



20TH HSC POSTER CONFERENCE 2015

Under the patronage of the president of Kuwait University



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20th HSC Poster Conference 2015
Organizing Committee

- Prof. Rajaa Al-Attayah, *Vice Dean Research & Postgraduate Studies, FOM*
- Prof. Yunus Luqmani, *Chairman & Coordinator; Scientific, Dept. of Pharmaceutical Chemistry, FOP*
- Prof. Khalid Khan, *Dept. of Anatomy, FOM*
- Dr. Yaqoub Al-Basarah, *Dept. of Pharmaceutics, FOP*
- Dr. Anwar Banaw, *Dept. of Medical Laboratory Sciences, FAHS*
- Dr. Rashed Al Azemi, *Dept. of Development & Preventive Sciences, FOD*
- Dr. Sahar Essa, *Dept. of Microbiology, FOM*
- Dr. James Craik, *Dept. of Biochemistry, FOM*
- Dr. Reem Al-Sabah, *Dept. of Community Medicine, FOM*
- Dr. Waleed Al Jassar, *Dept. of Obstetrics & Gynecology, FOM*
- Dr. Fatma Al-Saeedi, *Dept. of Nuclear Medicine, FOM*
- Dr. Ebaa Al Ozairi, *Dept. of Medicine, FOM*
- Dr. Jasem Al Hishel, *Dept. of Medicine, FOM*
- Dr. Entessar Hussein, *Dept. of Pediatrics, FOM*
- Dr. Munya Al-Fulaij, *Dept. of Pharmacology, FOM*
- Dr. Ahmed Al-Serri, *Dept. of Pathology, FOM*
- Dr. Slava Malatiali, *Dept. of Physiology, FOM*
- Mr. Jassim Al-Khorafi, *Administration Manager, FOM*
- Mr. Dheya H A Al-Hasan, *Finance Manager, FOM*
- Mrs. Amna Safar, *Technical Service Administration, HSC*

Special Acknowledgements

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



Photograph of Organizing Committee



Prof. Rajaa Al-Attiyah, Vice Dean for Research & Postgraduate Studies, FOM



*Prof. Yunus Luqmani
Chairman & Coordinator*



*Prof. Khalid Khan
Dept. of Anatomy, FOM*



*Dr. Yaqoub Al-Basarah
Dept. of Pharmaceutics, FOP*



*Dr. Anwar Banaw
Dept. of Medical Laboratory Sciences,
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*Dr. Munya Al-Fulaij
Dept. of Pharmacology, FOM*



*Mr. Jassim Al-Khorafi
Administrative Manager, FOM*



*Mr. Dheya HA Al-Hasan
Dept. of Finance, FOM*



Message from the Dean, Faculty of Medicine



It gives me great pleasure to write the introductory remarks of the Abstract book for the 20th Poster Conference 2015.

The Poster Conference throughout the years has continued to achieve the goals of fostering high quality medical research, stimulation of scientific endeavor and collaboration and interaction of faculty and students. This meeting is important as it provides a forum for all researchers to present and discuss basic and clinical research conducted in Kuwait.

We are extremely fortunate for this year to have one of the pioneers in the field of cancer cells, we would like to welcome Prof. Ramzi Mohammad, Director of Gastrointestinal Cancer Research, Karmanos Cancer Institute and Department of Immunology and Microbiology, Barbara Ann Karmanos Cancer Institute, Wayne State University, Detroit, Michigan, who will give the keynote speech on “The Future Healthcare: Personalized Medicine for Cancer Patients”.

The total number of research abstracts accepted this year is 265, which reflects the good progress in research in the Health Sciences in Kuwait. I am grateful to the Vice Dean Research and Postgraduate Studies Prof. Rajaa Al-Attiyah for her continuing support for the Poster Conference. I also thank the Chairman of the 20th Poster Conference Organizing Committee, Prof. Yunus Luqmani, and the Organizing Committee from HSC Faculties. They have all worked so hard to ensure the good quality of selecting abstracts and to make this conference successful.

Professor Adel K. Ayed
Dean, Faculty of Medicine



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



The first Poster Conference was introduced in April 1996 in the Faculty of Medicine. We have since then held this conference annually with great success with staff and students of all the faculties of Health Sciences Centre participating and presenting their research. Strong research is a prerequisite for academic excellence, and this concept was clearly understood when the First Poster Day was held 19 years ago, in April 1996, in the Faculty of Medicine. The founders of Poster Day started this event with a premise that scientific progress depends on investigation, critical analysis and exchange of ideas. The Poster Day started with an aim of stimulating 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).

In continuing the tradition of inviting internationally recognized Scientists whose work has great impact upon the Health Sciences, this year we would like to welcome Prof. Ramzi Mohammad, Director of Gastrointestinal Cancer Research, Karmanos Cancer Institute and Department of Immunology and Microbiology, Barbara Ann Karmanos Cancer Institute, Wayne State University, Detroit, Michigan, who will give the keynote speech on “The Future Healthcare: Personalized Medicine for Cancer Patients”. This year we have 265 poster abstracts and I have no doubt that the 20th HSC Poster Conference will be a great



success. I thank Kuwait University for the continuing support and sponsorship of the Poster Conference and Prof. Ramzi Mohammad for accepting our invitation as a keynote speaker in this year Poster Conference. I would like to express my appreciation to the Vice-President Health Sciences Centre, Deans of different Faculties of HSC for their encouragement and support and to all HSC technical and support staff who assisted in the organization and implementation of this meeting. I am especially very grateful to the Chairman and the members of the Organizing Committee for their commitment and efforts to make this a very successful event.

Prof. Raja'a Al-Attiyah

Vice-Dean for Research & Postgraduate Studies

Faculty of Medicine



**Message from the Chairman,
20th HSC Poster Conference Organizing Committee**



The HSC Poster Day was initiated in 1996, and so this year we celebrate the 20 year milestone. Enthusiasm for this event has remained undiminished over these two decades. In addition to the continuing support from the researchers of the HSC and Science Faculties of the University we receive contributions from clinicians working in the many hospital departments around Kuwait, and even from some outside of the country. The consistency in the number of submissions attest to the success of this endeavour, with discernible improvements in quality of presentations as a result of ever more rigorous standards being applied.

It should be appreciated that a university is a place not only of learning but where knowledge is created and disseminated. Basic science and clinical research by academics and clinicians is our most important and vital activity. The international reputation of a university is based principally on its research output. For the future development of the country, it is our responsibility to teach the next generation how to search for knowledge and appreciate the value of such a pursuit. And indeed, with the support of the College of Graduate Studies and the Research Sector of the university, our efforts in this respect are bearing fruition. This year 34% of the Posters are from undergraduate, postgraduate MSc and PhD students and clinical graduate residents. This is a reflection of both increased student interest in research, improved facilities and opportunities and greater encouragement from the academic staff. We certainly hope this trend will continue into future years and provide impetus for more innovative work.

One of the major aims of this event is to provide researchers with the opportunity of advertising their work in order to inform other interested individuals who might otherwise be unaware of their work, even within the same institution or department ! The increasing reliance of medical science upon innovative electronic technology means that we require



greater expertise in unfamiliar areas. It has become increasingly difficult to work in isolation, and collaboration has become essential to make any real impact in the international arena. We hope that you will avail of this opportunity to foster more mutually beneficial relationships with your colleagues.

As is our custom, the Poster Conference is inaugurated with a keynote address given by a distinguished researcher. Each year we have a different theme. On this occasion, the topic is on cancer. We are privileged to have Prof Ramzi Mohammed from the Karmanos Cancer Institute at the University of Michigan. He will deliver his lecture on the design, development and pre-clinical testing of novel small molecule drugs, and how these may be used to promote more personalized therapy for treatment of cancer based on genetic profiles.

Finally, I thank my colleagues in the Organising Committee for giving their time. Our task has been greatly facilitated by the Centre for Research Support and Conferences under the Vice Dean Research FOM. My thanks to them for their efficient administrative assistance, to the judges for their unenviable but hopefully rewarding task of selecting outstanding posters for awards, and to all participants for sharing their work.

Professor Yunus Luqmani
Chairman, 20th HSC Poster Conference Organizing Committee



Keynote Speaker

Prof. Ramzi M. Mohammad, Ph.D.

Director, GI-Cancer Research, Karmanos Cancer Institute,
Michigan, Department of Immunology and Microbiology,
Barbara Ann Karmanos Cancer Institute, Wayne State
University, MI



Prof. Ramzi Mohammad is an accomplished researcher who possesses about 30 years of cancer research experience. The primary focus of Prof. Mohammad's research is the design, development and pre-clinical testing of novel small molecule drugs for the treatment of cancer in a personalized manner. Being the Director of GI-cancer research at Karmanos Cancer Institute, Michigan, USA, he foresees the testing of new drugs in pancreatic and colon tumor models. In the past a number of agents have come from his lab to the clinic namely Dolastatin, Aurastatin, Bcl-2 inhibitor AT-101, MDM2 inhibitor and very recently the nuclear export protein CRM1 inhibitors KPTs and the DNA –Bcl2 inhibitor. He has active NIH funding on Bcl-2 inhibitor (AT-101); Mcl-1 inhibitor (UMI-77); KPTs and p53-MDM2-inhibitors. KPT and p53-MDM2i drugs happen to be among the fastest agents to come to the clinic and are being tested in multiple tumor types including colon cancer and very soon in pancreatic patients. He specializes in animal tumor model studies and has collaborated extensively with many basic, translational and pharmaceutical researchers to test novel agents in his advanced animal systems. His team is currently pursuing an approach to stratify cancer patient population to identify their responsiveness to certain personalized small molecule treatments with the goal to provide better treatment outcomes.



Keynote Abstract

The Future Healthcare: Personalized Medicine for Cancer Patients

What does personalized medicine mean to patients with cancer?
Should your doctor not know all about the genetics of your cancer?

We all need our physicians to truly understand our disease and go deeper into genetics than ever before. It is becoming a crucial issue for better understanding of diseases in general and more specifically for cancer where effective therapies are urgently needed. With a boom in high throughput technologies there are real opportunities for personalized healthcare and the power of genomics in this regard has become evident.

Science tells us that informations for good and bad health lie in our genes. We now understand that genes have a lot to say about the cancer from which we suffer. Cancer is a result of repeated hits to our genes. Tumors form when the switches inside our genes that control cell growth malfunction. Growth genes also known as Oncogenes are precisely regulated through an on and off switch. However, in cancer, there is a loss of this regulation resulting in some growth genes failing to switch off leading to uncontrolled cell division. We may be born with oncogenes, such as the BRCA breast cancer gene or the p53 gene. We may also be exposed to toxins in our environment that can damage our normal genes. Sometimes our genes simply wear out, as we age. Knowing precisely what oncogenes drive cancer in an individual, a successful genetic based therapy or precision medicine can be designed.

The concept of personalized medicine involves a treatment built on our gene-profile. These emerging concepts are anticipated to completely change how traditional treatments are given. Today, our doctors have only a limited capability to adjust therapy for cancer patients. In the near future, this approach will change dramatically. If an individual gets cancer, the tumor itself will be profiled to get quick answers to questions such as what oncogenes are turned on? What tumor suppressor genes are turned off? What caused this to happen? And most importantly, what meaningful strategies can be quickly designed to turn off those cancer genes and control the disease?

Last year, thousands articles were published on cancer care. The most exciting of these were related to personalized medicine.



In the recent past, many breakthroughs in personalized medicine have occurred. For example, using advanced profiling techniques researchers were able to pinpoint that Chronic Myelogenous leukemia (CML) is caused by a specific genetic translocation called BCR-ABL, also known as the Philadelphia Chromosome. A powerful drug has been manufactured (imatinib) which specifically target this gene. The drug can be taken orally and can actually cure patients with CML. Recently; Dr. Mohammad's team has taken similar approach to target the well-recognized promoters of cancer hallmarks and have introduced new drugs for a personalized treatment of pancreatic, colon and blood cancers based on the reactivation of p53 protein.



Best Poster Award Winners: 19th HSC Poster Conference 2014

PhD, MSc, Undergraduate, Graduate Resident Original Research and Case Report

➤ **Public knowledge and attitudes regarding organ donation in Kuwait**

Bosakhar B, Arab D, Al-Ali N, Al-Tawheid N, Al-Farhan S, Al-Mesailekh Z, Mitra AK

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

➤ **Low-dose exposure to lead during pregnancy effects spatial learning and neurogenesis in hippocampus in young rats**

*Al-Shimali HM¹, Al-Musaileem AF¹, Rao MS², Khan KM²

¹3rd Year Medical Student, Faculty of Medicine Kuwait University;

²Department of Anatomy Faculty of Medicine, Kuwait University, Kuwait

➤ **Anti-proliferative activity of 5-triazolylmethyl-and 5-acetamido-oxazolidinone derivatives**

*Hedaya OM, Mathew PM, Hassan F, Phillips OA, Luqmani YA

Department of Pharmaceutical Chemistry, Kuwait University Faculty of Pharmacy

➤ **Distribution of virulence genes in *Helicobacter pylori* cultured from native arab Kuwaiti patients with dyspepsia**

*Al-Abkal H^{1,2}, Siddique I³, Al-Ali J³, Junaid TA⁴, Albert MJ¹

¹Department of Microbiology, FOM, Kuwait University, Kuwait, ²Arabian Gulf University, Bahrain²; Departments of Medicine³; Pathology⁴, Faculty of Medicine, Kuwait University

➤ **Characterization of methicillin-resistant *Staphylococcus aureus* in Kuwait hospitals: 1992-2010**

*Boswihi SS, Udo EE, Al-Sweih N

Department of Microbiology, Kuwait University, Faculty of Medicine

➤ **Characterization of gallbladder stone, bile and tissue using time resolved fluorescence spectroscopy**

*Shuaib A¹, Kokaj J², Pichler G², Nair R², Joseph M²

¹Biomedical Engineering Unit, Physiology Department, Faculty of Medicine, Kuwait University; ² Physics Department, Faculty of Science, Kuwait



University

➤ **Efficacy of Botulinum toxin-A treatment in chronic migraine – first Middle East experience**

Al-Hashel JY^{1,2}, Nagarajan V¹, Ahmed SF^{1,3}

¹Department of Neurology, Ibn Sina Hospital, Kuwait; ²Department of Medicine, Kuwait University, Faculty of Medicine; ³Department of Neurology and Psychiatry, Minia University, Faculty of Medicine, Egypt.

➤ **Study of patatin-like phospholipase-3/adiponutrin I148M polymorphism and biochemical markers in nonalcoholic fatty liver disease**

*AlAnjeri AK¹, Al Serri AE², Gupta R³, El Baaly HA⁴, Kinatamith P⁵, Shaarawi O⁶, Mojiminiyi OA⁵

¹Clinical Biochemistry Laboratory, Mubarak Hospital; ²Unit of Human Genetics-Department of Pathology, Kuwait University, Faculty of Medicine; ³Department of Radiology, Kuwait University, Faculty of Medicine; ⁴Radiology Department, Mubarak Hospital; ⁵Department of Pathology, Kuwait University, Faculty of Medicine; ⁶Apheresis Unit, Kuwait Central Blood Bank



Past Poster day Keynote Speakers and Lectures

2014

Image-guided surgery – from bench to bedside; Professor Samuel Achilefu; Professor of Radiology, Mallinckrodt Institute of Radiology, Washington University School of Medicine

2013

Stem Cells: Building and Rebuilding the Nervous System; Professor Freda Miller; Senior Scientist, Research Institute, Developmental & Stem Cell Biology, University of Toronto

2012

Cardiovascular health in the 21st century; Professor Barry McGrath, Professor of Vascular Medicine & Medicine, Southern Clinical School, Monash University, Australia

2011

Cardiovascular Outcome Trials in Diabetes.; Prof. Rury Holman, Director of the University of Oxford Diabetes Trials Unit, University of Oxford, Canada

2010

New mycobacterial vaccine candidates: from lab to clinical trials. Prof. Abu Salim Mustafa, PhD, FRC Path. Department of Microbiology, Faculty of Medicine, Kuwait University

2009

Evidence-Based Medicine and Knowledge Translation Research for Better Health Care.; Prof. Brian Haynes, Professor of Clinical Epidemiology and Medicine, Chief of the Health Information Research Unit at McMaster University, Hamilton Ontario, Canada

2008

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



2007

From Molecular Imaging to Molecular Medicine.

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

2006

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

2005

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

2004

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

2003

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

2002

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

2001

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

2000

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



1999

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

1998

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

1997

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



Original Research Abstracts List By Subject Area



Allied Health

1

*Abdulrahman M, Deering J, Durkin L, Fierini D, MacGarvie D, Martino R, Nickerson V: Advancing multidisciplinary care and collaboration through the establishment of a dysphagia service at the Kuwait Cancer Control Center

2

*Al-Barjes TA, Sidky A, Al-Fadhli S: Screening and characterization of the disease-causing mutation for autosomal dominant congenital bilateral cataract in a multigenerational Kuwaiti family

3

*Al-Eisa A, Al-Rushood M, Al-Attiyah R: Pro-inflammatory cytokines IL1 beta, IL6 and IL8 release during relapse in children with nephrotic syndrome

4

*Al-Desoky MM, Al-Al-Johar WY, Al-Mufty SA, Aiesh A: Determination of ethanol in soya sauce in Kuwait market

5

*Al-Sayegh N, Al-Obaidi S, Al-Shuwai N, Ramadan S, Al-Qurba T: Benchmarking health of the health sciences community of Kuwait University: Health inventory and database development, a preliminary analysis

6

*AlMayouf S, AlShemmari SH: Kuwait's single transplant center laboratory experience of hematopoietic stem cell collection, processing and transplantation for haematological malignancies

7

*Fathelrahman Mahdi Hassan: Red cell alloimmunization among multi-blood transfusion cancer patients

8

*Prasad L, Ramachandran U, Al Kandari S, Ivanova M: Spinal injury rehabilitation in Kuwait -A ten year epidemiological analysis

9

*Yaseen H, Al-Madhoun A: Identifying potency markers in human umbilical cord wharton's jelly derived mesenchymal stem cells following Tri-lineage differentiation



Anatomy

10

*AbdelQader AA, Al-Bader M, Kilarkaje N: Resveratrol recovers hyperglycemia-induced oxidative stress and DNA damage in rat testis

11

*Alhussaini H, Jeffery G: Peripheral RPE cells have the capacity to proliferate and migrate to replenish central retina

12

*AlQattan H, Jamal D, Aljuwaihel H, Smitha S Rao MS: Thymoquinone enhances neurogenesis in lead exposed rats

13

*Alrumh M, Renno W, Pavlik A: Hsp70 involvement in hyperthermic preconditioning of excitotoxic neuronal damage in the hippocampus

14

Alsabah M, Renno W, Alsabah S, Alserri A, Alsabah SK: Laparoscopic Sleeve Gastrectomy (LSG) & Neuropathy

15

*Al-Sayegh R, Smitha S, Rao MS: Suppression of seizure frequency and mossy fiber sprouting and neurodegeneration in temporal lobe epilepsy in young rats by thymoquinone

16

*Brito SA, Smitha S, Rao MS: Mossy fiber sprouting and spontaneous recurrent motor seizures in chronic temporal lobe epilepsy in middle aged rats -effects of thymoquinone

17

*Eliwa J, Al-Ali H, Smitha S, Rao MS: Thymoquinone protects the spinal cord neurons from degeneration by enhancing GAP-43, Bcl-2 and decreasing Bax expression in sciatic nerve lesion model

18

*Faid I, Al-Hussaini H, Kilarkaje N: Resveratrol inhibits diabetes-induced testicular cell death by maneuvering oxidative stress and JNK signaling in rats

19

Mathai R, *Fahmy D, Lingegowda, *Sadek HL: Congenital coronary artery anomalies in adults; evaluation by dual source ECG gated CTA

20

*Rao MS, Smitha S, Joy J: Gliosis enhances the survival neurons in culture



21

*Upton H, Al-Bahouh NA, Smitha S, Rao MS: Thymoquinone improves cognitive functions and neurogenesis in intracerebro -ventricular model of Alzheimer's disease

Biochemistry

22

*Alenezi K, Benov L: Improving the efficiency of Zn-porphyrin-based photosensitizers for antimicrobial therapy

23

*Aleneze Yousef: Synthetic DNA construct design of HIV-1 induced VIF-resistant APOBEC3 expression towards degrading HIV-1 quasispecies into defective human endogenous retroviruses (HERV)

24

*Alkazemi NJ, O'Neill T, Formstone C, Freson K, Tissir F, Maguire PM: Wnt/planar cell polarity in platelets

25

*Al-Nasiri DA: Audit of thyroid function testing in Mubarak Al Kabeer hospital.

26

*Alrefae S: PSA as a marker of prostate problem

27

*Bader B, Benov L, Craik J: Mn(III)N-alkylpyridylporphyrins increase Vitamin C anticancer activity through generation of reactive oxygen species

28

*Iskandarani IN, Cheng B: Acth regulates adrenal mineralocorticoid receptor protein level: Evidence and implication

29

*Novotna B, Abdel-Hamid M, Koblizek V, Jarkovsky J, Hejduk K, Rehacek V, Bis J, Salajka F: Carnitines and amino acids in COPD patients: A metabolomic LC-MS/MS study

30

*Thomas M, Benov L, Batinic-Haberle I, Tovmasyan A: Do SOD mimetics protect against hydrogen peroxide?



Community Medicine

31

*Al-Essa D, Al-Hatem M, Al-Mutairi Y, Al-Shalal A, Al-Suwari I, Shamsaldeen H, Moussa MA: Patients' attitude toward medical student in Kuwait teaching hospitals

32

*Al-Hashash K, Al-Qattan H, Al-Ajmi M, Al-Omairah H, Al-Mutairi F, Al-Mutairat M, Ziyab AH: Prevalence of obstructive sleep apnea risk and associated factors among working population in Kuwait: A cross-sectional study

33

*Al-Kandari S, Alsalem A, Abohaimed S, Al-Orf F, Al-Zuabi M, Shah N: Sociodemographic profile and coping strategies of mothers with children suffering from ASDs in Kuwait.

34

*AlRasheedi S, AlKamali A, AlBader F, AlKandari D, AlOthman R, AlQuraishi H, AlBatineh A, AlMajran A: Perception of body image among adult residents of Kuwait

35

*AlRoumi M, AlMarri F, AlHashash H, Kartam M, Dannan R, AlSallal S, Shah N: Mistimed and unwanted pregnancies among postpartum women in Kuwait

36

*Farouk N, Farahat M, EL-Derea H, Abd EL-Moneim AL-Ahwal: Majorana as an organic food preservative for milk products and cereals

37

*Farouk N, Gheith O, Farahat M, EL-DereaH, Abd EL-Moneim AL-Ahwal: Chicken and meat products preservation by organum majorana

38

Lakha F, Pennefather P, *Badr H: Management of chronic non cancer pain in global cities: Current services and process.

39

*Rakhshani-Moghadam S, Alrefai S, Mohammad D, Al-Kilani F, Abdulaal N, Alsanad L, Moussa MAA: Knowledge levels, risk perceptions, and prevention methods regarding Ebola virus disease among primary health care physicians in Kuwait



Dentistry

40

*Al-Ali F, Nazar H, Al-Mutawa S, Ariga J, Soparkar P: Caries status among kindergarten children in Kuwait.

41

*Al-Ajmi S, Shaban A, Al-Azemi R: A comparison of treatment experience between invisalign aligner and fixed appliance therapy

42

Al-Anzi A, Soderling E, *Varghese A, Honkala E: Xylitol content of chewing gums in middle-east markets: A comprehensive study

43

*Al-Menezaa E, Nazar H, Al-Mutawa S, Ariga J, Soparkar P: Oral health knowledge and behavior among 12-year old female students.

44

*AlMujaweb T, Shyama M, Al-Mutawa SA, Al-Sumait A: Dental Fear among Dentists in Kuwait

45

*Al-Mutawa SA, Shyama M, Honkala E, Honkala S: Infant Feeding Practices among Disabled and Normal Children in Kuwait

46

*Al-Mutawa S, Ariga J, Nazar H, Al-Duwairy Y, Soparkar P: Evaluation of preventive services of school oral health program, Kuwait

47

*Al-Shamali W: Effect of turmeric on oral lichen planus erosive-erythematous form: A case series study.

48

*Jarrad A, Nazar H, Al-Mutawa S, Ariga J, Al-Duwairy Y, Soparkar P: Evaluation of stainless steel crowns on permanent teeth in the school oral health program, Kuwait.

49

Karched M, *Bhardwaj RG, Asikainen S: Coaggregation and biofilm growth of granulatella spp. with fusobacterium nucleatum and aggregatibacter actinomycetemcomitans



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*Karched M, Bhardwaj RG, Inbamani A, Asikainen S: Quantification of biofilm and planktonic life forms of coexisting periodontal species

51

*Lucas PW, Swapna MP, Al-Qeoud DN, Al-Drahim NA, Moule AJ: Nanoscale characterization of dental materials

52

*Nazar H, Al-Mutawa S, Ariga J, Al-Hawaj SH, Al-Duwairy Y, Soparkar P: Oral Health Status Among Adults in the State of Kuwait

53

*Philip SM, Darvell BW: Effect of heat treatment on the tensile strength of 'Elgiloy'

54

*Qasem JA, Al-Omer H, Qasem AA, Thomas JT: Helicobacter pylori prevalence in dental plaques of diabetic and gastritis patients, as a possible source of re-infection

55

*Shyama M, Al-Mutawa SA, Honkala E, Honkala S: Oral health habits among disabled schoolchildren in Kuwait

56

*Zeyad Al-Weher: Fluoride in bottled water found in Kuwait

Genetics

57

*Ali H, Hussain N, Naim M, Zayed M, Seaburg L, Sundsbak J, Harris PC: A novel PKD1 variant demonstrates a disease-modifying role in trans with PKD1 truncating mutation in Autosomal Dominant Polycystic Kidney Disease patients

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Original Research Abstracts By Subject Area



Allied Health

Category: Clinical

1

Advancing multidisciplinary care and collaboration through the establishment of a dysphagia service at the Kuwait Cancer Control Center

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Introduction:

Head and neck cancer (HNC) affects over 900,000 individuals globally. Of those newly diagnosed, 40% present with advanced disease, resulting in a high incidence of dysphagia – a comorbidity that leads to pneumonia and malnutrition. The objectives of this study were: to assess barriers and supports for a multidisciplinary dysphagia service for HNC patients; to promote the ongoing development of multidisciplinary collaboration; and to advance the scope of practice of dietitians and speech-language pathologists (SLPs) at the Kuwait Cancer Control Center (KCCC).

Methods:

Prior to the study, there was limited recognition of the risks associated with dysphagia, especially in HNC patients. A multidisciplinary team of local and international experts composed of dietitians, nurses, and SLPs analyzed the current state of service, conducted an educational needs assessment, developed discipline specific and joint education programs; and established a service level agreement between referring partners.

Results:

A formalized service was initiated whereby dietitians screen patients for suspected dysphagia followed by referral to speech-language pathology for assessment and management. Other outcomes of the project include: implementation of a local dysphagia screening and assessment process; development of texture modified diets by the dietitians; introduction of a dysphagia procedure and self-learning module to standardize practice by nursing and acceptance of recommendations to increase dysphagia training in the SLP curriculum at Kuwait University.

Conclusions:

Establishing a multidisciplinary dysphagia service at KCCC with nurses, dietitians and SLPs was critical to management and eventual recovery of HNC patients. A formalized dysphagia service has advanced the scope of practice of dietitians and SLPs at KCCC.

Key Words: Dysphagia; Multidisciplinary; Collaboration

Funding Agency: None



Allied Health

Category: Graduate MSc: Basic Science

2

Screening and characterization of the disease-causing mutation for autosomal dominant congenital bilateral cataract in a multigenerational Kuwaiti family

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Introduction:

Cataracts are an eye abnormality often known as Lens opacities. It is responsible for 51% of world blindness. Congenital cataract is an early onset cataract that causes blindness in infants. Recently many genetic studies were conducted to unravel the molecular background of the disease. Mutations in any of the genes encoding proteins that are responsible for lens structure, maintenance and transparency can lead to cataract. In here, we are genetically investigating autosomal dominant congenital cataract in a Kuwaiti multigenerational family.

Methods:

Ten members of the family suffering from ADCC were recruited from Al-Bahar Eye Centre. Clinical examination and assessment were completed. DNA was extracted from both affected and unaffected members. Genome-wide linkage analysis (GWLA) was performed using Affymetrix Gene Chip Human Mapping 250K Arrays. Appropriate statistical analysis tools were implemented. Direct sequencing is considered to screen candidate genes for mutations.

Results:

GWLA results of the investigated ADCC-Family revealed three high LOD scores (2.4, 2 and 1.75) for two distinguished loci 22q13.31 and 3q22. From Locus 3q22 only LEPREL1 showed clear relation to cataract, hence was picked as a candidate gene. Locus 22q13.31 yielded no genes involved in eye and lens development in the human. Nevertheless, WNT7b gene can be considered as potential candidate, because of its known involvement in eye/lens development in hens. Direct sequencing of the coding region and the exon-intron boundaries of both genes are being conducted in the lab.

Conclusions:

ADCC is considered a relatively rare disorder with only a few cases reported in Kuwait. More research in this field is encouraged in order to reach a better understanding of the disorder. Our ongoing research is in its initial stages. Currently, candidate gene sequencing is being performed. However, targeted loci sequencing is being considered as the next appropriate step.

Key Words: Genome-wide linkage Analysis, Cataract, Mutations

Funding Agency: YS 05/13



Allied Health

Category: Clinical

3

Pro-inflammatory cytokines IL1 β , IL6 and IL8 release during relapse in children with nephrotic syndrome

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Introduction:

The immune pathology of nephrotic syndrome has been widely postulated. The pro-inflammatory cytokines, IL1 β and IL6, and recently, the chemokine IL8 had been shown to induce proteinuria in various renal diseases. In this study we explore the release of the 3 cytokines during the relapse phase of the disease.

Methods:

IL1 β , IL6 and IL8 were measured in the urine of 37 nephrotic children during relapse. Twenty healthy children were used as controls.

Results:

A total 24 males and 13 females with a mean age of 6.4 years, were included. All patients had normal serum creatinine. Mean urinary IL1 β , IL6 and IL8 in patients during relapse were 132.94 \pm 654.97, 217.82 \pm 1124.31 and 150.227 \pm 523.97 pg/micromol, respectively. Compared to the same cytokines detected in controls (9.11 \pm 40.75, 0.146 \pm 0.652 and 6.455 \pm 24.53 pg/micromol, respectively), the difference was significantly higher during relapse than in controls (P=0.02, 0.03 and 0.014 respectively).

Discussion: Increased release of IL1 α , IL6 and IL8 in the urine of patients with nephrotic syndrome. IL1 α and IL6 are acute phase proteins and are involved in T-cell and macrophage activation. IL8 (CXCL8) is a chemokine, involved in leukocytes chemotaxis. We believe that elevation of these substances is consistent with the activation of the immune system during relapse and the generation of inflammatory response which might be the first step of initiating proteinuria.

Conclusions:

Relapses of nephrotic disease is an inflammatory process initiated by both the innate and adaptive immune systems. The use of cytokines blockers to induce remission in such patients is worth further studies.

Key Words: Relapse, Nephrotic syndrome, Cytokines

Funding Agency: None



Allied Health

Category: Basic Sciences

4

Determination of ethanol in soya sauce in Kuwait market

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Introduction:

Soy sauce originated in China and then spread to East and Southeast Asia. This traditional condiment has been used as a popular seasoning in eastern Asia for over 1,800 years. Soy sauce can be classified into Japanese-type and Chinese-type based on the amount of wheat used. In Japanese-type soy sauce, soybeans and wheat are used with the ratio of 1:1. However, Chinese-type use lower amount of wheat. Soy sauces are produced by mixing the grain and soybeans with fungi, such as *Aspergillus oryzae* and *A. sojae*. According to fermentation process the starch is fermented to alcohol and lactic acid and the proteins were broken down to peptides and amino acids. The objective of this study aim to determine and quantify the amount of ethanol in different brands of soya sauce located in Kuwait market.

Methods:

A total of 120 samples from 5 countries were collected during the period of June 2014 and December 2014. They were quantified using gas chromatography with flame ionization detector (GC-FID) coupled to headspace autosampler with the following conditions; Helium used as carrier gas. the injector temperature is 200°C, the detector temperature is 200°C and the column temperature is 65°C and held isothermally for 3 mint. For the headspace, oven temperature was 65°C, the needle temperature is 75 °C, and the transfer line temperature is 90°C. the samples incubated for 20 mint.

Results:

We determined and quantified the amount of ethanol in soya sauce samples from USA, Japan, Thailand, China and Korea .We found that the ethanol content in soya sauce is ranged from 0.05 % (v/v) to 7.3 % (v/v). According to this study 89 (74%) samples contain 0.5-0.5 %, 18 (15%) samples contain 0.5 to 3% and 13 (11%) samples contain 3 to 7.5% of ethanol content.

Conclusions:

This study highlights that the content of ethanol in soya sauce is differ in value and can reach to a high concentration till about 7.3 % according to the type of soya sauce, storing time and degree of fermentation.

Key Words: Ethanol, Soya sauce, Gas chromatography

Funding Agency: None



Allied Health

Category: Basic Sciences

5

**Benchmarking health of the health sciences community of Kuwait
University: Health inventory and database development, a
preliminary analysis**

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Introduction:

The faculties in the Health Sciences Center are committed to developing world class health care professionals. However, are the members of this community following the healthy lifestyles required of them to be credible role models for their patients? The objective of this study is to explore the health and lifestyle of the HSC community (students and staff).

Methods:

Longitudinal collection to evaluate health indicators of students, and staff over time. Health assessment included a health questionnaire and objective measures (heart rate, blood pressure, waist-to-hip ratio, and random blood glucose testing).

Results:

This preliminary analysis included 370 subjects (82 staff, 288 students). Students and staff had evidence of sub-optimal health, overweight/obesity (40%, 62%, $p < 0.001$), 11% of staff demonstrated high blood pressure and 26% abnormal random blood glucose levels. Significant differences between students and staff were observed for BMI, resting heart rate, and diastolic blood pressure ($p < 0.001$). Morbidity was more prevalent among staff compared to students (54% and 41% had more than one morbidities, $p < 0.05$). On average, both students and staff sleep 6.5 hours/night. Approximately half of students and staff reported being moderately physically active (3.5 hours of activity/week) (49% and 46%).

Conclusions:

Our findings support the need for general health education targeted differentially to students and staff to promote a culture of health. We identified some preliminary trends with respect to the need for health promotion and its delivery across these groups. These include the need for provision of fitness areas for men and women, walking programs, nutrition counseling, and sleep and stress management.

Key Words: Obesity and overweight; Health and wellbeing; Nutrition and physical activity

Funding Agency: None



Allied Health

Category: Clinical

6

Kuwait's single transplant center laboratory experience of hematopoietic stem cell collection, processing and transplantation for haematological malignancies

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Introduction:

Stem cell transplantation is a medical approach of using stem cells to repopulate the ablated bone marrow post chemo- and radiotherapy. This is used to help treat haematological malignancies such as leukaemia, lymphoma, multiple myeloma and genetic blood diseases such as thalassaemia. The Stem Cell Processing Laboratory in the Kuwait Cancer Control Center provides the support services for the stem cell transplantation programs. To date, over 300 autologous cell processing preparations have been conducted including over 200 autologous transplants and 32 allogenic stem cell transplants. Laboratory procedures performed contribute largely to the success of stem cell transplantations.

Methods:

Laboratory procedures include blood cell processing collected through apheresis and bone marrow aspirations. This includes red blood cell and plasma depletion for blood group incompatibility, CD34+ cell enumeration by flow cytometry, cryopreservation, slow-rate freezing, cell storage and thawing. Viability assays using Trypan blue and clonogenic cell culture are performed to assess stem cell function.

Results:

The number of CD34+ cells in the peripheral blood was used to predict the timing of apheresis and to optimize the yield for transplant. It has been shown that there is a correlation between the absolute CD34+ cell count in the peripheral blood and the total yield in the final cellular product. Different factors have been shown to affect stem cell mobilization. The cell viability ranged from 85% to 100% and there was an excellent outcome of colony forming units which was used as an indication of engraftment success along with the absolute neutrophil count.

Conclusions:

Stem cell transplantation is a life-saving therapy and the laboratory techniques play an important role in a successful outcome. Accurate cell enumeration and cell processing including cryopreservation have a crucial role in the harvest and vitality of the stem cells used for the transplantation.

Key Words: HSCT, Stem Cell Transplant, CD34

Funding Agency: None



Allied Health

Category: Graduate PhD (Basic Science)

7

Red cell alloimmunization among multi-blood transfusion cancer patients

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Introduction:

This is an observation, descriptive, cross-sectional study. Aimed to determining the frequency and specificity of alloantibodies against RBCs antigens among multi-transfused cancer patients in Khartoum state during the period from February up to April 2014.

Methods:

Two hundred and three cancer patients in the age range between 10-100 years old, treated or on follow-up in Radiation and Isotope Center-Khartoum (RICK). Patients with autoimmune disease were excluded from the study. Some information were obtained by questionnaire such as; age, sex, diagnosis, number of blood transfused and if there any previous hemolytic transfusion reactions . Verbal consent was obtained from multi-transfused cancer patients. The volume of 2.5 ml of venous blood was collected in EDTA from all patients, originally collected for routine clinical purposes. ABO, Rh D, screening test and antibody identification test was performed.

Results:

Collected data and tests results had been analyzed using the computer program SPSS 11 (statistical package of social sciences). The result showed that Red blood cells allo-antibodies were found in 29% of multi-transfused cancer patients, most common identified antibodies were anti-Kell (44%), anti-E (25%), anti-Leb (14%), anti-Kidd (7%), anti-e (7%), anti-s (5%), anti-c (5%), anti-duffy (5%), anti-N (5%), anti-Cw (3%), anti-E (3%) and anti-V (1%).

Conclusions:

There was no relationship between allo-immunization and sex; the present study found that there was no relationship between allo-immunization and age. No relationship between allo-immunization and type of cancer and between allo-immunization and number of blood transfusion, ABO and Rh blood group system.

Key Words: Red cell; Alloimmunization; Cancer

Funding Agency: None



Allied Health

Category: Clinical

8

Spinal injury rehabilitation in Kuwait: A ten year epidemiological analysis

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Introduction:

Spinal Cord Injury (SCI) is a major cause of disability in young adults and therefore an insight into the characteristics of the affected population is important to prevent SCI and improve the rehabilitation services. The objective of this study is to describe the data of spinal cord injury patients rehabilitated in the Physical Medicine & Rehabilitation (PMR) Hospital, Kuwait during the period 2000-2009. The study design is retrospective data analysis.

Methods:

Data pertinent to the study were collected from the case records of 370 patients admitted for SCI rehabilitation between 2000 and 2009 in PMR Hospital. The data was analysed using IBM SPSS version 22 software.

Results:

Of the total 370 cases, 265 males and 105 females ; 130 were Kuwaitis and 240 were non-Kuwaitis. Traumatic cases were more than non traumatic cases. In traumatic SCI, road traffic accident was the most common cause, followed by fall from height . Traumatic cases were more among non Kuwaiti than Kuwaiti, while rate of traumatic SCI was similar in both males and females. There was a significant difference in the causes of traumatic SCI according to nationality. RTA was the common cause among Kuwaitis and fall from height was the common cause among non-Kuwaitis. RTA and fall from height were more prevalent causes in male non-Kuwaitis while fall from height was more common cause followed by RTA in non-Kuwaiti females . Paraplegics were more in number than the tetraplegics. Post rehabilitation 45.9% of patients were wheelchair dependent, 19.5% needed wheelchair for long distances, 34.6% were functional walkers.

Conclusions:

The results of this study highlights the need to improve road safety and law enforcement to prevent road traffic accidents, to increase awareness and provide safety equipment to those who work at heights as well as early diagnosis and early intervention in non traumatic cases.

Key Words: Rehabilitation, Spinal cord injury, Epidemiology

Funding Agency: None



Allied Health

Category: Basic Sciences

9

Identifying potency markers in human umbilical cord wharton's jelly derived mesenchymal stem cells following Tri-lineage differentiation

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Introduction:

Wharton's Jelly-derived Mesenchymal stem cells (WJ-MSCs) have gained interest as an alternative source of stem cells for regenerative medicine because of their potential for self-renewal, differentiation and unique immunomodulatory properties. Although many studies have characterized various WJ-MSCs biologically, the expression profiles of the commonly used stemness markers have not yet been addressed.

Methods:

WJ-MSCs were isolated by microdissecting the Wharton's jelly from the umbilical cord and culturing in DMEM/F-12 medium supplied with 10% FBS. Pre-differentiation characterisation of cells was performed using flow cytometry and qPCR analysis. Growth kinetics was evaluated by calculating accumulative population doubling time. Cells were then induced into adipogenic, osteogenic and chondrogenic lineages following previously described protocols. Post-differentiation characterisation was performed using qPCR, immunocytochemistry and western blotting.

Results:

Flow cytometry, qPCR and western blot analysis revealed predominant expression of CD29, CD44, CD73, CD90, CD105 and CD166 in WJ-MSCs, while the hematopoietic and endothelial markers were absent. Our results demonstrated a reduced expression of only CD44 and CD73 in response to the tri-lineage differentiation induction.

Conclusions:

CD44 and CD73 are associated with undifferentiated state of WJ-MSCs which suggest a possible role for these two markers in determining the potency characteristics of these stem cells.

Key Words: Stem Cells; Cord blood; Differentiation

Funding Agency: This work was funded by the Kuwait Foundation for the Advancement of Sciences (KFAS) under projects numbers 2012-1302-03 for Hamad Ali and RA-2013-009 for Ashraf Al Madhoun.



Anatomy

Category: Graduate MSc (Basic Science)

10

Resveratrol recovers hyperglycemia-induced oxidative stress and DNA damage in rat testis

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Introduction:

Resveratrol (trans-trihydroxystilbene) is increasingly gaining importance as a pharmaceutical drug as it is said to have several beneficial effects. In this study, we investigated its modulatory effects on hyperglycemia-induced oxidative stress and DNA damage in the testis of diabetic rats.

Methods:

Adult male Wistar rats (n=6-8) were segregated into a) control, b) Resveratrol-treated (5 mg/kg; ip), c) diabetic (Streptozotocin-induced), and d) diabetes+ Resveratrol-treated groups. The animals were sacrificed at the end of 6th week and, during last 3 weeks before sacrifice, the animals received Resveratrol. Important sperm tests were conducted in samples collected from caudae epididymis. Total antioxidant (TAS) and oxidant (TOS) levels (plate reader assays), 8-oxo-dG levels (dot blotting and immunohistochemistry), testicular DNA synthesis, and DNA fragmentation assay (agarose gel electrophoresis) were measured in the testis tissue. Data were analyzed by one way ANOVA and LSD tests by using SPSS software and P<0.05 was considered significant.

Results:

Resveratrol improved diabetes-induced hypogonadism, sperm motility and sperm abnormality, and oxidative stress as compared to the controls (P<0.01). Resveratrol normalized diabetes-induced decrease in DNA synthesis and increase in 8-oxo-dG levels to control levels. However, interestingly, when given alone, Resveratrol inhibited DNA synthesis and enhanced 8-oxo-dG levels (P<0.05-0.01). The protective effects of Resveratrol on DNA double strand breaks in diabetic rats were minimum and did not show statistical significance.

Conclusions:

Our results indicate that Resveratrol protects testicular function and DNA damage in diabetic rats, but in normal rats it inhibits DNA synthesis and oxidizes deoxyguanosine base of DNA. Resveratrol may be a useful drug to treat oxidative stress-induced male hypogonadism.

Key Words: Hyperglycemia; Oxidative stress; DNA damage

Funding Agency: Kuwait University grant YM10/13, College of Graduate Studies and SRUL02/12



Anatomy

Category: Basic Sciences

11

Peripheral RPE cells have the capacity to proliferate and migrate to replenish central retina

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Introduction:

The retinal pigmented epithelium (RPE) is a monolayer of hexagonal cells that forms a part of the blood retinal barrier. It plays a critical role in supporting the neural retina. Studies have shown that RPE cells have the capacity to proliferate only in the periphery and suggested the possibility of RPE cell migration towards the central retina in an attempt to replenish age related cell loss (Del Priore et.al, 2002; Al-hussaini et al.,2008). In this study we used two methodologies to show RPE cell migration from peripheral to central retina.

Methods:

In the first method 10 Dark Agouti (DA) rats were injected with BrdU for 120 days. Labelled BrdU cells were then counted and mapped. In the second methodology Dil crystal, cell tracer, were injected into the peripheral region of the retina. DA rats were sacrificed at 10, 14, and 18 weeks after injections and labelled cells were identified.

Results:

Labelled BrdU cells were found mainly in the periphery, distributed in clusters, indicating potential clonal origin. However, some RPE cells were also found in the equatorial regions and very few in the center. Few RPE cells were found to be labeled with Dil crystals between the injection site and the optic nerve head.

Conclusions:

Our results shows that RPE cells have the capacity to migrate from central to peripheral retina.

Key Words: RPE; Migration; proliferation

Funding Agency: MA02/09



Anatomy

Category: Undergraduate

12

ThymoquiNone enhances neurogenesis in lead exposed rats

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Introduction:

Lead (Pb) is a neurotoxic substance showed to affect the postnatal neurogenesis and cognitive functions when exposed during fetal growth period. ThymoquiNone (TQ) is the active constituent of *Nigella sativa* (NS) seeds. TQ accounts for the pharmacological properties of NS. The aim of present study was to investigate the effects of TQ on postnatal neurogenesis in young rats born to pregnant rats that are exposed to low-dose Pb during pregnancy.

Methods:

Wistar rats were mated and after pregnancy was established, animals were given drinking water with 0.1% lead acetate alone (Pb group, n=6) or given drinking water with 0.1% lead acetate and treated with TQ (10mg/kg, ip, Pb+TQ group, n=6) from day one of pregnancy until parturition. Control animals (NC, n=6) received deionized water. Pups from all the groups were sacrificed and Pb level in hippocampus was measured by atomic absorption spectrophotometer on postnatal day 30. Sections of hippocampus were stained for doublecortin (marker for neurogenesis). Data were analyzed with one way ANOVA.

Results:

All Pb-exposed rats showed significantly ($P < 0.001$) higher level of Pb in comparison to NC. Pb-exposed rats showed significantly (30-40%) decreased number of doublecortin positive neurons in the hippocampus in comparison to NC ($P < 0.0001$) and Pb+TQ rats showed significantly (20-30%) more new neurons in comparison to Pb-exposed group ($P < 0.001$).

Conclusions:

Our data shows that low-dose exposure to Pb during pregnancy results in impairment of postnatal neurogenesis in the hippocampus and is restored (20-30%) by treatment with TQ.

Key Words: ThymoquiNone, Neurogenesis, Lead

Funding Agency: None



Anatomy

Category: Graduate MSc (Basic Science)

13

Hsp70 involvement in hyperthermic pre-conditioning of excitotoxic neuronal damage in the hippocampus

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Introduction:

Hsp70 is a major stress protein affording significant protection against adverse effects of hyperthermia and other insults. We used excitotoxic damage model in hippocampus to investigate if whole body hyperthermia (WBH) would precondition the excitotoxic neuronal damage.

Methods:

Female Sprague-Dawley rats (n= 60) weighing 160-200 g were subjected to preconditioning heat stress (HS) (HS: 41.5^oC x 30 min) and after 4, 24 or 72 hours they were injected with different intracerebroventricular (icv) kainite (KA) dose (KA: 0.05, 0.15 or 0.6 µg/kg). Then, the rats were sacrificed after 4 hours. Immunohistochemistry (IHC) stained sections were evaluated quantitatively by image analysis and non-parametric statistics.

Results:

KA-induced damage was dose dependent and extended through CA3 to CA4 and the hillus of the hippocampus. The HS preconditioning significantly decreased the hippocampal CA3a neural damage; while c-Fos expression was significantly attenuated only after the lowest (0.05 µg/kg) KA dosage by about 60 % (P<0.05) in the 4 and 72 hour intervals investigated. Blocking of Hsp70 expression by quercetine injection pre-and post-HS preconditioning (P<0.05) significantly abolished the HS-induced protection at 4 hours but it did not so at 72 hours after HS. Furthermore, we injected the heat-stress preconditioned animals icv with 50 µg PES/pifithrine, a new low molecular inhibitor of Hsp70 but this treatment did not attenuat heat induced-tolerance to kainate. Then, injecting PES/pifithrine to rats treated only with kainate disclosed that PES/pifithrine alone was protecting CA3a neurons against KA-induced excitotoxic damage.

Conclusions:

These results suggest that Hsp70 might be responsible for the observed early protection against excitotoxicity.

Key Words: Hsp70; Excitotoxic; Hippocampus

Funding Agency: Graduate studies at Kuwait University



Anatomy

Category: Graduate MSc: Basic Science

14

Laparoscopic sleeve gastrectomy & neuropathy

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Introduction:

A serious complication of LSG is neuropathy, unfortunately, little is known in terms of its risk factors. Due to an increase in obesity, rising numbers of bariatric surgeries, neurologic complications have become increasingly recognized. Our aim was to examine the biochemical, hormonal, and genetic factors that are associated with neuropathy in patients post LSG.

Methods:

A retrospective study of 1815 morbidly obese patients who underwent LSG at Al-Amiri Hospital, Kuwait (2008-2014). 32 patients included in the study; 16 patients with neuropathy (NG), 16 patients without neuropathy (CG). Diagnosis made by a consultant neurologist. Blood samples to examine vitamin deficiencies, biomarkers through genetic analysis, and hormones involved in neuropathy (GLP-1). DNA extraction and genotyping was performed to investigate rs6234 SNP in the PCSK1 gene. T test was used to compare between two groups.

Results:

Results showed the mean age of NG 34.9 while the CG was 26.6. The NG & CG's mean preoperative weight was 131 and 120.7, respectively with a mean BMI of 51 and 45.5, respectively. There was no significant difference between BMI ($p = 0.1$) as well as excess weight loss percentages post LSG at 12 months ($p = 0.6$). B12 levels were within normal range, but higher in NG ($p = 0.005$). B1 and B2 levels were significantly lower in NG; p values are 0.000 and 0.031, respectively. Vitamin B6 levels were significantly higher in NG ($p = 0.02$) Copper levels were lower in NG ($p = 0.009$). There was no significant difference in GLP1 levels. The genotypic frequency for GG, GC, and CC is 66.94%, 29.75%, and 3.31%, respectively. No significance between the three genotypes and GLP-1.

Conclusions:

Our data showed post sleeve neuropathy is associated with lower levels of B1, B2, copper, and are older in age. B6 was significantly higher in the NG, which is at toxic levels associated with neuropathy. No difference in preoperative BMI, excess weight loss % at 1 year, and GLP-1 levels, Rs6234 SNP were found.

Key Words: GLP-1, Bariatrics, Neuropathy

Funding Agency: College of graduate studies, Kuwait University



Anatomy

Category: Undergraduate

15

Suppression of seizure frequency and mossy fiber sprouting and neurodegeneration in temporal lobe epilepsy in young rats by thymoquiNone

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Introduction:

ThymoquiNone (TQ), the active constituent of *Nigella sativa* seeds has been shown to have anti-cancer, anti-inflammatory and neuroprotective roles. Present study was designed to investigate antiepileptic and neuroprotective properties of TQ in temporal lobe epilepsy in young rats.

Methods:

Status epilepticus was induced in 4-month-old Wistar rats by injecting kainic acid (0.5 μ g) into the lateral ventricles. They were divided into lesion only (LO) and lesioned and treated with TQ for 3 weeks (10mg/kg, ip, L+TQ, n=6 in both groups). Age matched normal and sham controls were maintained for comparison. Frequency of spontaneous recurrent motor seizures (SRMS) was quantified (3.0 to 3.5 months post lesion period) by video monitoring.

Results:

TQ treatment reduced the degenerating neurons in the dentate hilus and CA3 region on as revealed by Flurojade-B staining and increased neurogenesis in the dentate gyrus in kainic acid treated rats compared to LO group on the 4th post lesion day. TQ treatment reduced SRMS frequency significantly compared to LO group (5 \pm 0.1 seizures/day in LO vs 1.5 \pm 0.2 in TQ treated group) seizures/day, Student's t-test, P<0.001). Aberrant mossy fiber sprouting, as revealed by ZnT3 immunostaining and Timm's staining, showed significant reduction in TQ treated rats compared to LO group (35-40%, P<0.001). The number of new neurons in the dentate gyrus immunostained with doublecortin was significantly more in TQ treated chronically epileptic rats compared to LO (25-30%, P<0.001).

Conclusions:

Our data suggest that treatment with TQ reduces SRMS frequency, may be due to decreased aberrant mossy fibers sprouting. Enhanced neurogenesis in dentate gyrus suggests neurotropic role of TQ in acute and chronic phase of epilepsy progression. Results of the present experiment signify the use of TQ as a new antiepileptic drug to treat temporal lobe epilepsy in humans in the future.

Key Words: ThymoquiNone, Hippocampus, Epilepsy

Funding Agency:None



Anatomy

Category: Graduate MSc: Basic Science

16

Mossy fiber sprouting and spontaneous recurrent motor seizures in chronic temporal lobe epilepsy in middle aged rats; effects of thymoquiNone

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Introduction:

Studies have associated the brain inflammation as a causative factor for neural excitability and decreased neurogenesis in epilepsy. ThymoquiNone (TQ), active constituent of *Nigella sativa* seeds has anti-inflammatory and neuroprotective roles. Aim of the present study was to investigate the effects of TQ on frequency of spontaneous recurrent motor seizures (SRMS) and aberrant mossy fiber sprouting in kainic acid model of chronic temporal lobe epilepsy in middle-aged rats.

Methods:

Status epilepticus was induced in 12 months old Wistar rats by injecting kainic acid (0.5µg) into the lateral ventricles stereotactically and were divided into lesion only (LO) and lesioned and treated for 3 weeks with TQ (10mg/kg, ip, L+TQ, n=6 in both groups). After quantifying SRMS frequency from 3.0 to 3.5 months post lesion period, rats in both groups were sacrificed along with the age matched normal (NC) and sham (SH) control rats (n=6 in both groups). Brain sections were immunostained with ZnT3 and Timm's staining to stain mossy fibers and NeuN to quantify the neurons in the hippocampus. Data were analyzed with one way ANOVA or Student's t-test.

Results:

TQ treatment reduced the SRMS frequency significantly in comparison to LO group (4±0.1 seizures/day in LO vs 1.5±/-0.2 seizures/day in L+TQ group, P<0.001). Treatment with TQ suppressed the aberrant mossy fiber sprouting significantly compared to LO group (P<0.001). Number of neurons in the dentate hilus and CA3 regions in septal and temporal hippocampus was significantly more in TQ treated group in comparison to LO (P<0.001).

Conclusions:

We conclude that TQ protects the neurons from degenerating during early status epilepticus, prevents aberrant mossy fiber sprouting and thereby reduces SRMS frequency. Results of the present study suggests the use of TQ as new antiepileptic drug to treat temporal lobe epilepsy.

Key Words: ThymoquiNone, Hippocampus, Epilepsy

Funding Agency: None



Anatomy

Category: Undergraduate

17

ThymoquiNone protects the spinal cord neurons from degeneration by enhancing GAP-43, Bcl-2 and decreasing Bax expression in sciatic nerve lesion model

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Introduction:

Studies have established beneficial properties of thymoquiNone (TQ), the active constituent of Nigella Sativa seed oil. TQ has been shown to have anti-inflammatory and neuroprotective roles. Aim of the present experiment was to investigate the mechanisms of protection of spinal cord motor neurons by thymoquiNone in sciatic nerve lesion model.

Methods:

Sciatic nerve was exposed on the right side in 4 months old Wistar rats and transected at its point of entry to the thigh. They were divided into lesion only (LO, n=6, treated with saline-1ml/day ip for two weeks) and lesioned and treated with TQ (L+TQ n=6, treated with 10 mg/kg, TQ ip, for two weeks) groups. Age matched normal control (NC, n=6) and sham control (SC, n=6) were also maintained. Serial frozen sections of spinal cord were stained with cresyl violet and immunostained with NeuN, GAP-43, Bcl-2 and Bax. Number of immunostained neurons in the dorsal and ventral horn regions of the spinal cord were quantified. Data were analyzed with one way ANOVA.

Results:

TQ treatment rescued large number of neurons both in ventral and dorsal horn regions of the spinal cord from degeneration due to sciatic nerve lesion. Quantification of neurons stained with NeuN and cresyl violet showed a significant increase in the number of neurons in the anterior and posterior horns of the spinal cord in rats from L+TQ group in comparison to LO group ($P < 0.001$). Additionally, immunohistochemical examination of spinal cord sections revealed that TQ increased the expression of GAP-43 and Bcl2 ($P < 0.001$) and reduced the expression of Bax ($P < 0.001$).

Conclusions:

We conclude that the thymoquiNone has protective effects on the anterior horn motor neurons and posterior horn neurons after peripheral nerve lesion. It may be because of the anti-oxidant and the anti-apoptotic effects of TQ.

Key Words: ThymoquiNone, Spinal cord, Sciatic nerve

Funding Agency: None



Anatomy

Category: Graduate MSc (Basic Science)

18

Resveratrol inhibits diabetes-induced testicular cell death by manoeuvring oxidative stress and JNK signaling in rats

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Introduction:

As diabetes adversely affects functions of almost all organ systems, there is a need to invent counter strategies to protect the organ systems. The present study investigated the effects of Resveratrol on diabetes-induced alterations in oxidative stress, c-Jun N-terminal kinase (JNK) signaling and apoptosis in rat testis.

Methods:

Adult male Wistar rats (13-15 weeks; n=5-6) were segregated into four groups: 1) normal control, 2) Resveratrol-treated control, 3) Streptozotocin-induced diabetic, and 4) the diabetic+Resveratrol-treated (5 mg/kg; ip; given during last 3 weeks before sacrifice) groups. All animals were sacrificed on day 42 after the confirmation of diabetes. The oxidative stress was assessed by quantifying SOD, catalase, glutathione peroxidase (plate reader assays) and 4-HNE (dot blotting). The JNK pathway proteins ASK1, MKK4, JNKs, c-Jun and ATF-2, and apoptosis marker caspase-3 were quantified by Western blotting. Data were analyzed by One-Way ANOVA and LSD tests with the level of significance set at $P < 0.05$.

Results:

Resveratrol recovered diabetes-induced changes in the intra-testicular antioxidants, and 4-HNE levels and expressions of ASK1, JNKs, c-Jun and ATF2 to the control levels ($P < 0.05-0.001$). However, phosphorylated forms of the latter two proteins (p-c-Jun and p-ATF2) did not change in experimental groups. Resveratrol also recovered DM-induced increase in cleaved caspase-3 to control levels.

Conclusions:

Resveratrol reduces DM-induced oxidative stress, normalizes JNK signaling pathway and alleviates the induced apoptosis in rat testis. Further, these results suggest that the supplementation of Resveratrol to diabetics may be a useful therapeutic strategy to alleviate DM-induced male reproductive dysfunction.

Key Words: Antioxidants; Hyperglycemia; Male reproductive system

Funding Agency: Kuwait University grant YM11/13, College of Graduate Studies and SRUL02/12



Anatomy

Category: Clinical

19

Congenital coronary artery anomalies in adults; evaluation by dual source ECG gated CTA

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HSC-DASH

Introduction:

Congenital anomalies of the coronary arteries are rare and are often diagnosed incidentally during a conventional coronary angiography. Recently, the incidence of these congenital defects is on the rise particularly after the introduction of the electrocardiography (ECG) gated coronary computed tomographic angiography (CCTA). This innovative radiological screening modality has led to more precise mapping of the course of the coronary arteries on Computed Tomographic Scan.

AIM OF THE STUDY: To determine the prevalence of congenital anomalies of the coronary arteries and their variations in the local Kuwaiti community.

Methods:

In this study, we analyzed the CCTA data obtained consecutively from 842 patients admitted to Dar Al-Shifa hospital from the year 2013 until 2014, retrospectively. The inclusion criteria for the selection of the patients were: atypical chest pain, equivocal ECG, assessment of patency of coronary stents or grafts and pre-operative screening. Information was acquired by using a dual-source CT scanner with ECG gating.

Results:

Data analysis revealed that 21 (2.5 %) patients were found to have coronary artery anomalies out of the 842 patients who underwent CCTA. Out of these coronary artery anomalies, 13 cases showed more than two ostia, 7 cases showed ectopic origin of coronary artery from opposite sinus or non-aortic sinus, 2 cases showed single coronary ostium and one case showed coronary artery with pulmonary fistula. In addition, myocardial bridging was identified in 87 (9%) patients whereas ramus intermedius branch was identified in 160 (19%) patients.

Conclusions:

The prevalence of congenital coronary anomalies at Dar Al-Shifa institution in Kuwait was 2.5% during the year 2013 -2014, which is higher than most of the previous studies reported from different countries.

Key Words: Coronary artery; Anomalies; Coronary CTA

Funding Agency: NONE



Anatomy

Category: Basic Sciences

20

Gliosis enhances the survival neurons in culture

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Introduction:

Temporal lobe epilepsy(TLE) is characterized by loss of neurons, gliosis in the dentate hilus and CA3 regions and enhanced dentate gyrus neurogenesis following status epileptics in kanic acid (KA) model of TLE. Present study was aimed to investigate the role of astrocytes in survival of neurons in in-vitro KA lesion model of epilepsy.

Methods:

Hippocampal and neocortical primary cultures (n=12) were done from new born rat pups. On 5th day of culture, media was replaced with media containing 0.5µg/ml kainic acid (KA) for 6 hours to induce gliosis. Twenty four hours after KA stimulation, cultures were washed with fresh media and new cells from neonatal hippocampus or cortex were placed over the KA stimulated primary cultures or over cultures not treated with KA, [(control cultures (n=12)]. Media was changed every 72hrs. On 12th day, cultures were either fixed with 2% paraformaldehyde for glial fibrillary acidic protein (GFAP) and doublecortin (DCX-neuronal marker) immunosatining (n=6) or cells were frozen for western blot analysis of GFAP and DCX. Data were analyzed with one way ANOVA.

Results:

The KA treatment resulted in significant increase in the glial cell proliferation both in cortical and hippocampal primary culture as revealed by significant increase in number of GFAP positive astrocytes(P<0.001) and BrdU positive cells(P<0.001). Western blot analysis showed significant increase (P<0.001) in GFAP protein level in KA treated cultures compared to control cultures. Number of DCX positive neurons that survived on KA treated culture was found to be significantly increased compared to that survived on untreated control cultures.

Conclusions:

We conclude that enhanced astrogliosis in culture, facilitates survival of neurons from neonatal hippocampus and cortex [We acknowledge RCF, Faculty of medicine, Kuwait University (Grant No. SRUL02/13) for confocal microscopy].

Key Words: Culture, Gliosis, Doublecortion

Funding Agency: None



Anatomy

Category: Graduate MSc: Basic Science

21

ThymoquiNone improves cognitive functions and neurogenesis in intracerebro-ventricular model of Alzheimer's disease

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Introduction:

Alzheimer's disease (AD) is a progressive neurodegenerative disease and the most prevalent cause of dementia in adults. The hallmarks of the disease are cognitive impairment, amyloid deposits of aggregated β -amyloid (A β) peptides and neurofibrillary tangles. ThymoquiNone (TQ), the active constituent of *Nigella sativa* seeds has been shown to have anti-cancer, anti-inflammatory and neuroprotective roles. Objective of the present experiment was to study the effect of thymoquiNone on cognitive functions and neurogenesis in intracerebro-ventricular streptozotocin model of Alzheimer's disease.

Methods:

Streptozotocin (3mg/kg in citrate buffer) was injected into the lateral ventricles of 4-month-old Wistar rats. They were divided into lesion only (LO, n=6) and lesioned and treated with TQ for 4 weeks (10 mg/kg, ip, L+TQ, n=6). Age matched normal and vehicle controls were maintained for comparison. After four weeks of treatment rats in all group were subjected to water maze and radial arm maze behavioral tests. Finally rats were sacrificed, brain sections were processed for doublecortin immunostaining for neurogenesis analysis.

Results:

STZ injection into lateral ventricles resulted in significant cognitive impairment (both water maze and radial arm maze learning and memory retention, $P < 0.0001$) in LO group compared to control rats and cognitive function is improved significantly in L + TQ treated group compared to control group ($P < 0.001$). TQ treatment in L+TQ group protected the degenerating neurons in the dentate hilus and increased neurogenesis in the dentate gyrus compared to LO group. The number of new neurons in the dentate gyrus immunostained with doublecortin was significantly more in L+TQ treated rats compared to LO ($P < 0.001$).

Conclusions:

Our data suggest that thymoquiNone can prevent neurdegeneration and enhance neurogenesis in dentate gyrus in ICV-STZ model of Alzheimer's Disease.

Key Words: ThymoquiNone, Water maze, Alzheimer's disease

Funding Agency: None



Biochemistry

Category: Basic Sciences

22

Improving the efficiency of Zn-porphyrin-based photosensitizers for antimicrobial therapy

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Introduction:

Photosensitizers (PS) are non-toxic compounds that absorb visible light at specific wavelength to produce cytotoxic reactive species, mainly singlet oxygen, that kill the targeted cells/tissue in a process known as photodynamic therapy (PDT). Among the many uses of PDT is eradication of antibiotic-resistant microbial strains. Success of antimicrobial PDT depends on PSs which selectively and efficiently kill microbes and are harmless to the host cells. The aim of this study was to synthesize PSs with improved photoefficiency and to investigate their antibacterial potential.

Methods:

Zn(II)5,10,15,20-tetrakis(N-alkylpyridinium-2(3,4)-yl) porphyrins (ZnPs) with desired charges, lipophilicity, and size were synthesized and their antimicrobial activities were investigated using E.coli as a Gram-negative bacterial model. Cell damage and loss of viability were investigated using MTT assay and plating respectively. Each experiment was performed in triplicate. The results were analyzed for significant differences using student's t-test.

Results:

Keeping the positive charges and changing the tri-dimensional shape of the ZnPs, without altering the porphyrins core structure, improved the antimicrobial PDT efficiency of the PSs. Further increase of the antibacterial efficiency was achieved by moving the aliphatic substituents from ortho to meta position. Such PS were rapidly taken up by microbial cells and with only 5 min of illumination decreased microbial population by $> 5 \log^{10}$.

Conclusions:

The photoefficiency of ZnPs can be increased by orders of magnitude by changing the tri-dimensional structure and the lipophilicity of the molecule. Such modified compounds are potent antibacterial agents which at concentrations as low as 0.25 μM and short exposure to visible light, efficiently inactivate microbial cells.

Key Words: Zn-porphyrin; Antimicrobial; Photosensitizer

Funding Agency: Kuwait University grant MB02/12



Biochemistry

Category: Basic Sciences

23

Synthetic DNA construct design of HIV-1 induced VIF-resistant APOBEC3 expression towards degrading HIV-1 quasispecies into defective human endogenous retroviruses (HERV)

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Introduction:

Human intracellular restriction factors such as APOBEC3(A3) have defected many ancient retroviruses into endogenous retroviral elements found in ~8% of our genome. Human A3 (hA3) suppressed retroviruses through inducing loss-of-function (LOF) hypermutations in viral genome. However, HIV (a retrovirus) protects itself from hA3 by expressing VIF, a protein which targets hA3 for degradation. Nevertheless, studies have proven that some mammalian non-primate homologs of A3, such as the mouse homolog (mA3), can 'lethally' hyper-mutate VIF-competent HIV-1 and several types of SIVs. In this study, two main groups, (S/H)IV VIF-(i) Resistant and (ii) Affected A3 homologs (SHVRA3 and SHVAA3), were compared by their physicochemical properties to explore VIF-resistance characteristics in A3s. Furthermore, an HIV-induced SHVRA3 expression minicircle (MC-YAE) was designed using HIV regulatory (Reg) elements and mA3 cDNA.

Methods:

A phylogenetic tree was derived from sequence alignments of one non-primate SHVRA3, two primate non-hominid HVRA3s (HIV [but not SIV] resistant) and two hominid SHAAV3s. The variations of charged residues between the three groups (SHVRA3, HVRA3, SHVAA3) and VIF were analyzed. Additionally, HIV-1 RNA Reg elements from subtypes[A-K] were sequentially and structurally aligned to construct an HIV-1 quasispecies Reg element consensus structure. The consensus structure was then compared with the structure of MC-YAE's Reg element.

Results:

Both VIF and (S)HVRA3s had relatively less negatively charged residues compared to SHVAA3s, suggesting the possibility of strong salt-bridge interactions between VIF and SHVAA3s. The structure of MC-YAE's HIV Reg element was conserved with the quasispecies consensus structure. This implies that MC-YAE retains its HIV-1 specific gene control across HIV-1 quasispecies' spectrum.

Conclusions:

MC-YAE could be a promising DNA-based therapy to suppress HIV-1 quasispecies through introducing LOF mutations via SHVRA3.

Key Words: Artificial Gene Design, Structural Bioinformatics, Synthetic Biology

Funding Agency: None



Biochemistry

Category: Graduate PhD (Basic Science)

24

Wnt/planar cell polarity in platelets

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Introduction:

Wnt signalling is transduced through either the β -catenin-dependent pathway “canonical”, or β -catenin independent pathways “non-canonical”, which include the planar cell polarity pathway (Wnt/PCP). The two main features of PCP signaling involve the alignment of the cells together in a cooperative manner in polarized tissues, as well as local and global signals regulating the alignment with regard to the tissue axes. Wnt/PCP signaling has not previously been reported in platelets. Here we investigate the location, interaction, and possible functions of the core PCP proteins, including Cadherin EGF LAG Seven-pass G-type Receptor (CELSR), Frizzled, and Van Gogh-Like 1 & 2 (Vangl1,2), in resting and activated platelets.

Methods:

Platelets were acquired from healthy donors in accordance with approved guidelines from the University College Dublin (UCD) ethics committee. We investigated the Wnt/PCP core proteins location as well as any possible interaction within and between platelets under resting and different stages of activation to elucidate the possible function for this pathway in platelets using immunoblotting, immuno-fluorescence confocal microscopy, immuno-gold labelling electron microscopy, and immunoprecipitation. We also investigated the effect of Celsr2-deficiency on platelets by performing preliminary biochemical assays on Celsr2^{-/-} mice.

Results:

We provide evidence that human platelets express the Wnt/PCP core proteins, CELSR1, Frizzled and Vangl1&2, and show the location and interactions of Wnt/PCP components within resting and activated platelets.

Conclusions:

We have shown that Wnt/PCP proteins do not exhibit polarity between platelets, and are not involved in platelet-platelet contact, however, their function could be within platelets during resting or activation platelet conditions.

Key Words: Wnt Signalling; Planar Cell Polarity; Platelets

Funding Agency: Kuwait -CSC -Ministry of Health



Biochemistry

Category: Graduate (Resident)

25

Audit of thyroid function testing in Mubarak Al Kabeer hospital.

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Introduction:

Performance of audit is an essential part of the continuous quality improvement in the clinical biochemistry laboratory. An audit of thyroid function testing in the investigation of thyroid disease was performed in Mubarak Hospital.

Methods:

The audit looked at the requests received from all departments and outpatient clinics in Mubarak Hospital and polyclinics in Hawalli governorate, which are covered by Mubarak hospital laboratory. TSH, FT4 and FT3 requests were reviewed over one working week for the following aspects: diagnosis on requests and rate of requesting per patient. In addition, the audit aimed to identify the sources of thyroid function requests and if these are authorized personal (doctors only). The audit also evaluated the presence of any special conditions or preparations for patients prior to testing.

Results:

TSH and FT4 are extensively requested compared to FT3 and more than 50% of these requests come from polyclinics. In total, 103 requests were reviewed, 74 of these had request forms with irrelevant diagnoses that are not related to thyroid disease or symptoms that do not correlate with thyroid illness. 21 requests were repeated in less than 6 weeks period (2 out of these were ordered within a day) and 15 requests were repeated in less than one-month period. All physicians from all specialties and grades are authorized to ask for thyroid function test and repeat it at any time. There are no special appointments or preparations requested from the patient prior to testing.

Conclusions:

The audit highlights some aspects of misuse of laboratory service. It underlines the need for clear documented strategy for testing thyroid function that will discourage inappropriate and unnecessary repeat of thyroid function tests.

Key Words: Thyroid Function Testing; Mubarak Hospital; TSH and FT4

Funding Agency: None



Biochemistry

Category: Clinical

26

PSA as a marker of prostate problem

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Introduction:

The determination of serum prostate-specific antigen (PSA) has become an essential tumor marker for diagnosis, evaluation of the treatment and follow-up of the patients with prostate cancer. The ratio of free PSA in total PSA (fPSA/tPSA) has been reported to improve the diagnostic accuracy of prostate cancer in the group with slightly elevated serum PSA values, although the clinical significance of fit is still controversial.

Methods:

Retrospectively we studied our records for the results of randomly selected PSA requests starting from the end of 2013 to the beginning of 2015 for patients attending j.A Armed Forces Hospital. tPSA 4.0 ng/ml was used as a cut-off value for requesting fPSA. SPSS was used as Statistical package.

Results:

560 patients were involved (median 1.18 ng/ml) ; a group of 92 patients showed a result ≥ 4.0 ng/ml. Descriptive statistics of 92 patients are shown in table.1. Spearman's correlation showed positive relation between free and total PSA ($P < 0.01$; correlation coefficient 0.89). Positive correlation was found between the ratio and fPSA ($P < 0.0$; correlation coefficient 0.634) but not tPSA ($P = 0.41$; correlation coefficient = 0.087).

Conclusions:

fPSA seems to be useful marker for cancer susceptibility rather than tPSA. Further studies needed for confirmation.

Table.1. Descriptive statistics of 92 patients with tPSA ≥ 4.0 ng/ml

| | tPSA ng/ml | fPSA ng/ml | fPSA/tPSA |
|---------------|------------|------------|-----------|
| Median | 0.3 | 0.25 | 0.177 |
| Minimum | 0.003 | 0.001 | 0.01 |
| Maximum | 100 | 74 | 8.30 |
| 25 percentile | 0.63 | 0.21 | 0.127 |
| 75 percentile | 2.6 | 0.66 | 0.260 |

Key Words: tPSA; fPSA; fPSA/tPSA ratio

Funding Agency: None



Biochemistry

Category: Graduate MSc: Basic Science

27

Mn(III)N-alkylpyridylporphyrins increase vitamin C anticancer activity through generation of reactive oxygen species

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Introduction:

Ascorbate (Asc) administration has shown promising results in treatment of cancer. Mn(III)N-alkylpyridylporphyrins (MnP) are redox active superoxide dismutase mimetics with potential therapeutic applications. It is known that cancer cells accumulate porphyrins and show aberrant redox homeostasis. MnPs taken up by cancer cells can produce reactive oxygen species (ROS) by redox-cycling with ascorbate thus augmenting its cytotoxicity. This study investigates how structural modifications of MnPs affect their anticancer activity

Methods:

Rates of MnP catalyzed ascorbate oxidation, which corresponds to ROS generation, and MnP uptake were determined spectrophotometrically. Subcellular distributions of metalloporphyrins were investigated by confocal microscopy. MTT and SRB assays were used to quantify the combined effect of MnPs and Asc on human breast cancer PII/MDA and nontumorigenic breast epithelial HBL100 cell lines.

Results:

The hydrophilic meta and ortho isomers MnTE-2-PyP and MnTE-3-PyP produced the highest rate of ascorbate oxidation and oxygen consumption. A combination of 5 μ M MnTE-2-PyP and 1 mM Asc had the highest cytotoxic efficiency in PII, MDA and HBL100 cell lines and gave the greatest cell proliferation inhibition in PII cells. The lipophilic MnTnHexOE-2-PyP and MnTnOct-2-PyP showed greatest cellular accumulation in cells but displayed lower cytotoxicity than MnTE-2-PyP and MnTE-3-PyP which had lower cellular uptake. Addition of catalase prevented cytotoxicity. HBL100 cells were as susceptible to MnP+Asc as PII cells.

Conclusions:

Ascorbate (vitamin C) and MnP redox cycle to generate cytotoxic ROS, mainly H₂O₂. Anticancer efficiency of MnPs correlated with their ability to oxidize ascorbate while differences in uptake and subcellular distribution had a minor effect. This suggests that the main factor determining MnPs' anticancer activity is their redox potential.

Key Words: Ascorbate, Reactive oxygen species, Manganese porphyrins

Funding Agency: Supported by College of Graduate Studies (YM04/14)



Biochemistry

Category: Graduate MSc: Basic Science

28

**Acth regulates adrenal mineralocorticoid receptor protein level:
Evidence and implication**

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Introduction:

Adrenal cortex manufactures glucocorticoids upon stimulation by a pituitary hormone ACTH, and synthesizes aldosterone in response to low Na⁺/high K⁺ in circulation. Aldosterone action is through interaction with mineralocorticoid receptor (MCR) expressed in target cells and protected by 11 β HSD-2 enzyme activity. In perception, adrenal cortex itself is poorly reactive to its own steroids. However, the cortex expresses 11 β HSD-2, suggesting a possible MCR function. Prolonged ACTH-stimulation causes elevated glucocorticoidogenesis and suppresses aldosterone synthase (CYP11B2) gene expression. However, during an initial stage of stimulation (\leq 4 days), the rat adrenal CYP11B2 protein level is maintained and urinary aldosterone is higher than control. Thus, aldosterone action may be involved in glucocorticoidogenesis. We hypothesized that ACTH regulates the adrenal MCR level.

Methods:

Rats were independently injected with 30 μ g ACTH, and 50 μ g dexamethasone (DXM, blocking the pituitary release of ACTH), per 100g BW, and independently given 4% KCl-drinking water, for four consecutive days. Rats injected with saline and received tap-water served as respective controls. Adrenal MCR was studied by immunoblot with actin and renocortical MCR, respectively as loading and positive controls. Aldosterone and corticosterone were respectively measured by RIA and LC/MS. Statistical significance was determined by Student t-test.

Results:

ACTH-rats showed a 68% increase in adrenal MCR level ($P < 0.05$, $n = 7$). However, the MCR level decreased in the DXM-rats by 55% ($P < 0.005$, $n = 5$), but remained unchanged in the KCl-rats ($n = 6$).

Conclusions:

The evidence shows that the adrenal MCR protein level is regulated by ACTH-availability, but not by circulatory K⁺. Aldosterone may play an auto/paracrine role in the initial stage of glucocorticoidogenesis, likely through a MCR-mediated mechanism.

Key Words: Steroidogenesis, Mineralocorticoid receptor, Aldosterone synthase

Funding Agency: Supported by College of Graduate Studies



Biochemistry

Category: Clinical

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Carnitines and amino acids in COPD patients: A metabolomic LC-MS/MS study

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Introduction:

Metabolomic profiling involves studies of small molecules in biological fluids. It reflects metabolic changes of such molecules in the relation to a disease i.e. chronic obstructive pulmonary disease (COPD). The goal of our work was to perform LC-MS/MS metabolomic study to compare the abundance of several small biomolecules such as carnitines and amino acids in COPD patients in comparison to controls.

Methods:

The dried blood spot samples collected from COPD patients (n=24) and healthy controls (n=10) were simultaneously analyzed for free carnitine (CO), acylcarnitines (AC) and amino acids (AA) by liquid chromatography-tandem mass spectrometry. The concentrations of the diagnostic biomolecules in blood samples were automatically measured by NeoLynx software and were expressed as $\mu\text{mol/l}$.

Results:

COPD patients showed lower free carnitine levels 23.7 (15.4; 44.2) compared to controls 33.4 (19.10; 47.6). The total carnitines levels (free carnitine and acylcarnitines) (AC Total) for COPD and controls were 38.28 and 45.44 $\mu\text{mol/l}$, respectively. The free carnitine/ AC ratios (Co/AC) for the two groups were 0.59 and 0.73, respectively ($p=0.001$) indicating significant differences between groups. The total concentrations of amino acids including (alanine, valine, phenylalanine, tyrosine and leucine) were 491.54 and 590.35 $\mu\text{mol/l}$, respectively indicating significant low levels of amino acids in COPD patients ($p=0.039$). Gender and BMI had no significant effects on the results (Gender: $p = 0.387$; BMI: $p = 0.502$), whereas FFMI (fat-free mass index) had a positive effect on alanine levels in COPD patients (Spearman's coefficient 0.478, $p=0.021$).

Conclusions:

COPD is a chronic disorder associated with carnitines and amino acids deficiency which may be responsible of respiratory muscle weakness and morbidity. Carnitines and amino acids profiles may be useful for assessment of pulmonary status of COPD patients and supplementation may be recommended.

Key Words: COPD; Metabolomics; LC-MS/MS

Funding Agency: None



Biochemistry

Category: Basic Sciences

30

Do SOD mimetics protect against hydrogen peroxide?

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Introduction:

Hydrogen peroxide (H₂O₂) is a relatively stable intermediate of oxygen's reduction to water. As a potential source of hydroxyl radical, it is regarded as an extremely potent cell-damaging agent. In addition, it affects various redox-sensitive transcription factors and signaling pathways. It is claimed that the biological activity of superoxide dismutase (SOD) mimetics is due to their ability to catalytically decompose H₂O₂, i.e. act as catalase. Incorrect assignment of activity introduces not only confusion to the field and jeopardizes mechanistic considerations, but also hampers redox-based drug development. The aim of the present study was a comprehensive evaluation of the catalase activity of different classes of SOD mimics.

Methods:

H₂O₂ decomposition was measured by the production of O₂ using an oxygen monitoring system. The in vivo ability of the compounds to protect against H₂O₂ was assessed using catalase/peroxidase-deficient E. Coli mutants.

Results:

The k_{cat} (H₂O₂) for cationic Mn(III) N-substituted pyridylporphyrins (MnPs) of high SOD-like activity ranged from 23 to 88 M⁻¹s⁻¹. Analogous Fe(III) N-alkylpyridylporphyrins (FePs) showed about 10-fold higher activity than the corresponding MnPs, but the values were still 4 orders of magnitude lower than that of catalase (1.5 × 10⁶ M⁻¹s⁻¹). None of the tested SOD mimetics protected the catalase/peroxidase-deficient E. Coli mutants against H₂O₂.

Conclusions:

None of the SOD mimetics can catalytically decompose H₂O₂ with a rate high enough to compete with natural enzymes. Beneficial effects of such compounds can be attributed to scavenging of superoxide and peroxynitrite, but not to protection against H₂O₂.

Key Words: hydrogen peroxide; SOD mimetics; porphyrins

Funding Agency: Kuwait University grant MB02/12



Community Medicine

Category: Undergraduate

31

Patients' attitude toward medical student in Kuwait teaching hospitals

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Introduction:

Bedside teaching is essential to the education of medical students. Patients' cooperation with medical students is required to improve communication and promote clinical learning. Objectives: To assess the level of acceptance of patients to involve medical students in the clinical procedures performed on them, and study their attitudes toward students.

Methods:

This cross-sectional survey was conducted on 318 inpatients (121 general medicine, 197 general surgery) from four teaching hospitals. A self-administered questionnaire was used to collect data. An attitude score was devised based on 17 items. A logistic regression model was used to assess the association between patients' attitudes and patients' demographic and their acceptance to medical students.

Results:

The median attitude score of inpatients toward medical students was 12 out of 17, which is considered relatively low. However, the median overall acceptance level of patients for medical students was 80%. A high proportion of patients (91%) were not informed about bedside teaching. There was significant correlation between overall acceptance level of patients to students and patient's attitude score (Spearman rank correlation, $r_s=0.493$, $p=0.001$). The main reason for positive attitude was to help students in their education (86.5%), while for negative attitude was that students lack the experience to handle patients (44.3%). The logistic regression analysis showed that level of education (OR=2.688, $p=0.014$), patients who accept students in their clinical encounters (OR=9.003, $p=0.005$), patients who allow students to access their medical records (OR=3.508, $p=0.049$), and patients who allow students to examine them (OR=3.301, $p=0.004$) were independently associated with patients' positive attitudes after adjusting for confounding.

Conclusions:

A relatively low median attitude score of inpatients toward medical students was concluded. This result invites medical education authorities and Ministry of Health in Kuwait to establish a protocol to organize the relationship between patients and students, improving clinical teaching methods.

Key Words: Medical Students, Inpatients', Attitudes

Funding Agency: None



Community Medicine

Category: Undergraduate

32

Prevalence of obstructive sleep apnea risk and associated factors among working population in Kuwait: A cross-sectional study

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Introduction:

Obstructive sleep apnea (OSA) is characterized by frequent episodes of upper airway collapse during sleep leading to airflow cessation or reduction. Worldwide, OSA affects up to 7% of the general population with certain subgroups being at increased susceptibility. It has been shown that OSA is a risk factor for multiple adverse health conditions. This study aimed at estimating the prevalence of OSA and identifying factors associated with OSA in Kuwait.

Methods:

A cross-sectional study among working population in Kuwait was conducted (n = 651). The Berlin questionnaire was used to identify participants at high and low risk for OSA. Associations between potential risk factors and health consequences with OSA risk were evaluated using logistic regression. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were quantified.

Results:

The prevalence of high-risk OSA was estimated to be 13.8% in the total study sample, with more males (18.0%) than females (11.4%) being at higher risk for OSA (p-value = 0.02). The prevalence of high-risk OSA showed an increasing trend with age (p-value < 0.001). Diabetes was associated with increased odds of high-risk OSA (aOR = 2.95, 95% CI: 1.53 – 5.69, p-value = 0.001). Moreover, increased body mass index (BMI) was associated with high-risk OSA: overweight (aOR = 1.65, 95% CI: 0.86 – 3.15, p-value = 0.126), obese (aOR = 3.20, 95% CI: 1.55 – 6.61, p-value = 0.001), and morbidly obese (aOR = 5.12, 95% CI: 2.28 – 11.53, p-value < 0.001). In contrast, involvement in vigorous physical activity at least once per week was associated with decreased odds of OSA risk (aOR = 0.51, 95% CI: 0.32 – 0.83, p-value = 0.007).

Conclusions:

The prevalence of being at high-risk for OSA (13.8%) among the working population in Kuwait is nearly double the global average of 7%. Age, diabetes, and BMI were associated with increased risk for OSA; whereas, being physically active associated with reduced risk of OSA.

Key Words: Obstructive sleep apnea; Prevalence; Risk factors

Funding Agency: None



Community Medicine

Category: Undergraduate

33

Sociodemographic profile and coping strategies of mothers with children suffering from ASDs in Kuwait.

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Introduction:

Autism spectrum disorders (ASDs) affect approximately 60-70 of 100,000 children in developed countries; limited data is available on the prevalence of ASDs in developing countries. Raising a child with ASD places a significant burden on the family and increases stress levels of the primary caregivers. The purpose of this study was to provide a general profile of families of children with ASDs in Kuwait, emphasizing their sociodemographic characteristics and coping strategies used by mothers.

Methods:

All 25 schools enrolling children with ASDs were approached; 23 participated. 198 of 547 mothers of children with ASDs completed a questionnaire that assesses their sociodemographic characteristics, perinatal factors surrounding the birth of their autistic child, family management, and coping strategies (using the Brief COPE questionnaire).

Results:

Our study found that the majority of children with ASDs are male (79.6%). 84.3% of mothers reported to be the primary caregivers of their child. The majority (62.4%) said that their ability to perform social duties had decreased, and 50.5% reported that their ability to take care of themselves had decreased. 57.7% stated that their ability to enjoy life decreased; it had decreased more among non-Kuwaiti mothers than Kuwaiti mothers (p-value= 0.03), and among mothers with a bachelor's degree or higher (p-value=0.011). Results of the COPE questionnaire showed that "Religion", "Acceptance", and "Positive Reframing" were the 3 most common strategies used for coping with a child suffering from ASD. Finally, 83.9% reported the need for spousal support to help them cope, while 79.4% needed support from medical staff.

Conclusions:

Mothers suffer from considerable stress while trying to raise a child with ASDs, and measures should be taken to ensure adequate family and professional support is provided to help them cope.

Key Words: Autism; Coping; Profile

Funding Agency: None



Community Medicine

Category: Undergraduate

34

Perception of body image among adult residents of Kuwait

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Introduction:

With the increase in prevalence of obesity, body image dissatisfaction and the factors affecting it lead to a desire to have a thin body worldwide. Our objectives are to assess the prevalence of body image dissatisfaction among Kuwaiti adult residents, investigate the Feel-Ideal Difference (FID) association with body image dissatisfaction. Examine the association between gender and body image dissatisfaction, along with the socio-demographic factors influencing it.

Methods:

Our study included a cross-sectional survey that was conducted on 1016 adult residents, aged 21 and above, who visited a total of 12 co-ops in Kuwait. A self-administered questionnaire was used to collect data. It includes 38 questions on socio-demographic, diet, exercise, and body image related questions. Body image questions and body mass index (BMI) were compared with silhouettes body image figures and an (FID) index score was established by subtracting the score of the silhouette selected as 'Ideal' from the one selected as representing them currently, or 'Feel', and taking the absolute difference. We hypothesized that a higher FID index score is associated with more body image dissatisfaction.

Results:

The median (IQR) for the FID was 1.0 (1) and 2.0 (1) for the satisfied and not satisfied participants, respectively. A multinomial logistic regression model was used to study the association between body image dissatisfaction and other variables, adjusting for other covariates. It showed that for every 1 unit increase in FID score, the odds of being not satisfied (sometimes satisfied) about body image would be 2.4 (1.516) times more likely, compared to being satisfied, when all other variables in the model are held constant.

Conclusions:

The prevalence of body dissatisfaction in our population was (30.4%). FID score was significantly associated with more body image dissatisfaction. The odds of non-Kuwaiti Arabs to be dissatisfied of their body image is twice that for Kuwaitis.

Key Words: Kuwait, Body Image, Perception

Funding Agency: None



Community Medicine

Category: Undergraduate

35

Mistimed and unwanted pregnancies among postpartum women in Kuwait

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Introduction:

Background: Contraceptive use for spacing and preventing unwanted pregnancies is an important issue for women and their families all over the world.

Objectives: The main objective of this study was to assess the self-reported occurrence of mistimed and unwanted pregnancies with regards to traditional versus modern contraceptive methods among postpartum women in Kuwait. An additional objective was to examine the association of sociodemographic characteristics with the use of contraceptives and their effectiveness.

Methods:

Postpartum women in Kuwait were approached in all of the 4 government hospitals that have maternity wards through a face to face interview. A total of 643 were approached, 612 (95 %) of whom participated. A questionnaire based on the 2008 DHS Egypt Survey was developed.

Results:

Almost all women knew of at least one contraceptive method, while around 61% (n=375) had ever-used at least one method. Of all the methods, oral contraceptive pills were the leading method known by 95.9 % and ever-used by 34.3% of all the women. Among ever-users, 45.6 % reported their last child as unplanned; 20.5 % as mistimed and 25.1 % as unwanted. About 69.8% of those who were using a modern contraceptive method when they became pregnant did not want their last pregnancy at all compared with 45.1% women using traditional contraceptives. Irregular use as well as method failure resulted in unplanned pregnancies. Age and parity were positively associated while education and work participation were inversely associated with unplanned pregnancies.

Conclusions:

Although most women are aware of at least one method of contraception and the government provides free supply of contraceptives, there is a high unmet need among women in Kuwait that deserves policy intervention.

Key Words: Contraception; Unmet need; Unplanned

Funding Agency: None



Community Medicine

Category: Clinical

36

Majorana as an organic food preservative for milk products and cereals

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Introduction:

Many food products are perishable by nature and require protection from spoilage during preparation, storage and distribution. We aimed to evaluate the use of *Origanum majorana* hydrosol, oil and leaves as an organic food preservative in milk products and cereals after their storage for different periods.

Methods:

In this prospective, controlled study, *Origanum majorana* leaves were washed, air-dried and cut into small pieces and properly stored till use. Hydrosol and oil were prepared by hydrodistillation method. Different concentrations of different *Origanum* forms were added to milk products (white, ras and kareesh cheeses) and cereals (corn and wheat) and were monthly assessed microbiologically and organoleptically for 6 months.

Statistics: Kruskal Wallis, T-test and chi square tests were used for comparing continuous data and categorical data respectively with P value <0.05 to be significant.

Results:

The % of acceptable organoleptic properties of cheese samples treated with different forms and concentrations were significantly lower when compared to the control ($P < 0.05$), in case of the color of cheese samples treated with medium (66-70.4%) and high concentrations (15-25.9%) of leaves; the texture of treated samples with high concentrations of hydrosol (32-37.1%) and leaves (12-33.3%); the odor in samples treated with high concentrations of oil (50.5-51.9%) and hydrosol (49-51.8%) and finally in case of taste of samples treated with the high concentrations of all forms. The oil was more effective microbiologically than other forms. High concentration of all forms was successful in suppressing mesophiles below the limit of detection in all cheese samples except kareesh cheese ($p < 0.05$). Medium and high concentrations of leaves were the most effective in reducing mesophiles in wheat and corn samples compared to the control ($p < 0.05$).

Conclusions:

As bio preservative, we recommended *Origanum* oil (medium) for milk products and (high) leaf concentration for cereals.

Key Words: Origanum; Food preservation; Community

Funding Agency: None



Community Medicine

Category: Clinical

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Chicken and meat products preservation by *origanum majorana*

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DDI

Introduction:

Many food products-as meat and chicken-are perishable by nature and require protection from spoilage during preparation, storage and distribution .We aimed to evaluate the use of *origanum majorana* (hydrosol, oil and leaves) as an organic food preservative in chicken and meat products after their storage for different periods.

Methods:

In this prospective controlled study, *origanum* leaves was washed, air-dried and cut into small pieces and stored at room temperature in triple opaque plastic bags till use. Hydrosol and oil were prepared by hydrodistillation. Different concentrations (low oil, 0.062 mg/kg; medium oil, 0.125 mg/kg and high oil, 0.250 mg/kg) of different equivalent forms were added to chicken and meat products (minced and burger) and were assessed monthly for 6 months.

Results:

Both medium and high concentrations of all *origanum* forms were successful in suppressing aerobic mesophiles in beef burger and chicken samples -but not in minced meet-especially at 6th month of storage when the count reached below the limit of detection. Mesophilic counts in all treated samples were significantly lower than zero time values and control ($p < 0.05$). We observed significant continuous reduction in yeast and mold counts in minced meat compared to zero time values; and after one month of storage vs. the control till it reached below the limit of detection in oil and hydrosol treated samples at the 6th month especially with high oil concentration(1-2%)($p < 0.05$). We could not detect any mold or yeast at 6th month of storage in all treated chicken and beef burger samples; and the higher the concentration of the additive the earlier the disappearance of mold and yeast($p < 0.05$).

Conclusions:

As bio preservative, we recommended *origanum* oil(medium concentration) for chicken and meat products.

Key Words: Origanum; Food preservation; Community

Funding Agency: None



Community Medicine

Category: Clinical

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Management of chronic non cancer pain in global cities: Current services and process.

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Introduction:

The universal burden of pain and demonstration of effective management protocols for chronic non-cancer pain makes this a global priority. Yet several international organizations have reported slow transformation of pain management practices. Health systems play important roles in co-locating care resources and provision of globally recognized standards of care. There are no published studies of pain management services in Kuwait. This study aims to apply evaluation theory for assessing health system services in global city settings. The goal is to create a hybrid evaluation framework for characterizing quality of the output of structures, and processes, associated with chronic pain management services in global city settings. Observations made in Kuwait will be juxtaposed with observation in Toronto, Canada.

Methods:

Semi-structured interviews with key-informants are being used to characterize clinical services for chronic pain management in Kuwait and in Toronto. Key-informants are directors of clinics specializing in pain management located in those cities. Qualitative analysis of interview transcripts is being used to explore how local context and capabilities facilitate or impede development, deployment and accessibility of the ideal comprehensive patient-centered chronic pain management protocols currently being advanced as an international standard of care.

Results:

Data are being analyzed qualitatively to explore barriers to delivery of the internationally accepted standards of care. A combination of Donebedian and Logic model frameworks are used to organize analysis themes related to structure, process, and output elements in pain clinics. Barriers are related to infrastructure, services, education and research capacity themes.

Conclusions:

Health system structures and processes of those settings have impact on pain management outputs. Similar procedures are applied in the two cities but important differences are observed.

Key Words: Chronic non-cancer pain; Management; Kuwait

Funding Agency: None



Community Medicine

Category: Undergraduate

39

Knowledge levels, risk perceptions, and prevention methods regarding Ebola virus disease among primary health care physicians in Kuwait

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Introduction:

Primary health care physicians are the first high-risk front that are exposed to Ebola virus disease (EVD) patients. Little is known about their level of knowledge, risk perceptions, and prevention methods regarding EVD. The aim was to evaluate the knowledge level of primary care physicians (general practice and family medicine), investigate their perception about the risk of EVD and its prevention methods.

Methods:

This cross-sectional survey was conducted on 304 primary care physicians (230 general practice, 74 family medicine) from 51 centers, which represent 55% of primary health care centers in Kuwait. The sample represents 34.2% of primary care physicians in Kuwait. Data were collected through a self-administered questionnaire, which consisted of 4 sections: socio-demographic and work-related characteristics, knowledge, perception, and prevention methods regarding EVD. A knowledge score was devised based on 55 items.

Results:

The median knowledge score was 35 out of 55, which is relatively low. There was no significant difference in the knowledge level between general practice and family medicine physicians, who are supposed to be more knowledgeable due to their longer formal training. Moreover, there was no significant association between the knowledge level about Ebola and socio-demographic characteristics of physicians. However, there was significant difference in knowledge level according to rank (Kruskal-Wallis test, $p=0.046$), and governorate (Kruskal-Wallis test, $p=0.006$). A proportion of physicians failed to correctly respond to fundamental knowledge items, such as diagnostic methods for Ebola (27.9%) and case-fatality rate (13.7%).

Conclusions:

A relatively low knowledge score about EVD was found among primary care physicians in Kuwait. This result invites health authorities to launch awareness campaigns to promote the knowledge level of this high-risk group about Ebola and issue guidelines and public health policies for health workers.

Key Words: Primary health care physicians, Knowledge levels, risk perceptions, Prevention

Funding Agency: None



Dentistry

Category: Clinical

40

Caries status among kindergarten children in Kuwait

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Introduction:

Objectives: The aim of this study was to investigate the caries prevalence and severity in kindergarten children in Kuwait.

Methods:

In a cross sectional survey, a representative sample of 808 children were chosen from 23 kindergarten schools in Al-Farwaniya governorate in Kuwait. Two dental hygienists examined the children at their schools. Examination was done using mirror and periodontal probe with the presence of artificial light source on a portable dental chair. Dental data collected were: decayed, missed, and filled teeth along with other socio-demographic data.

Results:

In 2010, eight hundred and eight children were examined with the mean age of the children that were examined was 3.7 ± 1.1 years. Male children were 46% (n=370) and females were 54% (n=438). Caries prevalence in 4 year olds children was 61%. Children without caries experience were 39%. The mean dmft was 4.3 ± 5 . The mean decayed teeth were 4 ± 4.7 , the mean missing teeth 0.2 ± 0.7 , and the mean filled was 0.2 ± 0.7 . No statistical significant differences were seen between genders; both gender had almost similar caries prevalence and caries severity.

Conclusions:

Caries prevalence and severity in kindergarten school was high among the examined group. These results indicate an urgent need for a prevention program in Kuwait to control early childhood caries. Oral prevention program for children in age group of 1 to 4 years should be planned in future.

Key Words: Kindergarten; Caries prevalence; Dmft

Funding Agency: None



Dentistry

Category: Undergraduate

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A comparison of treatment experience between invisalign aligner and fixed appliance therapy

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Introduction:

Recent developments in the field of orthodontics have led to changes in patient interests in the provided treatment. Invisalign, a new treatment option, allows patients to enjoy better esthetics. Our aims are to (1) record and compare patients' experiences toward Invisalign and the buccal fixed appliance and (2) provide the general practitioners and orthodontist with a reference to help patients decide on the treatment modality that satisfies their needs.

Methods:

Data was collected through a questionnaire to 60 subjects, 30 in the Invisalign group and 30 in the buccal fixed appliance group. The study followed an observational design. Participants were asked about general activity, disturbances in eating, oral symptoms, treatment satisfaction, pain and analgesics.

Results:

Invisalign patients showed significantly more difficulty in speech ($p=0.035$), necessitating change to speech delivery ($p=0.003$). They reported better chewing ability ($p<0.001$) without restriction on amounts or types of food ($p=0.02$). Less mucosal ulcerations were also seen in the Invisalign group ($p=0.01$). No significant differences were found for general activity, other oral symptoms or treatment satisfaction. In addition, pain and analgesic use were the same between groups; however, pain lasted longer in the fixed appliance group ($p=0.022$).

Conclusions:

Adult patients treated with Invisalign reported more speaking difficulties, fewer limitations in food consumption, less mucosal ulcerations, and shorter pain duration than those treated with a buccal fixed appliance. Invisalign is no necessarily more pleasant, but could be more tolerable as it satisfies patient needs over food consumption, absence of mucosal ulcerations, and shorter pain duration.

Key Words: Buccal fixed appliance, Invisalign, Comparison

Funding Agency: None



Dentistry

Category: Basic Sciences

42

Xylitol content of chewing gums in middle-east markets: A comprehensive study

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Introduction:

Xylitol, a five-carbon sugar polyol is used as a natural sweetener in sugar-free chewing gums. Habitual consumption of xylitol containing chewing gums has been found to be effective in preventing dental caries. Xylitol is not fermentable by oral bacteria and makes mutans streptococci (MS) less adhesive to teeth. Objective: To measure the xylitol content in “sugar free” chewing gums available in the market of Gulf Cooperation Council (GCC) countries, Middle-East, in order to identify those products that can provide the recommended daily dose of xylitol for caries prevention (6-7g). The acid production from chewing gums was detected in vitro and in vivo.

Methods:

Twenty-one chewing gums containing xylitol were identified and collected from GCC market: Kuwait, Bahrain, Qatar, Saudi Arabia, UAE, Oman. Xylitol was extracted and its concentration was analyzed using special enzymatic kit. The pH of extracts was measured during 30-min incubation with *Streptococcus mutans*. Four subjects were taken to check if there is any change in saliva and plaque pH after the consumption of highly concentrated xylitol gums.

Results:

The xylitol content in grams was clearly mentioned on one product's label. Twelve products stated the percentage of xylitol (3.5% to 35%). The rest did not specify the amount. The mean measured weight of one gum piece was 1.67g ±0.38. The mean measured xylitol content/piece was 0.33g ±0.21. Xylitol content was <0.3 g/piece in 10 products, 0.3-0.5g/piece in 6 products, and >0.5 g/piece in 5 products. None of the highly concentrated xylitol gums showed pH drop in vitro or in vivo. One chewing gum, contained xylitol and glucose, resulted in low pH level (<5.5) when tested in vitro.

Conclusions:

The majority of xylitol chewing gums sold in GCC market does not provide the consumers with the recommended daily dose of xylitol for caries prevention. A better labeling on the product is also recommended.

Key Words: Xylitol; Caries prevention; Food labeling

Funding Agency: The study was funded by Kuwait University grants -DD02/13, GD01/11, SRUL02/13.



Dentistry

Category: Basic Science

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Oral health knowledge and behavior among 12-year old female students

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Introduction:

In Kuwait, the School Oral Health Program (SOHP) has well established oral health education department which conducts various oral health promotion activities targeting community as a whole and school children in particular.

Objective: To assess the oral health knowledge and behavior of 12-year olds female students in Kuwait. To evaluate the oral health promotion program in the SOHP.

Methods:

From 2011-2012, 977 self-reported questionnaire were answered by a convenience sample of female students belonging to middle schools either at the SOHP centers or in their schools. All the 6 governorates in Kuwait were included in this cross-sectional study. Seventeen oral health knowledge and 8 behavior questions were included in the questionnaire. These questions were focused on the oral health education information that had been delivered to schoolchildren by the SOHP oral health promotion team.

Results:

977 female students aged 12.8±2.3 participated in this study. Overall, 40% of mothers and 43% of fathers had bachelor degree. Almost half of the questionnaires were answered at the SOHP centers (44%) and half at the schools (55%). The most of the participants were from Al-Ahmadi (25%) and Al-Jahraa (24%) governorates. Knowledge questions were answered correctly by 65% of the students. Almost half (44%) brushed their teeth twice a day and 66% of the participants did not use floss. Only 33% visited the dentist for routine check-up. Half of the participants visited the dentist in last 6-months.

Conclusions:

Oral health knowledge among 12-year olds female students was satisfactory. This is not reflected in their oral health behavior which was not satisfactory. More efforts should be laid in future toward improving the oral health behavior of our schoolchildren.

Key Words: Oral health knowledge; Oral health behavior; Schoolchildren

Funding Agency: None



Dentistry

Category: Clinical

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Dental Fear among Dentists in Kuwait

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Introduction:

Dental fear is a universal problem and has been identified as a significant barrier to accessing dental care. Dental fear is a major problem encountered in the general population as well as among health care professionals. The aim of this study was to assess dental fear among the dentists in Kuwait.

Methods:

The study included 106 dentists; 53% dental specialists and 47% general dentists working in Kuwait. About 45% were Kuwaiti dentists and 55% were non-Kuwaitis. The majority of dentists were male (62%) and 38% were females. These dentists completed the Dental Fear Survey (DFS) questionnaire relating to their fear and anxiety. The chi-square test was used in the analyses.

Results:

About 43% of the dentists replied that they do not visit the dentist regularly for their own dental care. Significantly more general dentists (28%) indicated that they were afraid of visiting the dentist due to fear as compared to only 4% of specialists ($p < 0.001$). Also, more general dentists (44%) recalled bad dental experience during their childhood than the specialists (20%) ($p = 0.006$). Almost half (46%) of Kuwaiti dentists expressed nervousness or apprehension during their dental visit as compared to 24% among non-Kuwaiti dentists ($p = 0.016$). A quarter of the female dentists (25%) were afraid of visiting a dentist for dental care compared to about one-tenth of the male dentists (9%) ($p = 0.028$). The anaesthetic needle was the most fear-provoking stimuli among the dentists and nearly two-thirds recounted fear from the sight and sensation of the needle. Fear and anxiety were more frequently encountered during the treatment procedures among the dentists.

Conclusions:

Dental fear was a common problem encountered among the dentists in Kuwait. This may lead to the avoidance or delay in seeking the needed dental care by the dentists.

Key Words: Kuwait, Dental fear, Dentists

Funding Agency: None



Dentistry

Category: Clinical

45

Infant feeding practices among disabled and normal children in Kuwait

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Introduction:

Infant feeding practice is an important predictor of the future caries risk of children. The aim of this study was to describe infant feeding practices among disabled and normal children in Kuwait.

Methods:

This study involved 211 children with a physical disability, 97 with Down syndrome and 112 normal children. The parents completed a structured anonymous questionnaire about the feeding practices of their children. Chi-square and z-tests were used in the analysis.

Results:

A significantly higher proportion of physically disabled children (31%) were weaned from the bottle beyond the age of one year and had taken a bottle at bed time at night, left with the child, compared to both Down syndrome and normal children (20%) ($p = 0.023$). Physically disabled children were also older when permanently relinquishing the nursing bottle, while this happened after the age of two years in 24%, compared with 19% of Down syndrome and 11% of normal children ($p = 0.023$). A higher proportion of normal (34%) and physically disabled children (30%) had a bottle at bed time compared to those with Down syndrome (21%) ($p = 0.001$). Down syndrome children (17%) had a bottle left with the child at bed time more often compared to the physically disabled (14%) and the normal children (10%) ($p < 0.01$). A higher proportion of parents of disabled children with no education or with primary school education (26%) had left the bottle at bed time with the child compared to the parents with university education (7%) ($p < 0.01$). Shorter times for breast and bottle feeding were common among the normal children as the majority were weaned from bottle feeding by 18 months.

Conclusions:

The disabled children had poor infant feeding practices. The parents of the disabled children should be given health education on the healthy feeding practices of their children.

Key Words: Normal children, Infant Feeding Practices, Disabled children

Funding Agency: None



Dentistry

Category: Basic Science

46

**Evaluation of preventive services of school oral health program,
Kuwait**

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Introduction:

Aim: To evaluate the preventive services delivered through the School Oral Health Program, Kuwait (SOHP).

Methods:

This program provides oral health education, prevention, and treatment to almost 280,000 public schoolchildren in Kuwait. Preventive procedures performed under this program are bi-annual application of fluoride varnish along with placement of pit and fissure sealants on newly erupted permanent molars and pre-molars to all the children with positive consents. These services are evaluated on regular basis. Sealants are evaluated for quality on short-term and long-term basis. Outcome evaluation of these services is performed once in 5-6 years by performing oral health surveys among school children. Last survey was conducted during 2012-2013.

Results:

During recent years the SOHP has improved its coverage of children with prevention up to 80%. This has resulted in a considerable reduction in treatment needs which is evident from reduced number of composite restorations performed under this program during the last 6 years. More than 80% of the pit and fissure sealants are retained for at least one year after placement. Combination of all these factors has resulted in decreasing the severity of dental caries among school children.

Conclusions:

Improving the prevention coverage with proper follow-up of preventive services is key to success of this program.

Key Words: School children; Sealants; Fluoride varnish

Funding Agency: None



Dentistry

Category: Clinical

47

Effect of turmeric on oral lichen planus erosive-erythematous form: A case series study.

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Introduction:

Oral lichen planus is a chronic inflammatory oral condition. Its pathogenesis is attributed to secondary modification of keratinocyte surface antigens for which it's a primary target for cytotoxic cellular response. Steroid is the mainstay treatment albeit; minority OLP cases are poorly responsive. Turmeric is herb known for its medicinal properties due to its proven anti-inflammatory, anti-oxidant, and antimutagenic properties. The aim is to evaluate therapeutic effect of Turmeric on reluctant OLP lesions.

Methods:

A nine-month-study was carried out at Amiri Dental Center. A total of 7 patients (3 male and 4 female), aged between 27 and 69 years, fulfilling the diagnostic criteria for OLP were enrolled. All patients were nonsmoker. Each patient had a prescription of Turmeric capsule (500mg) to be used once daily for three months along with their usual Fluocinonide (0.05%) cream or/and Dexamethasone elixir 2.0mg/5ml. The symptoms and clinical sign of OLP lesions were followed by Thongbrasom modified OLP score and visual analogue scale (VAS) over 3, 6, and 9 months after Turmeric use.

Results:

Pre-Turmeric stage, erosive form was the most common clinical type seen in 5 (71.4%) followed by erythematous form 2 (28.6%) patients. Throngprasom score revealed; 5 (n=2), 4 (n=3) and 3 (n=2). All were moderately-severely symptomatic (average VAS= 8). Three months post-Turmeric therapy, those with Throngprasom score 5 and 4 regressed to score 2 in 2 patients, score 1 in 2 patients and score 0 in 1 patient. Those with score 3 reverted to score 1. All became less symptomatic with average VAS was 1. At 6-9 months, most OLP lesions were stable. The employ of topical steroids were significantly reduced. Only one patient was disease free.

Conclusions:

This study reveals the potential therapeutic effect of Turmeric on patient with erosive and erythematous OLP. Turmeric markedly abates OLP symptoms and does improve oral intake.

Key Words: Steriods, Oral Lichen Planus, Turmeric

Funding Agency: None



Dentistry

Category: Basic Science

48

Evaluation of stainless steel crowns on permanent teeth in the school oral health program, Kuwait

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Introduction:

To evaluate SSCs placed on young permanent posterior teeth.

Methods:

Children were randomly selected from the existing clinical records at the School Oral Health Program (SOHP). Inclusion criteria was: children who received at least one SSC on permanent teeth not less than 6 months from the date of examination. Clinical and radiographic examination was done by four calibrated dentists in a dental clinic. Clinical data was collected on extension and marginal adaptation of crowns, proximal contact, oral hygiene status, periodontal status, and dental caries. Radiographs were used to evaluate the extension and adaptation of crowns and the interproximal bone levels.

Results:

In this study, 465 children with 561 SSCs were included of which 59% were females and 41% were males. The mean age at examination was 10.4 ± 6.2 years. Mean duration of the examined crowns was 15.6 ± 11.7 months. The mean DMFT was 7 ± 4.2 . Half of children had poor oral hygiene. Only, 1.4% of the examined teeth had pocket depth < 3.5 mm and > 5.5 mm. Almost, 72% of crowns had proper extension and 26% had good marginal adaptation. Radiographic examination revealed that most did not have interproximal bone resorption (92%).

Conclusions:

Results were satisfactory which indicates the success of SSCs on young permanent teeth. Marginal adaptation was not ideal in most of the cases which can be attributed to the continuous eruption of these teeth. Success rate can be further improved by improving the oral hygiene status of these children.

Key Words: Stainless steel crown; Marginal adaptation; Oral hygiene

Funding Agency: None



Dentistry

Category: Basic Sciences

49

Co-aggregation and biofilm growth of granulicatella spp. with fusobacterium nucleatum and aggregatibacter actinomycetemcomitans

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Introduction:

Members of Granulicatella and Aggregatibacter genera belong to normal oral flora bacteria that cause infective endocarditis. Aggregatibacter actinomycetemcomitans has long been implicated in aggressive periodontitis, whereas DNA-based methods only recently showed an association between Granulicatella spp. and dental diseases. As bacterial coaggregation is critical for multispecies biofilms, our objective was to study coaggregation and biofilm formation patterns of Granulicatella spp. with A. actinomycetemcomitans in comparison with the multipotent coaggregator Fusobacterium nucleatum.

Methods:

For coaggregation, each bacterial strain was mixed with a partner species and OD600 was measured every 15 min for 2 h. Microscopy was used as a surrogate method to evaluate coaggregation. Mono- and dual-species biofilms grown in brucella broth in 24-well plates for 3 days in anaerobiosis were quantified by crystal violet staining and the absorbance read at 590 nm.

Results:

Fn exhibited significantly ($p < 0.05$) higher autoaggregation than all other test species, followed by Aa SA269 and Ge. Aa CU1000 and Ga did not autoaggregate. Ge with Fn exhibited significantly ($p < 0.05$) higher coaggregation than most others, but failed to grow as biofilm together or separately. With Fn as partner, Aa strains SA269, a rough-colony wild-type, and CU1000, a smooth-colony variant, and Ga were the next in coaggregation efficiency. These dual species combinations also were able to grow as biofilms. While both Ge and Ga coaggregated with Aa strain SA269, but not with CU1000, they both grew as biofilms with either of the Aa strains.

Conclusions:

Ge failed to form biofilm with Fn despite strongest coaggregation with it. The ability of Granulicatella spp. in general to coaggregate and/or form biofilms with Fn and Aa strains hint at the possibility that Granulicatella spp. have the potential to integrate into dental plaque biofilms.

Key Words: Endocarditis, Coaggregation, Granulicatella

Funding Agency: Kuwait University General Facilities grant GD01/11



Dentistry

Category: Basic Sciences

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Quantification of biofilm and planktonic life forms of co-existing periodontal species

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Introduction:

Complexity of oral polymicrobial communities has prompted a need for developing in vitro models to study behavior of coexisting bacteria. Little is known of in vitro co-growth of several periodontitis-associated species without early colonizers of dental plaque.

The Objective was to determine temporal changes in the quantities of 6 periodontal species in an in vitro biofilm model compared to parallel planktonic cultures and to assess their quantities in subgingival plaque and saliva, the natural representatives for the two bacterial life forms.

Methods:

Porphyromonas gingivalis (Pg), *Aggregatibacter actinomycetemcomitans* (Aa), *Prevotella intermedia* (Pi), *Parvimonas micra* (Pm), *Campylobacter rectus* (Cr) and *Fusobacterium nucleatum* (Fn) were anaerobically grown as mono- and multispecies biofilms and parallel planktonic cultures. After incubating 2, 4, 6, 8 days, the target species were quantified using qPCR with 16S rDNA primers. Periodontal species were also quantified from plaque and saliva samples from five non-periodontitis subjects by using qPCR as above.

Results:

The six species were found throughout 8-day period in all culture conditions, except Pg and Fn in multispecies planktonic cultures at day 8. In multispecies biofilm, Pg counts significantly increased from day 2 to day 8 and were higher ($P < 0.05$) than those of Aa and Cr, whereas in monospecies biofilm, Pg counts were lower ($P < 0.05$) than those of the other species, except Aa. Aa, Pm and Cr had higher ($P < 0.05$) counts in both mono- and multispecies planktonic cultures compared to respective biofilms. Aa, Pm, Fn and Cr were found in all subjects. The mean quantities of Aa and Pi were higher ($P < 0.05$) in subgingival samples than in saliva while those of Fn and Cr vice versa.

Conclusions:

Six periodontal species were able to form multispecies biofilm up to 8 days in vitro without pioneer plaque bacteria. Pg seemed to prefer multispecies biofilm environment whereas Pm and Aa planktonic culture.

Key Words: Plaque, Biofilm, Periodontitis

Funding Agency: Kuwait University General Facilities grant GD01/11



Dentistry

Category: Basic Sciences

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Nanoscale characterization of dental materials

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Introduction:

The aim of this study was to establish if quantitative atomic force microscopy (AFM) could be used to measure the material properties of dental materials at the nanoscale.

Methods:

We employed bimodal nanomechanical force microscopy (Asylum MFP-3D AFM, Oxford Scientific Instruments, fitted with an AMFM head) to examine the flat surfaces of standard homogeneous materials (sodalime glass, polycarbonate and polymethylmethacrylate), heterogeneous dental materials such as filled polymers and also dental enamel itself. Thin flat surfaces of each material were prepared. Square grids of 20 μm x 20 μm on these surfaces were examined with 512 taps made per line. Elastic moduli estimates that were obtained were compared to literature values. In addition, we also measured the moduli of some of the materials independently using a universal testing machine.

Results:

Generally, the distribution of the modulus estimations for homogeneous materials were narrow, but not Gaussian because of a common positive skew. The median modulus of polycarbonate was measured by AFM as 2.3 GPa (standard reported as 5.13 GPa; literature values lie below this), PMMA as 2.2 GPa (standard 3.1 GPa) and sodalime glass 73 GPa (literature 67-71 GPa). Heterogeneous materials showed wider distributions, but the capacity of the current experiments as a probe for the modulus depended on filling materials having a low enough modulus not to approach that of the silicon cantilevers used in this study. The median for dental enamel was 75 GPa, corresponding with theoretical predictions (Spears, I.R. J Dent Res 1997;76:1690-1697). Additional support for the theory was the observation that, measured at the nanoscale, the modulus of enamel may range from 20-110 GPa.

Conclusions:

This study verifies the ability of AFM to measure elastic moduli across a wide range and provides the first experimental confirmation of the behavior of enamel at a microstructural level.

Key Words: Dental materials; Atomic force microscopy; Elastic modulus

Funding Agency: Kuwait University General Facilities Project GD02/11



Dentistry

Category: Basic Science

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Oral Health Status Among Adults in the State of Kuwait

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Introduction:

Objectives: To describe the oral health status of adults in Kuwait.

Methods:

In 2011-2012, a cross-sectional study was done at the Ministries Complex in Kuwait. Oral health examination was performed to a convenience sample of adults during morning working hours (N=995). Portable Dental Chairs and light source was used for examinations. Six trained and calibrated dentists performed the examinations. The recording was done on a manual form by trained recorders. Only mouth mirror and periodontal probe (visual examination) was used. Data was collected about dental caries, oral hygiene and periodontal status. Data was entered and analyzed on Epi-info 3.5.3.

Results:

Total number of participants was N=995 in which 618 (62%) were Kuwaiti and 373 (37.5%) were from other nationality. Overall, the mean age was 36 ± 10.6 years. The gender distribution was 693 (69.5%) males and 293 (29.4%) females. Seventy nine of the adults were healthy and 7% were unhealthy. The mean number of teeth present was 28.5 ± 3.5 . The mean number of teeth with dental caries (coronal and root caries) was 3.08 ± 3.4 . The mean number of filled teeth was 3.9 ± 4.4 . Forty five percent of participants had gingival recession in at least one tooth. Only 3% of participants had soft tissue abnormality. Among participants, 33% reported that their oral health was good and 35% had oral pain at time of examination. Almost 16% of employees had good oral hygiene.

Conclusions:

The data suggests that there is high caries prevalence among adults in Kuwait which could be attributed to the poor hygiene. Efforts should be laid on introducing Oral health promotion activities in workplaces promoting oral hygiene practices among adults in Kuwait.

Key Words: Adult Survey; Caries; Oral hygiene

Funding Agency: None



Dentistry

Category: Basic Sciences

53

Effect of heat treatment on the tensile strength of ‘Elgiloy’

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Introduction:

Elgiloy is the trade name of a cobalt-chromium-nickel superalloy that is offered for orthodontic use as wire. Despite some years of use, there is very little information in the dental literature on its mechanical properties, and especially on the effect of the hardening heat treatment (HT) that may be used after forming on the tensile strength (TS) in relation to the four ‘tempers’ that are available.

Methods:

Straight lengths of round wire of the four available tempers, Blue, Yellow, Green and Red, were tested in direct tension at 5 mm/min in air at 23 °C to fracture, both as-drawn (AD) and with HT at 500 °C for 5 h, in air. HT was done in a high-uniformity, three-zone tube furnace in an alumina boat. The wires were then allowed to cool to room temperature in the boat, outside the furnace. . The nominal (original cross-sectional area) peak stress was calculated.

Results:

TS varied from 1.4 ~ 2.1 GPa, AD, and 1.6 ~ 2.8 GPa, according to temper, but with appreciable variation within tempers. Even so, the TS plot of HT vs. AD was very straight and of narrow distribution (intercept: -637.8 ± 63.8 , slope: 1.575 ± 0.036 , r^2 : 0.994918, $n = 12$ $F = 1957.66$, $p \sim 8 \times 10^{-13}$)

Conclusions:

The strengthening due to HT was highly regular and TS can be reliably predicted on the basis of the AD value, but this of course cannot be known without specific batch testing. However, the unexpectedly large variation in the AD values within tempers renders such a prediction of lower reliability and usefulness in practice. Indeed, the distinction between tempers can be negligible, making selection according to application demands problematic, and differential property expectation less than certain. No such product data are provided. Quality control is not as tight as might be expected. The implications for treatment need to be explored.

Key Words: Heat Treatment; Tensile strength; Elgiloy

Funding Agency: Kuwait University General Facilities Project GD02/11



Dentistry

Category: Basic Sciences

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Helicobacter pylori prevalence in dental plaques of diabetic and gastritis patients, as a possible source of re-infection

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Introduction:

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

Methods:

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

Results:

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

Conclusions:

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

Key Words: Helicobacter pylori; Diabetes; Gastritis

Funding Agency: PAAET-HS-01-2010



Dentistry

Category: Clinical

55

Oral health habits among disabled schoolchildren in Kuwait

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Introduction:

This study aimed to describe oral health habits among disabled schoolchildren in Kuwait.

Methods:

Altogether 308 parents of children either with physical disability (n = 211) or Down syndrome (n = 97), and parents of 112 normal children, participated, completing a questionnaire about their children's oral health habits. Chi-square and z-tests were used in analysis.

Results:

About one third of parents of Down syndrome children, 18% of normal children and 15% of physically disabled reported their children consuming both soft drinks and sweets at least once a day (p = 0.016). The proportions of children drinking soft drinks daily was higher among Down syndrome children (65%) than among physically disabled (52%) or normal children (48%) (p = 0.003). However, more normal children consumed sweets daily (79%) than disabled children (58%) (p = 0.012). Less than half brushed their teeth twice a day as recommended (48% of Down syndrome, 43% of normal and 38% of physically disabled). Of disabled children who brushed their teeth, 33% had no help with toothbrushing, 37% received some help from parents and 29% were extensively helped by parents or caregivers. About a fifth of disabled children and 37% of the normal children had never visited a dentist (p = 0.003). Disabled children had visited a dentist more frequently during the previous two years than normal children (65% vs. 57%). A larger proportion of disabled children (42%) visited the dentist due to toothache than normal ones (25%) (p < 0.01).

Conclusions:

Daily consumption of soft drinks and sweets was common. Less than half of the disabled children were reported to brush their teeth as recommended. Toothache was the main reason for dental visits. Disabled children had poor oral health habits and should be targeted for increased preventive dental care by the National School Oral Health Program in Kuwait.

Key Words: School children, Oral health habits, Disabled

Funding Agency: None



Dentistry

Category: Graduate (Resident)

56

Fluoride in bottled water found in Kuwait

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Introduction:

To measure the concentration of fluoride in various brands of bottled water and collect information about the type of water consumed in Kuwait.

Methods:

Fifty five brands of bottled water; local and imported were found in Kuwait. Three of each was collected from grocery shops, supermarkets and hypermarkets. Samples were spring, mineral, distilled, or carbonated mineral waters. Label fluoride values were recorded and three samples of each brand were blinded before sending for lab analysis. Lab values for fluoride in these samples were analyzed at Kuwait institute for Scientific Research (KISR) using Fluoride Ion-Selective Electrode Method (FISEM). Data on water consumption was obtained from questionnaire administered on 1430 adults visiting our centers in different governorates.

Results:

There were 55 brands of bottled water from 18 countries, mainly from Saudi Arabia (30.9%), Kuwait (14.5%), and UAE (9%). Overall, fluoride content in bottled water sold in Kuwait according to label was 0.4 ± 0.5 mg/L, whereas, the laboratory fluoride content was 0.5 ± 0.5 mg/L. Fifteen types of bottled water were having fluoride within the range of optimum level (0.7-1.2) mg/L, thirteen where from KSA, and the mean for all was 1.01 ± 0.11 mg/L. Most of the people (68.4%) consumed both bottled and tap water, whereas 7.3% consumed bottled water alone and 23.5% had only tap water.

Conclusions:

There was negligible difference between the lab and label values for fluoride in bottled water. There was a wide variation in fluoride concentration and most of them were below the optimum level needed for caries prevention. Since significant number of people consumed bottled water, there should be regulations to monitor the concentration of fluoride in bottled water. Also, more efforts should be made for educating the public about its importance.

Key Words: Bottled water; Optimum fluoride; Label fluoride

Funding Agency: None



Genetics

Category: Clinical

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A novel PKD1 variant demonstrates a disease-modifying role in trans with PKD1 truncating mutation in autosomal dominant polycystic kidney disease patients

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Introduction:

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common form of Polycystic Kidney Disease (PKD) and occurs at a frequency of 1/500 to 1/1000 affecting all ethnic groups worldwide. ADPKD shows significant intrafamilial phenotypic variability in the rate of disease progression and the occurrence of extra-renal manifestations, which suggests the involvement of heritable modifier genes.

Methods:

Clinical evaluation of a family with ADPKD was performed to diagnose and assess disease progression in each individual. PKD1 was genotyped in each individual by targeted sequencing.

Results:

Long range PCR and sequencing analysis showed that the patients with ADPKD in the family had the, p.Q2243X mutation in PKD1. A more severe disease phenotype, in terms of Glomerular Filtration Rate (GFR) and total kidney volume, was observed in two patients where in addition to the mutation, they carried a novel PKD1 variant, p.H1769Y. The first patient reached End Stage Renal Disease (ESRD) by the age of 29 with a height-adjusted Total Kidney Volume (htTKV) of 1362.63 ml/m, while the second patient had an htTKV of 1065.59 ml/m by the age of 26. Other patients from same family carrying only the p.Q2243X mutation showed milder disease manifestations while a carrier of only the p.H1769Y variant showed multiple renal cysts (<10) and normal kidney functions by the age of 58.

Conclusions:

ADPKD shows significant intrafamilial phenotypic variability that is generally attributed to other modifier genes. In this rare case, we have shown that a variant at PKD1, in trans with the PKD1 mutation, can also act as a modifier gene in ADPKD patients.

Key Words: PKD; Genetics; Nephrology

Funding Agency: This study has been funded by Kuwait University Research Grant NM01/13 and Mayo PKD center DK090728.



Genetics

Category: Basic Sciences

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Whole genome sequencing of *Brucella melitensis* isolates for the identification of biovar, variants and relationship within a Biovar

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Introduction:

Brucellosis, a highly infectious zoonotic disease, is endemic in Kuwait and the Middle East. The primary cause of Brucellosis in Kuwait is *Brucella melitensis*. The identification of *Brucella* genotypes is essential for epidemiological studies, including surveillance and contact tracing. However, the limited genetic diversity among *Brucella* genomes has made its genotyping a challenging task. The whole genome sequencing is emerging as a novel tool for genetic characterization of microorganisms. The aim of this study was to genotype human isolates of *B. melitensis* using whole genome sequencing.

Methods:

Fifteen clinical isolates of *B. melitensis* were grown on culture plates. The bacterial colonies from individual plates were suspended in saline and heated at 95°C for 10 minutes. DNA was purified using the QIAamp DNA Mini Kit (Qiagen) and checked for quantity and purity using a spectrophotometer (Epoch) and a fluorometer (Qubit). DNA libraries were prepared using the Nextera XT DNA Sample Preparation Kit (Illumina) and sequenced using MiSeq (Illumina). The sequence files were aligned to three biovars of *B. melitensis*, i.e. biovar 1 str. 16M, biovar 2 str. 63/9, and biovar 3 str. Ether. The alignment and variant calling were performed using 'bwa mem' and SAMtools/VCFtools, respectively.

Results:

The genome size of all the isolates was around 3.3 mega base pairs and belonged to *B. melitensis*. A neighbor-joining tree analysis identified isolate 2 as an outlier. However, variations (SNPs and indels) were spread all over the genome; but 138 SNPs were common among the 14 isolates, supporting the same ancestral origin. In addition, SNPs (2 -478) unique to each isolate were also identified, which divided the *B. melitensis* biovar 2 into two major variant groups.

Conclusions:

The biovar 2 is the most prevalent biovar of *B. melitensis* in Kuwait. Furthermore, isolate specific variations were identified, which may be useful in epidemiological investigations.

Key Words: Brucella melitensis; Whole Genome Sequencing; MiSeq

Funding Agency: Kuwait University Research Sector grant SRUL02/13.



Hematology

Category: Clinical

59

New conclusions in scintigraphy results of sickle cell disease bone involvements

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Introduction:

Sickle cells disease (SCD) is an inherited disease characterized by abnormally shaped red blood cells (RBC). Sickle cell anaemia (SCA) is a homozygous haemoglobin S disease. The abnormal haemoglobin S tends to polymerise under low oxygen concentration or increased body oxygen demands. Therefore, RBC become less pliable and are abnormally sticking. Some RBC becomes distorted into the sickle shape leading to tissue infraction. Imaging techniques are applied to diagnose avascular necrosis (AVN). Many sophisticated techniques are in used now a days starting from radiographs, bone scans and MRI. The recent modern Scintigraphy imaging provide merging of SPECT with computed tomography (CT) to better recognize the site of the lesion from anatomical and functional; aspects (SPECT-CT)

Methods:

The investigations conducted on 60 number respondent populations for determination incidence of illnesses or clinical assuagement through various tests. The data analysed by Microsoft excel included age, sex, haemoglobin phenotype according to the presence of AVN, sites of infraction and presence of osteomyelitis.

Results:

In this study the total spontaneous bone regeneration in AVN is 23.07%, which includes 60 SCD patients; they were 41 (68.33%) adults and 19 (31.66%) are children. The patients were aged 5-78 years. The percentage of AVN among children was found to be 20%, whereas the percentage of AVN in adults was 45%. In children the percentage of osteomyelitis was found to be 5%, no osteomyelitis was found in adult patients. The phenotypes in our sample are 15% have SCA, while 85% have SCD.

Conclusions:

Our preliminary results revealed:

1-AVN Spontaneous bone regeneration in SCD is a landmark observation in this project by using Scintigraphy; it could encourage more research work on using bone-rebuilding medications to restore the bone integrity in SCD.

2-SPECT/CT is safe and quick procedure. It gives the necessary information to localize AVN lesion in SCD patient

Key Words: Bone scan, Sickle cell disease, Avascular necrosis

Funding Agency: N one



Medical Education

Category: Undergraduate

60

Is rejection of bariatric surgery a result of a negative attitude towards obese patients?

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Introduction:

Kuwait was the only country in the world to impose a temporary ban on bariatric surgery in 2013. However bariatric surgery is strongly shown to be a very effective treatment for morbid obesity. It could be that the negative attitude in general towards obese subjects is what encouraged such measure. Therefore in this study we aimed to assess medical students' attitude towards the treatment of morbidly obese patients using a known validated questionnaire designed specifically for the purpose.

Methods:

The NEW scale questionnaire was administered to senior medical students (6th and 7th year) at Kuwait University Faculty of Medicine (KUFM). Participation was confidential, not related to assessments, and not rewarded. The results were compared to the results by second and fourth year medical students at Wake forest School of Medicine (WFSM). We also added a question to determine the student acceptance of bariatric surgery.

Results:

Ninety three students submitted filled questionnaires (52% participation rate). There were 29 male and 64 female students. On average the group scored 15.47 ± 19.40 , much lower than WFSM fourth year students, who scored 19.7 ± 20.6 , $p=0.039$. When compared by gender, the KUFM male students scored 18.33 ± 19.15 , lower than their female classmates, who scored 14.72 ± 19.74 . The difference, however, was not statistically significant, $p\text{-value} = 0.423$. Although not statistically significant, KUFM males scored lower than WFSM males, 15.47 ± 19.40 vs. 22.2 ± 20.5 , $p=0.304$. KUFM females scored significantly lower than WFSM females, 14.72 ± 19.74 vs. 25.9 ± 19.6 , $p<0.001$. The NEW score correlated to the students' acceptance of the bariatric surgery, $r = 0.3$ ($p=0.004$).

Conclusions:

Negative attitude towards obese patients may contribute to the rejection of bariatric surgery. In a country with one of the highest rates of obesity in the world this need to be addressed by proper education tools and curriculum.

Key Words: Bariatric Surgery; Obesity; Attitude

Funding Agency: None



Medical Education

Category: Clinical

61

Do students with better reported self-empathy communicate better with patients?

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Introduction:

Empathy is necessary for communication between patients and physicians to achieve optimal clinical outcomes. The objective of this study is (1) to examine association between students' self-reported empathy, and the grade scored of a communication station in an OSCE. (2), association between students' self-reported empathy and simulated Patients' (SPs) assessment of medical students' empathy.

Methods:

A total of 62 sixth-year medical students completed the Jefferson Scale of Physician Empathy (JSPE) before the OSCE exam. JSPE score was out of 140. During the communication station of the OSCE, SPs completed the Jefferson Scale of Patient Perceptions of Physician Empathy (JSPPE) with a score out of 35. The communication station was assessed by an examiner who rated the student's performance during the station with a maximum score out of 20.

Results:

There were 28 male students and 34 females. There were 10 students who failed the communication station (score ≤ 12), 20 students had average scores (13-15), 16 students had good scores (16-17) and 15 had excellent scores (18-10). A high correlation was found between the scores on JSPE and the communication station ratings by the examiner ($p < 0.01$). There was no correlation between scores of the JSPE and the JSPPE.

Conclusions:

There is a significant association between students' self-reported scores on the empathy and communication with patients. Empathy should be taught in medical curricula as it enhances doctor-patient communication.

Key Words: Empathy; Communication; Medical students

Funding Agency: None



Medical Education

Category: Clinical

62

Impact of structured education on diabetes management during Ramadan

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Dasman Diabetes institute

Introduction:

Fasting during Ramadan is an obligatory duty for all healthy adult Muslims. Although Islam exempts people with chronic medical conditions from the duty of fasting, many people with diabetes insist on fasting Ramadan despite the medical advice not to. Fasting among people with type 1 & 2 diabetes is associated with multiple risks such as hypoglycemia, hyperglycemia, and others.

Methods:

The impact of implementing a structured education program in preventing diabetes associate complications of fasting was evaluated in this study. A modified and customized version of Measured Approach for Diabetes And Ramadan (MADAR) has been adopted, adapted and implemented for this purpose. Educators, nutritionists, nurses and physicians were involved in this program. 50 patients (26 male and 24 female) were invited and accepted to participate in the program; the majority were T2DM (only 3 T1DM) with a mean age of 54.9y. All participants filled a questionnaire, covering different aspects of issues related to the effect of fasting and diabetes, before and after the course.

Results:

All patients attended education session before starting of Ramadan last year in Dasman Diabetes institute. Average confidence rate to manage diabetes outcomes during fasting period has been improved from 55% before education session to 88% thereafter. During last Ramadan, 38 patients (76%) reported at least one hypoglycaemic episode (by questionnaire), compared to 16 patients (32%) during the current Ramadan (by phone calls). Moreover, we observed that the mean reduction of HbA1c was 1.3% compared to pre-Ramadan value.

Conclusions:

Ramadan-focused structural diabetes education program (MADAR) can empower patients to change their lifestyle during Ramadan to minimize the risks associated with fasting in people with diabetes.

Key Words: Fasting Ramadan; Diabetes; Education

Funding Agency: None



Medical Education

Category: Graduate (Resident)

63

The educational environment of the undergraduate medical curriculum at Kuwait University

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Introduction:

The educational environment of an institution affects the quality of education. In this study, we aim to assess the educational environment of the undergraduate curriculum the Faculty of Medicine, Kuwait University (FOMKU).

Methods:

A cross-sectional study was carried out during April 2014. The validated Dundee Ready Education Environment Measure (DREEM) questionnaire was e-mailed to 607 students. The mean scores of the main domains of the questionnaire, and for each item, were calculated, and their association with the students' phase of study and gender was measured using the student t-test (p-value of ≤ 0.05 was considered as the cut-off level of significance).

Results:

Out of the 607 students, 117 (19.3%) completed the questionnaire. The total mean score for DREEM was 108.7/200 (54.3%). The mean score for students' perception of teaching, perception of teachers, academic self-perception, perception of atmosphere and social self perception were 25.2/48 (52.5%), 24.6/44 (55.9%), 18.4/32 (57.5%), 26.2/48 (54.5%) and 14.3/28 (51.0%), respectively. The highest mean score for an item of the DREEM questionnaire was for "my accommodation is pleasant" (3.48 ± 0.75), while the lowest score was for "there is a good support system for students who get stressed" (0.88 ± 0.86). The total mean score was not significantly different between the two phases of the curriculum, or among males and females; however, few significant differences among the main domains and items were noted.

Conclusions:

In conclusion, the educational environment of the FOMKU was suboptimal based on the learners' perspectives. Medical educators in Kuwait should work on improving this environment in order to improve the quality of the delivered curriculum.

Key Words: Medical education; Learning environment; Medical students

Funding Agency: None



Medicine

Category: Clinical

64

Circulating Bilirubin as a marker of adverse coronary heart disease risk profile in first degree relatives of patients with Type 2 diabetes mellitus

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Introduction:

Recent studies have shown that circulating total bilirubin (Tbil), often considered to be a toxic byproduct of haem catabolism, is inversely associated with risk for coronary heart disease and diabetic nephropathy. The objective of this study was to examine the associations of TBil with low grade inflammation, circulating adipokines, insulin resistance (IR), metabolic syndrome (MetS) and incident diabetes in first degree relatives (FDR) of diabetic subjects.

Methods:

Fasting Tbil, adiponectin, leptin, leptin receptor (sOB-R), insulin, glucose, high-sensitivity CRP (hsCRP), lipid profile were determined in 590 (238M and 352F) FDR. Free leptin index (FLI), insulin sensitivity (%S) and resistance (Homeostasis Model Assessment (HOMA-IR)) were calculated. Patients were categorised by IR, MetS (International Diabetes Federation criteria) and bilirubin quartiles.

Results:

Tbil showed inverse correlations ($p < 0.05$) with BMI, insulin, HOMA-IR, Triglycerides, Apo B, HbA1c and direct correlations with %S and sOB-R. Subjects in the first TBil quartile had higher ($p < 0.05$) BMI, waist circumference, triglycerides, HbA1c, insulin, HOMAIR, resistin, leptin, FLI, hsCRP and lower HDL-C and adiponectin compared to subjects in the 4th quartile. TBil decreased stepwise with increase in BMI and number of MetS components. The prevalence of MetS from 1st to 4th quartile were 40%, 40%, 13%, and 7%, respectively. The prevalence of IR from 1st to 4th quartile were 30%, 26%, 24%, and 20%, respectively. Binary logistic regression analysis showed odds ratio of the association of TBil with IR, MetS and incident diabetes were 0.88, 0.92 and 0.93 respectively.

Conclusions:

There is need for attending physicians to review results of the routinely estimated TBil as low levels could be a useful adjunct for the selection of high risk FDR for more aggressive intervention to lower the risk of progression to T2DM or development of CHD.

Key Words: Bilirubin; Metabolic syndrome; Type 2 Diabetes Mellitus

Funding Agency: KFA-2011-1302-01



Medicine

Category: Clinical

65

**Community acquired pneumonia in hospitalized patients:
Demographics and quality of care**

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Introduction:

Community acquired pneumonia (CAP) is a potentially preventable disease and one of the leading causes of hospitalization in Kuwait. The aim of this study was to identify the demographic characteristics of hospitalized adults (> 12 years) admitted with CAP, and to evaluate the quality of care provided to these patients according to the recommended international guidelines.

Methods:

An observational study was conducted, and the medical records were reviewed for all adults admitted with CAP from April 2013 to December 2014 in the Department of Medicine at Al-Sabah Hospital.

Results:

93 adults with CAP were hospitalized during the study period (53.8% males, 65.2% Kuwaiti nationals). The overall mean age was 58.5±19.0 years, and the median hospital stay was 8 days. Hospital stay was significantly longer in patients with diabetes and hypertension. The most frequent co-morbidities were Hypertension (57.0%), diabetes (54.8%), ischemic heart disease (30.1%), bronchial asthma (17.2%), dyslipidemia (14.0%), and chronic obstructive airway disease (11.8%). Although blood culture was indicated in 44.1% of the cases, it was performed in 88.2%. Blood culture was collected before the administration of the antibiotics in 96.3% of the cases. Empirical antibiotics were given according to the recommended guidelines in 98.9% of the cases. Ceftriaxone and clarithromycin were the antibiotics of choice in more than two thirds of the cases. Influenza and pneumococcal vaccines were given in 56.3% and 53.5% out of the eligible cases for vaccinations. Smoking status was assessed in 83.9% of the cases, and counselling to quit smoking for the current smokers (21.8%) was not satisfactory.

Conclusions:

This study highlighted important demographic characteristics and quality care indicators for hospitalized patients with CAP, which may help health policy makers to devise strategies to improve health care delivery system, and enhance patients' outcomes.

Key Words: Pneumonia; Hospitalization; Quality of care

Funding Agency: No



Medicine

Category: Clinical

66

Incident reporting system in Sabah hospital

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Introduction:

Adverse events occur every day in healthcare as well as other professions. There have been 44,000 to 98,000 patients reported to die every year in the USA as a result of adverse events. Thus, patients' safety and quality improvements are listed as a priority of health policy agenda of several developed countries. Despite implementing quality improvements and safety procedures in healthcare, medical adverse events still occur in developed countries with good healthcare systems. The reduction of these events requires understanding of their nature as well as the characteristics of the healthcare system. Effective reporting system should be prompt, non-punitive, and confidential. This is the first study of incident reports in a hospital in Kuwait. The aims of this study were to explore reporting incidents, and to assess the perception of staff in reporting incidents in Sabah hospital.

Methods:

This is an explorative descriptive study of the data from incident reports collected in 2013 (578 cases) and 2014 (606 cases). Analysis was to evaluate the general view of the type, nature and time of events, gender and age of the patients, as well as the degree of harms.

Results:

Most adverse events occurred during the morning shift compared to other shifts, and involved male patients. The nature of the events were more related to clinical and surgical procedures, and related mostly to omitted or missed treatment. Other most recurrent events were patients' falls and escapes from the hospital. There were many missing information in these incidents reports.

Conclusions:

Although there were various missing information and lack of reporting incidents from some departments, the study gives a good guidance to improve services and safety at Sabah hospital. Furthermore, this study paves the way for an environmental analysis to study the causes of falls and patients' escape, and guides the members of the Risk Management Committee to conduct several studies to evaluate the staff

Key Words: Adverse event, Incident report, Risk management

Funding Agency: None



Medicine

Category: Graduate (Resident)

67

The prevalence and associated factors of helicobacter pylori infection among the adult population of Kuwait

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Introduction:

Several studies have been carried out on asymptomatic individuals in Middle Eastern countries to evaluate the prevalence of *H. pylori* infection. Most studies evaluating the prevalence of *H. pylori* in Kuwait have been conducted with patients with gastrointestinal symptoms. To our knowledge, no study has evaluated the prevalence of *H. pylori* infection among the general population of Kuwait. This cross-sectional study aims to evaluate the prevalence of *H. pylori* infection among the adult working population of Kuwait and investigate its associated factors.

Methods:

A cross-sectional study was conducted that included 518 participants from two ministries. For each participant, a questionnaire was administered and a drop of blood, taken from a fingertip using a lancet, was tested for the presence of IgG antibodies specific to *Helicobacter pylori*. The questionnaire included 23 questions that were divided into three categories: sociodemographic characteristics, behavioral aspects, and health and co-morbidities. A chromatographic lateral flow immunoassay test kit was used to test the blood. The results were generated using IBM's SPSS Statistics.

Results:

The prevalence of those who had a positive test result for *H. pylori*-specific IgG antibodies was 16.6% (95% CI = 13–20%). On initial analysis, the variables that were associated with a positive IgG result included male gender (odds ratio = 2.385, p-value = 0.002), non-Kuwaiti nationality (odds ratio = 1.716, p-value = 0.0026), and an age >50 (odds ratio = 2.683, p-value = 0.013). However, upon using a logistic regression model, only male gender was found to be independently associated with a positive IgG result (adjusted odds ratio = 2.104, p-value = 0.047).

Conclusions:

Many studies have found *H. pylori* infection to be very prevalent worldwide with several associated risk factors. In our study, 16.6% of the participants were found to have IgG antibodies against *H. pylori*, and only male gender was found to be independently associated. A study that includes a larger sample size and that tests for more antibodies is recommended to generate substantial results.

Key Words: H. pylori infection, IgG antibodies, Prevalence in Kuwait

Funding Agency: Partially funded by: Takeda Pharmaceutical Company



Medicine

Category: Clinical

68

Efficacy of quadruple therapy versus standard triple therapy for eradication of helicobacter Pylori in Kuwait

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Introduction:

Chronic infection with helicobacter pylori is associated with chronic gastritis, peptic ulcer disease and gastric cancer. Eradication of helicobacter pylori improves morbidity of chronic gastritis and reduces the incidence of gastric cancer in high risk populations. Our aim was to test the efficacy of clarithromycin based triple therapy versus bismuth based quadruple therapy in eradicating helicobacter pylori in patients with chronic gastritis in Kuwait.

Methods:

Two hundred and eighteen dyspeptic patients of different nationalities with biopsy proven chronic gastritis were enrolled. All patients were naïve to helicobacter pylori eradication therapy. Patients were randomized in to two groups: group A received triple therapy (omeprazole, amoxicillin and clarithromycin) for 10 days and group B received quadruple therapy (omeprazole, bismuth sub citrate potassium, tetracycline and metronidazole) for 10 days. All patients were tested for eradication of helicobacter pylori by carbon -13 urea breath test four weeks after treatment.

Results:

Total response rate to eradication therapy in both groups was 77.5% (n=169). Group B (n=100) had higher eradication rate (88%) than group A (n=118) which had eradication rate of 68.6%. Helicobacter pylori eradication rate was significantly higher in males (84.2%) than females (70.2%) in both groups (p<0.01). There were no differences in eradication rates regarding median age or nationality.

Conclusions:

Bismuth based 10 day quadruple therapy was found to be more effective as first line therapy than clarithromycin based 10 day triple therapy for eradicating helicobacter pylori in patients with helicobacter pylori related chronic gastritis in Kuwait.

Key Words: Helicobacter pylori; Quadruple therapy; Triple therapy

Funding Agency: None



Medicine

Category: Clinical

69

Work-up of patients suspected of having a pulmonary embolus; are we doing the right thing?

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Introduction:

Pulmonary Embolism (PE) is a common, potentially lethal condition. CT Pulmonary Angiography (CTPA) is currently the gold standard investigation for the diagnosis of PE. We aim to assess the frequency of PE in patients who had CTPAs in our hospital, and what their pretest probability is according to Wells score.

Methods:

We retrospectively reviewed clinical information of 138 patients suspected to have a PE, and underwent imaging with CTPA over a 12 month period (January 1st 2013 through December 31st 2013) at Mubarak Hospital in Kuwait. The Wells score for each of the patients was calculated by two physicians, without knowledge of CTPA results.

Results:

Within the 12 month period, 192 patients had CTPA, 35 (18.2%) of which had a confirmed PE. The detailed medical records were available for 138 patients only. The mean age of patients with confirmed PE was 42.3 years, compared with 52.4 years for patients without PE (p 0.004).

In our study subjects, the percentage of patients with high wells score > 4 (High probability of P.E.) was only 23%. This percentage was much higher in patients with confirmed PE 69% versus 12.5% in patients without PE (p <0.001).

The most important predictors for the presence of PE in our study were; history of old DVT (p 0.019), presence of recent malignancy (p 0.05), and clinical signs of DVT (p 0.001). D dimer was done in 101 patients and the mean (SE) of D dimer was 3336 (658 ng/mL) for patients with confirmed PE versus 1650 (200 ng/mL) for patients without PE, p <0.01. However the majority of our patients 84% had high D dimer > 500 ng/ml.

Conclusions:

Our positive rate for PE is very low in patients who had CTPA for suspected PE. The majority of our patients who had CTPA had low wells score. This suggests that CTPA is over utilized in our hospital. The D dimer level was not a good discriminator in our acute care hospital setting.

Key Words: Wells criteria, PE Workup

Funding Agency: None



Medicine

Category: Clinical

70

The 2013 ACR/EULAR classification criteria for systemic sclerosis out-perform the 1980 criteria. Data from the Canadian scleroderma research group

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CSRG, McGill University

Introduction:

The goal of this study was to determine the sensitivity of the new 2013 classification criteria for systemic sclerosis (SSc) in an independent cohort of SSc subjects and to assess the contribution of individual items of the criteria to the overall sensitivity.

Methods:

SSc subjects from the Canadian Scleroderma Research Group cohort were assessed. Sensitivity was determined in several subgroups of patients. In patients without the criterion of skin thickening proximal to the metacarpophalangeal joints (MCPs), we re-calculated sensitivity after removing individual criterion.

Results:

A total of 724 SSc patients were included. Most were females (86%), mean age was 55.8 years, mean disease duration was 10.9 years, and 59% had lcSSc. Overall, the sensitivity of the 2013 criteria was 98.3% compared to 88.3% for the 1980 criteria. This pattern was consistent among those with lcSSc (98.8% versus 85.6%), anti-centromere antibodies (98.9% vs 79.8%), disease duration ≤ 3 years (98.7% vs 84.7%) and no skin involvement proximal to the MCPs (97% vs 60%). In the latter sub-group, removing Raynaud's phenomenon and sclerodactyly from the criteria reduced the sensitivity to 77% and 79%, respectively. Removing both sclerodactyly and puffy fingers reduced the sensitivity to 62%.

Conclusions:

The 2013 SSc classification criteria classify more SSc patients than the 1980 criteria. The improvement in sensitivity is most striking in those with lcSSc, especially those without skin involvement proximal to the MCPs. The addition of Raynaud's phenomenon and puffy fingers to the 2013 criteria accounts for important gains in sensitivity.

Key Words: Systemic Sclerosis; Classification criteria; Sine scleroderma

Funding Agency: None



Medicine

Category: Clinical

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Knee osteoarthritis in type 2 diabetes mellitus: Does insulin therapy retard the osteophyte formation?

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Introduction:

Despite many reports on the anabolic effects of insulin on connective tissue and cartilage metabolism in diabetes, data relating to the effect of insulin therapy in the progression of osteoarthritis (OA) is sparse.

Objective: To investigate whether radiographic changes in knee OA in Type 2 diabetes mellitus (T2DM) patients on insulin treatment differed from those not on insulin.

Methods:

A cross-sectional study was performed in 311 subjects (211 T2DM patients and 100 control subjects without diabetes), screened over a period of one year in a hospital-based setting. Patients were categorized into three groups, T2DM patients not on insulin (G1, n = 99), T2DM patients on insulin (G2, n = 112) and non-diabetic control group (G3, n = 100). Plain X-ray of knee was used to assess the changes of knee OA and graded using Kellegren-Lawrence (K-L) scale and the Osteoarthritis Research Society International (OARSI) Atlas grading scale.

Results:

A total of 622 knee X-rays were evaluated. A highly significant association ($p < 0.001$) was observed for OARSI-Joint Space Narrowing (JSN) as well as for osteophyte formation between the three groups. Comparing G2 and G3, highly significant association ($p < 0.0001$) was retained for JSN and for osteophyte formation. Comparing G1 and G2, though there was no association ($p > 0.05$) for JSN, significantly lesser osteophytes formation were noted in T2DM G2 patients compared to T2DM G1 patients (11.7% vs. 19.7%, $p=0.02$). Multivariate logistic regression analysis showed that T2DM G2 group had less osteophyte formation than both G1 T2DM group and G3 control group, (odds ratio = 0.294, $p < 0.008$ and odds ratio = 0.098, $p < 0.001$, respectively) after inclusion of confounders such as age, gender and BMI.

Conclusions:

Our findings suggest that insulin therapy might retard the radiographic changes in T2DM patients with OA knee.

Key Words: Osteoarthritis; Diabetes Mellitus; Insulin

Funding Agency: None



Medicine

Category: Clinical

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Clinical predictors of disease progression in multiple sclerosis patients with relapsing onset in a nation-wide cohort

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Introduction:

Prognosis of multiple sclerosis (MS) is variable. Predicting the progression of disability over time is challenging despite the florid clinical and paraclinical data provided. We aimed to assess whether baseline clinical variables of MS patients would predict the conversion to progressive phase of the disease.

Methods:

Utilizing the National MS Registry, patients who had relapsing onset and confirmed expanded disability status scale (EDSS) score at baseline and follow-up visits were included. Primary progressive MS and CIS patients were excluded. Clinical variables (gender, age at onset, disease duration, number of relapses, EDSS score) were collected. The end point was conversion to secondary progressive MS or reaching the stage of sustained irreversible neurological disability (EDSS 4). Chi Square and multivariable logistic regression were used to determine the influence of clinical variables on disease progression.

Results:

Data of 803 MS patients with relapsing onset were analyzed. Mean age at onset and mean disease duration were 26.62 and 8.12 years respectively. Eighty five (10.6%) patients reached the end point at last follow-up visit; 43.5% were male. The risk of disease progression was significantly higher in males (adjusted odds ratio (aOR) = 2.02; 95% confidence interval (CI): 1.16-4.16; P = 0.015), in patients who developed MS \geq 40 y of age (aOR = 4.36; 95% CI: 1.35-14.09; P = 0.041) and who had \geq 3 relapses during their disease course (P < 0.001). Spinal cord presentation at onset was predictive of progression (aOR = 2.01; 95% CI: 0.97-4.36; P = 0.06) while optic neuritis at onset was associated with lower risk of progression (aOR = 0.30, 95% CI: 0.10-0.87; P = 0.03).

Conclusions:

Males and patients who presented at age 40 years or beyond had increased risk of MS progression. Spinal cord symptoms at onset and 3 or more relapses were predictive of progression.

Key Words: Multiple Sclerosis; Disease Progression; Epidemiology

Funding Agency: None



Medicine

Category: Clinical

73

New onset diabetes after renal transplantation in Kuwait

Al-Otaibi T, Gheith O, Nampoory MRN, Said T, Halim M, Nair P, Abdulmoneim M, Fathy A,
Hassan R, Jude Yagan.
OTC

Introduction:

This is a retrospective observational study aimed at evaluating the prevalence and long-term outcome of renal transplant recipients with diabetes mellitus after renal transplantation: 14 years single center experience

Methods:

Out of 1229 renal transplant recipients-performed during the period between 2000 and 2014-370 (30.1%) were diabetic before transplantation, group 1 and 192(15.6%) developed NODAT after different periods of transplantation, group 2. Database of our transplant registry has been assessed regarding risk factors and outcome of transplant recipients with NODAT compared to non-diabetic recipients.

Results:

Most of patients with NODAT were males (Kuwait and non-kuwaiti arab) with mean age of 50.9 ± 13.4 in group 1 and 44.2 ± 13.9 in group 2. The two groups were comparable regarding original kidney disease (mainly glomerulonephritis in nearly 35 to 40 % respectively), type of donor and pre-transplant co-morbidities (tuberculosis, hepatitis C virus infection, hypertension, anemia and bone disease) ($p > 0.05$). However, ischemic heart disease was significantly more prevalent in pretransplant diabetic patients (13.5% vs. 11.1% $p = .03$). Induction immunosuppression was significantly less potent in diabetic patients (18.5 % vs. 12.1%, $p = .003$) but the maintenance regimen was comparable in both groups ($p > 0.05$). We found no significant difference in the 2 groups regarding post-transplant infections, graft or patient outcomes ($p > .05$).

Conclusions:

NODAT is not an uncommon complication in renal transplant. Meticulous evaluations to identify occult IHD and /or impaired glucose tolerance pre-transplant may be required to vent or decrease prevalence of this complication.

Key Words: NODAT; Renal transplant; Outcome

Funding Agency: None



Medicine

Category: Clinical

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Erythropoietin dependent anemia: Emerging issue among renal transplant recipients with different age groups

Al-Otaibi T, Nampoory MNR, Halim M, Abu Attia H, Mansour H, Abdulkawy H, Nair P.
OTC

Introduction:

Post-transplant anemia and its association with transplant outcomes have not been properly studied in the Middle East region in the era of EPO.

Methods:

Out of 2000 renal transplant recipients who were transplanted at Hamed Al-Essa Organ transplant center of Kuwait, 183 of them (9.15%) were maintained on erythropoietin. Patients were grouped according to their age into 4 groups: pediatrics, group 1 (<18years, n=19); adults, group 2 (18-40, n=54); middle age group 3 (40-60, n=83) and elderly group 4 (>60, n=27). We evaluated such cases for possible causes of resistant anemia.

Results:

The majority of patients in the four groups were females (52.9, 69.2, 64.7 and 70% respectively; $p=0.63$). The prevalence of anemia was 81.3%, 86.4, 79 and 88.9% ($p=0.68$) at the time of transplantation and decreased to 40, 38.1, 51.9 and 77.8% respectively after 6 months of transplantation ($p=0.24$). After 6 months of transplantation, target HB was achieved more commonly in adults (35.1%) but severe anemia was more prevalent among pediatric age group (46.2%) but this did not rank to significance ($p>0.05$). Most of patients had normal levels of CR protein, folic acid and vitamin b12, ($p>0.05$). Moreover, serum iron, transferrin, ferritin and transferrin saturation were comparable in all groups ($p>0.05$). The prevalence of anemia was significantly more common in cases with preemptive transplantation, especially with cadaveric or unrelated donors ($p0.04$). With multivariate analysis, we found that patient age had significant impact on serum iron, transferrin saturation and pre-transplant diabetes ($p<0.05$). There were no significant difference in patient or graft outcome among different groups ($p>0.05$).

Conclusions:

Post-transplant anemia is not uncommon in this EPO era, irrespective to age of recipients. The EPO dependency observed here posts a major issue in follow up and further studies are ongoing to identify its etiology.

Key Words: Anemia; Kidney transplant; Outcome

Funding Agency: None



Medicine

Category: Graduate MSc: Basic Science

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Radiofrequency catheter ablation of atrial tachycardia under navigation using the EnSite patch.

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Introduction:

Atrial tachycardia (AT) can originate from any site in the right or left atrium, and even from the proximal pulmonary veins or superior vena cava. Mapping and ablating atrial tachycardia is technically more challenging than other forms of paroxysmal supraventricular tachycardia. In this report, we describe the locations of the AT foci as well as evaluate the success of their treatment with radiofrequency ablation.

Methods:

Our study population consisted of 10 patients (7 females: 35 ± 14 years) with AT from a consecutive series of 231 patients in a single hospital experience who were evaluated for narrow complex tachycardia. AT was confirmed by several mapping criteria in addition to the EnSite patch, and the success of the radiofrequency ablation was established by the inability to induce tachycardia post ablation.

Results:

The site of origin of AT was the right atrium (RA) in 7 patients, left (LA) atrium in 2 patients and the non coronary cusp in 1 patient. Of the foci in the RA, 3 were septal and 1 was in the upper crista terminalis. The intervention was successful in completely ablating the AT foci in 9 patients while 1 case was partially successful requiring additional medical therapy to completely control the tachycardia.

Conclusions:

10 out of 231 patients with narrow complex tachycardia were diagnosed with AT. Using EnSite patch, complete success of radiofrequency ablation was achieved in 90% of the cases; this is comparable to the national data.

Key Words: Ablation, Atrial tachycardia, Radiofrequency

Funding Agency: None



Medicine

Category: Clinical

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Determinants of changes in chromogranin A concentration in normal female subjects

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Introduction:

Age-related changes and anthropometric relations of chromogranin A (CgA) levels in normal female subjects are unknown. This study aimed to investigate the determinants of changes in chromogranin A level with advances in age in normal female subjects.

Methods:

A random sample of 140 normal female subjects, aged between 20-69 years, was studied. Subjects were included into the study if they were not taking any medication and were not known to have any illness for at least 12 months. After taking baseline anthropometry, an overnight fasting blood was collected for the measurement of CgA (by ELISA). Body composition was then assessed using dual-energy X-ray absorptiometry (DXA) machine (lunar prodigy). From the DXA, we calculated % body fat (BF), % lean body mass (LBM) and % bone mineral content (BMC).

Results:

The (mean±SEM) age and BMI of the studied females were 44±1 years and 28.8±0.5 kg/m², respectively. Subjects were stratified based on age-decades into 5 groups (n1=29, aged 20-29 years; n2=19, aged 30-39; n3=42, aged 40-49; n4=35, aged 50-59; and n5=15, aged 60-69). As age advanced from group 1 to group 5, BMI (p=0.0001), waist (p=0.0001) and % BF (p=0.0008) demonstrated significant positive trends, whereas height (p=0.0117), % LBM (p=0.0052), and % BMC (p=0.0001) demonstrated significant negative trends. CgA demonstrated a non-significant negative trend as age advanced (group 1: 6.02±2.10, group 2: 5.99±2.30, group 3: 4.87±0.85, group 4: 3.77±0.89, group 5: 3.62±1.26ng/ml). However, log transformation of CgA demonstrated a significant negative correlation with % BF (Rho= -0.22, p= 0.029), and a significant positive correlation with % LBM (Rho= 0.20, p= 0.029). It demonstrated no relation with waist, weight, BMI, BMC, nor with age.

Conclusions:

Age-related changes in serum CgA concentration are determined by changes in components of body composition, namely % LBM and % BF.

Key Words: Body composition, Chromogranin A, Females

Funding Agency: None



Medicine

Category: Clinical

77

A Study of optimal screening for latent tuberculosis in patients with inflammatory bowel disease

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Introduction:

Reactivation of latent tuberculosis (LTB) in patients with inflammatory bowel disease (IBD), secondary to treatment with anti-TNF- α agents, can lead to serious and life-threatening illness. No gold standard exists for the detection of LTB and there is conflicting evidence regarding the best screening strategy. We aimed to assess whether the addition of interferon-g release assay (IGRA) to tuberculin skin test (TST) would improve the detection of LTB.

Methods:

Consecutive IBD patients being considered for anti-TNF- α treatment underwent testing with a TST, IGRA, chest x-ray (CXR) and completed a questionnaire. The association of both tests with demographic factors, LTB risk factors (RF), BCG vaccination and immunomodulators (IM) were evaluated using Fisher's exact test, and agreement between was evaluated using kappa statistics.

Results:

155 IBD patients underwent testing with both TST and IGRA. 24 (18%) patients had a history of BCG vaccination. 28 patients (19%) had at least 1 RF for LTB, including 4 (3%) with an abnormal CXR. 102 patients (70%) were on IM. 9 patients were TST positive (6%) and 7 patients (5%) were IGRA positive. Concordance between TST and IGRA was 91.9% (but kappa=0.21). Neither test was affected by age, gender or BCG. The presence of risk factors for LTBI was found to positively influence TST results (OR 19.8, 3.9-102.1), but not IGRA. IGRA was negatively influenced by IM therapy (OR 0.06, 0.007-0.5), but not TST. 4/5 patients who were IGRA positive but TST negative were advised to begin treatment for LTB by a respirologist.

Conclusions:

IGRA was negatively influenced by IM, while the presence of RF for LTB was found to positively influence TST. There is fair agreement between TST and IGRA. The addition of IGRA to the standard practice of TST and CXR increased the number of cases presumed to have LTBI and influenced management. Given these findings, dual testing with TST and IGRA should be considered in IBD patients.

Key Words: Inflammatory bowel disease; Latent tuberculosis infection; Anti-TNF- α
Funding Agency: None



Medicine

Category: Clinical

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Intermediate term outcome of bortezomib treated resistant Acute Antibody-Mediated Rejection among renal transplant recipients: single center experience

Gheith O, Al-Otaibi T, Nampoory MRN, Halim M, Nair P, Saied T, Yagan J, Al-Waheeb S, Muzeirei I, Ibraheim M

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Introduction:

The most vexing clinical condition caused by antibodies in organ transplants is antibody-mediated rejection. The effects of bortezomib on mature plasma cells may represent a quantum advance in antihumoral therapy.

Aim of the work:

We aimed to present our relatively long term experience with bortezomib as an anti-plasma cell therapy for the management of renal allograft recipients with resistant episodes of antibody mediated rejection (ABMR).

Methods:

During the last 4 years, we revised our data base, and collected demographic and clinico-metabolic parameters of patients who received bortezomib for resistant acute ABMR in Kuwait.

Results:

We are presenting 7 kidney transplant recipients who underwent live donor kidney transplantation in Kuwait during the period between July 2007 and December 2012. All patients were adults—except one child 12 years old—with their mean age 42.3 ± 13 years. Three out of four males received their 2nd allograft while all females were transplanted once. All patients—except two— received thymoglobulin as induction and were maintained on steroid, mycophenolate mofetil (MMF) and tacrolimus and the remaining two received basilixmab as induction and were maintained on cyclosporine based therapy and were converted to tacrolimus based regimen after acute ABMR episode. All cases experienced biopsy proven acute ABMR and were managed by plasmapheresis, IVIG and rituximab. Only two patients received 2 cycles of bortezomib. Good response was reported in 4 and partial response in 2 and no response in 1.

Conclusions:

Bortezomib represents a rescue therapy for early resistant acute ABMR among renal transplant recipients despite the associated risk of infection. Within the limitation of our small sample, it will need to be evaluated in prospective, randomized, and well-controlled studies

Key Words: Antibody-mediated rejection; Bortezomib; Outcome

Funding Agency: None



Medicine

Category: Clinical

79

Early versus late acute antibody mediated rejection among renal transplant recipients in terms of its response to rituximab therapy- single center experience

Gheith O, Al-Otaibi T, Nampoory MRN, Medhat H, Mahmoud T, Nair P, Abdul-moneim M, Al-Waheeb S, Hassan R
OTC

Introduction:

There are no comparable trials concerning the use of rituximab among renal transplant recipients with acute antibody mediated rejection.

Aim of the study:

We aimed to compare early and late acute AAMR among renal transplant recipients in terms of its response to rituximab therapy.

Methods:

Out of 1200 kidney transplant recipients performed in Hamed Al-Essa Organ Transplant Center of Kuwait over the last 10 years, 103 developed acute AAMR and were subcategorized into 4 groups according to the onset of rejection and rituximab management. All patients received the standard management of AAMR according to our protocol (PP and IVIG). We added rituximab to the management of cases of group 1 (n=27, early AAMR) and group 2 (n=38, late AAMR) while groups 3 and 4 represented non-rituximab groups (n=20, early AAMR & 18, late AAMR respectively). We compared the 4 groups regarding graft and patient outcome.

Results:

All patients were comparable regarding demographic data (patient age, sex, pre-transplant type of dialysis, viral profile, type of induction, donor criteria, and pretransplant co-morbidities). We observed that delayed and slow graft function were significantly higher in groups 1, 3 (p=0.016), however we found no significant difference in the 4 groups regarding NODAT, BK viral infection or malignancy. Graft outcome was significantly better in group 1, 2 compared to the other groups (p=0.028). However, patient outcome was comparable in the 4 groups (p>0.05).

Conclusions:

Early AAMR in renal transplant recipients had significantly better outcome when rituximab was added to the standard management.

Key Words: Early and late AAMR; Kidney transplant; Outcome rituximab

Funding Agency: None



Medicine

Category: Clinical

80

Bariatric surgery in obese renal transplants: Single center experience

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Introduction:

Obesity has been associated with poor graft and patient survival after kidney transplantation. Weight loss surgery may be a good alternative in this clinical scenario.

The aim of this report is to assess the outcome of bariatric procedures performed in patients after renal transplantation compared to conventional group of patients.

Methods:

In this retrospective study, collected database of obese kidney transplant recipients (BMI>38) who underwent bariatric procedures during the last 5 years (n=25cases, group 1) were analyzed in comparison to control obese group (n=41 cases, group 2). Roux-en-Y gastric bypass was the most common procedure.

Results:

The two groups of patients were matched regarding demographic data, type of donor, cases with IHD, induction and maintenance of immunosuppression. Most patients in bariatric group were females (60%) while males dominated the other group (84%, p=0.03). The basal BMI means were 38.3±8.9 vs. 44.2±5.6 while the last BMI were 33.3±7.3 vs. 44.2±6.7 with mean % of weight loss at 6 months as 15.4±5.1% vs. 0.4±0.2% in both groups respectively (p<0.001). We found no significant difference in the two groups regarding number of cases with pre-transplant diabetes or NODAT, however the total number of diabetics in the control group was significantly higher (73.3% vs. 40%, p=0.042). Moreover, we observed that rejection episodes, graft and patient outcomes were similar in both groups (p>0.05). There were no postoperative complications except in two patients: one with strangulated hernia; and the second with postoperative deep venous thrombosis and pulmonary embolism.

Conclusions:

Bariatric surgical techniques may be used safely and effectively-with some precautions-to control obesity among renal transplants. Long term follow up studies are needed to verify patient and graft outcome.

Key Words: Bariatric; Renal transplant; Outcome

Funding Agency: None



Medicine

Category: Clinical

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Successful cost effective prevention of cytomegalovirus disease in kidney transplant recipients using low dose valganciclovir

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OTC, Kuwait

Introduction:

Prophylaxis for cytomegalovirus infection is highly recommended for kidney transplant recipients. Using valganciclovir in low dose is still under investigation.

Our aim was to assess the cost effectiveness of 450mg valganciclovir prophylaxis compared with 900mg for kidney transplants.

Methods:

In this prospective trial, 201 kidney transplants were randomized (1:1) to receive 450mg valganciclovir prophylaxis (group1, n=100) or 900mg daily (group2, n=101) for the first 6months post-transplant. Patients were studied for incidence of CMV disease, leucopenia attacks, rejection episodes and graft outcome and associated costs during 1st year. Direct costs of immunosuppressive medications, diagnosing rejection, and hospitalizations were included. The cost data from our hospital records and the costs were measured in US dollars.

Results:

Demographic features of the studied groups were comparable. More patients have received tacrolimus in group1, while in group2 more patients were maintained on cyclosporine (p0.001). We found that the cost of CVM prophylaxis in patients of group 1 was significantly lower (by 50% at 6 months, p<0.001) with lower leucopenia attacks (p 0.04) and lower doses of granulocyte colony stimulating factor (by 30 % at 6 months, p 0.03) compared to group 2. Higher doses of mycophenolate mofetil (p 0.04) among group 1 patients were protective therefore they experienced less rejection episodes (p0.01). In group2; there were more cytomegalovirus infections requiring full treatment (p0.052) and more BK virus nephropathy (p0.03). Graft and patient outcomes were satisfactory in both groups. Mean estimated glomerular filtration rates were above 60 ml/min at baseline, at 6months and at 12months post-transplant for both groups.

Conclusions:

Conclusion: Low dose valganciclovir for cytomegalovirus prophylaxis after renal transplant is safer, effective and less costly than using usual dose.

Key Words: Kidney transplant; CMV cost benefit; Outcome

Funding Agency: None



Medicine

Category: Clinical

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Depression in stroke and its effect on functional outcome

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Kuwait

Introduction:

The prevalence of post stroke depression is reported to be between 20 to 30 % by various authors. The objective of this study is to find out prevalence of depression and its effect on functional outcome in stroke patients admitted to Physical Medicine & Rehabilitation Hospital in 2013.

Methods:

69 patients [42 males (60.9%), 27 females (39.1%)] out of a total of 79 patients admitted in P M R Hospital with hemiplegia were selected. Hemiplegia due to Cerebro Vascular Accidents were included, and causes like tumor, trauma and infection were excluded. Relevant data from the records, and clinical data, presence of depression, treatment, Functional Independence Measure(FIM) score on admission and discharge, and mobility status at discharge were collected.

Results:

A total of 20 CVA patients (29.0%) were diagnosed to have clinical depression by a qualified Psychiatrist and were on treatment. Out of this 9 patients were diagnosed with depression after admission to PMR Hospital. The mean FIM score of patients with depression on admission (55.5) were significantly lower compared to those without depression (65.1) and the percentage change in FIM at discharge was also less in depressed patients, but the difference was not statistically significant. There was a significant difference in the outcome between patients with and without depression. Most of the depressed stroke patients were wheel chair dependent (73.7%), with no one achieving independent walking, while in non-depressed patients, 11.6% achieved independent ambulation, and 34.9% were wheel chair dependent.

Conclusions:

This study showed a significant prevalence of depression in stroke patients and the functional outcome of depressed stroke patients is less than non-depressed patients even after treatment of depression. Hence early detection of depression will be helpful in proper rehab planning.

Key Words: Rehabilitation, Stroke, Depression

Funding Agency: None



Medicine

Category: Clinical

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Impact of donor source on graft and patient survival in pediatric renal transplant recipients

Mosaad A, Al Otaibi T, Nampoory MRN, Halim M, Said T, Abdul-Tawab K, Hosni W, Mansour H, Nair MP
OTC, Kuwait

Introduction:

Evaluation of the impact of kidney donor sources on the outcome of renal transplantation is not adequately studied.

Aim of the study:

We aimed to compare the long-term outcome of kidney transplantation from different sources among a pediatric recipient population.

Methods:

This study comprised 105 pediatric recipients who received their kidney grafts between 1994 and 2011 at Hamed Al-Essa Organ transplant center of Kuwait. These patients were further subdivided into three groups according to donor source (37 with LRDs); (31 with LURDs) and (35 with cadaveric donors). All patients' data were assessed with special emphasis on graft and patient survival as well as post-transplant medical complications.

Results:

All groups with mean follow up seven years-were comparable regarding pre-transplant demographic features especially diabetes, anemia, hypertension, tuberculosis, bone disease and viral profile. We found that patient survival at 1, 5, and 10 years was comparable in all groups. In our series, we observed that rejection rate in the 3 groups was comparable ($p>0.05$). However, kidney survival was poor among cadaveric group compared to other groups despite potent induction and maintenance immunosuppression. This could be explained by poor HLA match; high PRA; higher incidence of ATN and NODAT in the same group ($p<0.05$). This was translated as significantly higher mean serum creatinine. The overall incidence of post-transplant complications was comparable among the three groups except significantly higher post-transplant diabetes among LURD group ($p=0.004$).

Conclusions:

Pediatric renal transplants have good long term patient outcome whatever the donor source is; with poorer cadaveric grafts and higher risk of NODAT with unrelated donors

Key Words: Pediatric renal transplant; Kidney donor; Outcome

Funding Agency: None



Medicine

Category: Clinical

84

Pregnancy outcome after renal transplantation: Kuwait experience

Zakaria Z, Nair P, Al-Otaibi T, Mosaad A, Awdain W, Atta A, Balaha M, Yagan J, Said T,
MedhatHalim
OTC, Kuwait

Introduction:

The influence of pregnancy on graft function in patients after solid organ transplantation is still uncertain. Aim of the work was to evaluate the outcome of pregnancy in our kidney transplanted women.

Methods:

Our study is based on a group of 38 renal transplant recipients with 64 deliveries in the past 12 years and followed up in Hamed Al-Essa organ transplant center of Kuwait. We compared duration of pregnancy, mode of delivery, weight of neonates, and graft function in two groups (tacrolimusbased group and cyclosporinebased group) of patients.

Results:

The two groups were comparable regarding the viral profile (HBV,HCV and CMV),types of dialysis modalities,type of kidney donors and blood groups. Pregnant ladies maintained on tacrolimus were significantly younger with significant more diabetic patients($p<.05$). Ladies maintained on cyclosporine experienced more frequent abortions ; while the fetal mortality was higher in tacrolimus based group, however this did not rank to significance($p=.16$). The mean fetal body weight was comparable in both groups (2.5 ± 0.7 vs. 2.57 ± 0.6 , $p=0.97$). Most ladies who were maintained on tacrolimus delivered more females (63.6%vs. 40% in cyclosporine group) by caesarian section (81.8% vs. 53.8% in cyclosporine group)($p=0.16$ and $p=0.094$ respectively).The two groups were comparable regarding patient and graft outcomes.

Conclusions:

Pregnancy in kidney transplant recipients is high-risk, however with meticulous follow up the outcome might be fruitful without significant adverse effects regardless the calcineurin inhibitor used.

Key Words: Renal transplant; Pregnancy; Outcome

Funding Agency: None



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Comparative performance of conventional urine culture and an automated urine analyzer in terms of time, manpower and resources needed for the diagnosis of urinary tract infection in a tertiary hospital in Kuwait

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Introduction:

The time it takes to diagnose urinary tract infection is 48 – 72 hrs. Alfred 60 (Alifax), an automated urine analyzer, was introduced into the Microbiology Unit of Ibn Sina Laboratory Department in November 2013. This study was done to compare the total time taken to release negative as well as positive cultures by Alfred 60 and the conventional culture, together with the manpower and resources saved by Alfred 60.

Methods:

All urine specimens for culture received in the month of December 2014 are included in the study. They are processed by Alfred and conventional culture simultaneously. The time taken from receiving the specimens until the release of negatives by both Alfred 60 and conventional culture is calculated. The time taken for processing the positive cultures by Alfred 60 is calculated. Manpower and resource saving when using Alfred 60 compared to conventional culture is determined.

Results:

Out of 1590 samples processed in the month of December 2014 by Alfred 60, 1261(80%) are negative and 319(20%) are positive at the end of 4 hrs. The positives are then processed by the conventional culture method and the a total of 212 plates both blood agar and cysteine lactose electrolyte deficient agar (CLED) are used in comparison to a total of 1060 plates used when conventional method is used for all specimens. The total time saved in inoculating 319 positive samples from Alfred as compared to inoculating all the 1590 samples is 21.2 hrs. The total time saved when negatives are released within 5 hrs by Alfred is 21 hrs. The total manpower saved was from 3 to 1 technician per day when using conventional culture compared to Alfred 60.

Conclusions:

By using Alfred 60, time, manpower and cost were significantly reduced with a significant impact on the rapid confirmation and exclusion of UTI with its effect on antimicrobial stewardship.

Key Words: Conventional urine culture; Automated urine analyzer; Time, manpower and cost saving

Funding Agency: None



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Phenotypic and molecular characterization of candida haemulonii complex isolates and their emerging significance as human pathogens in Kuwait

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Introduction:

Non-albicans Candida species are being increasingly recognized as a major cause of nosocomial infections. Members of Candida haemulonii complex and other related species (Candida auris and Candida pseudohaemulonii) exhibit reduced susceptibility to antifungal agents and are often misidentified by phenotypic methods. Here, we report occurrence and distribution of C. haemulonii complex species in clinical specimens and their role in human disease in Kuwait.

Methods:

Candida species isolates exhibiting reduced susceptibility to amphotericin B and/or fluconazole were tested. Phenotypic identification was based on germ tube test, growth characteristics on CHROMagar Candida, and carbohydrate assimilation tests by VITEK 2 yeast identification system. For molecular identification, the internal transcribed spacer (ITS) region and D1/D2 domains of rDNA were sequenced and BLAST searches were used for species identification. Antifungal susceptibility was determined by Etest. The minimum inhibitory concentrations (MICs) were read after 24 h incubation at 35°C.

Results:

A total of 14 isolates of C. haemulonii complex and related species were identified. Of these, 5 were characterized as C. haemulonii, 2 as C. duobushaemulonii and 7 as Candida auris. Five of C. haemulonii, 2 C. duobushaemulonii and one C. auris isolates originated from patients with fungemia. All C. haemulonii, and C. duobushaemulonii isolates showed reduced susceptibility to amphotericin B (MICs 32 > µg/ml) and fluconazole (MICs >256 µg/ml).

Conclusions:

Isolation of C. haemulonii and other closely related species from blood and other clinical specimens suggests their emerging role in human infections in Kuwait. Since phenotypic methods cannot reliably identify these uncommon Candida species, increasing use of molecular methods is advocated, particularly when they exhibit reduced susceptibility to antifungal agents, which have direct implication in therapeutic management.

Key Words: Candida haemulonii Complex; Molecular characterization; Emerging significance
Funding Agency: None



Microbiology, Virology and Immunology

Category: Graduate PhD (Basic Science)

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Simple, low-cost detection of *Candida orthopsilosis* isolates and AFLP analysis for their molecular fingerprinting

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Introduction:

Objective: Recent molecular studies have shown that phenotypically identified *Candida parapsilosis* isolates represent a complex of three species, namely, *C. parapsilosis*, *C. orthopsilosis* and *C. metapsilosis*. *Lodderomyces elongisporus* is another species phenotypically closely related to *C. parapsilosis*. The aim of this study was to develop a rapid multiplex (m) PCR assay for rapid identification and molecular fingerprinting of *C. orthopsilosis* isolates.

Methods:

Species-specific forward primer targeting ITS1 region of rDNA and universal reverse primer designed to yield species-specific amplicons from *C. parapsilosis* (171 bp), *C. orthopsilosis* (109 bp), *C. metapsilosis* (217 bp) and *L. elongisporus* (258 bp) were used in mPCR. Reference strains of relevant species were used to establish mPCR. Clinical isolates (n=454) identified as *C. parapsilosis* by Vitek 2 were analyzed to evaluate mPCR. DNA sequencing of ITS region of rDNA were performed to validate the results of mPCR. All *C. orthopsilosis* isolates were genotyped by ITS sequencing and AFLP analysis.

Results:

Reference strains yielded expected results by mPCR. Phenotypically identified *C. parapsilosis* isolates (n=454) were identified as *C. parapsilosis* (n=431), *C. orthopsilosis* (n=19), *C. metapsilosis* (n=1) and *L. elongisporus* (n=3) by mPCR. The results were confirmed by DNA sequencing of ITS region of rDNA for 10 selected *C. parapsilosis*, 19 *C. orthopsilosis*, 1 *C. metapsilosis* and 3 *L. elongisporus* isolates. Molecular fingerprinting of *C. orthopsilosis* isolates by ITS sequencing and AFLP were in concordance and divided them into three clusters (A, n=5; B, n= 11; and C, n= 3).

Conclusions:

The mPCR accurately discriminated *C. parapsilosis*, *C. orthopsilosis*, *C. metapsilosis* and *L. elongisporus* strains. This rapid assay will be useful for characterizing large number of isolates for epidemiological studies. AFLP identified only 3 major clusters among 19 *C. orthopsilosis* strains indicating limited heterogeneity.

Key Words: Candida orthopsilosis; AFLP; Multiplex PCR

Funding Agency: Supported by College of Graduate Studies and Research Sector grant YM10/11 and Research Core Facility grant SRUL02/13.



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Economic burden of refractory chronic spontaneous urticaria on Kuwait health system

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Introduction:

Chronic spontaneous urticaria (CSU) is a common debilitating problem worldwide. Despite its prevalence in the Middle East, very little data is available on the economic impact of CSU on the public health system. This study evaluates the direct costs of treating refractory CSU patients in Kuwait. It also evaluates the impact of omalizumab use in these patients on the public health system budget.

Methods:

Prevalence of CSU was estimated through the Delphi method. Data regarding drug utilization, and the health care system utilization was collected retrospectively from charts of refractory CSU patients who are followed up at the Al-Rashed Allergy center in Kuwait. Costs were calculated from a health system perspective. One-way sensitivity analyses were conducted on the price and utilization of each cost component.

Results:

Before omalizumab use, the total direct costs of treating 1,156 refractory CSU patients was estimated to be 1 million Kuwaiti Dinars (KD) per year, corresponding to around 900 KD per patient per annum. The total cost was principally generated by outpatient visits (800,000 KD); which corresponds to 81% of the total cost. After omalizumab use, the cost was estimated to be 4.3 million KD per year, corresponding to around 3,700 KD per patient per annum. The total cost was principally generated by omalizumab costs (4.1 million KD); which corresponds to 97% of the total cost. All other direct costs of treating CSU patients were decreased after the use of omalizumab. Conventional medication costs and hospitalization costs were reduced by 90%. Cost estimates were most sensitive to variations in the prices and utilization of outpatient visits and the price of omalizumab.

Conclusions:

The economic burden of refractory CSU in Kuwait is high. The introduction of omalizumab on the health care system is costly because of its high cost; however, omalizumab has proven to be effective and is driving all other direct costs down.

Key Words: Kuwait, Economic, Chronic Urticaria

Funding Agency: None



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Lack of protection against *Campylobacter jejuni* after immunization with a double-mutant heat-labile enterotoxin of *Escherichia coli* (dmLT) in an adult mouse intestinal colonization model of infection

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Introduction:

We previously demonstrated that cholera toxin (CT) antiserum reacted with the major outer membrane protein (MOMP) from *C. jejuni* strains. Orally immunizing adult mice with CT significantly protected them against intestinal colonization upon oral challenge with *C. jejuni*. Humans cannot be immunized with CT as it is reactogenic. CT and LT are structurally and functionally related. A dmLT (R192G/L211A) has been shown to lose its toxicity for mice and humans while retaining its adjuvanticity. If dmLT cross-reacts with *C. jejuni*, the possibility remains that immunization of humans with dmLT will protect against *C. jejuni* diarrhea. To realize this goal, as a prelude, we carried out studies in the adult mouse colonization model of *C. jejuni* infection.

Methods:

A *C. jejuni* strain 111 (Penner serotype O:1,44) which cross-reacted with CT was used as the challenge strain. The reactivity of *C. jejuni* MOMP with rabbit dmLT antiserum (dmLT provided by JD Clemens, University of New Orleans, LO, and serum produced by us by standard protocol) was studied by immunoblot. Twelve, 6-8 weeks old BALB/c mice were orally immunized with a dose of 25 microg of dmLT three times at weekly intervals. Mice fed with phosphate-buffered saline (PBS, pH 7.2) served as controls. Animals were challenged with 2 X 10⁹ *C. jejuni* 111 a week after vaccination. Fecal shedding of 111 was studied daily for 9 days.

Results:

MOMP from *C. jejuni* 111 did not react with dmLT antibody. Most mice excreted challenge 111 strain showing no significant quantitative difference between the immunized and control mice.

Conclusions:

As dmLT did not cross-react with *C. jejuni* MOMP, immunization of mice with dmLT did not afford protection against colonization. The epitope(s) in CT responsible for cross-reaction with *C. jejuni* MOMP seems to be absent in dmLT. Therefore, it appears that immunization of humans with dmLT may not provide protection against *C. jejuni* diarrhea.

Key Words: E. coli heat-labile enterotoxin, C. jejuni, Vaccination

Funding Agency: Kuwait University grant number M103/13



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Infections in pediatric dialysis patients in Kuwait: 10 years' experience

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Introduction:

Objective: As the incidence of end-stage renal disease (ESRD) worldwide has increased, so has the need for performing hemodialysis (HD) and peritoneal dialysis (PD). We sought to identify risk factors and measure the rate of infections in pediatric patients undergoing dialysis.

Methods:

A retrospective review of pediatric patients at a single pediatric dialysis center in Kuwait from July 2003– July 2013 was performed. Risk factors and incidence of rate of infections were determined and also microbiological profile of commonest organisms causing dialysis -related infections was examined in patients undergoing either HD or PD.

Results:

A total of 91 patients underwent HD and 63 patients underwent PD during the 10 years period. The episodes of infection were documented in 13 patients in each of the two groups. The median age at presentation was 6.6 and 72 months for HD & PD groups, respectively. Our rates of infection were found to be one peritonitis episode per 20 patient months in PD group and 0.41 infection episodes per patient year in HD group. The commonest organisms isolated in PD-related infections were *Pseudomonas aeruginosa* and coagulase-negative staphylococci (CNST) whereas in HD-related infections CNST was the leading organism. Among the risk factors in both groups, personal hygiene was the most significant with a P value of <0.05. Mortality related to infection was 7.7% in PD with a median follow up of 6 months, and None was reported in HD.

Conclusions:

In this study of pediatric patients undergoing PD or HD at our center, the infection rates were found to be consistent with international reports. Furthermore, our data consistent with others, which showed a significant risk factor for infection with poor personal hygiene

Key Words: Hemodialysis; Peritoneal dialysis; Dialysis-related infection.

Funding Agency: None



Microbiology, Virology and Immunology

Category: Clinical

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Tumour necrosis factor alpha and pregnancy complications

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Introduction:

The aim of this study was to compare the levels of tumour necrosis factor-alpha (TNF- α) produced by peripheral blood mononuclear cells in normal pregnancy and complications such as recurrent miscarriage, premature rupture of membranes, pre-eclampsia and intra-uterine fetal growth retardation.

Methods:

Maternal peripheral blood mononuclear cells from women with a) recurrent spontaneous miscarriage, b) premature rupture of fetal membranes, c) preeclampsia and d) intra-uterine fetal growth retardation were stimulated with mitogen or antigen, and levels of TNF- α produced were compared to those produced by peripheral blood mononuclear cells from normal pregnancy.

Results:

Mitogen-induced median levels of TNF α at 1st, 2nd, 3rd and normal delivery were 1176.4, 4320.9, 7307.4 and 2463.0 pg/ml respectively, while those produced in recurrent spontaneous miscarriage, premature rupture of membranes and preeclampsia were 4159.8, 3489.5, 4149.2 pg/ml respectively. The differences were statistically significantly higher in these pregnancy complications ($p = 0.04$, 0.024 , and 0.014) as compared to levels in normal pregnancy. Further, antigen-induced TNF- α levels were produced at statistically significantly higher levels by women with IUGR (120.4 pg/ml) as compared to normal pregnancy (17.9 pg/ml) ($p=0.041$).

Conclusions:

Higher levels of tumour necrosis factor alpha are associated with these pregnancy complications suggesting possible pathogenetic roles for this potent inflammatory cytokine in such conditions.

Key Words: Intra-uterine growth retardation; Preeclampsia; Recurrent spontaneous miscarriage

Funding Agency: None



Microbiology, Virology and Immunology

Category: Graduate PhD (Basic Science)

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Diversity of Epidemic-Methicillin-Resistant Staphylococcus aureus - 15 (EMRSA-15) in Kuwait Hospitals

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Introduction:

Since its emergence in England in 1991, UK EMRSA-15 which belongs to ST22-MRSA-IV, has been reported globally. This study characterized EMRSA-15 isolates obtained from patients in Kuwait hospitals to ascertain their relatedness to EMRSA-15 obtained in the UK and elsewhere.

Methods:

A total of 37 EMRSA-15 isolates obtained in 2005 (4 isolates) and 2010 (33 isolates) were characterized using pulsed-field gel electrophoresis (PFGE), coagulase serotyping, SCCmec subtyping, multilocus sequence typing (MLST) and spa typing. DNA microarray was used to determine carriage of virulence and antibiotic resistance genes.

Results:

The isolates were resistant to trimethoprim (75.6%), ciprofloxacin (29.7%), erythromycin/clindamycin (24.3%), tetracycline (19.0%), gentamycin/kanamycin (21.6%). All isolates belonged to ST22, SCCmec IV, coagulase type XI, three PFGE types and 10 subtypes, and 10 spa types including t223 (51.3%), t852 (13.5%), t032 (8.1%), t790 (8.1%) and t3107 (5.4%). Spa types, t309, t2251, t3935, t5708, and t5983 occurred in single isolates. Spa type t032 carried SCCmec IVh, while t223, t309, t790, t2251, t3935, and t5708 carried SCCmec IVa. Spa types t852, t3107 and t5983 carried SCCmec IV. DNA microarray revealed that all isolates carried agr1, cap5, and egc gene cluster (seg, sei, selm, seln, selo, selu). sec was found only in t032 and t790 isolates. tst was detected in t223, t309, t2251, t3935, and t5708 isolates. t852, t3107, and t5983 isolates were positive for PVL and expressed multidrug resistance. The majority of the isolates carried dfrS1 and ermC that encodes trimethoprim and erythromycin resistance, respectively.

Conclusions:

The EMRSA-15 population in Kuwait hospitals belonged to diverse genetic backgrounds with 51.3% belonging to Middle Eastern variant of EMRSA-15 (ST22-IVa-t223) and only 8.1% belonging to UK EMRSA-15/Barnin MRSA clone (ST22-IVh-t032) suggesting multiple routes of acquisition for EMRSA-15 in Kuwait hospitals.

Key Words: MRSA; UK EMRSA-15; Kuwait

Funding Agency: YM 02/12



Microbiology, Virology and Immunology

Category: Clinical

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Correlation of Human Papillomavirus (HPV) with abnormal cervical cytology in the native and expatriate women in Kuwait

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Introduction:

Research has been conducted over recent years to determine the association of HPV with cervical cytological lesions such as atypical squamous cells of undetermined significance (ASC-US). Women with such lesions have a small but significantly higher risk of developing cervical cancer compared to those with normal smears. Our objective was to study the association of HPV, detected by a DNA-based assay (Hybrid Capture 2) in women with ASC-US cytology & prevalence of high-risk (hr) HPV in different age groups of these women.

Methods:

Kuwaiti (K=150) and expatriate (NK=125) women diagnosed with of ASC-US were tested for HPV by HC2 (Qiagen). Liquid-based cytology PreservCyt specimens were processed for screening smears and residual ThinPrep samples were used for HPV assay. The women were stratified according to age groups of < 30, 31-40, 41-50 and > 50 years.

Results:

HC2 assay detected HPV in 36 (24%) with hr types in 17 (47.2%), low-risk types (lr) in 11 (30.5%) and both (hr & lr) in 8 (22.2%) of K women. Among NK women, 24 (19.2%) tested positive for HPV with hr in 12 (50%), lr in 7 (29.1%) and both types in 5 (20.8%). Overall, hrHPV was detected in 69.4% and 70.8% of K and NK women, respectively with highest rates, 29.4% and 20.0% being in < 30 year age group of K and NK women, respectively. The rates of hrHPV detection in other age groups did not differ significantly among all women tested.

Conclusions:

The hrHPV infection was more prevalent among K and NK women in < 30 year age group with ASC-US. Further research is required to study the occurrence of hr types common in this region as also the follow-up of women with abnormal cytology who develop histological proven cervical cancer.

Key Words: Human Papilloma Virus; STD; Cervical carcinoma

Funding Agency: None



Microbiology, Virology and Immunology

Category: Clinical

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Acinetobacter spp. Bacteremia in a neonatal intensive care unit

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Introduction:

Acinetobacter spp.(AC) has recently emerged as an important nosocomial pathogen especially in intensive care units. It has also gained importance lately because of acquiring resistance to multiple antibiotics. This retrospective study is designed to evaluate the role of AC as important pathogen in neonatal blood stream infections, to identify the associated risk factors and to evaluate antibiotic susceptibility pattern (ASP).

Methods:

From 2012 through 2014, neonates with AC bacteremia were recorded with species identification of the isolate & ASP. In our laboratory blood cultures are performed using BACTEC^M & identification of organisms & AS testing is determined by Vitek 2 or Maldi-tof/MS. The case records of these neonates were retrieved for relevant clinical information including signs & symptoms, maternal & fetal risk factors, antibiotics received & the outcome.

Results:

During the study period 28,078 blood cultures were processed. Of these Gram-negative bacilli (GNB) were isolated from 371 neonates as compared to 806 & 133 being positive for Gram-positive & Candida spp., respectively. Among GNB 31.2%, 15.1%, & 13.7% were identified as K. pneumoniae, E. coli & AC respectively. Majority of AC belonged to baumannii (AB) complex 46/51 (90.2%) followed by A. lwoffii 3/51 (5.9%) & A. calcoaceticus 1/51(1.9%). All babies were born in hospital with 55% being females, birth weight > 1 kg in 51%, late-onset AC bacteremia in 88%, delivery by C-section in 59% & Apgar score of > 6 after 5 min. in 78%. The mortality rate was found to be 13/51 (25.5%). Multi-drug resistance (MDR) was observed in one strain of AB with susceptibility to only ciprofloxacin. All patients (except one) were treated either with piperacillin/tazobactam or meropenem with or without amikacin.

Conclusions:

Although MDR among these strains is not a major problem, mortality is similar to that reported from other NICUs globally.

Key Words: Acinetobacter; Bacteremia; Neonates

Funding Agency: None



Microbiology, Virology and Immunology

Category: Basic Sciences

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Phylogenetic analysis of human polyomaviruses WU from patients with respiratory tract infection in Kuwait

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Introduction:

Human polyomavirus WU (WUV) is a newly discovered respiratory virus and a limited data are available on the circulating strains. Here we investigated the circulating WUV strains among hospitalized patients with respiratory tract infections (RTI).

Methods:

Samples were screened by nested PCR using two sets of primers. Positive samples were sequenced and subjected to phylogenetic analysis. Patients with RTI were screened during a four years period from April 2010 to March 2014.

Results:

From four hundred fifty nine hospitalized children and adult patients with RTI, 17 patients (3.7%) were diagnosed with WUV infections. Genomic WUV DNA of three strains were sequenced and phylogenetic trees were constructed. Two of the circulating WUV strains belong to the type Ia and the third one belongs to the type IIIb. This study enabled us to identify the circulating WUV genotypes among patients with viral RTI in Kuwait.

Conclusions:

These finding allow us to develop an understanding of the circulating WUV genotypes among these patients. Precise classification and typing procedures will be important in the future for classifying WUV isolates and investigating what role these genetic groups play in human biology and disease.

Key Words: Human polyomavirus WU; Respiratory tract infections; Phylogenetic analysis

Funding Agency: Research No. (MI 03/08) by the Research Sector, Kuwait University.



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Molecular epidemiology and characterization of Multiple-Drug Resistant (MDR) clinical *Acinetobacter baumannii* isolates

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Introduction:

Acinetobacter baumannii is emerging as an important healthcare-associated pathogen worldwide with resistance to almost all known antibiotics. However, the antibiotic resistance mechanisms remain poorly characterized.

Methods:

We aimed to identify the genetic relatedness of multiple-drug resistance (MDR) in *Acinetobacter baumannii* clinical isolates recovered from a hospital in Los Angeles. Twenty one MDR *A. baumannii* isolates were collected and their antibiotic susceptibility were determined according to the CLSI guidelines. Genes coding for antibiotic resistance, were identified by PCR including plasmid-mediated quinolone resistant genes (QNR), oxacillinases (OXA-type), AAC, PER, GES, VEB, SIM, IMP, VIM, NDM and insertion elements. The identity of the amplicons was confirmed by DNA sequencing. Clonal relationships were studied by pulsed-field gel electrophoresis (PFGE) and multi-locus sequence typing (MLST).

Results:

MDR consistently correlated with the presence of oxacillinases, mostly in the form of plasmid-mediated OXA-23 enzyme which were detected in 12 (57.1%) isolates. GES-type carbapenemases were found in 20 (95.2%) strains, AAC in all 21 (100%) strains, PER in 7 (33.3%) strains and ISAbal has been detected in 16 (76.2%) isolates. The association between ISAbal and resistant genes researched in this study confirms insertion elements as a source of β -lactamase production. None of the clinical isolates harbored QNR-type genes. Of the 21 clinical isolates, 5 were found to be related to sequence type-1 (ST1) and 16 were found to belong to sequence type-2 (ST2) as analyzed by MLST. PFGE demonstrated that the majority of clinical isolates are highly related (>85%).

Conclusions:

This study supports a more complete understanding of genotyping of antibiotic resistance for better assessment of MDR strains transmission. Continuous surveillance is needed for monitoring the spread of these strains equipped with multiple drug resistance mechanisms.

Key Words: *Acinetobacter baumannii*; MDR; MLST

Funding Agency: None



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Microarray analysis for differential gene expression in multiple sclerosis

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Introduction:

Multiple sclerosis (MS) is an immune-mediated inflammatory demyelinating disease of the central nervous system. The peripheral blood mononuclear cells (PBMCs, i.e. lymphocytes & monocytes), induce active nerve demyelination in MS. Therefore, differential gene expression analysis in PBMCs of MS patients may be helpful in a better understanding of disease pathogenesis. In this study, the microarray technology was used to identify the genes expressed differentially in MS patients.

Methods:

PBMCs were isolated from the blood of newly diagnosed and drug naïve patients with relapsing-remitting MS and healthy subjects. Total RNA was purified from the cells by TRIzol reagent (Ambion) and quantified spectrophotometrically (Epoch, Biotek). The quality of purified RNA was assessed using Bioanalyzer 2100 (Agilent). The GeneChip 3' IVT Express kit (Affymetrix) was used for target RNA preparation and hybridized to HG-U133_plus_2 array (Affymetrix). The chips were scanned using the GeneChip scanner 3000 7G. The raw CEL files were scanned visually and quality control was done by the Expression Console Software. The *.chp files were exported to the Transcriptome Analysis Console (Affymetrix) for fold change estimation in gene expression.

Results:

The purity and quality of all the RNA samples were within the specified range. Principal component analysis clustering revealed that the healthy and the diseased samples formed separate clusters. Out of the total 54,613 transcripts studied, 357 transcripts were differentially expressed; 302 transcripts were up-regulated and 55 transcripts were down-regulated in MS patients. Interestingly, the majority of transcripts showing significant changes in MS PBMCs were associated with immune responses.

Conclusions:

The microarray analysis is a useful tool to study global gene expression in cells. It provides important information about the up or down regulation of genes that may have a potential role in disease pathogenesis.

Key Words: Gene Expression, Multiple Sclerosis, Microarray

Funding Agency: SRUL02/13 and MM 03/09



Microbiology, Virology and Immunology

Category: Basic Sciences

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Humoral immune responses in mice immunized with DNA vaccine constructs containing Mycobacterium tuberculosis-specific RD genes

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Introduction:

Recombinant DNA vaccine constructs are promising candidates to develop new vaccines against tuberculosis. Recent studies have suggested that both cellular and humoral immune responses are required to provide optimum protection against tuberculosis. We have previously shown the induction of cellular immune responses in mice after immunization with recombinant DNA vaccine constructs containing genes for Mycobacterium tuberculosis-specific proteins encoded by the region of difference (RD). The aim of this study was to investigate the induction of humoral immune responses in mice immunized with recombinant DNA vaccines constructs of pUMVC6 and pUMVC7 containing RD1 and RD9 genes of M. tuberculosis.

Methods:

Mice were immunized with the parent and recombinant plasmid DNA and sera were tested for antibodies against pure recombinant proteins of RD1 (PE35, PPE68, EsxA, EsxB) and RD9 (EsxV), peptide mixtures of each protein and their individual peptides using enzyme-linked immunosorbent assays. The optical density (OD) values were measured at 405 nm. E/C (OD in antigen-coated wells/OD in antigen uncoated wells) were calculated, and the values of E/C>2 were considered positive.

Results:

RD1 and RD9 antigen-specific antibodies were detected to all purified proteins in sera of mice immunized with the recombinant DNA vaccine constructs (E/C >2.0), but not in mice immunized with the parent plasmids. With respect to peptide mixtures and single peptides, PE35mix and P6 of PE35; PPE68 mix and P19, P24 of PPE68 showed antibody reactivity with sera of mice immunized with the corresponding recombinant pUMVC6 and/or pUMVC7 DNA vaccine constructs.

Conclusions:

The results confirm in vivo expression and the induction of humoral immune responses to of all the five RD1 and RD9 proteins whose genes were cloned in the DNA vaccine vectors. Furthermore, conformational as well as linear epitopes were recognized by the antibodies.

Key Words: ELISA, Antigens, Antibodies

Funding Agency: Supported by Kuwait University Research Sector grant



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Antimicrobial Susceptibility of OXA-48, NDM-1 and VIM-4 carbapenemase-producing clinical isolates of enterobacteriaceae from Kuwait government hospitals

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Introduction:

Emergence of infections due to multidrug-resistant Enterobacteriaceae presents a significant public health problem worldwide. Treatment alternatives for infections due to carbapenemase-producing Enterobacteriaceae are few and the resistant organisms have the potential for causing serious healthcare epidemics if not promptly detected and contained. The study was conducted to investigate types of carbapenemases-encoded genes and drug resistance among carbapenem-resistant Enterobacteriaceae isolates in 6 government hospitals in Kuwait.

Methods:

Enterobacteriaceae isolates resistant to carbapenems were collected over a period of 3 years (2010-2013). Susceptibility testing to 13 commonly used antibiotics was carried out by E test according to the CLSI guidelines. PCR assay was performed for detection of genes encoding ESBLs (blaCTX-M, blaSHV and blaTEM) and carbapenemases (blaOXA-48, blaVIM, blaNDM, blaIMP, blaGIM and blaKPC).

Results:

A total of 66 non-duplicated carbapenem-resistant isolates were collected over a period of 3 years. However, only 32/66 (48.5%) carried the carbapenemase resistance genes. Resistance genes analysis showed that 11 isolates carried blaOXA-48 gene, 11 carried blaVIM-4 gene and 10 carried blaNDM-1 gene. 9.1%, 72 and 80 % of blaOXA-48, blaVIM-4 and blaNDM-1-carrying Enterobacteriaceae, respectively were resistant to amikacin. 27.3, 18.2 and 40 % of blaOXA-48, blaVIM-4 and blaNDM-1 carrying isolates, respectively, were resistant to tigecycline and 9.1, 9.1, and 20%, respectively to colistin. Overall, almost 70% of the isolates were resistant to ciprofloxacin and cefepime.

Conclusions:

Treatment of carbapenemase-producing Enterobacteriaceae in Kuwait is problematic as some of our isolates are resistant to tigecycline at an unacceptable level and resistance to colistin is emerging.

Key Words: Susceptibility; Carbapenemases; Kuwait

Funding Agency: Kuwait University Research Grant No. MI 06/10 is fully acknowledged



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De novo assembly and comparative genome analysis of different Brucella genomes

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Introduction:

Brucellosis is a worldwide occurring zoonotic disease caused by the organisms of genus *Brucella*. The genome of *Brucella* is composed of two circular chromosomes without any plasmids. *Brucella* genome carries very limited variation across strains which makes it difficult to identify a particular strain. The aim of this study was to perform de novo assembly of *Brucella* genomes to identify the strain, and also to find the extent of differences at the gene level across the isolates of the same strain.

Methods:

Sequence data for draft was generated from 15 *Brucella* isolates using MiSeq platform. The generated reads were taken for further assembly and analysis. All the analysis was performed using Bioinformatics work station (8 core i7 processor, 8GB RAM with Bio-Linux operating system). FastQC was used to determine the quality of reads and low quality reads were trimmed or eliminated using Fastx_trimmer. Assembly was done by using Velvet and ABySS. Ordering of assembled contigs was done by Mauve. An online server RAST was used to annotate the contigs assembly. Annotated genome were compared using Mauve and ACT tools.

Results:

Q score was greater than 30 for 80% of reads with more than 100x coverage, which suggested that data can be utilized for de novo assembly. However when analyzed by FastQC, quality of four read out of fifteen reads was not good enough for creating a complete draft. So remaining samples were used for further analysis. The comparative genome analysis showed that despite sharing same gene set, the SNP and INDELS were prevalent across different genomes, which provided a variable extent of diversity to this bacteria.

Conclusions:

De novo assembly and comparative genome analysis can be utilized to find mutations and differences at gene level across different genomes within a strain. This information can also be exploited for identification of differences at a strain level along with discovery of novel genes present in a strain.

Key Words: De novo; Genome assembly; Brucella

Funding Agency: Supported by Kuwait University Research Sector grants SRUL02/13.



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Nucleic Acid Isolation, Purification and Quantification Using Manual Method and Biorobotic Method

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Introduction:

Nucleic acids are polymers, essential for all known forms of life and include DNA and RNA. Nucleic acid isolation is a

process of purification of DNA/RNA from samples using a combination of physical and chemical methods. The sources of nucleic acids include blood, tissues, bacteria, viruses and also PCR products and DNA recovered from agarose gels. The procedure includes four main steps: cell lysis, binding, washing and elution. The aim of this study was to compare the quantity and purity of nucleic acids using manual and automated methods.

Methods:

Nucleic acids were isolated using commercial kits. A manual method and a biorobotic method using QIAcube (Qiagen) were employed. QIAcube is a fully automated, closed, compact bench top system, avoids any manual errors, and safe to use. Whole blood samples obtained from healthy subjects and patients were used to isolate DNA using QIAamp DNA Blood mini kit (catalogue: 51104) and RNA QIAamp Blood mini kit (catalogue: 51104). Furthermore, PCR products and DNA from agarose gels were purified by both manual and biorobotic methods. The isolated and purified nucleic acids were quantified using Epoch spectrophotometer (Biotek), having a monochromator-base UV-Vis wavelength of 200 to 999 nm.

Results:

The concentration of nucleic acids from blood specimens varied from 20-120 ng/ μ l using manual as well as automated bio-robotic method. Furthermore, the purity was also similar for DNA ($A_{260}/A_{280} = 1.7-1.9$) and RNA ($A_{260}/A_{280} = 1.9-2.1$) using the two methods. The concentration of purified PCR products and DNA purified from agarose gels varied between 5-20 ng/ μ l using both methods ($A_{260}/A_{280} = 1.7-1.9$).

Conclusions:

The manual and biorobotic methods yielded similar results with respect to quantity and purity. However, the biorobotic method is more convenient and preferable because it can purify up to 12 samples at a time.

Key Words: Qiacube; Nucleic acid; Gel electrophoresis

Funding Agency: Supported by Kuwait University Research Sector grant SRUL02/13



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Species distribution and antifungal susceptibility of *Candida* bloodstream isolates in Kuwait

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Introduction:

Candida species are the fourth leading cause of nosocomial bloodstream infections worldwide. The epidemiology of candidemia is changing with non-*albicans* *Candida* species now accounting for more than half of all bloodstream isolates. This study reports on species distribution and antifungal susceptibility profiles of *Candida* bloodstream isolates obtained during the 10-year period (2005-2014) in Kuwait.

Methods:

All isolates were identified to species level by the germ tube test and/or by carbohydrate assimilation profile using the VITEK 2 yeast identification system. Antifungal susceptibility was determined by E-test against amphotericin B, fluconazole, caspofungin and voriconazole using RPMI agar. The minimum inhibitory concentrations (MICs) were read after 24 h incubation at 35°C. EUCAST/CLSI breakpoints were used to grade isolates as susceptible, susceptible dose-dependent/intermediate, and resistant.

Results:

A total of 1746 bloodstream *Candida* spp. isolates were obtained and included *C. albicans* (34.8%), *C. parapsilosis* (30.6%), *C. tropicalis* (12.1%), *C. glabrata* (8.7%) and others (13.8%). All *C. albicans*, *C. parapsilosis* and *C. tropicalis* isolates were susceptible to amphotericin B (MIC <1 µg/ml). Of 150 isolates of *C. glabrata* tested, only one (0.7%) exhibited resistance against amphotericin B (MIC ≥1 µg/ml). Resistance to fluconazole was observed in two (0.4%) *C. parapsilosis* isolates (MIC ≥8 µg/ml) and five (3.3%) *C. glabrata* isolates (MIC ≥62 µg/ml). All the isolates of *C. albicans*, *C. tropicalis*, *C. parapsilosis* and *C. glabrata* were susceptible to caspofungin (MIC < 0.5 µg/ml).

Conclusions:

Consistent with the global trends, non-*albicans* *Candida* species formed the major proportion of bloodstream isolates in Kuwait. Although amphotericin B and fluconazole are widely used in clinical practice, there is little evidence of emergence of resistance to these drugs in Kuwait.

Key Words: Candida; Candidemia; Antifungal susceptibility

Funding Agency: None



103

Serotype distribution and penicillin resistance of streptococcus pneumoniae in Kuwait: A ten-year study of impact of pneumococcal conjugate vaccines

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Introduction:

The pneumococcal conjugate vaccine (PCV)-7 was introduced in Kuwait in August 2006 and PCV-13 in August 2010 for children less than 2 years. The study is done to evaluate the impact of PCV-7 and PCV-13 on serotype distribution and antimicrobial resistance of invasive *Streptococcus pneumoniae* (*S. pneumoniae*) isolates.

Methods:

The study included all cases of invasive pneumococcal disease (IPD) divided into two periods, the pre-vaccination period is from August 2003 to July 2006 and the post-vaccination period is from August 2006 to July 2013. Serotyping and penicillin susceptibility testing were done using Quellung reaction and Etest method, respectively.

Results:

Sixty three invasive isolates (25%) were identified from children ≤ 5 years in the pre-vaccination period, and 156 invasive isolates (28%) from children ≤ 5 years in the post-vaccination periods. In the pre-vaccination period, PCV-7 and PCV-13 vaccine coverage in children ≤ 5 years is 50% and 70% in other age groups. In the post-vaccination period, the vaccine coverage for PCV-7 is 21% in children ≤ 5 years and 29% in other age groups and for PCV-13 is 46% in children ≤ 5 years and 51% in other age groups. The decrease in vaccine serotypes and the increase in the non-vaccine serotypes during post vaccination period compared to pre-vaccination period is statistically significant (p value 0.001). Penicillin resistance among *S.pneumoniae* isolates dropped from 67.9% in pre-vaccination period to 46.2% in post-vaccination period (p value 0.006)

Conclusions:

After 7 years of PCV use in Kuwait, new emerging serotypes of *S.pneumoniae* are seen.

Key Words: Streptococcus pneumoniae; Serotype distribution; Conjugate pneumococcal vaccine

Funding Agency: None



Microbiology, Virology and Immunology

Category: Basic Sciences

104

Flow cytometry quantifies multiple cytokines in culture supernatants of spleenocytes from BCG-vaccinated mice

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Introduction:

Cytokines are cell signaling molecules with a primary role in immunological function. They are broadly divided into T-helper (Th)1, Th2, Th17, Treg and proinflammatory cytokines. Traditionally, ELISAs in 96-well microtitre plates have been used for the detection and quantification of cytokines. In these assays, only one cytokine can be measured at a time and the minimum sample volume is 50µl. Recently, multiplex bead-based assays have been developed for simultaneous detection and quantification of a large number of cytokines. In this study, we have established and evaluated a 10plex cytokine assay using culture supernatants and antibody coated beads in flow cytometry.

Methods:

Spleenocytes were isolated from spleens of Mycobacteriumbovis BCG-vaccinated mice and stimulated in vitro with BCG. On day 6, the culture supernatants were collected and 25µl aliquots were analyzed for the simultaneous detection and quantification of 10 cytokines, i.e. GM-CSF,IFN-γ, TNF-α, IL-11, IL-2, IL-4, IL-5, IL-6, IL-10 and IL-17, by using a 10plex bead assay (BD Biosciences) and Cytomics FC 500 flowcytometer (Beckman Coulter).

Results:

The mycobacterial antigen stimulation of spleenocytes induced the secretion of all of the above cytokines. However, the quantity of IL-6 (a pro-inflammatory and Th2 cytokine) was the highest, followed by the Th1 cytokine IFN-γ and Th2 cytokines IL-4 and IL-5. Relatively lower concentrations of other cytokines were detected, i.e. Treg (IL10), Th17 (IL-17) and proinflammatory cytokines TNF-α and IL-11.

Conclusions:

Stimulation of spleenocytes with the mycobacterial antigen induces the secretion of a large number of cytokines, including proinflammatory, Th1, Th2, Th17 and Treg cytokines, which suggests a non-committed differentiation of T cells in response to complex mycobacterial antigens. Furthermore, the present study illustrates that detection of multiple cytokines by flow cytometry is a time saving and cost effective method.

Key Words: Flow cytometer; Cytokines; Spleenocytes

Funding Agency: Kuwait University Research Sector grant SRUL 02/13



Microbiology, Virology and Immunology

Category: Clinical

105

Validation of a rapid molecular assay for the detection of genes encoding the prevalent carbapenemases in Enterobacteriaceae.

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Introduction:

This test system is a microbiological rapid test for detection of variants of metallo- β -lactamases family and ESBL of the CTX-M group. Our objective was to evaluate this rapid molecular assay, Eazyplex® SuperBug CRE (ESB), for the detection of prevalent genes mediating carbapenem resistance in Enterobacteriaceae.

Methods:

Consecutive isolates of species of the family Enterobacteriaceae with elevated MICs for carbapenems, recovered from various clinical specimens from April to September 2014, were chosen for the study. The presence of carbapenamase was tested for by the Hodge-test and combined disk tests containing imipenem and meropenem plus EDTA. Subsequently, PCR and sequencing were performed to detect the presence of various resistance genes. ESB qualitative assay was performed according to manufacturer's protocol.

Results:

The combination of PCR and sequencing results was used as reference standard. A total of 88 clinical isolates was studied. Of these, a carbapenemase was present in 50 (56.8%) and CTX-M type ESBL in 55 (62.5%). No false negative results were observed using the ESB assay for NDM and VIM; the sensitivity and specificity were 100% and 100%, and 100% and 100%, respectively. Both positive and negative predictive values (PPV and NPV) were 100% each. However, for detection of OXA-48, we encountered 5 isolates that gave repeatedly negative results with sensitivity and specificity of 71.42% and 97.72%, respectively. The PPV and NPV were 93.75 and 87.75, respectively. ESB assay detected KPC (KPC-2 by sequencing) in 1 isolate. CTX-M-1 and CTX-M-9 were detected in 55 isolates.

Conclusions:

The assay demonstrated excellent sensitivity and specificity for the detection of CTX-M, NDM and VIM genes and a relatively good sensitivity for OXA-48, thus showing good results for the detection of the most prevalent carbapenemases. Sample-to-result took only 20 minutes.

Key Words: Carbapenemases; Enterobacteriaceae; Rapid molecular assay

Funding Agency: None



Microbiology, Virology and Immunology

Category: Graduate PhD (Basic Science)

106

Molecular cloning, expression and purification of low molecular weight Mycobacterium tuberculosis ESAT6-like proteins in Escherichia coli

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Introduction:

Tuberculosis is a major health problem that is responsible for 1.3 million deaths annually. In order to control and prevent the spread of TB, an effective vaccine is needed. Recent studies have suggested the potential of Mycobacterium tuberculosis-specific antigens as possible candidates for the development of new TB vaccines, particularly antigens encoded by RD genes. ESAT6-like proteins, ESXV and ESXW, are among the major antigenic proteins of *M. tuberculosis* with vaccine potentials. The aim of this study was to obtain these proteins in the recombinant form by gene cloning, protein expression and affinity purification.

Methods:

Molecular cloning of *esxV* and *esxW* was achieved by amplifying their genes using genomic DNA from *M. tuberculosis* and gene-specific primers in PCR. The amplified DNA were cloned into pGEMT-Easy cloning vector and subcloned in the expression vector pGES-TH1 for high level expression using glutathione-S-transferase (GST) as the fusion partner. The expression of recombinant fusion proteins in *Escherichia coli* (BL-21) was detected by SDS-PAGE and Western immunoblotting. The proteins were purified by loading the soluble or solubilized fusion proteins on Glutathione affinity columns. The column-bound proteins were treated with thrombin protease. The purified proteins from the column were eluted and then analyzed for purity by SDS-PAGE.

Results:

The genes for two ESAT6-like proteins, ESXV and ESXW, were successfully cloned in plasmid vectors and expressed in *E. coli*. The expressed fusion proteins were found in the soluble (ESXV) and pellet (ESXW) fractions of *E. coli* lysates. Both the proteins (free of GST) were purified to homogeneity by the affinity purification strategy.

Conclusions:

The recombinant ESXV and ESXW proteins were purified to homogeneity. These purified proteins can be used in downstream applications in order to evaluate their vaccine potentials against tuberculosis.

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

Funding Agency: Supported by the College of Graduate Studies and the Research Sector Project SRUL02/13.



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Differential proteomic analysis of Escherichia coli BL21 and recombinant Escherichia coli BL21 using the proteome™ Lab PF 2D platform

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Introduction:

The ProteomeLab™ PF2D protein fractionation system is a fully automated, two-dimensional system that resolves and collects proteins by isoelectric point and hydrophobicity. The system visualizes the complex pattern with a 2-dimensional protein map that is easy to interpret and the system's differential display allows to highlight differences in protein expression. The aim of this study was to generate a differential proteome map of the gram negative bacterium E coli BL21 and recombinant E-coli BL21.

Methods:

Single colonies of wild-type and recombinant E. coli BL21 were cultured in Luria Broth and the expression of the recombinant proteins was induced by the addition of isopropyl β-D-1-thiogalactopyranoside. The cells were centrifuged and the cell pellet (0.5 mg/ml) was lysed according to the protocol provided with the ProteomeLab PF2D chemistry kit. The cell lysate (2 mg protein/ml) was injected into the system and separated by PF2D. The 1st and 2nd dimension runs were carried out as per the optimized ProteomeLab PF2D method. The proteins were detected with UV light 280 and 214 nm, and the data were collected and analyzed using the MultiVue software package.

Results:

In the first dimension, the absorbance of pH profiles were recorded at 280 nm using high performance chromatofocusing chromatography and a total of 30 fractions were collected. From these, 24 fractions were separated in the second dimension using high performance reversed phase chromatography. A ProteoVue pI/hydrophobicity 2D protein expression map was generated and differential analysis of individual protein peaks in the two profiles was performed using the DeltaVue software application.

Conclusions:

The proteomic analysis of two bacterial samples with the ProteomeLab PF2D allows rapid and high sensitivity resolution of proteins, thereby facilitating the identification of differentially expressed proteins.

Key Words: Proteomics analysis; Escherichia coli; PF 2D Platform

Funding Agency: Kuwait University Research Sector grant SRUL 02/13



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Genome-wide differential expression reveals candidate genes involved in the pathogenesis of lupus and lupus nephritis in Arab females

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Introduction:

Systemic lupus erythematosus (lupus) is an autoimmune disease characterized by multiorgan pathology, accelerated apoptosis and hyper autoantibody production. The root cause of lupus remains unknown, although multiple susceptibility factors have been reported in different ethnic group. We aimed to explore the genome-wide differential expression spectrum of lupus and its severe form lupus nephritis (LN) in Arab females.

Methods:

A total of 98 subjects: 40 lupus, 18 LN and 40 age/gender/ethnically matched healthy controls (HC) were recruited. Carefully chosen subjects were employed for whole genome expression profiling using Human Exon arrays and statistical analysis was carried out using appropriate software. Validation cohorts were investigated to quantify the expression of candidate genes relative to GAPDH.

Results:

Genome-wide differential analysis revealed 7 candidate genes in lupus and 36 in LN, when individually compared to HC (ANOVA welch t-test, $p \leq 0.005$, Turkey's honestly post-hoc analysis). Analysis of differentially expressed genes with a fold change of 2, revealed 16 GO terms satisfying a $p \leq 0.05$. Five distinct inflammatory and metabolic pathways including TWEAK, osteopontin, endochondral ossification, Fluoropyrimidine activity and urea cycle and metabolism of amino groups that significantly contribute to the pathogenesis of lupus were detected. Validation of candidate genes (IRF9, ABCA1, APOBEC3, CEACAM3, OSCAR, TNFA1P6, MMP9, SLC4A1) revealed significant difference in expression indicating their promissory role in the pathogenesis.

Conclusions:

Our study provides central gene regulators of therapeutic potential, indicating the future prospects of the study.

Key Words: Lupus; Genome-wide expression; Arab females

Funding Agency: NM02/07



Molecular Biology

Category: Basic Sciences

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**Genome-wide peripheral blood transcriptome analysis of Arab female
Lupus and Lupus nephritis**

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Introduction:

Systemic lupus erythematosus is a genetically heterogeneous autoimmune disorder characterized by hyper-immune reactivity and autoantibody production against self-components. The exact etiopathology remains unknown, although multiple susceptibility genes have been reported in different ethnic population. With 92-94% of human genes exhibiting alternative splicing, gaining insights to such events may lead to novel biomarker discovery and better diagnostics. Herein, we aimed to explore the genome-wide peripheral blood transcriptome of lupus (SLE) and its severe form lupus-nephritis (LN) compared to healthy subjects (HC).

Methods:

Age/gender/ethnically-matched Arab female SLE, LN and HC were carefully selected for genome-wide expression profiling using Affymetrix Human Exon 1.0.ST arrays and statistical analysis was carried out using appropriate software.

Results:

Analysis of genome-wide expression spectrum revealed 15 splice-variants that are differentially expressed between SLE/HC and 99 variants between LN/HC ($p \leq 0.05$, $SI > 0.5$, Benjamin Hochberg False discovery rate correction). Comparison between LN/SLE revealed 7 variants that are differentially expressed. Pathway analysis of differentially spliced genes revealed 11 significant pathways in SLE and 12 in LN ($p < 0.05$). Analysis of peripheral blood transcriptome revealed signature causative genes that are alternatively-spliced, signifying their clinical relevance. The extent of differential splicing was found to be higher in LN than in SLE, signifying the need for further in-depth research in the same domain.

Conclusions:

Present study is the first to reveal the significance of alternative variants in susceptibility to SLE and LN.

Key Words: Lupus; Genome-wide; Splice variants

Funding Agency: NM02/07



Molecular Biology

Category: Basic Sciences

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Comparative evaluation of normal fluorescent and confocal laser scanning microscopes for detection of induced apoptosis

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Introduction:

Confocal laser scanning microscopes (CLSMs) are valuable tools for obtaining high resolution images of cells and tissues. The innovative Smart Setup function of LSM 700, a CLSM, takes care of the complex configurations of a wide range of fluorescent probes available. Furthermore, CLSMs, combined with immunostaining, have been used to study apoptosis. Anti-ACTIVE Caspase-3 polyclonal antibody (pAb), which is an apoptotic marker, specifically stains apoptotic human cells. An increase in apoptosis has been observed in normal cells after exposure to hydrogen peroxide (H₂O₂). The aim of this work was to determine the efficiency of LSM 700 in visualizing fluorescence signals from delicate samples after treatment with H₂O₂.

Methods:

Normal human fibroblast cells were grown in vitro, treated with H₂O₂, fixed and incubated with primary antibody (Anti-ACTIVE Caspase-3 pAb), followed by secondary antibody conjugated with AlexaFlour 555. After mounting with DAPI, which stains nuclei, the specimens were viewed under a normal fluorescent microscope (Zeiss Axio Imager) and LSM 700 (Carl Zeiss, Germany).

Results:

The ZEN imaging software, installed in LSM 700, automatically provided the most appropriate imaging strategies for the samples and collected data from in-focus information to create images as optical sections in two and three dimensions. As compared to Zeiss Axio Imager, LSM 700 created sharp, and detailed 2D images, and allowed collection of data in three dimensions. The induction of apoptosis by hydrogen peroxide was evident from the 2D images obtained by LSM 700. It was observed that the intensity and the morphology of cells were changed with increase in apoptosis.

Conclusions:

LSM 700 can visualize even weak fluorescence signals efficiently from delicate samples with an optimized light path. Additionally, it can produce images with greater sensitivity, contrast and resolution than those produced using a normal fluorescent microscope.

Key Words: Microscopes; Immunostaining; Apoptosis

Funding Agency: Supported by Kuwait University Research Sector Grant SRUL 02/13



Nephrology

Category: Clinical

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Performance of CKD-EPI versus MDRD among diabetic Egyptians

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Introduction:

Early changes in diabetic nephropathy involve increased urinary albumin excretion rate and/or a temporal increase in GFR (hyper-filtration), which are not necessarily inter-related. Current standards of clinical practice include annual measurement of ACR and serum creatinine-estimated GFR for staging of CKD.

Objective: The aim was to evaluate performance of The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula, modification of diet in renal disease (MDRD) formula in the prediction of glomerular filtration rate (GFR) as compared to renal isotope scan 99m Tc DTPA (TGFR) in diabetic patients with various degrees of albuminuria.

Methods:

GFR was measured in 52 diabetic patients using Tc99 DTPA renal scan (TGFR), and estimated (eGFR) from standardized creatinine, with MDRD and CKD-EPI equations, and their performance evaluated regarding clinical stages of albuminuria and chronic kidney disease.

Results:

In a group of 52 diabetic patients (67.3% were females, males were 32.7%) with Mean age was 54.75 ± 12.52 years and mean duration of diabetes 8.87 ± 7.05 years. Among all patients, the estimated bias of eGFR by MDRD than TGFR by isotope scan is -19.80 ± 33.98 , while estimated bias of eGFR by CKD-EPI than TGFR by isotope scan is -14.24 ± 15.00 (95% limits of agreement 15.2 – -43.6). In patients with measured GFR ≥ 60 ml/min, the estimated bias of eGFR by MDRD than TGFR by isotope scan was -38.13 ± 41.46 , while estimated bias of eGFR by CKD-EPI than TGFR by isotope scan is -24.01 ± 14.37 . The estimated bias of eGFR by MDRD than TGFR by isotope scan in diabetic patients with microalbuminuria was -23.73 ± 37.80 , while estimated bias of eGFR by CKD-EPI than TGFR by isotope scan is -15.80 ± 17.39 .

Conclusions:

CKD-EPI equation might be a better tool in estimating GFR in Egyptian patients with microalbuminuria and early stages of CKD in diabetes.

Key Words: GFR; CKD-EPI; MDRD

Funding Agency: None



Nephrology

Category: Clinical

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Value of urinary cystatin C in early detection of diabetic nephropathy in type 2 diabetes mellitus

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Introduction:

Small amounts of urinary proteins observed at early stages of diabetic nephropathy (DN) may result from both glomerular & proximal tubular dysfunction. Urinary α -1 microglobulin (U α 1), & Urinary β 2-microglobulin, urinary cystatin C (uCyC) are tubular proteins & enzymes used to detect proximal tubular injury. Increased uCyC concentrations allow accurate detection of tubular dysfunction among pure & mixed nephropathies. This study aimed to assess the value of uCyC in early detection of DN in type 2 diabetes mellitus (T2DM).

Methods:

42 patients with T2DM with normal serum creatinine (S.Cr) were selected from Diabetes clinic at Ain Shams University, & 6 normal adults were chosen as a control group. Patients were divided into 2 groups according to their spot urinary albumin/Cr. Ratio (ACR), 20 microalbuminuric patients (with ACR <30 μ g/mg); & 22 normoalbuminuric patients (with ACR ranging from 30 to 299 μ g/mg). All patients were subjected to assessment of S.Cr, microalbuminuria by ELISA in spot urinary sample, U α 1 by ELISA, serum Cystatin C (sCyC) & uCyC by ELISA.

Results:

No statistical significant difference was found when comparing S.Cr, & sCyC between both patients groups ($p > 0.05$). Also, no statistical significant difference was found when comparing U α 1 & urinary cystatin/creatinine ratio between both patients groups ($p > 0.05$), while there was a statistically significant difference found when comparing the 2 patients group together ($p \leq 0.05$). Plotting of the ROC curve for assessment of use of uCyC as a predictor for the presence of microalbuminuria resulted in an AUC = 0.701 with p value 0.026

Conclusions:

This study demonstrates that uCyC levels could be a useful marker for detection of microalbuminuria independent on any other tubular markers; in addition, it can be used as a good predictor for the presence of microalbuminuria in early DN.

Key Words: Cystatin C; Diabetic Nephropathy; Albuminuria

Funding Agency: None



Neurology

Category: Basic Sciences

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Effect of Interleukin-1 β (IL-1 β) on the Survival of cortical neurons and neurites outgrowth

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Introduction:

Reactive gliosis occurs as a result of the astrocytes response to insults to brain, which is associated with increased levels of cytokines secretion. Cytokines are thought to be a major mediator of reactive gliosis. The potent cytokine IL-1 β is both released by and acts on astrocytes. The hypothesis of this study is that IL-1 β acts on astrocytes to alter their chemical and physical properties affecting the survival of neurons. The author has examined the direct effect of IL-1 β on the survival of cortical neurons and how IL-1 β treated astrocytes support the survival of cortical neurons.

Methods:

Mouse astrocytes and cortical neurons were cultured. Morphological and neurites outgrowth assays using phase contrast microscopy and immunohistochemistry were done.

Results:

When neurons were cultured in the absence of astrocytes only a few of them grew and survived only for 5-6 days. These neurons had small cell bodies and few short neurites. When cultured neurons were treated with IL-1 β for 4 days, it was observed that more neurons survived up to 11 days. However, when the neurons were plated on a monolayer of astrocytes, more neuron grew and survived up to 16-18 days. They had large cell bodies and many long neurites that formed anastomosing networks. When the same number of neurons were plated on a monolayer of astrocytes pretreated with IL-1 β few neurons survived up to 13 days. When a 7-day old neuronal-astrocyte normal co-culture were treated with IL-1 β for 2-8 days (post-treated), the growth of neurons were affected but to a much lesser extent than the neurons grown on IL-1 β pretreated astrocytes and survived up to 15 days. In addition, IL-1 β stimulated the expression of glial fibrillary acidic protein by astrocytes. C

Conclusions:

Conclusions: This study indicates that IL-1 β supports the survival of cortical neurons and modulates the astrocytic support to the neuronal survival by acting directly on the astrocytes.

Key Words: Gliosis.; Neuronal survival; Cytokines

Funding Agency: None



Neurology

Category: Clinical

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Demographics and clinical characteristics of pediatric onset multiple sclerosis

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Introduction:

Although several studies indicated that the prevalence of pediatric multiple sclerosis (MS) is approximately 5% of the adult MS cohort, reports on clinical features of pediatric MS is scarce in our region. We aimed to study the demographics and clinical characteristics of MS patients whose disease started before the age of 17 years.

Methods:

Utilizing the national MS registry, we conducted a cross-sectional study to identify MS patients who had their disease onset before 17 years of age. Demographics and clinical characteristics (age, age at onset, symptoms presentation at onset, disease duration, disease course, relapses, expanded disability status scale (EDSS), and use of disease modifying therapies (DMTs)) were collected.

Results:

Records of 111 pediatric MS patients were analyzed; of whom 71.2 % were females. Mean age at onset and mean disease duration were 14.85 and 9.49 years respectively. Family history was reported in 12.6%. Supratentorial, optic pathway, cerebellar/brainstem, and spinal symptoms were the presenting symptoms in 28.8%, 23.4%, 35.1%, and 27% of patients respectively. 14.4% of patients presented with multifocal symptoms at onset. Most of patients 82% had relapsing remitting course, while clinically isolated syndrome group constituted 8.1%. The mean number of relapses was 3.36 and the mean EDSS at last visit was 2.51. Most of patients (75%) had EDSS less than 4. The mean time to secondary progressive MS was 14.63 years. Of 79.08% patients who were exposed to DMTs, 13.51% had aggressive course necessitating the use of natalizumab as a first line therapy while 37.36% escalated to second line therapies during their disease course.

Conclusions:

MS patients with pediatric-onset had comparable clinical characteristics to adult onset MS. Most patients had low EDSS scores despite the relatively higher percentage of patients with initial aggressive course and breakthrough disease throughout their disease course.

Key Words: Multiple Sclerosis; Pediatric onset; Epidemiology

Funding Agency: None



Neurology

Category: Clinical

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Pediatric onset multiple sclerosis patients tend to have slower disease progression

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Introduction:

Data on differences between pediatric and adult onset multiple sclerosis (MS) in terms of disease course and progression is scarce in our region. We aimed to compare the demographic and clinical characteristics between pediatric -onset and adulthood-onset MS.

Methods:

Utilizing the national MS registry, we conducted a cross-sectional study to dichotomize MS patients based on age of disease onset (<17 years or ≥ 17 years). Demographics and clinical characteristics (age, symptoms presentation at onset, disease duration, disease course, relapses, EDSS score, and use of disease modifying therapies) were collected. Simple descriptive statistical tests were used to describe numerical and non-numerical values. Variables of both groups were compared using chi-square and Student t-tests.

Results:

A total of 984 records of MS patients were assessed; of whom 111 (11.3%) had the disease onset before 17 years of age. Pediatric onset MS patients were more likely to be female (female: male ratio 2.5 vs. 1.85; $p < 0.05$), higher brain-stem / cerebellum (36% versus 26%, $p < 0.03$) and multifocal (15.3% versus 8.1%, $p < 0.01$) manifestations at onset. There was no significant difference in the mean EDSS score between the two cohorts (2.51 versus 2.69; $p < 0.38$) or mean number of relapses (3.38 versus 3.05; $p < 0.14$). The time to reach secondary progression MS was longer in the pediatric-onset MS (14.63 versus 11.03 years; $p < 0.0001$). A higher proportion of the pediatric cohort was treated with aggressive therapy (14.4% versus 8.8%; $p < 0.05$) and required earlier escalation therapy (33.3% versus 27.7 %; $p < 0.04$),

Conclusions:

MS patients, who had their disease onset before age 17, tend to be female and have brainstem/cerebellar and multifocal symptoms at disease onset. Despite the comparable relapse rate and disability measures between the two cohorts, patients with pediatric onset had slower disease progression

Key Words: Multiple Sclerosis; Pediatric onset; Disease progression

Funding Agency: None



Neurology

Category: Clinical

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Real world use of fingolimod in patients with relapsing remitting multiple sclerosis: A retrospective study utilising the national multiple sclerosis registry in Kuwait

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Introduction:

Fingolimod is an oral sphingosine-1-phosphate-receptor modulator, which has demonstrated efficacy in clinical trials and recently been approved for multiple sclerosis (MS) treatment in Kuwait. Post-marketing studies are important to demonstrate real-life efficacy and safety. We aimed to examine the efficacy and safety of fingolimod treatment in a clinical setting.

Methods:

Using the national Kuwait MS registry, Relapsing Remitting MS (RRMS) patients who had been prescribed fingolimod for ≥ 6 months were retrospectively identified. 3-monthly clinical evaluations and 6-monthly MRIs were performed. Patient status pre-and post-treatment was compared using chi-square and Student t-tests.

Results:

A total of 175 patients were included: 75.4% female (n=132); mean age 33.3 ± 9.2 years; mean disease duration 7.2 ± 5.2 years; mean fingolimod use 21.7 ± 9.1 months. Most had used previous disease-modifying therapy (78.9%; n=138), mainly interferons (66.9%; n=117). 23 patients (11.4%) discontinued/ withdrew fingolimod; of whom 8 had relapses. The proportion of relapse-free patients improved significantly (86.3% vs. 32.6%; $p < 0.001$), while the proportion of patients with MRI activity decreased (18.3.6% vs. 77.7%; $p < 0.001$). Mean Expanded Disability Status Scale (EDSS) score at last visit improved when compared to pre-treatment (2.26 ± 1.49 vs. 2.60 ± 1.44 ; $p = 0.03$). 43 (24.6%) patients experienced adverse events; headaches and lymphopenia were the most common reported adverse events.

Conclusions:

Fingolimod treatment was associated with reduced relapse and MRI activity, and improved EDSS score. Discontinuation/ withdrawal rates and adverse events were low. Fingolimod presents a promising treatment for MS in Kuwait.

Key Words: Fingolimod; Multiple Sclerosis; Disease stabilization

Funding Agency: None



Neurology

Category: Clinical

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Ventilator associated pneumonia an observational study in a single center neuro-ICU

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Faculty of Medicine, Health Sciences Center, Kuwait University², Kuwait

Introduction:

Ventilator-associated pneumonia (VAP) is the most common nosocomial infection in mechanically ventilated patients and the second most common cause of morbidity and mortality in general ICU patients. The incidence of VAP has significantly declined with the implementation of VAP bundle care in the general ICU settings, yet outcome studies from neurological ICUs are lacking.

Methods:

A pilot observational study is being conducted to analyze the epidemiology of VAP in a single center Neurological ICU since May 2014. Preliminary data analysis on a quarterly basis up to Dec 2014 was done to allow for comparison. In line with other studies [1, 2], patients were categorized as early-onset VAP (within 4 days) or late-onset VAP (after 4 days). The mean duration of onset, the culture results and sensitivity to antibiotics were noted. Strict adherence to the ventilator bundle by the nursing staff was done.

Results:

Out of the 212 patients admitted to the neurological ICU over an 8 months period, 17 patients were ventilated in the 1st quarter and 21 in the 2nd quarter. 4 patients developed VAP in each quarter with male: female 1:1 and 3:1 respectively and mean age \pm 51 years. The mean day to VAP was found to be 3.25 days and 9 days in the 1st and 2nd quarter respectively. 3 out of 8 isolated organisms were *Pseudomonas aeruginosa*. Despite full adherence to the ventilator bundle in both the quarters, 24% of cases and 19% of cases developed VAP in the respective quarters.

Conclusions:

In this pilot study, *pseudomonas aeruginosa* seems to be the most common cause of VAP still a longer observation study is deemed necessary to further understand the epidemiology and outcome of VAP in the neurological ICU.

Key Words: Neurocritical care; Ventilator associated pneumonia; Pseudomonas aeruginosa

Funding Agency: None



Nuclear Medicine and Radiology

Category: Clinical

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Changes in the diameter and valve closure time of leg veins in primigravida women during pregnancy

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Introduction:

The aim of this study was to monitor the changes that develop in leg veins of primigravida women during pregnancy.

Methods:

Sixty primigravida women volunteered to undergo clinical evaluation and duplex ultrasound examination of both lower limb veins to monitor changes in vein diameter (D) and valve closure time (VCT) during pregnancy and 3 months postpartum by using Duplex ultrasound. A total of four readings were taken for each subject, one reading for each trimester and the last reading was at 3 months postpartum.

Results:

The mean (\pm SD) age of participants was 26.82 \pm 2.47 years. 39 limbs (32.5%) and 65 limbs (54.2%) developed C1-C3 venous changes during the second and third trimesters, respectively. Three months postpartum, 36 limbs (30%) continued to have C1-C2 changes. Only four limbs in 4 subjects developed varicose veins along the great saphenous vein and their VCT was more than 1 second. These subjects were found to have family history of varicose veins. Duplex examinations showed that there was a gradual increase in the D and VCT from the second through the third trimester of pregnancy in all examined venous segments. These changes were statistically significant by Friedman and related-samples Wilcoxon-signed rank tests within the same legs ($p=0.001$) but not between legs in the same subject ($P>0.05$), even when adjusted for body mass index ($p=0.001-0.049$)

Conclusions:

In primigravida, lower limb veins showed gradual increase in vein D and in VCT starting from the second trimester. These changes reverted to baseline in most cases three months after delivery.

Key Words: Primigravida women; Varicose veins; Duplex ultrasound

Funding Agency: None



Nuclear Medicine and Radiology

Category: Clinical

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Risk of avascular necrosis of the femoral head in children with sickle cell disease on hydroxyurea: MRI evaluation

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Introduction:

There have been concerns about the safety of hydroxyurea (HU) in sickle cell disease (SCD) patients with the Arab/India haplotype because of potential osteonecrosis consequent upon increased Hct levels and blood viscosity. There has been an apprehension in using HU in our patients because of a risk of avascular necrosis of the femoral head (AVNFB).

Methods:

The present study documents the baseline and follow up MRI hips among Kuwaiti patients with SCD who have been on hydroxyurea for at least one year. The patients were screened for AVNFB by MRI using a 1.5 Tesla GE unit. Spin echo T1- and T2-weighted images and T2 FATSAT sequences in coronal and axial planes in 4mm-thick sections were obtained and the images were examined independently by at least two radiologists. AVNFB was graded I (mild), II (moderate), or III (severe).

Results:

Twenty five patients, made up of 13 SS, 10Sβ0 and 2 SD, had pre- and post-HU MRI of the hips for assessment of AVNFB. They were aged 8 to 20, with a mean of 14.5±4.0 years and had been on HU for 1 to 15 years. At pre-HU, 17 (68.0%) had normal images while 8 (32.0%) had varying degrees of AVNFB. The mean age of the former was 13.2±4.0 and the latter, 17.1±3.0 years; the difference was statistically significant (p<0.05). Post-HU, of the 17 that were initially normal, 15 (88.2%) remained normal, while 2 (11.8%) developed unilateral AVNFB. Of the 8 that had lesions in the initial MRI, 6 (75%) remained static, 2 (25%) had progressed with more florid lesions. Our previous study showed that, in SCD patients not on HU, AVNFB progressed in 64.7%, while 78% showed new lesions. In the present study, however, of patients on HU, only 11.8% developed new lesions, while 25% showed progression.

Conclusions:

In conclusion, our children with SCD have shown stability of AVN lesions in patients treated with HU. It may also prevent new lesions from developing. This may be due to the decreased expression of adhesion

Key Words: Hydroxyurea (HU), Magnetic resonance Imaging

Funding Agency: None



Nuclear Medicine and Radiology

Category: Clinical

120

Enhanced display of the pyramidal lobe by Tc-99m pertechnetate thyroid scan as corroborating evidence of thyrotoxic Graves disease

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Introduction:

Visualization of the pyramidal lobe by Tc-99m pertechnetate thyroid scan gives support to diagnosis of Graves disease due to uptake in the embryological remnants along the thyroid migration track, showing as a pyramidal lobe. The aim is to evaluate a novel computer processing method of the scan to enhance visualization of the pyramidal lobe as corroborating evidence for the diagnosis of Graves disease.

Methods:

75 thyroid scans were retrieved retrospectively. Patients' age, gender and scan diagnosis were recorded. The scans were visually evaluated in 4 magnified views: Anterior (with & without marker), Left Anterior Oblique and Right Anterior Oblique. Enhanced processing involved displaying the anterior view and thresholding it to show 10-100% uptake in 1 color (black on white) for definition of thyroid contour. A manual region of interest (ROI) was drawn around the contour and was superimposed on the original Anterior image. The content in the ROI was masked electronically for enhanced visualization of the structures outside the thyroid including the pyramidal lobe. The presence or absence of the pyramidal lobe for raw and enhanced images were recorded.

Results:

The average age of the patients studied was 41±16 yr (range: 4-81 yr) and 79% of scans were done in females. The scan diagnosis was: 54% Graves disease, 19% Subacute thyroiditis, 7% cold nodules, 5% normal, 5% Plummer's disease (toxic multinodular goiter MNG), 4% hot nodules, 4% MNG and 1% each Hashimoto's and Amiodarone effect. Pyramidal lobe visualization was seen in 32% of the raw and 44% enhanced display respectively (p<0.001). In patients with Graves disease 48% of the raw and 65% of the enhanced images showed a pyramidal lobe (p<0.001).

Conclusions:

Using the enhanced method described, visualization of the pyramidal lobe is improved and lends support for diagnosis of Graves disease.

Key Words: Pyramidal lobe; Thyroid scan; Graves disease

Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

121

In grand multiparous women with previous cesarean section: Is vaginal birth safe?

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Introduction:

There are limited studies on vaginal birth in grand multiparous women with previous cesarean section (VBAC). To determine the safety of attempted vaginal birth after cesarean section (VBAC) and the delivery outcome.

Methods:

This is a retrospective case control study performed at a tertiary hospital in Kuwait. The charts of 615 patients were reviewed from January 2010 till December 2014. 598 patients were fit for the this study. 299 patients were grand multiparous women attempting VBAC (Study Group [A]). The safety of this procedure along with delivery outcome of these women was compared to the outcome of 299 VBAC multiparous women (para 2-4) during the same period (Control Group [B]).

Results:

216 (72.2%) grand multiparous women were delivered vaginally compared to 225 (75.2%) in multiparous women, and this was not significant ($P > 0.05$). The rate of VBAC in the study group was 50%. 16 (5.2%) women in the study group needed labour augmentation with oxytocin compared to 43 (14.4%) in the control group ($P < 0.003$). The fetal weight, Apgar score and number of hospital days in the two groups was not significant ($P > 0.05$). In the study group 20 (6.6%) had post partum hemorrhage compared to 6 (2%) ($P < 0.002$). In the study group there was 1 (0.3%) uterine rupture, 4 (1.3%) uterine dehiscence and 2 (0.7%) still births due to placental abruption; compared to the control group in which there was no uterine rupture, 3 (1%) cases of uterine dehiscence ($P > 0.05$) and 2 (0.7%) still births due to abruption ($P > 0.05$).

Conclusions:

We conclude that vaginal birth after cesarean section (VBAC) in grand multiparous women appears to be a safe and an effective procedure with low adverse maternal and perinatal outcome. Vaginal birth after cesarean in multiparous women is a safe and efficacious procedure.

Key Words: Vaginal birth after cesarean section, Grand multiparous, Outcome

Funding Agency: None



Obstetrics and Gynecology

Category: Undergraduate

122

Maternal body mass index (BMI) and breastfeeding intention.

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Introduction:

The prevalence of maternal obesity remains unknown in Kuwait. Recently, it has been hypothesized that maternal obesity is linked to lower breastfeeding intention, initiation, and duration. This study aimed to estimate the prevalence of maternal obesity in Kuwait and investigate the association between maternal pre-pregnancy body mass index and the mother's intention to breastfeed.

Methods:

A cross-sectional study was conducted on 626 pregnant women attending public antenatal care clinics in Kuwait. Data were collected by a face-to-face interview using a structured questionnaire. Participants' current height and weight were also measured.

Results:

Out of the 670 pregnant women invited to participate in the study, 626 (93.4%) responded. The overall prevalence of pre-pregnancy overweight and obesity was 31.7% (95% CI: 26.9-36.9) and 19.8% (95% CI: 15.8-24.5), respectively. The prevalence of overweight and obesity in pregnant women in the first trimester was 29.0% (95% CI: 21.0-38.3) and 39.5% (95% CI: 30.6-49.1), respectively. A total of 95.1% of the participants intend to breastfeed their child when s/he is born. The median (interquartile range) of intended duration of breastfeeding was 12 (6-24), 18 (12-24), and 16 (12-24) months in under-/normal weight, overweight, and obese mothers, respectively (p-value 0.002). Obese and overweight mothers were more likely to intend to breastfeed their children >6 months compared to normal weight mothers but this lost statistical significance after adjusting for confounders.

Conclusions:

Maternal obesity and overweight is high in Kuwait. Efforts should be made to encourage ideal body weight in women planning for pregnancy. Despite that most mothers intend to breastfeed their children for >6 months, it is known that the prevalence of breastfeeding at 6 months is low. Future studies should investigate factors associated with early breastfeeding cessation.

Key Words: Maternal; Obesity; Breastfeeding

Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

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**Staples vs subcuticular sutures for skin closure at cesarean delivery:
A randomized control trial**

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Introduction:

Cesarean section is a common surgical procedure performed worldwide and the trend has been increasing across countries. The aim of the study was to compare staples with subcuticular sutures for skin closure in emergency cesarean section (CS) in women without previous abdominal delivery.

Methods:

This was a blinded randomized controlled study. 280 women (undergoing emergency CS without previous abdominal delivery) were randomly assigned to either staples or subcuticular skin closure (prolene 3-0). These women were assigned either to Group-1 for skin wound closure with surgical metallic staples (n=144) or Group-2 for continuous absorbable subcuticular sutures (n=136). Primary outcome of the study was cosmetic outcome (as assessed by patient and independent observer: Patient Scar Assessment Scale (PSAS) and Observer Scar Assessment Scale (OSAS), respectively), 6 weeks post-operative. Secondary outcomes were wound complications, operating time, post-operative pain (visual analogue scale on day 3 post-operative, and 6 weeks post-operative as assessed by patient), and duration of hospital stay.

Results:

262 women were available for evaluation of scar 6 weeks post-operative. Cosmetic result of staples was significantly better than subcuticular sutures (PSAS and OSAS: P <0.05 and P <0.001, respectively), with significantly lesser duration of surgery (26 vs 34 min: P <0.001) and comparable post-operative pain (Pain on day 3 and 6 weeks post-operatively: P >0.05 and P >0.05 respectively), and wound complications (P >0.05). However duration of stay in hospital was increased (7 vs 4 days p <0.01).

Conclusions:

Staples are the method of choice for skin closure in emergency CS as they are significantly better than subcuticular sutures with respect to cosmetic outcome and duration of surgery. Post-operative pain and wound complications were comparable in 2 groups. Staples are associated with a significantly increased duration of hospital stay.

Key Words: Staples, Cesarean section, Subcuticular sutures

Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

124

Prevalence of ovarian torsion: Trends in conservative surgical management

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Introduction:

Ovarian cysts occur commonly in women in the reproductive age group but less in prepubertal girls and postmenopausal women. Although most ovarian cysts are benign, they may be complicated by rupture, bleeding and torsion. Ovarian torsion may affect and cut off the blood supply and cause damage ovarian tissue death through ischaemia and impair the fertility potential of affected women. There are now reports of conservative management ovarian torsion.

Methods:

Between January 1, 2010 and December 31, 2014, all women with benign ovarian cysts including those with complications such as rupture, bleeding and torsion. The main focus however, has been on those with ovarian torsion with evidence of ovarian tissue ischaemia (gangrene) which were removed by Oophorectomy or conserved by Oophoropexy to the back of the uterus.

Results:

During the study period, there were 319 patients with benign ovarian cysts that were operated on at the Maternity Hospital Kuwait. Forty-five (14.1%) of them were admitted as acute surgical abdomen with predominance of torsion 31 (68.9%), Haemorrhagic 9 (20%) and rupture 5 (11.1%). 11 patients showed evidence of ischaemia and gangrene. Six of these patients had Oophorectomy . The remaining 5 had Oophoropexy. One patient had bilateral ovarian torsion with gangrenous appearance at 9 weeks of gestation and the second on the contralateral ovary at 22 weeks of gestation. She and another similar lady had emergency cesarean section at 38 weeks of gestation. Both ovaries looked normal but reduced in size and at postnatal clinic, they had started having their menstrual periods.

Conclusions:

There is limited information on the outcome of Oophoropexy following ischaemia of the torced ovary. Two of our five patients showed evidence of healthy ovarian tissue. We advocate a larger sample size with monitoring strategies like second look laparoscopy and Doppler studies.

Key Words: Oophorectomy and Oophoropexy

Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

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Unexpected malignant and premalignant gynecological lesions in women undergoing vaginal hysterectomy for utero-vaginal prolapse

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Introduction:

Asymptomatic women with utero-vaginal prolapse may have associated premalignant lesions which may not be detected by conventional screening methods.

Methods:

Eighty (80) women with asymptomatic utero-vaginal prolapse, were included in this prospective study for vaginal hysterectomy after preoperative preparation and after written informed consent. Women included in this study were screened preoperatively by high vaginal swab, Pap smear, endometrial biopsy and trans-vaginal ultrasound. Surgically removed uterus and ovaries were sent for histopathological examination. Results of histopathological examination as gold standard were compared with conventional gynecological screening methods.

Results:

Histopathological examination of surgically removed uterus and ovaries after vaginal hysterectomy treatment for uterovaginal prolapse showed abnormal findings in 61.25% (49/89) of studied cases (10 chronic cervicitis, 20 cervical intra-epithelial neoplasia-1 (CIN-I), 5 CIN-2, 2 CIN-3, 10 simple endometrial hyperplasia without atypia and 2 simple serous ovarian cyst). Also, histopathological examination showed premalignant changes in 33.75% (27/80) of studied cases (20 CIN-1, 5 CIN-2 and 2 CIN-3), which mean 50% sensitivity of Pap smear to detect premalignant cervical changes.

Conclusions:

Detection of Malignant and pre-malignant conditions by conventional screening methods should explained clearly preoperatively for women undergoing surgery

Key Words: Detection pre-operatively, Malignant, Pre-malignant lesions

Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

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A simple proline stitch is safe and easy to use for sacrospinous fixation: A prospective cohort study

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Introduction:

Pelvic organ prolapse (POP) is common and the health care impact of prolapse is likely to expand as life expectancy increases. Simple and safe approaches resulting in minimal short-and long-term complications are desirable. We therefore tested the reliability and efficacy of the use of a simple proline stitch for therepair of vaginal vault prolapse and POP.

Methods:

This was a prospective cohort study conducted between 2005 and 2010. Fifty patientswith vault prolapse after vaginal hysterectomy or complete procedentia with very weak pelvic floor muscleswere selected for study. All the patients underwentsacrospinous fixation (SSF) with a proline stitch using a cutting needle and traditional needle holder. Patients were followed up for two years. Sacrospinous fixation was done after vaginal hysterectomy in patients with complete procedentia. Patients had to fill Pelvic Floor Impact Questionnaire—short form 7 (PFIQ-7) preoperative and 12 months later.

Results:

16 patients completely recovered from prolapse. There were thirty four complications nine were short term six patients; three had post-operative dyspareunia with concurrent vaginal infection, three patients had vaginal candidiasis alone, and three had buttock pain. All received medical treatment and showed symptom free in their next postoperative visits. Twenty-five patients had long-term complications; six patients had recurrence 18 months, nine patients had cystocele two years after surgery and ten patients had sexual dysfunction. There was significant difference between Pelvic Floor Impact Questionnaire—short form 7 (PFIQ-7) preoperative and postoperative in all items.

Conclusions:

Sacrospinous fixation using a simple proline stitch can be performed without any special needle or applicator. Operative results are comparable to other standard surgical procedures with only minor post-operative complications requiring simple medical therapy. Quality of life is much improved.

Key Words: Gynaecologi Surgery, Pelvic organ prolapse; Sacrospinous fixation
Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

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Perinatal and maternal outcome of eclampsia over a decade at a tertiary hospital in Kuwait

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Introduction:

Eclampsia is defined as the development of convulsions and / or unexplained coma during pregnancy or postpartum in patients with signs and symptoms of preeclampsia. Eclampsia continuous to be an important cause of maternal and perinatal morbidity and mortality.

Methods:

Analysis of case records of all eclampsia cases from the study period of January 2005 to December 2014. This a retrospective study.

Results:

During the study period there were 30 cases of eclampsia. Total number of deliveries over 10 years was 70,000. The incidence of eclampsia was found to be 0.05% in our hospital. Antepartum eclampsia was seen in 15 patients (15%), intrapartum eclampsia in 6 patients (20%) and postpartum eclampsia in 9 patients (30%). There were no maternal deaths due to eclampsia. There was 1 perinatal death, hence the perinatal mortality rate for eclampsia was 33.3/1000. 22 (73%) of patients received MgSO₄ and 8 patients (27%) received Diazepam (valium), as MgSO₄ was introduced in early 2008. Only 1/8 (12.5%) patient, on Dizapam therapy had recurrence of convulsions and this was controlled . All 9 antepartum cases were delivered by uncomplicated cesarean section. 29 (95%) patients were unbooked, 21 (70%) of patients were primigravidas and 26 (85%) patients were less than 25 years of age. Only 6 (18%) patients were of low socio-economic status and were primary school educated. There were no cases of renal failure.

Conclusions:

Incidence of eclampsia was low, with no maternal deaths. Lack of antenatal care (which includes counseling) was a major risk factor. MgSO₄ was found to be highly effective in the treatment of eclampsia.

Key Words: Magnesium Sulphate, Eclampsia, Perinatal mortality

Funding Agency: None



Obstetrics and Gynecology

Category: Undergraduate

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Prevalence and risk factors of postpartum depression and health related quality of life among women in Kuwait

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Introduction:

Postpartum depression (PPD) is a major depressive episode that occurs within four weeks after delivery and continues for almost two years.

Methods:

A cross-sectional study was conducted in 18 randomly selected vaccination centers in Kuwait. Mothers visiting these centers to immunize their children (<=6 months) were eligible participants in the study. A self-administered questionnaire was anonymously completed by 658 women with a response rate of 90.6%. It included socio-demographic characteristics, current and past obstetric history, the Edinburgh Postnatal Depression Scale to assess PPD and the SF-12 questionnaire to evaluate the HRQOL(Health Related Quality Of Life).

Results:

PPD was prevalent among 45.9% (CI:42.1%-49.8%) of women. Multivariate analysis revealed that low educational level (OR=2.24, CI:1.11-4.51), experiencing severe stressful condition during the year preceding the study (OR=5.1, CI:2.76-9.32), unplanned pregnancy (OR=2.1, CI:1.22-3.60), non-breastfeeding mothers (OR=3.40, CI:1.32-8.79), and past history of PPD (OR=1.97, CI:1.10-3.51) were significantly associated with PPD. HRQOL overall mean score was 53.7 and the physical and mental health domains mean scores were 54.5 and 52.9 respectively. Multiple Linear regression analysis revealed that mean total scores of PPD and HRQOL (overall, physical and mental health domains) were inversely related. Being non-Kuwaiti, and giving birth in private hospital were associated with better HRQOL. However, gestational diabetes, having difficulty during delivery, giving birth to twins or more in a delivery and history of PPD were associated with lower HRQOL.

Conclusions:

PPD was highly prevalent among women in Kuwait. It was associated with poor physical, mental as well as overall HRQOL. Appropriate measures should be implemented to improve prenatal, natal and postnatal period to help reduce prevalence of PPD and its negative relation with HRQOL.

Key Words:

Funding Agency: Postpartum, HRQOL: Health Related Quality Of Life, PPD: PostPartum Depression, HRQOL: Health Related Quality Of Life



Obstetrics and Gynecology

Category: Basic Sciences

129

Maternal-Fetal transport kinetics of chromium in human placenta in vitro: Comparison with antipyrine

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Introduction:

Paucity of data on maternal-fetal transport of chromium, an essential trace element prompted us to explore placental transport kinetics of this element in perfused human placental lobule in vitro

Methods:

Human placentae from control pregnancies were collected post-partum. Chromium chloride (50 ug/), along with antipyrine (Concentration 100 ug/L) 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 perfusate. Concentration of chromium in perfusate samples was assessed by atomic absorption spectrophotometry while reference marker concentration in various samples was measured by spectrometry.

Results:

Differential transport rates of chromium and antipyrine in 12 perfusions differed significantly (Student's t-test ; $p < 0.05$) for 10%,75% efflux fractions of chromium&antipyrine while for efflux fractions for 25%,50% and 90% efflux fractions (Student's t-test ; $p < 0.05$) for 10%,75% efflux fractions of chromium and antipyrine. Chromium transport fraction(TF) averaged 59%, representing 73% of anipyrine TF. Student's t-test revealed that the difference between the chromium Tf and antipyrtine TF was statistically significant ($p < 0.05$). Pharmacokinetic parameters as well as absorption rate/elimination index of chromium differed significantly compared to antipyrine value as well.

Conclusions:

Our studies show for the first time in the literature that chromium is transferred freely from mother to fetus in control human pregnancies in late gestation. Further studies to explore maternal-fetal transport of essential trace elements in diabetic states in humans are in progress

Key Words: Placental Perfusion, Chromium, Maternal-Fetal Transport

Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

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Association between oxidative stress and butyrylcholinesterase activity in human semen

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Introduction:

Human spermatozoa exhibit a capacity to generate ROS and initiate peroxidation of the unsaturated fatty acids in the sperm plasma membrane, which plays a key role in the etiology of male infertility. Oxidative stress is a significant cause of Male infertility as a result of the imbalance between reactive oxygen species (ROS) and antioxidants. It is a powerful mechanism that can lead to sperm damage, deformity and eventually, male infertility. Significant levels of both AChE and BChE activities have been found in seminal fluid and homogenates from spermatozoids. The relevance and mechanism of BuChE activity have not been elucidated.

Methods:

Semen analysis was carried out according to WHO Guidelines (WHO 2010). Semen samples were centrifuged at 4000 rpm for 15 min and seminal plasma used for the assay. BuChE was determined using colorimetric method using the Randox kit (CE 7944). Estimation of Oxidants MDA and TNF- α and antioxidants Superoxide dismutase (SOD), Glutathione Peroxidase (GPX) and Total Antioxidant Capacity (TAC) also used Randox kits.

Results:

Increased levels of Oxidants MDA (6.46 \pm 1.23 versus 3.45 \pm 0.68 nmol/ml, P<0.05) and TNF- α (22.48 \pm 8.67 versus 9.82 \pm 2.86 pg/ml, P<0.01) in abnormal Sperm parameters-Oligozoospermia, Asthenozoospermia and Leukocytospermia, compared to normal sperm parameters but associated with decreased BuChE activity (0.362 \pm 0.148 versus 0.246 \pm 0.089 U/L, P<0.05). Similarly, SOD, GPX and TAC were also decreased and a linear positive correlation (r=0.56, P<0.05) between BuChE activity and total antioxidant activity in human semen.

Conclusions:

Oxidative stress plays an essential role in abnormal sperm parameters. Butyrylcholinesterase may be one of the first line of defense against poisons in human semen, such free radicals. It is tempting to speculate future interventional role for BuChE in male infertility with poor sperm parameters.

Key Words: Butyrylcholinesterase Activity, Oxidative Stress, Human Semen

Funding Agency: None



Obstetrics and Gynecology

Category: Clinical

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The implications of altered cytokine network in seminal plasma

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Introduction:

Cytokines are released by various immunocompetent cell subsets in the male urogenital tract and are thought to affect sperm cell function and reproductive process. There is evidence that cytokines are involved in male infertility

Objective of the study. To investigate factors that may affect expression of Cytokine network in seminal plasma

Methods:

Ninety-one men who sought consultation for their infertility of at least one year, were consecutively recruited into the study. Semen analysis was done for each patient according to WHO guidelines (2010). Cytokines TNF- α , IL-6, IL-12 and IL-4, IL-10 a IL 13 were estimated by Enzyme-linked sorbent-assay (ELISA), while Hormone profile-FSH, LH, prolactin and testosterone were estimated with Radio-immuno-assay.

Results:

Semen analysis apportioned the men into six groups according to the sperm parameters, Normozoospermia was associated with balanced T helper 1 and T helper 2 expression of cytokines such as TNF- α and Interleukin-10. Impaired sperm parameters such as Oligozoospermia, azoospermia, asthenozoospermia, teratozoospermia and leukocytospermia were associated with predominance of T helper 1 cytokine such as TNF- α 10.59 \pm 4.56 versus 6.56 \pm 2.34, P<0.01), IL -6 (50.80 \pm 29.12 versus 29.78 \pm 15.4, P<0.05) and IL-12 (55.62 \pm 30.42 versus 35.39 \pm 14.74 P<0.05) and reduced expression of T helper 2 cytokines -IL-4 (4.8 \pm 1.2 versus 4.62 \pm 2.12, P<0.09) IL-10 (5.28 \pm 3.46 versus 12.64 \pm 4.42, P<0.01) and IL-13 (5.18 \pm 2.95 versus 11.02 \pm 3.06, P<0.01) compared to levels in men with Normozoospermia as the benchmark. There was a strong correlation (r=0.74) between low testosterone (<5 nmol/L and proinflammatory T helper 1 Cytokine TNF- α .

Conclusions:

There is significant altered Cytokine network in men with poor sperm parameters such as Oligozoospermia, Asthenozoospermia and Leukocytospermia. This has important clinical implication in the management of male infertility

Key Words: Dominance, Impaired Sperm Parameters

Funding Agency: None



Oncology

Category: Graduate MSc: Basic Science

132

Invasion is promoted by alkaline pH induced bleb formation in endocrine resistant breast cancer cells

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Introduction:

Endocrine resistance is a major setback for hormonal therapy to women with estrogen receptor (ER)+ve breast cancer. We previously established links between resistance and epithelial to mesenchymal transition (EMT) induced by shRNA silencing of ER in MCF7 cells, producing a line (pII) with fibroblastic morphology. Such transformation was not observed in transfected lines without ER depletion (Sh2.1). This study determined involvement, in this phenomenon, of key molecules associated with motility/invasion.

Methods:

Cellular distribution (fluorescence confocal imagery for immuno-localisation) and expression (antibody arrays) of selected proteins was determined at pH 7.4, 8.3 and 6.5 in pII and Sh2.1 cells. Morphological behaviour was analysed by live cell imaging.

Results:

pII but not Sh2.1 exhibited alkaline-induced membrane ruffling, extensive actin-rich blebs and hair-like protrusions on the plasma membrane which could be prevented by cytochalasin D and inhibitors of Rho and myosin light chain kinases. Adhesion molecules integrin alpha2, JAM-1 and FAK, with diffuse cytoplasmic distribution at pH 7.4 and 6.5, showed enhanced expression in pII at pH 8.3 and also appeared in the newly formed blebs. Signaling molecules such as AKT were reduced or unchanged. Alkaline pH activated invasion related kinases, that were only slightly elevated at pH 6.5. Proliferation/growth signaling pathways were down regulated at both pH 8.3 and 6.5 reflecting a stress-related response that also resulted in lower intracellular protease expression at those pH conditions compared to pH 7.4. Culture medium at different pH conditions showed greater protease secretion at pH 6.5.

Conclusions:

Alkaline but not acidic extracellular environment leads to remarkable morphological transformation in ER silenced cells; increased motility is a consequence of re-mobilisation of cortical actin to form amoeboid-like structures containing matrix adhering proteins that will enhance invasion.

Key Words: Blebbing, Breast cancer, Proteomics

Funding Agency: YP03/03, SRUL02/13



Oncology

Category: Basic Sciences

133

Palliative performance scale differences between patients referred from tertiary cancer center and peripheral hospitals to palliative care center in State of Kuwait

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Palliative Care Center

Introduction:

Palliative care is changing from just end of life care to care delivered earlier in the disease trajectory. Metanalysis showed that Palliative Performance Scale (PPS) is associated with increased length of survival. Palliative Care Center (PCC) in Kuwait is the only standalone center in Eastern Mediterranean Region with a capacity of 92 beds. We compared clinical characteristics between patients referred from Tertiary Cancer Center and peripheral hospitals in Kuwait to PCC .

Methods:

Cross Sectional survey conducted since opening of PCC from January 2011 till June 2013. Data collection about demographics, type of the cancer, PPS score and referring hospital were done.

Results:

Total number of the patients was 142, Mean age was 61.05±14.79 years, number of males was 66 (47.1%) and females was 74 (52.9%). The most common cancers in males were lung (n=18, 27.3%) followed by head and neck cancers (n=8, 12.1%) and brain tumors (n=7, 10.6%) while in females, the most common cancers were breast cancer (n=12, 16.7%) followed by ovarian cancer (n=10, 13.9%) and Cancer Colon (n=8, 11.1%). Patients with PPS score 30% was 27.9% (n=39), 40% in 40.7% (n=57), and 50% in 17.1% (n=24). Patients referred from Tertiary Cancer Center had significantly higher percentage of PPS score >30% (73.4%, n=94) compared to patients coming from peripheral hospitals (33.3%, n=4), P value= 0.007.

Conclusions:

There was positive association between patients referred from Tertiary Cancer Center and PPS scores compared to patients referred from other hospitals. We encourage that all cancer patients should be treated in Tertiary Cancer Center to be referred earlier to Palliative Care Center Training workshops are needed for health care professionals working in general hospitals to be implemented for awareness about earlier referral of patients to palliative care services.

Key Words: Referral; Palliative Care; Cancer

Funding Agency: None



Oncology

Category: Clinical

134

Clinicopathological features and prognosis of triple negative breast cancer in Kuwait: A comparative/perspective analysis.

Fayaz MS, El-Sherify MS, El-Basmy A, Zlouf SA, Nazmy N, George T, Samir S, Attia G, Eissa H
Kuwait Cancer Control Center

Introduction:

AIM:

The aim of this study was to determine the incidence of TNBC in Kuwait, to analyze the clinicopathologic features and prognosis of this type of breast cancer, and compare it with reports from other regions of the world.

BACKGROUND:

Triple negative breast cancer (TNBC) is defined as a subtype that is negative for estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (HER2). There is growing evidence of the heterogeneity of such entities at the molecular level that may cause discrete outcomes.

Methods:

We analyzed the clinicopathologic features of 363 TNBC cases which were diagnosed in Kuwait from July 1999 to June 2009. The disease-free survival (DFS) and overall survival (OS) were analyzed by Kaplan-Meier method. Comparison was done with reports from USA, Europe, Middle and Far East.

Results:

Among 2986 patients diagnosed with breast cancer in Kuwait, 363 (12.2%) were TNBC. The median age was 48 y, 57.2% had lymph node (LN) metastasis, 56.9% were classified grade III tumor and 41.9% had stage II disease. 81% developed recurrences and 75% of deaths occurred by 2.5 y after treatment. There is marked variation of clinicopathologic features according to country of patients' cohort.

Conclusions:

The incidence of TNBC in our study is similar to other studies. TNBC patients showed an early major recurrence surge peaking at approximately year 2.5. Regional variation of clinicopathologic features indicates a need for molecular studies to define underlying molecular features and its impact on survival

Key Words: TNBC; Breast; Cancer

Funding Agency: None



Oncology

Category: Graduate MSc: Basic Science

135

Involvement of voltage-gated sodium channels (VGSCs) in the metastatic behaviour of endocrine resistant breast cancer cells

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Introduction:

Voltage-gated sodium channels have been reported to be expressed in several neoplasms. In breast cancer, the SCN5A gene expressing the Nav1.5 alpha subunit was found to be abundantly expressed and is believed to be involved in cell invasion. We recently reported that brief exposure of estrogen receptor (ER) silenced breast cancer cells to alkaline pH, induced morphological changes and enhanced their invasive potential. In this study, the effect of VGSC blockade in various functions of endocrine responsive (ER +ve) and resistant (ER -ve) cell lines was examined.

Methods:

The expression profile of VGSCs (Nav1.5) in ER+ve (MCF-7) and ER-ve (pII) cell lines at various pH conditions was determined using immunofluorescence. Cell invasion (under-agarose assay), motility (scratch assay) and proliferation (MTT assay) were assessed in pII cells in response to VGSC blockers [phenytoin (PHT) and tetrodotoxin (TTX)] and siRNA-mediated knockdown of the Nav1.5. Total matrix metalloproteinase (MMP) activity was also determined. The expression level/activity of Nav1.5, ERK1/2 and Akt were determined by western blotting.

Results:

A perinuclear expression pattern of Nav1.5 was observed in both MCF-7 and pII cell lines at pH 7.4. Upon cell exposure to pH 8.3, numerous bleb-like structures which were composed of F-actin were observed at the outer membrane of pII cells which were composed of F-actin. Nav1.5 was expressed inside the newly formed blebs. Treatment with PHT, TTX and siRNA significantly reduced pII cell invasion in part through reduced total MMP activity. Cells motility was inhibited by PHT, while proliferation was not affected by both inhibitors. PHT and TTX reduced ERK1/2 phosphorylation level, while siRNA transfection decreased pAkt.

Conclusions:

VGSCs play a significant role in breast cancer cell invasion and in the morphological/functional changes associated with exposure to alkaline pH conditions. Blockers of VGSCs may serve as potential anti-metastatic agents for breast cancer.

Key Words: MMP, Voltage-gated sodium channels, Invasion

Funding Agency: None



Oncology

Category: Clinical

136

The effect of weekly docetaxel and prednisolone for HRPC in Kuwaiti population

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Introduction:

To assess the effect of weekly dose of docetaxel plus prednisolone for HRPC in Kuwait.

Methods:

This is a phase II Pilot study in the Radiotherapy and Medical Oncology Departments of the Kuwait Cancer Control Center (KCCC) . Twenty patients with hormonal refractory prostate cancer (HRPC) were treated by a weekly regimen of docetaxel (30 mg/m²) plus prednisolone (10 mg daily). Measurement of overall biochemical response was assessed using the 50% decrease in the pre-treatment prostate specific antigen (PSA) . Subjective response,, toxicity profile and Quality of survival were also assessed.

Results:

A total of 20 patients were enrolled including 40% Kuwaiti nationals. More than 60% patients were diagnosed with stage IV disease followed by patients with stage II (20%) and stage III (15%) disease. Only 35% patients completed all 6 cycles of chemotherapy. PSA response was observed in 45% of patients with a mean value of 440, the median duration of the response was 392 days. A total of 57% patients did not show any disease progression, 28.6% demonstrated significant improvement in the performance status according to Karnofsky and ECOG scale. Only 1 (5.0%) patient reported Grade 4 toxicity which was hematological in nature. SAE was reported in 20% of patients including one incidence of Grade 4 hematological toxicity resulting in treatment discontinuation. The study reported 11 deaths and 9 deaths were assessed as disease related.

Conclusions:

Weekly regimen of docetaxel plus prednisolone was efficacious and well tolerated in HRPC patients treated in Kuwait. However, as small sample size was evaluated in this study, further studies need to be performed for better understanding of efficacy and toxicity.

Key Words: HRPC; Docetaxel; PSA

Funding Agency: None



Oncology

Category: Clinical

137

Docetaxel as a radiosensitizer with radical radiotherapy in locally advanced cancer cervix

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(KCCC)

Introduction:

The standard of care for locally advanced cancer cervix is radical radiotherapy with concomitant cisplatin. In some patients because of deranged renal functions cisplatin cannot be given also it requires longer time. Docetaxel is given by direct infusion, does not need hydration & has no nephrotoxicity hence it is worth to be investigated as an alternative drug when cisplatin cannot be used.

Methods:

Between 7/2003 & 11/2010, 47 patients consented to be enrolled in this pilot study. All patients were histologically confirmed & had advanced stage IIb(63.8%) or IIIb(34%) disease. Whole pelvis was given a median dose of 40Gy with 3DCRT(95.5%). Brachytherapy was given using Selectron LDR with dose equivalent of 36Gy. Parametrium was boosted to a median dose of 10Gy in 75% of patients. Docetaxel was given in a dose of 30mg/m²(36.2%) & 20mg/m²(63.8%) patients on weekly basis with external WPRT & occasionally with parametrial boost. Objective response was graded as NR, PR & CR along with calculation of medial survival.

Results:

A total of 75.6% of patients were non-Kuwaiti – non Arabs, median age was 46 years. Vaginal bleeding was the main symptom in 97.8%, ECOG, 0 – 1 was seen in 89.4% of the cases. Treatment was interrupted (≥1 week) in 19 patients due to acute treatment toxicity mainly GIT, only 2 had adverse events requiring hospitalization. Complete response was observed in 33/45 (73.3%) & partial response in 8/45 patients (17.7%). The median survival is 23 months from the time of diagnosis. The main late toxicities were vaginal narrowing, stenosis, dryness, synichae & telangiectasia. Sigmoiditis & proctitis was reported in 7 patients.

Conclusions:

Docetaxel as a substitute to cisplatin as concomitant drug with Radiotherapy in cancer cervix is well tolerated with similar response & toxicity. It has the advantage of quick delivery & can be given when renal functions are deranged.

Key Words: Docetaxel; Concomitant; Radiotherapy

Funding Agency: None



Oncology

Category: Clinical

138

Three dimensional conformal radiotherapy in the treatment of localized Prostate cancer: An overview-c (KCCC)

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Introduction:

Although radical prostatectomy for localized carcinoma of the prostate is considered as the standard of care, three dimensional conformal radiotherapy (3D-CRT) are equally effective. We report on the technique and preliminary results of 3D-CRT of cancer prostate in our center. Our objectives to assess the locoregional control (LRC), relapse free survival (RFS), and treatment related toxicities.

Methods:

From June 1998 to November 2007, a total of 109 patients were treated by external beam radiotherapy (EBRT) for cancer prostate. Patients treated for local recurrence post prostatectomy or with metastatic diseases were excluded from the study. Data of 45 patients with localized carcinoma of the prostate treated using 3D-CRT were retrospectively reviewed. Correlations between treatment results and Gleason score (GS), pretreatment prostate specific antigen (PSA) level, risk group and tumor grade were assessed.

Results:

The 3D-CRT has been well tolerated in our series, with 82% LRC and 66.7% RFS at median follow-up of 5.2 years. A total of 75.6% were alive and disease free (DF) and 24.4% were alive with disease. The RFS by GS were 96%, 70 % and 48 % for GS 2-6, 7, and 8-10 respectively (p=0.002). None of the patients with PSA < 10 ng/ml had relapse conversely, 35% of patient with PSA 10-20 and 50 % of PSA > 20 had disease relapse. The RFS by risk group were 100%, 81.1 % and 50 % for low, intermediate and high risk group respectively. According to tumor grade, the highest relapse (33.3%) was found in grade 3 tumors. Acute toxicities were occurred in 57.8 % of the patients, less than 5% had grade 3 late complications and 8.8% had urethral stricture.

Conclusions:

3D-CRT is an effective type of irradiation in the treatment of carcinoma of the prostate regardless of tumor size or risk group. More recent techniques are superior and allow more dose escalation and lower toxicity, but we need long term follow up.

Key Words: 3-D conformal radiotherapy; Prostate; Cancer

Funding Agency: None



Ophthalmology

Category: Clinical

139

The importance of visual screening in primary school children

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Introduction:

Visual problems are common in childhood and if undetected, can lead to poor scholastic performance at school. The objective of this study was to analyze the prevalence of visual impairment in a random sample of primary school children in an urban setting with adequate access to ophthalmology services.

Methods:

324 children between the ages 5 to 10 years with no apparent visual problems were randomly selected from 6 schools in and around Al Ahmadi area, and screened for errors of refraction, squint and other ocular disorders by a team of ophthalmologists and optometrists from Ahmadi Hospital. Children with glasses were excluded from the study.

Results:

There were almost equal samples of both genders -165 boys (50.9 %), and 159 girls (49.1%). 69 children (21.3%) had refractive errors which were previously undetected. Astigmatism was the most common (31.8%), followed by myopia (24.6%), and hypermetropia (21.7%). Four children had myopia with astigmatism, and nine had hypermetropia with astigmatism. Squint was detected in 46 children (14.2%) among which 50% were exotropic, and 36.9% esotropic. In addition to this 3 children had inferior oblique overaction, 2 had esotropia with inferior oblique overaction, and one child had exotropia with hypertropia. 5 children were detected to have red green colour blindness. Other disorders like blepharitis (8 cases), and vernal conjunctivitis (6 cases), one case each of congenital cataract, ptosis and nystagmus were also seen.

Conclusions:

A significant number of visual problems detected, mostly treatable ones, which were previously undiagnosed in spite of adequate access to healthcare facilities, underscore the need for more elaborate visual screening programs to be initiated in all schools on a regular basis and the need for increased awareness among parents and teachers. Early identification and intervention at an appropriate age is important to prevent amblyopia and permanent visual damage.

Key Words: School Children, Visual Screening, Refractive Error

Funding Agency: None



Orthopaedic Surgery

Category: Clinical

140

Hybrid external fixation for comminuted tibial plafond fractures

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Introduction:

Comminuted tibial plafond/pilon fractures represent a challenge for the treating orthopaedic surgeon. In this study, we aim to assess outcomes of using hybrid external fixation for this type of fractures.

Methods:

Patients with Orthopaedic Trauma Association (OTA) type C (C1 to C3) tibial plafond fractures who presented to our tertiary care orthopaedic hospital were included. The study started during August 2009 and ended by July 2012.

Results:

During the study period, 30 consecutive patients (mean age = 37.4 ± 10.7 years) with type C tibial plafond fracture were included. Motor vehicle accidents and fall from height were the cause of the fracture in 14 (46.7%) and 13 (43.3%) patients, respectively. Type C3 was present in 25 (83.3%) patients, while types C1 and C2 fractures were present in 2 (6.7%) and 3 (10.0%) patients, respectively. Nine (30.0%) fractures were open, while 21 (70.0%) were closed. Hybrid external fixation was used for all fractures. All fractures were united; clinical healing was achieved by a mean of 18.1 ± 2.2 weeks following the surgery, while radiologic healing at a mean of 18.9 ± 1.9 weeks. The fixator was removed at a mean of 20.4 ± 2.0 weeks post-operatively. At a mean follow-up of 13.4 ± 2.6 months, the mean modified Mazur ankle score was 84.6 ± 10.4 . The most commonly seen complication was ankle osteoarthritis (17 patients; 56.7%); however, it was of mild degree in more than 50.0% of the affected patients.

Conclusions:

The use of hybrid external fixation for type C tibial plafond fracture resulted in good outcomes. This, however, should be further investigated in studies of higher level of evidence.

Key Words: Tibia; Fracture; Hybrid external fixation

Funding Agency: None



Orthopaedic Surgery

Category: Graduate PhD (Basic Science)

141

The effect of induced brain injury and spinal cord injury on the union of femoral osteotomy in rabbits

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Jahra Hospital

Introduction:

The clinical observation that long bone fractures heal more rapidly in patients with associated head and spinal cord injuries remains controversial. The aim of this study is to compare the union potentialities and the amount of union callus formed in experimentally induced fractured femur of NZW rabbits subjected to experimentally induced brain and spinal cord injuries.

Methods:

The fracture union and the amount of union callus formed were determined radiologically at the end of 3 and 6 weeks and compared in groups of NZW rabbits subjected to the following experiments; A: brain injury + femoral fracture, B: spinal cord injury + femoral fracture, C: femoral fracture + addition of 1 ml sera from a rabbit with inflicted head injury on calcium sulphate cube as a carrier, D) femoral fracture + addition of 1 ml sera from a rabbit with spinal cord injury on a carrier, E) femoral fracture + addition of 1 ml sera from a rabbit with fracture of femur on a carrier, F) femoral fracture + addition of 1 ml sera from a healthy rabbit on a carrier, G) rabbit with femoral fracture + addition of cube of calcium sulphate carrier without any sera and H): femoral fracture only. There were 12 animals per experimental group.

Results:

At 6 weeks, all fractures in rabbits in groups A and B animals united completely with 0% nonunion. Groups C, D, E, F, G and H animals had nonunion rates of 58.3%, 66.7%, 50%, 58.3%, 41.7% and 50% respectively. The mean±SD of callus formed was 2.71±1.13 cm² for groups A and B animals compared to 1.85±0.25cm² for groups C, D, E, F, G animals (p<0.001) and 1.82±0.25cm² for group H animals (p<0.001). Indicating that sera from animals with fractures had no osteogenic effect on fracture healing.

Conclusions:

Data from these experiments suggest that central nervous tissue damage enhances healing of long bone fractures and sera from animals with nervous tissue injury have no osteogenic effect on that healing.

Key Words: Head and spinal cord injuries; Experimental fracture femur; Acceleration of bone healing

Funding Agency: KFAS project code No 2010/1302/04



Orthopaedic Surgery

Category: Basic Science

142

Estimation of mesenchymal stem cells and monocytes in peripheral blood of head and spinal cord injured patients with and without concomitant long bone fractures

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Ministry of Health, Jahra Hospital

Introduction:

There is some clinical evidence to suggest that long bone fractures heal more rapidly in patients with associated head and spinal cord injuries. The scientific basis for this clinical observation is yet to be elucidated. The aim of this study is to compare levels of circulating mesenchymal stem cells (MSCs) and monocytes in peripheral blood of patients with long bone fractures and concomitant head or spinal cord injuries with those with long bone fractures only.

Methods:

Blood samples were withdrawn from 52 patients with severe head injury only (group A), 50 patients with head injury and long bone fractures (group B), 21 patients with spinal cord injuries with paraplegia or quadriplegia (group C), 20 patients with spinal cord injuries and long bone fractures (group D), 60 patients with long bone fractures only (group E), and 50 healthy subjects/control (group F). Circulating MSCs and monocytes in peripheral blood of the patients were counted using the flow cytometer. The levels of the cells in circulation were compared amongst the groups of patients.

Results:

The results of the study showed increase statistically significant in MSCs (CD105+ve/CD14-ve) count in groups (A) to (D), especially 24 hours post-injury which started declining at the end of the first week, but it remained elevated statistically significant in comparison to its count in healthy subjects ($P < 0.05$). The monocytes count was found elevated statistically significant in all groups and remained elevated till end of the third week ($P < 0.005$).

Conclusions:

These results may indicate that following head or spinal cord injuries there is mobilization of endogenous distant bone marrow MSCs and monocytes recruitment to fracture site resulting in rapid healing of long bone fractures.

Key Words: Head injury; Mesenchymal stem cells; Monocytes

Funding Agency: KFAS 2010/1302/04



Orthopaedic Surgery

Category: Graduate (Resident)

143

Computed tomography-based morphologic and morphometric features of the coccyx among Arab adults

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Introduction:

Different sacrococcygeal morphologic features are associated with coccydynia. We aim to identify morphologic and morphometric features of the coccyx among adult Arabs.

Methods:

Retrospective review of 202 computerized tomography scans of adult Arab subjects was done (mean age: 47.98±16.46 years). Sacrococcygeal morphologic features including number of coccygeal segments, type of coccyx, joint fusion, joint subluxation, coccygeal spicule, coccygeal sacralization, ventral angulation of the terminal sacral segment (S5), and lateral deviation of coccygeal tip were recorded. Moreover, morphometric measurements including lengths and angles of the sacrococcygeal region were measured. Analysis of data was carried out using p-value of <0.05 as the cut-off level of significance.

Results:

Three coccygeal segments were present in 138 (68.3%) of individuals. The majority of the subjects had coccyx type I (96; 47.5%), II (70; 34.7%) or III (31; 15.3%); type I being more common among males (p = 0.004). Bony spicule was present in 109 (54.0%) individuals. Joint fusion, joint subluxation, coccygeal sacralization, ventral angulation of S5 and lateral deviation of coccygeal tip were present in 38.6%, 31.7%, 34.2%, 38.1% and 38.6% of the subjects respectively. Joint subluxation and ventral angulation of S5 were significantly more present among females (p = 0.015, p = 0.014 respectively). The mean straight and curved lengths of the coccyx were 3.3±0.7 cm and 3.7±0.8 cm respectively. The sacrococcygeal structures were longer in men than women. The mean sacrococcygeal joint angle was 149.2°±28.1°. Based on the morphometric measurements, the coccyx was more ventrally angulated among females.

Conclusions:

Coccygeal morphology and morphometry of Arab adults share some similarities and differences with individuals of other ethnic backgrounds. Future studies should investigate the relation between these anatomic features with coccydynia among this population.

Key Words: Coccyx; Coccydynia; Morphology

Funding Agency: None



Pathology

Category: Basic Sciences

144

BRAF V600E mutation in papillary thyroid cancer in Kuwait

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Kuwait University

Introduction:

Thyroid cancer is among the five most common cancers in Kuwait with Papillary thyroid cancer (PTC) being the most prevalent histological type. The mitogen-activated protein kinase pathway (MAPK) plays a fundamental role in cell proliferation, differentiation, and survival and aberrations of signaling molecules along this pathway have been implicated in thyroid carcinogenesis. In particular, BRAFV600E mutation has been described as the most frequent genetic alteration in PTC and to be associated with more aggressive behavior of the tumour. No molecular studies to describe the development or biological behavior of PTC have been reported from Kuwait. The aim of this study is to test for the presence of BRAFV600E mutation in thyroid tumours in Kuwait and its correlation with tumours' characteristics.

Methods:

Paraffin embedded tissues of 142 thyroid cases were collected along with patients' clinical and pathological information. Cases included: 103 cases of papillary thyroid cancer (PTC), 28 cases of nodular hyperplasia, 6 cases of Hashimoto's thyroiditis, 3 cases of follicular carcinoma and 2 normal thyroids. DNA was extracted by standard procedures and tested for the presence of BRAF V600E by Amplification Refractory Mutation System (ARMS) PCR, TaqMan mutation detection assay and dideoxy DNA sequencing.

Results:

BRAF V600E mutation was detected in 30% of PTC cases, while in None of the follicular carcinoma or other benign cases. The presence of the mutation was specific for the classic variant of PTC (92% of cases) and correlated with aggressive tumour characteristics such as extrathyroid extension, advanced tumour stage and lymph node metastasis.

Conclusions:

The specificity of BRAF V600E mutation to the classic variant of PTC among other thyroid tumours makes it a reliable diagnostic marker and identify patients with this histological subtype to be good candidates for anti-BRAF targeted therapy.

Key Words: Papillary thyroid cancer; MAPK; BRAF

Funding Agency: Kuwait university research administration grant# MG01/13



Pathology

Category: Graduate PhD (Basic Science)

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Associations of leukocyte telomere length with cardio-metabolic risk factors and circulating biomarkers of inflammation and oxidative stress

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Introduction:

Telomeres are tandem sequences at the end of chromosomes necessary for chromosomal integrity and activity of telomerase enzyme prevents telomere exhaustion. Telomeres and telomerase were linked to aging associated diseases namely obesity, and Type 2 diabetes mellitus [T2DM]. We hypothesize that shortened telomere length would be associated with cardio-metabolic risk factors, and that this relationship might be mediated by obesity-induced metabolic changes.

Methods:

Body Mass Index [BMI], Waist Circumference [WC], serum human Telomerase Reverse Transcriptase [hTERT], total adiponectin, Insulin, Myeloperoxidase [MPO], Total Oxidative stress status [TOS] and Leukocyte Telomere Length [LTL] were measured in 225 T2DM patients and 245 age and sex matched controls. Insulin resistance [IR] was estimated using Homeostasis Model Assessment [HOMA] calculator.

Results:

T2DM patients had significantly ($p < 0.0001$) lower LTL compared to controls [(Mean \pm SD:2.1 \pm 0.2) vs. (Mean \pm SD:4.1 \pm 0.1)] respectively. Levels of hTERT were higher in controls compared to T2DM patients [(Mean \pm SD: 32.9 \pm 8.9 ng/mL) vs. (Mean \pm SD: 21.4 \pm 4.7 ng/mL)]. LTL negatively associated with WC [$\beta = -5.7$, $p = 0.004$], HOMA-IR [$\beta = -1.1$, $p = 0.003$], MPO [$\beta = -0.6$, $p < 0.0001$], TOS [$\beta = -2.2$, $p < 0.0001$]. hTERT showed similar trends. LTL and hTERT were associated significantly and positively associated with adiponectin [$\beta = 3.1$, $p = 0.02$; $\beta = 1.5$, $p = 0.003$]. Shorter LTL were associated significantly with higher risk of T2DM [OR=7.5, $p = 0.003$].

Conclusions:

We show a link between telomere biology, cardiometabolic risk factors, and T2DM in the Kuwaiti population which has not been studied before. Metabolic changes such as the dys-regulation of adiponectin, hyper-insulinemia, IR and obesity associated inflammatory process, could play a role in mediating telomere shortening. Obesity and T2DM are increasing at epidemic pace in Kuwait; telomere attrition & telomerase levels could be potential cardio-metabolic risk markers of obesity and T2DM.

Key Words: Telomeres; Type 2 diabetes Mellitus; Obesity Metabolic Factors

Funding Agency: College of Graduate Studies, Research Sector Grant Number: YM06/11



Pathology

Category: Graduate MSc (Basic Science)

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Adipocyte size and metabolic consequences of obesity, Are they related?

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Introduction:

Although the excess fat mass in obesity has been associated with a large number of diseases, it is the function and location of the adipose tissue that is considered to be the major causal factor. During states of nutrient excess the way adipocyte expands (hypertrophic or hyperplastic) affects the function and distribution of adipose tissue. We hypothesized that the size of adipocyte affects its function which can be demonstrated by the reduction of adiponectin secretion and contributes to the adverse metabolic consequences of obesity.

Methods:

The current study population consisted of 39 patients (10 males and 29 females) underwent elective laparoscopic surgeries. Anthropometric measurements and biochemical analysis were performed including the assessment of adiponectin and its multimeric forms. Subcutaneous (SAT) and visceral (VAT) adipose tissue samples were collected during surgery and used for morphological analysis.

Results:

There was a significant association between enlarged adipocyte diameter in SAT 72.03 (5.71) μm and VAT 64.64 (7.67) μm and the metabolic syndrome (MetS) ($p = 0.016$ and $p = 0.002$ respectively). Insulin and HOMA-IR index were correlated positively with SAT ($r_s = 0.58, 0.58$ respectively) and VAT ($r_s = 0.55, 0.59$ respectively) mean adipocyte diameter ($p < 0.01$). Glucose ($r_s = 0.58$), plasma lipids [TAG ($r_s = 0.38$), TC ($r_s = 0.50$), LDL-C ($r_s = 0.49$)] were positively correlated with only VAT mean cell diameter. Total and HMW adiponectin were negatively correlated with mean adipocyte diameter in SAT ($r_s = -0.53, -0.57$ respectively) and VAT ($r_s = -0.65, -0.61$ respectively) while LMW adiponectin was negatively correlated with only VAT ($r_s = -0.35$).

Conclusions:

Our study suggests that while both VAT and SAT adipocyte diameter are correlated with metabolic disturbance that occurs in obesity, dysfunctional SAT is the initiating factor while VAT is a consequence of this dysfunction and is linked to a worse metabolic outcome.

Key Words: Adipocyte; Adiponectin Isoforms; Metabolic Syndrome

Funding Agency: College of Graduate Studies and the Research Sector (YS02/14)



Pathology

Category: Graduate MSc (Basic Science)

147

Are lipid accumulation product and visceral adiposity index useful for assessing adipocyte dysfunction?

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Introduction:

Lipid Accumulation Product (LAP) and Visceral Adiposity Index (VAI) are sex specific mathematical indices that use anthropometric and metabolic parameters to assess cardio-metabolic risk. Our aim was to find out whether VAI and LAP can be used to evaluate adipose tissue dysfunction in obesity.

Methods:

We studied 38 patients (10 males and 28 females) underwent laparoscopic surgeries. Adipose tissue samples Subcutaneous (SAT) and visceral (VAT) were collected during surgery and used for the measurement of adipocyte diameter. Anthropometric measurements and biochemical analysis were performed. Both LAP and VAI were calculated.

Results:

Weight, BMI, WC, WHtR and fat weight were positively correlated with LAP (rs = 0.65, 0.62, 0.71, 0.64 and 0.65 respectively) (p <0.001) while VAI did not show any significant correlation. Fasting glucose was positively correlated with LAP (rs = 0.66, p <0.001) and VAI (rs = 0.43, p = 0.007). The correlation was more significant between HOMA-IR and LAP (rs = 0.47, p = 0.004) than VAI (rs = 0.36, p = 0.034). Plasma lipid profile (TAG, TC and VLDL) were positively and significantly correlated with LAP [(rs = 0.69), (rs = 0.47), (rs = 0.54) respectively] and VAI [(rs = 0.88), (rs = 0.38), (rs = 0.48,) respectively]. LDL was positively correlated with LAP (rs = 0.39) while VAI was negatively correlated with HDL (rs = - 0.50). Total adiponectin was inversely correlated with LAP (rs = - 0.57) and VAI (rs = - 0.48). Mean adipocyte diameter in both SAT and VAT were positively correlated with LAP (rs = 0.34), (rs = 0.51) respectively and VAI (rs = 0.36). Logistic regression showed that LAP and VAI are associated with MetS (OR = 1.061, 95% CI = 1.017 – 1.107, p < 0.01) and (OR = 3.129, 95% CI = 1.204 – 8.132, p < 0.05) respectively.

Conclusions:

While both VAI and LAP are a potential simple mathematical indices to estimate adipocyte dysfunction in obese patients, LAP performed better than VAI.

Key Words: LAP; VAI; Adipocyte

Funding Agency: College of Graduate Studies and the Research Sector (YS02/14)



Pathology

Category: Basic Sciences

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Identification of the first gene CCNO causing a novel congenital ciliary respiratory disorder

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Introduction:

We recently discovered and reported the first gene causing a novel congenital respiratory disorder, CCNO (Cyclin O). We reported this phenotype as a pulmonary clearance disorder that misdiagnosed before as PCD.

Methods:

CCNO was firstly discovered in a multiplex consanguineous Kuwaiti family with five affected individuals using Whole Exome Sequencing and Autozygosity mapping technologies. The segregation of the identified mutations was performed using Sanger sequencing method. The ultrastructural defect was detected using Transmission Electron Microscopy (TEM).

Results:

Linkage analysis showed an Identical by descent (IBD) region at chromosome 5 that shared between all affected individuals with an interval of [50,317,612 -65,419,300]. Exome sequencing showed a mutation in CCNO gene that located within the IBD region. Sanger sequencing and segregation analysis showed a founder homozygous loss-of function mutations (c.252_253insTGCCC; p.Gly85Cysfs*10) in CCNO gene within all affected individuals that shared autozygous interval across the CCNO gene locus. TEM photographs of respiratory epithelial cells of the patients with CCNO mutations after in vitro ciliogenesis show severe reduction in the numbers of motile cilia and basal bodies at the apical cell region and mislocalization of basal bodies and rootlets within the cytoplasm.

Conclusions:

This indicates that this congenital pulmonary disease is caused by a marked reduction of the number of multiple motile cilia (MMC) covering the cell surface of respiratory epithelial cells. CCNO is the first gene reported to cause a defect in centriole amplification and migration due to reduced MMC and consequently develops an inherited a defective mucociliary clearance disorder which leads to severe defective respiratory system, the collaborative manuscript was published in Nature Genetics.

Key Words: Ciliopathy, Novel Congenital Respiratory Disorder, Genetics
Funding Agency: This work was funded by Dubai Harvard Foundation



Pathology

Category: Basic Sciences

149

Gender influence in EBV antibody response among Kuwaiti Multiple Sclerosis Patients

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Introduction:

Epstein-Barr virus (EBV) infection and altered EBV immunity is associated with multiple sclerosis (MS) risk, incidence, exacerbation, and progression. No such evidence was reported for MS patients from Kuwait where MS prevalence has witnessed an alarming 8-fold increase in a single decade. Our objectives was to determine the association of EBV infection and altered immunity with MS incidence in Kuwait.

Methods:

This is a case-control study involving 141 MS patients and 40 healthy controls from Kuwait. Antibody titers against viral coat antigen (VCA), and Epstein-Barr nuclear antigen 1 (EBNA1) were measured using ELISA to determine positive EBV infection, level of immune response, and infection stage.

Results:

Antibody titers against EBV antigens were significantly elevated in MS patients compared to healthy controls (anti-EBNA1 $p=0.008$; anti-VCA $p=0.028$), and infection reactivation was significantly higher in MS patients ($p=0.02$). Male MS patients had a more progressive MS course than females ($p=0.006$). Male MS patients also had a higher antibody response to EBNA1 than healthy male controls ($p=0.005$) and female MS patients ($p=0.03$).

Conclusions:

An increased immune response to EBV infection is associated with MS incidence in an antigen and sex specific manner. Anti-viral therapy might offer a new venue for curbing MS progression in male patients.

Key Words: Multiple Sclerosis; Epstein-Barr virus; EBNA1

Funding Agency: Kuwait University research sector, MG02/12



Pathology

Category: Clinical

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Molecular characterization of a population-based series of endometrial stromal sarcomas in Kuwait

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Introduction:

Endometrial stromal sarcomas (ESSs) frequently harbor genetic fusions, including JAZF1-SUZ12 and equivalent fusions in low-grade ESS (LGESS) and YWHAE-NUTM2 in high-grade ESS (HGESS). This study aims to classify a population-based series of ESSs in Kuwait based on the 2014 World Health Organization (WHO) classification system and to assess the diagnostic use of interferon-induced transmembrane protein 1 (IFITM1) immunomarker for ESSs.

Methods:

All ESSs diagnosed from 2002 to 2013 were identified from the pathology archive at Kuwait Cancer Control Center. The hematoxylin and eosin (H&E) glass slides were reviewed and the tumors were further characterized using fluorescence in-situ hybridization (FISH) and immunohistochemical studies. Clinical data were obtained including age, International Federation of Gynecology and Obstetrics (FIGO) stage, adjuvant treatment, and follow-up information.

Results:

Twenty ESSs including 19 LGESSs and 1 HGESS were identified. Thirteen (81.3%) of 16 LGESSs with interpretable results showed JAZF1 and/or PHF1 genetic rearrangements by FISH, and the only HGESS in the series showed YWHAE genetic rearrangement. All LGESSs with interpretable results showed positive immunostaining for CD10 compared with 11 (61%) of 18 that showed positive immunostaining for IFITM1; 4 of 7 IFITM1-negative LGESSs showed JAZF1 and/or PHF1 rearrangements. A series of uterine leiomyomas, leiomyosarcomas, adenosarcomas, and carcinosarcomas were included for comparison, and positive IFITM1 staining was found in 1 of 10 leiomyomas, 3 of 13 leiomyosarcomas, 3 of 4 adenosarcomas, and 3 of 8 carcinosarcomas, compared to 0 of 10 leiomyomas, 9 of 13 leiomyosarcomas, 3 of 4 adenosarcomas, and 5 of 8 carcinosarcomas that were positive for CD10.

Conclusions:

Our results demonstrated characteristic genetic rearrangements in a high percentage of LGESSs in this population. IFITM1 antibody appears to be less sensitive than CD10 for LGESS.

Key Words: Endometrial stromal sarcoma; JAZF1; IFITM1

Funding Agency: None



Pathology

Category: Basic Sciences

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**Swellings of the anterior and lateral chest wall, and the back:
Diagnosis by fine needle aspiration cytology**

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Introduction:

Swellings in the chest wall and back can be produced by infections, benign tumors and malignancies. Only a minority of these lesions may show characteristic clinical and diagnostic imaging characteristics. Fine needle aspiration (FNA) cytology can serve quick, simple, and economic diagnostic tool to arrive at a definitive tissue diagnosis in these lesions.

Methods:

Over a period of 5 years (2003-2007), 526 patients with superficial lumps in the anterior and lateral chest wall (173 cases), back (351 cases) and both these sites (2 cases) were subjected to FNA. The age of the patients ranged from 3 to 84 years with median of 40 years. Male to female ratio was 261:265.

Results:

The cytodiagnoses included lipomas (327 cases or 62.2%) or lipomatous lesions (72 or 13.6%), benign adipose tissue (30 or 5.7%), sebaceous/ epidermal inclusion cyst (46 or 8.7%), misc. benign tumors (5 or 1.0%), malignant tumors (6 or 1.1%), atypical cytology (1 or 0.2%), tuberculous lesions (4 or 0.8%), nonspecific inflammation (12 or 2.3%) and misc. benign lesions (8 or 1.5%). In 15 (2.9%) cases, the samples were inadequate. The malignant tumors included lymphoid malignancies (3 cases), pleomorphic sarcoma (1 case), metastatic adenocarcinoma (1 case), and malignancy, not otherwise specified (1 case). Significant difference in frequency of lesions on chest wall on one hand and back on the other were observed in case of lipomas (48.6% vs. 68.6%, $p=0.00001$), malignant tumors (2.9% vs. 0.6%, $p=0.01683$), tuberculous lesions (2.3% vs. None, $p=0.01179$), nonspecific inflammations (6.3% vs. 0.3%, $p=0.00004$), and inadequate cases (6.9% vs. 0.8%, $p=0.00022$).

Conclusions:

Lipomas were the most common lesions of chest wall and back. Lymphoid neoplasms were most common among malignancies. There was significant difference between chest wall and back in respect of frequencies in lipomas, malignant tumors, and tuberculous as well as non-specific inflammatory lesions.

Key Words: Chest wall swellings; Back swelling, Fine needle aspiration cytology

Funding Agency: None



Pathology

Category: Graduate (Resident)

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Dermatofibrosarcoma protuberance: A clinicopathological review of 42 cases from Kuwait Cancer Control Center (KCCC)

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Introduction:

Dermatofibrosarcoma protuberance (DFSP) is a rare superficial soft tissue sarcoma with a high risk of local recurrence. DFSP usually occurs in young to middle-aged adults, mostly on truncal sites. The aim of this study was to retrospectively review a case series of DFSP from KCCC.

Methods:

We searched the pathology archives at the KCCC for DFSP cases diagnosed between 2005 and 2012. Clinicopathological data were collected from pathology reports and patients' files. H&E and immunohistochemical glass slides were reviewed.

Results:

We reviewed a total of 49 cases diagnosed as DFSP during this period, 42 (86%) of which were confirmed, 4 (8%) were considered equivocal, 2 (4%) re-classified into cellular dermatofibroma and 1 (2%) into giant cell fibroblastoma. Of the 42 confirmed cases, 25 (60%) were males and 17 (40%) females. Mean age at diagnosis was 36 years (range 14-69). Trunk was the most common location (23/42; 55%), followed by limb girdle (10/42; 24%), lower extremity (3/42; 7%), head and neck (3/42; 7%), & upper extremity (2/42; 5%), with unknown location in 1/42 (2%). Histologically, all cases showed the characteristic storiform pattern and subcutaneous fat infiltration. Foci of myxoid change, collagenous stroma and pigmentation were seen in 13 (31%), 13 (31%), & 5 (12%) cases respectively. Diffuse CD34 immunostaining was seen in 33 (79%), patchy staining in 6 (14%), and unavailable in 3 (7%) cases. Six (14%) cases showed fibrosarcomatous transformation. Sixteen cases had available follow-up information of which 6 developed local recurrence 2-3 years after excision & 1 metastasized to the lung 2 years after diagnosis. The latter occurred in a fibrosarcomatous DFSP.

Conclusions:

This series describes the clinicopathological characteristics of DFSP diagnosed at KCCC over a 7-year period. Our findings are compatible with those in the literature. This study will form the basis for future molecular analysis, which will be our next goal.

Key Words: DFSP; Dermatofibrosarcoma; Protuberance

Funding Agency: None



Pathology

Category: Graduate (Resident)

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Comprehensive clinical and histopathologic profiling of salivary gland pathology in Kuwait: the Sabah hospital experience.

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Introduction:

A wide range of lesions can affect salivary glands. Numerous worldwide studies have revealed variations in incidence and prevalence of such lesions. To our knowledge, no such study was done in Kuwait. Herein, we aim to study the clinicopathologic profile of salivary gland pathology in a tertiary referral center in Kuwait: Sabah Hospital

Methods:

Cases were retrieved from the archives of Histopathology at Sabah Hospital(2011-2013). The criteria for inclusion are salivary and non-salivary-type lesions affecting major salivary glands and seromucinous glands of the upper aerodigestive tract. Available hematoxylin and eosin and special stains slides were reviewed. Stratification of the different pathoses was based on histomorphology and, when necessary, immunophenotypic characterization of the cases and was tabulated against clinical and histologic parameters.

Results:

105 cases were diagnosed in the 3 year period. The average age is 31.77yrs(2months-91yrs) and the M:F ratio is 1.39:1.37 of 105 cases (35.24%) were neoplastic, of which 75.67% were benign and 24.32% were malignant. The remaining 68(64.76%) cases were non-neoplastic, the most common site for which was the submandibular gland (35.29%). The parotid was the most common site for benign(71.43%) and malignant lesions(66.67%). Mucocele was the most common non-neoplastic lesion (35.29%). Pleomorphic adenoma was the most common benign neoplasm (60.71%). Mucoepidermoid carcinoma and adenocarcinoma (NOS) both tied for the most common malignancy(22.22% each).

Conclusions:

A wide variety of benign and malignant neoplasms and non-neoplastic lesions of salivary glands were seen in the place of the present study. Their frequency of occurrence, for the most part, reflects that seen in the studies conducted in North America. However, a multicenter study must be conducted in Kuwait to accurately assess the profile of salivary gland pathology in Kuwait.

Key Words: Salivary gland; Pathology; Kuwait

Funding Agency: None



Pathology

Category: Clinical

154

Epidermal growth factor receptor mutations in non-small cell lung carcinomas on fine needle aspirates of patients from Kuwait

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Introduction:

Non-small cell lung carcinoma (NSCLC) is the most frequently diagnosed form of lung cancer in Kuwait. NSCLC samples from the Kuwaiti population have never been screened for epidermal growth factor receptor (EGFR) mutations and gene amplification, which are known to affect treatment decisions and response to treatment. This pilot study investigated the mutational status of EGFR in fine needle aspirations (FNAs) of NSCLC samples from Kuwait.

Methods:

Eighteen confirmed NSCLCs from 5 Kuwaitis and 13 non-Kuwaitis were included in this study. DNA extracted from NSCLC FNA cell blocks was screened for EGFR gene mutations using PNA Clamp assay, EGFR gene amplification were assessed using fluorescent in-situ hybridization (FISH) in combination with EGFR protein expression using immunohistochemistry.

Results:

Five EGFR mutations were detected in five non-Kuwaiti NSCLC patients (27.8%). EGFR gene amplification was evident in 10 samples (55.5%) by direct amplification or as a result of chromosomal polysomy. Four samples had EGFR mutations and EGFR gene amplification, of which only one sample had simultaneous EGFR overexpression. EGFR protein expression was not associated with any EGFR gene aberration.

Conclusions:

Given the evidence of EGFR gene alterations occurring in NSCLC patients from Kuwait, there is a need to incorporate EGFR gene mutations/amplification screening of NSCLC patients and consider its consequent contribution to patient management and prognosis.

Key Words: Non-small cell lung carcinoma; Epidermal growth factor receptor-FISH; Fine needle aspiration

Funding Agency: Kuwait University Grant no. MG03/13.



Pathology

Category: Clinical

155

Relationship between adipokines, incipient nephropathy and endogenous markers of glomerular filtration rate: Evidence of gender-specific associations in patients with type 2 diabetes mellitus.

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Introduction:

Obesity and insulin resistance are known to contribute to the progression of renal disease via several potential mechanisms. We postulate that one of these mechanisms may involve retention of low molecular weight adipokines when glomerular filtration rate (GFR) decreases. Therefore, the main objectives of this study were to evaluate the relationships between adiponectin (Mr = 30kDa), resistin (Mr = 12.5 kDa) and leptin (Mr = 16 kDa) concentrations with estimated GFR (eGFR) in patients with Type 2 diabetes (T2DM) and varying degrees of diabetic nephropathy.

Methods:

Fasting adiponectin, resistin and leptin were determined in 153 T2DM patients who were classified as normoalbuminuric (microalbumin:creatinine ratio (MAR) < 30 mg/g; n=96) or microalbuminuric (MAR = 30–300 mg/g; n = 57). eGFR was determined by the abbreviated MDRD equation. Linear and multivariate regression (with inclusion of age, gender, waist circumference (WC), presence of coronary heart disease and smoking status as potential confounders) analyses were used to determine the associations of eGFR with adipokine concentrations.

Results:

35% of patients had eGFR < 60 ml/min/1.73 m²) and in these patients mean WC (105 vs 107 cm) was lower but mean adiponectin (15.8 vs 14.3 ng/ml), resistin (24.7 vs 23.3 ng/ml) and leptin (39.9 vs 39.2 ng/ml) were higher than in patients with eGFR < 60 ml/min/1.73 m²). Adiponectin (r = -0.38), leptin (r = 0.45) and resistin (r = 0.49) were significantly correlated with WC and these correlations remained significant after correction for eGFR. In uni and multivariate regression analyses, no significant associations were found between adiponectin, leptin and resistin and eGFR even in sub-group analysis of patients with eGFR < 60 ml/min/1.73 m²).

Conclusions:

Our results reject the hypothesis that there is GFR dependent retention of adipokines in patients with T2DM in whom the degree of adiposity appears to be the significant determinant of circulating adipokines.

Key Words: Adipokines; Nephropathy; Endogenous markers of Glomerular Filtration Rate

Funding Agency: KFAS-2011-1302-01



Pathology

Category: Graduate (Resident)

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Sessile serrated adenoma/polyps are infrequent at Mubarak Al-Kabeer Hospital: An audit over a 5-year period

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Introduction:

Sessile serrated adenoma/polyp (SSA/P) is a subtype of serrated colorectal polyps that can potentially give rise to colorectal carcinoma. SSA/P is typically flat, located on the right side of the colon, and has the same color as the background mucosa, therefore it is more challenging to detect endoscopically than conventional adenoma. SSA/Ps may also be challenging to pathologists and confused with hyperplastic polyps. Little is known about these lesions in the Middle East and Kuwait. Our aim was to study the frequency of SSA/P at our institution.

Methods:

We searched the pathology records of Mubarak Al-Kabeer Hospital, for all colorectal polyps labeled “serrated” or “hyperplastic”, between 2005 and 2009. Two pathologists re-evaluated the pathology slides. A third pathologist reviewed contentious cases. Age, gender, polyp size, and colonic location were retrieved from pathology reports.

Results:

Of 499 pathology reports of colorectal polyps, we identified 225 serrated polyps in 198 patients with a mean age of 55.4 and male to female ratio of 2.7 to 1. The majority of the polyps were left-sided (68%) and ≤ 1 cm in size (95%). Of the 225 polyps, 180 (80%) were originally diagnosed as hyperplastic polyp, 42 (19%) as “serrated adenoma” with or without dysplasia, and only 3 (1%) as SSA/P. Following histopathological reevaluation, a total of 149 (66.2%) polyps were re-classified, but the diagnosis of SSA/P remained infrequent at 4% (3 definite and 5 equivocal cases). All 3 confirmed SSA/Ps were right-sided measuring 0.3-0.7 cm.

Conclusions:

SSA/Ps are not commonly encountered at our institution, which may be a reflection of low endoscopic detection and/or true lower prevalence than in Western populations, which might be due to genetic or environmental factors. We illustrate the need for educational interventions to familiarize pathologists and clinicians in this part of the world with the nomenclature of serrated polyps and their clinical significance

Key Words: Serrated lesions; Colon; Colorectal polyps

Funding Agency: None



Pathology

Category: Basic Science

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Cardiac and aortic injuries caused by non penetrating blunt chest trauma: A pathological and autopsy based assessment of the injury pattern.

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Introduction:

Cardiac Concussion (or commotio cordis) was first described in 1930s, and now accounts for a cases of sudden death,with trivial non-penetrating impacts to anterior chest, leaving no visible trauma. no pathological changes may not be seen and no cardiac enzyme rise may not be noted.The misconception that non penetrating trauma to the heart is relatively rare, is primarily due to the fact that myocardial contusion or traumatic pericardial lesions are usually well tolerated and the clinical findings transient and often difficult to recognize. However,the sequelae of this type of cardiac trauma may be serious (However ECG & monitoring of cardiac Troponins are a must from medicolegal point of view).

Methods:

Out of 90 of autopsy cases referred from forensic medicine morgue to pathology departments, for morbid and histopathological assessment, five cases were detected with hemopericardium and cardiac tamponade, four out of them showed cardiac concussion with cardiac contusion.The fifth case showed ascending aortic aneurysm with thinning and perforation.

Results:

The hospital records and the relatives of all the expired and autopsy examined cases gave a history of a previous trauma with sudden deaths after few hours to few days from trauma.

Conclusions:

Any cases referred to causality departments with a history of non penetrating chest trauma especially RTA, must be carefully examined and fully investigated and to be kept under strict follow up for any serious effects and even sudden deaths.

Key Words: Chest trauma; Hemopericardium; Cardiac concussion

Funding Agency: None



Pathology

Category: Graduate (Resident)

158

Low-grade appendiceal mucinous neoplasm (LAMN): Eight cases from Mubarak Al-Kabeer Hospital

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Introduction:

Low-grade appendiceal mucinous neoplasm (LAMN) is a rare tumor of low malignant potential often discovered intraoperatively or during pathological assessment of appendectomy specimens. It may give rise to pseudomyxoma peritonei (PMP), a slow-growing but potentially fatal tumor. We have recently encountered 4 appendectomies with incidental LAMN, which has prompted a retrospective search in the pathology files of Mubarak Al-Kabeer Hospital to explore the extent to which LAMN has been reported.

Methods:

We searched a total of 10,236 appendectomy specimens, reported between 1990 and 2009, using the keywords "mucin", "mucinous", "adenoma", and "adenocarcinoma". Slide review was performed on cases meeting the search criteria.

Results:

After excluding secondary mucinous tumors, only 4 LAMN cases were confirmed (total= 8 including the 4 recent cases). These occurred in 4 males & 4 females with a mean age of 44.8 years (range 31-67). The appendices were invariably dilated grossly, up to 3cm in diameter, with a wall thickness of 0.8-1.2cm. Out of 7 cases with available slides, 5/7 (71%) showed mucin pools confined to the appendix histologically, and 2/7 (29%) showed mucin extending into peri-appendiceal tissues (no clinical information available on presence/absence of PMP). Acellular mucin was seen in 5/7 (71%) cases & luminal epithelial dysplasia in 7/7 (100%). Coexisting acute appendicitis was noted in 5 cases.

Conclusions:

LAMN was not diagnosed frequently between 1990-2009. It may have been overlooked for several reasons: a) appendices affected by LAMN usually look like a benign mucocele grossly, b) LAMN is not obviously invasive histologically, and c) lack of awareness amongst surgeons and pathologists. Any dilated mucin-filled appendix should be viewed with caution. This finding should prompt a search for extravasated mucin intraoperatively and careful pathological assessment. LAMN patients must be referred to a multidisciplinary oncology team.

Key Words: LAMN; Appendix; Mucinous

Funding Agency: None



Pediatrics

Category: Clinical

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Continuous subcutaneous insulin infusion versus multiple daily insulin injection in children with type 1 diabetes in Kuwait: Glycemic control, insulin requirement and BMI

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Introduction:

Continuous subcutaneous insulin infusion (CSII) and multiple daily insulin injections (MDI) are the two methods currently used for the management of type 1 diabetes (T1DM). The aim of our study was to report experience with CSII in a large cohort of children and adolescents in comparison with MDI in Kuwait.

Methods:

Patients less than 18 years of age, started on CSII during the period of July 1st 2007 until December 31st 2012 were included. Data on gender, age at diagnosis and at pump insertion, and diabetes duration were collected. Body mass index (BMI), HbA1c, insulin dose and adverse events were assessed at baseline and every 3 months. Similar data were collected on patients on multiple daily injections.

Results:

Although the drop of HbA1c was most significant in first year of pump therapy, it continued to be significantly lower in the CSII group compared to the MDI throughout the study period (CSII 7.94 ± 0.82 vs MDI 8.31 ± 1.03 ; $P < 0.001$). Daily insulin requirements were significantly lower in the CSII group. BMI z scores increased in both groups, more in the CSII, but the difference was not significant (0.76 ± 1.19 vs 0.71 ± 1.21 in 1st yr; $P = 0.69$ and 1.34 ± 0.89 vs 0.92 ± 1.28 ; $P = 0.15$ in 5th yr). The rate of ketoacidosis did not differ in both groups. CSII group had more severe hypoglycemia episodes at baseline (9.7 vs 3.7 event per 100 patient-year; $P < 0.05$). However, the rate of the episodes were decreased significantly in the CSII group (5.7 vs 17.7; $P < 0.05$ in the 1st year and 4.1 vs 19.7; $P < 0.05$ in the 5th yr).

Conclusions:

With available trained professional and financial resources available, CSII can be a safe alternative of intensive therapy in diabetic children with lower rate of severe hypoglycemia and better glycemic control.

Key Words: Type 1 diabetes; Children; Insulin pump

Funding Agency: Kuwait University (MK 02/13).



Pediatrics

Category: Clinical

160

Paraoxnase 1(PON 1) gene polymorphism in Kuwaiti arab children with nephrotic syndrome

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Introduction:

Paraoxonase -1 (PON1) is a serum enzyme bound to high density lipoproteins and has antioxidant as well as anti-atherogenic effect. Studies of its molecular basis revealed 2 polymorphic sites at aminoacids 55 and 192 giving 2 different alloenzymes of each site including L genotype(leucine/high activity) and M genotype(Methionine /low activity) at site 55 and A(Arginine/high activity) and B (Glutamine/low activity) at site 192. In this study we explore the role of Paraoxonase -1 gene polymorphism in Kuwaiti Arab nephrotic children.

Methods:

The Paraoxonase-1 gene, 55 and 192 polymorphisms were analyzed in 50 Kuwaiti children with nephrotic syndrome (NS) and 50 healthy control subjects. The patients included 32 children with Minimal change histology (MCNS) and 18 with focal glomerulosclerosis (FSGS) by using polymerase chain reaction-restriction fragment length polymorphism method.

Results:

The incidence of LL genotype (Leucine residue) was detected in 25/50 (50%) of the NS-patients group compared to 24/50 (48%) in the controls (p=0.84). The LM genotype was found in 21/50 (42%) in NS patients compared to 18/50 (36%) in controls (p=0.68). The MM-genotype (methionine residue) was detected in 4/50 (8%) NS patients compared to 8/50 (16%) in controls (p=0.35). The L allele frequency in both its homozygous LL and heterozygous LM genotypes was reported in 71% in NS patients compared to 66% in controls (p=0.54). The LL genotype was significantly more common in NS patients with FSGS histopathology when compared to minimal change histopathology (p=0.0001) as well as when compared to controls(p=0.0024).The LM genotype was also more common in FSGS group when compared to MCNS (P=0.0010) and when compared to controls (p=0.05).

Conclusions:

The L allele of PON1gene 55 polymorphism is might be a risk factor for FSGS pathology in Kuwaiti nephrotic children of an Arab race.

Key Words: Polymorphism, Nephrotic syndrome, Paraoxanase-1

Funding Agency: None



Pediatrics

Category: Clinical

161

Utility of ultrasonography in children with camptodactyly-arthropathy-coxa vara-pericarditis syndrome

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Introduction:

Early recognition of Camptodactyly-arthropathy-coxa vara-pericarditis (CACP) syndrome is very important for counseling and avoiding unnecessary treatment with anti-rheumatic drugs including biologic agents.

Objective:

to evaluate utility of ultrasonography in CACP syndrome patients and to compare the findings of the wrist and metacarpophalangeal joints with those in Juvenile Idiopathic arthritis(JIA) patients.

Methods:

The study cohort consisted of children with CACP syndrome and JIA with a poly-articular course. Each patient completed the same assessment: clinical examination of six joints (wrist, 2nd and 3rd metacarpophalangeal joints bilaterally), laboratory assessment, conventional radiography, and ultrasonography of the above-mentioned six joints. Ultrasonography assessment was performed in the same day as clinical and laboratory assessment.

Results:

A total of 24 patients have completed the evaluation: 19 JIA and 5 CACP syndrome patients with a total of 144 assessed joints, with each patient having completed the same assessment. Most patients had synovial membrane thickening. However, synovial proliferation was more prominent in CACP syndrome (26/30) compared to JIA patients (56/114) (P 0.0002). Interestingly, all CACP syndrome patients showed normal vascularity of the synovium as by color Doppler, while 25% of the assessed joints in JIA patients had increased synovial vascularity (P 0.0025). Joint effusion and bone erosion were more frequent in JIA patients compared to CACP syndrome. However, the difference was not statistically significant.

Conclusions:

Our findings suggest that ultrasonography is probably beneficial in differentiating inflammatory arthritis from non-inflammatory arthropathy.

Key Words: Ultrasound; Camptodactyly-arthropathy-coxa vara-pericarditis; Juvenile idiopathic arthritis

Funding Agency: None



Pediatrics

Category: Graduate (Resident)

162

Iron overload assessment in children with leukemia in Kuwait

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Introduction:

Leukemia patients are prone to severe anemia due to the disease itself and the medication. They receive multiple blood transfusions throughout their treatment. The aim of this study was to see whether intense chemotherapy affects the amount of blood transfusions received, hence leading to iron overload.

Methods:

This is a cross-section study of 50 children who were diagnosed with leukemia and treated at NBK pediatric hematology and oncology department, Sabah hospital. Serum ferritin level was tested in each patient while they were at different stages of treatment (after parents' consent).

Results:

There was a total of 50 children with leukemia: 29 males and 21 females, with 26 children being Kuwaitis and the rest from different nationalities. The youngest was one year old and the eldest was 16 years old. Twenty-four children were receiving their chemotherapy at the time of sampling and were at different stages of their treatment, whereas 26 children have already completed their chemotherapy in accordance to their chemotherapy treatment protocol. The risk of the disease did not affect serum ferritin level ($p=0.407$), nor the frequency of blood transfusions ($p=0.982$). The frequency of blood transfusions increases as the child progresses in the treatment protocol ($p=0.001$); however, it did not affect the serum ferritin level ($p=0.331$)

Discussion:

It is obvious that iron overload has an accumulative effect that can be clearly seen towards the end of the chemotherapy protocol. This cross-sectional study might not predict the long term effect of iron overload; however, it gives an insight to leukemia patient exposure to iron overload.

Conclusions:

Children with leukemia can develop iron overload due to necessary multiple blood transfusions received during their long term chemotherapy treatment that needs to be investigated further and possibly treated.

Key Words: Leukemia; Ferritin; Blood transfusion

Funding Agency: None



Pediatrics

Category: Clinical

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Evaluation of PTPN22 gene C1858T functional variant and HLA-DQ alleles as determinants of genetic susceptibility in Kuwaiti children with Type-1 Diabetes Mellitus

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Introduction:

The incidence of type-1 Diabetes Mellitus (T1DM) has increased steadily in Kuwait during recent years. An interaction between susceptibility genes, immune system mediators and environmental factors predispose susceptible individuals to T1DM. We have determined the prevalence of PTPN22 gene functional variant (C1858T; R620W) and HLA-DQ alleles in Kuwaiti children with T1DM to evaluate their impact on genetic predisposition to T1DM.

Methods:

This study included 191 Kuwaiti children with T1DM and 101 ethnically matched controls. The ISPAD diagnostic criteria was used to make diagnosis of T1DM. The control subjects were healthy Kuwaitis, None had close relative with T1DM and were evaluated by a Diabetologist. The genotypes for PTPN22 gene functional variant C1858T (R620W) were identified by PCR-RFLP method. HLA-DQ alleles were determined by sequence-specific PCR in 178 T1DM patients. The study was approved by the joint KIMS-FOM Ethics Committee.

Results:

The variant genotype of the PTPN22 gene (1858T) was detected in homozygous and heterozygous combination in 74/191 (39%) T1DM patients compared to 27/101 (27%) in the controls. The homozygous TT-genotype was detected in 8% T1DM patients compared to 0.99% in the controls (p <0.001). Nine different allelic combinations of HLA-DQ alleles were detected in T1DM patients. In 98 (55%) T1DM patients, the genotype was either homozygous for DQ2 or in combination with a DQ8 allele. In 58 (36%) T1DM patients, the genotype was homozygous DQ8 or with other alleles. Collectively, 91% of the T1DM patients had either DQ2 or DQ8 alleles in different combinations. In T1DM patients which carried TT-genotype for PTPN22 gene, 93% had at least one DQ2 allele and 60% carried either a DQ2 or a DQ8 allele.

Conclusions:

Our data demonstrate that the variant T-allele of the PTPN22 gene along with HLA-DQ2 and DQ8 alleles constitute significant determinants of genetic predisposition to T1DM in Kuwaiti children.

Key Words: Type-1 diabetes, Genotype, PTPN22 gene

Funding Agency: Kuwait University, Research Sector



Pediatrics

Category: Clinical

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Determinants of nutritional rehabilitation success in patients with growth faltering: Al-Adan experience

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Introduction:

The current study was conducted to assess the risk factors determining the outcome of the nutritional rehabilitation of patients with growth faltering following up in the Clinical Nutrition Pediatric Outpatient Clinic, Al-Adan hospital.

Methods:

This study was conducted on 122 patients 3-8 years old, 74 (60.6%) Males, Kuwaiti children suffering from faltering growth; 92 (75.4%) of those were underweight and 30 (24.6%) were wasted. Careful dietetic history was taken and each patient was clinically examined and laboratory tests were requested to exclude secondary causes. Caloric requirements were calculated and a clear dietetic regimen was given for each case in accordance to their own tolerance and preferences. The patients were followed for 6 months by assessing their anthropometric measurements and obtaining a dietary history in each visit. Success was determined when the anthropometric measurements fall above the -2 z scores on the WHO growth charts.

Results:

Underweight patients showed improvement after 1 and 3 months in comparison to more stunted children failing to respond after 6 months follow up ($p=0.041$). Patients cared for by mothers and family members showed statistically earlier improvement compared to those cared for by foreign care givers ($p=0.002$). More patients, receiving one fourth to one third of their calorie needs as supplementary milk and those using new recipes showed early improvement and less of them didn't respond after 6 months yet both comparisons didn't reach statistical significance ($p=0.69$ and $p=0.21$ respectively).

Conclusions:

Nutritional rehabilitation is easier for underweight patients and largely depends on the family participation. We recommend counselling the families explaining their role in the nutritional rehabilitation program of such patients with special emphasis on a tailored dietary regimen fulfilling the nutritional needs and including supplementary formulas.

Key Words: Underweight, Nutritional rehabilitation, Stunted

Funding Agency: None



Pediatrics

Category: Clinical

165

Acute gastroenteritis: An on going problem

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Introduction:

In Kuwait in spite of the relatively high social class, and the general improvement in public health, acute gastroenteritis (AGE) remains one of the most common reasons of childhood hospitalization, especially among children younger than 5 years. This is a descriptive study demonstrates that AGE is a major epidemiologic challenge which needs certain public health initiatives to reduce the economic resources wasted on it. This study highlights the importance of raising people awareness and implementing recent preventive measures to reduce AGE in Kuwait.

Methods:

The files of all patients aged 1 month to 12 years admitted with the diagnosis of AGE to unit B pediatric ward, Adan hospital over three month duration [29/6/2014 till 28 September 2014] were retrospectively reviewed.

Results:

901 children were admitted to general pediatrics wards Adan Hospital during 3 months period of these 432 patients admitted to ward 9. 96 patients were admitted with the diagnosis of AGE (i.e. 22% of all admissions). Mean age was 1 month to 1 year, mainly males (58 patients). Only 9 patients received exclusive breast feeding. Vomiting was the main presenting symptom in 87 patients, and diarrhea recorded in 93 patients. Only 7 patients had severe dehydration. 78 patients had metabolic acidosis. All patients received intravenous fluid. Hospital stay ranged from 1-7 days.

Conclusions:

This paper emphasizes the importance of encouraging exclusive breast feeding and promoting pre/probiotic containing milk formulas. It also demonstrates that rotavirus vaccination may substantially reduce medical cost and childhood hospitalizations caused by diarrhea.

Key Words: Acute Gastroenteritis; Rotavirus vaccination; Prebiotics vs probiotics

Funding Agency: None



Pediatrics

Category: Clinical

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**Vitamin-D levels in Kuwaiti children with Type-1 Diabetes Mellitus:
A prospective study from three hospitals in Kuwait**

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Introduction:

The prevalence of type-1 Diabetes Mellitus (T1DM) has been increasing in Kuwait over the past two decades. The disease results from a complex interplay between predisposing genes, immune system mediators and environmental factors. A variety of evidence indicate that Vitamin-D plays an important role in modulating the immune system and could thus impact the onset of T1DM. In this prospective study, we report Vitamin-D levels in Kuwaiti children with T1DM and healthy controls to explore its impact on disease predisposition.

Methods:

This study included 177 Kuwaiti children with T1DM from three hospitals in Kuwait (Mubarak, Farwania and Adan) over a 16-months period. The diagnosis of T1DM was based on the ISPAD diagnostic criteria. The control subjects (105 Kuwaitis) were healthy, had no close relative with T1DM and were evaluated by a Diabetologist. Vitamin-D levels were determined in serum samples from all study subjects using an enzyme immunoassay (EIA) method (25-Hydroxy Vitamin-D kit, IDS, UK). The study was approved by the Joint KIMS-FOM Ethics Committee.

Results:

The age of onset of T1DM was below 5 years in 61/177 (34%) patients. Vitamin-D levels were deficient (<21 ng/ml) in 151 (85%) of the 177 T1DM patients, insufficient (21-29 ng/ml) in 22/177 (12%) and sufficient (>29 ng/ml) in only 4/177 (2%) cases as per guidelines of the Task Force of Endocrine Society, 2011. In control group, Vitamin-D levels were deficient in 83/105 (79%), insufficient in 15/105 (14%) and sufficient in 7/105 (7%) respectively. The socio-economic status and educational background of the family had no correlation with the Vitamin-D levels in T1DM patients. However, in almost all the early onset T1DM cases, Vitamin-D levels were in the very low range.

Conclusions:

The Vitamin-D deficiency is highly prevalent in Kuwaiti T1DM patients and the control subjects and therefore can be considered an important determinant in high prevalence and/or early onset of the disease.

Key Words: Vitamin-D, Type-1 diabetes mellitus

Funding Agency: Kuwait University, Research Sector



Pediatrics

Category: Clinical

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Neuroimaging evaluation for first attack of unprovoked non-febrile seizure in pediatrics: When to order?

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Introduction:

The aim of this study is to assess the value of neuroimaging studies in pediatric patients presenting with their first attack of non-febrile seizure.

Methods:

We performed a cross-sectional, retrospective review of pediatric patients' records aged between 28 days and 12 years whom were admitted between January 1st and December 31st 2013 with first attack of unprovoked, non-febrile seizure. Only patients whom underwent a neuroimaging study were included. We excluded patients with febrile seizure, known epileptic disorder, history of status epilepticus, history of fits shortly after head trauma, and neonates or patients aged older than 12 years old presenting with seizures. Computed tomography (CT) scan and magnetic resonance imaging (MRI) were defined as either normal or abnormal. Abnormal neuroimaging studies were further classified as clinically insignificant and clinically significant (i.e. needs medical or surgical intervention). Descriptive analysis was performed to summarize the data.

Results:

Fifty children were included in our study, with a mean age of 5.2 ± 3.8 years. Of the subjects, 29 (58.0%) were males. Only sixteen (32.0%) patients were found to have abnormal neuroimaging scan; however, only one of them was considered to have clinically significant abnormal CT/MRI scan. This patient presented with disorientation, focal seizure and Todd's paresis, and was later diagnosed with Moyamoya disease.

Conclusions:

In conclusion, neuroimaging studies did not have a great value in evaluating pediatric patients presenting with their first attack of unprovoked, non-febrile convulsions among our patients. We therefore recommend the reconsideration of using these tests for this group of patients unless evidence of focal neurological deficit is present.

Key Words: Neuroimaging; Pediatrics; Non-febrile seizure

Funding Agency: None



Pharmacology and Toxicology

Category: Basic Sciences

168

MKP-2 attenuates doxorubicin-induced death in breast cancer cells

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Introduction:

Background: MKP-2/DUSP4 is one of MKPs family members, which is considered as an inducible enzyme. The main known function of MKP-2 is to negatively regulate mitogen activated protein kinases (MAPKs) by dephosphorylating their Tyrosine and Threonine residues. Although the DUSP4 gene has been connected to a number of cancers such as breast, its role in cancer cells growth and proliferation is still not well defined. We therefore examined whether MKP-2 might play a protective role in breast cancer.

Methods:

MDA-MB-231 and MCF-7 cells were stimulated with doxorubicin (DOX), an anthracycline anticancer drug, in the presence or absence of Sp600125 for indicated time. Extracted protein was subjected to western blotting to determine MKP-2, MAPK and Caspases levels. MKP-2 was overexpressed using adenovirus and silenced by shRNA. MTT assay was used to assess cells proliferation, while apoptosis was detected by Annexin V staining.

Results:

DOX induce a pro-apoptotic effect through significant activation of JNK 1/ 2 and ERK 1/ 2 in MDA-MB-231 cells. Also markedly inhibited MKP-2 at both mRNA and protein levels in a concentration-and time-dependent manner. By overexpressing MKP-2 or inhibiting phosphorylation of JNK by Sp600125, MDA-MB-231 and MCF-7 cells became more resistant to DOX-induced apoptosis. Knocking down MKP-2 expression by shRNA made cells became DOX-sensitive and subsequently increased apoptosis through caspase 3 dependent pathway.

Conclusions:

Data suggest that MKP-2/DUSP4 may serve as a biomarker for DOX sensitivity and a potential drug target for attempts to increase the efficiency and minimize the adverse side effects and resistance toward the present chemotherapeutic drugs.

Key Words: Caspase, DUSP4/MKP-2, Breast cancer

Funding Agency: Kuwait University Project NO: NM01/10



Pharmacology and Toxicology

Category: Graduate MSc: Basic Science

169

Action of the mas receptor in experimentally induced colitis

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Introduction:

Ang 1-7, a major component of the renin-angiotensin aldosterone system involved in the regulation of cardiovascular and renal functions, is thought to counteract the pro-inflammatory actions of angiotensin II and play a role in the etiology of many inflammatory diseases. In this study, we examined the effect of either exogenous administration of Ang 1-7 or inhibition of its function (by treatment with mas receptor antagonist A779) in inflammatory bowel disease (IBD).

Methods:

DSS-colitis model was established in balb/c mice. Physical parameters were assessed by monitoring body weight loss and colon length and thickness. Colitis severity was determined macroscopically and microscopically in Ang 1-7/DSS A-779/DSS treated groups. Circulating WBC in blood smear, colonic MPO activity for granulocyte infiltration and cytokine/chemokine expression in plasma by proteome array were also measured. Expression/activity of P-ERK1/2 and P-Akt and RAAS components was determined by western blotting. Ang 1-7 levels was measured by ELISA.

Results:

At 3.5% w/v dosing, DSS produced a consistent degree of colitis and was used to test the effect of Ang 1-7. All tested parameters indicated enhanced colitis severity with increased colonic MPO activity, elevated P-ERK1/2 and P-Akt, and cytokines and chemokines involved in chemotaxis, migration and activation of immune cells. Daily i.p injections of Ang 1-7 (0.01-0.06 mg/kg) resulted in significant improvement in colitis severity at gross and histological level, and paralleled the reduced circulating levels of various cytokines and chemokines. In contrast, A-779 significantly worsened colitis severity through up-regulation of these mediators.

Conclusions:

Enhanced expression of Ang1-7 and mas receptor in the colon of DSS treated mice suggests a role in colitis development. The anti-inflammatory properties of Ang 1-7 in the pathogenesis of IBD may provide a future therapeutic strategy to control disease progression.

Key Words: Ang1-7, Colitis, Mas receptor

Funding Agency: YP01/13, SRUL02/13



Pharmacology and Toxicology

Category: Basic Sciences

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Effect of ethanol and hyperthermia on the carotid artery

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Introduction:

Heatstroke is a serious condition and clinical studies indicate that vascular stroke increases with excessive consumption of alcohol (ethanol). It was our objective to test the influence of ethanol on cerebral perfusion at normal and higher temperatures.

Methods:

Twenty adult male New Zealand White rabbits were used in this study. Recording of isometric tension in rabbit carotid artery strips in organ baths with different concentrations of ethanol at normal temperature and during hyperthermia (+4 degree) and scintigraphic cerebral imaging were made.

Results:

Stepwise heating induced reproducible reversible graded contraction, proportional to temperature. At high concentrations (toxic levels) ethanol induced an increase in tension and heating potentiated these responses. During hyperthermia and ethanol scintigraphic isotope uptake was reduced in cortical and cerebellar regions. Ethanol also increased heating-induced vasoconstriction. Extracellular Mg²⁺ potentiated both heating-induced vasoconstriction and ethanol-induced vasoconstriction while extracellular Ca²⁺ had no effect on these responses. Capsazepine (vanilloid receptor antagonist) abolished the contractile effect of ethanol and prevented the potentiation between ethanol and heat.

Conclusions:

Carotid artery vasomotor tone is temperature dependent and heating induces vasoconstriction. Alcohol (ethanol) at normal temperature elicited carotid artery contraction only at high concentrations but at any concentration during elevated temperature. Ethanol potentiated the effect of hyperthermia-induced vasoconstriction and reduced cerebral perfusion. The synergistic effect of high-dose ethanol and hyperthermia may induce heat stroke and brain damage. The contraction to both heat and ethanol is mainly through intracellular and not extracellular Ca²⁺. The effect of ethanol is mainly via activation of vanilloid receptor TRPV1.

Key Words: Hyperthermia; Carotid artery; Scintigraphic cerebral imaging

Funding Agency: None



Pharmacology and Toxicology

Category: Basic Sciences

171

Paclitaxel causes electrophysiological changes in the anterior cingulate cortex via modulation of the GABAergic system

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Introduction:

The use of paclitaxel in the treatment of cancer is hampered by development of dose-limiting neuropathic pain. The aim of this study was to elucidate any supraspinal changes that may contribute to the development of paclitaxel-induced neuropathic pain (PINP).

Methods:

Sprague-Dawley rats were treated intraperitoneally with paclitaxel (8 mg/kg) on two alternate days. A week after the administration of the first dose, a time point when paclitaxel-treated rats have mechanical allodynia, animals were sacrificed to obtain slices of the anterior cingulate cortex (ACC; brain region involved in pain modulation). Field excitatory post-synaptic potentials (fEPSPs) were recorded in the ACC of control and treated animals and stimulus-response curves constructed. The observed effects were pharmacologically characterized by bath application of appropriate drugs.

Results:

Slices from paclitaxel-treated rats produced a significantly higher maximal response (E_{max}) than those from untreated rats ($p < 0.01$). This indicates increased excitability in the ACC of paclitaxel-treated rats. This may be due to a decrease in γ -aminobutyric acid (GABA)-mediated transmission. Enhancement of extracellular GABA with the GABA reuptake inhibitor, NO-711 (0.01 μ M) caused an increase in the E_{max} that was comparable to that obtained with paclitaxel treatment. This suggests that NO711 is causing a saturation of GABA receptors in the ACC of untreated rats, leading to a decrease in the overall effect of GABA. Reducing the effect of GABA by applying a GABA-B receptor blocker, CGP55845 (50 μ M) also increased the E_{max} in slices from untreated rats ($p > 0.05$).

Conclusions:

Paclitaxel causes supraspinal changes in excitatory synaptic transmission via modulation of GABAergic mechanisms involving GABA-B receptors. These changes possibly contribute to the pathophysiology of PINP. Thus, the GABAergic system is a potential therapeutic target for managing PINP.

Key Words: γ -amino butyric acid, Paclitaxel, Field excitatory postsynaptic potentials

Funding Agency: Kuwait University Research Sector grant number PTO



Pharmacology and Toxicology

Category: Graduate MSc: Basic Science

172

Investigating the desensitization and internalization of the incretin receptors

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Introduction:

Incretins (the gut hormones, glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1)), function to potentiate insulin secretion in a glucose dependent manner. This makes their respective receptors (GIPR & GLP-1R) attractive targets in the treatment of type 2 diabetes mellitus (T2DM). However, in T2DM there is an almost complete lack of response to GIP whereas this is not true for GLP-1. The aim of this project was to compare the desensitization and internalization of these two clinically important receptors.

Methods:

A myc-tag was introduced to the N-terminus of GIPR and GLP-1R, downstream of their putative signal peptides, by sequential overlapping PCR. myc-tagged GIPR and GLP-1R were expressed in HEK-293 cells. Homologous desensitization was assessed by pre-incubating cells with agonists for increasing periods of time, washing the cells and measuring the cAMP response to a second stimulation. Receptor internalization following agonist stimulation was monitored using an indirect ELISA-based method.

Results:

Pre-incubation of cells with agonist resulted in a rapid loss of response to a second stimulation for both GIPR and GLP-1R. In both cases, washing cells following pre-incubation failed to bring cAMP levels back to basal. Taking this into account, two rate of desensitization were calculated for GLP-1R; 'apparent' ($t_{1/2} = 19.3$ min) and 'net' ($t_{1/2} = 3.0$ min). GIPR desensitization was too rapid to accurately calculate rates. Incubation of cells with GLP-1 resulted in a time-dependent loss of GLP-1R cell surface expression ($t_{1/2} = 2.1$ min). However, GIP did not appear to induce internalization of GIPR.

Conclusions:

There appear to be fundamental differences in the regulation of GIPR and GLP-1R when expressed in HEK-293 cells. This may have relevance in the development of new incretin-based therapies.

Key Words: Internalization, GIP; GLP-1

Funding Agency: YM08/13



Pharmacy

Category: Basic Science

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Adolescent Knowledge and awareness of diabetes mellitus in Kuwait

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Introduction:

Diabetes mellitus is a major public health problem in Kuwait. This study aimed to evaluate the awareness and the knowledge of diabetes in adolescent about the disease which, will be of a great help to reduce the risk of developing diabetes and its complications.

Methods:

Across-sectional survey was done among the students of public and private secondary schools in Kuwait to evaluate their knowledge of diabetes. The questionnaire consisted of 37 questions focusing on different aspects of diabetes mellitus, namely: general knowledge, risk factors, symptoms, complications, treatment, management and monitoring of diabetes.

Results:

A total of 4333 students contributed. The mean total knowledge score was 25.0 (SD=7.1) out of 37 and the average correct answer was 63.2%, ranges from 33.3% to 87.1%. The average correct answer for different sections were highest for monitoring section (71%) followed by general knowledge section (69.8%) and the lowest for symptoms and complications section (55.5%). The percentage correct response to 18 questions were below the overall average. Only one third of students knew that pregnant women may become diabetic through pregnancy. Also, only about half of the participants knew that diabetes can result in weight loss, impaired vision and delay in wound healing.

Conclusions:

The students contributed in this study have good general information about diabetes except for a few areas. Our study will clarify these areas to help in designing educational programs to treat these deficiencies of knowledge about the disease and increase the awareness.

Key Words: Diabetes Mellitus; Adolescents; Kuwait

Funding Agency: PAAET



Pharmacy

Category: Undergraduate

174

Counterfeit medicines: Opinions of Health Science Center students and employees

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Introduction:

Counterfeiting medicines is a public health concern that has significant impact on health and quality of life. Increasing the awareness among the employees and students within educational institutions such as universities will help significantly to overcome the use of counterfeit medicines. The purpose of this study was to identify and explore the level of awareness on counterfeit medications among the Health Science Center (HSC) community at Kuwait University.

Methods:

The survey was conducted in November and December 2014. Ethical approval was obtained. Anonymous questionnaires were distributed throughout the four faculties (Medicine, Dentistry, Pharmacy and Allied Health) of the HSC including students and employees. The gathered data were analyzed using SPSS v. 21. Numbers and percentages were used to describe the data and chi-square test was used to compare between groups.

Results:

Among the 263 participants, 78.3% were students. Majority of participants were purchasing over the counter medicines (95%) and vitamins or supplements (71%) from pharmacies. Three-fourth of participants were aware of the existence of counterfeit medication in Kuwait and 72% believed that it is a problem in Kuwait. Only 15.3% knew what to do in case of finding a counterfeit medication in Kuwait and students were significantly lower in proportion in this matter compared to administrative and academic staff ($p < 0.001$). Overall 17.6% had the ability to detect counterfeit medication. The percentage of academic staff was significantly higher than that of the other two groups ($p = 0.014$). However, 67.6% had never received any information from authorities to improve the awareness about counterfeit medication.

Conclusions:

It is necessary to increase the awareness among students and employees of the HSC about counterfeit medicines and what to do in case of its existence, using multiple methods including workshops and formal seminars to spread the awareness.

Key Words: Counterfeit medicines; Pharmacy; Awareness

Funding Agency: None



Pharmacy

Category: Basic Sciences

175

Oral disintegrating tablets of desloratadine

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Introduction:

Orally disintegrating tablets (ODTs) are gaining importance as new drug delivery systems. These dosage forms dissolve or disintegrate in the oral cavity within a matter of seconds without the need of water or chewing. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets ideal for geriatric and pediatric patients. The aim was to prepare ODT of desloratadine, which is the major metabolite of loratadine.

Methods:

Twelve different placebos ODT were prepared (F1-F12) using different functional excipients. They were evaluated for their compressibility, hardness and disintegration time. The taste masking efficiency of the different formulations was tested a panel of 10 volunteers. The compressible non sticky formulations (F1, F3, F4, F5, F6, F7 and F 12) were subjected to further evaluation tests after addition of coated desloratadine, including weight uniformity, wetting time, and friability testing.

Results:

Desloratadine showed bitter taste when formulated as ODT without any treatment. Therefore, different techniques were tried in order to mask its bitter taste. Using Eudragit EPO resulted in complete masking of the bitter taste of the drug and increased the acceptability to volunteers. Fairly good weight uniformity values were observed in all the tested formulations. F12 exhibiting the shortest wetting time (14.7 seconds) and consequently the lowest (20 seconds) disintegration time. Dissolution profile showed that 100% desloratadine release was attained after only 2.5 minutes from the prepared ODT (F12) with dissolution efficiency of 95%.

Conclusions:

The suggested desloratidine-ODT showed 100% drug release, compared to 80% from conventional tablets (Aerius), after 2.5 minutes, with good taste masking.

Key Words: Taste masking, Desloratadine, Oral disintegrating tablets

Funding Agency: None



Pharmacy

Category: Basic Sciences

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Determination of the relative bioavailability of different paracetamol products in the rabbit

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Introduction:

The rate and extent of drug absorption are important determinants of the onset and intensity of effect for orally administered drugs. This study was designed to compare the rate and extent of paracetamol absorption after oral administration of a single dose of different brands in the rabbit.

Methods:

Five groups of rabbits (n=4 each) received a single oral dose of 30 mg/kg paracetamol using five marketed paracetamol products. The products were manufactured in the Kuwait, UAE, Nigeria, Germany, and UK. Paracetamol tablets were crushed, suspended in water and the dose was administered using pediatric feeding tube. Serial blood samples were obtained from each rabbit, plasma was obtained by centrifugation and paracetamol concentrations were determined using LC/MS/MS. A noncompartmental approach was utilized to calculate the pharmacokinetic parameters including C_{max}, t_{max}, AUC, and the obtained parameters for the different products are compared statistically.

Results:

The mean maximum plasma concentration after administration of the five products ranged from 2.48±0.57 ug/ml to 5.69±1.04 ug/ml, reflecting two fold difference. While the mean time to achieve the maximum plasma concentration ranged from 0.56±0.24 hr to 0.81±0.24 hr. Whereas the area under the curve calculated after administration of the five brands ranged from 6.75±1.21 ug-hr/ml to 10.37±1.98 ug-hr/ml, indicating about 60% difference. The bioavailability of the different paracetamol brands relative to the brand with the highest extent of absorption were 0.9, 0.9, 0.79, and 0.65. ANOVA showed that the relative bioavailability of the different products were significant difference for the different products.

Conclusions:

The results show that although paracetamol products are widely available in the market, and paracetamol products do not require special formulation strategies, large variation exist in the rate and extent of paracetamol absorption after the different products.

Key Words: Pharmacokinetics, Paracetamol, Bioavailability

Funding Agency: None



Pharmacy

Category: Clinical

177

Pharmaceutical care in hospitals of Kuwait: Pharmacists' attitudes and perceived preparedness

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Introduction:

Pharmaceutical care practice has been championed as the primary mission of the pharmacy profession, but its implementation has been suboptimal in Kuwait. Pharmacists must have sufficient knowledge, skills, and positive attitudes to practise pharmaceutical care. This study was designed to investigate hospital pharmacists' attitudes towards pharmaceutical care and perceptions of their preparedness to provide pharmaceutical care competencies.

Methods:

A descriptive, cross-sectional study was conducted among all pharmacists working in the governmental hospitals in Kuwait (n=385). Data were collected via a pre-tested self-administered questionnaire. Data analysis was performed using SPSS, version 20. Statistical significance was accepted at a p value of <0.05.

Results:

The response rate was 64.9%. Pharmacists agreed/strongly agreed with most of the statements of the standard Pharmaceutical Care Attitude Survey (PCAS), reflecting favorable attitudes towards pharmaceutical care. The highest perceived preparedness was in the psychosocial aspects of pharmaceutical care followed by communication, technical and lastly the administrative/management aspects. Pharmacists with more practice experience expressed significantly more positive attitudes towards pharmaceutical care (p=0.001) and they felt better prepared to provide pharmaceutical care competencies (p<0.001) than those with less experience as practitioners.

Conclusions:

Hospital pharmacists in Kuwait advocate implementation of pharmaceutical care. They felt well prepared overall to implement the various aspects of pharmaceutical care, even though they could benefit from further training in the administrative/management aspects. Professional experience seems to be influential in determining pharmacists' attitudes and preparedness level. More attention should be given to enhance pharmacists' actual pharmaceutical care competencies to expand their professional roles.

Key Words: Kuwait, Pharmaceutical care, Hospital pharmacists

Funding Agency: None



Pharmacy

Category: Basic Sciences

178

Enhancing ibuprofen dissolution rate using nanotechnology approach

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Introduction:

Nanoparticle engineering processes have become promising approaches for enhancing dissolution rate of hydrophobic drugs. The objective of the present work was to prepare ibuprofen (IBU) -PVP K30 nanoparticles using ultra homogenization to enhance the dissolution rate of IBU.

Methods:

Phase solubility study was done to investigate the effect of PVP K30 concentration on solubility of IBU. Nano-suspensions were prepared using different drug:polymer ratios by an optimized high pressure ultra-homogenization technique and were evaluated for particle size and zeta potential. The suspensions were then lyophilized and studied for drug content and dissolution. The effect of Tween 80 was also investigated and DSC and FTIR studies were also performed.

Results:

Phase solubility study indicated a linear increase in IBU solubility with increasing PVP K30 concentration. The saturation solubility of IBU (60 μm) was found to be 47 $\mu\text{g/ml}$. IBU-PVP K30 nanosuspensions were successfully prepared by an optimized ultra-homogenization technique. Increase in polymer concentration, number of homogenization cycles and pressure resulted in decrease in particle size up to 527 ± 31 nm. The suspensions also exhibited zeta potential values above -30 mV which is a pre-requisite for physically stable nanosuspensions. The lyophilized nanoparticles showed 100% drug release, compared to micronized IBU ($53.06 \pm 4.79\%$) after 60min. DSC endotherms demonstrated mutual interaction between IBU and PVP K30 which was further confirmed by FTIR. Nanosuspensions containing Tween-80 showed excellent re-dispersibility and further reduction in particle size up to 127 nm.

Conclusions:

IBU-PVP nanoparticles with improved aqueous solubility and dissolution rate have potential for better IBU formulation. These factors can enhance drug bioavailability, decrease gastric irritation and thus improve patient safety.

Key Words: Dissolution, Ibuprofen, Nanoparticles

Funding Agency: Kuwait University (Grant No. PP02/13)



Pharmacy

Category: Basic Sciences

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Structure-antibacterial activity relationships of N-substituted-(D/L-alaninyl) 1H-1,2,3-triazolyl oxazolidinones

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Introduction:

Introducing glycyl spacer with hydrogen bond acceptor and/or donor groups at N-4 position of terminal piperazine moiety of the phenyloxazolidinone pharmacophore yielded derivatives with potent antibacterial activity, due to enhanced interactions at the bacterial 50S ribosomal binding sites. Objective of the study is to investigate the influence of varied N-aryloxy- and N-arylsulfonyl-(D/L-alaninyl) on the antibacterial activity of piperazinyl-5-(4-methyl-1,2,3-triazolyl) oxazolidinones.

Methods:

The N-aryloxy- and N-arylsulfonyl-(D/L-alaninyl) oxazolidinones were synthesized and characterized by spectroscopic and other analytical methods. Antibacterial activity was evaluated against standard reference Gram-positive and -negative bacterial strains including *S. aureus*, *S. epidermidis*, *E. faecalis*, *E. coli*, *M. catarrhalis* and *H. influenzae*. Minimum inhibitory concentrations (MIC's, ug/ml) were determined by agar dilution method on Mueller Hinton agar.

Results:

Most of the compounds were generally more active against Gram-positive bacterial strains with MIC ranges of 2-16 ug/ml. There was no significant difference between the antibacterial activities of the D- and L-alaninyl oxazolidinones. Moreover, the N-nitrobenzoyl-alaninyl and N-aminobenzoyl-alaninyl oxazolidinones demonstrated comparable activity against all Gram-positive bacteria with MIC ranges of 2->16 ug/ml. However, N-nitroarylsulfonyl-alaninyl derivatives were less active against *S. aureus* (MIC: 16->16) in comparison to their activity against *S. epidermidis*, *E. faecalis* and *M. catarrhalis* with MIC ranges of 2-8, 4-16 and 4->16 ug/ml, respectively.

Conclusions:

The most active compounds are those bearing the N-3,5-dinitrobenzoyl-, N-3-nitrobenzoyl-, N-5-nitrothiophenecarbonyl groups with MIC values of 2 ug/ml against *S. aureus*, *S. epidermidis*, *E. faecalis* and *M. catarrhalis*, compared to linezolid (MIC: 2 and 8 ug/ml). Compounds exhibited moderate to strong activity against all Gram-positive cocci tested.

Key Words: N-Substituted-(D/L-alaninyl) 1H-1,2,3-triazolyl oxazolidinones

Funding Agency: Kuwait University, Research Sector Grant PC01/05



Pharmacy

Category: Clinical

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Influence of oral hypoglycemic agent on kininase II and nitric oxide activities in Kuwaiti patients with type 2 diabetes

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Introduction:

The current investigation was conducted to examine kininase II (angiotensin converting enzyme, ACE) and nitric oxide (NO) concentrations in healthy Kuwaiti control subjects and newly diagnosed Kuwaiti type 2 diabetic patients before and after treatment with oral anti-diabetic drugs.

Methods:

With the consent of volunteers (control and diabetic), blood and urine samples were collected after an overnight fasting. Samples were collected from diabetic patients before and after treatment of six weeks. Enzyme linked immunosorbent assay (ELISA) was carried out on the aliquoted samples to measure the concentration of kininase II. Nitric oxide was detected via colorimetry.

Results:

Plasma Kininase II or ACE levels were significantly ($p < 0.01$) increased by 18% in untreated diabetics when compared with healthy volunteers. However, after treatment there was a significant decrease of 20% in their ACE levels. NO levels were found to be significantly lower in plasma by 56% and in urine by 62% in untreated diabetic patients as compared with the healthy subjects. However, when the treated diabetic patients were compared with untreated diabetics, there was an increase of 50% in plasma and 37% in urine samples.

Conclusions:

The high levels of kininase II and reduced NO may be partly responsible for the induction of renal, cardiac and hypertensive complications associated with type 2 diabetes. Reduced NO level is an indication of endothelial dysfunction resulting in increased blood pressure. Oral anti-diabetic treatment is associated with protective effects through the reduction of kininase II (ACE) and elevation of NO levels. The results suggested that ACE inhibitors may have beneficial effect on renal system in diabetic patients.

Key Words: Diabetic; Kininase II; Nitric Oxide

Funding Agency: Kuwait University, Grant no. RP01/09



Pharmacy

Category: Basic Sciences

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Development and evaluation of metformin hydrochloride rectal suppository for treatment of diabetic patients

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Introduction:

Metformin hydrochloride (MtHcl) is an oral antidiabetic drug and has been used successfully to treat polycystic ovary and overweight patients. However, the available commercial dosage form (DF) is the oral tablets that have poor bioavailability, narrow absorption window and extensively metabolized in the liver. The aim of this work was to formulate MtHcl as a suppository DF to partially bypass the liver metabolism, improve the absorption and bioavailability and to be a good alternative for patients who cannot swallow the oral tablets.

Methods:

Suppository fatty bases (FB); Witepsol® and Suppocire® (different grades) and polyethylene glycol bases (PEG) 1000, 4000 and 6000 (different ratios), were used to prepare rectal suppositories each containing 500 mg MtHcl by fusion method. The formulations were inspected visually and characterized for weight uniformity, mechanical strength, melting time, penetration time, content uniformity, extraction efficiency and dissolution profile in phosphate buffer (pH 6.8).

Results:

The produced suppositories were elegant in shape and free of physical deformities. The average melting time for FB was 8 min, and the disintegration time for PEG bases ranged between 10-12min. The mechanical strength ranged between 7-8kg/cm and the penetration time ranged between 6.2-8.1min. All the formulations showed acceptable range of content uniformity (95-105%) and the drug could be efficiently extracted from the base. FB showed significant higher drug release compared to PEG (P=0.05) where more than 90% of drug was released in the first hour of dissolution.

Conclusions:

The results indicated that MtHcl rectal suppositories were successfully prepared and characterized and the FB showed better drug release than PEG bases. MtHcl suppositories could be a potential alternative to the oral tablets. Extra work will be done to get the optimized formulation that can be used later for bioavailability studies.

Key Words: Rectal Suppositories, Metformin Hydrochloride, Diabetes Type II

Funding Agency: None



Withdrawn



Physiology

Category: Graduate MSc: Basic Science

183

Administration of dexamethasone during pregnancy alters fetal brain development: Role of TAp73.

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Introduction:

Dexamethasone (Dex), is a glucocorticoid (GC) prescribed to pregnant women at risk of preterm delivery, or bearing fetuses at risk of congenital adrenal hyperplasia. Prenatal Dex administration is associated with several neuropsychological and behavioral disorders during infancy and adulthood. However, the mechanisms through which prenatal GCs induce these long lasting disturbances are not yet known. We have shown that fetal exposure to maternal GCs enhances the expression levels of the pro-cell death protein TAp73 in the fetal brain. In the present study, we explored the impact of maternal intake of Dex on fetal brain development and TAp73 protein expression and its associated neural cell death program.

Methods:

Pregnant dams received daily intra-peritoneal injection of either Dex (0.4 mg/kg, n = 6) or pyrogen-free saline (n = 6) from gestation day (GD)14 until GD21. TAp73 protein expression in the fetal brains was assessed using western blotting. The cellular expression of TAp73 and the neural cell death marker (cleaved caspase-3) and marker of mature neurons (NeuN) were monitored using fluorescent immunohistochemistry.

Results:

Maternal injection with Dex significantly reduced fetal body and brain weights and increased TAp73 protein expression. This enhanced TAp73 expression was associated with pronounced neural cell death as revealed by increased cleaved caspase-3 immunoreactive cells. Furthermore, Dex significantly reduced the number of mature neurons co-expressing TAp73 protein.

Conclusions:

The increased expression of TAp73 and the concurrent increase in neural cell death and reduction in the number of differentiated neurons, may be responsible for the restricted fetal brain development in Dex treated dams.

Key Words: Neural Cell Death, Prenatal Dexamethasone

Funding Agency: None



Physiology

Category: Undergraduate

184

The long lasting impact of prenatal immune challenge on the process of remyelination

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Introduction:

Early life stress has long lasting effects on brain function and plasticity. However, the impact of prenatal stress on remyelination after a demyelination insult has not yet been explored. Therefore, we explored the long lasting impact of prenatal immune stress on the process of remyelination during adulthood.

Methods:

At gestation day 12, pregnant Sprague Dawley rats were injected with either sterile saline solution or lipopolysaccharide solution (100 µg/kg, i.p.). A 2µl of the gliotoxin ethidium bromide (EB, 0.04%) was stereotaxically injected into the corpora callosa of male adult offspring. Brains were collected 7 days post-injection, a time corresponding to the peak of demyelination. Oligodendrocytes progenitor cells (OPCs) and mature oligodendrocytes in the vicinity of the lesion were detected by immunofluorescence using NG2 and CC1 antibodies respectively. Microglia were detected by immunofluorescent staining (Iba1). Microglial M1 and M2 types were monitored using antibodies against the inducible nitric oxide synthase and arginase-1 respectively. Western blotting was used to assess the activation of nuclear factor κB (NFκB) signaling pathway by measuring the levels of phosphorylated and total IκB.

Results:

Prenatal injection of LPS significantly increased the number of myelinating cells in response to EB-induced demyelination. This effect was not associated with a change in the levels of microglial activation or polarization. Prenatally immune-challenged animals showed significantly higher levels of total IκB when compared to those born to mothers given saline.

Conclusions:

These data strongly suggest that prenatal immune challenge has a long lasting impact on the offspring's response to the demyelination insult. This effect is manifested by an increase in the number of OPCs and mature oligodendrocytes at the lesion site. It is likely that this enhanced myelination is, at least in part, due to dampening of the NFκB signaling pathway.

Key Words: Myelin; Inflammation; Microglia

Funding Agency: None



Physiology

Category: Graduate MSc (Basic Science)

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Effects of lead exposure on early gene expression, apoptosis and oxidative stress level in rat's heart

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Introduction:

Lead pollution is an issue of concern in the recent days. The effects of lead on the heart are not completely understood. In this study we investigated the effects of lead toxicity and its oxidative stress on early gene expression and apoptosis in myocardial cells.

Methods:

Wister male and female rats (n=30) were subdivided into control with no treatment and treatment groups subjected to 0.5% lead acetate 5 or 45 days. Hearts isolated from these rats were perfused and separated into anterior and posterior walls. Anterior wall was embedded in paraffin to evaluate Ki-67, c-Myc, c-Jun protein expression and apoptosis. Posterior wall was homogenized to evaluate total oxidants and antioxidants levels.

Results:

Lead exposure significantly ($p < 0.002$) increased Ki-67 levels in male hearts in 45 days lead exposure compared to control and female hearts. 5 days lead exposure caused a significant ($p < 0.00001$) increase in c-Myc levels only in male rat hearts compared to control and female rat hearts. c-Myc levels were significantly ($p < 0.0001$) increased after 45 days lead exposure in both male and female rat hearts. c-Jun level increased significantly ($p < 0.00001$) in both male and female rat hearts after 5 and 45 days of lead exposures. c-Jun expression levels in the 45 days were significantly ($p < 0.00001$) higher than 5 days lead exposure. Apoptotic cell death was significantly ($p < 0.00001$) higher in both male and female rat hearts after 45 days lead exposure compared to their controls and 5 days lead exposure. Oxidants levels were significantly ($p < 0.0001$) lower in 5 and 45 days lead exposure in both male and female rat hearts compared to their controls. Antioxidants levels in male rat hearts were significantly ($p < 0.04$) lower than that of female rat hearts.

Conclusions:

Lead exposure amplified expression of stress related proteins and altered oxidant levels in cardiomyocytes. 45 days lead exposure resulted in a notable increase in the apoptotic cell death

Key Words: Lead; Toxicity; Heart

Funding Agency: YM 02/13



Physiology

Category: Graduate MSc: Basic Science

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Intrauterine growth restriction is associated with changes in placental expression of Metastasis Tumor Antigens in rats

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Introduction:

Objectives: Molecular mechanisms underlying placental formation in normal and intrauterine growth restricted (IUGR) placentas are not clearly known. We hypothesized that during IUGR, MTA1 and MTA2 expression decrease and that of MTA3 increases in placentas.

Methods:

Pregnant Sprague-Dawley rats (n=6/group) received daily i.p. injections of either Dexamethasone (0.4 ml/kg; DEX group), or saline (C group) starting from 14 days of gestation (dg) to either 19 or 21 dg. Gene and protein expression of MTA1, MTA2 and MTA3 in the basal (BZ) and labyrinth (LZ) zones of the placenta were investigated by real-time PCR, Western blotting and immunohistochemistry (IHC), respectively. The expression (IHC) of PCNA and Caspase-3 was investigated to assess cell proliferation and apoptosis, respectively. Statistical analysis was performed using SPSS, p-value<0.05 indicates significant change.

Results:

The gene expression of MTA1 increased on 19 dg (p<0.05) and its cytoplasmic protein expression increased on 21 dg in the LZ in DEX group (p<0.05). In the BZ, an increase in its cytoplasmic expression was seen on 19 dg (p<0.05) and a decrease in nuclear expression on 21 dg in the DEX group (p<0.001). The MTA2 gene expression decreased in the LZ on 19 and 21 dg in the DEX group (p<0.001 & p<0.05, respectively). The MTA2 protein expression increased in cytoplasm of BZ (p<0.05) and in LZ (p=0.52) on 19 dg in the DEX group. The MTA3 gene expression decreased on 19 and 21 dg in LZ (p<0.001 & p<0.05, respectively) and on 21 dg in BZ (p<0.001) of DEX group. In the BZ its protein expression decreased in the nuclear fraction on 21 dg (p<0.05) and increased in the cytosolic fraction on 19 dg (p<0.05) in the DEX group. Cell proliferation decreased and cell death increased in the DEX groups.

Conclusions:

IUGR is associated with molecular changes in MTAs expression in different placental zones and cell fractions. This could be linked to decreased cell proliferation and increased cell death

Key Words: Dexamethasone, Metastasis tumor antigens, Intrauterin growth restriction

Funding Agency: None



Physiology

Category: Graduate MSc (Basic Science)

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Effect of Cross Fit training on selected physical fitness components of adult males.

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Introduction:

Sports and exercise are a part of physical activity (PA) that is considered to be an essential risk factor for prevention of chronic diseases. Many types of physical fitness (PF) programs are available. CrossFit is a modern program recently gaining worldwide recognition due to the claim that it focuses on overall PF. The aim of this study was to investigate the effect of CrossFit on selected PF components of adult males. The components tested included: body composition, cardiorespiratory endurance, flexibility, muscle strength, muscle endurance, muscle power, speed, and agility. We also compared the effect of CrossFit with traditional fitness center training and with a control group.

Methods:

A total of 21 subjects were recruited, and allocated into three groups, each of 7: CrossFit, traditional fitness center, and control. In the CrossFit group, subjects participated in a minimum of 24 workout sessions within 8 weeks at a CrossFit facility. As for the traditional fitness center group, subjects participated in a minimum of 24 workout sessions within 8 weeks at a fitness center. Subjects in the control group did not perform any exercise for a period of 8 weeks. Tests of PF were conducted before and after each of the programs.

Results:

The results showed that CrossFit significantly improved six of the eight selected components of PF: flexibility ($p=0.002$), muscle strength ($p<0.001$), muscle endurance: push-ups ($p=0.002$) and sit-ups ($p=0.038$), power ($p<0.001$), agility ($p=0.009$), and speed ($p=0.001$). In the fitness center group, there was significant improvement in: flexibility ($p=0.039$), strength ($p=0.030$), and muscle endurance: push-ups ($p=0.014$) and sit-ups ($p=0.049$). The control group showed no significant improvement.

Conclusions:

CrossFit provided favourable results in improving the overall PF of the subjects when compared to the other groups. Moreover, this study confirms that PA on any level is better than None.

Key Words: Exercise; Fitness; CrossFit

Funding Agency: College of Graduate Studies, Kuwait University



Physiology

Category: Undergraduate

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The Role of ACE2, Angiotensin-(1-7) and mas receptor axis in glucocorticoid-induced intrauterine growth restriction

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Introduction:

Glucocorticoids are linked to intrauterine growth restriction (IUGR) and programming of cardiovascular and renal diseases in adulthood but the underlying mechanism is still unclear. Ang-(1-7) is a potent vasodilator produced mainly by the catalytic action of Angiotensin I-converting enzyme 2 (ACE2) on Angiotensin II. In mid and late pregnancy, the levels of ACE2 and Ang-(1-7) are elevated and are correlated with elevated placental angiogenesis, fetal blood flow, and rapid fetal growth. We hypothesized that ACE2, Ang-(1-7) and its receptor (Mas) are down regulated in response to glucocorticoid administration contributing to IUGR.

Methods:

Pregnant female Sprague-Dawley rats were injected with dexamethasone (DEX; 0.4 mg/kg/day) starting from 14 day gestation (dg) till sacrifice at 19 or 21 dg while control groups were injected with saline. The gene and protein expression of ACE2, Ang-(1-7) and Mas receptor in the placental labyrinth zone, the main area for maternal-fetal exchange, were studied by real-time PCR and western blotting, respectively.

Results:

DEX administration caused a reduction in the labyrinth zone at 19 and 21 dg compared to controls. IUGR, as shown by decreased fetal weights, was evident in DEX treated rats at 21 dg. ACE2 gene expression was elevated in the labyrinth zone of control placentas at 21 dg and DEX prevented this rise at both the gene and protein levels. In addition, Ang-(1-7) protein expression was significantly reduced in the DEX treated rats at 21 dg. On the other hand, Mas receptor expression was upregulated at 21 dg in both groups with higher protein expression at 21 dg in DEX compared to control group.

Conclusions:

The results of this study indicate that a reduced expression of ACE2 and an associated reduction in Ang-(1-7) in the placenta by DEX treatment may be responsible for IUGR and consequent disease programming later in life.

Key Words: Dexamethasone; IUGR; Ang-(1-7)

Funding Agency: None



Physiology

Category: Basic Sciences

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The role of reactive oxygen species, nitric oxide and natriuretic peptides in the protection of the heart against ischemia reperfusion injury

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Introduction:

Pacing-induced postconditioning (pacing postconditioning (PPC)), was proven to protect the heart against ischemia reperfusion (I/R) injury; however, its underlying mechanisms of protection are not completely understood. The aim of the present study was to explore the role of reactive oxygen species (ROS), nitric oxide (NO), Peroxynitrite (ONOO-), and natriuretic peptides in the heart protection and their role in PPC protection.

Methods:

Isolated (Langendorff) perfused rat hearts (n=6) were subjected to 30 minutes coronary occlusion and 30 minutes reperfusion. PPC consisted of 3 episodes of 30 sec left ventricular (LV) pacing alternated with 30 sec right atrial (RA) pacing during early reperfusion. Studied were control; with only ischemia and reperfusion, PPC, PPC in combination with selective agonists or antagonists of the molecules in question at the beginning of reperfusion. Hemodynamics were computed by a data acquisition program. Infarct size and area at risk were determined by 2,3,5-Triphenyltetrazolium chloride (TTC) and a blue dye.

Results:

Pacing postconditioning significantly ($p < 0.01$) improved cardiac hemodynamics and significantly ($P < 0.001$) decreased the infarct size. Blockade of BNP, NO, ONOO- and ROS completely abrogated the protective effect of PPC. However, ANP blockade did not affect this protection. When applied exogenously, ANP, BNP and NO donor, showed a significant ($P < 0.01$) recovery in the dysfunction of hemodynamics and significantly ($P < 0.001$) decreased the infarct size. Exogenous ROS completely blocked the improvement of hemodynamics and the decrease of infarct size induced by PPC compared to respective controls.

Conclusions:

Nitric oxide, ROS and the product of their interaction (ONOO-) protected the heart against ischemia reperfusion injury. Exogenous and endogenous BNP and NO protected the heart against ischemia reperfusion injury. However, endogenous ANP is not involved in this protection.

Key Words: Ischemia Reperfusion; Postconditioning; Reactive oxygen species

Funding Agency: MY 02/10 from Research Administration, Kuwait University.



Physiology

Category: Graduate MSc: Basic Science

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Differential cytokine expression by brain microglia / macrophages in primary culture after oxygen glucose deprivation and their protective effects on astrocytes during anoxia

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Introduction:

Activation of microglia/macrophages following cerebral ischemia may be beneficial or detrimental for survival of brain cells. This ambiguity was explained by findings that ischemia induces transformation of the microglia/macrophages into two different phenotypes, termed M1 and M2. To which extent this differentiation in vivo depends on paracrine signaling from other cells of the neurovascular unit (NVU) is not clear. This in vitro study used primary cultures of brain microglia/macrophages to explore if this transformation could occur in absence of other cells of the NVU.

Methods:

Primary cultures of rat microglia/macrophages were exposed to 2h oxygen glucose deprivation (OGD) and then incubated further under normal conditions, which was considered as a recovery period. Expression of phenotype-specific markers at transcript and protein levels and secretion of phenotype-specific cytokines were explored at different time points by real time PCR, immunostaining and ELISA, respectively. Viability of astrocytes was explored in the presence or absence of phenotype-specific cytokines during anoxia or in control conditions.

Results:

OGD protocol has triggered an increase in expression/secretion of M2 phenotype-specific markers/cytokines, with a similar time-pattern as it was revealed after ischemia in vivo. Expression and secretion of M1 phenotype-specific markers/cytokines did not show a common pattern, but there was a general tendency for an increase during the recovery period. Surprisingly, all M1 phenotype-specific and two out of the three tested M2 phenotype-specific cytokines revealed protective effects on astrocytes during anoxia.

Conclusions:

Polarization of the brain microglia/macrophages into the M2 phenotype following ischemia OGD appeared to be largely independent from paracrine signaling from the NVU. On the other hand, it appeared that a shift from the M2 into the M1 phenotype depends to a greater extent on paracrine signaling from the NVU.

Key Words: Cytokines, Microglia / Macrophages, Oxygen and Glucose Deprivation

Funding Agency: YM 04/12



Physiology

Category: Graduate (Resident)

191

Estradiol dampens the recruitment of oligodendrocyte precursor cells to the site of brain inflammation: Role of COX-2

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Introduction:

Conflicting findings have been reported on the immunomodulatory actions of 17 β -estradiol (E) in the central nervous system. We have previously shown that 17 β -estradiol exacerbates lipopolysaccharide (LPS)-induced cyclooxygenase-2 (COX-2) in the brain striatal region of ovariectomized (OVX) rats. Owing to the role of COX-2-produced prostaglandins in myelination, we investigated the effect of E on oligodendrocyte precursor cells (OPCs) and mature oligodendrocytes during brain inflammation.

Methods:

Ovariectomized adult Sprague Dawley female rats received intra-striatal injection of 2 μ l of LPS solution (500 ng/ μ l) using a stereotaxic apparatus. They were subsequently given either E (100 μ g/kg, s.c.) or sesame oil (s.c.) in conjunction with either the selective COX-2 inhibitor celecoxib (2.5 mg/kg, i.p.) or dimethyl sulfoxide (i.p.). The brains were collected on day 3 post-LPS injection, fixed and processed for immunofluorescent staining. Primary antibodies against OPCs and mature oligodendroglia, NG2 and CC1, respectively were used to detect the levels of these cells in the vicinity of the inflammatory lesion.

Results:

LPS injection into the striatum of OVX rats increased the number of OPCs, but not that of mature oligodendroglia, in the vicinity of the inflammatory lesion. Such cellular increase was significantly attenuated when OVX rats were given 17 β -estradiol. Interestingly, the co-administration of celecoxib with 17 β -estradiol restored the number of these myelinating cells in the vicinity of the lesion site.

Conclusions:

These preliminary results strongly suggest that 17 β -estradiol reduces the recruitment of OPCs to the site of inflammation. These modulatory effects are likely mediated through a COX-2 dependent mechanism.

Key Words: Striatum; Inflammation; Celecoxib

Funding Agency: None



Physiology

Category: Basic Sciences

192

Parasympathomimetic effects of chronic low dose ouabain treatment

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Introduction:

Ouabain may exhibit potentially useful pharmacological effects, different from other cardiotonic glycosides, e.g. digoxin, particularly when applied in nanomolar quantities. Some acute clinical studies showed that micromolar ouabain has negative chronotropic and dromotropic effects, stimulates acetylcholine release, and sensitizes baroreceptor reflex. All these effects are consistent with the stimulation of the parasympathetic nervous system. The aim of our study was to test whether chronic treatment with low dose ouabain is associated with the elevation of cardiac vagal activity.

Methods:

3-months-old male Wistar rats were implanted with telemetric transmitters to monitor arterial pressure, ECG, and core body temperature. A low dose of ouabain (63 µg/kg/day) was administered for 4 weeks, followed by a higher dose (324 µg/kg/day) for another 4 weeks. Heart rate variability in the high frequency band as well as complexity and fractality of RR-interval time series were used to estimate cardiac vagal activity.

Results:

Ouabain administration was associated with the elevation of several indices of cardiac vagal drive during the light (inactive) period: root mean square of the successive differences between neighboring RR-intervals increased by 30% (p=0.006), high frequency power of RR-interval variability by 18% (p=0.014), and Lempel-Ziv entropy by 26% (p=0.025). Strong correlations between RR-intervals occurring over longer time scales were reduced by 16% (p=0.001) and PQ-interval on the ECG was prolonged by 14% (p=0.027), also suggesting an augmentation of the cardiac vagal activity.

Conclusions:

Long-term administration of low dose ouabain stimulates cardiac vagal activity. This parasympathomimetic effect may contribute to the postulated cardioprotective properties of ouabain through restraining sympathetic activity and inflammation.

Key Words: Ouabain; Parasympathetic activity; Cardioprotection

Funding Agency: Kuwait University graduate student research grant YM 02/09



Physiology

Category: Graduate PhD (Basic Science)

193

Promyelinating properties of androstenediol in gliotoxin-induced demyelination in rat corpus callosum

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Introduction:

Experimental evidence showed that the adrenal steroid hormone; androstenediol, dampens the symptoms of demyelination. However, the cellular and molecular effects of androstenediol are not yet known. In the present study, we investigated the cellular and subcellular effects of this hormone in a gliotoxin-induced demyelination.

Methods:

Male Sprague Dawley rats received 2 µl of either sterile saline or the gliotoxin ethidium bromide (EB, 0.04%) into their corpora callosa. These rats received daily subcutaneous injections of either oil or androstenediol (5mg/kg). Their brains were collected at 2, 7, 14, and 28 days post-EB injection. Demyelination lesion was assessed using luxol fast blue staining while recruitment and differentiation of oligodendrocyte precursor cells to the lesion site were assessed using immunofluorescent staining. Remyelination was further explored using transmission electron microscopy. The expression levels of total and phosphorylated MBP isoforms were also explored using western blot.

Results:

Androstenediol decreased the size of demyelination lesion in the corpus callosum at 7 and 14 days post-EB injection. It enhanced the number of oligodendrocyte precursor cells, and promoted an increase in the number of mature oligodendrocytes. Androstenediol also stimulated the phosphorylation of MBP at the site of the lesion and promoted remyelination of the affected axons.

Conclusions:

These data strongly suggest that androstenediol is endowed with promyelinating properties in a model of focal gliotoxin-induced demyelination. It induces its promyelinating effects by enhancing recruitment of oligodendrocyte precursor cells and their maturation at the lesion site.

Key Words: ADIOL; EM; MBP

Funding Agency: Research administration, Kuwait University (YM 11/11)



Physiology

Category: Graduate PhD (Basic Science)

194

The differential effects of demyelination-induced microglial activation on neuronal and oligodendroglial progenitor cells: Impact of progesterone.

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Introduction:

Neuroinflammation is a major hallmark of demyelinating diseases. Many therapeutic approaches target this inflammatory response. However, the impact of such anti-inflammatory strategies on different cell types within the brain is unknown. In this study, we explored the anti-inflammatory effect of progesterone on microglial activation during demyelination and its consequent effect on both myelinating cells and newly born neurons.

Methods:

2 µl of 0.04% ethidium bromide (EB) solution was stereotaxically injected into the corpus callosum of adult male Sprague Dawley rats. Rats received daily injections of either oil or progesterone (5mg/kg, s.c.). The brains were collected 14 days following EB injection. Microglia (Iba-1), oligodendrocyte progenitor cells (OPCs; NG2), mature oligodendrocytes (CC-1) and newly born neurons (DCX) were monitored at the site of the lesion using immunofluorescent staining. Western blot was used to explore the impact of progesterone on MBP expression.

Results:

Focal demyelination elicited a strong microglial activation and a reduced number of OPCs at the site of demyelination. Interestingly, the inflammatory response was associated with enhanced newly born neurons in the white matter. Progesterone significantly reduced microglial activation and increased the number of OPCs at the demyelination site without a significant effect on either mature oligodendrocytes or the expression levels of MBP. Interestingly, progesterone dampened inflammation-induced neurogenesis around the lesion and in the subventricular zone.

Conclusions:

The present data are the first to show a differential effect of an anti-inflammatory treatment on two distinct progenitor cells, OPCs and newly born neurons and strongly suggest an eminent role of microglia in such differential cellular effect.

Key Words: Neurosteroid; Neurogenesis; Inflammation

Funding Agency: None



Psychology

Category: Basic Sciences

195

Gender differences in the big five personality factors

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Introduction:

Neuroticism (N), Extraversion (E), Openness (O), Agreeableness (A), and Conscientiousness (C) are the most common labels given to the Big Five Personality Factors, although they can vary from genders, depending on the culture. Therefore, the goal of the study was to examine gender differences on the Big Five Personality Factors among adults in the general population.

Methods:

The participants were 3067 (1339 males & 1728 females) Kuwait University students. The genders were matched in age (20.19 ± 1.56 & 20.67 ± 1.25 , $t=7.75$, $p<.001$). The Arabic versions inventory of the Big Five is Costa and McCrae's NEO PI-R and demographic surveys were administered to participants in the class. One-way ANOVA analysis was used in this study.

Results:

Internal consistency of NEO PI-R was satisfactory for males and females (Cronbach's α for N = 0.89, 0.91; E = 0.89, .86; O=0.87, 0.87; A=0.87, 0.85; & C=0.92, 0.90). Females scored significantly higher on Neuroticism ($f=9.79$, $p<0.002$), Openness ($f=11.01$, $p<0.001$), and Agreeableness ($f=4.71$, $p<0.03$). However, no significant gender differences were found on Extraversion ($f=0.01$, $p>0.05$), and Conscientiousness ($f=0.57$, $p>.05$). Moreover, based upon means of the factors, the order of the following factors: Conscientiousness, Extraversion, Agreeableness, Openness and Neuroticism, were consistent for both males and females.

Conclusions:

This study provided evidence for the association between gender and personality factors. Replication of these findings using longitudinal, epidemiologic designs may facilitate a better understanding of the mechanisms underlying the association between gender and personality.

Key Words: Gender Differences; Big Five; Personality factors

Funding Agency: None



Psychology

Category: Graduate MSc (Basic Science)

196

Openness to experiences and its relationship with artistic personality among a sample of students of higher institute of musical arts and higher institute of dramatic arts

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Introduction:

Openness to experience is one of five personality factors described by personality psychologists. Openness involves active imagination, aesthetic sensitivity, attentiveness to inner feelings, preference for variety, and intellectual curiosity. An abundance of psychometric research has demonstrated that these qualities are statistically correlated. Thus, openness can be viewed as a global personality trait comprised of a set of specific traits, habits, and tendencies that cluster together. This study aims to examine the nature of the relationship between openness to experience and artistic personality, as well as to identify gender differences in openness to experience, and artistic personality.

Methods:

The study used a total sample of (201) students, (118) students from the Higher Institute for Musical Arts, and (83) students from the Higher Institute of Dramatic Arts, and between the ages of 18-30 years. Applied to the sample measure of openness to experience (NEO-PI-R-O), and a measure of artistic personality (SDS).

Results:

showed the openness to experiences significantly positively correlated with artistic personality. Moreover, results revealed lack of significant gender differences in openness to experience, while there was a significant gender differences in artistic personality. The average score for females is higher than males, the results of factor analysis exploratory has revealed the extraction of three factors unipolar of variables of the study, and named as follows factor "artistic personality" and the factor "values and ideas," and workers "feelings and fantasy and aesthetics."

Conclusions:

The results of both correlation and exploratory factor analysis indicated that the three-factor model provided the best fit for the sample. The openness to experiences have no significant relationship with gender. Implications and suggestions for future research are discussed.

Key Words: Openness to experience; Artistic personality; Correlation

Funding Agency: None



Psychology

Category: Basic Sciences

197

Adaptation of the second version of beck hopelessness scale in Kuwait

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Introduction:

Hopelessness can be defined as a negative perspective of the future or a set of negative expectancies toward the future. Beck Hopelessness Scale (BHS) developed by Aaron Beck has been an internationally accepted and widely used measure in suicide prevention since its first publication in 1974. This study focuses on the adaptation of the scale in Kuwait and its psychometric characteristics.

Methods:

The BHS consisted of (20) items with two responses (true / false). The BHS has been applied to a random sample of (880) Kuwaitis including (440) males and (440) females of whom were studied at Kuwait University. The mean age of the sample was (20.04±1.35) years.

Results:

The BHS was positively correlated with Beck Depression Inventory-II BDI-II ($r=0.59$), Pessimism ($r=0.52$), and the Beck Anxiety Inventory -BAI ($r=0.39$). The Factorial validity of the BHS revealed three explanatory factors consisting of hopelessness (loss of motivation to change the future, the negative visions towards the future and the self and to renounce the hopeless future). Moreover, the mean of the corrected item total score were ranged (0.38 to 0.40) for females and males respectively. Furthermore, the test-retest coefficient was (0.71), Cronbach's α (0.80 -0.83), Spearman – Brown coefficient (0.81 -0.84), and Guttman split-half coefficient (0, 81 -0, 82). The results revealed the presence of significant gender differences ($f=206.60$, $p>.001$) in which females scored higher than males in hopelessness. The researcher presented a number of norms to BHS (means, percentiles, & T scores.)

Conclusions:

This study provided evidence for the reliability and validity of the Arabic BHS for Kuwaiti undergraduates. The strengths of the 20 core items of the BHS include their brevity and ease of scoring, which make them practical to use in both counselling and research. We do hope that BHS will be widely used as a proper measure in suicide prevention in Kuwait.

*Key Words: Beck Hopelessness Scale; Psychometric properties; Kuwait
Funding Agency: NONE.*



Psychology

Category: Graduate MSc: Basic Science

198

A confirmatory factor structure of beck anxiety inventory in secondary school students among Kuwaitis and Non-Kuwaitis

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FOM

Introduction:

The Beck Anxiety Inventory (BAI) has consistently been regarded as a strong tool for measuring cognitive and somatic aspects of self-reported anxiety symptomatology in both clinical and non-clinical populations. There is no study until this date that examines the factor structure of BAI within Kuwaiti and non-Kuwaiti from high school students. The current study investigated the original four-factor structure of the (BAI) in non-clinical sample of young adults.

Methods:

The sample consisted of 600 males and female students from secondary school of which 300 are Kuwaitis, and 300 non-Kuwaitis. The non-Kuwaitis nominated Bidoon, The genders were matched in age (males= 16.39 ± 0.91 & females= 16.20 ± 0.90 , $t=1.78$, $p>.05$) for Kuwaitis, and (males= $16.64 \pm .88$ and females= $16.54 \pm .98$, $t=0.99$, $p>.05$) for non-Kuwaitis. The inclusion criteria for all participants: sample of the population of Al-Jahra city, aged between 15 and 18 years old, school grade 10,11,12, and the social status of the parents (married)..The Arabic version of BAI was administered to participants. Explanatory and conformity factor analysis of BAI were used in this study.

Results:

The results revealed three structures of BAI in the two samples of Kuwaiti and non-Kuwaiti students. The first factor: Neurophysiological symptoms and symptoms of Subjective, and the second factor comprised symptoms of Panic and Subjective, while the third factor included panic and Autonomic symptoms. In addition, the results revealed no significant gender differences in the factor structure of BAI in the two samples of Kuwaiti and non-Kuwaiti students.

Conclusions:

The results of both confirmatory and exploratory factor analysis indicated that the original four-factor structures of the Beck Anxiety Inventory do not provide the best fit for either the Kuwaiti or non-Kuwaiti sample. Three-factor model provided the best fit for the two samples. Implications and suggestions for future research are discussed.

Key Words: Kuwait, Beck Anxiety Inventory, Explanatory and conformity factor analysis

Funding Agency: None



Surgery and Transplantation

Category: Clinical

199

Robotic surgery in Kuwait: The first experience

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Introduction:

Advances in urology have focused on minimizing the invasiveness of surgical procedures without compromising outcomes ultimately leading to introduction of robotic surgery. We hereby present our initial experience and outcomes in Kuwait with the da Vinci Si robot.

Methods:

After IRB approval data was recorded for all patients who underwent robotic surgery using the da Vinci Si at Sabah Alahmad Urology Center in Kuwait. Parameters recorded included demographic data, diagnosis, basic laboratory and imaging results, total operative time including docking and console time, estimated blood loss, need for transfusion, and duration of hospitalization. Complications were graded using the Clavien classification system. Major complications were defined as \geq Clavien 3.

Results:

A total of 23 cases were done robotically in Kuwait From February 2014 to January 2015. The first case was right robotic partial nephrectomy. Cases included 7 radical prostatectomies for prostate cancer, 6 radical nephrectomies and 3 partial nephrectomies for renal tumors, 3 pyeloplasties for ureteropelvic junction obstruction, 2 radical adrenalectomies for adrenal tumors, and 2 pyelolithotomies that failed ureteroscopic management. All cases were done transperitoneally. There was no conversion to open and None of the patients recieved a blood transfusion. There was no major complications. There was 3 Clavien grade II complications recorded in 2 patients (8.7%). There was considerably less docking and total operative time going from first to last case. Madian hospital stay was 3 days.

Conclusions:

Our results show good patient and operative outcomes in a diverse group of urologic robotic procedures in a newly established robotic unit. Establishing such unit requires proper patient selection and continuous staff training and supervision in the presence of a certified robotic surgeon to ensure good quality of care.

Key Words: Robotics; Urology; Oncology

Funding Agency: None



Surgery and Transplantation

Category: Basic Sciences

200

A new technique to induce experimental myointimal hyperplasia

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Introduction:

The development of arterial myointimal hyperplasia (MIH) has significant impact on long-term outcomes of peripheral vascular procedures such as by-pass surgery or angioplasty.

Methods:

In this study, we describe a new and innovative technique to induce MIH in Wistar rats by using a dental flossing cachet in the animal model. The intimal damage in the common carotid artery (CCA) was induced by inserting the tip of the dental flossing cachet through the external carotid artery (ECA) into the CCA and turned on for three rounds 20 seconds each. After two weeks, the animals were brought back, anaesthetized, both the experimental and the control (contralateral side) CCA's were harvested, preserved and stained for histopathological studies.

Results:

The experimental carotids showed impressive and significant intimal proliferation and thickening as compared with the controls.

Conclusions:

This technique is simple, inexpensive, highly reproducible and induces sufficient MIH to study this phenomenon in the animal model.

Key Words: Neointima formation, Myointimal hyperplasia, Carotid stenosis

Funding Agency: None



Surgery and Transplantation

Category: Clinical

201

Long term follow up of active management versus minimization of immunosuppressives of bk virus associated nephropathy after a kidney transplant

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Introduction:

There is no active treatment for post-renal transplant BK virus associated nephropathy (BKVAN) that has proven to be effective so far. We aimed to assess effectiveness of active management of BKVAN with combined leflunomide, IVIG and ciprofloxacin on the long term graft outcome compared to minimization of immunosuppressives.

Methods:

Our kidney transplant recipients were screened for BKVAN. Group1 (n=22): was composed of kidney transplant recipients with twice positive BK virus-PCR in urine and blood who underwent graft biopsy to confirm BKVAN. Once BKVAN was diagnosed, anti-metabolite (mycophenolate mofetil or azathioprine) was changed to leflunomide and a course of IVIG and oral ciprofloxacin were given. Group 2(n=33): was composed of BKVAN patients treated conventionally with reduced immunosuppressives.

Results:

Fifty five patients were treated, 69% were males, 50.9% were diabetics, mean HLA mismatches was 3.65 and 50.9% of patients were CW7 negative. All patients received induction therapy (thymoglobulin in 55.6%) and 52.7% received antirejection therapy before BKVAN diagnosis. Maintenance immunosuppression was prednisolone (96.3%), mycophenolate mofetil (94.5%) and tacrolimus (50.9%). Subsequent rejection episodes have occurred in 38% of the patients after BKVAN diagnosis. Basal mean eGFR was 52.5 ± 25.5 which has reduced significantly to 38.1 ± 27.8 ml/min/1.73m² (p <0.0001) at the end of the study without significant differences between the groups (p 0.08 and 0.17 respectively). Follow up period was 7.3 ± 4.99 years. There was no significant difference in the patient outcome. Graft survival was significantly better in group2 (p 0.032).

Conclusions:

Minimization of immunosuppressive drugs was more effective than actively treating BKVAN with a combination of leflunomide, IVIG and ciprofloxacin regarding long term graft outcome.

Key Words: Kidney transplant; BK virus; Allograft rejection

Funding Agency: None



Surgery and Transplantation

Category: Clinical

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The effect of epigallocatechin gallate on uncoupling protein 2 in acute liver injury

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Kuwait University

Introduction:

The aim of this study is to investigate in an acute liver injury-animal model the effect of Epigallocatechin gallate (EGCG), on Uncoupling protein 2 regulation.

Methods:

Twenty seven male Wistar rats were divided into three groups; control group (n= 9), TAA group (n= 9); acute liver injury induced by the intraperitoneal injection of Thioacetamide (200mg/kg) and EGCG/TAA (n = 9 rats): Epigallocatechin gallate given two weeks prior to the induction of acute liver injury by Thioacetamide. The levels of Uncoupling protein 2, CRP, TNF- α and interleukins (IL) 6 and 18 were analysed in the liver using PCR analysis.

Results:

Q-PCR analysis showed that the genetic expression of UCP2, TNF- α and CRP in the EGCG/TAA group was the least in comparison to other groups ($p \leq 0.005$). The IL-6 and IL-18 were upregulated after induction of acute liver injury, but this upregulation was significantly less in the group that received Epigallocatechin gallate (EGCG/TAA) compared to the TAA group. In addition, histological examination showed a reduction in hepatocyte injury in EGCG/TAA compared to the TAA group.

Conclusions:

Epigallocatechin gallate administration prior to induction of acute liver injury down regulates Uncoupling protein 2 expression and reduces IL-6, IL-18, TNF- α and CRP.

Key Words: Hepatitis; Uncoupling protein 2; Epigallocatechin gallate

Funding Agency: REG grant from Kuwait University



Surgery and Transplantation

Category: Graduate (Resident)

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Bibliographic study about the feasibility and efficacy of transplanting autologous lymph node with gracilis free flap for post mastectomy breast reconstruction

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Introduction:

Microvascular lymph node transfer technique provided a fresh hope for patients with postoperative lymphedema after mastectomy. We aimed to combine this new method with the standard breast reconstruction, to find out the feasibility and efficacy of transplanting autologous lymph node with gracilis free flap

Methods:

This is a bibliographic study that is divided into three sections. First part talked about the anatomy of the axillary and inguinal lymph node and inguinal region. Second part discussed the Lymph node transplant; we summarized 27 recent articles about lymph nodes transplant. Finally, we discussed the gracilis myocutaneous free, and we summarize 53 recent articles that talked about. Our main resource was ‘‘PubMed’’

Results:

27 articles used superficial inguinal lymph nodes as a pedicle. 6 of these articles used the superficial circumflex artery for harvesting the inguinal Lymph nodes pedicle; 1 out of them used the superficial epigastric artery. Gracilis muscle has a class 2 vascular pedicle, with a dominant vascular pedicle which is the medial circumflex femoral artery 90%. One to four perforators were seen within an area of 6 x 6 cm² at the entrance of the main pedicle into the proximal gracilis muscle with diameter ranged from 0.5 to 1.0 mm. Dissections identified both septocutaneous and musculocutaneous perforators from the proximal gracilis pedicle, supplying the cutaneous territory over the adductor longus and sartorius anteriorly and extending for > 5 cm beyond the posterior margin of the gracilis muscle

Conclusions:

Simultaneous breast and lymphatic reconstruction is an ideal option for patients who suffer from lymphedema after mastectomy and axillary dissection. Transplanting autologous inguinal lymph node with gracilis free flap is feasible and efficient to perform for post mastectomy breast reconstruction on:

Key Words: Lymphedema; Chronic pain Lymph node

Funding Agency: None



Original Research Case Report By Subject Area



Allied Health

Category: Clinical

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In-patient cardiac rehabilitation post LVAD implantation

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CASE REPORT

Background:

A left ventricular assist device (LVAD) is a mechanical circulation support implanted for patient with end-stage heart failure. It may be used either as bridge to cardiac transplantation or as destination therapy. We present the first successful case of implanted LVAD in Kuwait who received an in-patient cardiac rehabilitation service.

Case summary:

A 70 years old man with history of ischemic heart disease presented to the hospital with massive anterior wall myocardial infarction, cardiogenic shock and severe left ventricle systolic dysfunction (ejection fraction=10%). After failed Percutaneous Coronary Intervention, Intra-Aortic Balloon Pump was inserted and removed. Subsequently patient was established on Extra Corporeal Membrane Oxygenation, and a decision to place the patient on LVAD was taken. Even though patient had multiple setbacks in his clinical course, the patient continued to receive In-patient Cardiac Rehabilitation. There was significant improvement in exercise capacity and quality of life following our cardiac rehabilitation. The patient was discharged home with LVAD.

Conclusion:

We reported the effect of exercise therapy for the first successful implanted LVAD patient in Kuwait.

Key Words: LVAD; Rehabilitation; Exercise therapy



Anatomy

Category: Clinical

205

An unusual arterial variation in the abdomen: An abnormal meandering artery

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CASE REPORT

Background:

The superior (SMA) and inferior mesenteric (IMA) arteries supply blood to midgut and hind gut derivatives, respectively. These two arteries show variations in branching pattern, courses and anastomoses of their branches. The variations of the mesenteric arteries and their branches are clinically important during laparoscopic abdominal surgery. Here we report an unusual variation in meandering artery, its branching pattern and anastomosis in a 50 year-old male.

Case summary:

During routine dissection of a cadaver, the following arterial variations were noted. The right and the middle colic branches originated independently from the SMA, but soon after they formed an anastomosis in an 'H'-shaped manner, and thereafter continued separately toward their destination. Interestingly, a small-caliber branch arose from the anterolateral aspect of the SMA above the level of origin of the middle colic artery. This artery resembled, to a large extent, the meandering artery rarely described in literature. It looped above the duodeno-jejunal flexure or root of the mesentery to enter the arterial zone of the hindgut derivatives. This so called meandering artery descended towards the lower end of the left colon and anastomosed with the sigmoidal branch of the IMA. The left colic artery, instead of arising from the IMA, originated directly from the meandering artery. Another direct colic branch arose from the meandering artery and coursed towards the left one-third of the transverse colon.

Conclusion:

For our knowledge, although the meandering artery and arc of Riolan have rarely been described in literature, this is the first case of the meandering artery arising directly from the SMA and anastomosing with the IMA. This abnormal artery may be important for inter-mesenteric collateral circulation, and may be an important variation to consider during surgical procedures related to the location of the artery.

Key Words: Abdominal laparoscopy; Superior mesenteric artery; Vascular variations



Community Medicine

Category: Basic Sciences

206

Could the leadership and conflict management styles translated into a consistent organisational culture?

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CASE REPORT

Background:

Culture is a group personality resulted from people's interactions over time and planted by the organisation founder's effect. A 2ry care hospital's Quality department culture was assessed using Goffee & Jones (G&J) tool. Depending on levels of solidarity (task-based) and sociability (people-based), G&J identify 4 cultures: Networked (high sociability, low solidarity), Communal (high sociability & solidarity), Fragmented (low sociability & solidarity) and Mercenary (low sociability, high solidarity). The tool is composed of 4 analysis parts. The 1st 2 parts look at Physical space, Time, Communication and Identity. The 2nd 2 parts assess the culture impact. Plotting person's behavior along 2 dimensions: assertiveness and cooperativeness identifies 5 conflict handling modes: compromising, accommodating, competing, avoiding and collaborating. A 3rd tool assessing the leadership style gives scores for task and people-oriented dimensions.

Case summary:

The author and the 8 department's staff answered G&J tool. Staff's main response for the 1st part were communal. Their 2nd part's responses were communal. The author's responses for both parts were communal. Author and staff's answers of the 3rd and 4th parts identified 9 +ve versus 5 -ve aspects. The author's conflict handling modes –by answering Conflict Mode Instrument–were compromising 90% and accommodating 75%. Answering the Leadership Style Questionnaire by the author resulted in a task-oriented score=20 and people-oriented score=16.

Conclusion:

The department's founder (author) had a vision of what the department should be, and its small size made it easy to impose that vision on all staff and embed his personality in the culture. The high sociability and solidarity communal +ve strong culture was created by the founder's balanced task and people-oriented leadership together with the medium assertive and cooperative compromising and low assertive high cooperative accommodating conflict handling modes.

Key Words: Organisational culture; Conflict Management Style; Leadership in Kuwait



Community Medicine

Category: Clinical

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ED overcrowding: A global concern reaching us

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CASE REPORT

Background:

Emergency Department (ED) overcrowding (OC) is defined as a situation where the demand for services exceeds the capacity of the department to provide them in a high quality and timely manner. It is a key global issue for more than 20 years, as they result in patient suffering, deteriorating levels of service, adverse patient outcomes, ambulance diversions, treatment delays, reduced safety, medical errors, unnecessary mortality and inability to retain experienced ED staff. EDOC is associated with increased ED Length of Stay (LOS) of some patients beyond the accepted limit that varies from above 4 hours in UK to above 8 hours in Australia. ED staff of the general hospitals in Kuwait and ED patients are reporting a progressively increased EDLOS and EDOC. No measurements have been done to assess the situation.

Case summary:

The team selected a day from 7 am till 7 pm to collect data and calculate wait times. ED nurses were requested to observe and register timing of the steps using a data collection form. During that 12 hour period, 22 patients were observed. The selection was based on Willoughby et al. (2010) strategy to overcome the infeasibility of documenting all ED visits, so only the apparently more acute patients were observed. Out of those 22 observed patients, 10 patients stayed less than 5 hrs in the ED, 7 patients stayed between 5 to 7 hrs and 5 patients stayed more than 7 hrs, 2 of them stayed more than 12 hrs. Further mapping of one case revealed that around 78% of the total time of the patient at the observation room was waits, receiving no service.

Conclusion:

This 12 hour observation revealed alarming signs. 22% of the sample had long EDLOS and most of the time spent was waits. A national-wide measurement project should be considered to define the exact problem volume, its impact and identify its causes. Setting ED performance indicators for clinical and service times together with the whole EDLOS might be helpful to track progression.

Key Words: ED Overcrowding; ED Patient flow; Kuwait



Dentistry

Category: Clinical

208

A rare cause of macroglossia in an adult

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CASE REPORT

Background:

Lymphangiomas are uncommon, developmental malformations of the lymphatic system and have marked predilection for the head and neck region. They are usually present at birth or arise in early childhood. Intraoral lymphangiomas are rare and are more frequently seen on the dorsum of tongue. Here, we present a rare case of intraoral lymphangioma of tongue in an adult patient.

Case summary:

A 29 year old male patient reported to the Oral Medicine Clinic of Kuwait University Dental Center with the chief complaint of swelling and pain with repeated episodes of bleeding from his tongue since a few months. On intraoral examination, generalized macroglossia with deep fissuring and a pebbly surface was noted. Multiple, papillary, vascular hyperplastic lesions were seen on the posterodorsal and ventral surfaces of the tongue, which blanched on applying pressure with a glass slide. On palpation, the tongue was soft to firm in consistency and very tender. A working diagnosis of haemangioma/lymphangioma was established. Multiple incisional biopsies were performed under local anaesthesia and sections showed numerous dilated, endothelial-lined spaces containing lymph. The lymphatic channels were located directly close to the overlying epithelium without any apparent intervening connective tissue. These features were consistent with a histopathological diagnosis of cavernous haemangioma. Systemic steroids were prescribed for a week and there was marked improvement in the swelling and pain. The patient is on regular follow up every three months.

Conclusion:

Although rarely encountered, lymphangiomas represent a condition that must be recognized. They may cause significant morbidity due to the large size and critical location. Inflammation from secondary infection or trauma results in severe pain, swallowing difficulties and airway obstruction. The early recognition allows proper initiation of treatment and prevents the occurrence of complications.

Key Words: Macroglossia; Lymphangioma; Intraoral



Ethics

Category: Undergraduate

209

Is the accreditation program enough to ensure patient safety? A students' reflection on a patient safety required area

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CASE REPORT

Background:

Developing a protocol containing informed consent completion as a part of the pre-intervention patient's verification is a patient safety required area mandated by The National Accreditation program to ensure performance of correct procedure at correct body site. Completion of the consent is required by medical records regulations as well. The informed consent is not merely a form but an internationally accepted way of communicating verified information about the patient, the procedure and the surgeon through an actual process that entails a doctor-patient interaction. The objective of this case report is to focus on the use of informed consent forms as an educational tool during the elective course "Patient Safety: Better Knowledge for Safer Care".

Case summary:

The Burton's approach to reflection with the 3 core questions of: What? So What? Now What? was used during the assessment of masked non-identifiable consent forms retrospectively reviewed as part of a hospital based audit. The WHAT? component revealed: Total of 41 masked informed consents were used during this ethical analysis to identify the deviation from the standard of care and the potential ethical and safety issues relevant to the review. The full name of the patient absent (19. 5%), date of birth absent in (100%) of cases, medical record number absent (9. 8%), full description of the name/site/side/level of procedure was not adhered to (12. 2%), procedure name without abbreviation present (80.5%), physician's name present (100%), physician's signature absent (12. 2%), patient's signature absent (4. 9%). The SO WHAT? component revealed the students' uncomfortable feelings and thoughts especially at a time when there is a national accreditation program in the country. The NOW WHAT? component showed a clear commitment "to do the right thing" and "first do no harm".

Conclusion:

The Burton's reflection approach was successfully used as a tool in teaching a clinical ethics course on patient safety.

Key Words: Burton's Approach to Reflection, Ethics, The National Accreditation program



Ethics

Category: Clinical

210

Ethics case consultation personalized medicine is more than our genes: Faith-based treatment with camel milk and urine

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CASE REPORT

Background:

In clinical care, when there is concern about the right thing to do, ethics consultants work with staff, patients and families to help them make good decisions to resolve these concerns.

Case summary:

Mr. X, a 50 old patient diagnosed with Axillary metastatic poorly differentiated carcinoma requested an ethics consultation to resolve a conflict with his treating oncologists regarding the use of a complementary substance. The scientific literature refers to this patented substance obtained from dried camel urine as PMF. History: Seen at a polyclinic for 6/12 with wrong diagnosis and treatment; excisional biopsy revealed metastatic adenocarcinoma with no identified primary cancer; 3 oncologists consulted in Kuwait, Egypt and Canada (2 advised no difference in prognosis with Chemotherapy & Radiotherapy and potential risks with treatment, one in Kuwait advised treatment “to be on the safe side”); patient rejected treatment and oncologist asked him to sign a no liability form; In 2011, new supraclavicular lymph node felt and biopsied with similar pathology; advised to have surgical clearance and chemotherapy; while waiting for surgery, the patient came across scientific literature about the use of camel milk and urine in the treatment of cancer; during a pre-operative assessment after 40 days of use, the surgeon could not feel the lump nor see a surgical scar; he insisted in knowing what the patient was doing?; The patient admitted a faith-based use of a combination of camel milk/urine and was referred back to his oncologist; he was faced with rejection and was continually referred to a new oncologist every visit. The patient didn't follow up since 2012!

Conclusion:

Given the patient's faith-based decision that is informed and voluntary with a no liability release; treating doctors should encourage follow up to provide care when needed in a respectful environment despite feelings that the patient decision might compromise their professional standards.

Key Words: Camel Milk and Urine, Ethics, Faith-Based Decision



Ethics

Category: Undergraduate

211

**Students' reflection on current practice to avoid tubing
misconnection: A simple solution, a difficult compliance, a training
opportunity**

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CASE REPORT

Background:

Learning consists of cognitive, emotional and social dimensions. In medical education, the cognitive dimension is usually measured through assessments or performance, while the social and emotional dimensions are more challenging to capture. One of the objectives of the course on “Patient Safety: Better Knowledge for Safer Care” is to support emotional reflection in the learning process to enable a critical assessment of both self as a professional –in our case a future doctor– and as an agent of change. The Kolb’s cycle begins with a concrete experience or task, reflecting on the experience and then applying the learning to new situations. In this case report, we present the task of carrying out a patient safety hospital round as an object of reflection to explore adherence to the “Avoiding Catheter and Tubing Misconnections” protocol which is one of the World Health Organization (WHO) “Nine Patient Safety Solutions” adopted by the Ministry of Health in Kuwait.

Case summary:

The students completed a hospital round of 19 wards and inspected 152 patients who had different catheters and tubes for the following criteria: correct labelling of proximal and distal ends of tubes (fully implemented in 53%); routing tubes and catheters in correct directions (fully implemented in 94.4%); name or number and date of insertion (fully implemented in 55.4%); documentation of tubes and catheters in nursing notes at the start of the shift (fully implemented in 85%).

Conclusion:

Harming patients can take place at different levels within health care like lack of funding, system level (structure or process), or at the point of interaction between patients and practitioners. When asked to reflect about their experience, it was evident that the students in this elective course successfully developed a new realisation of the role of human factors in errors and the concept of system failure suggesting that training for patient safety should start early during medical education.

Key Words: Avoiding Catheter and Tubing Misconnections, Future Doctors, Ethics



Ethics

Category: Undergraduate

212

Exploring students feelings counts in education: The use of Gibbs reflective cycle in teaching clinical ethics

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CASE REPORT

Background:

One of the objectives of the ethics and professionalism elective course on 'Patient Safety: Better Knowledge for Safer Care' is to apply different reflection tools to the students' hospital experiences to enable their development as future doctors. The Gibbs Reflective Cycle was applied to the students' experience of one of the nine World Health Organization (WHO) 'Patient Safety Solutions' adopted by the Ministry of Health in Kuwait. In this case presentation, the four steps of the Gibbs cycle: to describe, to express feelings, to evaluate and finally to make sense of experience were applied to the 'Performance of Correct Procedure at Correct Body Site' protocol. The first step in the protocol is the verification of the intended patient, procedure, site laterality (right or left without abbreviation) and any implant or prosthesis.

Case summary:

the students were able to identify that in a recent retrospective audit of 33 medical records of surgical procedures involving a body part that needed to be specified in terms of side laterality, there were 6 records that included at least one wrong entry. Out of a total of 86 different opportunities to enter the specific site of the procedure in the six patients' records the following were identified: a wrong side identified 13 times (15%); abbreviated site (Rt or Lt) 52 times (60%); and in only 17 opportunities the correct non abbreviated site was used (19.7%). In one case the surgery was actually performed on the wrong site. The students' feelings were initially those of 'shock and frustration, fear and need to be precautious going into the world of medicine, motivation to learn, and finally excitement and ambition to attain new perspectives about clinical ethics and patient safety'.

Conclusion:

Reflection can be used as a tool to facilitate the teaching of hospital based clinical ethics and patient safety in medical education.

Key Words: World Health Organisation, Ethics, Patient Safety



Genetics

Category: Clinical

213

**Adenosine kinase deficiency in two sisters with a novel mutation in
ADK gene**

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CASE REPORT

Background:

Hypermethioninemia is known to be caused by four inborn errors of metabolism causing deficiency in enzymes that directly interfere with the methionine cycle. These enzymes are methionine adenosyl-transferase (MAT) (1), glycine N-methyl transferase (GNMT) (2), S-adenosyl-homocysteine hydrolase (SAHH) (3), and CBS, cystathionine beta-synthase (4). In 2011 Bjursell et. al. described 6 patients, two from a Swedish family and four from two Malaysian families, with severe developmental delay, facial dysmorphism, liver dysfunction and hyper-methioninemia. Using whole exome sequencing, each family was found to have a deleterious homozygous missense mutation in the ADK gene encoding adenosine kinase, thus defining a novel form of hypermethioninemia.

Case summary:

We report two sisters born to double first degree cousin parents, who presented with severe global developmental delay, seizure disorder, progressive spasticity, facial dysmorphism, impaired liver function with recurrent hypoglycemia and high methionine. Homozygosity-guided mutation analysis revealed a novel homozygous deletion of exon 3 in the ADK gene.

Conclusion:

Adenosine kinase deficiency is a new genetic cause of hypermethioninemia by disrupting the futile cycle, which regulates the adenosine and adenine nucleotide levels. (5). resulting in early onset liver disease with recurrent hypoglycemia, global developmental delay, mental retardation, facial dysmorphism and progressive neurodegenerative disorder resulting in seizures and progressive spasticity.

Key Words: Hypermethioninemia; Adenosine kinase; Neurodegenerative disorder



Hematology

Category: Clinical

214

Long standing eculizumab treatment without anticoagulant therapy in high risk thrombogenic paroxysmal nocturnal hemoglobinuria

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CASE REPORT

Background:

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare hematopoietic stem cell disease affecting all haemopoietic cell types [1]. The abnormality of the red blood cells (RBCs) predisposes them to intravascular complement-mediated haemolysis. Thrombosis is the key cause of death in PNH patients in about 40% to 67% [7]. Venous thrombosis can occur anywhere, including hepatic splenic, portal and the cerebral veins [8]. However, others may die of complications such as bone marrow failure meyelodysplastic syndrome, renal failure, and leukaemia [9]. Hepatic vein thrombosis is documented as one of the most common sites of thrombosis affecting PNH patients [10].

Case summary:

2006 seen this patient first seen by hepatologist because of abdominal pain hepatosplenomegaly and thrombocytopenia. Abdominal doppler ultrasound and CT abdomen revealed Budd-Chiarie syndrome. She was put on oral anticoagulant Coumadin. Transjugular intrahepatic portacaval shunt (TIPS) was successfully placed a hepatic vein stent. The results of laboratory tests showed pancytopenia

2007 She had pancytopenia at that time where she was referred to haematologist. Bone marrow for pancytopenia showed only 35% hypocellularity on trephine biopsy and peripheral blood test for PNH revealed positive result.

2010 Eculizumab was commenced on early 2011, since that time she showed progressive marked clinical and laboratory improvements. Since Eculizumab was started on 2011, she refused to carry on her anticoagulant over the last three years up to date without any thrombotic events although she is in high risk of thrombosis due to the Budd-Chiarie syndrome and the insertion of stent, which need continuous anticoagulant treatment.

Key Words: Eculizumab, Paroxysmal Nocturnal Hemoglobinuria



Hematology

Category: Clinical

215

Successful off label nilotinib treatment in a child with chronic myeloid leukaemia

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CASE REPORT

Background:

Chronic myeloid leukaemia (CML) is a rare malignant neoplasm in paediatric age. A Philadelphia chromosome, a translocation between chromosomes 9 and 22, results in an abnormal fusion called BCR-ABL oncogene. BCR-ABL fusion encodes a chimeric BCR-ABL protein. This protein is the underlying cause of CML. Nilotinib is a newly licensed drug for CML in adults, structurally it is similar to Imatinib the older tyrosine kinase inhibitor, but it is much more potent in inhibiting BCR-ABL. Nilotinib was used with these patients as off label drug use because it is not licenced for children. A 16 years child female diagnosed indecently to have CML in chronic phase and she showed a complete remission.

Case summary:

A 16 years old Kuwaiti paediatric female presented to emergency clinic with only common cold, she showed with high WBC counts, she was treated with paracetamol. After one year she presented again to the emergency clinic with common cold, with much higher WBC count, bone marrow aspiration confirmed a diagnosis of CML. Nilotinib tablets were started at a dose of 150 mg twice daily. After one month the dose was shifted to 400 mg. Her liver enzyme derangements after one month. The dose was reduced to 200 mg until the liver enzyme improved, after one month she put again on 400 mg. This patient now still on Nilotinib treatment with continuous complete molecular remission

Conclusion:

CML historically was treated with conventional busulfan or hydroxyurea and was associated with a poor prognosis. The development of imatinib TKI targeted against the causative BCR-ABL oncoprotein has resulted in hematologic and cytogenetic remissions in all CML phases. Some patients are resistant to imatinib or develop resistance during treatment. Nilotinib an orally highly selective TKI which is structurally similar to imatinib but much more potent in inhibiting BCR-ABL. It has, therefore been approved as first-line therapy for adult patients with CML in chronic phase by the Food

Key Words: CML, Nilotinib, Off label drug, Tyrosine kinase



Medicine

Category: Clinical

216

Cerebral haemorrhage and polycystic kidney disease

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CASE REPORT

Background:

Autosomal dominant polycystic kidney disease is characterized by cysts in the kidneys and, in many cases, is associated with cysts in the liver and pancreas. In addition, patients may have a variety of other abnormalities. The major extrarenal complications of autosomal dominant polycystic kidney disease include cerebral aneurysms, hepatic and pancreatic cysts

Case summary:

50-year old male, known to have hypertension since long time, admitted with headache, confusional state and vomiting. His blood pressure was elevated 200/110. Computerized tomography scan of the brain done and showed large left intra axial blood collection involving the left basal ganglia, thalamus and frontoparietal region, with surrounding area of edema, midline shift to the right and effacing of the left lateral ventricle with impending left subfalcin herniation. Abdominal examination showed fullness of both flanks more on the right. Abdominal ultrasonography showed both kidneys enlarged near total replacement of the renal parenchyma by innumerable variable sized cysts, some are seen showing mural calcifications and septations. Normal liver and pancreas.

His renal function is impaired with raised serum creatinine 233 umol/L (normal 44 – 120). His liver function is normal. Haemoglobin is 90 g/L normocytic normochromic, normal platelet and white blood cell count.

The patient was seen by the neurosurgeon and craniotomy done with mild improvement of his conscious level. He is bed bound with flexion contracture of the limbs.

Conclusion:

A ruptured cerebral aneurysm, resulting in a subarachnoid or intracerebral hemorrhage, is the most serious complication of polycystic kidney disease. Aneurysms occur in approximately 5 to 20 percent of patients. Aneurysm rupture in polycystic kidney disease most often occurs with larger aneurysms, usually before the age of 50 years and/or in patients with poorly controlled hypertension.

Key Words: Polycystic; Haemorrhage; Craniotomy



Medicine

Category: Clinical

217

Schistosomal myelopathy at the level of conus medullaris with good response to treatment; a case report

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CASE REPORT

Background:

Schistosomiasis (also known as Bilharziasis) is a disease caused by parasitic worms of the Schistosoma type. It affects over 200 million people worldwide. In Africa it is endemic in Egypt and South Africa. Schistosomiasis of the spinal cord is rare. It is commonly caused by schistosoma mansoni although schistosoma haematobium has been isolated. Spinal cord schistosomiasis is the most severe ectopic form of schistosomal infection.

Case summary:

We report a case of an Egyptian farmer who presented with acute urinary retention and ED. His MRI showed enhancing lesion at the level of conus medullaris. Laboratory workup confirmed the clinical diagnosis of Schistosomiasis. Anti-schistosomal treatment Praziquantal was given with steroids and the patient responded well both clinically and radiologically.

Conclusion:

Schistosomal infection of the spinal cord is a rare entity but should be considered in the differential diagnosis of cases with myelopathy especially at the level of conus medullaris.

Key Words: Conus Medullaris, Schistosomiasis, Myelopathy



Medicine

Category: Clinical

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A case report of vitamin B12 deficiency presenting with neurological, hematological and dermatological manifestations with complete resolution after treatment

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CASE REPORT

Background:

Vitamin B12 is a water-soluble essential vitamin. It is also called 'cobalamin' because it contains the metal cobalt. Vitamin B12 is essential for the rapid synthesis of DNA during cell division thus formation of red blood cells and maintenance of a healthy nervous system as well as the skin. Vitamin B12 is synthesized by bacteria and is found mainly in meat, egg, and dairy products but lacks a reliable plant source. Vitamin B12 deficiency occurs due to either poor intake or absorption. Among the commonest causes are Pernicious anemia, Atrophic gastritis, Celiac disease or following Bariatric Surgery. Deficiency of this essential vitamin can lead to neurological, psychiatric, hematological and dermatological symptoms.

Case summary:

We report a case of a male patient who presented with gradual onset of weakness and spasticity of both lower limbs and upper limbs, parathesia of all limbs with loss of joint position and vibration sensation. These symptoms were associated with memory changes, weight loss and hyperpigmentation of the skin. Our patient had a long history of recurrent gastritis. MRI showed a long demyelinating lesion in the cervical spinal cord. Extensive laboratory investigations were done to confirm Vitamin B12 deficiency and to rule out other common mimicks. Our patient showed marked improvement of all his neurological and non-neurological symptoms following Vitamin B12 supplementation with complete resolution of the cervical demyelinating lesion.

Conclusion:

Vitamin B12 Deficiency is a common but underdiagnosed entity that needs to be highlighted. Early diagnosis and treatment of Vitamin B12 Deficiency could reverse the symptoms and could prevent the disability that would ensue if untreated.

Key Words: Megaloblastic Anemia, Vitamin B12 Deficiency, Myelopathy



Medicine

Category: Clinical

219

Unexpected etiology of abdominal pain

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CASE REPORT

Background:

The evaluation of abdominal pain requires an understanding of the possible mechanisms responsible for pain as there are broad differential of common causes. All patients do not have classic presentations. Thus, unusual causes of abdominal pain must also be considered, especially in elderly and immunocompromised patients.

Case summary:

74-year old lady, with past history of diabetes mellitus, hypertension, chronic kidney disease, chronic atrial fibrillation on warfarin, admitted with abdominal pain and vomiting of one month duration, with similar attacks before. Her blood pressure was 80/40, afebrile, not dehydrated. Abdominal ultrasound done and showed biliary sludge in the gall bladder, but the common bile duct was not dilated. Colonoscopy done and two sessile polyps were accidentally found and were removed. Laboratory investigations showed normal electrolytes with impaired renal function. Thyroid function done and showed low TSH. Serum cortisol, luteinizing and follicle stimulating hormones were also low. Magnetic resonance imaging of the pituitary done and showed evidence of empty sella, together with age-related brain atrophic changes. The patient started on eltroxin 50 mcg per day and prednisolone tablets 10 mg morning and 5 mg evening with good response to treatment.

Conclusion:

Damage to the anterior pituitary can occur suddenly or slowly, can be mild or severe, and can affect the secretion of one, several, or all of its hormones. As a result, the clinical presentation of anterior pituitary hormone deficiencies varies from hypotension to abdominal pain as in our case. A good response occurred after starting therapy in the form of resolution of pain and normalized blood pressure.

Key Words: Hormone, Vomiting, Sella



Medicine

Category: Clinical

220

Unusual cause of abdominal pain

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CASE REPORT

Background:

Abdominal pain is a common problem. Most patients have a benign and/or self-limited etiology, and the initial goal of evaluation is to identify those patients with a serious etiology for their symptoms that may require urgent intervention. Abdominal pain has a wide varieties of underlying pathology. The abdominal ultrasound can give a clue to the diagnosis.

Case summary:

We reported a 34 years married with 5 children presented with right upper quadrant abdominal pain, dull aching, not related to meals associated with nausea but no vomiting of about 4 days duration. She has past history of hypothyroidism well controlled on replacement therapy. Physical examination revealed tenderness over the right hypochondrium, no organomegaly. Abdominal ultrasonography demonstrated that the liver showed diffuse homogenous echogenicity and distended portal vein with a heterogeneous thrombus along its course to the portal venous confluence. This finding was further confirmed with computerized tomography scan. Laboratory findings showed normocytic normochromic anemia. Revising the patient history she was on oral contraceptive pills for the last 2 years and was advised to stop them. Screening for hypercoagulable state came later and showed low antithrombin (67%: reference 83-128) and low protein S (58. 9%: reference 63. 5-149). She was started on clexane followed by oral anticoagulation with improvement.

Conclusion:

Despite an increased likelihood of having inherited thrombophilia, acute thrombosis can reduce the plasma concentrations of antithrombin, protein C and protein S. Anticoagulation perse can affect the level and activity of such anticoagulant factors. So the diagnosis showed be confirmed by repeat testing two weeks following the discontinuation of anticoagulation

Key Words: Abdominal pain; Contraceptives; Portal vein thrombosis



Medicine

Category: Clinical

221

Unsuspected cause of gastro-enteritis

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CASE REPORT

Background:

Gastroenteritis is a common condition usually caused by a viral or bacterial infection most often caused by salmonella or campylobacter bacteria causing food poisoning. When Gastro enteritis is not resolved, we should look for another underlying disease.

Case summary:

68 year old lady, with past history of diabetes and hypertension. Admitted because of repeated vomiting and watery diarrhea without mucous or blood for about two months during which she lost 20 kg. No oral ulcer and no contact with sick persons.

On examination, her vital signs were normal, no clubbing and no lymphadenopathy.

Laboratory investigations showed normal renal and liver function tests. C-reactive protein was negative. Stool routine showed no ova or parasite and no red blood cells. Stool culture showed no salmonella or shigella.

Abdominal ultrasound done and was normal. Upper gastro intestinal endoscopy done and showed normal oesophagus, moderate gastritis and normal duodenum. Colonoscopy done and showed rectal polyp which was excised.

Basal serum cortisol = 233.14 nmol/L (n 138 – 635)

TSH = 0.15 mIU/L (n 0.3 – 4) Free T4 = 50 pmol/L (n 7.5 – 21.1).

Thyroid ultrasound showed picture suggesting multinodular goitre.

Then thyroid scan done and showed increased thyroid uptake 5. 6% (normal up to 4%). Both thyroid lobes showed avid uptake of tracer and homogeneous distribution.

The patient started on inderal 10 mg three times daily and neomercazol 15 mg three times daily and showed marked improvement.

Conclusion:

The prolonged gastro enteritis and the loss of weight can be caused by many diseases as toxic multinodular goitre. We should take into consideration that thyroid storm can occur as a result of viral gastroenteritis. So the early diagnosis of the cause and the proper management can avoid many complications.

Key Words: Weight loss, Gastroenteritis, Hyperthyroidism



Medicine

Category: Clinical

222

Adult respiratory distress syndrome during Basiliximab treatment in renal transplantation

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CASE REPORT

Background:

Basiliximab is used as an induction immunosuppressive agent in renal transplants. It has an excellent safety profile but hypersensitivity reactions leading to adult respiratory distress syndrome (ARDS) following Basiliximab therapy have been rarely reported. We report 2 such cases of ARDS following Basiliximab administration.

Case summary:

Case 1:-A 48-year-old lady with end stage renal failure and normal cardio respiratory status underwent renal transplantation with Basiliximab induction (2 doses on day 0 and day 4) followed by steroids, mycophenolate and tacrolimus as immunosuppression. There was immediate postoperative diuresis with excellent graft function. She developed acute respiratory distress with clinical and radiological evidence of pulmonary edema on day 2 and day 4 post operatively, not responding to fluid restriction and diuresis. Cardiac and respiratory workup was normal and she was successfully treated with assisted ventilation and ultrafiltration. Case 2:-A 28 year old lady with end stage renal failure underwent a live renal transplant with Basiliximab induction on day of transplant followed by maintenance immunosuppression with steroids, mycophenolate and cyclosporine. She had normal cardiorespiratory status pre transplant and the operative and immediate postoperative periods were uneventful with good diuresis and improvement of renal function. On the 2nd postoperative night she developed acute respiratory distress with features of ARDS. Investigations did not reveal any cause for the ARDS. The second due dose of Basiliximab was not given and she responded to assisted ventilation, fluid restriction and diuresis.

Conclusion:

Basiliximab induced cytokine release and increased capillary permeability leading to ARDS is a serious adverse event and improved awareness and prudent management can be life saving.

Key Words: Basiliximab; ARDS; Renal Transplantation



Medicine

Category: Clinical

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Posterior reversible encephalopathy syndrome

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CASE REPORT

Background:

This is a clinical radiographic syndrome of heterogeneous etiologies that are grouped together because of similar findings on neuroimaging studies. It was first described in 1996. It is also often referred to as: Posterior leukoencephalopathy syndrome, Hyperperfusion encephalopathy, Brain capillary leak syndrome.

Case summary:

21 years old lady, not hypertensive or diabetic before, delivered nine days back with normal vaginal delivery. She was admitted with two attacks of generalized tonic clonic convulsions not associated with tongue bite or urinary incontinence. The patient gave history of headache and vomiting in the last two days. She was agitated and her blood pressure at that time was 120/70. So the patient was intubated to protect her airways. Computerized tomography of the brain done with and without contrast and was normal. Her renal and liver functions were normal. Complete blood count was normal. D-dimer was elevated.

Magnetic resonance imaging of the brain done and showed posterior reversible encephalopathy syndrome and multiple parieto-occipital hyperdense lesions in FLAIR mode. Then the patient started to have high blood pressure reaching 160/100, so intravenous labetalol and epanutin started. The blood pressure was then controlled and the patient was extubated and then discharged on labetalol tablets and epanutin capsules.

Conclusion:

It is a clinical syndrome of insidious onset of headache, confusion or decreased level of consciousness, visual changes, and seizures, which was associated with characteristic neuroimaging findings of posterior cerebral white matter edema. The syndrome is not always reversible, and it is often not confined to either the white matter or the posterior regions of the brain.

Key Words: Encephalopathy; Seizure; Headache



Medicine

Category: Clinical

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Auto-immune inflammatory brain stem encephalitis

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CASE REPORT

Background:

autoimmune brain disease is generally assumed to be related to either antibodies or immune cells that cause damage to the brain. Autoimmune encephalopathy represents a complex category of disease with diverse immunologic associations, clinical manifestations, and therapeutic outcomes.

Case summary:

55-year old lady, with past history of sero positive rheumatoid arthritis since 2001, admitted with generalized weakness and inability to stand up from sitting position, then she developed dysphagia, hoarseness of voice and nasal regurgitation of fluid. No fever, no history of infection or diarrhea. Nasopharyngeal fiberoptic examination showed left vocal cord palsy with mild movement of the right vocal cord. Neurological examination showed wide based gait, bilateral rotatory nystagmus, no facial palsy. Normal sensation and deep tendon reflexes. Coordination: severe tetra ataxia. Motor function: 3/5 motor power bilaterally, proximal more than distal. Investigations showed normal liver and renal functions, normal complete blood count. ESR = 84, Normal serum B12, folate and thyroid function. Positive antinuclear antibody, rheumatoid factor and anti extracted nuclear antibody. Lumbar puncture showed normal white blood cell count, mild elevation of protein, presence of oligoclonal bands and positive titres for anti-ganglioside antibodies. CT brain and MRI brain normal. Nerve conduction study and electromyography normal. Intravenous immunoglobulin and plasmapheresis given without improvement. Full investigations for an underlying malignancy were negative.

Conclusion:

The presence of oligoclonal bands in the CSF and positive titres for anti-ganglioside antibodies point towards an auto-immune inflammatory brain stem encephalitis with residual deficits. Besides the cerebellar syndrome, there is no clinical or electro-physiological evidence of a lesion of the motor and sensory spinal tracts and the peripheral nerves.

Key Words: Dysphagia, Cerebellar, Immunoglobulin



Medicine

Category: Clinical

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Herbal medicine and fulminant hepatic failure

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CASE REPORT

Background:

Herbal therapy is used frequently. Many cases reported severe acute hepatocellular liver injury occurring within weeks. When a patient presents with unexplained hepatic abnormalities, it may be worthwhile to consider non-orthodox self-treatment with herbal remedy as a potential cause.

Case summary:

33-year old lady with no past history of any illness, admitted with jaundice after using some herbal medicine including curcuma and unknown others for one week. Her liver enzymes were elevated 13 times the normal level. Autoimmune, virology and metabolic screen were sent and came negative. Unfortunately, over the next 2 weeks, only small improvement in her enzymes was noted, and her ultrasonography showed hepatomegaly. Liver biopsy decided but the patient refused and left the hospital against medical advise. Around 6 weeks later, she presented to the hospital with deep jaundice and elevated liver enzymes about 10 times the normal level. The patient admitted to having had 5 days of unknown herbs claiming that it will cure her jaundice, after which she decompensated. Clinically she was deeply jaundiced, drowsy, with nausea, vomiting and anorexia. No bleeding or ascites. She had improved initially, but she rapidly deteriorated. So an urgent transjugular liver biopsy done and showed signs of acute hepatitis, intact liver architecture, scattered areas of spotty necrosis, bridging fibrosis, mild interface hepatitis, mild plasma cells and few areas of lobular collapse, bile duct proliferation and cholestasis. Picture was not consistent with autoimmune hepatitis. This lady went rapidly from Child class A to class C. The patient was transferred to a liver transplantation centre, as she will need an orthotopic liver transplantation.

Conclusion:

The use of herbs is now increasing for many reasons especially for losing weight. Some has hepatotoxic effect and can lead to fulminant hepatic failure necessitating liver transplant.

Key Words: Transplant, Jaundice, Herbal



Microbiology, Virology and Immunology

Category: Clinical

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Meningitis and bacteraemia by rare organism *Actinobacillus ureae*

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CASE REPORT

Background:

Actinobacillus ureae, formerly known as *Pasteurella ureae* is an uncommon commensal of the upper respiratory tract. This case is being reported as the clinical microbiology laboratories may face difficulties in identifying this rare pathogen which can cause meningitis & Bacteraemia.

Case summary:

A 70-day-old boy presented with meningitis. *Actinobacillus ureae* was isolated from blood as well as from the cerebrospinal fluid culture. It was identified as *Haemophilus* sp. by API-NH But VITEK 2 & VITEK MS identified it as *Actinobacillus ureae* which was confirmed by Polymerase Chain Reaction of 16 S rRNA gene sequencing. The boy was successfully treated with intravenous ceftriaxone for two weeks and was discharged home without any neurological sequelae.

Conclusion:

Actinobacillus ureae being a rare pathogen, may be misidentified, especially with API-NH, with which may masquerade as *Haemophilus* sp. Other modalities like VITEK 2, VITEK MS and molecular techniques play a vital role in its correct identification and in guiding the antimicrobial therapy.

Key Words: Actinobacillus ureae; Meningitis; Bacteraemia



Microbiology, Virology and Immunology

Category: Clinical

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Central line associated blood stream infection by an unusual organism

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CASE REPORT

Background:

Cellulomonas species are environmental Gram positive bacilli rarely implicated in human infections. We present a case of central line associated blood stream infection (CLABSI) in an immunocompromised child.

Case summary:

A six month old Egyptian male child, who was a known case of methyl-malonic aciduria, presented with recurrent fever. He was having a long term central venous catheter (porta-cath) & diagnosed as having CLABSI with an unusual Gram positive bacillus – Cellulomonas species. It was isolated repeatedly and the differential time to positivity was more than two hours on each occasion. It was identified by using VITEK 2 and API-CORYNE. The child responded to removal of the Central Venous Catheter (CVC) and a course of intra venous vancomycin for 10 days. The same organism was isolated in significant count from the tip of CVC. Within one month prior to this episode he had presented with fever on two occasions, blood culture from the CVC had grown the same organism, which on both the occasions was disregarded as contaminant, as the child's fever was self limiting and no parallel peripheral venous specimen was sent for culture.

Conclusion:

This case highlights the importance of sending the peripheral venous blood cultures in parallel to the CVC specimens. It also underlines the necessity to look into the identity of a blood culture isolate from an immunocompromised patient with long term indwelling CVC.

Key Words: CVC; CLABSI; Bacteraemia



Microbiology, Virology and Immunology

Category: Clinical

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**A case of cutaneous mucormycosis caused by Apophysomyces elegans:
A devastating complication post-aesthetic surgery**

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CASE REPORT

Background:

Mucormycosis is a rare, aggressive and life threatening infections that is caused by organisms belonging to the order Mucorales. It is usually acquired by ingestion, inhalation or inoculation and mostly affects the immunocompromised patients. Cutaneous mucormycosis is associated with disruption of cutaneous barriers, which usually occurs after trauma. This form of infection is locally aggressive and proven to be fatal if not treated adequately.

Case summary:

A previously healthy 41 year old lady was admitted to the Burns and Plastic Surgery Department after undergoing aesthetic surgery (abdominoplasty, liposuction, lipofilling) with extensive tissue inflammation and necrosis in both gluteal regions. Upon admission, she was started on empirical antimicrobial therapy which included piperacillin/tazobactam and teicoplanin. The laboratory investigations showed WBC of 46. 69/109/L, procalcitonin of 1. 46 ng/ ml and temperature of 38⁰C. The patient underwent incisional drainage and excision of necrotic tissues. The affected tissue was sent for microbiological and histopathological examination. The KOH-digested tissue as well as histopathological sections showed non-septate fungal elements suggestive of mucor elements. The patient was empirically started on voriconazole. The fungus was identified in the Mycology Reference Laboratory as Apophysomyces elegans. Since the isolate was resistant to voriconazole (MIC 24µg/ml), she was switched to liposomal Amphotericin B, 5mg/kg once daily. The wound showed healing and good granulation after regular surgical debridement and liposomal Amphotericin B which was continued for 3 weeks.

Conclusion:

Apophysomyces elegans is an uncommon cause of cutaneous mucormycosis. Unlike other mucoraceous fungi, it usually affects immunocompetent individuals. As in this case, liposomal amphotericin B, together with regular debridement are necessary to achieve clinical cure.

Key Words: Cutaneous mucormycosis; Apophysomyces elegans; Aesthetic surgery



Microbiology, Virology and Immunology

Category: Clinical

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Primary cutaneous aspergillosis in a leukemic child

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CASE REPORT

Background:

Primary cutaneous aspergillosis (PCA) is a rare disease principally caused by *Aspergillus fumigatus* and *Aspergillus flavus* (*A. flavus*).

Case summary:

Here we report a case of PCA in a 34-month-old caused by *A. flavus*. The child had Down's syndrome and acute myeloid leukaemia. He developed a cutaneous lesion when he was profoundly neutropenic following a course of chemotherapy. Apparently, the infection was acquired by trauma inflicted by the adhesive tape placed to hold the cannula. The diagnosis was established by demonstrating septate fungal elements in the direct microscopy of the tissue and by isolating *A. flavus* in culture. To the best of our knowledge, this appears to be the first report of PCA from Kuwait.

Conclusion:

This report highlights the importance of tissue specimen over the superficial swabs, and underlines the importance of clinical suspicion on seeing such lesions in immunocompromised patients. Unfortunately histopathological report was not available, but direct Gram's stain established the invasive nature of the infection.

Key Words: Aspergillus flavus; Primary Cutaneous Aspergillosis; PCA



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Black water fever in severe falciparum malaria

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CASE REPORT

Background:

Black water fever (BWF) is a syndrome characterized by intravascular hemolysis, hemoglobinuria, acute renal failure and the passage of bloody urine. The massive hemolysis of red blood cells occurs in severe *Plasmodium falciparum* infection when treated with quinine. The death due to severe falciparum malaria occurs in 20% to 30% and the mortality rate is higher among non-immune patients.

Case summary:

A 20 year old Nigerian boy came to IDH on 22nd September with high fever (40.8^oC), abdominal pain, nausea and vomiting. The initial laboratory tests revealed mild anemia (Hb, 120g/L and HTC, 0.352 L/L, RBC, 4. 12 10¹²/L, WBC, 4. 2 10⁹/L and platelets 16 10⁹/L). His G6PD was normal, 214. 6 mU/10⁹ erythrocytes. The thick and thin blood examination confirmed the severe infection of *Plasmodium falciparum* with 41. 0% parasitemia. The patient was admitted to the hospital and started intravenous Quinine. The patient was feeling much better on next morning but became unconscious by evening and shifted to ICU. His all CBC parameters were higher and started passing cola colour urine. The 12 units of whole blood was exchanged on 24th September and became fully conscious on 4th day. His anemia and thrombocytopenia was improved and the colour of the urine also became normal. He was transferred to the general ward on 7th day and discharged from the hospital on 9th day.

Conclusion:

Quinine is managing both complicated and uncomplicated malaria and may precipitate black water fever in severe infection of *P. falciparum*. The black water fever is caused by the hemolysis of erythrocytes due to malaria and also with the metabolism of quinine by the cytochrome enzyme.

Key Words: Black Water Fever; Malaria; Quinine



Nephrology

Category: Clinical

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Successful management of surgical wound mucormycosis in recent renal transplant recipient

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CASE REPORT

Background:

Cutaneous mucormycosis is a rare entity related to kidney transplantation. It usually presents with ecthyma-like lesions and black necrotic cellulites. We report an unusual case of primary cutaneous mucormycosis presenting as erythema-gangrenosum-like lesions in a man who had received a renal transplant.

Case summary:

A 33-year-old man who was suffering end stage kidney disease secondary to membranous nephropathy received a living-unrelated kidney transplant in Pakistan (12. 2014). His post-transplant course was uneventful except for new onset diabetes after transplant and cutaneous lesions in the abdominal wall near the surgical wound. Later these lesions became multiple, painful, erythema-gangrenosum-like. Mucormycosis was diagnosed by skin biopsy. Microscopic examination also showed panniculitis. The patient was treated successfully with liposomal amphotericin B and repeated surgical debridement. To our knowledge, this is the first description of primary cutaneous mucormycosis with erythema-gangrenosum -like lesions and panniculitis after renal transplantation.

Conclusion:

Cutaneous mucormycosis should be considered in the differential diagnosis when a kidney transplant recipient develops erythema-gangrenosum-like lesions with panniculitis.

Key Words: mucormycosis, renal transplant, erythema gangrenosus



Neurology

Category: Clinical

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Status migrainosus as an initial presentation of multiple sclerosis

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CASE REPORT

Background:

Multiple sclerosis (MS) demyelinating plaques may induce headache through disruption of the pathways which are implicated in the pathogenesis of migraine.

Case summary:

A 25-year-old female presented with status migrainosus fulfilling the criteria of international classification of headache disorder, third edition. There were no accompanied clinical features in her initial neurological examination. At the onset of status migrainosus, magnetic resonance imaging (MRI) revealed multiple subcortical, juxtacortical and periventricular T2/Flair hyperintense lesions involving corpus callosum, temporal lobes and middle cerebellar peduncles fulfilling Barkhof Criteria. She was started on migraine prophylactic treatment but there was no response to anti-migraine medication. One year later, she presented with another attack of status migrainosus and a follow-up MRI brain and spine revealed multiple gadolinium-enhancing and new T2/ flair hyperintense lesions in the brain and spinal cord. She was treated with abortive migraine medications but she continued to have chronic migraine. Within one year, she developed ascending parasthesia and weakness of both lower limbs indicative of myelitis in association with recurrent status migrainosus. A diagnosis of MS was established based on a follow-up MRI that satisfied the revised 2010 McDonald criteria. Both the headache and neurological signs improved with IV methylprednisolone pulse therapy. Her headache entered remission after the initiation of disease modifying therapy.

Conclusion:

Status migrainosus can be the initial presentation of MS. Unresponsiveness to migraine abortive and prophylactic therapy in the presence of active demyelinating plaque in MRI brain may pose a diagnostic challenge in clinical practice and MS should be considered in the differential diagnosis.

Key Words: Multiple Sclerosis; Migraine; MRI



Neurology

Category: Clinical

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Spinal segmental myoclonus as an unusual presentation of multiple sclerosis

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CASE REPORT

Background:

Unusual presentations of multiple sclerosis (MS) at onset may pose a diagnostic dilemma to the treating neurologists. Spinal myoclonus is rare in MS and may lead to perform extensive investigations to rule out other etiologies affecting the spinal cord.

Case summary:

We described a 31-year-old male who presented with involuntary brief jerky movements of the left shoulder and arm with significant wasting of shoulder muscles. In retrospect, the patient had a progressive right leg weakness one year prior to his presentation. Needle electromyography confirmed the presence of rhythmic irregular burst discharges in motor units of muscles expanding from the third to the sixth cervical region with normal nerve conduction parameters. There was no evidence of cortically generated myoclonic jerks using time-locked electroencephalogram. Magnetic Resonance Imaging of the brain and cervical cord along with the presence of oligoclonal bands in cerebral spinal fluid confirmed the diagnosis of MS. Based on the history and progressive clinical features, a diagnosis of primary progressive MS was established.

Conclusion:

Spinal myoclonus can be the presenting manifestation of MS in association with demyelinating plaques in the root exit zones of the spinal cord. Spinal myoclonus may pose a diagnostic challenge when it presented at the disease onset and especially in patients with progressive course at onset. Our patient represents the first reported primary progressive MS case in the literature with spinal myoclonus presentation.

Key Words: Multiple Sclerosis; Spinal myoclonus; Cervical demyelination



Neurology

Category: Clinical

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Severe cerebral salt wasting in aneurysmal subarachnoid hemorrhage: A case series

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CASE REPORT

Background:

Hyponatremia secondary to cerebral salt wasting (CSW) is an electrolyte disorder seen in aneurysmal subarachnoid hemorrhage (aSAH) patients during the vasospasm period. CSW is a disorder of sodium and water handling that occurs as a result of cerebrovascular disease in the setting of normal kidney function. Different degrees of hyponatremia complicate 30% of aSAH cases which induces natriuresis and reduces total blood volume, resulting in a risk of symptomatic vasospasm and delayed cerebral ischemia. Patients with asymptomatic cerebral vasospasm reportedly become symptomatic when CSW occurs, and symptomatic vasospasm is reported to be closely related to hyponatremia in CSW. Furthermore, severe CSW after SAH is associated with an increased risk of cerebral ischemia. Early diagnosis and development of an effective treatment for hyponatremia is critical. In severe hyponatremia, apart from 3%NaCl infusions, mineralocorticoid administration has been reported to be of benefit. Fludrocortisone acetate, a potent mineralocorticoid, enhances sodium reabsorption in the renal distal tubules and may prevent post-SAH hyponatremia.

Case summary:

We present a retrospective case series of 3 aSAH cases that were diagnosed with severe CSW during their vasospasm period despite high dose 3%NaCl. These patients were treated in a Neuro-ICU with an established aSAH treatment protocols and developed CSW despite treatment with continuous infusions of up to 80mls/hour 3%NaCl. Two patients received supplementary fludrocortisone with mixed results. Mean ICU stay was 15±2. 6 days. Daily serum Na and osmolarity, and urine Na and osmolarity are presented along with the total daily urine output and total volume of infused fluids. Response to the given medications, complications and outcome up to discharge were recorded.

Conclusion:

Severe CSW secondary to aSAH leads to prolongation of ICU stay yet effective treatment modalities still lack.

Key Words: Aneurysmal subarachnoid hemorrhage; Severe cerebral salt wasting; Mineralocorticoid



Nuclear Medicine and Radiology

Category: Clinical

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The added value of FDG PET/CT in the diagnosis of chronic osteomyelitis

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CASE REPORT

Background:

The clinical role of FDG PET CT imaging shows incremental value in detecting chronic musculoskeletal infections. Multiple studies revealed higher sensitivity, specificity and accuracy of 18F-FDG-PET/CT modality in the assessment of chronic bone infection and overlying soft tissue.

Case summary:

A fifty year old male patient had a remote history of road traffic accident in 1981. He had left tibia fracture that was treated with multiple surgeries including bone grafting until complete recovery in 1987. One and half year ago, he got an episode of high grade fever, tenderness and swelling at the old surgical site, treated conservatively with antibiotics and recovered. Again three weeks ago He relapsed with the same clinical symptoms. A three phase bone scan was obtained which showed increased uptake at the left tibial shaft. SPECT/CT images revealed a corresponding small osteolytic lesion with sclerotic margin as well as increased cortical thickening. As well, there is increased soft tissue uptake with corresponding fatty stranding on the CT images. The leukoscan showed mild soft tissue uptake at the left leg with no abnormal bone uptake to suggest for acute osteomyelitis. FDG PET/CT study was arranged to rule out chronic osteomyelitis. The study demonstrated FDG uptake at the osteolytic lesion suggesting active chronic osteomyelitis and sequestrum formation. There is also increased soft tissue uptake with fatty stranding on CT images. Multiple ipsilateral enlarged inguinal lymph nodes were also seen with increased FDG uptake suggesting reactive process.

Conclusion:

Combined radionuclide bone scan and leukoscan studies are the imaging method of choice in cases of post-traumatic and implanted musculoskeletal infection. FDG PET/CT showed an added value in the diagnosis active chronic osteomyelitis which was not detected by leukoscan.

Key Words: PET/CT; Osteomyelitis; Leukoscan



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Total anomalous pulmonary venous connection supracardiac type draining into the vertical vein in a 22-years-old female: multidetector computed tomography angiography diagnosis

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CASE REPORT

Background:

Total anomalous pulmonary venous connection (TAPVC) is very rare in adults but accounts for approximately 1-5% of cardiovascular congenital anomalies in children which the pulmonary veins fail to connect with the left atrium and connect directly to the right atrium or to one of the systemic veins.

Case summary:

A 22 years old young female was came to the chest hospital pre employment without any symptoms. A chest radiography showed widening mediastinum without any lung parenchymal lesions. Echocardiography showed a large atrial septal defect. No connections between the pulmonary veins and left atrium could be visible. In order to demonstrate this congenital anomaly and vascular structures in detail, With a GE HD 64 MDCT scanner (General Electrics Medical Systems, USA), Three-dimensional (3D) images were reconstructed using MIP and 3D volume rendering algorithms. MDCT angiography clearly showed the pulmonary veins draining both lungs formed a vertical vein. Volume rendered 3D CT image showed the right side pulmonary veins joined with the left side pulmonary veins then connected to the left vertical vein which drained into large right superior vena cava. Axial cuts showed a large atrial septal defect (ASD).

Conclusion:

TAPVR is an admixture lesion classified into supracardiac, cardiac, infracardiac, and mixed types, depending on the routes of venous drainage. TAPVC should be considered for differential diagnoses in patients presenting with respiratory distress and cyanosis. Knowledge of the presence and type of TAPVC is highly important in preoperative surgical planning. MDCT angiography is an excellent imaging method to detect TAPVC. Multiplanner reformat (MPR) and 3D Volume rendering (VR), VR imaging in particular provide important and detailed information on these anomalies, revealing pathology that may cause clinical symptoms

Key Words: VR volume rendering, MPR multiplanner reformat, TAPVR total anomaly pulmonary venous connection



Nuclear Medicine and Radiology

Category: Clinical

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Advantage of FDG PET/CT brain imaging in the characterization of dementia

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CASE REPORT

Background:

Accurate diagnosis of the dementia type is critical in patient management and new disease-targeting drug development. A pure clinical classification of dementia subtypes may be challenging because of overlapping presentations. FDG PET/CT proved to be a valuable method in reaching an appropriate characterization of dementia.

Case summary:

67 years old female patient referred for FDG PET/CT brain study because of memory loss, aphasia and inability to walk. The patient was injected 351 MBq 18F-FDG intravenously, and after an initial uptake period of 60 minutes, a CT scan without oral or IV contrast at low mA level was acquired for the purpose of attenuation correction and anatomical localization. Subsequently, PET images of the brain were obtained. The CT, PET and fused images were reconstructed in transaxial, coronal, and sagittal projections and interpreted from a work station. The study showed severe hypometabolism involving the temporal and parietal lobes extending to the frontal lobes bilaterally, with sparing the primary somatosensory area and the occipital lobes. The hypometabolism extends from the cortical to the subcortical structures of the basal ganglia bilaterally. Multiple bilateral areas of absent metabolism are seen scattered within both cerebral hemispheres corresponding to hypodense lesions on the grey matter seen on CT images, representing cerebral multi-infarcts. There is also diffuse bilateral cerebellar hypometabolism. Dilated ventricles were also seen.

Conclusion:

18F-FDG PET/CT of the brain is a valuable diagnostic tool in differential diagnosis of dementia subtypes. In this case, the scan pattern suggests advanced Alzheimer's disease with multi-infarct dementia.

Key Words: FDG PET/CT; Dementia; Brain



Nuclear Medicine and Radiology

Category: Clinical

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A rare case of giant Cowper's gland syringocele in an adult male patient

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CASE REPORT

Background:

Cowper's gland syringocele is an uncommon abnormality of the male urethra, consisting of a cystic dilatation of the main duct of Cowper's bulbo-urethral gland showing various radiographic patterns.

Case summary:

A 42 years old male patient presented to emergency department with features of perineal abscess managed by incision and drainage. Subsequently he presented with urinary leakage from the site of incision. MCUG and MRI revealed a large complex cystic lesion arising from bulbar urethra extending around the membranous and prostatic urethra and then coursing anteriorly around the penile urethra. Diagnosis of Cowper's gland syringocele was established. Transperineal ligation and excision of syringocele was successfully performed.

Conclusion:

Cowper's gland syringocele is rare in adult male patient, it should be considered in the differential diagnosis of periurethral diverticula, lower urinary tract symptoms and persistent post void dribbling as it can be treated easily.

Key Words: Cowper's gland, Synringocele, Bulbar urethra, Periurethral diverticula.



Obstetrics and Gynecology

Category: Clinical

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Successive successful pregnancies subsequent to intravenous immunoglobulin therapy in a patient with recurrent spontaneous miscarriage

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CASE REPORT

Background:

Recurrent Spontaneous Miscarriage [RSM] has a multifactorial aetiology, mainly due to karyotype abnormalities including balanced translocation, anatomical uterine disorders and immunological factors, although, in 50-60%, the aetiology is unexplained. The treatment of RSM remains challenging and the role of intravenous immunoglobulin in RSM controversial.

Case summary:

Mrs. H. M., 37years old, P0+1+13+1, married to an unrelated 47 year-old man, known case of hypothyroidism/PCOS, presented to our RSM clinic in early January 2014 for investigation and treatment. She has had multiple failed IVF trials and 13 first trimester missed miscarriages terminating at 6-7weeks, all without IVIG therapy. Her 10th pregnancy was spontaneous, managed in London, UK, with multiple supportive therapy and courses of IVIG starting from the 3rd to the 30th week of pregnancy. The pregnancy ended at 36weeks' gestation through caesarean section[C/S] and delivery of live baby girl who is doing very well. She had balanced translocation, 46XX t (7:11) (p10;q10). PGD/ICSI/IVF were performed with embryo transfer on 29/05/2014 and a pregnancy. She was commenced immediately on metformin, luteal support and IVIG therapy started at 6weeks gestation and at monthly intervals until 30weeks' gestation. She received additional therapy. The pregnancy, monitored with ultrasound, progressed uneventfully until admission at 35 weeks' gestation with mildly elevated liver enzymes and suspected fetal growth restriction. She was managed conservatively and in the light of non-reassuring fetal status, she was delivered by emergency C/S on 14/01/2015 of a live female infant, Apgar score 8 and 9, weight 2.29kg, with mild respiratory distress, admitted to the SCBU for intensive therapy. The mother and baby made satisfactory progress and were discharged on 24/01/2015.

Conclusion:

Two successive successful pregnancies in Mrs. HM with multiple causes of RSM after IVIG strongly suggest that IVIG has a role in RSM

Key Words: Recurrent Miscarriage, Translocation



Obstetrics and Gynecology

Category: Clinical

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Atypical hemolytic uremic syndrome [a HUS]: A postpartum complication.

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CASE REPORT

Background:

Atypical hemolytic uremic syndrome (a HUS) is a very rare life threatening progressive disease caused by uncontrolled chronic activation of the alternate complement pathway resulting in microvascular thrombosis, organ ischemia and damage.

Case summary:

A 28 years old primigravida was admitted at 39 weeks gestation to a tertiary Maternity Hospital in Kuwait and underwent emergency LSCS on 20/9/14 for failure to progress to deliver a live male baby 3.4 Kg, with apgar score 8 & 9 at 1 and 5 minutes respectively. Intraoperatively, there was atonic Primary Post Haemorrhage and 2 pints packed RBC and 2 units of Fresh Frozen Plasma were transfused. Initial postoperative Hb 8.9 gm/dl and platelets 209,000 dropped to 6 gm/dl and thrombocytopenia-platelets 86,000. and Hb 5.5 gm/dl, platelets 23,000 by second post-operative day. Th reticulocytes 9.73%, serum lactate dehydrogenate (LDH) = 1680. Liver function tests were normal. Peripheral smear reported microcytic hypochromic anemia, thrombocytopenia and plenty of fragmented RBC's (schizocytes). Renal function tests reported raised levels of urea 12.8, creatinine 173 and uric acid 485. Based on the triad of microangiopathic hemolytic anemia, fragmented RBC's (schizocytes), and elevated renal function tests led to a diagnosis of atypical HUS. Twenty sessions of plasma exchange and 3 doses of methyl prednisolone were given. Renal function tests stabilized after 2 weeks of hospital stay and hemoglobin, platelet count and reticulocyte count showed an improving trend after the 10th sessions of plasma exchange. She was discharged in an excellent condition with Hb 9.2 gm/dl, platelet count 332,000 and normal renal function tests, on October 17, 2014. At the postnatal clinic on November 6, 2014, both mother and child were healthy.

Conclusion:

Establishing the diagnosis of atypical HUS is challenging. The case described illustrates the complexity and importance of rapid diagnosis in a rare disease.

Key Words: Plasma Exchange, Atypical hemolytic uremic syndrome, Postpartum Complication



Oncology

Category: Clinical

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Wernicke's encephalopathy in head and neck cancer patients under radical chemoradiation Case reports

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CASE REPORT

Background:

Diagnosis of Wernicke's encephalopathy (WE) was only reported in autopsy cases for long time. Uncertainties still exist and clinic-radiological diagnosis is often delayed. The underlying cause is deficiency of thiamine. It is uncommonly malignancy. Classical triad of confused state, ocular symptoms and gait ataxia is characteristic. Delay in diagnosis and intervention can lead to the irreversible and fatal Korsakoff syndrome. We report 2 cases of WE occurring during the course of chemoradiotherapy (CRT) for head and neck cancer.

Case summary:

Case 1-A 49 years old Indian lady, diagnosed with T4N2bM0 well differentiated squamous cell carcinoma of hard palate, was treated by hyperfractionated CRT. Developed sepsis which complicated the clinical picture and led to delay in diagnosis of WE. MRI brain was characteristic showing bilateral symmetrical hyperintensity signals on third ventricles, thalamus, hypothalamus, brain stem and peri-aqueductal gray matter. Mammillary bodies and colliculi showed post contrast enhancement. This patient was managed with thiamine supplement but she did not recovered from encephalopathy. She died 4 months later.

Case 2-A 46 years old Indian male, diagnosed with T4N2cM0 poorly differentiated squamous cell carcinoma of oropharynx, was treated by hyperfractionated CRT. Two weeks after completion of radiotherapy, he presented with confusion, nystagmus and ataxia. Early suspicion of WE was raised which was confirmed by MRI brain and serum thiamine level. He was managed with thiamine intravenously. His ocular symptoms and ataxia have completely recovered while higher functions are slowly recovering.

Conclusion:

Prompt clinical diagnosis, backed up by necessary laboratory investigations and MRI brain help in averting the irreversible damage. Careful nutritional assessment and support during and after treatment is of paramount importance. Intravenous thiamine should be given without delay as its toxicity profile is safe.

Key Words: Wernicke's Encephalopathy; Thiamine Deficiency; head and neck cancer.



Oncology

Category: Clinical

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Extra-ventricular ependymoma involving thalamus

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CASE REPORT

Background:

Extra-ventricular Ependymomas are extremely rare. They can originate from the Ependymal rests. Only a few cases of Extra-ventricular Ependymoma occurring in the cerebral hemisphere mainly involving frontal, parietal, temporal lobes of the brain have been reported in the literature. So far, no case of occurrence of Thalamic Ependymoma in human beings has been reported. Furthermore, an extensive review of the literature showed that a case of thalamic Ependymoma has been reported in a white tailed Deer in veterinary Pathology journal.

Case summary:

A 61 years old Pakistani male presented with 2 months history of patchy altered sensation in the left side of face and left half of body. He did not have any focal signs of any neurological deficit. A CT scan of the brain showed a low density mass lesion occupying right thalamus. MRI of the brain showed a vaguely hyper-intense mass lesion with post contrast enhancement after Gadolinium, representing possibility of a low grade Glioma involving almost whole of right thalamic region. No features of ventricular obstructions or mid line shift noted. MRI spectroscopy revealed increased choline & creatinine levels & decrease in NAA levels. Histo-pathological examination showed typical features of Ependymoma (WHO grade II) and it was further confirmed by histochemical and immune-histochemical stains. MRI of the spine did not show any drop metastases. Currently, the patient is being treated with a curative course of radiotherapy using 3-Dimensional conformal external beam radiotherapy. A dose of 50 Gy/25 fractions/5 weeks has been planned.

Conclusion:

To the best of our knowledge, this is the first case report on an Ependymoma occurring in the region of Thalamus in human beings. Because of the difficult location of the tumour, surgery was not contemplated, thus a course of primary radical Radiotherapy has been planned.

Key Words: Extra-ventricular ependymoma, Thalamic Ependymoma



Oncology

Category: Clinical

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Spinal metastases from Glioblastoma multiforme

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CASE REPORT

Background:

Glioblastoma multiforme (GBM) was first described by Rudolph Virchow in 1863 and represents the most common and most lethal malignant tumor of the brain, usually arising between the ages of 40 and 60 years. Extra-cranial metastasis of GBM is extremely rare with reported frequency of only 0.44%. Spinal metastases from GBM are quite rare. They usually occur late in the course of the disease. They may manifest clinically or may even remain silent.

Case summary:

We hereby report a 51 years old male patient with a diagnosis of Glioblastoma multiforme involving left temporal lobe. He underwent subtotal resection of his tumour in June 2014 and received adjuvant post operative Radiotherapy (60 Gy/30 fractions over 6 weeks period) along with daily Temozolamide. He completed radiotherapy on 1st September 2014. Subsequently, he was started on a monthly course of 5 days Temozolamide. After the first cycle of Temozolamide, he developed severe low backache, pain and weakness in the lower extremities and difficulty in walking. MRI of the spine revealed extensive and widespread dural metastases involving almost whole spine. There was a soft tissue mass lesion in the region of L2 spine causing spinal cord compression. MRI of the brain also revealed residual primary lesion. He underwent surgery in the form of leminectomy at L2 and removal of 70% tumour from L2 region was performed. The histopathological examination revealed metastatic Glioblastoma, which was similar to the primary tumour. Following surgery, he was started on a palliative course of local Radio Therapy (RT). The patient developed bilateral Pulmonary embolism and septicemia. He died due to uncontrolled and progressive malignant disease, pulmonary embolism and septicemia.

Conclusion:

A rare case of Glioblastoma multiforme of the temporal lobe of the brain with rare occurrence of extensive spinal metastasis is being reported.

Key Words: Glioblastoma multiforme (GBM), Spinal metastasis



Orthopaedic Surgery

Category: Clinical

244

Avulsion injuries of the flexor digitorum profundus tendon: A report of an unclassified pattern of injury

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CASE REPORT

Background:

Closed avulsion of the flexor digitorum profundus (FDP) tendon is a common injury of the hand. This condition is classified based on the impact of the injury on the management plan.

Case summary:

In this report, we present a 44 year-old lady with unclassified pattern of FDP tendon avulsion. The injury involves an intra-articular fracture of the volar part of distal phalanx of the little finger resulting into two bony fragments, one attached to the retracted avulsed tendon and another separated and incarcerated at A4 pulley, and an intact dorsal cortex of the phalanx. This pattern was not described before in the literature. The bony fragments and the tendon were reduced and fixed using a pull-out suture which was tied over a button on the dorsum of the finger by inserting one limb of the suture through the proximal fragments and the other limb through the distal fragment. Post-operative rehabilitation was done accordingly. The final functional assessment of the patient six months following the surgery was excellent.

Conclusion:

Based on the frequent reports of unclassified pattern of FDP avulsion injuries, the development of a new classification scheme for this condition should be considered.

Key Words: Flexor digitorum profundus tendon; Fracture; Avulsion



Pathology

Category: Clinical

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An unusual case of prostate tuberculosis

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CASE REPORT

Background:

Tuberculosis of the prostate is a complication of miliary tuberculosis. Involvement of the prostate is rare and often asymptomatic.

Case summary:

We report a young man diagnosed as a case of miliary tuberculosis affecting the prostate. The patient was admitted to the hospital with convulsions. Computerized tomography increased the clinical suspicion of miliary tuberculosis extending to the prostate where a transrectal urethral biopsy was obtained. The biopsy revealed multiple necrotizing granulomata suggestive of tuberculosis.

Conclusion:

A high incidence of clinical suspicion and availability of sophisticated and reliable test are needed in order to avoid misdiagnosis of a complicated miliary tuberculosis cases.

Key Words: Miliary; Tuberculosis; Prostate



Pathology

Category: Clinical

246

Case of multiple myeloma with plasmacytoma breast and meningeal involvement -Case report and review of literature

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CASE REPORT

Background:

Extramedullary plasmacytomas can present as primary tumor or as secondary involvement in multiple myeloma(MM). Breast and CNS involvement is exceedingly rare with only few cases reported in the literature. We report a case of multiple myeloma with breast plasmacytoma and leptomeningeal myelomatosis.

Case summary:

A 44 year old Kuwaiti woman presented in September 2010 with periodontal swelling, fatigue and fever. Investigations revealed impaired renal function, hypercalcemia, anaemia, osteolytic bone disease and left maxillary gingival biopsy revealed a plasmacytoma. Sonomammography showed a well defined heterogenous solid nodule (BIRADS IV) in upper outer quadrant of left breast. FNA revealed singly dispersed and occasional clusters of immature plasmacytoid cells with prominent nucleoli. Diagnosis of plasmacytoma was made. Bone marrow biopsy showed replacement of marrow by plasma cells and serum chemistry showed the presence of Ig A Kappa paraprotein confirming the diagnosis of multiple myeloma. Cytogenetics revealed 13q deletion. She was given Vecade, thalidomide and dexamethasone chemotherapy. In July 2011 she developed symptoms of raised intracranial tension. MRI showed diffuse infiltrative process affecting orbits, greater wing of sphenoid, skull base and epidural intracranial extension but no intraparenchymal lesions. CSF cytology showed infiltration by myeloma cells. Six months later she developed multiple subcutaneous swellings and a soft tissue lesion in the midline of lower back which on FNA showed a myeloma deposit. Patient was lost to follow up.

Conclusion:

Metastatic tumors to the breast are rare and involvement of the breast by either solitary plasmacytoma or disseminated multiple myeloma is exceedingly rare. Cases have been reported. Extension into central nervous system is uncommon, estimated at 1% of patients. To the best of our knowledge this is the first case of MM with breast and leptomeningeal involvement diagnosed on cytology

Key Words: Multiple myeloma; Breast plasmacytoma; Meningeal involvement



Pathology

Category: Graduate (Resident)

247

Adipocyte atrophy within a lymph node: A diagnostic pitfall

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CASE REPORT

Background:

Atrophy of adipose tissue of the body occurs as part of the generalized atrophy of prolonged starvation, cancer cachexia and severe weight loss following bariatric surgery. Atrophic adipocytes are shrunken in size and can mimic signet ring cells. The main goal of the pathologist is to distinguish pseudoneoplasms from malignancies. The awareness of the presence of mimickers of malignant signet ring cells and attention to cytomorphologic details are necessary for proper interpretation. Immunohistochemistry along with appropriate clinical history and awareness of the histological appearance of markedly atrophic fat are helpful in reaching the correct diagnosis.

Case summary:

A 28 year-old female with a history of sleeve gastrectomy 2 years ago, presented with redundancy all over the body due to significant weight loss. The patient underwent Belt lipectomy and during surgery, an enlarged left inguinal lymph node was incidentally found and removed. Gross examination of the specimen revealed an irregular piece of fatty tissue with a lymph node (1.5 cm). The entire lymph node was submitted for evaluation. Microscopically, the lymph node showed reactive lymphoid hyperplasia with patent subcapsular sinuses. Clusters of signet ring-like cells are identified in interfollicular areas as well as in the medulla. Immunohistochemical markers were performed. The signet ring-like cells are weakly positive for S-100 but negative for other melanoma markers, and negative for cytokeratin which excluded signet ring-cell adenocarcinoma. The light microscopic and immunohistochemical findings were therefore, in keeping with adipocytic cells.

Conclusion:

This is a case of massive weight loss with small round vacuolated cells present in a lymph node. Ruling out metastatic signet ring adenocarcinoma is the most important consideration. However, clinical, morphological and immunohistochemical interpretation favour the diagnosis of adipocyte atrophy.

Key Words: Weight loss, Adipocyte atrophy, Signet ring cells



Pathology

Category: Graduate (Resident)

248

Dermatofibrosarcoma protuberans masquerading as a breast mass in a male patient

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CASE REPORT

Background:

Dermatofibrosarcoma protuberans (DFSP) is a rare neoplasm of low-grade malignancy that arises in the cutaneous region and superficial soft tissue with predilection for the trunk and proximal extremities. DFSP accounts for 1-6% of soft tissue sarcomas. We report a case of DFSP in a male masquerading as breast malignancy.

Case summary:

A 37-year-old male presented with recent increase in size of a firm right breast mass, present for the past 10 years. On ultrasound the mass was retroareolar and oval, measuring 5 x 5 x 4.5cm with heterogeneous echo pattern and positive color Doppler suspicious for malignancy. Ultrasound-guided needle core biopsy showed a spindle cell lesion suggestive of DFSP. CT chest was performed for pre-operative evaluation revealing that the mass was skin based with moderate heterogeneous enhancement, resting on the chest wall, with no evidence of metastasis to lymph nodes or lung parenchyma. The patient underwent wide local surgical excision and histopathology examination of the excised specimen confirmed the diagnosis of DFSP. Grossly, the tumor had a "protuberant" fleshy cut surface. Histologically, it showed a monomorphic spindle cell proliferation with a storiform growth pattern. On immunohistochemistry, diffuse immunopositivity for CD34 characteristic of DFSP was seen. Epithelial markers were negative. Ki67 proliferation index was not elevated and there were no features of high-grade fibrosarcomatous transformation.

Conclusion:

Our case of DFSP occurring in the breast region posed a diagnostic dilemma, presenting as an intramammary mass mimicking a primary breast tumor without a hint of dermal origin neither clinically nor sonographically. CT was helpful in characterizing and accurately localizing the tumor for surgical planning. Radiologic-pathologic correlation and knowledge of this entity are important in reaching the diagnosis because of its propensity for local aggressive growth and high recurrence rate.

Key Words: Breast, Male, DFSP



Pathology

Category: Graduate (Resident)

249

Mixed medullary and poorly differentiated follicular cell carcinoma of the thyroid

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CASE REPORT

Background:

Thyroid carcinoma commonly arises from follicular cells and less likely from parafollicular cells as medullary carcinoma. In rare cases, a mixed medullary and follicular cells carcinoma can be seen. These mixed tumors are usually medullary carcinoma associated with well differentiated tumors including: papillary or follicular carcinoma. Herein a report of extremely rare case of mixed medullary and poorly differentiated follicular cell carcinoma.

Case summary:

A 43 y old women previously healthy presented with right sided neck mass. Ultrasound examination showed enlarged right thyroid lobe with a 3.6 cm mass with central cavitation and associated with multiple lymph nodes enlargement. Pathological examination of the mass revealed a single mass with central necrosis. There were two distinct tumors within the mass. One was characterized by small cells with eosinophilic cytoplasm and round nuclei with stippled chromatin characteristic of neuroendocrine tumor. The second tumor was composed of sheets of cells with focal insular arrangement and tumor cell necrosis. The nuclei were vesicular with irregular nuclear membranes. Immunohistochemical testing showed that the former tumor expressed calcitonin and chromogranin confirming medullary carcinoma. The later tumor expressed thyroglobulin and TTF-1 and was negative for calcitonin and chromogranin confirming follicular origin.

Conclusion:

Mixed medullary poorly differentiated follicular cell carcinoma is an extremely rare tumor. There are several hypotheses for these mixed tumors whether they arise from common stem cell origin or as simultaneous tumors. The management for such tumors will be challenging, as both components should be treated with different modalities.

Key Words: Follicular, Medullary, Thyroid



Pathology

Category: Graduate (Resident)

250

Malignant phyllodes tumor with osteosarcomatous differentiation metastasizing to small bowel causing intestinal obstruction

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CASE REPORT

Background:

Phyllodes tumors are relatively uncommon breast neoplasms constituting 0.3-1.0% of all breast tumors according to the 2012 World Health Organization (WHO) classification system. Up to 10-20% of all phyllodes tumors are malignant and thus potentially capable of hematogenous metastatic spread particularly to the lungs and bones. Metastasis to the gastrointestinal tract, however, is unusual and might lead to diagnostic confusion particularly in the absence of relevant background clinical information. Phyllodes with osteosarcomatous and chondrosarcomatous heterologous differentiation may be particularly prone to metastasis.

Case summary:

We report an unusual case of metastatic phyllodes tumor to small bowel that demonstrated extensive osteosarcomatous and chondrosarcomatous stromal elements in a 49-year-old woman. In view of the limited history available to the pathologist at presentation, a non-specific diagnosis of "high-grade sarcoma" was rendered. Further investigation, however, revealed a history of breast surgery 2 years prior to the current presentation with a pathological diagnosis of malignant phyllodes tumor. Slide review of the breast specimen together with the current bowel tumor confirmed the histological similarity between the two. The patient died two months post-operatively due to surgical complications.

Conclusion:

Osteosarcomatous tumors of the bowel and mesentery are extremely rare and when encountered should prompt a meticulous search for metastatic disease such as metastatic phyllodes tumor. Clinicopathological correlation and a thorough search in the patient's past medical records are of paramount importance in such cases.

Key Words: Osteosarcomatous, Phyllodes tumor, Small bowel



Pathology

Category: Graduate (Resident)

251

Intracapsular salivary duct carcinoma ex pleomorphic adenoma: A therapeutic dilemma

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CASE REPORT

Background:

Pleomorphic adenoma (PA), a benign biphasic salivary gland neoplasm, is the most common neoplasm of salivary glands. Carcinoma ex pleomorphic adenoma (CXPA), a malignant epithelial neoplasm arising from a PA, accounts for only 3.6% and 12% of all salivary gland neoplasms and malignancies, respectively. Herein, we report a case of intracapsular salivary duct CXPA.

Case summary:

A 44 year old Syrian male presented with a long standing swelling of 8 years duration in the left parotid. A sudden increase in size was noted 2 years ago. Fine needle aspiration cytology was consistent with PA, and a left superficial parotidectomy was performed. Formalin fixed specimen revealed a 4.0cm, encapsulated, firm, solid, tan mass occupying the bulk of the specimen. The histologic sections showed an encapsulated PA with pseudopodia and extensive fibrosis. Foci of apocrine metaplasia of ductal cells were present, adjacent to which ductal overgrowth with "Roman Bridging" architecture was evident within the PA, with no extension outside the PA capsule. The diagnosis rendered was intracapsular salivary duct CXPA (4.0 cm). The lesion was completely excised and the patient was disease free 13 months post operatively.

Conclusion:

Generally speaking, the behavior, and thus the treatment, of CXPAs is dictated by the malignant component. Salivary duct carcinoma (SDC), arguably the most common CXPA, is a high-grade malignancy with an aggressive behavior due to its metastatic potential. However, and of particular interest to our case, intracapsular, and 'minimally invasive', CXPA has a very indolent behavior, similar to that of a benign pleomorphic adenoma with only rare instances of aggressiveness. Additionally, most of the SDC foci in our case showed a rim of myoepithelial cells, as highlighted by immunohistochemistry, indicating that the malignant changes are in fact intraductal or in-situ, further supporting an anticipated indolent behavior.

Key Words: Intracapsular; CXPA; SDC



Pathology

Category: Graduate (Resident)

252

Calcifying nested stromal-epithelial tumor of the liver

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CASE REPORT

Background:

Calcifying nested stromal-epithelial tumor is a rare primary liver neoplasm with less than 35 cases being reported in the English literature. This tumor of uncertain histogenesis and unclear malignant potential, is usually discovered incidentally. It affects children and young adults with female predilection and it commonly involves the right lobe of the liver. The histology of this nonhepatocellular tumor is characterized by nests of spindle and epithelioid cells associated with myofibroblastic stroma and variable calcification.

Case summary:

A 25-year-old female presented with a liver mass, which was discovered incidentally, during her workup for a weight reduction surgery. A further CT scan revealed a huge well-defined solid lesion with irregular scarring, enhanced septations and calcification measuring 18x13.5x12cm. An initial diagnosis of hamartoma was made on a core needle biopsy. Followed by extended right hepatectomy that showed a well demarcated tan/lobulated mass measuring 18x17x12cm, histopathology of which showed a lesion composed of spindle cells arranged in nest and sheets with focal calcification in a fibrous stroma. The tumor cells were positive for pan cytokeratin, WT1 and EMA and negative for HapPar1 and TTF-1. Integrating the histomorphology and immunohistochemical findings a diagnosis of calcifying nested epithelial tumor was established.

Conclusion:

Calcifying nested stromal-epithelial tumor, an extremely rare mixed tumor of the liver. It should be included in the differential diagnosis of liver masses when encountered in the proper clinical setting. Recognizing such an entity can help in identifying additional cases that lead to more information on the clinicopathological and prognostic features of this unusual hepatic tumor.

Key Words: Calcifying nested stromal-epithelial tumor; Hepatic mixed tumor; Liver



Pathology

Category: Clinical

253

Rare adult alveolar rhabdomyosarcoma of paranasal sinus diagnosed on fine needle aspiration cytology

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CASE REPORT

Background:

Rhabdomyosarcoma (RMS) involvement of paranasal sinuses in adults is rare comprising only 1.5% of reported head and neck rhabdomyosarcomas. We report a case of alveolar RMS involving paranasal sinus and orbit with cervical metastases diagnosed on fine needle aspiration cytology.

Case summary:

A 43 year old Kuwaiti female was referred to KCCC for aspiration of cervical lymph nodes. She had swelling of left side of face with proptosis and ptosis of left eye. MRI showed large neoplastic mass involving left ethmoid and sphenoid sinus, left nasal cavity with extension to left frontal and maxillary sinuses, left orbit and extradural intracranial extension. Left cervical lymph node aspirate was cellular comprising of small round cells with high nucleocytoplasmic ratio. Few plasmacytoid cells with eccentric round to lobulated nuclei having moderate eosinophilic cytoplasm were also seen along with extensive necrosis. Tumor cells stained positive for desmin, myoglobin, Chromogranin and vimentin and negative for CK, LCA, CD99, HMB 45, melan A, GFAP, and SMA. Myogenin was noncontributory. A diagnosis of rhabdomyosarcoma was rendered. Molecular cytogenetic by FISH technique revealed FOXO1 rearrangement at 13q14 which was consistent with diagnosis of alveolar rhabdomyosarcoma. Patient was evaluated as inoperable and advised induction chemotherapy followed by concomitant chemo radiotherapy. The patient received 2 cycles of chemotherapy and was lost to follow up.

Conclusion:

Alveolar RMS is difficult to distinguish from other primitive round cell neoplasms without immunohistochemistry and/or genetic studies. In adults, the differential diagnosis includes small cell carcinoma, lymphomas and neuroepithelial tumors. Initial immune-profiling may not include myogenic markers while aberrant expression of epithelial and neuroendocrine markers may be a potentially serious diagnostic pitfall. Radiotherapy and chemotherapy is preferred with a combination of surgery for treatment.

Key Words: Alveolar rhabdomyosarcoma, Paranasal sinus, Fine needle aspiration



Pathology

Category: Graduate (Resident)

254

Follicular lymphoma in situ with hyaline vascular Castleman disease-like features: A case report

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CASE REPORT

Background:

Hyaline vascular Castleman disease (HV-CD) is a benign lymphoid hyperplasia characterized by hyperplastic follicles with atrophic germinal centers rich in hyaline deposits and vascular proliferation. Several B-cell lymphomas should be considered including follicular lymphoma before a diagnosis of CD is rendered.

Case summary:

A 36 year-old lady presented with 3 days history of epigastric pain and nausea. Physical examination was unremarkable. Initial laboratory investigations were within normal limits. Upper GI endoscopy revealed multiple small gastric polyps. Ultrasound abdomen and pelvis revealed multiple hypoechoic solid mesenteric lymph nodes. CT scan of the abdomen and pelvis shows multiple enlarged lymph nodes in mesentery and retroperitoneum. PET-CT imaging demonstrated large hypermetabolic lymph nodes in the para-aortic, mesenteric, retroperitoneal and right inguinal and femoral nodes. Other laboratory results including LDH, and viral studies for HIV, HBV, HCV and HHV-8 were negative. Right inguinal lymph node biopsy for histopathological examination showed focal localization of monotonous groups of small cells that display strong staining for BCL-2 protein and CD10 in occasional germinal centers that otherwise appear reactive. The background nodal tissue shows hyaline vascular Castleman disease-like changes. A diagnosis of in situ follicular lymphoma on a background of Castleman disease-like changes was established. Bone marrow biopsy shows paratrabecular atypical lymphoid aggregates. FISH analysis showed positivity for t(14;18) translocation involving the IGH/BCL2. Also, monoclonal population of B-cell was detected by PCR.

Conclusion:

HV-CD has been associated with several B-cell lymphomas. However, there is no case reported showing the association between in situ follicular lymphomas and HV-CD. To our knowledge this is the first reported case. We highlight the clinicopathologic features of the case with integrating a multifaceted approach.

Key Words: Castleman disease; Follicular lymphoma; In situ



Pathology

Category: Clinical

255

Primary cutaneous $\gamma\delta$ T cell lymphoma

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CASE REPORT

Background:

Primary cutaneous $\gamma\delta$ T –cell lymphoma (PCGD-TCL) are rare, representing approximately 1% of all cutaneous T-cell lymphoma, composed of a clonal proliferation of mature activated $\gamma\delta$ T –cells with a cytotoxic phenotype which was previously known as subcutaneous panniculitis-like T-cell lymphoma with a $\gamma\delta$ phenotype. PCGD-TCL occurs in adults, often presenting with generalized skin lesions, preferentially affecting the extremities and can show epidermotropic, dermal and subcutaneous involvement. PCGD-TCLs are aggressive lymphomas resistant to multi-agent chemotherapy and/or radiation and have a poor prognosis with a median survival of approximately 15 months.

Case summary:

A 24-year-old male presented with two weeks history of ulcerated and indurated plaques and nodules on the skin predominantly involving the lower limbs and genital ulcer, associated with fever. Clinical examination revealed hepatosplenomegaly. PET-CT scan demonstrated multiple cutaneous and subcutaneous soft tissue lesions scattered throughout the body and hypermetabolic genital ulcer, suspicious of cutaneous T-cell lymphoma.

A skin biopsy was performed and subsequent histopathology showed ulcerated epidermis, deep dermal and subcutaneous infiltrate of large blasts with irregular nuclei containing coarsely clumped chromatin, inconspicuous nucleoli and increased mitotic activity. Necrosis, perineural and angioinvasion were demonstrated. The tumor cells were immunopositive for CD2, CD3, CD56, GRANZYME B and negative for CD4, CD5, CD8, & CD7. Based on histology and immunohistochemistry, a diagnosis of PCGD-TCL was made.

Conclusion:

PCGD-TCL usually run an aggressive course and portend a poor prognosis and can also be associated with complications such as haemophagocytic syndrome and multi-organ failure.

Key Words: Skin; $\gamma\delta$ T –cell; Lymphoma



Pathology

Category: Clinical

256

2,8-dihydroxyadenine nephrolithiasis identified as cause of renal failure after renal transplant

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CASE REPORT

Background:

Adenine phosphoribosyl transferase (APRT) deficiency is a rare hereditary cause of nephrolithiasis, transmitted in an autosomal recessive fashion. APRT is an enzyme in the purine metabolism pathway that converts adenine into adenosine monophosphate. A lack of this enzyme results in accumulation of adenine, which is alternatively converted to 2,8-dihydroxyadenine (DHA) by xanthine oxidase. The low solubility of DHA cause recurrent urolithiasis or nephropathy secondary to crystal precipitation into renal parenchyma (DHA nephropathy). If unrecognized prior to renal transplant, can recur causing graft failure. The prevalence of APRT deficiency is 1:33000 to 1:250000 but may be underestimated because of lack of awareness and under diagnosis. This case happens to be the first to be reported from Kuwait. Treatment of APRT deficiency relies on allopurinol therapy, which acts by blocking xanthine dehydrogenase which allows renal function to improve and prevents recurrence after renal transplantation.

Case summary:

A 41-year-old female was admitted in the nephrology centre for a renal transplant following end stage renal disease due to recurrent nephrolithiasis which were identified as calcium oxalate and urate stones by standard analysis. She underwent live related renal transplant and native nephrectomy. Histopathology of the native kidney showed tubulointerstitial nephritis with abundant brown crystals which were present in the tubular lumina, tubular cell cytoplasm and focally within the interstitium arranged as rods, irregular shapes and annular formations of striated crystals. The possibility of DHA crystalline nephropathy was raised and was confirmed biochemically.

Conclusion:

A high index of suspicion for APRT deficiency and performing the appropriate investigations are mandatory in patients with recurrent urolithiasis and renal failure. A delay in diagnosis can result in irreversible renal failure which could otherwise be treated with one pill a day.

Key Words: Kidney; Stone; 2,8-dihydroxyadenine



Pathology

Category: Graduate (Resident)

257

Colonic muco-submucosal elongated polyp: An under-recognized entity

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CASE REPORT

Background:

Colonic muco-submucosal elongated polyp (CMSEP) is a relatively new entity which, until recently, has been exclusively reported by Japanese researchers. The prevalence of these polyps is reported to be between 0.1% in a Western series and 0.39% in a Japanese series. However, this might be an underestimate as CMSEPs are frequently asymptomatic. They are usually detected incidentally on colonoscopy but can occasionally be associated with non-specific gastrointestinal symptoms including abdominal discomfort, bowel habit alteration or a positive fecal occult blood. CMSEP is being encountered more often due to colon cancer screening programs. Based on 50 cases reported in the literature, there appears to be a male preponderance and a wide age range, with a mean age of 62 years. These polyps have a predilection for the transverse colon (28%) and sigmoid colon (26%)³. The pathogenesis of CMSEP is not well established; a plausible theory is that traction secondary to peristaltic motions allows the polyp to develop over time.

Case summary:

We discuss four examples of such polyps encountered in our practice. The polyps were all incidental findings discovered either in isolation or adjacent to another pathological finding in the colon. Grossly, the polyps were characteristically long with a slender stalk, narrow base, and sometimes a rounded tip imparting a “drumstick” appearance. Histologically, the polyps were composed of almost normal-looking colonic mucosa lacking specific pathological alterations, and an underlying submucosal stalk containing dilated blood vessels and lymphatic channels. The polyps were initially confused with other types of polyps.

Conclusion:

CMSEPs can mimic a variety of other colorectal polyps. Pathologists should be aware of their morphological features in order to avoid confusion with other more clinically significant polyps.

Key Words: Colon; Colonic muco-submucosal elongated polyp; Non-neoplastic polyp



Pathology

Category: Clinical

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Role of fine needle aspiration cytology and immunocytochemistry in the diagnosis of intrathoracic neuroendocrine tumors

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CASE REPORT

Background:

Neuroendocrine tumors are a highly diverse group originating from neuroendocrine cells. There are several distinct types of pulmonary neuroendocrine tumors, such as carcinoid tumors (typical and atypical), large cell neuroendocrine carcinoma and small cell carcinoma. We present two cases of intrathoracic neuroendocrine tumors diagnosed by imaging guided FNA cytology and immunocytochemistry (ICC).

Case summary:

Case 1: A 47-y old man was admitted to Mubarak Al-Kabeer Hospital with CT-scan finding of a large mediastinal mass, suggestive of lymphoma. Ultrasound (US)-guided FNA smears showed tumor cells arranged in loosely cohesive clusters as well as dispersed singly having round to oval nuclei and little or no cytoplasm. Nuclear moulding was a prominent feature. An occasional acinar formation was noted. ICC results showed, the tumor cells were positive for cytokeratin (CK) and neurone specific enolase (NSE), and negative for leukocyte common antigen (LCA) and chromogranin. Cytological diagnosis was malignant small round cell tumor, most likely small cell anaplastic carcinoma. Case 2: A 60-y-old man was admitted to Mubarak Al-Kabeer Hospital with a mass in the left lung; CT scan examination showed a large mass in the upper lobe. US-guided FNA smears showed round tumor cells with minimal nuclear pleomorphism and salt and pepper chromatin along with scanty to moderate amount of cytoplasm and fine reddish cytoplasmic granules in occasional cells. Cytodiagnosis was suggestive of carcinoid tumor. ICC results showed the tumor cells were positive for CK and chromogranin and were negative for synaptophysin. Following ICC studies, small cell carcinoma was a strong possibility. Both these patients were referred to HMJ Center for Specialized Surgery, for further management.

Conclusion:

Small cell anaplastic carcinoma has usually typical cytological features. In absence of these features, immunocytochemical studies may be of help to arrive at a diagnosis.

Key Words: Fine needle aspiration cytology, Intrathoracic, Neuroendocrine tumor



Pediatrics

Category: Clinical

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Van der Woude Syndrome: Case report and literature review from Kuwait

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CASE REPORT

Background:

Van Der Woude syndrome (VDWS) is an autosomal dominant genetic disorder characterized by the combination of lower lip pits, cleft lip with (CLP) or without cleft palate (CP), and cleft palate alone. VDWS is distinct from other clefting syndromes due to the positive family history of CLP AND CP and presence of other associations including hypodontia, congenital heart disease, syndactyly, ankyloglossia, and cerebral abnormalities. We present a rare case of VDWS in a patient from Kuwait to highlight the clinical features essential for diagnosing this syndrome and to emphasize the importance of the multidisciplinary team approach for management of those patients.

Case summary:

A 3 year old Kuwaiti boy, ex-preterm (33+2 weeks) second of mono chorionic monoamniotic twin, birth weight=1.650 kg, born to 35 years old diabetic mother, having history of cleft palate in 2 previous offspring. He was found to have cleft palate, congenital heart disease (TGA, ASD, & VSD) and spine deformity (double canal scoliosis segmentation). He required an intensive multidisciplinary team management regarding his CP and CHD corrective surgeries. Currently, He is mentally subnormal and on gastrostomy feeding and speech therapy.

Conclusion:

VDWS should be considered in the differential diagnosis of patients present with lower lip pits and CP/CLP especially if family history for CP/CLP is positive. Early diagnosis and collaborative management of different specialties would improve the outcome and prognosis of this condition.

Key Words: Van Der Woude syndrome; Cleft palate syndrome; Familial cleft lip



Pediatrics

Category: Clinical

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Pseudo-TORCH syndrome: Case report and literature review

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CASE REPORT

Background:

Pseudo-TORCH syndrome is a condition characterized by the presence of microcephaly and intracranial calcifications at birth accompanied by neurodevelopmental delay, seizures and a clinical course similar to that seen in patients after intrauterine infection with *Toxoplasma gondii*, Rubella, Cytomegalovirus, Herpes simplex (so-called TORCH syndrome), but despite repeated tests revealing the absence of any known infectious agent. It is an autosomal recessive immune-mediated neurodevelopmental disorder caused by mutations in the SAMHD1, TREX1, or Ribonuclease H2 (RNASEH2A, RNASEH2B, RNASEH2C) genes. In this case report, we describe a 3 year old Kuwaiti girl with congenital TORCH like syndrome emphasizing the importance of early diagnosis and genetic counselling for the patient's family.

Case summary:

3 year old Kuwaiti girl presented with global developmental delay. She is the first baby to consanguineous parent, product of full term normal delivery with birth weight of 2 kg. She has microcephaly, cataract, ASD, and spastic quadriplegia. CT head showed calcification within basal ganglia and white matter, bilaterally. All investigations including TORCH screen and metabolic screen were repeatedly negative. Family history is positive for mental retardation, microcephaly, and basal ganglia calcification (first degree cousin). Kuwait Genetic center registry records revealed 9 cases with 7 are Kuwaiti from the same family and 2 are non Kuwaiti. The diagnosis was confirmed in one patient with RNASEH2B 13q.

Conclusion:

Pseudo-TORCH syndrome should be considered in the differential diagnosis of patients with microcephaly, intracranial calcification and congenital heart disease and other findings resembling congenital infectious diseases, if TORCH screen is negative and family history is positive. Early diagnosis restricts investigation and empowers prognosis plus and genetic counselling.

Key Words: Aicardi-Goutieres syndrome; Baraitser-Reardon syndrome; Pseudo-TORCH syndrome



Pediatrics

Category: Clinical

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Varicella gangrenosa with toxic shock-like syndrome due to group A streptococcus infection in a 3 year old girl: A case report from Kuwait

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CASE REPORT

Background:

Chickenpox (Varicella) is a common childhood infection which is usually regarded as a trivial condition. Varicella gangrenosa is one of the rare most serious life threatening complications of chickenpox. Varicella gangrenosa is a term used to describe the gangrenous ulceration of the skin and/or deeper tissues that may follow chicken pox infection. We report a case of an immunocompetent 3 year old Kuwaiti girl with varicella gangrenosum caused by group A streptococcal superinfection of the skin lesions due to chickenpox. With the prompt recognition and the great plastic surgery management beside the intensive medical treatment, this patient survived with the least possible body disfigurements. Awareness and early aggressive intervention might reduce the high morbidity and mortality associated with this condition.

Case summary:

A three and a half year old girl presented on the fourth day of her mild chicken pox with toxic shock like syndrome. She had a huge hemorrhagic cutaneous necrosis involving bilateral hips along with clinical and laboratory features of disseminated intravascular coagulation. Group A streptococcus was isolated from the skin lesion. She improved with broad spectrum antibiotics, acyclovir and immunoglobulin infusion. After the gangrenous area was demarcated she underwent surgical debridement followed by split thickness skin grafting. Finally, she was discharged home after 35 days of hospitalization in well condition.

Conclusion:

Chicken pox is not always a benign infection. In certain circumstances and in special populations it can present with unusual serious complications. Awareness of Varicella gangrenosa as a potentially life threatening complication of chicken pox will enable prompt diagnosis, more aggressive management and a better prognosis. Multidisciplinary team of approach plastic surgery beside medical management will yield excellent clinical outcomes.

Key Words: Chicken pox; Varicella gangrenosum; Acute infectious purpura fulminans



Pediatrics

Category: Clinical

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Glucose transporter type 1 (glut1) deficiency syndrome: First reported case from Kuwait

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CASE REPORT

Background:

Glucose transporter type 1 deficiency syndrome (Glut1 DS) is a rare genetic metabolic disorder caused by deficiency of a protein that is required for glucose to cross the blood-brain barrier. The condition is described as a developmental encephalopathy characterized by infantile onset refractory epilepsy, acquired microcephaly, and mixed motor abnormalities. Some patients suffer from abnormal movements with or without seizures. Cognitive impairment, ranging from learning disabilities to severe intellectual disability, is typical. We report a case of Glut 1 deficiency to raise the awareness of this condition, highlighting the importance of ketogenic diet in management it.

Case summary:

7 year old Kuwaiti boy, first child to consanguineous parent, product of full term normal uneventful delivery. He showed normal neurodevelopment in the first year. Mother noticed paroxysmal attacks of multifocal dystonic movements of the limbs, and attacks of dystonic ataxic gait. Attacks were triggered by fasting and relieved by sleeping or eating. Investigations including metabolic screen, EEG and MRI brain were normal. Glut 1 deficiency was considered and CSF analysis showed low glucose (1.8mmol/l) and low lactate (0.9mmol/l) with low CSF/plasma glucose ratio (0.4). Molecular analysis found a heterozygous 26bp deletion (c615_640del26bases p. 206Afs*22) confirming the diagnosis. Ketogenic diet was started and within one month the paroxysmal episodes almost disappeared and sleep, attention and behavior improved.

Conclusion:

Glut1 DS should be considered in the differential diagnosis of intractable epilepsy or movement disorders especially if cerebrospinal fluid glucose is low. Ketogenic diet is the main treatment improving seizure control, cognitive function and long-term neurologic outcome. Awareness of the broad clinical spectrum associated with Glut1 DS will enable early diagnosis and management of this treatable condition.

Key Words: Glucose transporter type 1 (glut1) deficiency synd; Developmental encephalopathy; Ketogenic diet



Surgery and Transplantation

Category: Clinical

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Bariatric surgery: An emerging cause of malnutrition in Kuwait

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CASE REPORT

Background:

Malnutrition often evokes images of starvation, commonly associated with developing poor countries. However, many people are unaware that poor nutritional status also exists in regions where food is plentiful. Micronutrient deficiency of vitamins and minerals is a form of malnutrition, which is increasingly seen in Kuwait, the fifth richest country in the world. As health care providers, we have to recognise the signs and symptoms of micronutrient deficiency and be aware of underlying causes that might be missed if relevant history is not explored.

Case summary:

A 51 year Kuwaiti female attended a health education booth organized by the “SHOOF ZAIN: The Community Eye Health Initiative in Kuwait” where members of the public can get a free “Visual Functioning Quality Assessment”. The only deficient aspect in her vision assessment was a progressive reduction in night vision. Her medical history included Asthma and Hypothyroidism on treatment. Visual Acuity was 6/6 in both eyes for distance and N5 for reading with glasses. There was no family history of any hereditary eye disease. This lady was very reluctant to share information about a Sleeve Gastrectomy surgery, which she had at a private hospital in 2011 to control her obesity leading to a loss of more than 40 Kg during the past 3 years and a recent treatment with Iron and vitamin A supplements.

Conclusion:

Obesity in Kuwait, the second-most obese nation in the world, has escalated to epidemic proportions with 74% of men and 77% of women are overweight or obese and “as waistlines are expanding, so too will the business of obesity or bariatric surgery”! Due to the malabsorption, reduced gastric volume and alterations in eating behaviours induced by this procedure, there is an increased risk of developing certain mineral and vitamin deficiencies. This case highlights the ethical and medical importance of recognizing an emerging cause of malnutrition in Kuwait with potential serious effects on health.

Key Words: Vitamin A deficiency and night vision, Bariatric Surgery



Surgery and Transplantation

Category: Graduate (Resident)

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Reporting 3 cases of sarcoma treated with pedicled DIEP flap

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CASE REPORT

Background:

Soft tissue reconstruction following wide resection of soft tissue sarcoma or skeletal sarcoma remains a challenge. Pedicle flap and free tissue transfers are an essential part of limb sparing surgery. Deep inferior epigastric perforator (DIEP) flap is usually our choice of flap to reconstruct the loss of skin after large size sarcoma excision. Our goal is to evaluate the functional outcome of this procedure and emphasize its usefulness even after radiation therapy.

Case summary:

We report 3 cases of sarcomas, all of them were men, and their ages were 26, 57 and 39 years old. The first patient had femur osteosarcoma, the second had dermatofibrosarcoma of the left inguinal region, and the third patient had supra-pubic epithelioid sarcoma respectively. Their stages were T0N0M0, T2N0M0, T1N0M0 respectively. All of them were having a large size of sarcoma approximately 20x25cm. Angiogram were done before each operation. We used the pedicle DIEP flap as our reconstruction choice for reconstructing the defects. Our patients were all treated without any morbidity post-op. All the wounds closure was treated by primary intention healing. Our patients were happy and satisfied after their reconstruction, regaining their normal life without difficulties and no morbidities.

Conclusion:

The use of DIEP pedicle flaps has proven to be invaluable in numerous reconstructive procedures, and more recently in soft-tissue sarcomas reconstruction. It has a lot of valuable qualities that was mentioned earlier. All our patients had a better quality of life and better functional outcome. We proved the success of using this technique in reconstructing the part of large skin defects that is obviously in our cases much proper than Anterolateral Thigh flap or Taylor's flap. It allows the safe transfer of soft tissue from the abdomen for the construction of the indicated area without sacrificing the rectus muscle or fascia.

Key Words: Diep, Sarcoma, Pedicled Diep Flap, Soft Tissue Rec



Dentistry

Category: Undergraduate

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Measuring the intensity of pain or discomfort after initial placement of orthodontic elastomeric separators

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Introduction:

Objectives: The aims of this study were to measure the intensity of pain and discomfort following the initial placement of orthodontic elastomeric separators and to determine whether a topical anesthetic agent or systemic analgesic drugs are needed before the placement of the elastomeric separators.

Methods:

Forty subjects (ages 21-40 y) took part in this study. Orthodontic elastomeric separators were placed randomly in right or left interproximal contact area between the second maxillary premolar and the first maxillary molar of each subject. The subjects were asked to record the intensity of pain or discomfort experienced every two minutes for a total period of ten minutes using a Visual Analogue Scale (VAS) scale. After the procedure, the subjects were asked to complete a questionnaire consisting of 5 questions.

Results:

Most of the subjects reported having pain and discomfort with an intensity ranging from 10 -70%. The most frequent type of pain experienced by the subjects was pressure discomfort. Almost half of the subjects preferred having a topical anesthetic agent applied before the placement of elastomeric separators.

Conclusions:

The initial placement of orthodontic elastomeric separators can lead to pain and discomfort. Use of topical anesthetic agents could relieve the pain and discomfort associated with the initial placement of orthodontic elastomeric separators.

Key Words: Topical Anesthetic, Orthodontic, Separators

Funding Agency: None



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