fetus in the other sac. The monoamniotic twin pair shared 1 placenta, 1 chest, 1 liver and 1 heart and had concordant anomalies: thoracopagus, omphalocele containing bowel and cystic hygroma denoting accumulation of lymphatic fluid secondary to cardiac overload. A morphologically normal male singleton fetus with normal length and internal organs was noted in the other sac. Follow up scan at 22 weeks gestation will assess fetal cardiac morphology. Further management includes intensive counselling of the couple with close follow-up of the patient. Delivery by cesarean section at 34 weeks, with possible separation of the twins is a viable option. Duplication of the cardiac vessel and absence of malformations incompatible with life are essential parameters for twin separation with one being sacrificed.

Conclusion:

Dizygotic, dichorionic-diamniotic triplet pregnancy is presented with an equally rare combination of thoracopagus with cystic hygroma and omphalocele. Multidisciplinary care with early involvement of the pediatric cardio-thoracic team is essential. The occurrence of such a case has not been reported in literature.

Key Words: Triplet pregnancy; Dichorionic - Diamniotic; Conjoint twins



Oncology

Category: Clinical

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Leiomyoma of the upper respiratory tract: A case report

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CASE REPORT

Background:

Primary pulmonary leiomyomas are extremely uncommon, constituting less than 2% of benign lung tumors. Leiomyomas develop from the smooth muscle of the bronchi or bronchioles and can present as parenchymal, endobronchial, or tracheal lesions, the latter being least common. Reported here is a rare case of tracheal leiomyoma identified and treated in Kuwait.

Case summary:

A 34 year-old Bangladeshi non-smoker male prisoner was brought to hospital with fever, shortness of breath, productive cough, and haemoptysis. He was previously diagnosed with bronchial asthma and was admitted twice over the last 3 months with chest infections. On examination: he was febrile, tachypneic, and tachycardic. Chest examination revealed reduced air entry and inspiratory crackles on the right lung base. Chest X-ray confirmed a right basal pneumonic patch. The patient had neutrophilic leucocytosis (WBC=42. 2), with raised inflammatory markers (ESR=123, CRP=388). Sputum culture/microscopy was negative for acid-fast bacilli and H1N1. Testing for HIV, connective tissue diseases, vasculitides, and immunodeficiency were negative. Computed tomography of the chest demonstrated a round carinal mass measuring 17x14x11 mm arising from the posterior wall of the carina and extending into the right main bronchus. Fiberoptic bronchoscopy detected a pedunculated well demarcated mass at the carina obstructing the right main bronchus. Bronchoscopic biopsy showed spindle-shaped cells arranged in fascicles, compatible with smooth muscle. The diagnosis was established as bronchotracheal leiomyoma. Right thoracotomy and excision of the tumour was performed. Immunohistochemistry showed a positive reaction with smooth muscle actin and desmin.

Conclusion:

Bronchotracheal leiomyoma is a rare entity that can present with recurrent respiratory symptoms. The diagnosis can be established through bronchoscopy and biopsy, and successfully treated through bronchoscopic or surgical excision.

Key Words: Leiomyoma; Bronchotracheal; Tumor



Pathology

Category: Graduate (Resident)

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Dyshormonogenetic goiter with follicular adenoma.

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CASE REPORT

Background:

Dyshormonogenetic goiter (DG) is a rare disease that results from defects in thyroid hormone biosynthesis. Although a goiter may be present at birth, it more often develops at 1-2 years. Most of the enzymatic defects are inherited as autosomal recessive traits. DG is very rarely associated with thyroid tumor. We report a case of follicular adenoma a DG.

Case summary:

A 27 years old Indian male tailor who had been diagnosed with hypothyroidism and had been on levo-thyroxin therapy, presented with a goiter that had enlarged over 2 years. He had a TSH of 71. 75 and T4 of 5. 2 at presentation in July 2010. He received further therapy for the hypothyroidism and had total thyroidectomy in December 2010. Prior to surgery, his thyroid function tests showed a TSH of 2. 62 and T4 of 10. 9. Histopathological examination of the multinodular thyroid showed dyshormonogenetic goiter with a focus of follicular adenoma.

Conclusion:

Because Dyshormonogenetic goiters are rarely associated with neoplasm, it is important to submit them for histopathological examination to exclude co-existent neoplasm.

Key Words: Dyshormonogenetic goiter (DG); Thyroid hormone; Follicular adenoma



Pathology

Category: *Clinical*

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Abdominal pain GIST and the testis

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CASE REPORT

Background:

Testicular tumours most often present as masses in the testes but may uncommonly present with features more representative of sites of their metastases. When this occurs the possibility of a primary testicular tumour maybe overlooked.

Case summary:

A 24 yr old previously healthy man presented with vague abdominal pains that cumulated in a laparotomy. At surgery a retroperitoneal mass thought to arise from the intestines was resected. The tumor was initially diagnosed as a gastrointestinal stromal tumour (GIST). Subsequent review of the histopathological slides showed it to be a germ cell tumour. Clinical attention was then directed to the testes resulting in the resection of the right testis where the primary tumour was found.

Conclusion:

Testicular tumours are common in young men aged 15-40 yrs and may be haboured even in a normal size testis. Complete clinical examination of such patients is advised to prevent delay in the diagnosis of a potentially curable cancer.

Key Words: Abdominal pain; Abdominal mass; Testicular tumour



Pathology

Category: Clinical

206

**Marked myoepithelial proliferation arising in salivary gland inclusion:
A unique case that can resemble metastatic carcinoma**

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CASE REPORT

Background:

Lymph node inclusion is a benign ectopic tissue that is found within a lymph node as result of embryological development. There are different types of inclusions that have been reported to occur within the lymph nodes. Rarely, this heterotopia may undergo reactive changes and can be a pitfall for diagnosis of metastatic carcinoma. In this report we are describing very unusual salivary gland inclusion with proliferative changes that resembled metastatic carcinoma.

Case summary:

A 63-year-old man presented with constitutional symptoms and enlarged lymph nodes in the parotid region. Histopathological examination revealed salivary gland inclusion with marked proliferation of myoepithelial cells resembling metastatic carcinoma. The nature of the cells was confirmed by immunohistochemical stains.

Conclusion:

This is an unique case of reactive changes occurring in salivary gland inclusions. Pathologists should be aware of such changes to avoid inaccurate diagnosis as a metastatic carcinoma.

Key Words: Salivary gland; Inclusion; Lymph node



Pathology

Category: *Clinical*

207

Diagnosis of endometriosis by fine needle aspiration cytology

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CASE REPORT

Background:

Endometriosis is a fairly common disease found in a variety of extrauterine locations. It primarily affects women of reproductive age group and has varying symptoms. Occasionally it produces clinically palpable subcutaneous nodules/cysts or lesions in deep soft tissue which are detected radiologically. Fine needle aspiration diagnosis can be challenging since it needs to be differentiated from primary/metastatic malignancy. We describe one such case which was accurately diagnosed by fine needle aspiration cytology(FNAC).

Case summary:

A 35 year old Pakistani lady presented to surgical out patient with a dull non-cyclic pain in right iliac fossa. It was unrelated to posture or food intake There was a vague fullness in this area on clinical examination , no definite lump was felt. Ultrasound(US) revealed an irregular hypoechoic intramuscular lesion and an US guided FNA was done. Cytological examination showed classical features i. e. groups of epithelial cells admixed with stromal cells and presence of few hemosiderin laden macrophages. A diagnosis of endometriosis was offered which was confirmed by histopathology.

Conclusion:

Endometriosis can show worrisome cytological features & should be kept in mind while dealing with skin&soft tissue nodules specially in abdomen. FNAC is safe and effective tool for identification of endometriosis obviating the need for diagnostic surgical procedure in some patients.

Key Words: Endometriosis; Soft tissue; FNAC



Pathology

Category: *Clinical*

208

Role of molecular genetics in the diagnosis of Liposarcoma- A case report.

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CASE REPORT

Background:

Liposarcomas are one of the common soft tissue tumours in the retroperitoneum. Interpretation of hematoxylin –eosin stained slides by light microscopy remains the bedrock of anatomic pathology. However molecular assays are becoming a vital component in the diagnosis of liposarcomas particularly when difficulty arises on the distinction between benign and malignant lipomatous tumours on routine light microscopy. Liposarcomas are associated with a variety of molecular genetic abnormalities occurring in the q arm of chromosome 12. We present a case of retroperitoneal liposarcoma with an uncommon chromosomal abnormality.

Case summary:

A 42 year old female presented with a retroperitoneal mass. Surgical resection was done and a nodular greywhite mass weighing 430 gm with myxoid cut surface was received. Histopathological examination showed Liposarcoma of mixed type(well differentiated and myxoid) . Molecular genetic analysis were done on the paraffin embedded tissue block.

Interphase cytogenetics was demonstrated by the Fluorescence in situ hybridization (FISH), Vysis DDIT3 Break Apart FISH Probe kit (Previously Vysis LSI CHOP (12q16) Dual color, Break Apart Rearrangement Probe). Molecular genetic analysis showed amplification at the 12q13 region encompassing the CHOP(DDIT3) gene which supported the diagnosis of well differentiated liposarcoma with myxoid differentiation. Considering both the histomorphology and cytogenetic findings, this case was reported as myxoid liposarcoma with uncommon chromosomal abnormality.

Molecular genetic abnormalities associated with Liposarcomas include a t(12;22)(q13;11) or a t(12;22)(q13;12) translocation, which is a hallmark of myxoid liposarcoma, as well as amplification of 12q13-15 region seen in atypical lipomatous tumours/well differentiated liposarcomas but these are not demonstrated in lipomas.

The karyotypic hallmark of myxoid/round cell liposarcoma(MLS/RCLS) is the t(12;16)(q13;p110) present cytogenetically in more than 90% cases. The translocation leads to the fusion of the CHOP(DDIT3) and the FUS genes and the resulting fusion gene encodes a FUS-CHOP chimeric protein. The FUS-CHOP fusion is present in approximately 95% of the cases. The remaining 5% cases harbor a variant translocation t(12;22)(q13;q12) in which CHOP fuses instead with EWS.

Conclusion:

The molecular genetic analysis done on this case brought out chromosomal abnormalities which not only confirmed the histological diagnosis but also led to a more refined diagnosis. This case underlines the importance of molecular testing in the contemporary anatomic pathologist's armamentarium for a more specific diagnosis.

Key Words: Liposarcoma; molecular; genetics



Pathology

Category: *Clinical*

209

Follicular adenomatoid odontogenic tumor in mandibular dentigerous cyst

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CASE REPORT

Background:

Follicular Adenomatoid odontogenic tumor (FAOT) is a recently described variant of adenomatoid odontogenic tumors of slowly growing, asymptomatic and uncommon lesion, mainly noticed in young females. The tumor arising from reduced enamel epithelium of the dental follicle

Case summary:

We describe and discuss a case of follicular adenomatoid odontogenic tumor in a dentigerous cyst, in a 41 year old Indian male who had been presented with mandibular cyst. A panel of immunohistochemistry markers was performed for calretinin, Ki67, P63, factor XIII-a and cytokeratins to rule out malignant potential and ameloblastic defferentiation.

Conclusion:

In conclusion, follicular adenomatoid odontogenic tumor is a neoplasm with low proliferation potential, a variant of AOT should be differentiated from encysted ameloblastoma. It could be presented as a mandibular cyst, at any age and both sexes are affected.

Key Words: Adenomatoid odontogenic tumor; Immunohistochemistry; Neoplasm



Pathology

Category: *Clinical*

210

**Peri-Iliac Unilocular Cystic Gastrointestinal Stromal Tumor (GIST)
Unusual Presentation**

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CASE REPORT

Gastrointestinal stromal tumors (GISTs) arise from the precursor cell of the interstitial cell of Cajal. Mutations in c-kit and PDGFRa appear to be alternative and mutually exclusive oncogenic mechanisms in GISTs. This report presents a case of small bowel cystic GIST in a Kuwaiti female patient 79 years old, presented by cyst. Grossly, It was attached to the antimesentric side of the small intestine segment and measured 10 X7 cm. wall thickness was 0.5 cm and histologically occupied by spindle cell fascicles. A panel of Immunohistochemistry antibodies markers was performed to identify the nature of the cyst. Tumor spindle cells were strongly positive for c-kit and CD34 proteins. Proliferation marker (Ki67) was less than 10%. The cyst nature and prognostic factors will be discussed. GIST that has undergone cystic change must be differentiated from other cystic lesions to guide the treatment approach.

Key Words: Cystic GIST; C-Kit; Ki67



Pathology

Category: *Clinical*

211

Non-ossifying fibroma (metaphyseal fibrous defect) of the mandible

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CASE REPORT

Background:

Metaphyseal fibrous defect(non ossifying fibroma) is a tumor-like condition that typically occur in the metaphysis of growing long bones in children, most commonly above the knee. In this report we describe a case of non ossifying fibroma of the mandible in a 15-year-old boy.

Case summary:

A 15-year-old boy presented with a swelling in the posterior part of left mandible. Conventional radiograph showed a well-defined expansile unilocular radiolucent lesion involving the angle of left mandible. Computed tomography scan showed it to be an expansile soft tissue density mass with heterogeneous enhancement. The lesion was curetted with a wide soft tissue margin and a miniplate was implanted at the excision site. On microscopy, it was composed of cellular proliferation of uniform spindle shaped cells with prominent storiform pattern, characteristic of non-ossifying fibroma. Follow-up radiography revealed good healing of the area . Six months later, radiography revealed fracture at the site of implannation plate. The lesion was re-explored with curettage of soft tissue, which on microscopy demonstrated similar lesion.

Conclusion:

We present this case to highlight the importance of recognizing this unusual lesion in the mandible which can mimic common mandibular lesions such as radicular cyst, ameloblastoma, central giant cell lesion, aneurismal bone cyst etc. Correct identification is important considering its benign clinical course. Conservative surgery is usually curative.

Key Words: Metaphyseal fibrous defect; Non ossifying fibroma; Benign fibrous histiocytoma



Pathology

Category: *Clinical*

212

Medullary carcinoma of the breast with cystic change: Diagnostic Dilemma in Fine Needle Aspiration Cytology.

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CASE REPORT

Background:

Medullary carcinoma of the breast is an uncommon to rare subtype of invasive breast cancer, which has a better prognosis despite its high grade morphology. Medullary carcinoma with cystic change is even a rarer entity, which is likely to pose a diagnostic challenge to the pathologists/cytopathologists.

Case summary:

A 60 year old female patient presented to Mubarak Al Kabeer hospital surgical outpatient with the complaints of left breast mass. Mammography and ultrasonography examination showed a complex cyst measuring about 5x5 cm, with internal septations and small solid component, at 3 'o clock position in the left breast. Fine needle aspiration was performed under ultrasound guidance from the solid component of the cystic mass. Approximately 12 ml. of dark brown hemorrhagic fluid was aspirated. Smears show clusters of malignant ductal cells, some with papillary configuration. These tumor cells show pleomorphic nuclei with prominent nucleoli and irregular nuclear outline. A few large cells with vacuolated cytoplasm are also seen. Numerous foamy histiocytes, reactive lymphoid cells, dendritic cells and plasma cells intermixed with the tumor cells were present. The diagnosis of high grade carcinoma with the possibility of medullary carcinoma with cystic change was given. Core biopsy was performed from the left breast mass. The section showed high grade carcinoma. The differential diagnosis between ductal carcinoma, not otherwise specified and medullary carcinoma was difficult due to the fragmented nature and small size of the biopsy.

Conclusion:

While evaluating a solid mass within a cystic breast lesion, the possibility of an extremely rare entity like medullary carcinoma, cannot be ruled out.

Key Words: Breast medullry carcinoma; Cystic Change; Fine needle aspiration cytology



Pathology

Category: *Clinical*

213

Signet ring cell adenocarcinoma of the rectum with bilateral breast metastasis: A case report and review of literature.

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CASE REPORT

Background:

Breast metastases from non-breast primaries are rare, constituting about 2% of all breast metastases in female patients. Lymphoma, metastatic melanoma and bronchial carcinoma are the malignancies that account for the majority of cases. Breast metastases from colorectal carcinoma have been described in a small number of cases in the literature.

Case summary:

A 30-year old pregnant woman presented to Al Amiri hospital with a circumferential rectal mass in February 2010. Biopsy was reported as signet ring cell carcinoma (the origin of which was not known). The patient was referred to Kuwait Cancer Control Center for pre-operative chemoradiotherapy. After four radiotherapy sessions, MRI was done which revealed multiple bone metastases with locally advanced rectal mass. Carcinoembryonic antigen and Cancer antigen 19-9 were elevated. Then she developed intestinal obstruction which was relieved by a diverting colostomy. In November 2010 patient presented with bilateral retroareolar breast lumps. Ultrasound revealed well-defined mass lesions. Cytology of both breast nodules showed loosely cohesive tumor cells with moderate pleomorphism, vesicular nuclei and intracytoplasmic vacuoles. Signet ring cells were also seen in a mucinous background. On morphology the possibility of a lobular carcinoma or a metastasis from the rectal carcinoma was considered. Tumor cells in both breasts stained positive for ER and PR receptors, CK7, CDX2, CEA and E-cadherin and were focally positive for CK20. Cells stained negative for GCDFP-15. However a final diagnosis of mucinous carcinoma, metastatic from primary colorectal carcinoma was entertained.

Conclusion:

Although colorectal metastasis to breast is rare, it should be included in the differentials for any patient with a known history of colorectal cancer. Accurate differentiation is necessary because treatment differs significantly for patients with breast metastasis as compared with patients with a second primary breast cancer.

Key Words: Colorectal carcinoma; Breast metastasis; FNAC



Pediatrics

Category: *Clinical*

214

Severe refractory coagulopathy as a diagnostic clue to a metabolic disorder

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CASE REPORT

Background:

Tyrosinemia type 1 is an inborn error of tyrosine metabolism that is inherited in an autosomal manner. It is attributed to a deficiency in the enzyme, fumarylacetoacetate hydrolase (FAH), a terminal enzyme in tyrosine catabolic pathway. Consequently, conversion of accumulated intermediate metabolites to succinylacetate and succinylacetone is responsible for the biochemical toxicity and the clinical disease. Affected individuals may present with a spectrum of signs and symptoms involving renal, hepatic and neurologic manifestations along with growth failure and rickets. Death, due to hepatic failure or hepatocellular carcinoma, may occur in untreated patients.

Case summary:

We report a 3-month old male who presented with one day history of high grade fever with no focus. His blood culture grew *Aeromonas hydrophilia*, for which he received cefotaxime for 10 days. Despite being clinically well, the child had severely deranged coagulation profile as manifested by INR of 8 that failed to be corrected despite intervention with fresh frozen plasma, cryoprecipitate and vitamin K. His laboratory investigations revealed persistent metabolic acidosis, mildly elevated liver transaminases, very high alkaline phosphatase (ALP) and hyperammonemia. Metabolic workup panel demonstrated increased excretion of tyrosine metabolites and succinyl acetone in the urine, high plasma methionine, tyrosine and phenylalanine, and high alpha-fetoprotein confirming the diagnosis of tyrosinemia type 1. The child was commenced on NTBC (nitro-trifluoromethyl benzoyl cyclohexanedione) combined with low tyrosine formula that resulted in normalization of his INR and other biochemical abnormalities.

Conclusion:

Severe refractory coagulopathy in an apparently well infant can be considered as a diagnostic clue to tyrosinemia type 1.

Key Words: tyrosinemia type 1; coagulopathy; inborn error of metabolism



Surgery

Category: Clinical

215

**Adult intussusception secondary to small bowel lipoma: A case report
and literature review**

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CASE REPORT

Background:

Intussusception is a relatively common etiology of abdominal pain in pediatric population and is usually idiopathic. In adults, on the other hand, it's rare and challenging condition due to the variety of non specific and chronic symptoms such as abdominal pain, nausea, vomiting, recurrent bowel obstruction and fresh rectal bleeding. In adult intussusception, an underlying pathological lead point is frequently found. Small bowel lipoma is rare benign tumor which may predispose the condition in adults.

Case summary:

A 26 year old male, who has no past medical or surgical history, presented with colicky abdominal pain, nausea, vomiting and intestinal obstruction of four days duration. He reported similar attacks in the past with few episodes of passing fresh blood per rectum. Clinically he was dehydrated, tachycardic, abdomen was distended and tender all over. Abdominal XR showed dilated small bowel loops with multiple air-fluid levels. CT Scan showed complete intestinal obstruction with ileoileal intussusception with intraluminal mass. Laparotomy revealed ileo-ileal invagination with an intraluminal mass of 7X3 cm, about 100 cm from ileocecal valve. Segmental resection and end-to-end anastomosis were performed. Pathological study revealed small bowel lipoma composed of lobules of mature fat cells. The patient made a satisfactory recovery.

Conclusion:

This case highlights an unusual cause of small bowel obstruction and the role of CT Scan in diagnosis of such rare condition. Adult Intussusception must be suspected in young previously healthy patient, with complex symptoms of recurrent bouts of abdominal pain, passing fresh blood per rectum and intestinal obstruction. Surgical resection remains the treatment of choice and produces an excellent prognosis.

Key Words: Adult Intussusception; Ileoileal; Lipoma



Surgery

Category: Clinical

216

**Scoliosis as a rare risk factor for colon perforation during colonoscopy:
The second reported case and literature review**

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CASE REPORT

Background:

Colonoscopy has been accepted as the best method for the screening, diagnosis, treatment and follow-up of colorectal pathologies. It's an invasive procedure with many recognized complications such as iatrogenic colonic perforation (CP). Knowledge of the factors influencing (CP) is of decisive importance, especially with regard to the avoidance or minimization of the perforations. This is the second case in the literature with such unreported and rare risk factor for iatrogenic colonoscopic perforation.

Case summary:

We reported a 66 year old female, not known to have any medical problems who underwent colonoscopy screening. No abnormalities were detected up to the rectosigmoid junction when the gastroenterologist noted sudden and massive abdominal distension and the patient started complaining of severe generalized abdominal pain, was hemodynamically stable. The procedure was abandoned. Abdominal X-Ray showed severe scoliotic deformity of the lumbar spine with massive pneumoperitoneum. Diagnostic laparoscopy showed a small perforation at the anterior wall of sigmoid colon which was repaired. No fecal soiling of the peritoneal cavity was found as she was prepared for colonoscopy. Her course was unremarkable, and she was discharged 7 days later. A 2-weeks follow-up revealed that she is asymptomatic with healed laparoscopic surgery scars and normal bowel motion.

Conclusion:

Patients with skeletal deformity such as scoliosis undergoing colonoscopy have a higher risk of iatrogenic colonoscopic perforation. Symptoms of abdominal pain and distension during colonoscopy in this group of patients should alert the treating doctor for the possibility of colon injury which should be managed accordingly.

Key Words: Colon Perforation; Iatrogenic Perforation; Colonoscopic Perforation



Surgery

Category: Clinical

217

Trans-abdominal pre-peritoneal laparoscopic repair of a primary acquired lumbar hernia: A case report

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CASE REPORT

Background:

Lumbar hernias are rare postero-lateral abdominal wall hernias; traditionally their repair by open surgical techniques was marred by technical difficulties and high recurrence rate. The laparoscopic repair offers several advantages over traditional open techniques; it allows exact localization of the hernial defect and the placement of a prosthetic mesh in a tension free manner between the defect and the pressure compartment.

Case summary:

We reported a 52 years old diabetic laborer presented with 5 months history of a growing left loin painful lump. Physical examination revealed a 7x5 cm hemispherical tender mass in the left costovertebral angle. The diagnosis of a lumbar hernia was suspected and was subsequently confirmed by CT scan abdomen. The patient underwent trans-abdominal pre-peritoneal repair of the hernia. He had a smooth post operative course and discharged on the 2nd post operative day. He was back to work within 10 days of discharge. Post operative follow up 3 months later showed a solid repair.

Conclusion:

Lumbar hernias are rare and high index of suspicion and use of appropriate imaging studies is essential to make the diagnosis. Laparoscopic management of lumbar hernia is associated with several advantages and is recommended for most lumbar hernias.

Key Words: Lumbar Hernia; Laparoscopic



Surgery

Category: Clinical

218

Marjolin's ulcer, incidence & management, our experience in Kuwait

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CASE REPORT

Background:

Marjolin's ulcer has been defined as malignant transformation of any chronic wound, including postburn, osteomyelitic, venous, or pressure sore ulcer. Malignancy is most commonly Squamous skin cancer (SCC), followed by basal skin cancer (BCC). The pathogenesis of malignant transformation remains controversial. Diagnosis of malignant transformation is challenging because of tissue necrosis and misdiagnosis with chronic inflammatory reaction (pseudoeplitheliomatosis).

Case summary:

Prospective clinical study for 45 cases with chronic (more than 6 months) post-burn and osteomyelitis ulcers. Clinical suspicion of malignancy was confirmed by histopathologic analysis. 10 cases were diagnosed with SCC. Evolution time from scar to malignancy onset ranged from 10 to 50 years. Management was followed according to the American academy of cancer control protocol. Excision of the tumor with safety margin 2-3 cm was done for 6 cases, with no recurrence rate after 1 year follow up. Below knee amputation was done for 4 cases with deeply infiltrated ulcer and with underlying bone destruction. Here, 2 cases showed malignancy recurrence and died within 6 months of surgery. Regional lymphadenectomy and postoperative radiotherapy were done to some cases.

Conclusion:

It is important to thoroughly investigate long lasting chronic ulcer (especially post burn scar exceeding 10 years) if becomes painful, infiltrated, or secreting. Multiple biopsies are paramount to avoid misdiagnosis. Excision of ulcer with no more than 2.5 cm safety margin was enough. It is preferred not to surgically intervene in advanced cases with bone infiltration, as generalized metastasis shall be aggressive and uncontrollable.

Key Words: Chronic ulcer; Squamous cell; Histopathology



Surgery

Category: Clinical

219

Pancreaticoduodenectomy for pancreas head cancer in a patient with advanced multiple sclerosis.

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CASE REPORT

Background:

There are no reports in the literature, up to our knowledge, on the outcome of major abdominal surgery in patients with multiple sclerosis (MS). In this case report, we present the outcome of pancreaticoduodenectomy surgery (Whipple's operation) for pancreatic head cancer in a patient with advanced progressive MS.

Case summary:

A 48-year-old Kuwaiti female diagnosed with progressive MS in 1996. Her neurological manifestations included quadriplegia and unilateral facial palsy. She has been bedridden since 1999. The patient has intact cognitive abilities and swallowing function. She does not have history of chest infection in the past. T2 brain MRI showed wide spread variable MS plaques.

She presented with painless jaundice that led to further workup, which detected resectable peri-ampullary adenocarcinoma with no evidence of distal metastasis. The case was discussed in our weekly multidisciplinary meeting and the main worry was post-operative ventilator dependency. Patient underwent uneventful Whipple's operation and was successfully extubated shortly after transfer to ICU. The histopathology of the specimen showed the adenocarcinoma to be arising from the head of the pancreas (stage pT3, N1, Mx).

Her post-operative course was complicated by a pancreatic leak on day 7 that was managed conservatively by existing intra-abdominal drain and additional placement of transhepatic biliary drain to divert the bile away from the leak site at pancreaticojejunostomy anastomosis. Patient did well afterwards and was discharged from hospital on post-operative day 60. Adjuvant therapy for the tumor included a single agent Gemcitabine chemotherapy. Ten month follow-up patient is still alive and back to her baseline neurological status.

Conclusion:

Major abdominal surgery is feasible in patients with MS. Multidisciplinary team approach is recommended in the management of such difficult cases.

Key Words: Multiple sclerosis; Pancreas cancer; Pancreaticoduodenectomy



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