Abstract Book

23rd HSC POSTER CONFERENCE 2018

Under the Patronage of the President of Kuwait University

13-15 March 2018

Health Sciences Center
Kuwait University

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Inaugural Ceremony: Tuesday 13 March 2018

Venue: HSC Auditorium, Health Sciences Centre, Jabriya

Moderator: Professor Mariam Yousif

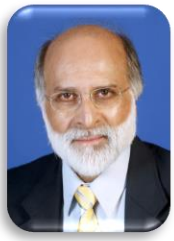
9:00 AM	***National Anthem, Recitation of Holy Quran***
9:10 AM	***Welcome Address: Professor Rajaa Al-Attiyah*** *Vice-Dean for Research & Postgraduate Studies, Faculty of Medicine*
9:15 AM	***Introduction of Keynote Speaker: Professor Yunus Luqmani*** *Chairman of Organizing Committee*
9:25 AM	***Keynote Lecture:* "The internal exposome – a global approach to a better understanding of human disease"** *Professor Paolo Vineis; Chair in Environmental Epidemiology* *Imperial College London, UK*
10:20 AM	***Opening of Poster Conference*** *Vice President for Research, Assistant Vice President for Research, HSC Deans and Vice-Deans, All Participants*
10:25 AM	***Poster Viewing: Faculty of Medicine Lobby***
Closing Ceremony: Thursday 15 March 2018	
12:00 PM	***Welcome Address: Dr. Maitham Khajah***
12:05 PM	***Announcement of Awards by Chief Judge*** *Presentation of Awards to the Winners by Dean, FoM and Chairman*
12:30 PM	***Vote of Thanks: Dr. Maitham Khajah***

Online Registration for CME Credits: www.hsc.edu.kw/poster

Photographs of Organizing Committee

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

Prof Yunus Luqmani, Chairman, Pharmaceutical Chemistry, FoP



Prof. Khalid Khan, Anatomy

Prof. Moussa Khalaf, Biochemistry

Prof Saeed Akhtar, Community Medicine

Prof Mariam Yousif, Pharmacology

Prof. Nandakumaran M, Obse & Gyne

Dr. Hanady Amoudy
Director of CRC; Microbiology

Prof. Noura Sweih
Vice Dean Accademic FoM, Microbiology

Dr. Babu Chulliparambil, Medicine

Dr. Fatma Khalil Ali, Medicine

Dr Fawzi Babiker, Physiology

Dr. Issa Loutfi, Nuclear Medicine

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Diagnostic Sciences (FoD)

Dr. Janvier Gasana, Environmental & Occupational Health, FoPH

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Dr. Anwar Al-Banaw, MLS (FAHS)

Dr. Mohammad Jamal, Surgery

Mr. Dheya HA Al-Hasan; Dept. of Finance, FoM

Message from the Vice-Dean for Research and Post-Graduate 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 22 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. Paolo Vineis, Chair in Environmental Epidemiology, Imperial College, London, U.K., who will give the keynote speech on "The internal exposome – a global approach to a better understanding of human disease". This year we have 212 poster abstracts and I have no doubt that the 23rd HSC Poster Conference will be a great success. I thank Kuwait University for the continuing support and sponsorship of the Poster Conference and Prof. Paolo Vineis for accepting our invitation as a keynote speaker in this year's Poster Conference. I would like also 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
23rd HSC Conference Committee

This year marks the 23rd Poster Day event since it was initiated in 1996. The number of contributions grew steadily in the early years to reach a peak in 2006 and has since fluctuated between 200 and 280 posters per year. Given the diversity of research interests of the contributors and participants, there is something for everyone to appreciate. The occasion provides an excellent forum for dissemination of information and increased awareness particularly between the university and other institutions, and opportunities for establishing collaborations. Over the years the contribution from students has grown to now approximately a third of all posters, a positive sign of interest of the new generation.

With the fast moving pace of medical research, it has become increasingly difficult to accomplish all of one's aims individually and the value, and necessity, of collective efforts is becoming all too apparent with greater demands from high impact journals for publication. While we may not yet have arrived to the 'publish or perish' reality of many 'western universities', the era of plentiful funding may be gradually receding and we must look to consolidating our research capabilities. The Faculties of the Health Sciences Centre, Science and Engineering have all established common use Research Core Facilities which afford access to technologies that are difficult, and indeed unnecessary, to acquire individually. More effective use of these resources should be actively promoted. Focus on specific areas through formation of Research Groups or Units would be another means of enhancing our capabilities in an ever more competitive global arena, and making a more significant impact. Discovering new information and acquiring new knowledge attracts attention but real recognition comes from innovative ideas and applications. Whilst quantity remains an important consideration, it is quality that will be remembered and valued.

Following in the tradition of past years, this event will be inaugurated by a keynote lecture given by an invited speaker who has made significant contributions in the field of medical science. This year we have an individual who's expertise overlaps two very different yet somehow complimentary areas that have been literally thrust upon us in recent years. He uniquely combines issues associated with climate change and the analysis and ability to alter our genetic make-up. Both are highly controversial and evoke emotive and often irrational responses. How to deal with the masses of genetic data that are now being generated by innovative technology is a new problem faced by researchers. We look forward to a stimulating lecture from Professor Paulo Vineis from Imperial College, London.

Finally, I extend my thanks and gratitude to my academic colleagues in the Organising Committee for giving their time. Increasingly over the years the tasks of this committee have been facilitated by the contribution of the Centre for Research Support and Conferences operating under the auspices of the Vice Dean Research FoM. My thanks to them for their efficient administrative assistance and organisation, and of course also to the judges for their unenviable but hopefully rewarding task of selecting outstanding posters for the various awards. Lastly, and indeed most of all, my thanks go to all the contributors of the posters for sharing their work.

Professor Yunus Luqmani

Chairman, 23rd HSC Poster Conference Organizing Committee

Keynote Speaker

Professor Paolo Vineis

Chair in Environmental Epidemiology,
Imperial College London, UK

Paolo Vineis is professor of Environmental Epidemiology at Imperial College London, School of Public Health. He is a leading researcher in the field of molecular epidemiology and his latest research focuses on examining biomarkers of disease risk, complex exposures, and intermediate markers from omic platforms in large epidemiological studies. He also studies the effect of climate change on non-communicable diseases. He is Head of the Unit of Molecular and Genetic Epidemiology at the Italian Institute of Genomic Medicine in Torino, Italy. Dr. Vineis is coordinator of the European Commission funded Exposomics (on air pollution) and Lifepath (H2020, on socio-economic inequalities and ageing) projects, and is a principal investigator or co-investigator of numerous international projects. He has more than 850 publications in journals such as Nature, Science, Nature Genetics, Lancet, and Lancet Oncology. He is the author of "Health without Borders. Epidemics in the Era of Globalization", Springer 2017. Additionally, he is a member of various international scientific and ethics committees and vice-chair of the Ethics Committee at the International Agency for Research on Cancer. Dr. Vineis received his MD from the University of Torino, Italy (https://en.wikipedia.org/wiki/Paolo_Vineis).

Keynote Abstract

The internal exposome – a global approach to a better understanding of human disease

It is generally accepted that the majority of important chronic diseases are likely to result from the combination of environmental exposures to chemical and physical stressors and human genetics. There is also evidence that the effects are location-specific and influenced by lifestyle and socioeconomic characteristics. Although information on both environmental and genetic causes of disease is growing as a result of large-scale epidemiological research, exposure data (including diet, lifestyle, environmental and occupational factors) is often fragmentary (in time and depth), non-standardized, at crude resolution and often does not include estimates at the level of the individual. The information on environmental factors is often incomplete or inaccurate and the subsequent estimation of overall risks associated with these factors is severely hindered. As a result, important associations can go undetected. This limitation has recently been framed within the context of the exposome, the environmental counterpart of the genome. The concept of the exposome refers to the totality of environmental exposures from conception onwards, and has been described in detail elsewhere including its external and internal components (Wild, 2005; Rappaport and Smith, 2010; Anon, 2016; Vineis et al.,2009).

The exposome approach has been proposed to improve the identification of environmental risk factors for disease, by applying to epidemiological research new tools emerging from exposure sciences and high-throughput omic technologies. Environmental contaminants have been argued to lead to the perturbation of one or more “Adverse Outcome Pathways” which consist of a sequence of events including molecular initiating events, biochemical responses, cellular responses, tissue organ responses, individual responses and lastly population responses. Pathway perturbation can be used as a conceptual framework for organising and evaluating the strength of existing evidence concerning steps necessary for progressing from molecular initiating events to an adverse outcome. Pathway perturbation makes particularly sense within the causal model called the “sufficient-component-cause framework”. This considers exposures or hits that together lead to the outcome under consideration. The model provides a way to account for how multiple factors, whether environmental exposures or genes, combine to result in disease in an individual or population. Another important component of the “pathway perturbation” paradigm is the life-course approach.. The early stages of life allow individuals to build-up their ability to respond to strains of different kinds (chemical, physical, biological and psychological) and this response “build-up” constitutes a “reserve” that allows variable resilience, very often depending on socio-economic status in addition to environmental and behavioural agents. These concepts have been systematically developed in the context of the US National Academy of Sciences 2st Century Risk Assessment report (NAS 2017), that refers extensively to the exposome.

Best Poster Award Winners: 22nd HSC Poster Conference 2017

Dr. Nael Al-Nakib Award (undergraduate)

Award No. 1: **Poster # 165**

Gender-dependent effect of prenatal immune challenge on adult hippocampal neurogenesis.

Al Mutairi R*, Ashqar A, Kalakh S, Mouihate A.

Department of Physiology, Faculty of Medicine, Kuwait University.

Award No. 2: **Poster # 150**

Antibacterial and antiproliferative activity of novel triazolyl oxazolidinones

*Almufarreh SA [1], Udo EE [2], Novotny L [1], Paulikova H [3], Kozurkova M [4], Phillips OA[1]

[1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University; [2]Department of Microbiology, Faculty of Medicine, Kuwait University; [3] Department of Biochemistry and Microbiology, Slovak University of Technology, Bratislava, Slovak Republic; 4Institute of Chemistry, Department of Biochemistry, P. J. Šafárik University, Kosice, Slovak Republic

Graduate – MSc

Award No. 1: **Poster No. 126** (Khoushiash, Abaza, Bahman, Al-Attiya – Microbiol.)

Natural phenolic compounds enhance the lethality of the multi-kinase inhibitor Sorafenib in human hepatocellular cancer cells.

Khoushiash S [1], Abaza MS [1], Bahman AM [1], Alatiyah R [2].

[1] Department of Biological Sciences, Faculty of Science Kuwait University; [2]Department of Microbiology, Faculty of Medicine, Kuwait University.

Award No. 2: **Poster No. 5** (Al-Harbi, Rahman, Khan – Fac. Biol. Sci./Anatomy)

Developmental vitamin D deficiency impairs spatial learning but has no effect on memory

*Al-Harbi A[1], Rahman A[1], Khan KM[2]

[1]Department of Food Sciences and Nutrition, College of Life Sciences; [2] Department of Anatomy, Faculty of Medicine, Kuwait University

Graduate – PhD

Poster 50 (Safar, Amoudy, El-Hashim, Mustafa – Microbiol./Pharmacy)

Live recombinant Mycobacterium smegmatis as an antigen delivery system for the induction of antigen-specific and protective cellular immune responses in mice.

Safar HA [1], Amoudy H [1], El-Hashim A [2], Mustafa AS[1]

[1] Department of Microbiology, Faculty of Medicine; [2] Department of Pharmacology & Therapeutics, Faculty of Pharmacy

Graduate – Resident

No Award

Case Report:

Poster # 208, (Aleneizi, Alhussaini, Atyani)

Atraumatic splenic Rupture in adult patient with chickenpox

Alenezi AO"*", Alhussaini A.

Surgery Department, Jahra hospital, Jahra, Kuwait

Young Researcher – Basic Sciences

Poster No. 13 (Dhanya, Khadir Kavalakkat, Tiss – Dasman Diabetes Inst.)

Protective effects of GLP-1 analogues against cellular stress in glucose up-taking tissues under lipotoxic conditions

*Madhu D, Khadir A, Kavalakatt S, Tiss A

Functional Proteomics and Metabolomics Unit, Dasman Diabetes Institute, Kuwait City

Young Researcher – Clinical Sciences

Poster No. 152 (Alwayesh, Ahmed, Al-Hashel, Alroughani)

Economic Burden of Multiple sclerosis on Kuwait Health care system

*Alowayesh MS [1], Ahmed S [2], AL-Hashel J[2], Alroughani R[2]

[1]Department of Pharmacy Practice, Faculty of pharmacy, Kuwait University; [2]Ibn Sina Hospital, Ministry of Health

Past Poster day Keynote Speakers and Lectures

2017

Vascular stiffness and systolic hypertension; Prof Pierre Moreau,
Dean and Professor, Faculty of Pharmacy, Health Sciences Center, Kuwait University

2016

Chemokines: Key players in immune surveillance and aging. Prof Bernhard Moser, Chair (Infection & Immunity), Institute of Infection and Immunity, Cardiff University

2015

The Future Healthcare: Personalized Medicine for Cancer Patients; Prof Ramzi M. Mohammad, Director, GI-Cancer Research, Karmanos Cancer Institute, Michigan, Department of Immunology and Microbiology, Barbara Ann Karmanos Cancer Institute, Wayne State University, MI

2014

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

2013

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

2012

Cardiovascular health in the 21stcentury; Prof 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, 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, 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. Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

2006

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

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.

2004

The Nitric Oxide/Cyclic GMP Pathway: Targets for Drug Development.
Prof Ferid Murad, (Nobel Laureate), 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 Medicien, University of Oxford.

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.

2000

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

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**

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.

Original Research Abstracts List

By Subject Area

Allied Health

1

*Al-Awadhi A, Adekile A, Marouf R: Von Willebrand Factor and ADAMTS-13 antigen and activity levels in adult sickle cell disease patients in Kuwait

2

Al-Sayegh N, Mohammad Shaban, Saud Al-Obaidi, Tahani Al-Qurba, Khazna Al-Enezi, Elizabeth Dean: Three-year analysis of changes in lifestyle behaviors and health status of the health science community of Kuwait University

3

*Rajan CJ, AlObaid F, Nawaz I, AlMusaileem N: Tinnitus In Adolescents and Adults with Normal Hearing: A Pilot Study

Anatomy

4

*Abd-El-Basset EM, Rao MS: Dibutyryl cyclic adenosine monophosphate (dBcAMP) rescues the neurons from Degeneration in kainic acid injured hippocampus and enhances learning and memory and neurogenesis

5

Alhussaini MS*, Almutairi AS, Ridha FM, Sadek HL, Kumar J, Renno WM: Curcumin treatment improved the Neurobehavioral recovery and neuronal regeneration more than Neurobion® in the sciatic nerve crush injury rat model.

6

Al-Hussaini H, Kilarkaje N: Trans-resveratrol modulates diabetes-induced alterations in retinoic acid metabolism pathway in retinal pigment epithelium of Dark Agouti rats

7

AI-Mutairi A, Rao M, Rahman A: Effect of Thymoquinone and Ferulic acid on Breast Adenocarcinoma cell lines

8

*Alshawaf S, Ashkanani H, Kabli A, Joy J, Najem A, Abd-El-Basset EM: Tumor necrotic factor-alpha (TNF- α) induces astrogliosis and promotes survival of cortical neurons

9

Khan KM, Rao MS, Rahman A: Infusion of quinolinic acid in the lateral ventricle of young rats affects spatial learning and memory

10

Rao M, Smitha S: Neurogenesis and cognition in STZ model of Diabetes- Role of Thymoquinone, BDNF and VEGF

Behavioral Sciences

11

Tolma EL, Stoner JA, Batterton C, Dougherty L: Developing health communication messages through quantitative research: The Native's Women's Health Project example

Biochemistry

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Allaho R*, AL-Rifae T: Stability study of Hormones

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Alhajji S: Adherence to Current Lipid Guidelines by Physicians in Kuwait

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Alrefaee S, Hattab M, Mahmoud E, Mohammad T, Maqseed M, Alajmi M, Almosaed S, Alqenaee M, Abutaher T, Hfith A, Alyouha A: Roche NT-proBNP assay in intensive care sitting

15
Alrefae S, Hattab M, Almosaed S: SPE: A tool for clinical diagnosis

16
Al-Mutairi R, Benov L: Can bacteria become resistant to photodynamic inactivation?

17
Al-Somali HF, *Botras MS, Qadhi IQ, Al-Maghrebi M, Renno WM: Lutein modulates transcription dysregulation of adhesion molecules and spermatogenesis transcription factors induced by testicular ischemia reperfusion injury: it could be SAFE

18
*Hussein J, Al-Mohanna Z, Al-Laho R, Al-Sayed S, Humoud M: Prevalence of heterozygous familial Hypercholestrolemia

19
*Kavalakatt S, Khadir A, Tiss A: Dysregulated Heat shock response and unfolded protein response in obese humans and its modulation through physical exercise.

20
*Kotb T, Al-Oan D: Stability of Serum 25(OH) vitamin D under different storage conditions

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*Madhu D, Hammad M, Kavalakatt S, Khadir A, Tiss A: Exendin-4 modulated MAPKs and protected against cellular stress in insulin-responsive tissues

22
Olusegun AM, Al Khaldi RM, Abdella N: Associations of Fetuin-A with Leukocyte Telomere Length and Human Telomerase Reverse Transcriptase in Patients with Acute Myocardial Infarction.

23
AlQenaie S, Abdur Rahman, Rao M: Synergistic Neurotoxic Effects of Lead and Quinolinic Acid on Cultured Rat Embryonic Hippocampal Cells: Protection by Memantine

Biomedical Engineering

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Shuaib A, Saleh T, Bourisly A: Optimization of Low-Level Light Therapy's Illumination Parameters for Spinal Cord Injury in a Rat Model

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*Ahmed N Albatineh, Alroughani R, Al-Temaimi R: Predictors of Multiple Sclerosis Severity Score among Multiple Sclerosis Patients in Kuwait

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Aldhafeeri E, Alshammari F, Jafar H, Malhas H, *Botras M, AlNasrallah N, Akhtar S: One-Year Period Prevalence of and Factors Associated with Road Traffic Crashes among Kuwait University Students: A Cross-sectional Study

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*Alhajeri A, Alajmi R, Alsulaiman A, Algharibah A, Ghuloum K, Alyaqoub E, Tardos N, Longenecker J: Association of Mother's Perception of Overweight with BMI-for-Age and Other Factors among Preschoolers in Kuwait

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Al-Aazmi N, Al-Shammari N, *Haider A, Al-Mutairi M, Al-Mutairi R, Al-Sabah R: Knowledge of Preconception Care Among Female Students at Kuwait University

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Alkhabbaz M, Al-Taiar A, Saeed M: The burden of acne vulgaris and its association with vitamin D deficiency among school students in Kuwait

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*Al-Mousawi T, Al-Dousari H, Al-Azimi F, Al-Khaledi M, Al-Azemi R, Al-Dhufairi Sh, Badr H: Diabetes Self-Management: A factor associated with health related quality of life in patients with diabetes

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Al-Jasem RM, Ramadan MA, Al-Awadhi KW, Al-Ghuwainem HA, Al-Bousairi FS, Prof Akhtar S: Exposure to active and environmental tobacco smoke and prevalence of allergic morbidity among young adults in Kuwait

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*Akbar F, Al-Baghli J, AlBesharah M, Bulbul F, Mohammad D, Qadoura B, Al-Taiar A: Low back pain among public high school students in Kuwait in relation to weight of school bag

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*Al-Sheridah N, Akhtar S: A matched case-control study of risk factors for colorectal cancer in Kuwait

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Bin Sabt A, *Bahzad Z, Ali F, Alramzi R, Makhseed A, Hussain A: Association between smoking, physical activity and mental health status amongst university students in Kuwait

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*El-Muzaini H, Hamada G, El-Enezi K, Aljunid SM: Cost analysis and potential cost savings in transurethral resection of prostate procedure for treatment of benign prostatic hyperplasia in Kuwait.

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*Kenawy M, Qureshi M, Adil S, Al-Awadhi K, Al-Ali M, Sadeq A, Ali A, AlMutawa N: Patient satisfaction: Public vs Private Hospitals in Kuwait

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Alqandi N, Jeragh F, Mulla Ali F, Al Zahraa S, Al-Bader B, Tadros N, Longenecker JC: Survey of Knowledge, Attitudes and Practices regarding Childhood Vaccinations among Employed Adults in Kuwait

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Naser J, Al-Zaabi A, Al-Saeedi A, Al-Munefi Kh, Al-Houli Sh, Al-Rashidi D, Badr H: Childhood Maltreatment: a Correlate of Mental Health Problems among Adolescents and Young Adults

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*Mohammad Z, Al-Tawheed S, Husain F, Al-Taleb A, Bulbul F, Moradi H, Al-Mutawa N: Knowledge, Attitude, and Practice of Bariatric Surgery among the Adult population of Kuwait

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*Ridha H, Bouzaber F, Al-Sallal M, Almutairi A, Al-dhubaiei R, Akhtar S: Prevalence and factors associated with self-reported noncompliance with mandatory seatbelt use law among adults in Kuwait

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*Shuaibi S, Al-Zuabi M, Sabti M, Behbehani A, Bouhamad M, Al-Majran A, Albatineh AN: Knowledge beliefs and barriers toward colorectal cancer screening among older adults in Kuwait: a cross-sectional study

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*Al-Matouq S, Abdulaziz F, Al-Mutairi H, Al-Mutairi, Al-Enzi M, Al-Basri D, Al-Taiar A: Dysmenorrhea among High-school Students and its Associated Factors in Kuwait

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*Kapila K, Al Temaimi R, Al Ayadhy B, Jaragh M, Mothafar F, Alath P, George SS, Francis I: Hormone receptors and HER2 expression in fine needle aspirates from metastatic breast carcinoma in Kuwait - Role in patient management

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*Al-Hennawi D, AlSumait A, Ariga J, Shyama M, Al-Mutawa SA: Prevalence of Molar Incisor Hypomineralisation among Schoolchildren in Kuwait

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*Al-Mutawa SA, Shyama M, Honkala S, Honkala E: Correlations between General Oral Health Assessment Index items among parents and teachers of special needs schoolchildren in Kuwait

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*Al-Nafisi M, Shyama M, Al-Mutawa SA: Cephalometric dental values for Kuwaiti adults with a malocclusion

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Alotaibi J, Swain MV: Characterization of the Time Dependence of the Mechanical Properties and Associated Chemical Reactions of Biodentine Following Preparation

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*Drobiova H, Bhardwaj R, Karched M: Detection of phosphoryl choline epitope in oral bacteria

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*Hanif A, Bhardwaj RG, Karched M: Effect of streptococcal biofilm-secreted components on the biofilms of fluconazole-resistant and -susceptible clinical isolates of Candida

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*Shyama M, Al-Mutawa SA, Honkala S, Honkala E: Oral hygiene habits among parents and teachers of special needs schoolchildren in Kuwait

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Layla A: The Effectiveness of Diabetes Nutrition Out-patient Clinic Program on HbA1c level of Kuwaiti Type 1 Diabetes

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Wasti N: Determination and modification of cardiovascular risk factors in patients with type-2 diabetes in Kuwait.

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*Almari M, Ziyab AH: Associations of parental diabetes and markers of adiposity with prediabetes among adolescents in Kuwait: a cross-sectional study

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Alsayegh R, Alnajem A, E-mail A, Alharbi M, Eliwa J, Bouhaimed M: Attitudes and Experiences Regarding Medical Errors and Disclosure Among Physicians in Kuwait

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Omu AE, Al-Serri A, Al-Harmi J, Omu FE, Al-Azemi MK: Effect of Zinc Deficiency on the Pregnancy outcome in the Rat

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Faisal AM, *Aljunid SM: Cost of assisted reproductive technology using activity-based and step-down costing methods: A case study in a private hospital in Kingdom of Saudi Arabia

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*Aljunid SS, Mohd Taib MZ, Abu Samah Z, Aljunid SM: Users satisfaction with the interior design quality of inpatient units of public hospitals in Malaysia

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Original Abstracts

Allied Health

1

Von Willebrand Factor and ADAMTS-13 antigen and activity levels in adult sickle cell disease patients in Kuwait

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Introduction:
Sickle cell disease (SCD) is a severe form of hemolytic anemia characterized by chronic hemolysis and is often associated with increased thrombotic risk. The thrombophilic status in SCD has been well documented as multifactorial, involving hemostatic changes, stimulation of the coagulation cascade and endothelial activation as shown by high levels of endothelial adhesion proteins including von Willebrand factor (vWF). Elevated vWF levels in SCD have been attributed to increased secretion and impaired processing by its cleaving protease ADAMTS-13. In light of the mild form of SCD reported in the local population and lack of reports of ADAMTS-13 activity in SCD patients in Kuwait, this study aims at assessing vWF and ADAMTS-13 antigen and activity levels in adult SCD patients in comparison to healthy controls.

Methods:
Hematological and biochemical parameters for 39 adult SCD patients (23 SS and 16 Sβ0thal) were analyzed and compared to 41 age- and sex-matched controls. Commercially available ELISA kits were used to measure vWF and ADAMTS-13 antigen and activity levels. .

Results:
There was no difference in age between patients and controls ($p=0.47$). Patients, of both genotypes, showed higher vWF antigen levels ($p<0.001$) compared to normal controls, but ADAMTS-13 antigen and activity levels were comparable between the two groups ($p>0.05$). We also report lower ADAMTS-13 activity to vWF:Ag ratio in patients compared to controls ($p< 0.003$), which reflects the ability of ADAMTS-13 to degrade vWF

Conclusions:
Increased vWF in adult SCD patients may be attributed to increased production rather than ADAMTS-13 deficiency. Despite normal levels of ADAMTS-13, its proteolytic activity seems insufficient to degrade the increased vWF antigen levels in SCD patients.

Key Words: Sickle cell disease; Von Willebrand factor; ADAMTS-13 protease;

Funding Agency: Kuwait University

Allied Health

2

Three-year analysis of changes in lifestyle behaviors and health status of the health science community of Kuwait University

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Introduction:
Health professionals who adopt healthy lifestyles are more likely to promote healthy living practices in their community and with their patients. Therefore, our study's aim was to evaluate health indicators of students, and staff of the Health Sciences Center of Kuwait University. This knowledge base overall will help inform the elements of a culture of health on campus for both students and staff.

Methods:
We extracted data on health behavior profiles related to smoking, physical activity, stress and sleep and objective measures such as systolic and diastolic blood pressure (SBP and DBP), heart rate (HR), random blood sugar (RBS), Body mass index (BMI), and waist-to-hip ratio (WHR).

Results:
206 participants (107 staff, 99 students) attended three academic years. Pairwise analysis showed a significant changes from unhealthy in 2014-15 to healthy in 2016-17 among all participants in WHR (4.4%, p=0.001), HR (27.3%, p=0.001), and stress (15.3%, p=0.020). Subgroup analyses reported similar changes among female and student participants. Male participants remained unhealthy in BMI (74.2%), SBP (81.2%), and WHR (72.7%). Amongst female participants, healthy to unhealthy changes were in sleep (83.5 %) and BMI (74.2%), while unhealthy to healthy changes were observed in HR (67.6%), Stress (18.8%), and DBP (82.0%).

Conclusions:
Three-year analysis showed significant improvements in WHR, HR and stress. Health indicators that were a concern for males were BMI and blood pressure while for females they were sleep and BMI. We shall continue to encourage students and staff to participate in annual health assessments and take advantage of individualized health coaching, advice and follow-up. In this way, the baseline of student and staff health will be expanded and evaluated in terms of change over years in students' academic program or staff members' years of employment.

Key Words: Health promotion; Lifestyle behavior; Health sciences students;

Funding Agency: Kuwait University, NP02/14

Allied Health

3

Tinnitus in Adolescents and Adults with Normal Hearing: A Pilot Study

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Introduction:

The audiology clinic of Farwaniya Hospital encounters a rising number of adolescent and adult patients complaining of tinnitus yet normal hearing. Aim: To investigate tinnitus in adolescents and adults with normal hearing in reference to use of personal media devices.

Methods:
A cross-sectional study was conducted in 20 gender matched participants aged 9 – 18 (10 adolescents) and 20 – 30 (10 adults) with tinnitus and 20 participants without tinnitus. Tinnitus history and use of Personal Media Devices (PMD's) history were noted followed by Impedance Audiometry (IA), Pure Tone Audiometry (PTA), Loudness Discomfort Level (LDL) and Otoacoustic Emmision (OAE). Patient with hearing loss were excluded from this study.

Results:
Irrespective of bilateral and unilateral tinnitus, adult males reported more use of PMD's and sleep disturbances due to tinnitus. Although auditory habits were near universal, a marginal significance ($p = 0.070$) was noted in PMD's users of ≥3 hours more likely reported tinnitus. Adolescents and adults reporting or not reporting tinnitus had a difference in LDL of 10 – 15db with no significant difference ($p = 1.000$) observed. No discrimination was found in PTA or IA, but adults with tinnitus obtained OAE in refer criteria with lower wave reproducibility <75% with significant difference ($p < 0.0001$)

Conclusions:
Increased use of PMD's in various daily activities could take a toll on both adolescents and adults in the form of tinnitus. Further studies in PMD's usage, LDL and OAE are highly required in tinnitus patients with normal hearing.

Key Words: Tinnitus; Adolescents; Adults;

Funding Agency: NONE

Anatomy

4

Dibutyryl cyclic adenosine monophosphate (dBcAMP) rescues the neurons from Degeneration in kainic acid injured hippocampus and enhances learning and memory and neurogenesis

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Introduction:

Dibutyryl cyclic adenosine monophosphate (dBcAMP is a cell-permeable synthetic analog of cyclic adenosine monophosphate (cAMP. Although elevation of cAMP levels was reported to promote the functional recovery in spinal cord injury, its role in hippocampal injury is unknown.
Objective: To study the effects of dBcAMP on learning and memory in the hippocampal injury.

Methods:
A lesion was created in the hippocampi of four months-old BALB/c mice by injecting 1µl kainic acid (0.25µg into the lateral ventricles. Lesioned mice (L were divided into L+ dBcAMP and L+PBS. Sham surgery was done (S, by injection of 1µl of saline into the lateral ventricles. The S mice were divided into S+dBcAMP and S+PBS. Mice in groups L+dBcAMP and S+dBcAMP were treated with dBcAMP for one week (ip,50mg/kg whereas, mice in groups L+PBS and S+PBS were treated with PBS. Mice in all groups were subjected to water maze and passive avoidance tests at the end of 4th week. Morphological studies using Cresyl violet staining, NeuN immunostaining (for neuron and DCX immunostaining (for neurogenesis of brain sections were done.

Results:
During water maze learning sessions, distance traveled by L+dBcAMP mice was significantly less compared to L+PBS mice, suggesting better learning performance. Memory retention test showed that L+dBcAMP mice had significantly short entry latency and higher target quadrant time/distance traveled compared to L+PBS group suggesting better memory retention. Passive avoidance test showed that L+dBcAMP had significantly improved memory retention compared to L+PBS mice. Morphological studies showed significantly more number of neurons and more neurogenesis in the hippocampus in L+dBcAMP compared to L+PBS group. There was no significant difference between S+dBcAMP and S+PBS groups in water maze/passive avoidance tests and number of neurons.

Conclusions:
dBcAMP protects the hippocampal neuron from degeneration and enhances the learning, memory and neurogenesis.

Key Words: Hippocampus; Learning and memory; Neurogenesis

Funding Agency: Project No. MA01/14

Anatomy

5

Curcumin treatment improved the Neurobehavioral recovery and neuronal regeneration more than Neurobion® in the sciatic nerve crush injury rat model.

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Introduction:
Curcumin is a compound found in the dietary spice turmeric, Curcuma longa. It has been used as a traditional medication for centuries. Curcumin has a broad spectrum of pharmacological activities including antioxidant, anti-inflammatory, anti-cancer, and neuroprotective effects on the CNS and PNS. The present study was designed to compare the therapeutic effect of curcumin and the widely used medicine Neurobion® on sciatic nerve regeneration, neuroprotection of spinal neurons and sensory-motor functional recovery in the sciatic nerve crush injury model.

Methods:
Adult male Wistar rats were assigned to, i) Sham, ii) Sciatic nerve crush treated with saline, iii) Sciatic nerve crush treated with Curcumin (100 mg/kg orally for 14 days), iv) Sciatic nerve crush treated orally with Neurobion and v). Sciatic nerve crush treated with both Neurobion and Curcumin groups (n=12/group). All rats were tested for the motor and sensory neurobehavioral parameters from the week 1 to week 5 (Hoping reflex, hot plate test, tail flick test, extensor postural thrust, foot position, toe spread test, mechanical hyperalgesia test). At the end of the study, sciatic nerve and spinal cord tissues were harvested and processed for morphometric and stereological analyses.

Results:
Crush+Curcumin group showed significant improvement in sensory and motor behavioral tests compared to Crush+Saline and Crush+Neurobion groups. The morphological study showed a significantly increased number of nerve fibers in sciatic nerve, with better myelination pattern in Crush+Curcumin treated group. Spinal cord ventral horns showed a significant increase in the number of NeuN-immunoreactive neurons in the Crush+Curcumin treated group compared to Crush+Saline and Crush+Neurobion groups.

Conclusions:
Curcumin treatment remarkably improves the motor and sensory impairment and revealed significant histomorphological evidence of neuronal regeneration compared to Neurobion® in sciatic nerve crush injury model.

Key Words: Neuroprotection; Neuroregeneration; Neurobehavioral

Funding Agency: None

Anatomy

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Trans-resveratrol modulates diabetes-induced alterations in retinoic acid metabolism pathway in retinal pigment epithelium of Dark Agouti rats

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Introduction:
Diabetic retinopathy is a common microvascular complication of hyperglycemia, which results in blindness. This study investigated the modulatory role of resveratrol (R) on diabetes (DM)-induced changes in vitamin A metabolism pathway in retinal pigment epithelium (RPE) of type 1 DM rats.

Methods:
In experiment 1, 15 male Dark Agouti rats (13-15-week-old) were divided into 3 groups (n=5/group)- control (C), DM (Streptozotocin, 50mg/kg; ip), and DM+R (DR). The rats received R (5 mg/kg, ip) once daily up to day 14, and the RPE was sampled, and RNA was extracted. Global gene expression was analyzed by Affymetrix microarray. In experiment 2, the rats were divided into 4 groups (n=5/group) in 2 sets- C, R, DM, and DR. The RPE was collected from one set on day 14, and from the other set on day 28. RT-PCR and Western blotting were used for gene and protein studies. Unpaired Student t-test analyzed the microarray data, and the other data were analyzed by one-way ANOVA LSD test with significance level set at $P<0.05$.

Results:
DM affected the expression of 833 genes and R further increased the differentially expressed genes to 1249 in DR rats ($P<0.05$). DM downregulated genes of vitamin A metabolism enzymes, namely-Lpl, Lrat, RPE65, Rdh5, Rdh10, Rdh12, Rlbp1, and Rbp1. On day 28, R normalized Rdh5 and Cyp3a and increased Lrat and Rdh10 in DM rats. R exaggerated already inhibited RPE65, and decreased the elevated Crabp1, and increased the inhibited Cyp26b1 in DM rats. Resveratrol inhibited DM-induced increases in Rdh5, Rdh10, and Cyp3a, and increased Cyp26b1 protein levels on day 28.

Conclusions:
Short-term hyperglycemia for 2 weeks inhibits transcription of enzymes involved in vitamin A metabolism. R normalizes long-term DM-induced changes in transcription of the pathway proteins. Thus, long-term R supplementation in DM rats appears to be beneficial in reducing the adverse effects of hyperglycemia on vitamin A metabolism pathway.

Key Words: Retina; Micro-array; Diabetes

Funding Agency: Supported by Kuwait University grant # RM01/16

Anatomy

7

Effect of Thymoquinone and Ferulic acid on Breast Adenocarcinoma cell lines

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Introduction:

Poor cancer survival statistics call for the need of alternative/complementary methods of treatment. Plant/food derived phytochemicals have been shown to be effective in cancer treatment and protection. Nigella sativa and Ferula asafoetida are plants as well as food ingredients with anticancer properties shown in several cancer cell lines with bioactive constituents Thymoquinone(TQ)and Ferulic Acid(FA), respectively. Anti-cancer properties of TQ and FA individually have been reported in the literature but not synergistically. We investigated the effects of TQ and FA, individually and in combination, on proliferation, viability, apoptosis and cell cycle of MDA-MB 231 breast cancer cells.

Methods:

Cells were grown for 24h and treated with various concentrations of TQ (25, 50 and 100µM), FA (250,350 and 450µM) and various combinations of TQ+FA for 24 or 48 h. MTT assay and crystal violet and AO/PI staining were used for proliferation and viability while RNase A and Annexin-V/FITC assays were used for cell cycle analysis and apoptosis.

Results:

Our results showed that relatively high doses of TQ (50 &100µM) and FA (350 & 450µM) were effective individually in reducing proliferation and viability, and inducing apoptosis in MDA-MB 231 cells after 48h of treatment. At these doses TQ and FA significantly inhibited cell proliferation by76.4 and 80.4% respectively. Combination of relatively low doses of TQ+FA (TQ 25 µM +FA 350 µM) showed significant synergistic anti-cancer effect by reducing cell proliferation and viability to 90%. Individually these doses were less effective. No synergistic effects were observed on cell cycle and apoptosis.

Conclusions:

These data suggest that low doses of TQ and FA, which are physiologically achievable through foods, when used in combination are effective as anti-cancer therapeutics in the model used. Further research is needed to validate these findings in a breast cancer animal model.

Key Words: Breast cancer; Thymoqionone; Ferulic Acid;

Funding Agency: College of Graduate Studies Kuwait University, the Research Sector, Kuwait University, (Graduate Student Research Grant No. YF02/15)

Anatomy

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Tumor necrotic factor-alpha (TNF- α) induces astrogliosis and promotes survival of cortical neurons

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Introduction:
Neuro-inflammation occurs as a sequence of brain injury and is associated with production of cytokines. Cytokines can modulate the function and survival of neurons and astrocytes. Although the pro-inflammatory cytokine TNF-α is thought to be one of the major mediators of neuro-inflammation, its role in brain injury remains ill-defined. The objective of this study is to examine the effect of TNF-α on the neurons and astrocytes in normal brain and stab wound brain injury.

Methods:
Two groups of BALB/c mice were used. The first group (I) was subjected to stab wound brain injury. This group was subdivided into IA and IB groups. The second group of mice (N) was not subjected to injury and subdivided into NA and NB. Groups IA and NA received IP injections of TNF-α every day for five days, whereas groups IB and NB received five IP injections of PBS. Animals were killed 1, 3, 7, and 9 days post treatment. Immunostaining of frozen brain sections for glial fibrillary acidic protein (GFAP) specific for astrocytes, NeuN (specific for neurons) and Fluoro-Jade B (specific for degenerating neurons) were used. Western blotting and ELISA were done from the tissues isolated from the injured sites of group I and non-injured brain (N).

Results:
In group N (NA and NB) there was no significant change in the number of neurons and there was significant increase in the number of astrocytes (astrogliosis) in TNF-α treated group (NA). In group I there was a gradual increase in the number of both astrocytes and neurons with a significant increase in TNF-α-treated group IA. The number of degenerating neurons significantly decreased in TNF-α -treated group IA. In addition, it was found that TNF-α stimulated the expression of GFAP and BDNF in NA and IA groups.

Conclusions:
TNF-α induces astrogliosis in normal and injured brain, and promotes the survival of cortical neurons in stab wound brain injury. The upregulation of BDNF by TNF-α may contribute to the neuronal protection.

Key Words: TNF alpha; Astrogliosis; Brain injury;

Funding Agency: none

Anatomy

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Infusion of quinolinic acid in the lateral ventricle of young rats affects spatial learning and memory

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Introduction:
Quinolinic acid (QA), metabolite of kynurenine pathway of tryptophan metabolism, is a known neurotoxicant. QA toxicity affects hippocampal, striatal and cortical neurons. QA induces tau phosphorylation and reduces the expression of serine/threonine phosphatases. These effects are associated with age-related memory loss. We investigated the effects of infusion of QA in lateral ventricle of young Wistar rats on spatial learning and short- and long-term memory.

Methods:
QA (9 mM) was infused into right lateral ventricle of 21-day old rats for 7 days using osmotic pumps (Durect Corporation, CA, USA). Rats infused with the same volume of normal saline served as vehicle control (VC). Learning and memory was assessed by Morris Water Maze test on postnatal day 30 (PND30) and PND45.

Results:
Two-way repeated measure ANOVA analysis revealed that learning was significantly impaired in QA-infused rats compared to VC group ($p < 0.05$) at PND30 but not at PND45. Short-term memory(STM) tested 2 days after the last learning session showed significant memory deficits in QA-infused rats compared to VC at both PND30 and PND45 ($p < 0.05$ and 0.01, respectively). However, long-term memory (LTM) tested 10 days later showed no significant difference between the QA-infused saline-infused rats of both ages ($p > 0.05$).

Conclusions:
These results show that intraventricular infusion of QA causes learning and STM impairment, but has no significant effect on LTM. It is tempting to speculate that the difference in STM and LTM results is due to time-dependent clearance of QA.

Key Words: Quinolinic acid; Intraventricular perfusion; Spatial learning & memory

Funding Agency: Kuwait University Research Administration Grant No. RW01/14

Anatomy

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Neurogenesis and cognition in STZ model of Diabetes- Role of Thymoquinone, BDNF and VEGF

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Introduction:

Thymoquinone (TQ), the active principle of Nigella sativa seed, proved to have antioxidant, anti-inflammatory, antibacterial, hepatoprotective, antimutagenic, and antitumor activities. A recent study showed antihyperglycemic effect of thymoquinone in diabetic rats. Diabetes has adverse effects on neurogenesis, cognitive function, and trophic factors levels. Aim of the present experiment was to study the effects of TQ on learning and memory in diabetic rats and neurogenesis, brain derived neurotropic factor (BDNF), vascular endothelial growth factor (VEGF) levels and gliosis in the hippocampi of the diabetic rats.

Methods:

Five months old Wistar rats were divided into control (C), diabetic (DI) and diabetic + TQ groups (DI+TQ, n=12 in all groups). Diabetes was induced by single intraperitoneal streptozotocin (60mg/kg) injection. DI+TQ rats were treated with TQ (10mg/kg, ip) for 5 or 10 days. Control and diabetic rats were treated with PBS. Learning and memory was assessed by Morris water maze test. Hippocampal tissue was analyzed for neurogenesis, gliosis and trophic factors.

Results:

TQ treatment did not decrease the blood glucose levels in DI+TQ group both at 5 and 10 days. Five days treatment with TQ did not show any effects on all parameters studied. 10 days treatment with TQ showed significant effects. Morris water maze test revealed significant memory deficit in DI rats compared to control rats and TQ treatment significantly improved the memory in DI+TQ rats ($p<0.01$). Immunostaining and Western blot analysis of the hippocampus for newly born neurons and astrocytes (GFAP) showed significantly increased neurogenesis ($p<0.001$) and astrocytes in DI+TQ group. ELISA for BDNF and VEGF in the hippocampus showed significant increase ($p<0.001$) in D+TQ group compared to DI group.

Conclusions:

We conclude that TQ enhances glial cells, BDNF and VEGF levels in the hippocampus, which in turn enhance the neurogenesis and cognitive function in diabetic rats.

Key Words: HIPPOCAMPUS; BDNF; VEGF

Funding Agency: nil

Behavioral Sciences

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Developing health communication messages through quantitative research: The Native's Women's Health Project example

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Introduction:
There is limited research in developing health communication messages (HCMs) especially through quantitative research among indigenous populations. This study aims to demonstrate how quantitative research can be used to develop HCMs on breast health among American Indian/Alaska Native (AI/AN) women in the USA.

Methods:
Data were collected from a random sample of 255 AI/AN women, eligible for screening mammography, at a rural tribal clinic in Oklahoma. Variables of interest included demographics, intention to get a mammogram, cognitions (e.g. self-efficacy) and related knowledge. A recursive partitioning algorithm, with five-fold cross-validation, was used to identify subgroups with low, moderate, and high intention of undergoing mammography within six months of the survey. Models were adjusted for certain demographic and personal characteristics. JMP software was used to fit the decision trees (JMP® version 11.2.0, 2013 SAS Institute).

Results:
Sixty-one percent of participants intended to undergo screening mammography (95% CI: 55% to 67%). Three (low, moderate, high) intention groups were revealed. The low intention group, reported more uncertainty regarding scheduling mammography and a negative attitude toward the value of mammography in preventing breast cancer. The high intention group, reported higher confidence in scheduling/arranging a mammogram, a more favorable attitude toward the value of mammography in preventing breast cancer and assuring women that they do not have breast cancer, and less support of the belief that a woman does not want to know if she has breast cancer because she does not want to know if she is dying from it.

Conclusions:
There is a spectrum of the decision making process on screening mammography among AI/AN women, accompanied by a variation of beliefs and attitudes. The "one size fits all approach" might not be appropriate in developing HCMs promoting breast health.

Key Words: Breast cancer; Health communication; Prevention

Funding Agency: Susan G. Komen® Grant Number: KG111046

Biochemistry

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Stability study of hormones

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Introduction:

Serum and other blood products are often stored in the refrigerator (4 ℃) prior to analysis in biochemistry laboratories, but sometimes are mistakenly left out in room temperature. Therefore, the temperature at which the samples are stored is an important pre analytical factor that may affect test results. The aim of this study was to determine whether the stability of analytes is affected by temperature or other storage conditions.

Methods:

The study was performed in Amiri biochemistry laboratory during seven days. A total of 42 samples were pooled. Pool A included vitamin B12 and serum folate (s. folate). Pool B included luteinizing hormone (LH), follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), prolactin, estradiol, progesterone, testosterone, free thyroid hormones (FT3 and FT4), cortisol, and ferritin. Pool C involve total and free prostate specific antigen (tPSA, FPSA) and parathyroid hormone (PTH). All analytes were measured at baseline and at different timings. Vitamin B12 and s. folate were additionally stored with and without foil wrapping. Percent bias was calculated for each result and compared with total allowable error.

Results:

Our study showed that LH, FSH, prolactin, TSH, testosterone, estradiol, FT4, FT3, cortisol, ferritin, and tPSA were all stable in room temperature and at 4 ℃ until 7 days with no clinically significant change. PTH was stable in room temperature till 48 hours, but in 4 ℃ till 7 days. Vitamin B12 showed similar stability with and without foil wrapping in both temperatures. Regarding s. folate, it was stable in room temperature without foil wrapping for 3 days, but with foil for 6 days. And in 4 ℃, it was stable without foil for 7 days.

Conclusions:

In conclusion, most analytes, except for PTH and s. folate, showed no clinically significant change during storage in either room temperature or refrigerator during 7 days.

Key Words: Stability; Analytes; Hormones;

Funding Agency: NONE

Biochemistry

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Adherence to Current Lipid Guidelines by Physicians in Kuwait

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Introduction:

Alarmingly high rates of dyslipidemia have been found among the Gulf region in patients presenting with acute coronary syndrome, with the highest frequency of dyslipidemia found in Kuwait (37%). Therefore, it is of utmost importance to identify and treat dyslipidemias promptly and effectively. In an effort to understand local physicians' practice and use of evidence-based medicine and lipid treatment guidelines, the objective of this study was to survey and assess the current standards of care.

Methods:

Between October 2015 and June 2016, 279 surveys designed to assess physicians' attitudes and practice towards lipid guidelines were conducted as paper or web questionnaires among physicians working at governmental hospitals and polyclinics. Statistical analysis was done using SPSS.

Results:

Over 90 percent of physicians claimed to use lipid guidelines with 92.3 percent of them rating themselves as knowledgeable. Younger physicians were found to be less knowledgeable and consequently, used guidelines less. The most important factor influencing clinical decision was clinical guidelines. The majority (72.4%) of physicians required more time to use guidelines more frequently. The most commonly selected lipid guideline for daily practice was the Guideline on the Treatment of Blood Cholesterol published by ACC/AHA (2013). The most common risk assessment tool used was Framingham risk score.

Conclusions:

Three types of barriers to guideline adherence were identified; these were knowledge, attitude, and behavior. There was a clear difference identified between guidelines awareness and familiarity. Recommendations to improve physician adherence were proposed and included educating and familiarizing physicians with more recent guidelines as well as improving workplace accessibility to lipid guidelines.

Key Words: Lipid Guidelines Use; Physicians Adherence; Dyslipidemia;

Funding Agency: None

Biochemistry

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Roche NT-proBNP assay in intensive care sitting

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Introduction:
N-terminal pro natriuretic peptide (nt-probnp) primarily used to detect, diagnose and evaluate severity of heart failure. It can also be used to distinguish type of shortness of breath. Different automated assays were developed in which natriuretic peptides being studied under different conditions however; remains few the studies which monitored the assay's performance under conditions of routine use. In this study we studied Roche nt-probnp assay as test of heart failure and pulmonary diseases.

Methods:
84 samples sent for procalcitonin (PCT) from intensive care unit (severe cardiac, respiratory diseases) were analyzed for nt-probnp on Cobas 6000. Nt-probnp precision, interassay variation, stability for the assay, % nt-probnp recovery & effect of hemolysis were tested. probnp & PCT tests were compared. 20 volunteers selected from laboratory staff. SPSS used for statistical analysis.

Results:
Intraassay precision measured as mean 107.5 ng/ml ± 4.9 S.D. Controls were within range for control1mean 4520.3 ±706 ng/ml; control 2 mean: 246.23 ng/ml ± 352.6 S.D. Assay was stable storage times (wilxocson test; p = 0.1). Recovery 122%, 114% and 108.8%. No effect of hemolysis p>0.05.23-86 years old patients showed median nt-probnp 2142 pg/ml that correlated significantly with PCT (p = 0.000; spearman correlation) . ROC curves for cardiac diseases showed area 0.79; p = 0.002. Cut-off 331 ng/ml nt-probnp showed 100% sensitivity & 70% specificity for cardiac diseases. ROC curve for respiratory diseases showed area for nt-probnp 0.78; p = 0.04. Cut-off 331 ng/ml nt-probnp showed 100% sensitivity & 70% specificity for respiratory diseases. PCT didn't showed significant relation either for cardiac diseases: area 0.69; p = 0.1 nor respiratory diseases area 0.69; p = 0.1.Volunteers 26 - 61 years old showed: range 5.0 pg/ml - 74.7 pg/ml, mean 107.9 pg/ ml & median 107.3 pg/ml.

Conclusions:
Roche nt-probnp is a promising test for severe cardiac and respiratory diseases once conjugated with proper functional test.

Key Words: nt-probnp; PCT; ICU;

Funding Agency: Roche; Yiacho, Ministry of defense.

Biochemistry

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SPE: A tool for clinical diagnosis

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Introduction:

Serum protein electrophoresis (SPE) is usually ordered to diagnose multiple myeloma (MM). Although levels of proteins in the serum change in predictable way in response to different clinical situations that can be detected from SP bands on a gel. This test is underestimated due to insufficient diagnostic evidence. We studied SPE as tool for detecting other clinical changes than MM.

Methods:

44 patient's samples negative for MM (20 males & 24 females) were analyzed using Automatic agarose gel electrophoresis system / compact Microgel Interlab. Nephlometry testing for immunoglobulin (IgA, IgM &IgG) were also done using Beckman Immage immunoassay system while routine biochemical analysis including total protein (TP), transferrin (TRN), low density lipoprotein(LDL) and Lactate dehydrogenase (LD) were analyzed using Beckman DXc600 I analyzer. Readings for bands were compared to each other's and compared to albumin /globulin ratio (G/A).

Results:

Bands studied showed 14 cases with polyclonal bands, one with sign of hemolysis, other hyperlipidemia, and one with low serum globulin. All bands showed significant positive correlation with A/G except for α2 that showed negative correlation; $p<0.05$. Using linear regression α1 ($p = 0.29$; $t = 10.7$) & albumin ($p = 0.4$; $t = 0.9$) were independent variables of γ band while α2 ($p = 0.03$; $t = -2.25$) is inversely related to γ compared to β that was directly related ($p = 0.024$; $t = 2.34$). No significant gender differences affected bands readings.

Conclusions:

Analysis of SPE may give a rough idea about clinical situation of a patient and guide towards further analysis.

Key Words: Electrophoresis; Multiple myeloma; Albumin /globulin ratio;

Funding Agency: none

Biochemistry

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Can bacteria become resistant to photodynamic inactivation?

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Introduction:

Excessive and improper use of antibiotics has led to a dramatic decline in antibiotic efficiency. This stimulates the efforts for development of new methods for microbial eradication, which would allow antibiotics to be spared for cases where their use is unavoidable. A promising alternative of antibiotics is the use of a photosensitizer (PS) and light for photodynamic inactivation of microorganisms (PDI). It has proven efficient against various classes of microbes, but investigations about development of resistance and ability of PDI to inactivate antibiotic-resistant bacteria are scarce. The aim of this work was to investigate how bacteria respond to prolonged exposure to sublethal PDI and how efficient is PDI against antibiotic-resistant Gram-negative and Gram-positive strains.

Methods:

E. coli and S. aureus resistant to multiple antibiotics, and corresponding antibiotic-sensitive strains, were exposed to sublethal PS concentrations and light intensity. Effect on cell metabolic activity was determined by the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] assay, and ability to proliferate was assessed by the clonogenic assay. All experiments were repeated at least two times with 3 -5 replicates. Statistical analysis was performed using SigmaPlot 11.0.

Results:

Microbial cultures grown under sublethal levels of PS and light, did not develop resistance. Prolonged exposure to sublethal PDI and multiple cycles of PDI treatment and regrowth did not produce PDI-resistant or antibiotic-resistant mutants. Gram (+) and Gram (-) bacteria resistant to antibiotics were as susceptible to PDI as were their antibiotic- sensitive counterparts.

Conclusions:

Neither growth under sublethal PDI nor prolonged PDI exposure induces resistance. Strains resistant to multiple antibiotics can be efficiently killed by PDI.

Key Words: Antibiotic resistance; Photodynamic inactivation; Antimicrobial;

Funding Agency: NONE

Biochemistry

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Lutein modulates transcription dysregulation of adhesion molecules and spermatogenesis transcription factors induced by testicular ischemia reperfusion injury: it could be SAFE

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Introduction:

Testicular ischemia reperfusion injury (tIRI) is considered as the underlying mechanism of testicular torsion, which can cause male infertility. tIRI-induced damage was investigated by assessing the gene expression of spermatogenesis master transcription factors and that of major adhesion molecules of the blood-testis barrier. The effect of lutein, a hydroxyl carotenoid, in alleviating tIRI-induced damage was also studied.

Methods:
Male Sprague-Dawley rats were divided into three groups: sham, unilateral tIRI, and tIRI + lutein (0.2 mg/kg). tIRI was induced by occlusion of the testicular artery for 1 h, followed by 4 h of reperfusion. Lutein was injected 15 min after the start of ischemia.

Results:
Histological analysis and real-time polymerase chain reaction revealed significant decreases in tissue biopsy scores, reduced seminiferous tubule diameters, and down-regulated the mRNA expression of the TFs cAMP-responsive element modulator, TATA box-binding protein-related factor 2, and regulatory factor X 2 compared with the sham group. Lutein treatment reversed these effects. The mRNA expression of the adhesion molecules N-cadherin, nectin-2, claudin- 11, occludin, and connexin-43 was significantly down-regulated during tIRI, but this change was prevented by lutein treatment. In addition, lutein normalized the tIRI-induced increase in total antioxidant capacity, increased malondialdehyde levels, augmented number of TdT-mediated dUTP-X nick-end labeling (TUNEL)-positive nuclei, and activated caspase-8 pathway. The components of survivor activating factor enhancement (SAFE) were also activated during tIRI. Increased tissue expression of TNF-α and its receptor, TNFR1, was accompanied by increased phosphorylation of Janus kinase and STAT3, which was prevented by lutein treatment.

Conclusions:
Our findings suggested that tIRI-induced spermatogenic damage may involve modulation of the SAFE pathway and could benefit from lutein treatment.

Key Words: Transcription dysregulation; Testicular ischemia; Lutein;

Funding Agency: None

Biochemistry

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Prevalence of heterozygous familial Hypercholestrolemia

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Introduction:

Heterozygous familial hypercholesterolemia (heFH) is a common autosomal dominant disease with a prevalence of 1:500 in the general population. The prevalence in Kuwait is unknown. Our objectives is to estimate the prevalence of heFH in Kuwaiti population using the Dutch Lipid Clinic Network criteria (DLCN) for the diagnosis of FH, and to identify their genetic mutations.

Methods:
The Eastern Mediterranean Approach for Control of Non-Communicable Diseases (EMAN) survey database, which was collected between March and September 2014 and included 4391 subjects aged 18-69 years randomly selected, was used to estimate the prevalence of FH in Kuwaiti population. Subjects with LDL values equal or higher than 4 mmol/L (321) were selected in our study. Those subjects were contacted and interviewed with a questionnaire including personal and family history and physical examination. In addition, a blood sample was taken from the participants and sent for genetic study. The DLCN criteria score was applied on the participants. Based on DLCN criteria, a diagnosis of FH was considered definite, possible, or probable.

Results:
We interviewed total of 40 subjects. Based on the DLCN scoring system, 23 are unlikely to have FH (scores ≤ 3), 12 subjects are possible FH (score 3-5), 4 subjects are probable FH (Score 6-7), and 1 is definite FH (score ≥ 8). The estimated prevalence of possible, probable, and definite FH is 0.4%. Genetic study results are pending.

Conclusions:
heFH, defined by the Dutch Lipid Clinic criteria, affects around 1 in 200 Kuwaiti adults. This ratio is underestimated due to our inability to interview all selected patients. Genetic testing may further confirm our findings.

Key Words: Hypercholestrolemia; Prevalence; Kuwait;

Funding Agency: KFAS

Biochemistry

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Dysregulated Heat shock response and unfolded protein responsein obese humans and its modulation through physical exercise.

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Introduction:

Obesity induced insulin resistance and Diabetes is characterized by impaired heat shock response (HSR) and endoplasmic reticulum (ER) stress. However, their expression pattern in adipose tissue (AT) is yet to be elucidated. Here, we investigated the status of key unfolded protein response (UPR) markers and heat shock proteins (HSP) in adipose tissue of lean and obese humans along with its modulation through physical exercise and diabetes.

Methods:
Adult subjects consisting of 40 lean and 40 obese were recruited and enrolled for a 3-month supervised exercise program. Subcutaneous adipose tissue (SAT) biopsies and venous peripheral blood were collected before and after exercise.Plasma inflammatory and metabolic markers were measured using Bioplex-200 system. The expression levels were studied using immunohistochemistry, confocal microscopy, western blotting and Real Time-PCR. Marker circulating levels were estimated using ELISA. All statistical analyses were done using SAS version 9.2.

Results:
Levels of the major heat shock proteins; HSP60 and Hsp72 and the major UPR protein GRP78 along with its downstream sensors; ATF6, IRE1α and PERK were increased in obese subjects. This pattern was concomitant with increased inflammatory response reflected by enhanced Interleukin 6 (IL6), Tumor necrosis factor-α (TNFα) and RANTES expression. Physical exercise significantly attenuated their expression levels with parallel reduction in the inflammatory markers. Though the levels of IL6 and TNFα significantly increased with the diabetic status in SAT, it showed reduced HSP and enhanced GRP78 expression.

Conclusions:
Perturbation of HSR and UPR are landmarks of metabolic complications in relation with obesity and diabetes. Physical exercise modulated those systems in obese subjects. Hence, enhancing the UPR and HSR defense system through exercise might relieve cellular stress, enhance metabolic homeostasis and consequently have a beneficial impact in diabetes prevention

Key Words: Heat Shock Response and Heat shock proteins; Unfolded Protein Response;

Funding Agency: KFAS

Biochemistry

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Stability of Serum 25(OH) vitamin D under different storage conditions

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Introduction:

Processing 25(OH)–vitamin D samples cannot be instant, and sometimes they sit on the bench for several hours before being analyzed. The aim of our study is to assess the stability of 25(OH)–vitamin D in direct light and room temperature. The established allowable bias for 25(OH)–vitamin D measurement is 10%.

Methods:
Twenty 25(OH)–vitamin D serum samples free of hemolysis, icterus, and lipemia were pooled in one container, mixed thoroughly, and were separated into 3 pools. The pools were Labeled as Pool 1 to 3 per the following conditions; -Both Pool 1 &2 were stored on the bench at room temperature. Pool 1 was protected from direct light while pool 2 was exposed to direct light -Pool 3 was stored in the fridge (2-8 °C). Baseline 25(OH)–vitamin D level was performed on the 3 pools (time=0) then Pool 1 and 2 were analyzed at 4h, 24h, 48h, 72h and 168h. Pool 3 was analyzed at 72h, 144h, and 168h.

Results:
None of the storage conditions exceeded the allowable bias.

Conclusions:
All results were within the total allowable error. 25(OH)–vitamin D samples are stable in room temperature and direct light up to 7 days from the time of collection.

Key Words: Vitamin D; Stability; Biochemistry;

Funding Agency: None

Biochemistry

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Exendin-4 modulated MAPKs and protected against cellular stress in insulin-responsive tissues

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Introduction:
Lipotoxicity is an important factor in the pathogenesis of type 2 diabetes resulting in defective β-cell proliferation and increased apoptosis. GLP-1 and its mimetics act on pancreatic β-cells to decreases blood glucose, enhance β-cell function. Recent studies have shown beneficial effect of these peptides on insulin-responsive tissues such as adipose tissue, muscles and liver. We investigated here the potential beneficial effects of GLP-1 mimetics on those peripheral tissues using established cell lines under stressing levels of palmitic acid.

Methods:
Using cell lines from adipose tissue (3T3-L1), skeletal muscle (L6), liver (HepG2) and pancreatic cells (BTC-6), we analyzed the effect of Exendin-4 on global protein expression pattern using LC-MS/MS Orbitrap system and label-free quantification in the presence of stressing amounts of palmitic acid (400uM). Dysregulated pathways were analyzed using Ingenuity Pathway Analysis software. Results were validated using Western blotting and RT-PCR.

Results:
Under lipotoxic conditions, a set of proteins related to lipid homeostasis were modulated by Exendin-4 aside with key canonical signaling pathways such as EIF2, ILK, PKA and Rho. Interestingly, the phosphorylation levels of MAPKs (JNK, ERK1/2 and p38) were clearly increased in the presence of Exendin-4 alone. In the presence of palmitic acid, Exendin-4 attenuated the MAPKs phosphorylation. By contrast, the heat shock response, known to relieve cellular stress, was not affected by Exendin-4 regardless the used conditions. Furthermore, cell viability assays have shown that exendin-4 alleviated the palmitic acid-induced cell death. Finally, Exendin-4 decreased the oil droplet accumulation in liver and adipose cells.
Conclusions:
In conclusion, identifying new pathways modulated by GLP-1 analogues provides insight into further beneficial effects of GLP-1 in energy homeostasis in glucose up-taking organs

Key Words: GLP-1, Proteomic profiling; diabetes; MAPKs;

Funding Agency: KFAS, RC14015001

Biochemistry

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Associations of Fetuin-A with Leukocyte Telomere Length and Human Telomerase Reverse Transcriptase in Patients with Acute Myocardial Infarction.

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Introduction:
Telomeres, tandem repeats of DNA sequences at the end of eukaryotic chromosomes, are maintained by human Telomerase Reverse Transcriptase (hTERT). Leukocyte telomere length (LTL) has been shown to be a risk marker of cardiovascular diseases (CVDs). Fetuin A, an anti-inflammatory glycoprotein, inhibits apoptosis of vascular smooth muscle cells and prevents heterotropic calcification. Low Fetuin A concentration has been shown to be associated with overproduction of inflammatory cytokines, mitral and aortic calcification and cardiac fibrosis. This study explores potential associations between LTL, hTERT and Fetuin A as potential markers in patients with Acute Myocardial Infarction (AMI).

Methods:
LTL (singleplex qPCR), hTERT (Enzyme Linked Immunosorbent Assay [ELISA]), Fetuin A (ELISA), Troponin I (Beckman Access), and lipid profile (DxC 800 analyzer) were measured in 144 patients with AMI and 192 age and gender matched healthy control subjects.

Results:
AMI patients had significantly ($p<0.05$) shorter (mean ± SD) LTL and lower (mean ± SD) hTERT levels compared to controls - [0.9±1.1 vs 4.5±3.9] and [23.0±5.5 vs 32.9±8.9 ng/ml] respectively. Levels of Fetuin A were significantly lower in patients with AMI compared to control subjects - [31.9±9.5 vs 38.5±12.9 ng/ml]. LTL significantly correlated negatively with Troponin I and Fetuin A levels ($r = -0.13$; $r = -0.36$). hTERT levels significantly correlated negatively with Troponin I ($r = -0.19$) and Fetuin A ($r = -0.28$). Binary logistic regression analysis showed that the odds ratio (OR) of having shorter LTL and lower hTERT were 2.1 (95%CI 1.5-6.2) and 1.6 (95%CI 1.2-8.8) respectively in patients with AMI compared to control subjects.

Conclusions:
Short LTL and lower levels of hTERT and Fetuin A are risk factors that may play significant roles in the pathogenesis of AMI. Estimation of LTL, hTERT and Fetuin A could be useful adjuncts for the identification of patients with high risk of CVDs.

Key Words: Fetuin A, Leucocyte Telomere Length, human Telome; Telomere Shortening;

Funding Agency: (KFAS) 2012-1302-05 and Kuwait University College of Graduate Studies Research Sector Grant number YM06/11.

Biochemistry

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Synergistic Neurotoxic Effects of Lead and Quinolinic Acid on Cultured Rat Embryonic Hippocampal Cells: Protection by Memantine

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Introduction:
Quinolinic acid (QA), an excitotoxic metabolite of the kynurenine pathway of tryptophan metabolism, is produced in response to inflammation and oxidative stress. Lead (Pb) a neurotoxic heavy metal, causes oxidative stress and thus may produce neurotoxicity by increasing QA production. In this study we investigated the in vitro synergistic neurotoxic effects of Pb and QA, and whether these effects could be abrogated by the NMDA receptor antagonist, memantine.

Methods:
We treated primary cultures of embryonic hippocampal cells from Wistar rats with different concentrations of Pb and/or QA without and with memantine. Cell viability was determined by MTT ["3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) tetrazolium reduction] and crystal violet assays. Cell cycle, apoptosis and necrosis were analyzed by flow cytometry. For cell cycle analysis, cells were stained with propidium iodide (PI); for apoptosis and necrosis analysis cells were stained with Annexin-V and PI. Number of neurons and astrocytes were determined by immunostaining the cultures with β3-Tubulin (Tuj1) and glial fibrillary acidic protein (GFAP) respectively.

Results:
Pb at 20 µg/dL and QA at 500 nM showed significant neurotoxic effects, as evidenced by decreased cell viability, increased apoptosis and mitosis, and decrease in the number of both astrocytes and neurons. At lower doses of both Pb and QA, significant synergistic neurotoxic effects were observed. Memantine (500 nM) was largely protective against the neurotoxic effects of both Pb and QA.

Conclusions:
These results suggest that the neurotoxic effects of both Pb and QA involve NMDA receptor activation and that memantine may be protective against Pb- and QA-induced neurotoxicity.

Key Words: Lead and Quinolinic Acid; Neurotoxicity; Memantine;

Funding Agency: RW01-14

Biomedical Engineering

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Optimization of Low-Level Light Therapy's Illumination Parameters for Spinal Cord Injury in a Rat Model

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Introduction:
Spinal cord injury (SCI) can result in complete or partial loss of sensation and motor function due to interruption along the severed axonal tract(s). SCI can result in tetraplegia or paraplegia, which can have prohibitive lifetime medical costs and result in shorter life expectancy. A promising therapeutic technique that is currently in experimental phase and that has the potential to be used to treat SCI is Low-level light therapy (LLLT). Preclinical studies have shown that LLLT has reparative and regenerative capabilities on transected spinal cords, and that LLLT can enhance axonal sprouting in animal models. However, despite the promising effects of LLLT as a therapy for SCI, it remains difficult to compare published results due to the use of a wide range of illumination parameters (i.e. different wavelengths, fluences, beam types, and beam diameter), and due to the lack of a standardized experimental protocol(s). Before any clinical applications of LLLT for SCI treatment, it is crucial to standardize illumination parameters and efficacy of light delivery.

Methods:
Therefore, in this study we aim to evaluate the light fluence distribution on a 3D voxelated SCI rat model with different illumination parameters (wavelengths: 660, 810, and 980 nm; beam types: Gaussian and Flat; and beam diameters: 0.1, 0.2, and 0.3 cm) for LLLT using Monte Carlo simulation

Results: The results, in general, showed that the wavelength had the most definite effect on LLLT fluence distribution, followed by beam size and beam type. These findings were verified by calculating the fluence accumulated in the SCI site.

Conclusions:
This study provides an efficient approach to guide researchers in optimizing the illumination parameters for LLLT spinal cord injury in an experimental model and will aid in quantitative and qualitative standardization of LLLT-SCI treatment.

Key Words: Low-level light therapy; Spinal cord injury rat model; Monte Carlo

Funding Agency: NONE

Community Medicine

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Predictors of Multiple Sclerosis Severity Score among Multiple Sclerosis Patients in Kuwait

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Introduction:
Multiple Sclerosis (MS) is a complex demyelinating autoimmune disorder. Several environmental and genetic factors have been shown to associate with MS severe clinical progression. Here we investigated the influence of different life style factors on MS clinical severity as assessed by MS severity Score (MSSS).

Methods:
A questionnaire was administered to 128 Kuwaiti MS patients recruited at Dasman Diabetes Institute MS clinic to assess the association between passive smoking, smoking status, food allergy, physical activity and education with MSSS. A multiple linear regression model was used to test the significance of associations of interest. Gender, history of blood transfusion, MS age of onset, marital status, and disease duration were included in the model to control for their confounding effects

Results:
Smoking status and passive smoking were not associated with MSSS. Patients with food allergy, have on average 1.33 higher MSSS compared to those without food allergy (β =1.33, p = 0.097). Patients with graduate or professional degree have on average 2.61 (1.68) lower MSSS compared to those with less than high school education (β = - 2.61, p = 0.082), (β = - 1.68, p = 0.109); respectively. Finally, patients who perform rigorous physical activity, score on average 2.03 lower on the MSSS compared to those with no physical activity (β = - 2.03, p = 0.005).

Conclusions:
Physical activity is significantly associated with reduced MSSS, while educational level is marginally significant at the 10% level. Physical activity and education level both contribute to a less severe MS clinical progression. Current MS management protocols should consider life style changes to improve the quality of life of MS patients.

Key Words: Multiple Sclerosis; Smoking; Physical Activity;Multiple Sclerosis severity

Funding Agency: None

Community Medicine

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One-Year Period Prevalence of and Factors Associated with Road Traffic Crashes among Kuwait University Students: A Cross- sectional Study

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Introduction:

Objectives: This cross-sectional study aimed to ascertain the one year period prevalence of road traffic crashes (RTCs) and their associated factors among students in various faculties of Kuwait University. The objectives of this study are to assess the prevalence of RTCs among Kuwait University students and examine the factors associated with RTCs.

Methods:
During December 2016, 1100 Kuwait University students 15 different colleges were asked to participate. Students who drive and/or are above 18 years old were eligible. Data collection was done using self-administered questionnaires. We computed the RTC prevalence during the past year and the frequencies of other variables. Statistically significant variables related to RTA on Chi-Square analysis were considered for inclusion in the multivariate analysis while evaluating various factors related to RTA.

Results:
Of 1465 participants, 71.5% were female, 56.4% were aged between 21 and 25 years, and 67.1% were Kuwaitis. One-year period prevalence of RTC was 38.9%. The multivariable logistic regression model showed that after adjusting for the influences of other variables in the model, participants were more likely to have had at least one RTC during the past one year if they habitually sped over limit (adjusted OR = 1.34; 95% CI: 1.03 – 1.75), crossed a red light (adjusted OR = 1.37; 95% CI: 1.04 –1.81), or if they have had three or more speeding tickets (adjusted OR = 2.14; 95% CI: 1.31 – 3.48) compared to those who reportedly had no RTC during the same period.

Conclusions:
A high one-year prevalence of RTCs was reported among Kuwait University students. Habitual speeding, having had three or more speeding tickets, and practice of crossing a red light and being a patient of epilepsy was significantly associated with at least one RTC during the past one year. Targeted education and enforcement of existing traffic laws may reduce the RTCs frequency in relatively young population.

Key Words: Road Traffic accidents; Kuwait university students; one year prevalence;

Funding Agency: None

Community Medicine

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Association of Mother's Perception of Overweight with BMI-for-Age and Other Factors among Preschoolers in Kuwait

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Introduction:

Mother's perception of her child's weight may play an important role in the high prevalence of childhood obesity in Kuwait. The primary aims of this study are to measure BMI-for-age among preschoolers in Kuwait, to assess their mother's perception of their child's weight status, and to assess the prevalence of and factors associated with mother's underestimation of their child's weight in this population.

Methods:

This cross-sectional study enrolled 458 mother-child pairs attending Kuwait Ministry of Health Primary Healthcare Centers in all governorates. Mothers of preschoolers aged 24 to 71 months were interviewed using a structured questionnaire consisting of 46 questions. Height and weight of the child were measured, and BMI-for-age was calculated using the standard WHO definitions. Overweight and obesity were defined as a BMI-for-age z-score +2 or +3 standard deviations above the standard WHO mean, respectively. A binary "underestimation" variable was defined and used as the dependent variable in multivariate logistic regression models to adjust for potential confounding factors.

Results:

In this study, 24.0% of children were obese or overweight while only 8.1% of mothers perceived their children as "overweight". Overall, 46.7% of mothers underestimated their child's weight. However, over 90% of mothers of overweight children underestimated their weight; 54.3% of mothers of obese children underestimated their weight; and 39% of mothers of normal weight children perceived them as "underweight." Mother's education with a bachelor's degree or higher was associated with less underestimation of the child's weight, but not any other sociodemographic characteristics.

Conclusions:

A majority of overweight and obese preschoolers' mothers underestimated their actual weight. This may be a contributing factor to the high prevalence of childhood obesity in Kuwait. Health promotion program planners should consider this issue to control childhood obesity.

Key Words: Mothers perception; Obesity; Childhood obesity;

Funding Agency: None

Community Medicine

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Knowledge of Preconception Care Among Female Students at Kuwait University

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Introduction:
Maternal behavior before, during, and after conception affects both the mother and the child's health. Although globally the benefits of preconception and antenatal health care are well recognized and the attention focused on them has grown substantially over the past decades, these practices remain under recognized in Kuwait. The aim of this study was to determine the level of knowledge and attitudes regarding preconception and antenatal care among female students at Kuwait University.

Methods:
A cross-sectional study design targeted 1200 female students at Kuwait University from 8 different colleges. Data were collected through a self-report questionnaire designed to assess knowledge related to preconception health and pregnancy.

Results:
There was a statistically significant difference between the eight colleges in terms of their knowledge of the timing of preconception care visits. Students from the Colleges of Medicine (20%), and Engineering and Petroleum (17.7%), were more knowledgeable about this topic than students from the Colleges of Education (9.1%) and Social Sciences (7.4%).

Conclusions:
Although great variability in preconception care knowledge was observed both within as well as between the eight selected colleges, general knowledge of this topic appears to be inadequate. Even colleges from the Health Sciences Center did not demonstrate superior knowledge. Since most students reported that preconception care visits should take place after marriage, it is important to introduce preconception care to all females in their reproductive age before marriage.

Key Words: Preconception Care; Antenatal Care; Pregnancy;

Funding Agency: None

Community Medicine

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The burden of acne vulgaris and its association with vitamin D deficiency among school students in Kuwait

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Introduction:
The prevalence of Acne Vulgaris (AV) among adolescents in Kuwait remained mostly unknown. Although AV is not fatal, it has an enormous impact on the quality of life of adolescents. This study aimed to estimate the prevalence of AV and its impact on the quality of life among students in public schools in Kuwait. The study also aimed to investigate the association between vitamin D level and AV.

Methods:
Cross-sectional study on 714 participants who were randomly selected from public school using multistage cluster random sample with probability proportional to size sampling. Vitamin D levels were measured in previous project using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Global Acne Grading System (GAGS) score was used to assess the severity of AV whereas Cardiff Acne Disability Index (CADI) was used to assess the impact of AV on quality of life. Unconditional logistic regression was used to investigate the association between vitamin D level and the presence or absence of AV.

Results:
Of 714 participants, 320 (44.8%; 95%CI: 41.1-48.6%) self-reported AV. By clinical examination, AV was found in 479 (67.1%; 95%CI: 63.5-70.5%). Those with AV reported no or minimum impact on the quality of life, the median (Interquartile) for CADI score was 1 (0-3). There was no significant association between vitamin D level and AV before or after adjusting for potential confounders.

Conclusions:
The prevalence of self-reported AV seems to be lower than that reported in other settings; while the prevalence of AV by clinical examination resembles that reported in many other countries. No association was found between vitamin D status and AV. It is important to improve vitamin D level among adolescents for several other health benefits regardless of its association with AV. Our study does not support providing vitamin D neither to treat nor to prevent AV.

Key Words: Acne Vulgaris; Vitamin D deficiency; Global Acne Grading System;

Funding Agency: None

Community Medicine

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Diabetes Self-Management: A factor associated with health related quality of life in patients with diabetes

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Introduction:

Purpose: This study aimed to assess health-related quality of life (HRQOL) among patients with diabetes attending primary health care (PHC) diabetes clinics in Kuwait, and to examine the factors associated with their HRQOL.

Methods:

A cross sectional study was conducted among 503 patients with diabetes attending 26 PHC diabetes clinics in Kuwait. Self-administered questionnaire was filled by each participant after signing an informed consent. The questionnaire included participants' socio-demographic and clinical characteristics. It also comprised the Diabetes Self-Management Questionnaire (DSMQ) to assess patients' DSM. SF12 was employed to assess the HRQOL, producing two outcomes: Physical health composite (PHC) and Mental health composite (MHC).

Results:

The mean age of participants was 52.06±10.8 years, 53.1% were males, and 49.0% were Kuwaitis. The median DSM sum score was 6.5. Males showed significantly better median DSM sum score than females. The overall median score of HRQOL was 61.7/100 with better median score of physical health composite (PHC) than mental health composite (MHC) of quality of life (66.7/100 and 56.7/100, respectively). Multivariate analysis revealed significant direct association between DSM and better PHC and MHC. It also showed that female gender, reporting two or more diabetes complications were significantly correlated to poor PHC.

Conclusions:

Kuwaiti patients with diabetes showed a modest level of HRQOL. Patients' DSM, gender, and diabetes complications, were significant independent correlates to HRQOL. Appraisal of HRQOL as an essential component of diabetes management in clinical settings is suggested. Further intervention studies to examine the impact of good DSM on HRQOL improvement are needed.

Key Words: Diabetes mellitus; Quality of life; Diabetes self-management care;

Funding Agency: NONE

Community Medicine

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Exposure to active and environmental tobacco smoke and prevalence of allergic morbidity among young adults in Kuwait.

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Introduction:

Objectives: This study aimed to assess the prevalence of tobacco smoking (active and passive), assess the prevalence of a tobacco smoke related allergic morbidity including asthma, eczema, allergic rhinitis, and examine the association between tobacco smoking and allergic morbidity (one or more of asthma, eczema, and rhinitis vs. none) among young adults in Kuwait.

Methods:

During March 2017, we conducted this cross-sectional study among Kuwait University students. Participants of any gender, aged 20 to 39 years were enrolled as a sample of convenience. A structured questionnaire was used to collect data on socio-demographics, tobacco smoking (active and passive), and physician-diagnosed allergic morbidities. Bivariate association of demographics and smoking variables with the outcome variable (at least one allergic condition vs. none) were evaluated using Chi-square and logistic regression analysis.

Results:

Of 1412 invited students, 1254 (88.8%) participated. Of whom, 56.2% were female and 88.2% were Kuwaiti. Prevalence of active smoking was 18.8%. Furthermore, 96.6% participants have one or more smokers in the family and 91.7% spent weekly at least one hour at public places (e.g. café, dewanyia) wherein people smoke. Prevalence of asthma, rhinitis, and eczema was 20.3%, 16.4%, and 9.9%, respectively. Logistic regression analysis showed that participants spending four or more hours at public places were significantly more likely to have at least one allergic morbidity compared to those who spent no time in such places (Crude OR = 1.8; 95% CI: 1.1-2.8; $p < 0.001$).

Conclusions:

We recorded high prevalence of active smoking, passive smoking, and allergic morbidities in this study population. Spending weekly 4 or more hours at public places wherein people smoke was significantly associated with at least one allergic morbidity. Targeted educational efforts may help reduce the exposure to environmental tobacco smoke and resultant allergic morbidities.

Key Words: Tobacco; Smoke; Allergy;

Funding Agency: None

Community Medicine

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Low back pain among public high school students in Kuwait in relation to weight of school bag

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Introduction:

Published data on low back pain (LBP) amongst adolescents in Kuwait and Middle East are scarce. The association between school bag weight and LBP amongst students remains under debate worldwide. This study aims to estimate the prevalence of LBP amongst public high school students (14 to 19 years) in Kuwait and its association with school bag weight.

Methods:

A cross-sectional study using multistage cluster sampling with probability proportional to size method was conducted on 950 public high school students from all governorates. Data on LBP were collected through interviews using a standardized questionnaire. The students' height, weight, and weight of their school bags were measured using appropriate weight and height scales. Logistic regression analysis was used to investigate the association between the weight of school bags and LBP while adjusting for potential confounders.

Results:

The estimated lifetime, 6-month, and 1-month prevalence of LBP were 70.3% (95% CI: 67.30–73.21 %), 49.1% (95% CI: 45.83–52.28%), and 30.8% (95% CI: 27.81%–33.78%) respectively, with significantly higher prevalence amongst females compared to males (p-value<0.001). The absolute weight of school bags was not significantly associated with LBP neither in univariate nor multivariate analysis. The relative weight of school bags (as percentage of body weight) was significantly associated with LBP in univariate analysis but not multivariate analysis. Students' perception towards their bag weight was found to be significantly associated with LBP throughout the analysis (p-value<0.001).

Conclusions:

LBP amongst high school students in Kuwait is common with a prevalence resembling that of high-income countries. Our data suggests that students' perception toward their bag weight is more important than the actual weight. Current recommendations about school bag weight are not supported by evidence and should be revised to take into account the perception of school bag weight.

Key Words: Prevalence; Back pain; Bag weight;

Funding Agency: None

Community Medicine

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A matched case-control study of risk factors for colorectal cancer in Kuwait

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Introduction:
Cancer of colon and rectum (colorectal) is one of the most common cancers worldwide. There is a paucity of published data on the risk factors in colorectal cancer from the Middle-East. Therefore, this matched case-control study examined the risk factors associated with colorectal cancer in Kuwait.

Methods:
Multivariable conditional logistic regression model showed that cases were 4.3 times more likely to have had attainted obesity in their lifetime compared to controls (mORadj = 4.3; 95% CI: 1.6 – 11.4). Additionally, compared to controls, cases rarely consumed fruits and vegetable (mORadj = 20.8; 95% CI: 4.4 – 99.5), tended to consume red meat 2-3 times a week (mORadj = 3.8; 95% CI: 1.6 – 8.7) or more than 4 times a week (mORadj = 9.4; 95% CI: 2.5 – 35.4). Moreover, cases compared to controls frequently (nearly every week) suffered from constipation (mORadj = 5.6; 95% CI: 1.9 16.5). However, compared to controls, colorectal cases tended to report less frequently the history hypercholesterolemia (mORadj = 0.3; 95% CI: 0.2 – 0.7) or diabetes mellitus type II (mORadj = 0.4; 95% CI: 0.2 – 0.8).

Results:
Multivariable conditional logistic regression model showed that cases were 4.3 times more likely to have had attainted obesity in their lifetime compared to controls (mORadj = 4.3; 95% CI: 1.6 11.4). Additionally, compared to controls, cases rarely consumed fruits and vegetable (mORadj = 20.8; 95% CI: 4.4 99.5), tended to consume red meat 2-3 times a week (mORadj = 3.8; 95% CI: 1.6 8.7) or more than 4 times a week (mORadj = 9.4; 95% CI: 2.5 35.4). Moreover, cases compared to controls frequently (nearly every week) suffered from constipation (mORadj = 5.6; 95% CI: 1.9 16.5). However, compared to controls, colorectal cases tended to report less frequently the history hypercholesterolemia (mORadj = 0.3; 95% CI: 0.2 0.7) or diabetes mellitus type II (mORadj = 0.4; 95% CI: 0.2 0.8).

Conclusions:
Overcoming identified pitfalls in dietary pattern and lifestyles may help minimize the colorectal cancer risk in Kuwait and perhaps other countries in the region.

Key Words: Colorectal cancer; Case-control study; Risk factors;

Funding Agency: None

Community Medicine

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Association between smoking, physical activity and mental health status amongst university students in Kuwait

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Introduction:
Mental health such as depression, anxiety and stress are widely prevalent among adults with majority starts to have these problems during adolescence. The associations between smoking and physical activity with mental health status need to be further examined and understood.
Objectives
This study aimed to i) assess the prevalence of mental health problems, smoking and physical activity among university students in Kuwait; ii) examine the association between smoking and physical activity with their mental health status.

Methods:
A cross-sectional study was conducted among 1158 students in Kuwait's public and private universities using self-administered anonymous questionnaire, which included questions on participants' socio-demographic characteristics, DASS-21 test to assess students' mental health status, Godin test to assess physical activity levels, the Fagerstorm nicotine dependency test to evaluate smoking dependence. Statistical analysis involved Chi-square test, Spearman's correlation, and binary logistic regression model. The significance level was at p-value < 0.05.

Results:
The prevalence of depression, anxiety and stress among students was 44.8%, 59%, and 44.2% respectively. About 15% of them were smokers (significantly higher in males) and 35.6% were physically inactive (significantly higher in females). Multivariate analysis revealed that younger age and female gender were significant correlates to all mental health problems. However, low monthly income was associated with depression and stress. Poor academic performance was also associated with stress. Smoking was a significant correlate to depression and anxiety, while physical inactivity was a correlate to stress.

Conclusions:
Prevalence of mental health problems were high in university students. Socio-demographic factors, physical inactivity, and smoking correlated to poor mental health status. Cohort studies to understand the causality of mental health problems in relation to smoking and physical inactivity are needed.

Key Words: Mental Health; Smoking; Physical activity;

Funding Agency: None

Community Medicine

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Cost analysis and potential cost savings in transurethral resection of prostate procedure for treatment of benign prostatic hyperplasia in Kuwait.

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Introduction:
Benign prostatic hyperplasia BPH) is a condition where the prostate gland enlarges leading to different degrees of urinary tract obstruction. The overall prevalence worldwide is 6% among men aged 4564. The objective of this study is to conduct a costanalysis of transurethral resection of prostate (TURP) for cases of BPH from the perspective of healthcare providers.

Methods:
The study was conducted in a public hospital with 866 beds that provides secondary care in Kuwait. Sources of costing information include Ministry of Health (MOH) Financial Report, Medical Stores Administration and National Health Information Centre Reports. Doctors and nurses involved in carrying out the procedure were interviewed to understand the usual practice of TURP and to obtain additional information for validation and refinement of the costing calculation. A combination of stepdown and activity based costing was carried out to impute the total cost.

Results:
The overall length of stay of patients that undergone TURP is 5 days. The cost of TURP is KD 475 (USD 1,566) per patient, which is equivalent to 3.3% of percapita GDP. Staff salary is the main component of the cost contributing 52% of the total cost, followed by drugs (13%), equipment (12%) and consumables (10%). Sensitivity analysis showed that the minimum cost of TURP procedure is KD 434 (USD 1,441) and the maximum cost is KD 569 (USD 1,876). Based on 6% prevalence BPH for population in age 4564 years, 4,327 cases will be potentially operated yearly with the cost of KD 2.1 million (USD 6.8 million). If these cases were operated on a daycare surgery, there will be an annual cost saving of KD 765,915 (USD 2.52 million).

Conclusions:
The cost of TURP is moderate but may potentially consume significant amount of financial resources for health care services in Kuwait in the future with the aged population. There will a significant costsavings if the hospital changes their practice to the more efficient daycare surgery

Key Words: Cost-analysis; Transurethral resection of prostate; Benign prostatic

Funding Agency: None

Community Medicine

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Patient satisfaction: Public vs Private Hospitals in Kuwait

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Introduction:

Patient satisfaction with the healthcare being provided is an essential part of the healthcare system, and increasing satisfaction has been associated with better patient outcomes. Measurement of patient satisfaction levels with various aspects of the healthcare system allows recognition of where deficiencies lie and can help shape policy making decisions. The objective of this study was to assess satisfaction of patients between public hospitals and private hospitals.

Methods:
This cross sectional study was conducted in the outpatient departments of four public and two private hospitals in Kuwait. Self-administered questionnaires were used to collect data. The questionnaire consisted of socio-demographic factors and short form of the standardized Patient Satisfaction Questionnaire (PSQ- 18) questionnaire. The answers to each of the PSQ- 18 questions were via a five-point Likert scale ranging from one (strongly agree) to five (strongly disagree). Mean scores were calculated for each part. The Statistical Package for Social Science (SPSS) was used for data analysis. The mean satisfaction scores were compared using the independent t-test.

Results:
There was a statistically significant difference ($p < 0.05$) between mean patient satisfaction scores in public versus private hospitals with regard to all aspects if the PSQ-18 except for the financial aspect, which was not significant ($p > 0.05$).

Conclusions:
Overall satisfaction rate was significantly ($p < 0.05$) higher in the private hospitals as compared to the public hospitals regarding all aspects of the PSQ- 18 questionnaire, with the exception of financial aspect, where although the difference in the mean scores was higher in the private sector as compared to public, statistical significance was not established ($p > 0.05$)

Key Words: Patient satisfaction; Outpatient departments; Kuwait;

Funding Agency: None

Community Medicine

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Survey of Knowledge, Attitudes and Practices regarding Childhood Vaccinations among Employed Adults in Kuwait

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Introduction:

The anti-vaccination movement has reduced vaccination rates in some countries. This study's aim is to assess parental knowledge, attitude, and practice of childhood vaccination in Kuwait.

Methods:
This cross-sectional study enrolled 736 working parents 8 government ministries. The questionnaire consisted of 45 questions in 4 sections (sociodemographic, knowledge, attitudes, and practices). The parental attitude toward childhood vaccination survey was used to calculate a "vaccination hesitancy" score (range: 0-100%). A validated "high" hesitancy score is considered ≥50%. A vaccination knowledge score was also developed (range: 0-100). Multivariate logistic and linear regression models were used to assess associations, as appropriate.

Results:
Prevalence of "high hesitancy" was 12%. Participants expressed concern regarding safety (39%) and severe side effects (36%) of vaccines. Prevalence of ever delaying or not vaccinating a child previously were 18.4% and 14.7%, respectively. Hesitancy was significantly lower among those with ≥3 children compared with fewer children (AOR=0.49; $p<0.03$). The overall trust in doctors was high and negatively associated with hesitancy ($p<0.001$). Mean knowledge score was 52.6%, and 67% answered "some vaccines may cause autism" incorrectly. Knowledge score was higher in Kuwaiti's than non-Kuwaiti's (Adjusted mean difference = 5.4%, p=0.007) and those with income <1000KD compared to income >1500KD (5.8%, p=0.004). Barriers to vaccination include fear of side effects (40%), fear of becoming diseased for which he/she was vaccinated (36%), and the lack of time (23%).
Conclusions:
Hesitancy towards vaccination is low and the practice of vaccination is generally high among working parents in Kuwait. However, substantial number of respondents expressed concerns about the likelihood of serious side effects and development of autism following of vaccination of their children. Vaccination programs should consider these concerns when developing awareness programs and policies.

Key Words: Knowledge; Attitude; Vaccination;

Funding Agency: None

Community Medicine

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Childhood Maltreatment: A Correlate of Mental Health Problems among Adolescents and Young Adults

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Introduction:
Child maltreatment is a risk factor for detrimental effects that may extend to adulthood. This study aimed to examine the association between exposure to childhood maltreatment, and students' mental health and self-esteem.

Methods:
A cross-sectional study enrolled a representative sample of 1270 university students. An anonymous self-administered questionnaire was used that included students' socio-demographic characteristics, history of exposure to childhood physical and/or emotional maltreatment, DASS-21 to assess mental health status, and Rosenberg self-esteem scale. Chi-square test and binary logistic regression models were applied.

Results:
Among participants, 49.6%, 63.0%, and 43.8% reported having depression, anxiety, and stress respectively. Moreover, 22.5% and 18.6% reported exposure to childhood physical and emotional maltreatment, respectively; while 12.7% reported both types of maltreatment. Multivariate analysis revealed that experiencing childhood physical and emotional maltreatment were independent contributors to reported depression and anxiety; while exposure to only emotional maltreatment contributed to reporting stress. Female gender, low GPA, childhood enrollment in private schools, no/low number of close friends, were other contributors to mental health problems. Participants' median score of self-esteem was 17/30, and only childhood emotional maltreatment was a significant correlate to low self-esteem after adjustment for other confounders.

Conclusions:
Mental health problems, and experiencing childhood physical and emotional abuse were relatively highly prevalent among university students. Childhood corporal and emotional maltreatment were independent correlates of adolescents and young adults' mental health problems. Experiencing childhood emotional maltreatment predicted low self-esteem. Further research to assess cultural factors associated with childhood maltreatment is recommended.

Key Words: Child maltreatment; Mental health status; Adolescents;

Funding Agency: None

Community Medicine

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Knowledge, Attitude, and Practice of Bariatric Surgery among the Adult population of Kuwait

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Introduction:

There is an epidemic of obesity encompassing 13% of the world's adult population. Kuwait ranks as the second most obese population worldwide. This tremendous rise in the prevalence of obesity is associated with an increase in obesity related co-morbidities (e.g. type 2 diabetes, hyperlipidemia, hypertension, obstructive sleep apnea, heart disease, and hormonal disorders). Thus, bariatric surgery is expanding exponentially to meet this global and local epidemic of morbid obesity and it seems to be the only effective therapy for it.

Methods:
A cross sectional study was conducted on randomly selected employees from 6 ministries in Kuwait. Data was collected using a self-administered questionnaire. We also used standardized scales to measure the participants' height and weight. Associations were analyzed using logistic regression.

Results:
Out of 1453 questionnaires distributed, 1151 (79.2%) were completed. In our study, the prevalence of bariatric surgery was 7.8%. Gender, nationality, number of children and educational level were statistically significant factors associated with the practice of bariatric surgery. All co-morbidities except for diabetes, and all aspects of attitude towards bariatric surgery along with the knowledge of its complications were statistically significant with undergoing the surgery.

Conclusions:
We estimated the prevalence of bariatric surgery in Kuwait to be 7.8%, which is slightly lower than what we hypothesized. Different social factors and patterns of knowledge and attitude were associated with having the surgery. Future studies aiming to evaluate the knowledge, attitude, and practice of bariatric surgery among the adult population of Kuwait should be conducted among a more diverse sample for more precision followed by awareness campaigns to educate the public on this practice.

Key Words: Bariatirc Surgery in Kuwait; Obesity in Kuwait; BMI in Kuwait;

Funding Agency: None

Community Medicine

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Prevalence and factors associated with self-reported noncompliance with mandatory seatbelt use law among adults in Kuwait

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Introduction:
The cross-sectional study assessed the prevalence of self-reported noncompliance with mandatory seatbelt use law while driving and examined the factors related with noncompliance with seatbelt use law in adult working population in Kuwait.

Methods:
During October 2017, 822 public sector employees aged 21-60 years were enrolled in this study. Data were collected using a self-administered questionnaire. Prevalence of self-reported noncompliance with mandatory seatbelt use while driving was computed, and the factors associated related to noncompliance with seatbelt use law were examined using multivariable logistic regression model.

Results:
Of 822 participants, 64.4% were female, 56.6% aged between 21 and 30 years, 86.5% Kuwaitis, and 70.3% had college and/or university education. Prevalence of self-reported noncompliance with mandatory seatbelt use law while driving was 55.5%, whereas, prevalence of noncompliance with self-reported mandatory use seatbelt laws as a passenger was 80.9%. The variables independently related to noncompliance with mandatory seatbelt use law included 'the belief that seatbelt offers no protection during RTC' (adjusted OR (aOR) = 2.3; 95% CI: 1.1 - 4.6), 'ever fined for not wearing seatbelt' (aOR = 4.0; 95% CI: 2.7-6.0), 'being unaware of seatbelt law in Kuwait (aOR = 1.6; 95% CI: 1.1 - 2.1), 'being regular user of mobile phone while driving (aOR = 1.6; 95% CI: 1.02 - 2.4) or 'suggesting no penalty for noncompliance with seatbelt law (aOR = 2.0; 95% CI: 1.03 - 3.8).

Conclusions:
A high prevalence of self-reported noncompliance with mandatory seatbelt use law in the adult working population was recorded. Unawareness of seatbelt law, benefit of seatbelt use, attitude towards use of seatbelt use were main contributors to noncompliance with seatbelt law. Focused educational campaign along with strict enforcement seatbelt law may enhance the seatbelt usage among drivers. Future studies may look at the impact of the such efforts.

Key Words: Noncomplinace; Seatbelt law; Adults;

Funding Agency: None

Community Medicine

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Knowledge beliefs and barriers toward colorectal cancer screening among older adults in Kuwait: a cross-sectional study

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Introduction:
Colorectal cancer (CRC) is the third most common cause of cancer deaths worldwide with more than 550,000 annual deaths. CRC is the most common cancer among males and second most common among females in Kuwait. Approximately, 747 cases of CRC were diagnosed during 2000-2009 with 93 deaths during this period. The age-adjusted incidence rates for CRC among Kuwaiti males have increased by about five folds over the last 33 years.

Methods:
This study aims to evaluate knowledge, beliefs, and identify barriers toward CRC screening for individuals 45 years and older using a cross-sectional design. Data were collected from 1,118 individuals attending general hospitals and primary health care clinics using convenient sampling from the six governorates in Kuwait. Men and women who were not diagnosed with CRC were invited to participate.

Results:
About 51.7% of the participants have never heard of CRC screening. About 67.5% of participants with elementary education or less have never heard of CRC screening. Only 38.8% think 50 years or older is the age for CRC screening. Around 61% believe that CRC can be present without any symptoms. There is significant association between ever heard of CRC/CRC screening and education level, nationality, and income. Only 13.4% believe that colonoscopy screening is not effective in detecting CRC or its precursors like polyps and 67.1% are not up-to-date on their CRC screening. Finally, the most common barriers to CRC screening among those never been screened are "having no symptoms" (40.0%), "not aware of CRC screening by colonoscopy" (36.1%), and "waiting long time for an appointment" (36.0%).

Conclusions:
Findings indicate that many participants older than 45 years old are unware of CRC or CRC screening. This knowledge is mainly low among people with low education, non-Kuwaiti Arabs, income less than 1000KD. Awareness campaigns and better communications between primary care physicians and patients at risk should be established.

Key Words: Colorectal Cancer; Colonoscopy; Screening, Kuwait;

Funding Agency: None

Community Medicine

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Dysmenorrhea among High-school Students and its Associated Factors in Kuwait

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Introduction:

Although dysmenorrhea is not a serious health issue, it can cause a substantial burden on individuals and communities. There is no data on the prevalence of dysmenorrhea in Kuwait; and the data from Arab states in the Gulf region or the Middle East is scarce. Objectives: This study aimed to estimate the prevalence of dysmenorrhea among female public high-school students in Kuwait and investigate factors associated with dysmenorrhea.

Methods:

A cross-sectional study using multistage cluster sampling with probability proportional to size method was carried out on 763 twelfth grade female public high-school students in five governorates. We used face-to-face interview with a structured questionnaire to collect data on dysmenorrhea and presumed risk factors. Weight and height of the students were measured using appropriate weight and height scales in a standardized manner. The association between dysmenorrhea and potential risk factors was assessed using multiple logistic regression.

Results:

The one-year prevalence of dysmenorrhea was found to be 85.6% (95%CI: 83.1-88.1%). Of the participants with dysmenorrhea, 26% visited a public or a private clinic for their pain and 4.1% were hospitalized for their menstrual pain. Furthermore, 58.2% of students with dysmenorrhea missed at least one school day and 13.9% missed at least an exam. Age of menarche (p-value=0.005), regularity and flow of the menstrual period (p-value=0.025, p-value=0.009; respectively), and drinking coffee (p-value=0.004) were significantly associated with dysmenorrhea in multivariate analysis.

Conclusions:

Dysmenorrhea seems to be highly prevalent among female high-school students in Kuwait, resembling that of high-income countries. Because of the scale of the problem, utilizing school nurses to manage students with dysmenorrhea and referring suspected cases of secondary dysmenorrhea is recommended.

Key Words: Dysmenorrhea; Risk Factors; Prevalence;

Funding Agency: None

Cytopathology

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Hormone receptors and HER2 expression in fine needle aspirates from metastatic breast carcinoma in Kuwait - Role in patient Management

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Introduction:
Estrogen receptors (ER), progesterone receptors (PR) and epidermal growth factor (HER2) are important prognostic factors which dertermine management of breast carcinoma. In our study we determined them by immunohistochemistry (IHC) on cell blocks from fine needle aspirates (FNA) of metastatic breast carcinomas to axillary lymphnodes and compared them with that reported in the primary breast carcinoma (PBC). The aim was to document any change in the expression of ER, PR and HER2 in the metastatic tumor which would guide future management.

Methods:
ER, PR and HER2 by IHC and HER2 oncogene by Fluorescent in-situ hybdridisation [FISH] were studied on cell blocks of FNA of axillary lymphnodes in 53 of 94 cases of PBC in HMJCSS during 2013-2016.

Results:
In 25 of 38 (65.8%) ER, PR+ PBC the metastasis on FNA was ER, PR+ while all the 15 (28.3%) ER, PR- PBC remained negative in the metastatic tumor. In 10 of 11 (91%) of HER2-IHC+ PBC the metastatic tumor was positive for HER2-IHC. In 7 of 32 (21.9%) HER2 negative PBC, HER2-IHC was positive in the metastatic tumor. HER2-FISH was performed in 37 cases on FNA which included 27 equivocal and negative cases of HER2 on FNA and ten HER2+, ER, PR- cases by IHC on FNA. Six of 37 were HER2 amplified/positive while 9 and 19 remained equivocal and negative for HER2 copy number and 3 were not interpretable. All the HER2-FISH positive cases were positive by IHC. In our study, 34.2% of ER, PR+ cases of PBC became ER, PR- in the metastatic tumor and 21.9% of HER2-IHC negative PBC were HER2-IHC+ in the metastatic aspirate.

Conclusions:
ER, PR and HER2 can be evaluated by IHC in cell blocks of FNA material from metastatic lymphnodes with fair reliability. A change in receptor status (34.2%) and HER2 status (21.9%) was documented in the metastatic tumor which is of great clinical significance as these patients warrant a change of therapy and management.

Key Words: Metastatic breast carcinoma; Hormone receptors; HER2;

Funding Agency: Kuwait University-MG01/15

Dentistry

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Vital pulp therapy of immature permanent molars with long term follow up

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Introduction:

Deep caries or traumatic injuries can arrest the development of immature tooth resulting in a tooth with short roots wide-open apex, and thin dentinal walls. Vital pulp therapy (VPT) is a conservative approach aimed at treating reversible pulpal injuries by preserving the vitality of the tissues and sealing the pulp in order to prevent further microbial contamination.

Methods:
Four cases of cariously exposed immature vital first permanent molars were treated with mineral trioxide aggregates (MTA) with the purpose of continued maturogenesis of the roots.

Results:
All the cases treated with MTA demonstrated successful out come up to 5 years Clinical and radiographic follow up

Conclusions:
The immature permanent tooth had an excellent capacity to respond to apexogenesis. Whether dealing with caries or trauma, as long as the clinical treatment is performed quickly and properly. Whenever the tooth is vital and the apex is open, apexogenesis should be considered as the first option of treatment, rather than conventional endodontic treatment.

Key Words: Pulp therapy; Immature teeth; Mneral trioxide aggregates;

Funding Agency: None

Dentistry

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Dentists' perception, knowledge, and clinical management of molar-incisor hypomineralisation in Kuwait: A cross-sectional Study

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Introduction:
Molar-incisor Hypomineralisation (MIH) is considered as a global dental problem. There is little knowledge among general dental practitioners (GDPs) and dental specialists (DSs) about this condition in different parts of the world, particularly in Gulf Cooperation Council (GCC) countries. Hence, this study has been carried out to assess the knowledge of GDPS and DSs in Kuwait about MIH condition, its clinical presentation and with MIH.

Methods:
A structured questionnaire was distributed to 310 attendees of the 18th Kuwait Dental Association Scientific Conference, Kuwait. Data concerning demographic variables, prevalence, diagnosis, severity, training demands and clinical management of MIH were collected.

Results:
A response rate of 71.3 % (221/310) was reported. 94% of respondents noticed MIH in their practice. Yellow/brown demarcation has been observed as a common clinical presentation (>50%). Almost 10-20% of MIH prevalence has been reported by the participants. Resin composite was the dental material often used in treating MIH teeth (~65%), and fewer than half would use it for treating moderately affected molars. Most respondents would use preformed metal crowns for severe MIH (63%). Dental journals were the information source for DSs; whereas, the internet was the information source for GDPs. Child's behaviour was the main reported barrier for treatment of MIH affected children. Many GDPs felt unconfident when diagnosing MIH compared to dental specialists. Respondents supported the need to investigate MIH prevalence and to receive a clinical training.

Conclusions:
Molar incisor hypomineralisation is a recognised dental condition by practitioners in Kuwait. GDPs reported low levels of confidence in MIH diagnosis which necessitates conducting continuing education courses to provide high- quality dental care for children management.

Key Words: Molar incisor hypomineralisation; Perception; General dental

Funding Agency: None

Dentistry

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Prevalence of Molar Incisor Hypomineralisation among Schoolchildren in Kuwait

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Introduction:
The aim of this study was to determine the prevalence of molar incisor hypomineralisation (MIH) among schoolchildren in Kuwait.

Methods:
This cross-sectional epidemiological survey included a total of 631 children aged 8 to 11 years attending government primary and intermediate schools from 4 governorates of Kuwait. Clinical examinations were performed using a mouth mirror and periodontal probe in the fixed and mobile school dental clinics. All data were collected in a record chart designed for this study in which European Academy of Paediatric Dentistry (EAPD) diagnostic criteria was used for scoring MIH. Each molar and incisor was examined for the presence and severity of demarcated opacities. Lesions 2mm in diameter or larger were included. Hypoplasia and post eruptive enamel break down were distinguished by means of visual inspection of the borders of the defect. Surfaces that were examined were the buccal, lingual/palatal and occlusal surface of permanent first molars and labial surfaces of upper and lower incisors. Chi square tests were used for testing the associations of the variables with the prevalence of MIH.

Results:
The mean age of the children examined was 9.7 years. The gender distribution was 48% male and 52% female. Overall the prevalence of MIH in the sample was 42%. There was a significant difference in the occurrence of MIH between governorates. The prevalence of MIH varied from 27 to 66% across the various governorates ($p<0.001$). Also, higher prevalence was observed in females (45%) compared to males (38%) ($p=0.036$). There was no significant difference in the prevalence of MIH with age.

Conclusions:
MIH prevalence is high and must be taken into account when planning dental care. The early identification of children with MIH will allow monitoring so that remineralisation and preventive measures can be instituted. Oral health education must be emphasised early and parents should be educated on the importance of regular check-ups.

Key Words: Molar Incisor Hypomineralisation; Schoolchildren; Kuwait;

Funding Agency: None

Dentistry

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The influence of different components of dental esthetics on social perception

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Introduction:

To determine how different components of dental esthetics affect the social perception of laypersons in Kuwait, and whether these perceptions differ among genders.

Methods:
Frontal facial photographs of four volunteers were used to build a questionnaire to assess the effect of three different components of dental esthetics: color, mal-alignment and form on social perception. Each volunteer had four images, one representing each dental component; and a fourth one with ideal smile as control. The dental components were scored using Likert scales based on four aspects of social perception, attractiveness, intelligence, popularity and trust.

Results:
The 282 participants consisted of 151 (53.5%) females and 130 (46.1%) males. The subjects' photographs with ideal smile were rated higher when compared to color, in terms of social perception. This difference was statistically significant (p-value <0.01). Both genders were affected the most by color, however, males were less affected by mal-alignment than females (p-value <0.01)

Conclusions:
Tooth color had the greatest impact on social perception followed by mal-alignment, while tooth form had the least impact on social perception.

Key Words: Dental esthetics; Social perception; Comparison between genders;

Funding Agency: None

Dentistry

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Correlations between General Oral Health Assessment Index items among parents and teachers of special needs schoolchildren in Kuwait

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Introduction:
The aim of this study was to assess oral health as a quality of life and evaluate correlations between General oral health assessment Index (GOHAI) items in parents and teachers of special needs schoolchildren in Kuwait.

Methods:
Impact of perceived oral health was measured by 12 GOHAI questions, which evaluated three dimensions of oral health-related quality of life: (1) physical function, (2) pain or discomfort, and (3) psychosocial function. The GOHAI questions had a 3-point scale (always, sometimes, never). Pearson's correlation coefficient (r) was used to measure the inter-item and item-scale correlations among all the respondents. The internal consistency was measured by Cronbach's alpha.

Results:
The response rates were 92% (n=308) among parents and 75% (n=112) among teachers. Two thirds (66%) of parents and three fourths (76%) of teachers were always able to swallow comfortably. About 40% of parents and 37% of teachers were able to eat without discomfort. Altogether, 43% of parents and 37% of teachers were always pleased and happy with the looks of their teeth. All the inter-item correlations were positive. The strongest inter-item correlations were observed between 'uncomfortable eating in front of people' and 'able to eat without discomfort' (r=0.52); 'limit contacts with people' (r=0.52) and 'self-conscious of teeth' (r=0.48). There was also a strong correlation between 'being able to eat without discomfort' and 'having trouble biting or chewing' (r=0.46); 'being unable to speak clearly' (r=0.44). The weakest correlations were between 'being pleased with look of teeth' and 'limiting food because of teeth' (r=0.12). Cronbach's alpha (0.83) showed a high degree of internal consistency between different GOHAI items.

Conclusions:
The GOHAI could be used as a practical instrument for measuring oral health-related quality of life and it seemed to provide important information about oral symptoms, psycho-social and functional problems.

Key Words: GOHAI; Parents; Special needs schools;

Funding Agency: None

Dentistry

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Cephalometric dental values for Kuwaiti adults with a malocclusion

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Introduction:
The aim of this study was to retrospectively evaluate cephalometric dental values among Kuwaiti adults and to compare these to Middle-Eastern norms.

Methods:
Lateral cephalometric radiographs for 120 Kuwaiti adults (58 males, 62 females) aged 18-40 years, regardless of malocclusion were digitally traced by a single examiner using Dolphin® version 11. Statistical analysis was performed using IBM SPSS software version 21.0. Descriptive statistics including mean and standard deviation were calculated for the cephalometric measurements. The significance level was $p < 0.05$.

Results:
The cephalometric dental values for Kuwaiti adults revealed a mean upper incisor inclination of 115.95° ± 7.4, interincisal angle 119.2° ± 14.4, increased overjet (4.66 mm ± 2.7) and a reduced overbite (0.30 mm ± 2.3). Kuwaitis had increased maxillary incisors to the maxillary plane angle (115.95° ± 7.4), similar mandibular incisor to mandibular plane angle (94.25° ± 7.10), similar interincisal angle and slightly decreased lower incisor tip to A-Pogonion line (3.42 mm ± 2.99) compared to the Jordanian adults.

Conclusions:
It is recommended to use the obtained Kuwaiti adult cephalometric dental values as a standard for orthodontic treatment planning.

Key Words: Cephalometric dental values; Kuwaiti adults; Malocclusion;

Funding Agency: None

Dentistry

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Characterization of the Time Dependence of the Mechanical Properties and Associated Chemical Reactions of Biodentine Following Preparation

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Introduction:

Biodentine (Septodont, Saint Maur des Faussés, France) is novel dental cement based on hydrated tricalcium silicate compounds. It is being used in a variety of dental clinical applications. Hence in a variety of clinical application, knowing more details regarding the reaction involved during the setting of this cement, as well as the strength development over time following preparation will assist clinicians to a better understanding of its material properties.

Methods:
Samples of the cement to be investigated were prepared according to the manufacturer's instructions. Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), and indirect tensile strength test (DTS) were conducted according to literature guidelines.

Results:
FTIR techniques offer powerful tools for monitoring the complex chemical reactions taking place during the hydration process of Biodentine. The development of the phases, such as tricalcium silicate (Ca3SiO5), dicalcium silicate (Ca2SiO5), calcium silicate hydrate (CSH), calcium carbonate (CaCO3), calcium hydroxide (Ca(OH)2), and zirconium oxide (ZrO2) are followed using the XRD. The results of the DTS of the Biodentine increased as a function of time with P value = 0.000.

Conclusions:
Measuring the tensile strength of Biodentine will help us better understand the possible course of clinical application and its limitations. Moreover, knowing the changes in the crystallography and chemical composition before and during setting will provide a more critical basis for clinicians to use this novel dental cement reliably.

Key Words: Biodentine; FTIR; XRD, DTS;

Funding Agency: None

Dentistry

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Antifungal activity of Honokiol from plant origin against oral clinical Candida isolates

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Introduction:
Treatment of oral candidosis has continued to be problematic because of the potential toxicity of available antifungal drugs in clinical use, and also development of drug resistance among the infected patients. Therefore, the aim of this study was to examine the antifungal potential of plant derived Honokiol molecule against the oral clinical isolates and ATCC strains of Candida species. Honokiol is a polyphenol molecule mainly present in Magnolia spp.

Methods:
The Minimal Inhibitory Concentration (MIC) of Honokiol molecule was determined by broth microdilution as per NCCLS document M27-A3 [1]. Anti-biofilm effect of honokiol was estimated by MTT reduction assay and cell damage was examined through Confocal Laser Scanning Microscope (CLSM) using propidium iodide (PI). Ultrastructure of cells was examined by Scanning Electron Microscope (SEM) and Transmission Electron Microscopy (TEM).

Results:
MIC of honokiol molecule against 4 ATCC strains and against the 60 oral Candida isolates ranged between 32 and128 µg/ml. However MIC of Amphotericin B was ranged between 0.06 and1.95 µg/ml. Honokiol at MIC and Sub-MIC levels reduced biofilm by 69.5% and 46.7% respectively. CLSM studies revealed the membrane permeabilization of Honokiol treated Candida cells. In addition, SEM result showed damage of the cell wall and plasma membrane which is sharply defined by the a change in cell shape, deformaty in cells and formatio of deep furrows and wrinkles on the cell surface. TEM image of honokiol treated cells showed the complete disintegration of cell walls, rupturing of the plasma membrane and oozing out of intracellular content.

Conclusions:
Honokiol is found to be effective anti-candida agent that leads to damage of cell membrane and cell wall. The results infer that the Honokiol is a promising source for anti-candida compounds.
Reference: [1] Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeast (2008), CLSI; M27-A3, USA.

Key Words: Antifungal; Biofilm; Honokiol;

Funding Agency: Research sector, Kuwait University (DR04/14)

Dentistry

52

Detection of phosphoryl choline epitope in oral bacteria

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Introduction:

Phosphoryl choline (ChoP) is a small molecule harbored on cell surface structures by many bacteria. It helps bacteria in evading host immunity through mimicry. ChoP also promotes bacterial adhesion to surfaces. ChoP is present on cell surfaces of several oral bacteria that are implicated in oral infectious diseases. Recent studies utilizing Next Generation Sequencing tools have uncovered that the microbiota of oral infections is highly complex. The objective of this study was to explore the presence of ChoP epitope in oral bacteria that are not studied earlier.

Methods:
A total of 33 oral bacteria reference strains were screened for the occurrence of phosphorylcholine. Bacterial whole cell lysates were prepared in PBS (pH 7.2) diluted in gel loading buffer and heated at 100 C for 5 min. The lysates were separated using a 15% SDS-PAGE and transferred onto a PVDF membrane. Bands containing ChoP were detected using a monoclonal antibody TEPC-15 (1:100 dilution) against ChoP and anti-mouse IgA conjugated with peroxidase as secondary antibody.

Results:
Of the 33 strains tested, 7 (21%) showed binding to anti-ChoP antibody. These included A. odontolyticus, C. hominis, F. nucleatum, G. morbillorum, G. elegans, P. pallens, and S. noxia. Most of them showed only one protein band of sizes ranging from 11-23 kDa that reacted with the antibody. C. hominis, F. nucleatum (11 and 15 kDa) and G. elegans (17 and 18 kDa) exhibited two bands to which ChoP was bound. Currently, identification of the ChoP-harboring bands using 2D gel electrophoresis and 2D immunoblotting followed by mass spectrometry is underway.

Conclusions:
The presence of ChoP on hitherto unexplored oral bacteria suggestive of a role for ChoP in virulence mechanisms of these species.

Key Words: Oral bacteria; Phosphoryl choline; Endocarditis;

Funding Agency: SRUL 01/14

Dentistry

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Effect of streptococcal biofilm-secreted components on the biofilms of fluconazole-resistant and -susceptible clinical isolates of Candida

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Introduction:

Microbial interactions in multispecies biofilms like dental plaque include competition, synergism and antagonism. In addition to contact-dependent interactions, residents of biofilms use secreted extracellular products to interact with other species. Streptococci and Candida generally function synergistically in biofilms. However, interaction between streptococci and drug-resistant Candida species has not been studied. It is long known that drug-resistant microbes may have advantages for survival in complex niches. The aim was to investigate the effect of streptococcal biofilm supernatants on the biofilms of fluconazole resistant and -susceptible Candida isolates

Methods:
Supernatants of 48-h old biofilms of Streptococcus mutans CCUG 11877, Streptococcus gordonii CCUG 33482 and Streptococcus sanguinis CCUG 17826 were added to biofilm cultures of fluconazole-resistant (Flu-R) and –susceptible dose-dependent (Flu-SDD) Candida isolates at the beginning (for biofilm inhibition) or after 24 h (for biofilm killing). Biofilms were quantified by crystal violet staining and viability of preformed Candida biofilms upon treatment with streptococcal biofilm supernatants was assessed by MTT assay.

Results:
Streptococcal biofilm supernatants inhibited the biofilm formation by Flu-R isolates of Candida albicans and Candida glabrata. S. mutans supernatant showed the highest reduction in biofilm formation by Flu-R C. glabrata (5.4-fold), while Streptococcus sanguinis showed maximum biofilm inhibition in Flu-R (6.2-fold) and Flu-SDD C. albicans (11.8-fold). The supernatants decreased the viability of the preformed biofilms of C. albicans but not of C. glabrata isolates. S. mutans showed highest reduction in the viability of Flu-SDD (5.5-fold) and Flu-R (1.1-fold) isolates of C. albicans.

Conclusions:
Streptococcal biofilm supernatants hindered the biofilm forming capacity of Flu-R Candida isolates. Seemingly, species-dependent variation was seen in biofilm killing.

Key Words: Candida biofilm; Streptococci; Fluconazole resistant;

Funding Agency: SRUL 01/14

Dentistry

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Oral hygiene habits among parents and teachers of special needs schoolchildren in Kuwait

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Introduction:
This study aims to determine oral hygiene habits among the parents and the teachers of special needs schoolchildren in Kuwait.

Methods:
A total of 308 parents of the children with a physical or developmental disability and 112 teachers from four special needs schools were enrolled in this study. Information was collected by structured anonymous questionnaires. Oral hygiene habits were assessed through questions on toothbrushing frequency and usage of dental floss, tooth pick and the traditional chewing stick (miswak).

Results:
The mean age of the parents was 45 + 9.9 years and of the teachers 38 + 8.4 years. The response rate of the parents was 92% and of the teachers 75%. Of these, 66% of the parents and 72% of the teachers reported brushing their teeth at least twice daily. Nearly a quarter of the parents and the teachers (28% vs. 24%) stated brushing only once a day. Majority of the parents and the teachers (88% vs. 92%) were using fluoridated toothpaste. Usage of dental floss was less than a quarter; only by 19% of the parents and 24% of the teachers. Tooth picks were used by one-thirds (38%) of them. Habit of miswak use was more common among the parents than among the teachers (28 vs. 13%; $p = 0.023$). Half of the parents (52%) and the teachers (55%) had visited a dentist during the last 12 months. Adequate toothbrushing habits were significantly associated with the dental visits among the parents ($p = 0.049$) and the teachers ($p = 0.008$).

Conclusions:
Although two-thirds of the subjects followed the recommended toothbrushing frequency of twice daily, the use of dental floss was uncommon (< 25%). More emphasis should be laid towards educating the parents and the teachers about the importance of proper oral hygiene practices and use of oral hygiene aids as an adjunct to toothbrushing.

Key Words: Oral hygiene habits; Parents; Teachers; Special needs schools; Kuwait

Funding Agency: None

Diabetes

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The Effectiveness of Diabetes Nutrition Out-patient Clinic Program on HbA1c level of Kuwaiti Type 1 Diabetes

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Introduction:

Aim: To evaluate the effectiveness of specialized diabetes nutrition clinic program compared to the general nutrition clinic program in the management of type 1 diabetes mellitus in Kuwaiti society.

Methods:
The retrospective study was conducted on 75 randomly selected Kuwaiti subjects with type1 DM, aged 12 or above who had been under multiple daily insulin therapy for at least one year before attending the nutrition clinic. They were divided into treatment group consisting of 45 cases as DM diet subject who attended at least 3 specialized diabetes nutrition sessions and a control group of 30 subjects who did not attend the specialized diabetes nutrition sessions or only attended general nutrition session or did not attend any nutrition session at all. The HbA1c mean and median difference of pre-and post-intervention data, collected from the specialist dietitian Database and hospital medical records, was compared between and within both groups. A paired t-test to assess statistical significance revealed a p value of 5% ($P < 0.05$).
Results:
Statistically there was no significant difference in HbA1c results ($P > 0.05$) between the treatment DMdiet group and the controlled group, but clinically as effectiveness on HbA1c Mean and Median Differences, DMdiet group had greater reduction of (-1.9 and –1.5, respectively) compared with the Control group (-0.9 and -1.9, respectively). This study highlights and supports the importance of including specialist clinical diabetes dietitian within the diabetes medical team. Individual sessions are needed more often to ensure effective discussion of any personal concerns, which is preferred according to individuals' differences. The importance of modifying some points of DM nutrition guidelines.

Conclusions:
Attending sufficient sessions of diabetes nutrition therapy and education program provided by specialist diabetes dietitian has helpful effect on improving glycemic level.

Key Words: Type 1 diabetets; Nutrition; Therapy;

Funding Agency: None

Diabetes

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Determination and modification of cardiovascular risk factors in patients with type-2 diabetes in Kuwait.

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Introduction:

Type 2 diabetes (T2D) is a major health burden in Kuwait with a high prevalence of cardiovascular (CV) risk factors. Objective: To determine and modify CV risk factors in T2D patients in Kuwait with lifestyle, dietary intervention and optimization of medical treatment.

Methods:

The study was based on 141 consecutive patients with T2D in a Primary Care Clinic in Kuwait. The pre-intervention data for CV risk factors were collected from patients at the time of initial assessment, based on the American Diabetes Association guidelines. The 10-year CV risk was calculated using the Framingham and UKPDS CV risk calculator. Presence of metabolic syndrome was determined by the National Cholesterol Education Program and Adult Treatment Panel III criteria (NCEP-ATP III). The intervention included adjustment of the patients' pharmacologic therapy and a standardized 1800 kcal diet and counseling about smoking cessation and exercise. Post-intervention CV risk factor calculation was done after a period of 3 months.

Results:

There were 71 (50.4%) males and 70 (49.6%) females (Kuwaitis 44.7%). The mean age of the patients was 50.0 ±8.8 years and 20.6% were smokers. Post-intervention, there was reduction in obesity from 79% to 77.3%. The mean A1C declined from 8.6±2.0 to 7.8±1.5% ($p<0.005$), with LDL reduction from 2.9±0.9 mmol/L to 2.5±0.8 mmol/L. Comparison of values (pre-and post-intervention) determined the effectiveness of risk management, as well as any change in the 10-year CV risk. The 10-year Framingham CV risk percentage decreased from a 5.3±6.5% at baseline to 4.9±6.2% with the intervention (p=NS). The UKPDS risk calculator also showed a significant CV risk reduction from 8.6±13.1% to 7.5±11.4% ($p<0.05$).

Conclusions:

The risk of CV diseases in T2D patients can be reduced by life style modifications and optimization of pharmacologic therapy in a primary care setting. Implementation of such measures over a longer term may have a more significant impact.

Key Words: Diabetes; Cardiovascular diseases; Life-style modification;

Funding Agency: None

Epidemiology of Diabetes

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Associations of parental diabetes and markers of adiposity with prediabetes among adolescents in Kuwait: a cross-sectional study

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Introduction:
In the past few decades, diabetes and prediabetes, a high-risk state for developing diabetes, have become more prevalent among children and adolescents. This study sought to estimate the prevalence of prediabetes and assess its association with markers of adiposity among adolescents in Kuwait. Also, to determine whether maternal and paternal diabetes associate with offspring prediabetes in a sex-specific manner.

Methods:
A cross-sectional study was conducted by enrolling students (n=1,959; aged 14-19 years) attending public high schools across Kuwait. Participants and their parents were asked to complete self-administered questionnaire on clinical history of diabetes and relevant lifestyle factors. Glycated hemoglobin A1c (HbA1c) was measured in capillary blood using point-of-care testing. In the absence of prior diabetes, prediabetes was defined according to the diagnostic criteria of the American Diabetes Association (ADA; 5.7≤ HbA1c% ≤6.4) and the International Expert Committee (IEC; 6.0≤ HbA1c% ≤6.4). Adjusted odds ratios (aOR) and 95% confidence intervals (CI) were estimated using multivariable binary logistic regression.

Results:
According to the ADA criteria, 33.3% (620/1,845) of participants had prediabetes; whereas, 8.5% (157/1,845) met the IEC definition of prediabetes. Subjects classified as obese (based on body mass index-for-age) had higher prevalence of prediabetes compared to children in the thinness/normal group (aOR = 2.25, 95% CI: 1.78, 2.85). Analysis stratified by offspring sex showed that maternal history of diabetes is associated with prediabetes among male offspring (aOR = 1.47, 95% CI: 1.07, 2.19). In contrast, paternal history of diabetes showed an association with prediabetes among female offspring (aOR = 1.36, 95% CI: 1.02, 1.85).

Conclusions:
Prediabetes affects a substantial proportion of adolescents in Kuwait and obesity and parental diabetes being the main risk factors for prediabetes.

Key Words: Prediabetes; Epidemiology; Prevalence;

Funding Agency: None

Ethics

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Attitudes and Experiences Regarding Medical Errors and Disclosure Among Physicians in Kuwait

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Introduction:
Avoiding harm to patients from the care that is intended to help them and disclosing it is an ethical must. In addition, many hospital accreditation standards worldwide require disclosure about "unanticipated outcomes". This study aims at exploring the attitudes and experiences regarding medical errors and its disclosure among physicians.

Methods:
A cross-sectional study enrolled physicians from governmental hospitals utilizing a self-reporting survey. Descriptive statistics and logistic regression models were used. Analyses were performed with a significance level of 0.05 (SPSS v22).

Results:
A total of 374 physicians completed the survey (response rate 65%) with 58.8% admitted to 'ever been personally involved" in minor errors, and 14% reported the same for serious medical errors. A significant association was noted between "being involved in a minor error" and gender (p-value 0.024), age (p-value 0.001), nationality (p-value 0.017), and rank (p-value 0.000); "disclosing to the patient" with gender (p-value 0.004), nationality (p-value 0.019), rank (p-value 0.004), and medical school (p-value 0.015). Additionally, "medical errors are reaching an alarming rate in Kuwait" was associated with gender (p-value 0.042), age (p-value 0.015), rank (p-value 0.001), and medical school (p-value 0.010); and "fear of legal consequences as a reason for not disclosing" with nationality (p-value 0.000), rank (p-value 0.000), and medical school (p-value 0.000). The odds of a senior physician "ever committing a minor error" is 3.18 higher compared to those with less experience (95% CI 1.24-8.13), and the odds of disclosing a committed error to the patient was 4.98 higher with seniority (95% CI 2.235-20.088).

Conclusions:
Medical errors- regardless of their perceived severity- are reported more by physicians in senior positions. Additional research is needed to understand how disclosure decisions are made to encourage its practice and consequences in Kuwait.

Key Words: Medical Errors; Disclosure of Errors; Ethics;

Funding Agency: None

Genetics

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Effect of Zinc Deficiency on the Pregnancy outcome in the Rat

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Introduction:
Zinc deficiency is known to have adverse effects growth, spermatogenesis and sperm function in human and animals. Objective of the study is to investigate the effect of Zinc Deficiency on the pregnancy outcome in the rat.

Methods:
Zinc deficiency was induced in 10 Sprague-Dawley rats with ethylenediamine tetraacetic acid (EDTA) and 10 controls had diet containing 28 mg Zinc/kg. Both groups were maintained on a cycle of 12hour light and 12 hour darkness at 22^0C and mated with male rats. Day 1 of pregnancy was designated when sperm were detected in the vaginal smear. On Day 21, the pregnant rats were sacrificed and dissected to evaluate resorption, congenital anomalies, liter size, placental weight and vilitis. Blood was collected from all the rats for estimation of Zinc, Selenium, Magnesium and superoxide dismutase and glutathione peroxidase

Results:
Zinc deficiency had significant effect on the outcome of the pregnancy compared to rats on normal zinc diet: with reduced pregnancy rate-70%vs 100%, $p<0.05$, liter size 12 vs 18, $p<0.04$ Placental vilitis, $p<0.01$, Congenital anomalies of the head in form of micrognathia 16%vs 4%. $P<0.01$ and Agnathia12% vs 6%, $p<0.04$ and Resorption 18% vs 12%, $p<0.01$. The serum levels of Zinc, Selenium and Magnesium and superoxide dismutase and glutathione peroxidase were significantly lower in the Zinc deficient group.

Conclusions:
Zinc deficiency is associated with poor pregnancy outcome in the rat.

Key Words: Zinc Deficiency; Poor Obstetric outcome; Congenital anomalies;

Funding Agency: None

Health Economics

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Cost of assisted reproductive technology using activity-based and step-down costing methods: A case study in a private hospital in Kingdom of Saudi Arabia

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Introduction:
About 6.5 million babies have been born since the first In-Vitro Fertilization (IVF) was introduced in 1978. Since then, IVF and other techniques of Assisted Reproductive Technology (ART) have been implemented in health facilities around the world to manage infertility. ART services were started in the Kingdom of Saudi Arabia (KSA) in mid-eighties. Presently there are around 35 ART centers performing around 25, 000 IVF cycle and 5,000 Intra-Uterine Insemination (IUI) cycles annually in the Kingdom. A total of 1,413 ART procedures were performed in 2015 in the private hospital in this study. The aim of this study was to calculate and compare the cost of two modalities of ART treatment: IVF and IUI.

Methods:
A cost-analysis of ART was conducted from January to December 2015 in one of the biggest private hospital in KSA. Activity-Based Costing (ABC) and Step-Down Costing methodology with expert interviews was used to impute the cost of IVF and IUI. Three hundred procedures had been observed by the embryologist in-charge. The capital and recurrent cost was calculated from the provider's perspective.

Results:
The total cost of IVF and IUI was SR 6,534 (range: SR 4,900-8,167) and SR 1,692 (range: SR 1,269-2,115), respectively. The highest cost component for IVF procedure was drugs (57.3%) followed by consumables (18.4 %). For IUI cost of drugs was also the highest component (44.3 %) followed by the staff cost (30.4 %). The estimated annual cost of IVF and IUI service in the Kingdom was SR 171,846,000, which represents 0.143% of annual health care expenditures.

Conclusions:
The cost of providing IVF is 80% higher than IUI. Drugs used for hormonal stimulation were the main cost component for both IVF and IUI. Efficiency of ART services can potentially be improved if IUI is used as the first line treatment in the management of infertility

Key Words: Cost; Assisted Reproductive Technology; Saudi Arabia;

Funding Agency: None

Health Economics

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Cost Analysis of Percutaneous Transluminal Coronary Angioplasty for Management of Coronary Heart Disease in a public Cardiac Centre of Kuwait

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Introduction:
Coronary Heart Disease (CHD) is one the leading cause of mortlity that account for 17.3 million deaths annually. Percutaneous transluminal coronary angioplasty (PTCA), is a non-surgical procedure that relieves narrowing and obstruction of the arteries in patients with CHD. This is one of the most common procedures done in Kuwait with more than 7,000 cases per year in the Cardiac Centre. The objective of the study is to conduct the cost analysis of PTCA procedures on CHD cases from provider's perspective.

Methods:
This study was conducted in a 154-bed public Cardiac Centre that provides tertiary care to the population. Sources of costing information include Ministry of Health (MOH) Financial Report, Medical Stores Administration and National Health Information Centre Reports. Doctors and nurses involved in carrying out the procedure were interviewed to understand the usual practice of PTCA and to obtain additional costing information. A combination of step-down and activity based costing was carried out to impute the capital and recurrent cost.

Results:
Most of the cases had three days of stay and used two drug-eluding stents. The overall cost of PTCA is KD 1,392 (USD 4,589) per patient, which is equivalent to 11% of per capita GDP. The main components of the cost were drug-eluding stents (63%), followed by other disposables (16%) and laboratory investigations (11%). The minimum cost of PTCA is KD 920 (USD 3,033) and the maximum cost is KD KD1,892 (USD 6,238). The annual cost of PTCA based on the total cases of patients treated in the centre is KD 9.9 million (USD 32.9 million). If the cases were managed as day-care surgery and using only one drug-eluding stent, there will be an annual cost saving of at least KD 3.4 million (USD 11.2 million).

Conclusions:
The cost of PTCA is high and may not be affordable by most individual patients. There will be a significant cost-savings if the hospital changes their practices to the more efficient day-care surgery.

Key Words: Cost analysis; Percutaneous Transluminal Coronary Angioplasty;

Funding Agency: None

Health Policy and Management

62

Users satisfaction with the interior design quality of inpatient units of public hospitals in Malaysia

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Introduction:
Hospital is one of the most complex building types to design and build. Although there has been substantial progress in the healthcare facilities in many developing countries, minimal progress has been made in the design of inpatient units. It is known that physical environment plays an important role in occupants' well being. Objective: The main objective of this study is to determine the level of users' satisfaction towards the interior design quality of the inpatient units.

Methods:
This study employed the combination of both qualitative and quantitative methods. Quantitative data were collected through self-administered questionnaires. Respondents were asked to rate their level of satisfaction of items on a Likert type response scale of 1 to 5. Qualitative information was gathered by conducting semi-structured interviews and walkthrough observations. Five out of 12 public hospitals located in Klang Valley were randomly selected. Respondents of the study were patients, staff, and visitors.

Results:
Respondents were found to be the least satisfied with the wayfinding system (mean score =2.98, sd=0.75) and furniture (mean score =3.04, sd=0.74). This is most probably the result of poor planning at the design and construction stage due to lack of local experts and experienced personnel in hospital designing. However, safety features (mean score=3.69, sd=0.82) were the most satisfying aspect. The result of the qualitative study revealed that most of these facilities suffered from faulty design. Although the respondents seemed to be satisfied with the aspect of privacy (mean score=3.36, sd=0.91), the qualitative data proved otherwise.

Conclusions:
Based on the results, the overall performance of the facilities does not meet the users' satisfaction. The interior design quality of inpatient units of these hospitals needs major improvement. This study significantly contributes to gathering information to reveal the current design status of inpatient units in Malaysia

Key Words: Interior design; Inpatient; public hospitals;

Funding Agency: None

Medical Education

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Electronic cigarettes: Knowledge, attitudes, and prevalence among students of Kuwait University

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Introduction:
Electronic cigarettes became a widespread phenomenon across the borders. Their publicity owes to producers' marketing and the postulated theories about its potential to help tobacco smokers quit smoking. This study aims to assess the prevalence, knowledge and perceptions towards electronic cigarettes among Kuwait University students.

Methods:
A cross-sectional study was conducted in December 2016, targeting Kuwait University students from all campuses. An anonymously self-administered questionnaire was used, asking questions about the participants' sociodemographic characteristics, smoking status, and smoking related variables. Knowledge of electronic cigarettes and their contents, as well as perceptions towards its advantages and disadvantages were assessed through the structured questionnaire. Multivariable logistic regression analysis was conducted to study the factors associated with electronic cigarettes use.

Results:
Overall, 23.4% of Kuwait University students used e-cigarettes at least once, with more males (46.7%) being ever users than females (6.7%). Also, 35.9% of students thought that e-cigarettes were less harmful than tobacco cigarettes, and 44.2% believed it aids in smoking cessation. When asked about their knowledge about contents of e-cigarettes, only 14.3%of respondents claimed they knew the contents.

Conclusions:
The prevalence of electronic cigarettes use among students is quite high, and it is higher among males, tobacco ever smokers, and hookah users. The dual use of e-cigarettes and tobacco cigarettes urges public health professionals to understand smoking risk factors and why the youth are more prone to using cigarettes. Further investigations and educational programs would enhance the social awareness towards such recent phenomena.

Key Words: Electronic cigarettes; Prevalence; Kuwait University;

Funding Agency: None

Medical Education

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Professionalism narratives of Kuwait's future physicians: impact of the hidden curriculum

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Introduction:
Medical students' experiences in clinical settings is the most powerful determinant of future physicians' perceptions and practices of professionalism. This study assesses the professional attitudes of medical students in Kuwait and the impact of the informal and hidden curriculum.

Methods:
A questionnaire assessed professional attitudes and was distributed to a random stratified sample (n=150). A thematic and inductive qualitative analysis was conducted on 508 stories yielded from an online survey (n=150) and narratives collected from 5 semistructured interviews (n=47).

Results:
Most students (88%) recognize and agree with standard professional norms, including honesty with patients (79%) and reporting medical errors (72%). Most narratives (61%) involved witnessing negative embodiment of professional values, 89% of which were conducted by attending physicians. Two main thematic categories were evident: medical-clinical interactions and teaching-and-learning environment. 38.8% of negative narratives reflected a lack of manifested respect in clinical interactions towards patients, colleagues, and medical students. 31% of negative experiences reflected discrimination practiced by physicians, mainly towards expat patients (40%). Students reported witnessing discrimination by clinical tutors based on gender (18%). 26.6% of negative narratives reflected poor communication skills by attending physicians with patients, including lack of empathy (29%). 24.6% of negative narratives revealed a lack of respecting patient autonomy. Most students did not report any unprofessional incidents out of fear of the potential consequences to their academic performance and career

Conclusions:
Our results suggest that students' reflective narratives reflect the informal curriculum that shapes them into physicians. Medical students in Kuwait have a strong sense of professional norms. However, they do not usually witness norms being practiced by attending physicians.

Key Words: Medical education; Professionalism; Hidden curriculum;

Funding Agency: None

Medicine

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Linking Nephropathy, Neuropathy and Ischaemic Heart Disease in Type 2 Diabetes Is Fetuin A the missing Link?

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Introduction:
Fetuin-A (FA), an anti-inflammatory glycoprotein synthesized in the liver, inhibits insulin action, apoptosis of vascular smooth muscle cells and prevents heterotropic calcification. This study evaluates the relationship between FA, insulin resistance (IR), and micro- and macro-vascular complications in patients with type 2 diabetes mellitus (T2DM).

Methods:
Fasting plasma FA, lipid profile were measured in 201 T2DM patients. Anthropometric and clinical data were recorded and subjects were classified on the basis of the degree of adiposity and homeostasis model assessment of insulin resistance (IR). Ratio of urine microalbumin to creatinine was determined to categorize subjects as normo- (NAO, ratio <30mg/g); micro- (MIA, ratio 30-300mg/g) and macro-albuminuric (MAA, ratio >300 mg/g). Univariate and multivariate analyses were used to compare study subjects and binary logistic regression analyses were used to evaluate associations with micro- and macro-vascular complications.

Results:
FA was significantly higher in subjects with IR > 2 compared to subjects with IR < 2 (350 vs 331 ug/ml). FA significantly correlated with Total Cholesterol; LDL-cholesterol; Triglycerides; ALT and inversely correlated with age. FA was significantly lower in subjects with ischaemic heart disease (IHD) (310 vs 331 ug/ml); MIA and MAA (308 vs 340 ug/ml), sensory neuropathy (SN) (318 vs 348 ug/ml); autonomic neuropathy (AN) (305 vs 337ug/ml) and retinopathy (319 vs 350 ug/ml) compared to T2DM patients without these complications. Binary logistic regression showed significant associations with MIA and MAA, AN, SN, retinopathy and IHD.

Conclusions:
Lower FA could predispose to arterial calcification which is common in T2DM in association with neuropathy and nephropathy. Estimation of FA could be used to identify patients at risk of these adverse prognostic complications that are also independent risk factors for cardiovascular disease and all-cause mortality.

Key Words: Fetuin A; Type 2 Diabetes mellitus; Diabetic complications;

Funding Agency: KFAS-2011-1302-01

Medicine

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Metabolic control, cardiovascular risk factors, and the prevalence of chronic complications among adults with type 2 diabetes: Identifying the impact of structured diabetes care services

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Introduction:

Diabetes mellitus is a chronic disease that needs a structured care to achieve optimal outcomes. The aims of this study (i) to determine the level of metabolic control, cardiovascular (CV) risk factors, and the prevalence of chronic complications among adults with type 2 diabetes, and (ii) to identify the impact of delivering a structured care on diabetes outcomes.

Methods:
The medical records of 253 adults with type 2 diabetes were reviewed as part of an audit conducted for patients attended the diabetes OPD clinics at Al-Sabah Hospital in 2011. The data abstracted included demographics, diabetes-related data, and cardiovascular risk factors. To identify the impact of structured diabetes care, the results of Kuwaiti adults were compared with data published previously.

Results:
This audit included 253 adults with type 2 diabetes (55% females, and 67% Kuwaiti nationals). Overall, mean age was 54.1+8.4 years, and mean duration 12.7+8.3 years. Current smoking was 5.9%. Overall, the mean BMI was 32.9+6.7 and the mean HbA1c 8.6+1.6 %. The mean systolic and diastolic BP was 126.6+11.7 and 78.3+6.5 mmHg respectively. Mean levels for LDL, HDL, and triglycerides were 2.6+0.8, 1.1+0.3, 1.7+1.0 mmol/l respectively. Albuminuria and any retinopathy was present in 33.7% and 29.5% of the patients respectively. Compared with previous data, there is significant reduction of HbA1c % (-0.6), systolic and diastolic BP (-9.6 and -3.6 respectively), LDL, and HDL levels (-1.1, and -0.1 respectively). Although Kuwaiti adults in the present audit were older and had longer mean duration of diabetes, the prevalence of any retinopathy and albuminuria was lower compared with previous study population (38% vs. 40%; p=0.32, and 31.1% vs. 43.5%; p=0.03 respectively).

Conclusions:
The findings of this audit underscore the value of providing structured diabetes care services to improve metabolic control, reduce CV risk factors, and prevent chronic diabetes complications.

Key Words: Diabetes; Type 2; Outcomes;

Funding Agency: None

Medicine

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Baseline Characteristics of Ulcerative Colitis Patients from Kuwait in an Observational Study (ICONIC)

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Introduction:
Ulcerative colitis (UC) is a chronic inflammatory bowel disease of unknown etiology. Since epidemiology, clinical characteristics and natural history of UC are still unknown, there is a need for local data analysis to understand its burden in Kuwaiti population.

Methods:
ICONIC is an ongoing, prospective, observational study assessing UC-associated burden in adult patients under routine care. In this analysis, we evaluate the baseline data of a cohort of Kuwaiti patients to better understand the demographics and clinical characteristics of UC. This analysis looks at a correlation between patient and physician perception of UC disease burden. Quality of life and disease burden are measured using Patient Modified Simple Clinical Colitis Activity Index (P-SCCAI) and Short Quality of Life in Inflammatory Bowel Disease Questionnaire (SIBDQ).

Results:
Of 52 patients (25 females, 26 males, 1 missing; mean age: 33.2±13.2 years), 42.3% had symptoms for ≥1 year prior to diagnosis. Though improvement in disease was noted in 75% patients, UC was assessed to be moderate to severe in 69.3% patients on self-assessment (63.5% as assessed by the investigator). In total, 92.3% patients were receiving treatment for UC with one third (36.5%) achieving complete response while 50% patients had only a partial response. Comorbidities were seen in 36.5% patients; fatigue was the most common (23.1%), followed by low body weight (13.5%), and anxiety/depression, skin diseases, and sleep disorders (7.7% each). Patients reported a higher mean score for SCCAI (5.1±3.8) as compared to physicians (4.7±3.3). Patients' SIBDQ score was 47.0±13.7.

Conclusions:
At baseline, majority of patients had received treatment for UC and showed improvement since diagnosis. However, both patient and physician assessments indicate a high proportion still had moderate to severe disease. A good correlation was seen in patient and physician's SCCAI scores, highlighting unaddressed disease burden

Key Words: Ulcerative Colitis; Burden; Baseline data;

Funding Agency: None

Medicine

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Interim results from PROOF a 5-year observational study of long-term disease outcome in axial spondyloarthritis subanalysis from Kuwait

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Introduction:
PROOF is a large, multi-country, observational study evaluating long-term progression of axial spondyloarthritis (axSpA). The disease course of full-spectrum axSpA, including ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA), has not yet been studied in large patient groups; local data in Kuwait are lacking.

Methods:
PROOF is a large multi-country prospective, observational study evaluating disease burden and progression of axSpA over 5 years. Patients with axSpA, fulfilling the ASAS classification criteria (either AS or nr-axSpA), were eligible, if diagnosed ≤12 months prior to enrollment. Pelvic x-rays were collected at baseline and during yearly follow-up visits. Images were read by a local reader and validated by ≤2 blinded and central readers. Subdiagnosis I is based on investigators' clinical judgment before x-ray grading. Subdiagnosis II is based on combined local and central x-ray readings. Baseline data was analyzed on June 2015. The second data cut, presented here, captures Year 2 of the 5-year period.

Results:
Of 2126 patients enrolled globally, 28 were from Kuwait. Overall, the mean age of patients was approximately 35.6±8.4 and 19(59.4%) were male. Of these, 16 patients (57.1%) were classified as having AS and 12 (42.9%) as having nr-axSpA, the first data cut revealed that of those originally diagnosed as having nr-axSpA (12, 42.9%) in Subdiagnosis I, only 2(7.1%) retained their original classification after Subdiagnosis II. In this data cut, there was no change observed in comorbidities and biomarker profiles from baseline.

Conclusions:
There was a long duration from onset of symptoms to seeing a rheumatologist possibly due to delay in considering AS/nr – AxSpA as an important differential diagnosis reflecting the need to increase disease awareness among general practitioners and others.

Key Words: Spondyloarthritis; Rheumatology; Kuwait Axial SpA;

Funding Agency: AbbVie

Medicine

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Prevalence of joint hypermobility in Kuwait

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Introduction:
Joint hypermobility (JH) is defined as a more-than-normal range of movement (ROM) in a joint, beyond the 95th percentile for the general population. JH is an autosomal dominant genetic disorder, affecting genes that encode various connective tissue proteins. Hypermobility not associated with systemic disease occurs in 4% to 13% of the population. The aim of our study was to determine the prevalence of joint hypermobility (JH) among young Kuwaiti adults.

Methods:
This was a cross-sectional study of 390 randomly selected healthy undergraduate university students, aged 18–29 years from the Health Sciences Centre, Kuwait University, Safat, Kuwait. Beighton score at four peripheral sites bilaterally (knees, elbows, thumbs and fifth fingers) and forward flexion of the trunk were used to evaluate joint hypermobility. Any student who met four out of the nine criteria was considered hypermobile. Joint pain was documented in all subjects through personal interview.

Results:
A total of 390 subjects (male: female ratio 1.0:0.9) were assessed. Of those, 87 (22.3%) were found to have JH: 60 (29.4%) males and 27 (14.5%) females, showing a significantly higher male predominance ($P < 0.001$). Beighton score was inversely correlated with age ($\rho = -0.15$, $P = 0.003$). A higher incidence of finger signs was noted in comparison to elbow-knee hyperextension and hands-to-floor. Knee joint, back, neck and shoulder pains, in descending order, were the commonest type of joint complaints, although not statistically significant ($P > 0.05$) in subjects with and without joint hypermobility. It was also observed that the left side, at all the sites, was slightly more hypermobile in hypermobile subjects.

Conclusions:
The prevalence of joint hypermobility is not uncommon among young Kuwaiti adults, and was comparable to the data published in other Asian-Pacific regions. General practitioners should be familiar with the condition and its clinical associations, while assessing musculoskeletal complaints.

Key Words: Hypermobility; Arthralgia; Kuwait;

Funding Agency: None

Medicine

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Proposed Sickle Cell Disorders Nomenclature

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Introduction:
Sickle cell disease (SCD) is an autosomal recessive disease it forms a group of disorders which are different from each other in laboratory and clinical findings. SCD classified in this study to the known two main groups. I-Heterozygous or trait (T) classified to three subgroups 1- Sickle cell anemia trait (SCA-T) , 2- Sickle cell thalassemia trait (SCThal-T), 3- Sickle cell variant trait (SCVx-T) . II-Homozygous group which are patients with the disease. They are also classified to three subgroups 1-Sickle cell anemia disease (SCA-D), 2- Sickle cell thalassemia disease (SCThal-D) with alpha or beta thalassemia trait, 3-Sickle cell variant disease (SCVx-D), x is the hemoglobin variant as Hb C, D, G. Etc. Aim: creat an easier nomenclature for SCD to make better understanding for both the genotype and the related clinical status.

Methods:
The High-performance-liquid-chromatography (HPLC) results from 2010 -2016 were classified into 2 groups heterozygous and homozygous groups of sickle cell disorders according to HbS level. Each group classified into 3 subgroups. The including criteria was patients with sickle cell hemoglobin with or without thalassemia trait or other hemoglobin variants. Test done were CBC (Hb, MCV, MCH), reticulocytes, LDH, bilirubin, HPLC, abdominal ultrasound.

Results:
Table [1] show the different laboratory and clinical findings between heterozygous and homozygous: 1- Spleen in SCA and in SCV is atrophied, while it is enlarged in SCThal. 2- MCV and MCH are normal in SCA and in SCV but lower in SCThal.

Conclusions:
SCD is a group of disorders which are different in laboratory and clinical findings. The proposed SCD nomenclature gives better understanding for laboratory genotype and clinical status. The heterozygous sickle cell group is better named SCA-T, SCThal-T and SCV-T. The Homozygous or sickle cell disease is more informative if it is named SCA-D, SCThal-D and SCV-D.

Key Words: Sickle cell disease; varient; thalassemia;

Funding Agency: KFAS

Medicine

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Prevalence and characteristics of Restless Arm Syndrome in Kuwait

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Introduction:

Restless arm syndrome (RAS) is an underrecognized movement disorder that is sometimes related to restless leg syndrome. The aim of this study is to evaluate the prevalence and characteristics of RAS in the general population of Kuwait.

Methods:
A cross sectional study was conducted to assess the prevalence and sociodemographic characteristics of RAS in the general population of Kuwait. A web-based questionnaire was distributed online via several social network applications. The diagnosis of RAS was based on a modified International Restless Legs Syndrome Study Group (IRLSSG) diagnostic criteria to determine RAS symptoms.

Results:
In this study, 1021 individuals (80.4% females) participated in answering the questionnaire. Approximately 33% were younger than 20 years of age. The majority (93.6%) were from Gulf Cooperation Council (GCC) countries. The prevalence of RAS was 55%. It was also found that 81.5% of those with RAS were females. Fifty-four (9.3%) of RAS were diabetics, compared to 79 (7.7%) from all the sample. More than a third (37.5%) had anemia. The prevalence of smoking in those with RAS was 114 (20.3%).

Conclusions:
In the first study to look at RAS in Kuwait, we found that RAS is very common condition in Kuwait, especially among females. It can be accompanied by comorbid conditions. It is underrecognized and easily treatable.

Key Words: Restless; Arm; Prevalence;

Funding Agency: NONE

Medicine

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An Exploratory Pilot Study on Knowledge, Attitudes, and Perceptions Concerning Antibiotics' Resistance and Use Practices Among Primary Healthcare Practitioners in Kuwait

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Introduction:
Inappropriate use of antibiotics is a global public health problem. 'In 2009, almost 40% of prescriptions at 50 primary centers in Kuwait involved an antibiotic'. Antibiotics resistance is known to affect therapeutic effectiveness, lead to longer and severe illness and costs more. The objective of this study is to explore knowledge, attitude and perceptions of antibiotics resistance and use practices among primary healthcare practitioners in Kuwait.

Methods:
Data collected utilizing a self-reporting questionnaire from a sample of convenience from 28 primary health care centers.

Results:
A total of 100 completed surveys were analyzed (response rate 85%). The majority of participants (69%) were <45 years, 63% females, 58% registrars, 48% Kuwaiti, and 67% graduated from a medical school abroad. A total of 74% identified that "inappropriate use of antibiotics puts patients at risk" and 66% identified resistance as a problem in their daily practice. While 89% of doctors reported that they "feel confident about their knowledge and practice", only 31% indicated that they received regular training and education in this area. When exploring the prescription patterns, 19% prescribed "empiric" therapy for one week, 45% prescribed antibiotics to >30 patients/month, 33% prescribe for 10-30 patients/month. Two thirds prescribe antibiotics based on the clinical condition versus one third who would prescribe based on positive microbiological results. Cost effectiveness was a determining factor for 61% of doctors and was significantly associated with rank (37.5% residents, 16.7% consultants, 13.8% registrars) with P value 0.042. Around 30% use their clinic guidelines, which were described as limited by 52%, and accessible with difficulty by 34%.

Conclusions:
Antibiotics resistance is still a problem in daily practice at primary care. More education and training is requested by health care providers and clear institutional guidelines need to be developed and made accessible.

Key Words: Antibiotics Resistance; Knowledge; Primary Healthcare;

Funding Agency: None

Medicine

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Circulatory levels of oxidative stress markers and BMD in postmenopausal women

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Introduction:
Osteoporosis is a significant health issue which is set to rise alarmingly worldwide. In addition to some well-characterized factors, oxidative stress is also suggested to contribute to bone loss in osteoporosis seen in menopause. Oxidative stress is the result of an imbalance between the production of reactive oxygen species (ROS) and the removal of their reactive intermediates. There is much controversy regarding the possible pathological role of oxidative stress on bone mineral density (BMD). This study was aimed at measuring serum oxidative stress parameters i.e., Catalase, Peroxiredoxin 2 (PRX2), Superoxide dismutase 1 (SOD1), Superoxide dismutase 2 (SOD2) and Thioredoxin (TRx1) in postmenopausal women with normal, osteopenic and osteoporotic bone density.

Methods:
The study population included 64 post-menopausal women of whom 23 had normal BMD, 38 had osteopenia and 13 had osteoporosis. Serum oxidative stress parameters were measured using the Multiplex system (Millipore) and read on the Magpex ELISA platform.

Results:
Serum levels of Catalase, SOD2 and PRX2 were found significantly lower in postmenopausal women with low BMD group as compared to women with normal BMD ($p=0.031$, 0.044 and 0.041 respectively). These findings support that oxidative stress plays an important role in pathogenesis of postmenopausal osteoporosis. However, levels were not significantly different in women with osteopenia as compared to those with osteoporosis. Furthermore, levels did not correlate significantly with BMD of the hip or spine.

Conclusions:
These data provide insights into the possible role of oxidative stress on the pathogenesis of postmenopausal osteoporosis. However the lack of association between studied oxidative stress markers and BMD may indicate that osteoporosis may be rather multivariate and complex.

Key Words: Osteoporosis; Oxidative stress; Postmenopause;

Funding Agency: This study is supported by Kuwait Foundation of Advancement of Science (KFAS) projects no. 2013-1302-02 and PR17-18SL-01.

Medicine

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Idiopathic Erythrocytosis Reality and Treatment Modality

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Introduction:
In absolute erythrocytosis, the persistently raised red blood cells are involved with increased hemoglobin (Hb) and hematocrit (Hct). The identified types of erythrocytosis are primary polycythemia (PV), secondary polycythemia (SP), and relative polycythemia (RP).WHO diagnostic criteria specified the treatment based on the Erythrocytosis type. However, Erythrocytosis could be idiopathic and not consistent with these recognized types. Aim: The idiopathic erythrocytosis (IE) with normal erythropoietin level could be considered as a new polycythemia subclass in treatment.

Methods:
A prospective study over two years, 75 patients with high hemoglobin (Hb), hematocrit (Hct) had major criteria tests Red Cell Mass (RCM), JAK2 V617F mutation (except JAK2 exon 12 mutation) and minor criterion test erythropoietin level . RCM was done by Cr-51 RBC radiolabeling method. All subjects consented to the study approved by the ethics committee. Statistical analysis involved descriptive statistics and chi-square test.

Results:
There were 71 male and 4 female, the mean age 46y (range17-75y). The diagnosis results were as follow PV 5/75 (7%), SP 28/75 (37%), RP 34/75 (45%) and 8/75 (11%) are not consistent with any identified types of erythrocytosis. The major criteria used in classification were high level RCM, Hb, Hct and positive JAK2 and the minor criterion was Erythropoietin level.

Conclusions:
The Idiopathic Erythrocytosis (IE) could be considered as a fourth type of erythrocytosis. It has particular importance in diagnosis and treatment modality. IE does not meet the criteria of any other types of polycythemia. It has a normal erythropoietin level and a positive JAK2 mutation and a high RCM, Hb, and Hct level. Patients with IE are causing clinical confusion. Therefore, it might be useful to take into consideration that IE type is a new type of polycythemia and treated according to the clinical presentation without being restricted to any other types of polycythem

Key Words: Idiopathic Erythrocytosis; JAK2; RCM;

Funding Agency: NA

Medicine

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The association between Restless Arm Syndrome and cigarette

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Introduction:

People with restless arm syndrome (RAS) have uncomfortable sensations in their upper limbs and an irresistible urge to move their hands to relieve the sensations. Sometime RAS can affect other parts of the body especially the legs (restless leg syndrome). The urge of smokers to pick up a cigarette at a certain time is not clear. We hypothesize that RAS plays a role in making smokers want to smoke to relieve the uncomfortable sensations in their hands. If confirmed, then physicians could help smokers through anti-RAS medications or even cognitive behavioral therapies. The aim of this study is to assess for an association between RAS and smoking.

Methods:
A cross sectional study was conducted using a web-based questionnaire that was distributed online via several social network applications. The diagnosis of RAS was based on the presence of the four mandatory diagnostic criteria that were assessed by answering certain questions. The questionnaire included questions on participants' smoking behaviors to study the association between RAS and smoking.

Results:
A total of 1021 answered the survey. The prevalence of smoking in those with RAS was 114 (20.3%). Among smokers, 8.8% with RAS started smoking before the age of 10 years, compared to 4.5% without RAS. Whereas, those who started smoking after the age of 30 years, 3 (2.6%) had RAS compared to 6 (8.9%) without RAS. Among the smokers who had RAS, 67.9% said that the discomfort in their arms gave them the desire to smoke in order to relieve this feeling.

Conclusions:
This is the first time to our knowledge that an association between RAS and smoking has been demonstrated. Further research is needed to confirm RAS as a risk factor for smoking and whether treating RAS would help patients quit smoking.

Key Words: Restless; Arm; Smoking;

Funding Agency: NONE

Medicine

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Prevalence of Myasthenia Gravis in Kuwait: A tertiary referral study

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Introduction:
Background: Epidemiological study on myasthenia gravis (MG) in Kuwait is scarce. Objectives: To assess the prevalence of MG at Ibn Sina Hospital, a tertiary neurological referral hospital in Kuwait.

Methods:
This cross-sectional study was conducted between January 2011 to December 2015. Medical files of all patients >12 years of age were reviewed. Patients were a diagnosis of clinical MG, a positive antibody test for acetylcholine receptor (AChR MG) or muscle-specific kinase (MuSK MG), or sero-negative MG, confirmed by an electrophysiological test were included.

Results:
Of 17815 admitted patients during the study period, 85 out of them had MG (0.4%). Female: male ratio was 1.4:1. The mean age at onset was 32.49±13.01 years (males 42.40 ±13.03 years versus females 25.65 ±7.29 years; $p < 0.001$). Ocular MG was diagnosed in 27% of the patients whereas generalized MG were observed in 73%. Acetylcholine receptor (AchR) antibodies were assessed in 72 patients of whom 50 (69.4%) were seropositive. Thymoma was found in 42.4% and thymic hyperplasia in 11.8%. Thymoma was more prevalent in males (27% vs. 21%; $p < 0.02$)

Conclusions:
The prevalence of MG in Kuwait is comparable with international figures. It is more common in young females while thymoma is more prevalent in males.

Key Words: Myasthenia Gravis, prevalence, tertiary hospital; Thymoma; Prevalence;

Funding Agency: None

Medicine

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Renal transplantation in patients with Systemic lupus erythematosus: single center experience.

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Introduction:

Long term outcome of renal transplantation among systemic lupus erythematosus (SLE) patients remains a debated topic.
Aim of the study:
We compared the long-term outcome of kidney transplantation in ESRD patients secondary to lupus nephritis with that in an age, sex, and donor matched control group of recipients.

Methods:
This study comprised 192 kidney transplant recipients who received their grafts between 1994 and 2011 at Hamed Al-Essa Organ transplant center of Kuwait. These patients were further subdivided into two groups according to original kidney disease (36 secondary to SLE) and (156 secondary to non-SLE causes). All patients' data were assessed with special emphasis on graft and patient survival as well as post-transplant medical complications.

Results:
The two groups were comparable regarding pre-transplant patient demographic features (age and sex of both donors and recipients), moreover pre-transplant diabetes, anemia, hypertension, tuberculosis, bone disease, dialysis type; immunosuppression and viral profile were also matched. The overall incidence of post-transplant complications was comparable among the two groups especially NODAT, BK nephropathy and coronary heart disease ($p>0.05$). Lupus patients needed significantly more anti-hypertensives ($p=0.003$) and had higher prevalence of CMV ($p=0.001$). On the other hand, we noticed higher prevalence of hyperlipidemia in the control group ($p=0.01$). We found that the mean number of rejection episodes were significantly higher among lupus patients compared to the control group (0.94 ± 1.1 vs. 0.42 ± 0.66; $p=0.011$). Kidney graft survival was worse among the lupus group compared to the control group ($p=<0.001$); however, patient survival was comparable in both groups at 1, 5, and 10 years ($p<0.05$).

Conclusions:
SLE as a cause of ESRD in renal transplant recipients is associated with worse allograft survival possibly due to higher prevalence of CMV, hypertension and acute rejection

Key Words: renal transplant; lupus; outcome;

Funding Agency: none

Medicine

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Impact of early post-transplant graft function at the time of transplantation on long term outcome in pediatric renal transplant recipients

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Introduction:

Background and Objectives: A successful kidney transplant is the most effective renal replacement therapy for children with end-stage renal disease (ESRD). Delayed graft function has detrimental effect on graft and patient outcomes as adults. Therefore, this study was conducted to assess variable peri-transplant conditions that may affect the postoperative graft function and its impact on long-term patient and graft survivals in our pediatric recipients.

Methods:
Ninety-one pediatric kidney transplant recipients were included in this retrospective study (53 males and 38 females). The patients were categorized into three groups: group 1 (with immediate graft function, 76.9%), group 2 (with slow graft function, 9.9%) and group 3 (with delayed graft function, 13.2%). The impact of pre-transplantation co-morbidities (infections especially HBV, HCV, CMV, TB, anemia, urologic problems, hypertension and DM), bone disease, dialysis type, donor type, donor origin, type of induction and maintenance immunosuppression, NODAT and post-transplantation BK and CMV infection on the graft function were studied. Graft and patient outcomes were evaluated in relation to the graft function at the time of transplantation.

Results:
Recorded graft function was significantly affected by donor type (P=0.005), donor origin (P=0.002), and type of induction therapy (P=0.013). No significant difference was found among the three groups in relation to pre-transplantation infections (HBV, HCV, CMV, and TB), anemia, urologic problems, hypertension, DM, bone disease, dialysis type or post-transplantation type of maintenance immunosuppression, NODAT, BK or CMV infection. Moreover, the three groups were comparable regarding both graft and patient outcomes.

Conclusions:
Donor type, donor origin, and type of induction therapy are major determinants of postoperative graft function, although none has detrimental effect on long-term patient or graft outcomes.

Key Words: Pediatric kidney transplantation; Delayed graft function; Graft outcome;

Funding Agency: None

Medicine

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Importance of Accreditation for Patient Health Care

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Introduction:
Every number in Medical diagnostic tests is a life. Interest in accreditation is growing in developing countries, but there is little published information on the challenges faced by new programs. Impact of Accreditation on the Quality of Healthcare Services is crucial. The increased focus on improving patient outcomes, safety and quality of care advocate healthcare provider to adopt standardized protocols for evaluating healthcare.
Objectives and Aim
The objectives of this study gives an insight into the crucial requirement in fulfilling the minimum laboratory accreditation standards protocols in medical laboratories and diagnostic examinations. The aim of this present study is to control and optimize, in a permanent manner, good professional practice by internationally established standards to maintain the accuracy and reliability to maintain patient health.

Methods:
The path to achieve accurate results is by implementing quality standard protocols through the whole three phases of investigation cycles (pre-analytical, analytical and post-analytical phases) starting from patient identification, collection of samples and various diagnostic analysis using systematic standards protocols used in methodologies, reagents, equipments, internal and external proficiency testing. In addition implementing personnel, safety and overall management policies.

Results:
Policies and procedures were written in all three phases pre-analytical, analytical and post-analytical phases of analysis and all procedures, equipments and machines were validated and calibrated and employees demonstrated the crucial aspects of evaluating a checklist through each examination.

Conclusions:
Accreditation improves quality and minimizes errors and mistakes which affect patient's health and recovery. Non accredited laboratory not only jeopardizes the patient health but risks the compromise safety of workers. All health sectors of various categories should implement quality control standards for patient health care.

Key Words: Accreditation; Quality Assurance; Quality Standard Protocol;

Funding Agency: none

Medicine

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Zero-HLA mismatches renal transplant recipients: Kuwait expereince

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Introduction:
Background: The higher the HLA match the better the renal graft outcome. Therefore the compatibility at all three HLA loci is desirable for optimal graft outcome. Aim: To assess the long-term outcome of HLA zero-mismatched renal transplant recipients in Kuwait.

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

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

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

Key Words: Renal transplant; HLA zero mismatch; Outcome;

Funding Agency: none

Medicine

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Association of protein tyrosine phosphatase non-receptor type N22 gene functional variant C1858T with systemic lupus erythematosus

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Introduction:
Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease which involves the loss of self-tolerance with hyperactivation of autoreactive T- and B-cells. Protein tyrosine phosphatase non-receptor type 22 (PTPN22) encodes for lymphoid specific phosphatase (LYP) which is a key negative regulator of T lymphocyte activation. The aim of this study was to investigate the association between PTPN22 gene functional variant R620W and systemic lupus erythematosus (SLE) by comparing its prevalence in Kuwaiti SLE patients and controls.

Methods:
The study included 134 SLE patients and 214 controls from Kuwait. The genotypes of PTPN22 gene functional variant R620W were determined by PCR-RFLP and confirmed by DNA sequence analysis in both SLE patients and the controls.

Results:
A relatively high prevalence of the variant 620W (T-allele) of the PTPN22 gene was detected in the SLE patients from Kuwait. 35.7% of the SLE patients had at least one variant allele (T-allele) compared to 15.9% in the controls. A statistically significant difference was detected in the frequency of variant genotypes, TT and CT between SLE patients and the controls ($p < 0.0001$). No association was detected between the PTPN22 gene variant and the Raynaud's phenomenon, renal involvement and severity of the SLE.

Conclusions:
The frequency of PTPN22 gene functional variant R620W reported in this study is amongst the highest compared to other world populations. A high prevalence of this variant in SLE patients in comparison to the healthy controls suggests its significant contribution in conferring susceptibility to SLE along with other factors.

Key Words: Systemic lupus erythematosus; PTPN22 gene; Kuwait;

Funding Agency: None

Microbiology and Immunology

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Disputed rpoB mutations detected among drug-resistant and polydrug-resistant Mycobacterium tuberculosis isolates phenotypically susceptible to rifampin in Kuwait

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Introduction:
Increasing incidence of MDR-TB is a serious threat to global TB control. Liquid culture-based phenotypic drug susceptibility testing (DST) methods fail to detect Mycobacterium tuberculosis strains with disputed rpoB mutations which exhibit low-level but clinically significant resistance to rifampin. We evaluated the occurrence of rpoB mutations in drug-resistant M. tuberculosis strains phenotypically susceptible to rifampin in Kuwait.

Methods:
A total of 238 isolates including pansusceptible (n=60), monoresistant to isoniazid (INH) (n=51) or streptomycin (SM) (n=15) and polydrug-resistant to INH+SM (n=75) or INH+EMB (ethambutol) (n=26) or INH+SM+EMB (n=11) were tested. Phenotypic DST was performed by MGIT 960 system. Mutations in rpoB hot-spot region (HS-rpoB), katG codon 315 and inhA regulatory region were detected by Genotype MTBDRplus assay. Mutation I572F in rpoB was detected by multiplex allele-specific PCR. Results were confirmed by PCR-sequencing of rpoB.

Results:
All pansusceptible or INH- or SM-monoresistant strains contained wild-type rpoB sequences. Two INH+SM-resistant isolates contained H526N mutation, one INH+EMB-resistant isolate contained D516Y mutation and one INH+SM+EMB-resistant isolate contained S531C mutation in HS-rpoB. All isolates with a disputed rpoB mutation were resistant at least to isoniazid (MDR-TB) and contained S315T mutation in katG. Occurrence of disputed rpoB mutations increased from 3/101 (3.0%) in isolates resistant to any two drugs to 1/11 (9.1%) in isolates resistant to three drugs and was also higher in isolates with additional resistance to EMB (2/37, 5.4%) compared to isolates with additional resistance to SM (3/86, 3.5%).
Conclusions:
Disputed rpoB mutations occur frequently among polydrug-resistant M. tuberculosis isolates. Since patients infected with such strains often relapse or fail treatment, all isolates with polydrug-resistant phenotype should be subjected to rpoB analysis to detect such mutations.

Key Words: Mycobacterium tuberculosis; Polydrug resistance; Disputed rpoB

Funding Agency: KU Research Sector grant MI 03/16

Microbiology and Immunology

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Comparison of in vitro activity of tedizolid and comparator antimicrobial agents against MRSA isolated in a tertiary care hospital in Kuwait

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Introduction:
Treatment of multidrug-resistant infections caused by methicillin-resistant Staphylococcus aureus (MRSA) poses a clinical challenge due to limited therapeutic options and drug toxicity. Tedizolid phosphate is a novel oxazolidinone antibiotic against infections caused by Gram-positive bacteria, including MRSA.
Objectives
This study was done at Ibn Sina Microbiology Laboratory to compare the in vitro antimicrobial activity of tedizolid and comparator antimicrobial agents including linezolid, vancomycin and teicoplanin against MRSA isolates from various clinical specimens and to determine the MIC50, MIC 90 and percentage resistance to those antibiotics.

Methods:
A total of 87 MRSA isolates from various clinical specimens including skin and soft tissue, respiratory tract, blood stream and other sites of infections were evaluated. The mimimal inhibitory concentration (MIC) to vancomycin, teicoplanin, linezolid and tedizolid were determined using the Epsilometer test method (E-test) according to the manufacturer's instructions (Etest® bioMérieux and Liofilchem® MIC Test Strip). MIC50 and MIC90, range and percentage resistance was determined. The MIC breakpoints for all the evaluated antimicrobials were determined according to the criteria defined by CLSI, 2016.

Results:
Out of the 87 MRSA isolates, 50 were isolated from skin and soft tissue, 6 from blood-stream, 13 from respiratory tract, 9 from urine and 9 from other sites. The MIC ranges for tedizolid, linezolid, vancomycin and teicoplanin was 0.094 – 0.75, 0.023 -2.0, 0.25 – 2 and 0.125 – 2 respectively. The MIC50 for the above mentioned antibiotics was 0.38, 1.0, 1.0 and 1.0, respectively, and the MIC90 was 0.50, 1.5, 2.0 and 2.0, respectively. Tedizolid showed the lowest MIC50 and MIC90 values.

Conclusions:
Tedizolid is a promising alternative antimicrobial agent for the treatment of infections caused by MRSA.

Key Words: Tedizoild; MRSA; MIC;

Funding Agency: None

Microbiology and Immunology

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Whole genome characteristics of Helicobacter pylori from native Arab Kuwaitis

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Introduction:
As information on the genotype(s) of Helicobacter pylori causing disease in Kuwait is scarce, we carried out whole genome sequencing and comparative analysis of three H. pylori strains isolated from native, Arab, Kuwaiti patients.

Methods:
Three H. pylori strains-HP22, HP45, HP59-were cultured from gastric biopsies of three patients with gastritis treated at Al Amiri Hospital, during Dec 2012 to Feb 2013. Sequencing was done on MiSeq Illumina platform. Reads were assembled using velvet assembler. CLA was used to assemble draft genome with H. pylori 26695 genome as the reference. Genomes were analyzed using Artemis, tRNAscan-SE, RNAmmer, ISfinder and PHAST and RAST. Whole-genome SNP-based and MLST-based phylogenetic trees were constructed along with 31 other H. pylori representing several genotypes from NCBI database using Harvest and visualized with FigTree. cagA gene-based phylogenetic tree was constructed using neighbor-joining algorithm. Protein sequences were compared using OrthoMCL and functional categories identified using CDD database. Virulence genes were identified using VFDB database.

Results:
H. pylori strains had approximately 1600 genes. They possessed cagA and vacA genes, oipA gene in "on" position, up to seven phage-associated regions, a plasmid and a complete cag-PAI and a plasticity zone. They had a cagA AB-C EPIYA motif. HP22 and HP45 encoded cagA with a EPIY(T) B-type motif and HP59 encoded a EPIY(A) B type motif. vacA gene type combinations for HP45, HP59 and HP22 were s1/m1, s1/m2 and s2/m2 respectively. Another 58 virulence-associated genes were conserved. Strain-specific genes encoding hypothetical proteins were present. In phylogeny, Kuwaiti strains formed a single group adjacent to HpEurope strains. The EPIYA-AB-C type motif of CagA confirmed the European ancestry.

Conclusions:
The comparative genomic analysis of Kuwaiti H. pylori strains revealed a European ancestry and a high pathogenic potential.

Key Words: Helicobacter pylori; Genome; Sequence;

Funding Agency: None

Microbiology and Immunology

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Seroprevalence and associated risk factors of T. solium infection in Kuwait

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Introduction:

Taenia solium (pork tapeworm) causes an intestinal infection (taeniasis) in humans. Adult stage parasite eggs are shed in feces of a taeniasis carrier which may contaminate food/water. Consumption of contaminated food/water may result in development of larval stage cysts in brain (neurocysticercosis) causing severe, often fatal disease. In Kuwait, swine handling and pork consumption are prohibited. Infection is imported via taeniasis carriers which remain undetected due to low sensitivity of current screening based on stool microscopy. This study screened suspected taeniasis carriers using a more sensitive and specific ELISA-based serology.

Methods:
Five hundred newly-arriving immigrants and 500 food handlers at the Public Health Department, Ministry of Health, were asked demographic, socioeconomic and health-related questions and a blood sample was collected. Using T. solium-specific rES33 antigen, we developed an in-house, indirect ELISA to screen and detect anti-T. solium taeniasis-specific IgG antibodies in blood samples.

Results:
ELISA screening has shown that seroprevalence of T. solium taeniasis in Kuwait is 4.2% among expatriate population arriving from endemic Asian and African countries, particularly Ethiopia, Philippines, India and Sri Lanka. Significantly higher O.D. values ($p < 0.05$) were seen among females compared to males, in Ethiopians compared to other nationalities, in expatriates from poor/low-income background compared to middle/high-income background, and those with lower education levels. None of the seropositive cases were detected at Public Health Labs using standard stool microscopy.

Conclusions:
Our in-house ELISA has shown higher sensitivity and specificity in screening the expatriate population for detection of T. solium taeniasis carriers. Therefore, we propose that Public Health Departments of Ministry of Health, Kuwait may adopt this assay for more sensitive screening of T. solium taeniasis carriers.

Key Words: Taenia solium; Taeniasis; Cysticercosis;

Funding Agency: Kuwait University, Research Sector, Project No. YM06/14

Microbiology and Immunology

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Molecular basis of resistance to echinocandins in clinical Candida glabrate isolates in Kuwait

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Introduction:

Candida glabrata is second/third most common Candida species causing candidemia or invasive candidiasis in at-risk patients. It is inherently less susceptible to azole anti-fungal drugs and can also develop resistance to echinocandins, mainly due to missense mutations in hot-spot (HS)-1 and HS-2 regions of FKS1 and FKS2, as a result of prolonged drug exposure. This study determined the molecular basis of resistance in phenotypically identified echinocandin-resistant C. glabrata isolates in Kuwait.

Methods:
C. glabrata isolates (n=75) recovered from various clinical specimens were studied. The isolates were initially identified by Vitek2 system. Identity was confirmed by multiplex (m) PCR assay that simultaneously detects C. glabrata sensu stricto, Candida nivariensis and Candida bracarensis and/or by PCR-sequencing of rDNA. Antifungal susceptibility testing to fluconazole, caspofungin, micafungin and amphotericin B was determined by E-test. Mutations in HS-1 and HS-2 of FKS1 and FKS2 were detected by PCR-sequencing of the respective gene fragments.

Results:
All 75 isolates were identified as C. glabrata by Vitek2 and also by mPCR. Based on EUCAST breakpoints, 71 (95%) isolates were susceptible (MIC = ≤0.032 µg/ml) and 4 (5%) isolates were resistant (MIC = >0.032 µg/ml) to micafungin. Three of four isolates phenotypically resistant to micafungin contained S663P mutation in HS-1 of FKS2 gene. Forty-seven C. glabrata isolates randomly selected from 71 isolates phenotypically susceptible to micafungin contained wild-type sequences in HS-1 and HS-2 of FKS1 and FKS2 genes.

Conclusions:
Although acquired echinocandin resistance is rare among Candida species, its incidence is increasing in C. glabrata resulting in clinical failure among infected patients. Other data show that most echinocandin-resistant C. glabrata isolates contain mutations in HS-1/HS-2 of FKS1/FKS2 genes and their rapid detection will contribute to better management of infected patients.

Key Words: Candida glabrata; Echinocandin resistance; FKS mutations;

Funding Agency: supported by CGS and RS grant YM08/17

Microbiology and Immunology

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Glucose fluctuation enhance macrophages pro-inflammatory expression and the development of atherosclerotic plaques

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Introduction:

Cardiovascular disease (CVD) is the major cause of death in patients with type 2 diabetes (T2D). More than 60% of T2D patients die of CVD related outcomes even under normal glucose levels at the time of death. It is well-established that hypo/hyperglycemia are both in part responsible for the chronic low grade inflammation experienced by diabetic patients, which is an underlying cause for a myriad of diabetic-associated pathologies such as atherosclerosis. This study assessed whether the effect of glucose fluctuation on macrophage inflammation and foam cell formation play a major role in CVD progression.

Methods:
THP-1 transformed macrophages were challenged with a fluctuation (3 and 15mmol/ml) in glucose levels every six hour for three days. Inflammatory markers were measured with flow-cytometry and ELISA. MMP's and TIMP's were also measured in the supernatant by ELISA. Transcription factors was assessed by western blot and RT-PCR.

Results:
Glucose fluctuation induced inflammation in macrophages with no significant difference to hyperglycemic conditions.

Conclusions:
These results suggest that although diabetic patients attempt to avoid hyperglycemic complications via insulin treatment that they are still at risk of inflammation due to the fluctuating glucose levels and require an addition approach to treatment such as Non-Steroidal-Anti-Inflammatory Drugs.

Key Words: CVD; Macrophages; Diabetes;

Funding Agency: KFAS

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First Time Description of Nosocomially Acquired Oxa-181 Carbapenemase-Producing Enterobacteriaceae in Two Major Teaching Hospitals in Kuwait

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Introduction:

OXA-48 carbapenemase-producing Enterobacteriaceae (CRE) has been reported before in a Kuwaiti patient who travelled to France. What has not been reported before in Kuwait is OXA-181-producing CRE, a single amino-acid mutation of OXA-48. The objective of this study was to investigate and characterize rectal isolates of CRE from patients admitted to the intensive care units (ICUs) of major hospitals in Kuwait.

Methods:
Specimens consisted of non-duplicate rectal swabs of patients admitted to the ICUs of 2 hospitals for more than 48 h from April-September, 2017. Enterobacteriaceae isolates were identified by VITEK-2 and susceptibility preformed with the E-test. Ertapenem non-susceptible isolates were subjected to molecular characterization by PCR. Amplicons were sequenced and clonal relatedness of the positive isolates was assessed by pulsed-field gel electrophoresis (PFGE).

Results:
Of the 608 isolates, 61 (10%) were CRE. Of these, 56 (91.8%) were carbapenemase-producers (CPE) and harbored one or more carbapenemase genes. Forty-three (76.8%) harbored blaOXA-181 gene, 7 (12.5%) blaKPC-2, 6 (10.7%) blaOXA-48, 3 (5.4%) blaNDM-5, 3 (5.4%) blaVIM-1 and 3 (5.4%) blaNDM-1. Twelve OXA-181 CRE co-harbored 3 blaNDM-5, 6 blaKPC-2 and 3 blaVIM-1 genes. Seven isolates with indistinguishable banding patterns were singletons after PFGE, and epidemiological investigations revealed that these cases were present in the same ICU unit of same Hospital; 6 isolates were closely related. The patients were of mixed nationalities with no history of prior hospitalization or recent travels.
Conclusions:
Our study revealed 4 compelling findings: 1) alarming high prevalence of CRE among asymptomatic ICU patients, 2) overwhelming prevalence of OXA-181 among our ICU CRE, 3) emergence of OXA-181, NDM-5 and KPC-2 CPE for the first time in Kuwait, and 4) identification of a relatively large number of clonal OXA-181 strains suggesting possible horizontal spread within the ICU.

Key Words: OXA-181 CARBAPENEMASE; ENTEROBACTERIACEAE; ICU

Funding Agency: Faculty of graduate study

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Emergence of Alarming Clindamycin and Erythromycin Resistant Streptococcus group B over 2004-to-2016 in Kuwait

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Introduction:

Group B streptococcus (GBS) is an important neonatal pathogen known to be associated with high morbidity and mortality. GBS is a known etiology of postpartum infection and is considered to be an emerging pathogen in adult causing severe and invasive infections. The aim of this study was to study clindamycin and erythromycin resistance among GBS isolated from invasive and non-invasive specimens over 13 years.

Methods:
From 2004-to-2016, 134invasive and 2,311non-invasive, non-repetitive isolates were included in the study. The identification was done by Vitek2 and MIC determined by E test.

Results:
Among 134 invasive isolates, 124 (92.5%) were from blood and 10 (7.5%) were from CSF. Non-invasive isolates were mainly from genital, urine and wound swabs. The study period was divided into 2004-2006, 2007-2010, 2011-2014 and 2015-2016. The most prevalent serotype in invasive GBS isolates was type III 32 (28.8%), while in non-invasive was type V (31.4%). Resistance pattern to clindamycin and erythromycin of non-invasive GBS isolates was as follow: (5.2% and 4.8%) in 2004-2006, (16.3% and 21.3%) in 2007-2010, (18.8% and 25%) in 2011-2014 and (52.5% and 49.4%) in 2015-2016. Invasive GBS isolates resistance pattern to clindamycin and erythromycin was as follow: (5.3% and 13.2%) in 2004-2006, (5.7% and 25.7%) in 2007-2010, (23.7% and 31.6%) in 2011-2014 and (43.5% and 40.4%) in 2015-2016. A high level erythromycin and clindamycin- resistant strains with MIC > 256 µg/ml was (20% & 61.5%) respectively. Resistance to either erythromycin and/or clindamycin was (50%) among serotype IV, (43.8%, 33.3%, 30%,23.5% & 17%) among serotype III, Ib, V, II &Ia respectively.

Conclusions:
GBS resistance to clindamycin and erythromycinwas significantly increased over the study period. These findings strongly support ACOG recommendations that clindamycin use for intrapartum prophylaxis to be restricted to penicillin allergic women and all GBS isolates to be tested for clindamycin.

Key Words: GBS; Clindamycin; Resistance;

Funding Agency: None

Microbiology and Immunology

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Characterization of MRSA isolates belonging to spa type t688 in Kuwait hospitals

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Introduction:

Methicillin-resistant staphylococcus aureus (MRSA) is a major cause of life threatening infections. MRSA isolates can be characterized using different molecular techniques including Spa typing, multi locus sequence typing and DNA microarray. Objectives: To characterized MRSA isolates belonging to spa type t688 in Kuwait hospitals.

Methods:
MRSA isolates were obtained from various samples in different Kuwait hospitals from January 1st to December 31 in 2016 and characterized using antibiogram, Spa typing and DNA microarray.

Results:
In total, 240 (10.4%) of the 2305 MRSA isolates belonged to spa type t688. Other major spa types identified included t304 (9.1%) and t860 (8.2%). The t688 MRSA were isolated from Nasal (21.20%), skin and soft tissue infections (20.4%) and other clinical samples in 11 hospitals. The t688 isolates were resistant to chloramphenicol (98%), tetracycline (85.8%), fusidic acid (82%), trimethoprim (79.1%), erythromycin and clindamycin (16.2%), ciprofloxacin (8.7%), gentamicin (0.8%), kanamycin (0.4%), and high-level mupirocin (0.4%,) and carried fexA, tetM, fusC and dfrS1. DNA microarray analysis showed that all t688 isolates belonged to clonal complex 5 (CC5) with the majority belonging to CC5-MRSA-VI+SCCfus (69 isolates) followed by CC5-MRSA-V [SED/jr+] (7 isolates), CC5-MRSA-V (3 isolates) and CC5-MRSA-VI, [New Pediatric Clone] (3 isolates). All CC5 genotypes belonged to accessory gene regulator type II, capsular polysaccharide type 5, harbored enterotoxins genes, (sed, sei and selu) and hemolysins genes (hld, hl, hla, hlb, hlll).
Conclusions:
The study revealed the transmission of t688 isolates belonging to CC5-MRSA in Kuwait hospitals in 2016, and highlights the importance of molecular typing in detecting the spread of new MRSA strains in a healthcare facility.

Key Words: MRSA; Molecular typing; Spa tying;

Funding Agency: None

Microbiology and Immunology

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Molecular characterization and epidemiology of multidrug-resistant Mycobacterium tuberculosis (MDR-TB) and identification of possible cases of local transmission of MDR-TB in Kuwait

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Introduction:

Increasing incidence of multidrug-resistant tuberculosis (MDR-TB) is hampering efforts to control TB. Kuwait is a low (25/100,000) TB incidence country and ~1% of Mycobacterium tuberculosis strains are resistant to rifampin, RIF and isoniazid, INH (MDR-TB). Analysis of resistance conferring mutations in seven genes was combined with spoligotyping for detecting local transmission of MDR-TB in Kuwait.

Methods:
MDR-TB strains (n=131) from 88 TB patients and 50 susceptible strains were used. Susceptibility testing was done by MGIT 960 system, gMTBDRplus assay and PCR-sequencing of three regions of rpoB, katG codon 315 (katG315) + inhA regulatory region, embB (embB306/embB406/embB497 regions), rpsL + rrs-500-900 regions and pncA for RIF, INH, ethambutol (EMB), streptomycin (SM) and pyrazinamide (PZA), respectively. Sequencing data were used to construct phylogenetic tree by MEGA7 software. Spoligotypes were identified by SITVIT2 and phylogenetic tree was made by MIRU- VNTR plus software.

Results:
Mutations were detected in most isolates in rpoB, katG+inhA, embB, rpsL+rrs and pncA which confer resistance to RIF, INH, EMB, SM and PZA, respectively. Phylogenetic analysis of multi-locus concatenated sequences showed unique patterns for 51 patient's isolates while 37 patient's isolates grouped in 14 clusters. Spoligotyping identified 35 patterns (19 unique patterns and 69 patients's isolates in 16 patterns) including 11 orphan patterns. Sixteen isolates yielded 6 clusters (each containing 2-5 isolates) by both fingerprinting methods.

Conclusions:
Our study provides the first insight into molecular epidemiology of MDR-TB in Kuwait and identified six potential cases of local transmission of MDR-TB involving 2-5 subjects (including 5 Kuwaiti patients) which had escaped detection by routine surveillance studies. Prospective detection of resistance conferring mutations thus identifies possible cases of local transmission of MDR-TB in low TB incidence countries.

Key Words: Mycobacterium tuberculosis; MDR-TB; Molecular fingerprinting;

Funding Agency: supported by grant YM08/14

Microbiology and Immunology

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Colonization with multi-drug resistant rods among in-patients in a general hospital in Kuwait

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Introduction:
Since the incidence of infections due to multi-drug resistant rods (MDRR) is increasing worldwide reliable detection of these organisms is critical for infection control. The study aims at presenting institutional experience with MDRR colonization at specific anatomical sites of in-patients.

Methods:
Microbiological samples for identification of MDRR such as, carbapenem -resistant Enterobacteriaceae (CRE), -Acinetobacter baumannii (CRAB) andPseudomonas aeruginosa (CRPA) were routinely collected from patients admitted to different wards including intensive care units (ICU). Anal and throat swabs were cultured on McConkey agar with and without addition of meropenem (10 mg/L). Colonies isolated on selective media then subjected to identification and antimicrobial susceptibility by Phoenix and MDRR were confirmed for resistant markers by EasyplexR SuperBug, to detect target genes including KPC, VIM, NDM and OXA-48 enzymes and ESBL of CTX-M variety of Enterobacteriaceae.

Results:
During a one year study period, the rate of isolation of aforementioned MDRR among a total of 2955 samples tested was found to be 4.2% (124/2955). The proportion of isolated organisms was CRAB (67.7%), CRPA (20.2%), and CRE (12.1%). Anal swabs were more often positive (76; 61.3%) than throat swabs for MDRR and their isolation rate (43.5%) was found to be lower from ICU patients as compared to other wards. The resistant markers detected among these isolates were: A. baumannii (OXA23=59.5%; NDM=15.5%); P. aeruginosa (VIM=32%); K. pneumoniae (NDM=42.8%; CTX-M=28.6%; OXA48=7.14%).

Conclusions:
Our study confirms that colonization with MDRR is not necessarily restricted to ICUs. Determination of resistant markers can aid in timely detection of new clones, risk factors and implementation of contact precautions. Screening for intestinal carriage of MDRR is of significant importance to optimize antimicrobial use and for the development of infection control strategies

Key Words: Colonization; Multi-drug resistant rods; Resistant markers;

Funding Agency: none

Microbiology and Immunology

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Surgical site infection following cesarean section in a secondary-care center in Kuwait: trends and risk factors

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Introduction:
Surgical site infections (SSI) are a significant cause of post-surgical morbidity and mortality. The objectives of this study were to determine the incidence of SSI and identify risk factors for infections following cesarean section (CS).

Methods:
A prospective study of SSI after CS was carried out from January 2014 to December 2016 using the methodology of the American National Nosocomial Infection Surveillance System. Follow-up of women was carried out in the Obstetrics and Gynecology outpatient department for any post-discharge SSI. Suspected SSIs were confirmed clinically by the surgeon and or by culture.

Results:
During the study period, 7235 CS were performed with infection rate estimated at 2.1%, increasing from 1.7% in 2014 to 2.95% in 2016 (p=0.010). The infection rate was 46.7% in women ≤ 30years as compared to 53.3% in women > 30 years (p=0.119). Most of the infections were categorized as superficial (98.0%) and presented more often following emergency (73.7%) than elective CS (26.3%) (p=0.554). Of 148 culture samples from as many women, 112 (75.7%) yielded growth of microorganisms with 42 (37.5%) being multi-drug resistant. Women who did not receive prophylactic antibiotics (35.5%) developed SSI more often than those who did (p< 0.0001). SSI appeared following discharge from hospital (99.3%), becoming evident within the first 13 days (median 11 days) following surgery (median duration 40 min.). Majority of the women (103) had ASA score of 1and 136 women presented with a risk score of 1.

Conclusions:
Our study demonstrates that most of SSI following CS are detected only after patient's discharge from the hospital. Emergency CS and improper prophylaxis, are important risk factors in the development of SSI. In the light of the emergence of MDROs there is a need to implement revised prophylactic antibiotic policy as part of antimicrobial stewardship to bring down the SSI rate to zero.

Key Words: Surgical site infection; Cesarean section; Antibiotic prophylaxis;

Funding Agency: None

Microbiology and Immunology

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Effect of human coronavirus OC43 structural and accessory proteins on the transcriptional activation of antiviral response Elements

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Introduction:

In Kuwait, human coronavirus OC43 (HCoV-OC43) causes 25-30% of common cold, and 8.8% of respiratory infections in hospitalised patients. It is also associated with severe respiratory symptoms in infants, elderly, and immunocompromised patients. Our previous results showed that the expression of antiviral genes in human embryonic kidney (HEK) 293 cells is downregulated in the presence of HCoV-OC43 proteins. To understand the role of HCoV-OC43 proteins in antagonising antiviral responses of the host, we investigated the effect of HCoV-OC43 structural and accessory proteins on the transcriptional activation of interferon-stimulated response element (ISRE), interferon-beta (IFN-beta) promoter, and nuclear factor kappa B response element (NF-kappaB-RE).

Methods:
HCoV-OC43 ns2a, ns5a, membrane (M), and nucleocapsid (N) mRNA were amplified and cloned into the pAcGFP1-N expression vector, followed by transfection in HEK-293 cells. Two days post-transfection, the cells were co-transfected with a reporter vector containing firefly luciferase under the control of ISRE, IFN-beta promoter, or NF-kappaB-RE. Renilla luciferase vector was used as an internal control for transfection efficiency. Following 24 hours of incubation, the cells were treated with either IFN or tumour necrosis factor for 6 hours. Thereafter, promoter activity was assayed using the dual-luciferase reporter assay system. Influenza NS1 protein was used as positive control for antagonism.

Results:
The transcriptional activity of ISRE, IFN-beta promoter, and NF-kappaB-RE was downregulated in the presence of ns2a, ns5a, M, or N protein as there was a sharp fall in firefly luciferase levels. Overall, HCoV-OC43 proteins reduced firefly luciferase levels for ISRE and IFN-beta promoter by at least ten fold, whereas for NF-kappaB-RE the firefly luciferase levels were reduced by at least five fold.

Conclusions:
HCoV-OC43 has the ability to block the activation of different antiviral signaling

Key Words: Coronavirus OC43; Antiviral response elements; Luciferase reporter gene

Funding Agency: College of Graduate Studies, Research Administration Grant number YM04/15

Microbiology and Immunology

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Diversity and emergence of novel methicillin-resistant Staphylococcus aureus genotypes in Kuwait hospitals

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Introduction:
The epidemiology of Methicillin-resistant Staphylococcus aureus (MRSA) is constantly changing in healthcare facilities worldwide driven by international travels. Regular surveillance is essential to monitor changes in the composition of MRSA strains in healthcare facilities. This study was conducted to characterize MRSA isolates obtained during a surveillance exercise to provide information on the types of MRSA strains circulating in Kuwait hospitals.

Methods:
A survey of MRSA was conducted from February to July, 2016. One thousand and fifty-eight MRSA were isolated from clinical samples in Kuwait hospitals and typed using antibiogram, SCCmec typing, spa typing, and DNA microarray.

Results:
A total of 168 different spa types were obtained. The majority belonged to spa types t688 (111; 10.4%), t304 (90; 8.5%), t860- (85; 8.0%), t044 (69; 6.5%), t127 (65; 6.1%), t002 (61; 5.7%); and t223 (54; 5.1%). One hundred and sixty-eight isolates were selected for DNA microarray analysis. Twenty-one clonal complexes (CCs) consisting of CC1, CC5, CC6, CC8, CC15, CC22, CC30, CC45, CC59, CC72, CC80, CC88, CC96, CC97, CC121, CC152, CC361, CC398, CC913, CC1153, CC2250/2277 were obtained with the majority belonging to CC5 (94; 55.9%) and CC22 (73; 43.4%). Some strains including CC15-MRSA-V+SCCfus; ST59-MRSA-IV WA MRSA-118; ST59/952-MRSA-VT [PVL+] Taiwan clone; CC96-MRSA-IV [PVL+] Central Asian CA-MRSA; CC152-MRSA-V [PVL+]; CC398-MRSA-IV; CC2250/2277-MRSA-V WA MRSA-114 were identified for the first time in Kuwait hospitals.

Conclusions:
The results demonstrated the diversity of MRSA strains circulating in Kuwait hospitals. The study also revealed the emergence of new MRSA strains including Livestock- associated MRSA (CC398). The emergence of new MRSA strains can impose different challenges for the physicians and infection control teams for treatment and control of MRSA infections in Kuwait hospitals.

Key Words: MRSA; Genotyping; Spa typing;

Funding Agency: None

Microbiology and Immunology

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Antimicrobial resistance of Escherichia coli isolates from women and children with urinary tract infections

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Introduction:

Urinary Tract Infections (UTIs) are very common disease both in women and children. They are associated with risk for developing medical complications in pregnancy and childhood. Escherichia coli (E. coli) is the most common infecting organism in patients with UTIs and it possess specific virulence determinants. The study was undertaken to determine the antibiotic resistance trends of E. coli strains isolated from women and children with UTIs over a period of seven years. We analysed also the distribution of haemolysin production in E. coli strains.

Methods:

During 01.01.2011 - 30.06.2017 retrospective epidemiological study involved: 71 pregnant women, 350 non-pregnant women and 23 children. They all were with UTIs and visited London Hospital. Isolation was performed and the identification - by the API system. The disk diffusion method was used for susceptibility testing and the results were interpreted according to CLSI guidelines.

Results:

The cumulative results of the resistance rates of E. coli isolates are analysed. High resistance development observed in E. coli isolates against the antibiotics which are frequently used in empiric treatment of patients with UTIs - 41,4 %. We analysed also multidrug resistance rates (in 2011 - 4,8 % and in 2016 - 7,3 % of the strains E. coli are multidrug-resistant) and haemolysin production in E. coli isolates (28,8% and 34,15% respectively).

Conclusions:

The clinicians must consider current resistance rates when prescribing the antibiotics. We believe that it is necessary to stop prescription of some antimicrobials in our hospital and to rationalize prescription of other, in order to prevent a further increase of resistance in E. coli isolates. Knowledge of E. coli antimicrobial resistance patterns in women and children is essential to provide clinically successful antimicrobial therapy for UTIs, good evolution and decreasingly the risk of complications.

Key Words: Resistance rates; Complications; Haemolysin production;

Funding Agency: None

Microbiology and Immunology

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The impact of Persistent Genotype-4 Hepatitis C Virus Infection on Cellular Immune Subsets before, during and after treatment.

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Introduction:
Hepatitis C virus (HCV) infection is a major public health problem with an estimated 3-4 million people infected each year worldwide. 20–30% of individuals acutely infected with HCV will spontaneously clear the virus, with the remaining 70–80% developing persistent HCV infection. The interplay between the virus and host innate and adaptive immune responses determine the outcome of HCV infection. The present study aims to determine the level of cellular immune subsets in responders and non-responders HCV-infected patients as a result of the standard treatment (PEG-IFN and ribavirin) and to correlate the results with the major HCV genotypes in Kuwait.

Methods:
Data of the immunophenotyping for cellular subsets include 60 genotype-4 HCV-infected patients (39 responders vs. 21 non-responders) at baseline (before treatment) and after treatment. The immunophenotyping was evaluated by flow cytometry using antibodies specific to mature T cells, T cytotoxic cells, regulatory T cells, T helper cells, activated T cells, natural killer (NK) cells, NKT cells, pan B cells, and regulatory T cells.

Results:
There were significant differences in the mean values of percentages for T helper cells, T cytotoxic cells, B cells, NK cells, NKT cells and activated T cells between HCV-responder vs. HCV-non-responder patients. Also, significant differences were noticed in the mean values of the absolute counts for T helper cells, B cells, NK cells, and T cells.

Conclusions:
Cellular subsets of the immune system play an important role in the pathogenesis, progression, and clearance of HCV. The screening for multiple cellular markers in the present study showed significant variations in the absolute counts and percentages of essential immune cellular subsets. These findings could lead to new possibilities for immune-based interventions and/or vaccine development with the aim of restoring functional antiviral T cell responses combined with improved viral clearance.

Key Words: Hepatitis C virus; Immunophenotyping; Trearment;

Funding Agency: Research grant MI02/13 by the Research sector, Kuwait

Microbiology and Immunology

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Antibody Reactivity to M. tuberculosis RD1 and RD9 Proteins and Peptides in Rabbits, Mice and Humans

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Introduction:
The immunogenicity of antigens may vary depending upon the species tested. The aim of this study was to compare the antigen-specific antibody responses in rabbits, mice and humans to proteins and peptides encoded by M. tuberculosis-specific regions of difference (RD) genes, i.e. RD1 (PE35, PPE68, ESXA and ESXB) and RD9 (Rv2346).

Methods:
Sera were obtained from i. rabbits immunized with pure recombinant proteins of PE35, PPE68, ESXA, ESXB and nRv2346, ii. mice immunized with DNA vaccine constructs of pUMVC6 and pUMVC7 containing RD1 and RD9 genes, and iii. Tuberculosis patients and healthy humans. ELISAs were performed with the sera to determine the antibody reactivity to purified proteins, peptide pools and individual peptides of RD1 and RD9 proteins. The optical density (OD) values were measured at 405 nm. E/C were calculated, and the values of E/C>2 were considered positive.

Results:
The ELISA results with sera from rabbits immunized with pure proteins showed positive antibody reactivity with all of the immunizing proteins and their peptide pools. Testing of the sera with individual peptides showed positive antibody reactivity with PE35 peptides P1, P2, P5 and P6, PPE68 peptides P9, P11, P14, P22, P23 and P24, all peptides (P1 to P6) of ESXA and ESXB, and RV2346 peptides P1, P2, P3, P5 and P6. The sera from mice immunized with DNA vaccine constructs showed antibody reactivity to the peptide P6 of PE35 and peptides P19 and P24 of PPE68. In humans, peptides of PPE68 (P11, P14, P22, P23 and P24) and Rv2346 (P4, P5 and P6) showed positive reactivity with sera from tuberculosis patients and healthy subjects.

Conclusions:
The results suggest that all of the tested proteins have several antibody-inducing epitopes, and demonstrate the superiority of rabbits for studying antibody responses to various antigens.

Key Words: Mycobacterium tuberculosis; Recombinant vaccine vectors; ELISA, Antigens,

Funding Agency: Supported by Kuwait University Research Sector grants YM01/03 and SRUL02/13.

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Metagenomic Analysis of Viral Diversity in Respiratory Samples from Patients with Respiratory Tract Infections in Kuwait

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Introduction:
A metagenomic approach based on target independent next-generation sequencing has become a known method for the detection of both known and novel viruses in clinical samples. This study aimed to use the metagenomic sequencing approach to characterise the viral diversity in respiratory samples from patients with respiratory tract infections.

Methods:
We have investigated 86 respiratory samples received from various hospitals in Kuwait between 2015 and 2016 for the diagnosis of respiratory tract infections. A metagenomic approach using the next-generation sequencer to characterise viruses was used.

Results:
According to the metagenomic analysis, an average of 145, 019 reads were identified, and 2% of these reads were of viral origin. Also, metagenomic analysis of the viral sequences revealed many known respiratory viruses, which were detected in 30.2% of the clinical samples. Sequences of non-respiratory viruses were detected in 14% of the clinical samples, while sequences of non-human viruses were detected in 55.8% of the clinical samples. The average genome coverage of the viruses was 12% with the highest genome coverage of 99.2% for respiratory syncytial virus, and the lowest was 1% for torque teno midi virus 2. Our results showed 47.7% agreement between multiplex Real-Time PCR and metagenomics sequencing in the detection of respiratory viruses in the clinical samples.

Conclusions:
Though there are some difficulties in using this method to clinical samples such as specimen quality, these observations are indicative of the promising utility of the metagenomic sequencing approach for the identification of respiratory viruses in patients with respiratory tract infections.

Key Words: Respiratory Viruses; Metagenomic Sequencing; Kuwait;

Funding Agency: Research Sector, Kuwait University. Project No. MI03/15

Microbiology and Immunology

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Molecular characterization of Methicillin-Resistant Staphylococcus aureus in a General hospital in Kuwait

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Introduction:
Methicillin-resistant Staphylococcus aureus (MRSA) is a major cause of healthcare-associated and community-associated infections worldwide. determining the dominant MRSA clones in a local healthcare facility is important for better management of infections.The objective of this study was to investigate the prevalence and clonal composition of MRSA strains in a General hospital in Kuwait.

Methods:
Bacterial strains: A total of 209 MRSA isolates were obtained from clinical samples in Farwaniya hospital from 1st January to 31st December, 2016. Antibiotic susceptibility testing: Antibiotic susceptibility testing was performed by disc diffusion method. MIC was determined using E-test and interpreted in accordance with Clinical Laboratory Standards Institute (CLSI) guideline 2016.Carriage of Panton–Valentine leukocidin (PVL) genes: All MRSA isolates were investigated for the carriage of PVL (lukS/F-PV) encoding genes using primers and PCR protocol previously published. Molecular typing SCCmec typing: All isolates were typed by multiplex PCR using previously published primers.Spa typing: All isolates were spa typed using primers and PCR protocol published by Harmsen et al.

Results:
Specimens source: The majority of the MRSA isolates were obtained from wound (n=52), blood (n=25) and pus (n=22). Antibiotic susceptibility testing: All MRSA isolates were susceptible to vancomycin, teicoplanin, and rifampicin. Carriage of PVL: Fifty-nine (31%) MRSA isolates carried PVL encoding genes. Molecular typing: Five SCCmec types (II-VI) were detected in the MRSA isolates. The majority of the isolates belonged to SCCmec types IV (74; 35%) and V (55; 26.3%), followed by type III (71; 33.9%), IV (8; 3.8%), and II (1; 0.47%) SCCmec type I was not found in any of the isolates. Based on SCCmec typing, MRSA isolates were classified into CA-MRSA and HA-MRSA. A total of 126 (60%) isolates were CA-MRSA, and 83 (39.7%) isolates were HA-MRSA. Fifty-five spa types were detected in MRSA isolates.

Conclusions:
The study showed that MRSA isolates circulating in Farwaniya hospital belonged to a mix population of HA-MRSA and CA-MRSA with the majority (126; 60.2%) belonging to CA-MRSA. The isolates were mostly (99; 47.3%) obtained from invasive infections (wound, blood and pus). Molecular typing revealed that HA-MRSA and CA-MRSA isolates belonged to diverse genetic backgrounds. CA-MRSA isolates belonged to 48 different spa types with the majority belonging to t688 (14 isolates), t127 (14 isolates), t304 (13 isolates), and t044 (12 isolates), while HA-MRSA isolates belonged to t860 (50 isolates) and t945 (18 isolates). Sixty-three (50%) CA-MRSA isolates exhibited multi-resistance to non-beta-lactams including kanamycin (24 isolates), fusidic acid (21 isolates), erythromycin (20 isolates), tetracycline (18 isolates), gentamicin (18 isolates), clindamycin (16 isolates), trimethoprim (17 isolates), and chloramphenicol (8 isolates). PVL testing revealed that 31% of the isolates carried PVL encoding genes with the majority belonging to CA-MRSA. The emergence of multi-resistant CA-MRSA isolates with different genetic backgrounds in Farwaniya hospital is alarming since it can complicate treatment. Therefore, non-beta-lactam antibiotics (other than vancomycin and teicoplanin) should be rationally used to stop the spread of these isolates.

Key Words: HA-MRSA health care associated MRSA; CA-MRSA community-associated

Funding Agency: None

Microbiology and Immunology

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Food Safety Knowledge and Hygiene Practices among Food Handlers Working in Community and Healthcare Settings in Kuwait Districts

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Introduction:

Food handlers (FH) play an important role in ensuring food hygiene during food production. Unsafe food handling or poor personal hygiene could be potential sources of dissemination of bacterial infection. The study objective was to assess food safety knowledge and practices among food handlers in both community and Healthcare catering services.

Methods:
The survey was conducted among food-handlers in Kuwait via a face-to-face interview using structured questionnaire, from September 2015 to June 2016.

Results:
A total of 405 participants were enrolled in the study; 182 (44.9%) were community food handlers (CFH) and 223 (55.1%) were Healthcare food handlers (HCFH). Indian nationality formed the bulk of the HCFH (140: 62.8%) whilst the Philippinos formed the majority of the CFH (67: 35.8%). Analysis by age stratification showed that higher proportion of the 44%, the FH were aged 29-39 years. The majority (343: 84.7%) were male participants. Approximately 43% of them had a high school certification, particularly the HCFH (58.7%). About 63.7% of the CFH had college degrees. A total of 191 (48%) traveled back home. Assessment of fingernails trimming habit showed that 348 (85.9%) cut their nails once a week and 33 (8.1%) rarely did with hardly any difference between HCFH and CFH. Only 24 (5.9%) gave a history of previous hospitalization. About 65.4% knew of the necessity for changing utensils while handling unwrapped raw or cooked foods. However, an unacceptable proportion (44.9%) of the FHs wore the same gloves when handling meat and fresh food. Equally, high proportion (42.2%) of the FHs went home with their working clothes.

Conclusions:
The awareness of hygienic measure by majority of the FHs was very appropriate. However, the study revealed some practices which were below recommended standards and which may pose a significant risk to the consumers. Therefore, regular food safety training is highly recommended to improve food handler's hygiene knowledge.

Key Words: Food safety; Demographic characteristics; Food handler;

Funding Agency: Kuwait University, College of Graduate Studies and Research administration (Grant No. YM07/15).

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Explosive Emergence of Colistin-resistant and Carbapenem-resistant Enterobacteriaceae (CRE) Among Community Food- handlers in Kuwait.

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Introduction:
Background: Colistin is an antimicrobial agent used as last resort for the treatment of carbapenem-resistant Enterobacteriaceae (CRE). Anecdotal and published reports from our country have shown that as high as 8% of the significant Enterobacteriaceae in 4 Kuwaiti hospitals were CRE and 10% of the CRE were colistin-resistant. The extent of colistin resistance and CRE among healthy individuals in the community is currently unknown. The aim of this study was to determine the prevalence of CRE and colistin-resistant carriage in food handlers.

Methods:
We included 405 food handlers throughout Kuwait during their routine screening for Salmonella spp. The rectal swab was collected and cultured using routine methodology for isolation. The identification was performed by Vitek-2 and MIC was determined by E- test.

Results:
A total of 679 non-duplicate isolates were included in the study. Out of these, 423,125 and 53 were Escherichia coli, Klebsiella pneumoniae and Enterobacter cloacae, respectively. Seventy-seven (11.3%) individuals were positive for faecal carriage of colistin-resistant isolates (MIC, > 2mg/L). These isolates included E. coli (n=43), K. pneumoniae (n=14) E. cloacae (n= 6), P. mirabilis (n=5) and 9 other species. The faecal carriage rate of CRE was (5.3%, 36). Isolates included E.coli (n=16), K. pneumoniae (n=8), E. cloacae (n=3), Citrobacter spp. (n=2) and 7 other species. CRE was detected among 16.8% of colistin-resistant isolates however, colistin resistance was detected in 15 (41.6%) of the CRE isolates.

Conclusions:
This study highlighted an unexpected and alarming high prevalence of colistin-resistant Enterobacteriaceae among healthy individuals in community. These findings call for introduction of preventive measures by Public Health Authority to prevent dissemination among the general population at large. Further genetic study is needed to evaluate the determinants of colistin resistance among the Enterobacteriaceae in our community.

Key Words: Colistin; Carbapenem; Enterobacteriaceae;

Funding Agency: Collage of Graduate Studies and Research Administration, Kuwait University Grant No. YM07/15 which is fully acknowledged.

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A comparison of Multiplex PCR, ERIC-PCR, 16S rDNA sequencing, and Whole Genome sequencing for identification and/or typing of clinical Acinetobacter baumannii strains isolated in two major hospitals in Kuwait

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Introduction:
Acinetobacter baumannii is a rising concern in the medical field as one of the most dangerous MDR (multiple drug resistant) opportunistic bacterial pathogens in nosocomial settings. The phenotypic methods for identification and typing of A. baumannii are unsatisfactory in distinguishing between A. baumannii and genotypically related species. The objective of this study was to test the abilities of multiplex PCR, Enterobacterial Repetitive Intergenic Consensus (ERIC)-PCR, 16S rDNA sequencing and Whole Genome sequencing (WGS), for identification and/or typing of A. baumannii strains isolated in Kuwait.

Methods:
Sixty-seven phenotypically identified clinical strains of A. baumannii, isolated at Al-Sabah, and Farwaniya hospitals in Kuwait, were used in this study. The genomic DNA were isolated from the bacterial cultures using Qiagen kits. The isolated DNA were quantified by Qubit fluorometry. The DNA samples were used for multiplex PCR, ERIC-PCR, 16S rDNA sequencing and whole genome sequencing using standard methods. The band profiles (in case of multiplex PCR and ERIC-PCR) and the DNA sequence data (in case of 16S rDNA and whole genome sequencing) were analyzed by BioNumerics software for species identification and genotyping analysis.

Results:
All of the 67 isolates were identified as A. baumannii by multiplex PCR, and 16S rDNA and whole genome sequencing. The clustering pattern of 16S rDNA, ERIC PCR, and WGS single nucleotide polymorphisms (SNP) analyses gave a discriminatory index of 0.37, 0.52, 0.36.

Conclusions:
The molecular methods used in this study confirm the identity of the isolates as A. baumannii and suggest genetic heterogeneity among them, with the ERIC-PCR showing the maximum groups/genotypes with highest discriminatory power.

Key Words: Acinetobacter baumannii; Molecular methods; Typing;

Funding Agency: The College of Graduate Studies and Research Sector grant YM07/16

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Evaluation of five antigen delivery systems for the induction of antigen-specific and protective cellular immune responses to a major Mycobacterium tuberculosis-specific antigen Rv2346c

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Introduction:
Vaccination against Mycobacterium tuberculosis has only been partially successful. The only available vaccine, BCG introduced in 1921, displays limited efficacy against adult pulmonary tuberculosis, the most common outcome of the disease. Due to limitations of BCG vaccine, the development of new vaccines has gained significant interest in recent years. The identification of major M. tuberculosis-specific antigens has led to study their role in inducing protective immunity against tuberculosis. However, the delivery of these antigens is an important issue. The aim of this study was to test four delivery systems, i.e. chemical adjuvants (Alum and IFA), two non-pathogenic mycobacteria (M. smegmatis and M. vaccae), and a DNA vaccine vector, for induction of protective and pathologic cellular immune responses to a major M. tuberculosis-specific antigen Rv2346c.

Methods:
The gene of Rv2346c was cloned into three expression plasmids. The appropriate recombinant plasmids were used to obtain recombinant Escherichia coli and mycobacteria. Mice were immunized and boosted with (1) recombinant (r) protein emulsified in chemical adjuvants, (2) r-mycobacteria, and (3) the r-DNA vaccine. Mice were sacrificed and the spleenocytes were stimulated in vitro with a mitogen and 25-mer peptides covering the sequence of Rv2346c. The culture supernatants were assayed for the protective Th1 cytokine IFN-ɣ and the pathologic Th2 (IL-5), Treg (IL-10) and Th-17 (IL-17A) cytokines in ELISA.

Results:
RV2346c was successfully cloned and expressed in E. coli and mycobacteria. The mice immunized with the protein in IFA, r-mycobacteria and rDNA vaccine showed positive responses to the peptide pool in Th1 assays but not in Th2 and Treg assays.

Conclusions:
The study suggests that live non-pathogenic mycobacteria and DNA vaccine vectors could be useful delivery systems for the induction of protective immune responses against tuberculosis.

Key Words: Rv2346c; Cytokines; Vaccines;

Funding Agency: College of Graduate Studies, Research Sector Projects YM06/15 and SLU02/13.

Microbiology and Immunology

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Candida growth in urine cultures: Contemporary analysis of species and current trends in antifungal susceptibility in a general hospital in Kuwait

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Introduction:
Urinary tract infections (UTIs) due to Candida species are becoming common, especially in hospitalized patients. Although it can be challenging to differentiate colonization from true candiduria, denying treatment to appropriate patient can lead to increased morbidity and mortality. The aim of this study was to find the frequency of Candida among uropathogens, speciation and determining the susceptibilities profile.

Methods:
A prospective study conducted from October 2016 to September 2017 and data from urine samples cultured during this period were collected in a general hospital. Suspicious colonies on Sabourauds dextrose agar and or blood agar were identified and susceptibility to antifungal drugs was determined by VITEK® 2 fungal susceptibility card (bioMérieux, France).

Results:
A total 49,156 urine samples were received. The cultures were positive for uropathogens in 6156 samples. Although Candida was isolated in 375 (6.1%) samples, only culturally significant 307 (5.0%) isolates were subjected to identification and susceptibility testing. The isolation rates of C. albicans, C. tropicalis, C. glabrata, C. parapsilosis and C. krusei were 60.3%, 19.5%, 9.1%, 3.9% and 2.6%, respectively. All the isolates were susceptible (100%) to flucytosine except none of C. krusei and C. dubliniensis strains. Fluconazole also showed good activity (100%) against most of the isolates except C. glabrata (96.4%), C. parapsilosis (91.7%). All Candida spp. were susceptible (100%) to voriconazole, caspofungin, amphotericin B and micafungin. Only 83.3% of S. ciferri isolates exhibited susceptibility to fluconazole, voriconazole and amphotericin B.

Conclusions:
C. albicans exceeded the number of non-albicans Candida among the urinary isolates. All Candida spp. were susceptible to most of the antifungal agents tested. Unusual Candida spp. may be present in the urine cultures.

Key Words: Candiduria; Candida speciation; Antifungal susceptibility;

Funding Agency: None

Microbiology and Immunology

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Proportion of positive blood cultures that yielded extended-spectrum β-lactamase (ESBL) and carbapenem-resistant Enterobacteriaceae (CRE) isolates in a Teaching Hospital in Kuwait over a 2-year period.

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Introduction:
Extended-spectrum beta-lactamase (ESBL)-producing organisms and carbapenem-resistantEnterobacteriaceae (CRE) pose unique challenges to clinical microbiologists, infectious diseases physicians, infection control professionals and antibacterial-discovery scientists. This study was undertaken to determine the prevalence of extended-spectrum β-lactamase (ESBL)-producing and carbapenemase-positive members of the family Enterobacteriaceae isolated from positive blood cultures of patients in Mubarak Al Kabeer hospital.

Methods:
Enterobacteriaceae isolates from proven cases of blood stream infections (BSI), from January 2014 to December 2015, were included in the study. They were identified and tested for their susceptibilities to 18 antibiotics by conventional methods and semi-automated VITEK-2 system. ESBL and carbapenem resistance (CR) were detected by phenotypic and molecular PCR methods, and characterized by sequencing.

Results:
A total of 4133 blood cultures were positive. Of these, 543 (13.1%) were positive for Enterobacteriaceae, 135 (24.9%) of which were ESBL producers and 28 (5.2%) identified as CRE. The most common of the ESBL-producing isolates were Escherichia coli (81:60%) and Klebsiella pneumoniae (44:32.6%). Resistance rates of E. coli to the cephalosporins ranged from 47-100%, ciprofloxacin 70.4%, imipenem 2.5% and meropenem 1.2%. Higher proportions of K. pneumoniae were resistant to the cephalosporins (68.2-100%), imipenem (27.3%) and meropenem (22.7%). Sequence analysis of the ESBL revealed CTX-M-15 as the commonest enzyme (75%). The CRE harbored mainly the blaVIM (28.6%) and blaNDM-1 (35.7%) genes.

Conclusions:
Our study demonstrated a high prevalence of Enterobacteriaceae harboring ESBL of CTX-M-15 variety and equally high prevalence of CRE producing predominantly VIM and NDM-1 enzymes among blood culture isolates at our hospital. This result should guide the use of carbapenem for empirical therapy in patients with bloodstream infections.

Key Words: Prevalence; ESBL and CRE; Blood culture

Funding Agency: None

Microbiology and Immunology

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Prevalence and Diversification of Healthcare- Associated MRSA Genotypes in Kuwait hospitals.

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Introduction:
Background and Purpose: Methicillin-resistant Staphylococcus aureus (MRSA) remains an important healthcare-acquired pathogen. Understanding the epidemiology of local MRSA isolates is important for better patient's care. This study characterized MRSA isolated in public hospitals in Kuwait for their clonal composition and carriage of genes for virulence and antibiotic resistance.

Methods:
In total, 1,326, non-repeat MRSA isolates obtained between 1 January and 31 December 2016 were characterized using antibiogram, Staphylococcal cassette chromosome mec (SCCmec), Spa typing and DNA Microarray.

Results:
Molecular typing revealed that 325 (24.5%) of the isolates consisting of 195 ST22-MRSA, 117 ST239-III-MRSA, 11 ST5/ST225-II-MRSA and two ST36-II-MRSA were healthcare-associated MRSA. Spa typing grouped ST5/ST225-II-MRSA and ST36-II-MRSA into four and one spa types respectively. ST239-III-MRSA belonged to 11 spa types with t860 (52.1%), t945 (15.4%), t16187 (11.1%), as the dominant spa types. ST22 -MRSA had 60 spa types with t223 (21.9%), t005 (14.8%), t852(10.7%) and t032 (9.2%) as the common spa types. The ST239-MRSA isolates had our subtypes: ST239-III-MRSA (N=3), ST239-III+ SCCmer +ccrC-MRSA (N=11), ST239-III+SCCmer-MRSA (N=101) and ST239-III-MRSA +ccrC (N=2). They expressed multi antibiotic resistance, carried ermA, aacA-aphD, and aphA3; were positive for agr1 and cap8. The ST22-MRSA consisted of nine subtypes with ST22-IV-MRSA[tst1+]-Middle Eastern Variant (N=91), ST22-IV-MRSA[PVL+] (N=55) as the dominant subtypes. Twenty-four isolates carried novel composite genetic elements consisting of ST22-IV+V-MRSA (N=12), ST22-IV+V-MRSA [PVL+] (N=1) and ST22-IV-MRSA [tst1/PVL+] (N=11). ST22-MRSA isolates were positive for agr1 and cap5.

Conclusions:
The study revealed the emergence of heterogeneous subtypes of ST239-III-MRSA and ST22-MRSA isolates with some harboring novel composite SCCmec elements. These may have adverse impact on infection control and patient management.

Key Words: MRSA; Antibiotic resistance; Molecular typing;

Funding Agency: None

Microbiology and Immunology

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Lack of detection of Candida nivariensis and Candida bracarensis among a large collection of clinical Candida glabrata complex isolates in Kuwait as revealed by simple, low-cost multiplex PCR assay

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Introduction:

Candida glabrata is an important fungal pathogen that can rapidly evolve resistance to azoles. Two phenotypically similar species, Candida nivariensis and Candida bracarensis are members of C. glabrata complex. They are indistinguishable by CHROMagar Candida and Vitek2 yeast identification system. C. nivariensis and C. bracarensis are even less susceptible to azoles. Species-specific identification of C. glabrata complex isolates is essential for better management of these infections. This study developed a multiplex (m) PCR assay for species-specific identification of C. glabrata complex isolates and evaluated the protocol by screening a large number of C. glabrata sensu lato isolates originating from clinical specimens in Kuwait for detection of C. nivariensis and C. bracarensis.

Methods:
Reference strains of several Candida species were used for developing the mPCR assay. The mPCR was evaluated on clinical C. glabrata sensu lato isolates (n=430) identified by Vitek2. DNA sequencing of internal transcribed spacer (ITS) region of rDNA was performed for selected isolates to validate the results of mPCR.

Results:
Species-specific amplicons for C. glabrata (212 bp), C. bracarensis (299 bp) and C. nivariensis (414 bp) were obtained by mPCR while no amplicon was obtained from other Candida species, as expected. The mPCR performed on 430 C. glabrata sensu lato isolates yielded an amplicon of 212 bp from all the isolates, thus identifying all isolates as C. glabrata sensu stricto. No isolate was identified as C. nivariensis or C. bracarensis. The mPCR results were confirmed by PCR-sequencing of ITS region of rDNA from selected isolates.

Conclusions:
We have developed a simple, low-cost mPCR assay for rapid differentiation of C. glabrata sensu stricto from C. nivariensis and C. bracarensis. Our data obtained from a large collection of clinical C. glabrata sensu lato isolates also show that C. nivariensis and C. bracarensis are rare pathogens in Kuwait.

Key Words: Candida glabrata complex; Multiplex PCR; Differentiation;

Funding Agency: MI01/15

Neurology

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Burden of migraine in a Kuwaiti population: a door-to-door survey

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Introduction:
Migraine prevalence and disability imprints on Kuwaiti population are underreported. We aimed to measure the prevalence of migraine and its burden in Kuwait.

Methods:
A cross sectional community based study included biologically unrelated Kuwaiti adult population aged 18–65 years. They were randomly recruited from all six governments of Kuwait using stratified multistage cluster sampling. The Headache Attributed Restriction, Disability, and Social Handicap and Impaired Participation questionnaire was used to collect the data.

Results:
A total of 15523 subjects were identified; of whom 3588 (23%) were diagnosed as episodic migraine and 845 (5.4%) as chronic headache. Prevalence of episodic migraine was 31.71% in female versus 14.88% in males ($P < 0.01$) with a mean age of 34.56 years. Most of migraine cohort (64.4%) sought medical advice. The majority 62.4% were seen by general practitioners while neurologists assessed 17.2% and 3.7% was seen by other specialties. Tension type headache and sinus related headaches were diagnosed in 8.9% and 2.1% of migraine subjects respectively. The majority 94.6% of migraine subjects used symptomatic drugs for headache attacks, whereas 39.9% were taking preventive medication. In the preceding 3 months to the survey, subjects with episodic migraine had lost a mean of 1.97 days from their paid work or school attendance compared to 6.62 days in chronic headache sufferers ($P < 0.001$). Additionally, subjects with episodic migraine lost a mean of 1.40 days from household work compared to 5.35 days in subjects with chronic headache ($P < 0.001$). Participants with episodic migraine and chronic headache missed a mean of 2.81 and 3.85 days on social occasions, in the preceding 3 months ($P < 0.001$).

Conclusions:
Migraine in Kuwait is highly prevalent and it has a significant impact on activity of daily living, schooling/employment and social occasions of patients.

Key Words: Epidemiology; Burden; Migraine;

Funding Agency: Kuwait University, Research Sector.

Neurology

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The use of Alemtuzumab in multiple sclerosis patients in a clinical setting, Kuwait experience

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Introduction:
Alemtuzumab is anti-CD52 monoclonal antibody which has demonstrated efficacy in clinical trials and recently been approved for treatment of multiple sclerosis (MS) patients in Kuwait.
We aimed to examine the efficacy and safety of Alemtuzumab treatment in a clinical setting.

Methods:
Using the national Kuwait MS registry, MS patients who received alemtuzumab and had at least 6-month follow-up were identified. Demographics, clinical, MRI characteristics, and adverse events were collected. Patients` status pre- and post-treatment was compared using chi-square and Student t-tests.

Results:
A total of 20 patients were included of whom 60% (n=12) were female. The mean age and disease duration of the cohort were 31.8 ±6.3 and 11.2 ±5.2 years respectively. The cohort included 14 relapsing and 6 active progressive MS patients. Most patients (90%) received prior disease-modifying therapies versus two naïve patients. The mean follow-up duration after the first infusion of alemtuzumab was 17.7±7.1 months with 55% of the patients received 2 courses of alemtuzumab. The annualized relapse rate was significantly reduced (0.1 versus 1.1; $p < 0.001$) and the mean Expanded Disability Status Scale (EDSS) score at last visit improved when compared to pre-treatment scores (3.6 ±2.4 versus 4.2 ±1.9; $p = 0.001$). Only one patient continued to have persistent gadolinium-enhancing lesion on follow-up MRI. Majority of patients 17(85%) developed mild to moderate infusion-related reaction and three patients (15%) developed autoimmune thyroiditis; two of whom were subclinical.

Conclusions:
The effectiveness of alemtuzumab therapy in clinical practice mirrors the results seen in pivotal clinical trials. Autoimmune thyroiditis is common necessitating prompt vigilance and identification.

Key Words: Alemtuzumab; Multiple sclerosis; Kuwait;

Funding Agency: None

Nuclear Medicine and Radiology

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Tc-99m tetrofosmin gated-SPECT myocardial perfusion imaging for assessment of left ventricular contraction dyssynchrony in patients with myocardial ischemia and infarction

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Introduction:
Gated-SPECT Tc-99m tetrofosmin myocardial perfusion (MPI) studies are used to check reversible perfusion defects denoting ischemia or fixed defects indicating scarring from myocardial infarction (MI). Also, functional information is given on cardiac contraction in terms of regional left ventricular wall motion, ejection fraction (LVEF) and timing of regional contraction of the left ventricle, what is known as dyssynchrony analysis. The aim of this study is to compare myocardial perfusion, function and dyssynchrony in a group of patients that had MPI for work up of ischemic heart disease (IHD).

Methods:
This is a cross-sectional study on 19 sequential MPI studies at the Nuclear Medicine Dept, Mubarak Al Kabeer Hospital from Aug to Nov 2017. The studies were reconstructed and analysed quantitatively for perfusion, function and dyssynchrony using the Corridor 4DM software (Invia) on a HERMES station. The results were scored as normal or abnormal and quantitative data were recorded as displayed by the analysis software.

Results:
The mean age of the patients was 62.5 yr (n=19, Range: 44-78 yr, SD: 11.0). There were 74% females. Risk factors were diabetes in 15 patients (79%), hypertension: 18 (95%), dyslipidemia: 10 (53%), previous history of MI 3 (16%) and smoking 3 (16%). There were 10 (53%) abnormal perfusion studies with ischemia in 8 (42%) and scar in 2 (10%). Dyssynchrony was abnormal in 17 (90%) of the stress studies and 19 (100%) Rest studies. The mean LVEF was 56% and was abnormal in 3 (16%) of the studies. Cross correlation of the perfusion and LVEF was tending towards significance (p=0.073) while correlation with the dyssynchrony score was not significant (p=0.115).

Conclusions:
Myocardial perfusion, function and dyssynchrony analysis provide complementary information on cardiac function that could be useful for the diagnosis and management of IHD. Further study of more patients using this approach is warranted.

Key Words: Ischemic heart disease; Dyssynchrony; Myocardial perfusion imaging;

Funding Agency: Research under KuMSA SCORE Scheme

Nuclear Medicine and Radiology

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Risk factors for Helicobacter Pylori: Are diabetics more at risk?

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Introduction:
The association between the Helicobacter pylori (HP) infection and Diabetes is still controversial and a significant gap is present in the discrepancy of the study's findings which have been conducted on this issue. Objective: This case-control study aims to estimate the risk of acquiring the HP infection among diabetic patients.

Methods:
The 14C Urea Breath test was applied to correlate the positive infection of HP with Diabetes. A total of 200 subject's data was collected included 130 female and 70 male. Two groups were used, one with positive infections of HP and a control group of negative infections; the mean age of the positive group is 38 years, SD ± 12.7 and the mean age of the control group is 35 years SD ± 13.2. SPSS software package (version 21) involved descriptive statistics and chi-square test of 2×2 contingency cross tables to compare positive HP infections with the exposure to Diabetes.

Results:
Statistical analysis of the association of exposure to Diabetes with positive HP infection shown p-value = 0.398, odds ratio = 0.688 for diabetic patients compared to non-diabetic (95% CI = 0.288 -1.643); the prevalence of positive infection among those 200 subjects was 66%, (female 70.3 % vs. male 29.6%, p = 0.022); The correlation of age ≤ 30 with positive infection of HP was 27.5%, the age between 30 and 50 was 55.5% and the percentage of age more than 50 was 17%.

Conclusions:
The statistic calculation has not shown that Diabetes is a significant risk factor for the H. pylori infection. No association between the exposure to Diabetes disease and the positive infection of H. pylori. The female gender variable was the only variable which reported a significant statistical association with the positive HP infection. A larger sample size in a cohort study design is recommended to be sufficient to present the relationship between Diabetes and H. pylori, which may exist.

Key Words: DIABETES; Helicobacter Pylori; Risk factor;

Funding Agency: None

Nuclear Medicine and Radiology

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Effect of microbiologic characteristics of causative micro-organisms on patterns of labeled WBCs uptake in osteomyelitis

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Introduction:
The diagnosis of osteomyelitis can be challenging and depends on clinical findings, laboratory tests and imaging studies. Gram-positive bacteria are the primarily causative agent of osteomyelitis and Staph aureus is by far the most common in all age groups. Occasionally, the infection can be caused by gram-negative bacteria especially in patients with certain predisposition. A preliminary animal study with rabbits confirmed that gram-negative infections in vertebral and femoral osteomyelitis is associated with low to no accumulation of labeled WBCs resulting in false-negative scan. The aim of our work was to study the correlation between the scintigraphic pattern on labeled-WBC scans and the microscopic characteristics of the causative bacterial organisms in cases of non-vertebral osteomyelitis.

Methods:
Retrospective analysis of 25 cases referred to nuclear medicine department in Kuwait's general hospital. Bone scans and labeled WBC scans were cross-referenced with microbiological culture and inflammatory laboratory markers.

Results:
Total of 16 patients were eligible for this study, seven females and nine males. The diagnosis of osteomyelitis was confirmed on all patients based on their clinical, laboratory and positive culture results. Of these, seven patients had gram positive while nine patients had gram negative bacterial infection. The majority (85.7%) of gram-positive organisms had positive scans whereas only one-third (33.3%) of patients with gram-negative organisms had a positive scan.

Conclusions:
The pattern observed in this study shows that the false negative results of labeled-WBC scans are mainly noted in patients with gram-negative as opposed to gram-positive bacterial infections. This observation may be due to the anti-chemotactic factors that gram-negative organisms are known to secrete, which may prevent the migration of labeled-WBCs to the site of infection decreasing the accumulation of labeled-WBCs and resulting in a false-negative scan.

Key Words: Osteomyelitis; Labeled-WBC scan; Gram-negative bacteria;

Funding Agency: NONE

Nuclear Medicine and Radiology

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The Efficacy of the available peptide receptor radionuclide therapy for neuroendocrine tumors: A meta-analysis

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Introduction:
This study is a meta-analysis of work previously published which was performed to compare the efficacy of 90Y, 177Lu and combination of both radiotracers (tandem) peptide receptor radionuclide therapy (PRRT) in patients with inoperable and metastatic neuroendocrine tumors.

Methods:
Systematic searches of PubMed and SciVerse Scopus data bases were obtained till December 2016. Keywords used were octreotide, octreotate, 90Y, 177Lu, PRRT and neuroendocrine. Only human studies of more than ten patients were included, and duplicated data were excluded. The data was sorted out into three groups: 90Y-, 177Lu- and tandem-PRRT. Each group was subdivided into two subgroups based on the response criteria used: Response Evaluation Criteria in Solid Tumors (RECIST) or Southwest Oncology Group (SWOG) criteria. Each subgroup was analyzed for disease response rate (DRR) and disease control rate (DCR). The data was analyzed with Excel as described by Neyeloff et al.

Results:
From the electronic search, 90Y-PRRT had 162 and 177Lu-PRRT had 224 related publications. Studies eligible for analysis were 6 for 90Y-PRRT, 9 for 177Lu-PRRT and 3 for tandem-PRRT. For RECIST criteria group, 90Y-PRRT DRR ranged from 23-56% with pooled effect of 43% and DCR was 100%. 177Lu-PRRT DRR ranged from 28-57% with pooled effect of 33%, and DCR between 72-100% with pooled effect of 79%. As for tandem-PRRT, DRR ranged between 42-67% with pooled effect of 51% and DCR between 93-100% with pooled effect of 98.97%. For SWOG criteria group, 90Y-PRRT DRR ranged from 5 -27% with pooled effect of 13% and DCR ranged between 77-86% with pooled effect of 81%. 177Lu-PRRT DRR ranged from 6-60% with pooled effect of 26%, and DCR between 48-85% with pooled effect of 75%.

Conclusions:
From this meta-analysis, 90Y-PRRT had the highest DCR under both criteria. 177Lu-PRRT had the highest DRR in the SWOG criteria, while tandem-PRRT had the highest DRR in the RECIST criteria. So PRRT should be customized for m

Key Words: Neuroendocrine Tumors; PRRT; Octreotide;

Funding Agency: None

Nuclear Medicine and Radiology

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Efficacy of 3D GSPECT Reconstruction Filters in LVEF Evaluation in the Presence of Low to Intermediate Perfusion Defect Correlation with ECHO.

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Introduction:
LVEF is a reliable diagnostic and prognostic value in coronary artery disease. Several modalities including ECHO, GSPECT, cMRI and RNV can assess the LVEF. Filtering contributes to the variation of LVEF with influence on spatial resolution and statistical noise in the reconstructed images. The authors investigated the impact of Wiener and Butterworth filters variation for accuracy of LVEFs in CAD pts.

Methods:
Scans of 17 patients; 12 males and 5 females, 25-76 years old, with suspected CAD who underwent the 99mTc Myoview GSPECT using QPS and QGS were reconstructed with Winer filter based on the outcome of an earlier SPECT-CT optimisation of two chest phantoms. The patient results compared to the previous reports using a standard Butterworth filter and the ECHO for comparison.

Results:
47%, 29% and 24% of pts reported normal, equivocal (EV) and having CAD based on LVEF respectively and prior to modified filtering. A good correlation between ECHO and the calculated LVEF with Winer and Butterworth (r= 0.944 & r=0.94) and for small heart (r= 0.94 & r=0.96) was observed. There was an absolute correlation between GSPECT and ECHO after modifying filter parameters (r=1). To achieve less variation in LVEF measurement, we established a mean cut-off value for Butterworth (0.26 ±0.09) and a mean point value for Winer (4.9 ±1.19) in correlation to ECHO. Pts. With LVEF of <40 showed greater variation in points- setting for Winer, but less fluctuation in cut-off for Butterworth. No remarkable difference noticed for LVEF between two filter techniques for normal cases after adjusting parameters.

Conclusions:
There was an absolute agreement between LVEF derived from GSPECT and ECHO after adjusting parameters with 10% higher accuracy in EV cases at this stage. The accuracy of intermediate CAD reporting for both rest and stress studies was elevated, though more pts. are assessed.

Key Words: GSPECT; LVEF; Echocardiography;

Funding Agency: None

Nuclear Medicine and Radiology

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Impact of Filtering on SPECT Reconstruction for Quantitative & Qualitative assessments and Improvement of Intermediate CAD - Comparison with Angiography and CT Angio.

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Introduction:
Filtering has great impact on the processing and quantitative/qualitative assessment of SPECT images, with more effect on intermediate clinical cases. Much discrepancy in selection of proper filter and its parameters for individual cases are exist. The authors investigated the impact of most common available filters on NM images of patients with CAD, and compared the results with the CT- Angio and invasive angiography for accuracy evaluation.

Methods:
The investigation initiated by performing the various SPECT / CT scan of Jaszczak & NEMA chest phantoms having hot and cold inserts (9.5-37 mm). Data acquired on GE 670 PRO SPECT/CT; 360Ø, 64 frames, 60s, 128, LEGP with CT attenuation (120 kV & 170 mA). The images reconstructed with FBP and ITERATIVE OSEM utilizing filters; Hann, Butterworth, Metz, Hamming and Wiener. The Image contrast measured to assess absolute nearness of the inserts. Scans of 20 patients with CAD, 17 males and 3 females, age 41-77 year old who had been reported earlier reprocessed with the nominated filter and were reported by 2 NM consultants. The results compared to the earlier reports and to the CT –Angio and Angiography.

Results:
The optimization suggested 3 filters; Wiener (Wi), Metz and Butterworth (But) provide highest contrast (99% to 3%) and (81% to 32%) for the cold and hot inserts respectively, with the (Wi) filter to be the best option. The reprocessed patients scan with the (Wi) presented an elevated improvement in diagnostic accuracy, correlated well with the CT-Angio and Angiography results (p=9.36E-7 & r=0.910 for Wi vs p=0.047 & r=0.501 for But). Four out of five cases that reported normal, appeared to have moderate to severe Ischemia, and one remained normal when reprocessed with the Winer filter (r= 1 for Wi vs r=0.577 for But).

Conclusions:
Results of reprocessed CAD scan with the (Win) filter are more consistent with angiography than the other filters, with the elevated accuracy in intermediate cases.

Key Words: SPECT/CT; Multifunctional filters; Cardiac imaging;

Funding Agency: None

Nuclear Medicine and Radiology

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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 the potential risk of avascular necrosis of the femoral head (AVNFH), which is a common complication among patients in Kuwait.

Methods:
The present study documents the baseline and follow-up MRI of the hips among Kuwaiti patients with SCD who have been on hydroxyurea for at least one year.The patients were screened for AVNFH 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. The images were examined independently by two radiologists. AVNFH was graded I (mild), II (moderate), or III (severe).

Results:
Forty patients, made up of 18 (45%) SS, 19 (47.5%) Sβ^0-thal and 3 (7.5%) SD, had pre- and post-HU MRI of the hips for assessment of AVNFH. They were aged 6 to 20, with a mean of 12.9±4.2 years and had been on HU for 1 to 15 years. Pre-HU, 29 (72.5%) had normal images while 11 (27.5%) had AVNFH of grade I in 5 and grade II in 3. The mean age of the former was 11.9±4.0 and the latter, 15.3±3.7 years; the difference was statistically significant (p=0.02).Post-HU, of the 29 that were initially normal, 27 (93.1%) remained unchanged, while 2 (6.9%) developed new AVNFH.Of the 11 that had lesions in the initial MRI, 5 (45.5%) remained static while 5 (45.5%) had progressed with more florid lesions and 1 (9%) improved. A previous study from our center showed that, in SCD patients not on HU, AVNFH progressed in 64.7%, while 78% showed new lesions.In the present study, however, of patients on HU, only 6.9% developed new lesions, while 45.5% showed progression.

Conclusions:
There is no evidence of enhanced progression of AVNFH lesions in children with SCD treated with HU in Kuwait.The drug may, in fact, prevent new lesions. This may be due to the decreased expression of adhesion molecules that has been reported with the use of HU.

Key Words: AVN; SCD; MRI;

Funding Agency: None

Obstetrics and Gynecology

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The weight reduction in adolescents with Polycystic Ovarian Syndrome is associated with increase in serum adinopectin

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Introduction:
Adinopectin is produced and expressed by adipose tissue, which is prevalent in Polycystic Ovarian Syndrome with increased Body Mass Index (BMI), Adiponectin has profound insulin – sensitizing, anti-inflammatory and anti-atherogenic effects.Objective of the study is to investigate the association between weight reduction in obese adolescent with PCOS and adinopection and TNF-α and C-R-P.

Methods:
Fifteen obese adolescents with Polycystic Ovarian Syndrome between 12 and 20 years of age with anovulation and hyperandrogenemia were recruited for the gynaecological clinic of Maternity Hospital and Polyclinic. All had clinical evaluation including history and physical examination – weight and height and Body Mass Index. They were randomized into 3 treatment groups: Metformin only, Metformin and Exercise and Exercise only.Serum levels of adinopectin, c-creatine protein, TNF-α, and C-reactive protein were estimated by ELISA technique initially before treatment and repeated after 3 months of treatment.

Results:
All the three methods of treatment resulted in weight reduction – Metformin with exercise had a more significant increase of adinopection (3.42 Vs 8.48 $P < 0.001$), decrease of TNF-α (11.08 Vs 48.4 $P<0.020$), and C-RP (20.8 Vs 11.4 $P<0.031$)

Conclusions:
Weight reduction in Obese adolescents with PCOS is associated with increase level of adiponectin and decrease levels of TNF-α, and C-Reactive Protein.

Key Words: Adolescent, Adiponectin; Weight reduction, Metformin; Tumor Necrosi

Funding Agency: None

Obstetrics and Gynecology

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Significance of Adiponectin and Leptin in Preeclampsia and Gestational Diabetes.

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Introduction:
Adipokines are involved in a wide range of physiological processes including haemostasis, blood pressure regulation, insulin sensitivity and angiogenesis. Objective of the study. To investigate the relationship between Adiponectin, Leptin and C-reactive protein and Preeclamsia and gestational Diabetes mellitus (GDM)

Methods:
In this comparative study, 4 groups of women were evaluated in 120 females (30 healthy non-pregnant, 30 healthy pregnant women and 30 women with preeclampsiaand 30 with GDM referred to and followed up at the Maternity Hospital Kuwait. Blood samples collected from study participants were refrigerated and centrifuged at 4°C. Plasma and serum samples were stored at −70°C until assayed. Leptin and adiponectin were analysed by DRG ELISA kit.

Results:
The leptin concentrations were higher in women with gestational diabetes mellitus; 31.9±17.1 vs 23.6±17.8 ($P<0.03$) and compared with controls, levels of adiponectin were significantly lower in women with mild or severe PE ($P<0.01$ for both groups) whereas levels of leptin were significantly higher in women with mild or severe PE, Adiponectin 5.7±1.6 vs 8.4±6.3 ($P<0.001$) and CRP 19.9±4.4 vs11.5±11.5±3.3 ($P<0.025$). There was a negative correlation between plasma levels of adiponectin and leptin in pre-eclamptic women ($r=-0.76$, $P<0.01$).

Conclusions:
Circulating adiponectin levels are reduced in patients with Preeclampsia and GDM. Further investigations in early pregnancy to identify women that would develop preeclampsia or GDM are necessary.

Key Words: Adiponectin, Leptin,; Gestational Diabetes Mellitus; Preeclampsia;

Funding Agency: None

Obstetrics and Gynecology

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Effect of Metabolic Syndrome on Male Infertility

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Introduction:
Metabolic Syndrome is a constellation that encompasses Abdominal Obesity, Hypertriglyceridemia, Low high density lipoprotein Cholesterol, High blood pressure and high fasting glucose. It has a direct effects on male infertility through impairment of sperm parameters. Objective of Study: To investigate the effect of Metabolic Syndrome on male infertility through its impairment of sperm parameters.

Methods:
During the 10 year period of 2006-2016, there were 114 men with Metabolic Syndrome out of 1,200 men seen at the infertility clinic at the Maternity Hospital. Semen analysis was carried out on all the men according to WHO guideline and 100 control men.

Results:
Incidence of Metabolic Syndrome was 9.5%. There was a significant increase of Metabolic Syndrome between 2006 and 2016. Effect of Metabolic Syndrome on sperm parameters was significant – Normozoospermia 14.8 vs 48.4% ($P<0.001$), Oligozoospermia 29.3% vs 15.2 ($P<0.04$), Asthenozoospermia 41% vs 16.4 ($P<0.01$) Azoospermia 31 vs 16.2 ($P<0.05$). Single entities of Metabolic Syndrome were individually shown to cause impairment of sperm parameters.

Conclusions:
Metabolic Syndrome definitely has adverse effects on the sperm parameters. The mechanism of this effect needs to be investigated.

Key Words: Metabolic Syndrome; Male Infertility; Impairment of Sperm Parameters;

Funding Agency: None

Oncology

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Extracellular Vesicles as Modifiers of Phenotypic Behavior of Co-cultured Recipient Breast Cells

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Introduction:
Microvesicles (MVs) are a subclass of extracellular vesicles (EVs) shed by numerous cell types and thought to be involved in inter-cellular communication. We hypothesized that MVs derived from estrogen receptor positive (ER+) breast epithelial cells (EII) could be used to deliver cellular content to the aggressive ER silenced (ER-) mesenchymal-like cells (pII), to induce reversion back to their original less invasive epithelial phenotype.

Methods:
MVs were isolated from EII cell cultures by differential ultracentrifugation and analyzed by atomic force and confocal microscopy. Three preparations of conditioned media from EII cells were co-cultured with pII cells: complete media with all extracellular vesicles (CM1), depleted of MVs (CM2), and MVs alone. Modifications in cell behavior were assessed by morphological assessments, invasion and motility assays, gene and protein expression of E-cadherin (epithelial marker) and vimentin (mesenchymal marker) using qPCR and fluorescence immunocytochemistry.

Results:
MVs of mean 250nm were isolated from E11 culture supernatants and shown to contain cellular components by virtue of the presence of green fluorescent protein expressed by these cells. The MVs were endocytosed by pII cells when co-cultured. Alone MVs had no discernible effect on pII, neither did CM2 but CMI significantly reduced motility and invasive capacity of pII cells following two days of co-culture, without altering expression levels of E-cadherin and vimentin.

Conclusions:
EII cells shed cytoplasm containing MVs. However, only the complete EII conditioned medium containing all EVs was effective in reducing the aggressive properties of pII cells but without altering its mesenchymal-like properties. This suggests that there may be suppressive factors released from EII cells which actively prevent them from becoming invasive and these may be absent from pII cultures; these may be highlighted by analyzing their respective proteomic profiles.

Key Words: Extracellular vesicles; Breast cancer; Epithelial mesenchymal transition;

Funding Agency: College of Graduate Studies and the Research Sector, Kuwait University, YP02/16.

Oncology

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The Biological Function of miR-7 in Thyroid Tumorigenesis

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Introduction:
Papillary thyroid carcinoma (PTC) represents 80% of all thyroid cancers. MicroRNAs (miRNAs) are endogenous non-coding RNAs that contribute to the pathogenesis of multiple cancers by interfering with many biological processes. Our previous miRNA profiling work showed that miR-7 is downregulated in PTC. The functional role of miR-7 in PTC carcinogenesis is still largely unknown. This study aimed to investigate the diagnostic potential and the biological functions of miR-7 in PTC.

Methods:
The expression of miR-7 was assessed by quantitative real time PCR in different variants of PTC (82 samples), 20 cases of noninvasive follicular thyroid neoplasm with papillary-like nuclear features, NIFTP, (a newly classified benign tumour previously considered in clinical diagnosis as PTC variant) and 10 cases of multi-nodular goiter (MNG). MiR-7 mimic was transfected into primary thyroid cultured cells and the activity of 10 signaling pathways were assessed by luciferase assay. The obtained results were confirmed by immune-fluorescence staining in transfected cells. The effect of miR-7 on cancer cells growth was examined using apoptosis assay by flow cytometry.

Results:
The real time PCR results followed by analysis with the Receiver operating characteristic (ROC) curve showed that miR-7 significantly differentiates NIFTP from MNG (87% sensitivity and 90% specificity). Transfection with miR-7 mimic resulted in activation of the WNT, Notch, P53, TGFβ and, Hypoxia signaling pathways and increased the number of apoptotic cells.

Conclusions:
miR-7 displayed a diagnostic role in distinguishing the NIFTPs from the hyperplastic (MNG) nodules. Functional experiments proved the role of miR-7 in activating the cell signaling pathways related to tumor suppression. Overexpression of miR-7 reduced the survival of PTC cells in culture. Down-regulation of miR-7 detected in PTC and NIFTP cases advocates for its potential role in neoplastic transformation in thyroid tissue.

Key Words: MicroRNA; Papillary thyroid cancer; Noninvasive follicular thyroid

Funding Agency: YM08/15, MG02/13

Oncology

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Combination strategies with natural phenolic compounds to enhance the anticancer activity of the multikinase inhibitor sorafenib on human colorectal cancer cell.

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Introduction:
Sorafenib (Sora) is an FDA approved multi-kinase inhibitor drug, with potent antiangiogenic & antitumor activities. Effective strategies to reduce the side-effects & enhance the activity of Sora are required. In this study, we endeavored to investigate the effects of combination treatment of Sora & natural phenolic compounds (NPCs), on human colorectal cancer (CRC) cell growth, cell cycle & apoptosis.

Methods:
MTT assay was used to monitor the cytotoxicity of 14 NPCs on fibroblast cells CRL1554 & to measure the lethality of Sora, NPCs & their combinations on CRC cells; SW1116 & SW837; using three different treatment approaches; sequential, reverse sequential & simultaneous. Cell cycle was analyzed by flow cytometry. Apoptosis was assessed by; DNA fragmentation, Annexin V/PI double staining assay & mitochondrial membrane potential assay. Finally, expression of genes controlling apoptosis & cell cycle was evaluated by western blot analysis.

Results:
Four NPCs; curcumin (Cur), quercetin (Que), kaempferol (Kmf) & resveratrol (Rsv) were selected, for their low % cytotoxicity (0 - ≤ 20%) on CRL1554 cells. NPCs markedly potentiated the therapeutic efficacy of Sora in a schedule-, type, & dose of NPC-, & cell line-dependent manner. Simultaneous treatment of SW1116 cells with Sora & Cur (Sensitization Ratio, SR= 13.8) or Que (SR=8), & sequential treatment of SW837 cells with Sora & Cur (SR= 23.7) or Kmf (SR=9) were associated with the highest efficacy of combination treatments. Combination treatments with Sora & Cur or Kmf or Que arrested CRC cell lines in the S-phase & the G2/M-phase, & markedly induced apoptosis compared with single treatments with Sora, Cur, or Kmf or Que. Combined treatment reduced the levels of cell cycle related protein & increased the levels of apoptotic proteins in a dose-dependent manner.

Conclusions:
Our results clearly indicate a marked enhancement of Sora efficacy on CRC cells by combined treatment with NPCs. Further in vivo studies are needed.

Key Words: Colorectal cancer; Sorafenib; Natural phenolic compounds;

Funding Agency: College of Graduate Studies & Research Sector, Project No. YS01/15.

Oncology

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Invasive capacity of endocrine resistant breast cancer cells is enhanced by Na^+/K^+ ATPase activity by increased phosphorylation of its downstream signaling molecules

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Introduction:
The Na+/K+-ATPase (NKP) is a cation transporter that can also modulate signal transduction through a protein kinase cascade. In view of its reported involvement in the etiology of various tumours including those of the breast, we determined, with the use of pharmacological inhibitors and gene down-regulation, its effect on normal breast epithelial cells and on estrogen receptor (ER) positive and negative endocrine resistant cancer cells

Methods:
NKP was silenced by siRNA transfection. Protein expression was measured by western blot, cellular localisation by immunofluorescence and NKP activity by a colorimetric-based assay. Cell proliferation, apoptosis and cell cycle stage were determined using MTT, annexin V and flow cytometry. Cell motility and invasion were determined using wound healing and matrigel assays.

Results:
Both membrane localised expression and activity of NKP was significantly greater in the cancer cell lines compared to the normal breast cells. Treatment with epidermal growth factor (a potent proliferative agent) enhanced NKP activity and induced its internalization from the cell membrane into the cytoplasm. NKP inhibitors (ouabain and 3,4,5,6-tetrahydroxyxanthone) as well as siRNA-mediated silencing of the NKP alpha subunit effectively inhibited cell proliferation, motility and invasion. In addition, alkaline pH-induced membrane blebbing, a mechanism involved in ER negative cell motility, was completely abolished. Ouabain also inhibited EGF-induced phosphorylation of Rac/cdc42, profillin, ERK1/2 and P70S6K implicating these NKP induced downstream events in the aggressive activities of the cancer cells.

Conclusions:
NKP activity appears to be a driver of cancer cell progression and may present a novel therapeutic target in breast cancer patients, particularly those who have acquired endocrine resistance. This would help improve therapeutic strategies and enhance survival rate.

Key Words: Breast cancer; Na/K ATPase; Invasion;

Funding Agency: PT01/14

Oncology

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Contribution of the RAS/ERK pathway in papillary thyroid carcinogenesis

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Introduction:
Papillary thyroid carcinoma (PTC) accounts for more than 70% of all thyroid cancers and ranks among the five most common cancers in Kuwait. Deregulated signaling through the extracellular signal-regulated kinases 1/2 (Erk1/2) pathway is a central signature of many epithelial cancers including PTC where it is attributed mostly to RAS and BRAF oncogenic mutations. The well-known role of the ERK pathway has been in regulating cell survival and differentiation, but recently a new role in mediating growth arrest has been described. The purpose of this study is to explore the activation status of the ERK pathway including testing for the most common RAS mutations in PTC.

Methods:
30 PTC and 10 benign tumour samples were studied. DNA was extracted, the NRAS codon 61 and codon 12/13 gene were amplified by PCR and sequenced by Sanger sequencing. Tissue sections were stained for phospho-ERK by immunofluorescence technique and the active ERK expression and subcellular localization were analyzed by confocal microscopy.

Results:
NRAS codon 61 mutation was detected in one PTC sample. Nuclear expression of phospho-ERK, denoting activated ERK, was detected in thyroid follicular cells in the benign tumour cases and in the normal looking follicles adjacent to the tumour in PTC samples. The PTC tumour follicles were all negative.

Conclusions:
NRAS mutation is a rare event in PTC in Kuwait. ERK pathway is activated independently of NRAS mutation in the benign and normal thyroid follicular cells. Lack of ERK activation in cancer cells suggest that ERK pathway is regulated by some negative feedback mechanisms pointing to its role in tumour suppression in PTC.

Key Words: Papillary thyroid cancer; Ras oncogene; ERK Pathway;

Funding Agency: MG02/13

Pathology

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Accuracy of axillary ultrasound findings in detection of metastases on fine needle aspiration cytology of primary breast carcinoma cases.

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Introduction:
Ultrasound guided fine needle aspiration (USG-FNA) is universally used for detection of abnormal lymph nodes in cases of primary breast carcinoma (PBC). The technique has good diagnostic accuracy with sensitivity and specificity of 65-99% and 80-100%. The aim of this study is to evaluate the US findings namely- size, shape, cortical thickness (CT) and loss of hilar fat which contribute to detection of nodal metastases in PBC.

Methods:
In 50 PBC cases who underwent USG-FNA of axillary lymph node (ALN) over a period of 6 months (January – June 2017) at KCCC, the size, shape, cortical thickness and presence or absence of hilar fat were reviewed.

Results:
Of the 50 PBC cases17 were Kuwaitis and 33 non Kuwaitis .The age ranged from 29-78yrs with a mean of 51. The primary was infiltrating ductal carcinoma (IDC) in 46 ,infiltrating lobular carcinoma (ILC) in 2 and ductal carcinoma in situ (DCIS) in 2. While 49 patients had ipsilateral ALN one had contralateral. There were 23 patients with single ALN and 33 with multiple lymph nodes. ALN of size >2.5cm were malignant in 100% while nodes <1.5cm were benign in 52.6% and malignant in 47.6%. CT of > 6mm was positive for malignancy in 100% while CT of <5mm was benign in 56.5% of cases. ALNs with absent hilar fat were malignant in 89.3% of cases while 100% of ALNs with irregular shape showed malignancy.
Conclusions:
In the present study the ultrasound findings of ALN, size >2.5cm, irregular shape, absent hilar fat and a CT of > 6mm when present alone or in combination is highly suggestive of nodal metastasis in PBC.

Key Words: Axillary lymph node; Ultrasound; Primary breast cancer;

Funding Agency: None

Pathology

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Genetic Aberrations in Non-Small Cell Lung Cancers at Kuwait Cancer Control Center

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Introduction:
Targeted therapy guided by molecular diagnostics has become a standard of care in advanced non-small cell lung cancer (NSCLC). Targetable genetic aberrations in NSCLC include those of EGFR, ALK and ROS1 genes. This pilot study aims to examine the frequency of these aberrations in a cohort of NSCLC patients treated at Kuwait Cancer Control Center (KCCC).

Methods:
NSCLC tissue samples referred to KCCC from Jan 2015 to Sep 2017 were identified. EGFR testing was performed using the Cobas EGFR v2 PCR Kit. ALK & ROS1 were evaluated by fluorescence in-situ hybridization using Vysis & ZytoLight SPEC breakapart probes, respectively. Pathology slides were reviewed.

Results:
We identified 185 NSCLC samples from 174 patients (130 males and 44 females) with a mean age of 58.9 years (range 18-91). The majority of the samples were small biopsies (160;90%) followed by resections (17;8.5%) and only a few cytology specimens (3;1.5%). Most were obtained from primary lung masses (134;75%) followed by metastatic sites (51;25%). Adenocarcinoma constituted 84% of the histological types. EGFR mutations occurred in 31(17%) of the tumors while ALK and ROS1 rearrangements occurred in 20(11%) and 3(1.5%) tumors respectively. These were mutually exclusive. Aberrations were more common in females than males (38.6% vs 28.4%). Respective mean ages were 61.4, 43 & 42 years for EGFR-mutated, ALK-rearranged and ROS1-rearranged tumors. Exon 19 deletions and exon 21 point mutations were the most common EGFR aberrations accounting for ≈90% of all EGFR mutations. Histopathological exam did not reveal morphological differences across the different aberration types or between wild-type and mutant tumors.

Conclusions:
In this pilot study the frequency of EGFR mutations in NSCLC (17%) is closer to that of European populations (as opposed to Asian populations that are known to have the highest mutation frequency). Our ALK & ROS1 aberration frequencies are similar to global ones.

Key Words: Lung cancer; ALk; EGFR;

Funding Agency: None

Pathology

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Preclinical optimization and validation of the Ion Torrent S5 XL Sequencer and Oncomine Solid Tumor panel for molecular testing of lung and colon cancers

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Introduction:
Molecular characterization of cancer using next generation sequencing (NGS) technology has become a key tool for facilitating targeted therapy. The Oncomine Solid Tumor NGS assay enables detection of hundreds of somatic mutations across 22 genes relevant to current cancer therapy. At Kuwait Cancer Control Center we validated the analytical performance of this assay and the Ion Torrent's S5 XL sequencer for KRAS, BRAF and EGFR mutations in stage IV colorectal and lung cancer samples.

Methods:
We included 92 formalin-fixed paraffin-embedded cancer samples (49 lung, 43 colon), previously tested at reference laboratories using a variety of methods. Genomic DNA was extracted using MagMAX™ FFPE DNA/RNA Ultra Kit and isolated by Kingfisher Duo Prime Purification System. DNA concentration was measured on a Qubit 3.0 Fluorometer. An amplicon library was generated using 10ng of DNA from each of the FFPE samples and the libraries were sequenced using Ion Torrent S5 XL Semiconductor (ThermoFisher Scientific). Data analysis was performed using the Ion Reporter software.

Results:
Mutation analysis of 43 colon cancers revealed: 22(51%) KRAS mutations, 2(5%) BRAF mutations and 19(44%) wild type. Analysis of 49 lung cancers revealed: 12(25%) EGFR mutations & 37(75%) wild type. All expected single nucleotide variants and indels were successfully identified with a full concordance between our results and that of the reference labs (100% specificity and sensitivity). This included rare coexisting EGFR variants in one lung sample (L861Q & G719X). All sequencing run metrics were in the acceptable range and base coverage showed over 92% uniformity in all runs. The sequencing reads covered the region of interest evenly and gave a total number of 3-6 million reads for a 520 chip and 15-20 million reads for a 530 chip.

Conclusions:
We confirmed that our NGS platform and assay are accurate and practical for diagnostic solid tumor testing in a clinical laboratory.

Key Words: Ion Torrent NGS; Colon; Lung;

Funding Agency: None

Pathology

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HER2 FISH characteristics of breast cancer cases at KCCC Cytogenetics Laboratory

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Introduction:
Fluorescence in-situ hybridization (FISH) is considered the gold standard for assessment of human epidermal growth factor receptor 2 (HER2) status in breast cancer to select patients for anti-HER2 therapy. The aim of this study was to review the clinicopathological and HER2 FISH characteristics of breast cancers tested at our Cytogenetics Lab over a 3-year period.

Methods:
A total of 808 consecutive tissue samples of breast cancer (from 675 patients), tested for HER2 FISH between Jan 2015 to Dec 2017, were reviewed. These were highly enriched for HER2 2+ cancers by immunohistochemistry. FISH was performed using a dual-color probe and interpreted according to current ASCO/CAP guidelines.

Results:
The patients included 664(98.4%) females & 11(1.6%) males, aged 25-93yrs (mean 54) with 83(12%) patients younger than 40 years of age (81 females, 2 males). The majority of submitted samples were breast biopsies (461; 57%) followed by breast resections (305; 38%), then non-breast specimens (42; 5%). Tumor statuses were: 675(84%) primary, 71(9%) post-neoadjuvant therapy, 42(5%) metastatic, and 20(2%) recurrent. FISH results of the 808 samples were: 552(68%) non-amplified, 129(16%) amplified, 99(12%) equivocal, and 28(4%) failed. More amplification was seen in invasive ductal carcinomas (114 of 684; 17%) compared to invasive lobular carcinomas (4 of 53; 8%) but the difference was not statistically significant (p value=0.1). Amplification occurred predominantly in histologically grade 3 cancers (73 out of 285 tumors; 57%) that were estrogen receptor & progesterone receptor positive (ER+/PR+). Repeat FISH testing on 20/48 equivocal cases clarified the HER2 status in 14 cases (9 became non-amplified and 5 became amplified while 6 stayed equivocal).

Conclusions:
In our cohort 16% of breast cancers referred for HER2 FISH testing showed amplification, which confers eligibility for anti-HER2 therapy. Our results are compatible with that in the literature.

Key Words: Breast cancer; HER2; FISH;

Funding Agency: None

Pathology

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The association of ANGPTLs with multiple sclerosis pathogenesis and response to therapy

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Introduction:
Angiopoietin-like proteins (ANGPTLs have functional attributions encompassing lipid metabolism, angiogenesis, and inflammation. ANGPTLs have been investigated in many disorders, but their involvement in demyelinating, neurodegenerative disorders, such as Multiple Scleorsis, has been overlooked. Our objective was to investigate ANGPTL's involvement in MS progression and response to treatment.

Methods:
A total of 100 MS patients and 77 healthy controls plasma samples were used in this study. Plasma levels of the ANGPTL 2, 3, 4 and 6 were assessed using the multiplexing immunobead array platform and analyzed using the Bioplex-200 system.

Results:
High ANGPTL6 levels significantly correlated with lower Expanded disability status scale (EDSS in the MS cohort (r= -0.3107, p= 0.0017 and lower MS Severity Score (MSSS (r= -0.274, p= 0.0057. Dividing MS patients by treatments (Fingolimod: n = 39, Natalizumab: n = 34, we found MS patients on Fingolimod to have higher levels of ANGPTL6 (r= 0.235, p= 0.045 and ANGPTL4 (r= 0.241, p= 0.039 than those on Natalizumab. Longitudinal 2.5 years follow-up of patients on Natalizumab subdivided them into responsive (n= 23 and non-responsive (n= 11 based on EDSS, MSSS, and MRI. ANGPTL4 levels were higher in those responsive to Natalizumab than poorly responding MS patients to the same drug (p= 0.012. Moreover, MSSS values before and after Natalizumab treatment were lower in patients with high ANGPTL4 levels (p<0.001, whereas MSSS values increased in patients on Natalizumab with low ANGPTL4 levels (p= 0.02.

Conclusions:
ANGPTLs significantly associated with MS progression and response to therapy. While ANGPTL6 associated with disease progression, ANGPTL4 association with response to Natalizumab proposes it as a candidate predictor of response to Natalizumab. Our findings support the need to investigate ANGPTLs' roles in inflammation, neuronal regeneration, and wound healing.

Key Words: Multiple sclerosis; Angiopoietin like-Proteins; Natalizumab;

Funding Agency: KFAS grant # 2012-1302-02

Pathology

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GP6 rs2304166 polymorphism is associated with response to Natalizumab in multiple sclerosis patients from Kuwait

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Introduction:
Currently, there are no pharmacogenetic predictors of response to treatment in Multiple Sclerosis (MS) patients. Commonly used second line treatments, including Natalizumab have proven to be successful in slowing MS progression in a subset of patients; albeit some patients do not respond well. Our aim was to determine pharmacogenetic factor(s) associated with MS patients' response to Natalizumab.

Methods:
Ten MS patients unresponsive to natalizumab and 23 MS patients responsive to Natalizumab were selected for exome sequencing. DNA was extracted from blood using Qiagen DNA mini kit. Exome sequencing was performed on an Illumina HiSeq2000 platform using TruSeq v5 chemistry with target coverage of 50X. Patient exome sequences were analyzed using Tute Genomics application. Additional 86 MS patients were rs2304166 genotyped to confirm exome results.

Results:
Exome analysis revealed a missense mutation in Glycoprotein VI (GP6) rs2304166 (p.P314A) associated with homozygosity in Natalizumab non-responsive patients (p=0.0012). An additional cohort of 86 MS patients of which 19 were natalizumab non-responsive and 67 responsive was used. Rs2304166 CC was significantly associated with poor response to natalizumab (p=0.0000027) and disease progression as assessed by worse expanded disability status scale, occurrence of relapse, and new MRI activity (Odds ratio 22.18, 95%CI: 5.758 - 95.88, p=0.000000011).

Conclusions:
Natalizumab is a commonly used second line treatment for MS, and poor response to natalizumab is associated with rs2304166 CC genotype MS patients. In addition, rs2304166 CC was associated with disease progression as assessed by worse expanded
disability status scale, occurrence of relapse, and new MRI activity despite Natalizumab treatment. Our findings support the need to investigate GP6 role as a potential pharmacogenetic factor in MS patient's response to Natalizumab.

Key Words: Multiple sclerosis; Natalizumab; Glycoprotein VI;

Funding Agency: KFAS grant # 2012-1302-02

Pathology

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Molecular alterations in gastrointestinal stromal tumors (GISTs) using targeted next-generation sequencing

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Introduction:
Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the GI tract, driven by gain-of-function mutations in either KIT or PDGFRA genes, with 10-15% being KIT/PDGFRA wild type. Mutational status predicts response to targeted therapy. Our aim was to study the molecular alterations in a cohort of GIST cases from Kuwait Cancer Control Center.

Methods:
Between 2005-2015, a total of 114 GISTs from 100 patients were identified in our pathology archive. Of these, 24 formalin fixed paraffin embedded tissue samples were sequenced on the Ion S5 XL NGS system using the Oncomine Comprehensive Assay, which covers 161 cancer driver genes. Pathology slides and reports were reviewed, & immunohistochemistry (IHC) was performed for KIT, DOG1, and CD34.

Results:
Of 100 patients, 63 were males & 37 females (mean age 54.7 years; range 5-84). Of 24 tumors tested, 12(50%) showed KIT mutations, 4(16.7%) PDGFRA mutations, and 8(33.3%) KIT/PDGFRA wild type. KIT mutations included exon 11 in-frame deletions and point mutations (n=10) & exon 13 K642E (n=2). KIT-mutated tumors were located in the stomach (n=5), small bowel (n=3), rectum (n=2), & peritoneal cavity (n=2). The majority was of spindle-cell type histologically (92%) showing fascicular architecture ± palisading & cell vacuolation and included low- to high-risk tumors. On IHC, KIT and DOG1 were detected in all of the tumors tested while CD34 was seen in 45.5%. PDGFRA-mutated GISTs (exon 18 D842V, exon 12 V561D) were all located in the stomach, showed epithelioid/mixed histology, and were of low to moderate risk. On IHC, all showed reduced KIT but preserved DOG1 expression. KIT/PDGFRA wild GISTs constituted a heterogeneous group of tumors of variable histology and risk.

Conclusions:
Our results are compatible with those in the literature. This is the first study in Kuwait to evaluate GISTs at the molecular level, which will serve as the foundation for more comprehensive studies.

Key Words: GIST; KIT; PDGFRA;

Funding Agency: Research Grant No. MG02/15, Research Sector, Kuwait

Pathology

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Non-Classical HER2 FISH Results in Breast Cancer Cases at Kuwait Cancer Control Center (KCCC) Cytogenetics Laboratory

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Introduction:
Accurate HER2 assessment by fluorescence in-situ hybridization (FISH) is critical for selecting breast cancer patients for HER2-targeted therapy; however, "non-classical" FISH patterns may be a source of confusion. The aim of this study was to examine the frequency and clinicopathological features of breast cancers with non-classical HER2 results at KCCC Cytogenetics Laboratory.

Methods:
HER2 FISH results of 299 consecutive breast cancer samples, from Jan-Dec 2016, were reviewed retrospectively. Non-classical amplification categories were defined according to ASCO/CAP 2013 criteria as follows: low amplified (ratio≥2.0, HER2/cell 4.0–5.9); co-amplified/polysomy (ratio <2.0, HER2/cell ≥6.0); monosomy (ratio ≥2.0, HER2/cell <4.0); and heterogeneity (clusters of amplified cells representing at least 10% of tumor). Clinicopathological information was obtained from pathology reports.

Results:
Of 286 interpretable samples, 23(8%) had a 'non-classical' HER2 amplified result compared to 21(7%) 'classical' amplified. Non-classical categories were as follows: 13(4.5%) low-amplified, 8(2.8%) co-amplified, 1(0.3%) monosomy, and 1(0.3%) clustered heterogeneity. The non-classical cases had the highest frequency of patients (57%) younger than 50 years old compared to the classically amplified (19%). Non-classical amplified and classical amplified showed Nottingham grade 3 cancers in 61% and 67% of cases, respectively. The non-classicals had a higher frequency of ER-positive cancers compared to classicals (91% vs 86%). Six of the non-classical cases changed category upon repeat testing by a different scorer: 4 cases from equivocal to low-amplified, 1 from equivocal to co-amplified, and 1 from co-amplified to equivocal.

Conclusions:
This study offers an insight into HER2 non-classically-amplified breast cancers at KCCC. Larger studies with data on clinical outcomes and response to targeted therapy are needed.

Key Words: HER2; Breast cancer; FISH;

Funding Agency: NONE

Pathology

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Impact of implementing a laboratory information system on surgical pathology turnaround time at Kuwait Cancer Control Center (KCCC)

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Introduction:
A robust laboratory information system (LIS) can make a dramatic difference in reducing the turnaround (TAT) in surgical pathology by eliminating gaps in laboratory processes and enabling prioritization & tracking. Acceptable TAT is variable depending on specimen complexity & other factors, but it is generally between 2-7 days. Herein, we present our experience with a new LIS and its impact on TAT at our pathology lab.

Methods:
We identified specimens over a period of 21 months: prior to LIS (Jan-Dec 2016) and after LIS (Jan-Sep 2017). TAT was measured in working days from the time of specimen accessioning to the time of sign-out. TAT targets were determined based on specimen priority & complexity: ≤2 days for Rapid Diagnostic Breast Clinic (RDBC), ≤5 days for small specimens, ≤7 days for complex specimens, & ≤7 days for elective surgical skin specimens. In each category, TAT was considered satisfactory when ≥85% of specimens met the TAT target, monthly.

Results:
Of 5297 specimens prior to LIS, 182 (3%) were RDBC, 1426 (27%) small, 772 (15%) complex, & 656 (12%) elective skins. Of 4667 after LIS, 109 (2%) were RDBC, 1470 (32%) small, 784 (17%) complex, & 485 (10%) elective skins. Prior to LIS, RDBC biopsies meeting the TAT target of 2 days fluctuated from 44% to 100%, across the defined 12-month period. After LIS, a significant improvement was noticed with 100% of cases meeting the target across the defined 9-month period. Other categories also showed improved TATs and less fluctuations: small specimens 72%-93% vs 78%-100%, complex specimens 68%-96% vs 78-91%, elective skins 73%-100% vs 92%-99% (before vs after LIS respectively).

Conclusions:
Overall, TAT trends after LIS implementation were more consistent with no abrupt dips (less outliers); therefore we conclude that LIS has improved TAT at our lab. Other variables that may potentially affect TAT remained unchanged. Long-term monitoring of TAT is needed for more in-depth evaluation.

Key Words: Turnaround time; Quality; Pathology;

Funding Agency: NONE

Pathology

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T-cell-rich B-cell lymphoma: Is it an over-diagnosed entity in fine-needle aspiration cytology?

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Introduction:
T-cell-rich B-cell lymphoma (TCRBCL) or T-cell/histiocyte-rich B-cell lymphoma (TC/HRBCL) represents a rare subtype of diffuse large B-cell lymphoma (DLBCL), characterized by presence of a few neoplastic large B-cells with a background of reactive T cells and/or histiocytes, which has been usually misdiagnosed as Hodgkin lymphoma (HL), peripheral T-cell lymphoma or anaplastic large cell lymphoma (ALCL). We intend to find out the extent of misdiagnosis as other entities in our material and suggest how to limit this error.

Methods:
The study, spanning over a period of 10 years (2005-2014), included 15 cases in which the possibility of TCRBCL was considered in FNA cytology and/or corresponding histopathology. The sites of FNA were lymph nodes in 14 (cervical in 12, axillary in 1 and inguinal in 1) and nodal (cervical) as well as extranodal (thyroid) in one.

Results:
The age of the patients ranged from 17 to 61 years with a mean± SD of 41.1±15.05 and median of 45 years. Male: female ratio was 11:4. The initial cytodiagnoses in these cases were TCRBCL in 2, HL/TCRBCL in 3, HL/ALCL/TCRBCL in 2, ALCL/TCRBCL in 1, NHL-B cell in 2, and NHL-SC/CLL, suggestive of (S/O) NHL, S/O lymphoma, lymphoma/reactive hyperplasia (RH) and atypical lymph node cytology (ALC) in one case each. The reviewed cytodiagnosis or one of the possibilities was TCRBCL in 13 cases, NHL-SC in 1 and nodular lymphocyte predominant HL in 1. The histopathological diagnoses were TCRBCL in 4, DLBCL in 5, HL in 4, and follicular lymphoma and reactive hyperplasia in one case each. Immunocytochemical (ICC) studies performed in 9 cases revealed cyto-histological correlation for TCRBCL or DLBCL in 7 (77.8%) but in none of the 6 cases without ICC studies there was exact cytohistological correlation for TCRBCL/DLBCL (P=0.00720).

Conclusions:
TCRBCL is over-diagnosed in FNA cytology, Hodgkin lymphoma being the main differential diagnostic consideration; to avoid it ICC studies are essential.

Key Words: T-cell-rich B-cell lymphoma; Hodgkin lymphoma; fine-needle aspiration

Funding Agency: None

Pathology

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PD-L1 expression in non-small cell lung cancer: A pilot study from Kuwait Cancer Control Center (KCCC)

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Introduction:
Programmed cell death ligand 1 (PD-L1) expression measured by immunohistochemistry (IHC) is now used to predict response to anti–programmed cell death 1 (PD-1) immunotherapy in patients with non-small cell lung cancer (NSCLC). NSCLCs diagnosed at KCCC are currently tested for PD-L1 at a reference laboratory. We conducted this preliminary validation study in order to evaluate inter-laboratory concordance of PD-L1 testing between the reference and KCCC pathology lab.

Methods:
Of 42 NSCLCs with available PD-L1 result, 15 were included in this study and deemed satisfactory (containing ≥100 viable tumor cells). PD-L1 immunostaining was performed on formalin-fixed paraffin embedded tissues using the 22C3 pharmDx anti-PD-L1 antibody (Dako) on autostainer Link 48 platform. Two pathologists analyzed the slides using FDA-approved cutoffs: ≥50% positive cells (high PD-L1 expression; patients in this category are offered Pembrolizumab as first-line), 1-49% positive (weak expression; Pembrolizumab given as second-line), <1% (negative; no treatment).

Results:
The 15 cases were all males, mean age 63.8 years (range 37-78). Specimens tested were lung biopsies (n=7), lung resection (n=1), pleural biopsies (n=3), lymph node biopsies (n=2), and metastatic sites (n=2). Agreement was observed in 12 of 15 cases with a moderate inter-laboratory concordance (kappa=0.59). Discordance occurred between high-expression and weak-expression categories in 3 cases.

Conclusions:
The 22C3 anti-PD-L1 assay is reproducible at our lab. Source of discordance may be technical (different staining protocols), biological (intratumoral heterogeneity) or analytical (subjective analysis, lack of standardized approach, & borderline results that are close to cutoffs). This study is limited by small sample size. A larger study is needed to thoroughly evaluate the performance of this test and correlate the findings with pathological features, driver mutation status and clinical outcome.

Key Words: NSCLC; PD-L1; Lung cancer;

Funding Agency: None

Pathology

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High risk human papillomavirus genotypes other than 16,18 and 45 account for the most predominant genotypes amongst women with abnormal cervical smear cytology residing in Kuwait.

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Introduction:
Persistent infection with high risk types of human papilloma virus (HR-HPV) causes cervical cancer. The HR-HPV genotypes 16 and 18 are considered to be the most prevalent genotypes causing cervical cancer worldwide. Detection of HR-HPVs and their genotyping are used as adjuncts to cervical cytology for early detection of cervical cancer. The Aptima assay is an mRNA based assay for detection of HR-HPV and genotyping for types 16, 18 and 45.

Methods:
The period of study was from July 2015 to September 2017. During this period all cases which were diagnosed as "epithelial abnormality" were subjected to HR-HPV assay using the Aptima HR-HPV assay. A particular number of cases amongst the above which were positive for HR-HPV, were further genotyped.

Results:
749 cases which on cytology smears were diagnosed to be epithelial abnormalities, were subjected to HR-HPV assay on Aptima.229 (30.57%) of these cases were found to be positive for HR-HPV and 520 cases were negative (69.43%). Out of these, 116 cases were subjected to HR-HPV genotyping. The 116 specimens were from 51(43.96%) Kuwaiti and 65(56.17%) non-Kuwaiti women. Out of the 116 specimens, 36 (31.03%) were positive for HPV 16, seven (6.03%) for HPV 18/45 and 73 (62.93%) were negative for HPV 16, 18 and 45 (indicating HPVs other than 16,18,45). There was no significant difference in genotyping results between Kuwaiti and non-Kuwaiti women.

Conclusions:
The study shows that amongst women residing in Kuwait with abnormal cervical smear, high risk HPV types other than 16,18 and 45 account for the most predominant genotypes. This is in contrast with the commonly held paradigm that types 16 and 18 cause most cases of cervical cancer worldwide..This could have serious implication for the success of any HPV vaccination strategies since both the HPV vaccines target types 16 and 18.

Key Words: HPV; Genotyping; Cytology;

Funding Agency: None

Pathology

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Audit of Amended Reports and Addenda in Surgical Pathology at Kuwait Cancer Control Center (KCCC)

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Introduction:
The surgical pathology report is a critical document that guides clinical management. Not uncommonly, pathologists may need to amend or add information to the final pathology report after its release. An "amended report" overwrites a previously issued report in order to communicate critical information to treating physicians, whereas an "addendum" simply supplements a previous report without modifying original text. Studies show lack of standardization in the use of amendments and addenda among pathologists. Our aim was to evaluate the use of such reports at our institution and identify misclassified addenda over a 9-month period.

Methods:
We searched the pathology reports at KCCC, from April-December 2016, for the keywords "supplementary", "addendum", "amendment", & "revised". The reports were reclassified as either amendments or addenda based on CAP guidelines and were categorized according to accession class, subspecialty, and indication. Amendments were subdivided into 4 defect areas: misinterpretation, misidentification, specimen defect, and report defect.

Results:
Of a total of 4424 pathology reports, 461 had at least one subsequent amended/additional report, 61% of which belonged to in-house surgical cases and 39% to review cases. The majority were breast reports (51%). Major indications for issuing an addendum were reporting of molecular results (55.5%) and prognostic immunohistochemical results (33%). After revision, 97.2% (n=562) were appropriately reclassified as addendum and 2.8% (n=16) as amendment. Amendment defect areas: 62.5% misinterpretation, 25% misidentification, 6.2% a report defect, and 6.2% a typographic error. Seven original addenda were deemed to contain critical information that warranted an amendment instead (misclassified addenda).

Conclusions:
Standardized use of the addendum and amendment functions in surgical pathology is needed and periodical review of such reports is essential for quality improvement.

Key Words: Addendum; Amendment; Pathology report;

Funding Agency: None

Pathology

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Nodular fasciitis revisited: Review of 27 cases referred for consultation

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Introduction:
Nodular fasciitis (NF) is an uncommon mass-forming myofibroblastic lesion that may potentially be misdiagnosed as sarcoma (i.e. pseudosarcoma) due to its rapid growth and variable morphological features. Our aim was to review cases of NF referred to our institution to identify reasons of referral and problematic areas faced by pathologists.

Methods:
A total of 27 NFs were referred between 2012-2017 to exclude sarcoma. A sarcoma pathologist reviewed the histopathological features and immunohistochemical stains retrospectively. Reason of referral was assessed.

Results:
The 27 patients included 10 females and 17 males, aged 6-62 years (mean 31.8). The lesions were 0.7-4.0cm in size (mean 2.2cm). Head and neck was the most common location (40.7%), followed by upper extremity (29.6%), trunk (25.9%), & lower extremity (3.7%). Lesions were subcutaneous (60.9%), fascial (26.1%), intramuscular (4.3%), intraparotid (4.3%), or mucosal (4.3%). A location in the head and neck, trunk, or deep soft tissues (e.g. intramuscular or intraparotid) was considered problematic by some pathologists and was a reason for referral. Irregular tumor border, which is commonly seen in fascial-type NFs, was another pitfall. Histologically, myxoid NF was the most alarming to pathologists, usually raising suspicion of a myxoid sarcoma e.g. myxofibrosarcoma. Cellular NF with a storiform pattern and hyalinization was confused with benign fibrous histiocytoma and rarely with dermatofibrosarcoma protuberans when there was focal fat infiltration. NF with a prominent inflammatory component raised the question of inflammatory myofibroblastic tumor especially in children. Another reason for referral was specimen fragmentation that prevented proper assessment.
Conclusions:
Problematic areas that influenced referral of NF cases for second opinion included unusual anatomical location, myxoid morphology, irregular tumor borders, pediatric age group, and specimen fragmentation.

Key Words: Nodular fasciitis; Pseudosarcoma; Pathology;

Funding Agency: None

Pathology and Oncology

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Genetic Variants in Vitamin D Metabolic Pathway are Associated with Breast Cancer Risk and Clinical Characteristics in Kuwait

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Introduction:
Vitamin D (VD) deficiency is associated with increased risk of several cancers including breast cancer (BC). VD is found in the circulation bound to vitamin D binding protein (VDBP) and interacts with target cells through vitamin D receptor (VDR). The aim of this study was to investigate the expression of VDR in BC tissues in relation to common genetic variants in VDBP and VDR genes.

Methods:
A hundred and eighteen Kuwaiti female BC tissues were used in the study. Immunostaining of VDR was performed in all BC tissues. DNA extraction was performed using Qiagen DNA mini kit. Taqman genotyping assays for VDBP variants rs7041, rs4588; and VDR variants rs2228570 & rs731236 were used.

Results:
Two variants were associated with BC risk: VDBP rs7041 and VDR rs731236 (p-value ≤0.001, odds ratio (OR) 3.88, 1.791, 95% confidence interval (CI): 1.9-7.7, 1.06-2.97; respectively). VDR rs2228570 (AA) correlated inversely with VDR cytoplasmic staining (r= -0.21, 95% CI: -0.39-(-0.024), p = 0.023) and rs7041 (C) negatively correlated with VDR nuclear staining (r= -0.2, 95% CI: -0.37-(-0.01), p = 0.01). VDBP rs4588 (T) associated with HER2 negative BC (p-value= 0.04) and correlated negatively with HER2 expression (r= -0.19, 95% CI: -0.367- (-0.004), p-value= 0.049).

Conclusions:
Genetic variants in VD metabolic pathway are associated with BC risk, and influence the pattern of VDR expression in cancer tissues. This suggests that VD metabolism is altered in BC and warrants further investigations.

Key Words: Breast cancer; Vitamin D; Genetic polymorphisms;

Funding Agency: None

Pediatrics

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Kuwait national sickle cell disease registry

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Introduction:
The Kuwait National Sickle Cell Disease Registry (KNSCDR) was inaugurated in 2013. The main objectives are to document the number, distribution, presentation and complications of patients with sickle cell disease (SCD), and to eventually unify its management in the country.

Methods:
Data are obtained via questionnaire forms and by the review of patients' records to document the age, Hb genotype, clinical presentation, complications and treatment. These are obtained on site, at the participating hospitals (Mubarak, Amiri, Adan, NBK, Sabah, Farwaniya and Jahra Hospitals), involving both pediatric and adult patients. The data are entered into a database purposely-designed for the project.

Results:
A total of 396 patients have been registered. Most, 351 (88.6%) patients are Kuwaiti nationals with 52% males and 48% females. Most (62.1%) are SS, 34.8% Sβ and 2.8% SD. Their ages ranged from <1 to 73, with a mean of 19.2± 15.6 years while the HbF ranged from 1 to 55, with a mean of 21.2 ± 9.8%. Most (63.6%) patients had a mild phenotype (0 -1 pain episodes per year), while 18.7% had >3 pain episodes per year. The most common complication was gallstones (33.3%), followed by avascular necrosis (AVN) of the femoral head (21.2%); 13.9% had acute chest syndrome. Only 3.0% had priapism and 1.5% had stroke. There were no recorded cases of leg ulcers. These complications were more common in the older age group (>16 years) and also among Sβ0thal patients. One hundred and sixty seven (42.2%) patients had been transfused, but none was currently on chronic transfusion therapy. The use of hydroxyurea was documented in 158 (40.0%) patients; the commonest indication was frequent severe painful episodes.

Conclusions:
SCD is a significant cause of morbidity in Kuwait. The clinical phenotype is however, different from patients in other parts of the world. Some of the usual complications like priapism, leg ulcers and stroke are uncommon.

Key Words: Sickle cell disease; Registry; Kuwait;

Funding Agency: KFAS Grant 2013-1302-07

Pediatrics

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Transcranial Doppler in peninsular Arab patients with sickle cell

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Introduction:

Stroke is a common devastating complication in sickle cell disease (SCD), but not so much among Gulf Arab patients with the disease. Transcranial Doppler (TCD) is the gold standard to identify patients with SCD at risk for stroke. We have carried out TCD studies in patients from 4 countries in the Arabian Peninsula (Kuwait, Oman, Southern Iraq and UAE) to document the prevalence and pattern of TCD findings.

Methods:

We have pooled data from independent cross-sectional studies in the 4 centers, carried out in the last 5 years. The patients were recruited from outpatient clinics and studied in steady state. TCD was performed using standard equipment with experienced operators. Time-averaged mean of maximum velocity (TAMMV) of blood was documented in the arteries of the Circle of Willis. The hemoglobin (Hb) genotype was confirmed and the fetal Hb (HbF) level and complete blood counts were determined in addition to other selected clinical and laboratory parameters.

Results:

There were 415 patients in the study, aged 2 to 18 years (mean of 8.6±3.5). None of the patients had abnormal TAMMV (i.e. >200 cm/sec), while only 13 (3.1%), all from Iraq had conditional values in the right middle cerebral artery (MCA) and 7 (1.7%) in the left MCA. There were no significant gender differences, and the Hb genotype (SS, $S\beta^0$thal or SD) showed no influence. Hydroxyurea, but not history of blood transfusion, caused significant lowering of TAMMV. Total hemoglobin, reticulocyte count, serum bilirubin and HbF showed varying degrees of association with TAMMV in the different vessels.

Conclusions:

This study has demonstrated the rarity of abnormal TCD findings among Peninsular Arab patients with SCD. This might be related to the haplotype, elevated HbF or may represent a racial variation. It is also consistent with the rarity of stroke among our SCD patients. The guidelines for TCD screening in this population need further studies and recommendations.

Key Words: Sickle cell disease; Stroke; Transcranial Doppler;

Funding Agency: Kuwait University Grant MK 01/08

Pharmacology and Toxicology

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The impact of linker region between receptor and fluorescent protein on arrestin recruitment assays.

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Introduction:
Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), are secreted from the gut in response to nutrient ingestion. They potentiate glucose dependent insulin secretion through their specific receptors (GLP-1R and GIPR, respectively) expressed on pancreatic beta-cells. Using fluorescence resonance energy transfer (FRET) between YFP-tagged receptors and CFP-tagged arrestin3, we have previously reported that GLP-1R interacted robustly with arrestin3 in response to agonist whereas GIPR did not. In subsequent experiments a GIPR construct was employed that used a modified version of YFP (SYFP2). This receptor was found to recruit arrestin. The objective of this study is to discover why.

Methods:
Arrestin3 recruitment to GIPR was investigated by monitoring FRET between YFP-labelled GIPR and CFP labelled arrestin in transiently transfected HEK-293T cells. Cells were perfused with buffer or GIP. Arrestin recruitment was observed as an increase in FRET. The original GIPR-YFP construct contained a 10 amino acid linker between the receptor and a XbaI restriction site. There is no linker between GIPR and the XbaI site in GIPR-SYFP2. However, this results in the introduction of a serine residue to the end of GIPR's C-terminal tail which could potentially be a phosphorylation site. The serine/arginine (SR) coded by the XbaI site was subsequently substituted with glycine/glycine (GG) by site-directed mutagenesis.

Results:
Deletion of the 10 amino acid linker between GIPR and the XbaI site results in a receptor that can recruit arrestin. However, substitution of SR with GG between the receptor and YFP abolishes arrestin recruitment (n=5).

Conclusions:
These results highlight the importance of the linker between receptor and fluorescent protein in arrestin recruitment assays. The use of the commonly used XbaI restriction site may introduce an additional phosphorylation site, potentially resulting in false positive results.

Key Words: GPCR; Arrestin; FRET;

Funding Agency: Kuwait University Grant RM01/15.

Pharmacology and Toxicology

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Free radicals scavenging potential of Cassia fistula extract against hydrogen peroxide-induced toxicity in human intestine cells

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Introduction:
Overproduction of free radicals within the cells induced oxidative damage of biomolecules. Present study tested the protective efficacies of Cassia fistula extract against the hydrogen peroxide(H2O2) induced free radicals in human intestinal epithelium cells(INT-407).

Methods:
Cassia fistula fruit pulp methanolic extract was tested for free radicals scavenging potential using DPPH (1,1-diphenyl-2-picrylhydrazyl) and hydroxyl radicals scavenging assays. Cytotoxicity was examined by MTT assay. Free radicals scavenging enzymes activities [catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and glutathione reductase (GR)] were estimated in extract treated and untreated INT-407 cells [1]. The experiment was performed in triplicate.

Results:
The IC50 of pulp extract against the INT-407cells was 1.104 mg/mL and against H2O2-exposed INT-407 cells (50µm H_2O_2 treated for 2h) was 0.775 mg/mL at 24 h. At 0.3 mg/mL of extract, the viability of H2O2 exposed cells was 90.64%. H2O2 -exposed cells showed decrease levels of CAT (61.3%), SOD (67.9%), GPx (62.3%), and GR (15.0%) enzymes activities as compared to the untreated control. Although, H_2O_2-exposed cells incubated with extracts (0.3 mg/mL), showed increase levels of CAT (60.2%), SOD (56.3%), GPx (40.4%), and GR (10.6%) enzymes activities as compared to the control, i.e., H2O2-exposed cells ($p<0.05$). The EC50 of pulp extracts against DPPH and hydroxyl radicals were 0.915 and 0.889 mg/mL, however, EC50 of ascorbic acid were 0.102 and 0.105 mg/mL, respectively.

Conclusions:
Cassia fistula fruit pulp extracts treated cells have shown to increased level of free radicals scavenging enzyme activities, that might be protect from subsequent cells damage induced by the H2O2 or OH* radicals. From both results, present study provided clear evidence that the Cassis fistula pulp have potential source of natural antioxidants.Reference: [1]. Ahmad I., et al. (2017). J Plant Biochem Physiol.,5,1-8.

Key Words: Cassia fistula; Free radicals; Superoxide dismutase;

Funding Agency: None

Pharmacology and Toxicology

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Chemical composition and antifungal efficacy of Paganum harmala from Kuwait

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Introduction:
Bioprospecting is the process of discovery and commercialization of new products based on biological resources. Reports show that limited research has been carried out to examine the biological potential of Kuwait's native plants. Not even a fraction of native plant species (1- 10%) with bioprospecting potential have been studied till date. The aim of this study was to assess the phytochemical composition and in vitro antifungal activity of methanolic seed extract from P. harmala native to Kuwait.

Methods:
The chemical components of the extract were identified through GC-MS analysis. The antifungal activity of the extract was examined against 3 standard and 10 oral Candida isolates. The MIC of the extract for each isolate was determined through broth microdilution assay. Biofilm formation was measured by MTT assay. Effect on ultrastructure of the cell was examined through Scanning Electron Microscopy, and Transmission Electron Microscopy.

Results:
GC-MS analysis lead to the identification of thirty three chemical compounds. The major compounds present were Harmine (79%), 3,5-Bis (P-Dimethylaminostyrl)-2,2-Dimethyl-2H-Pyrrole 1-Oxide (7.53%), and 9,12-Octadecadienoic acid (Z,Z) (6.24%). The MIC of the test extract against Candida isolates ranged 0.625-2.5 mg/ml. Biofilm results obtained for the three Candida spp. demonstrated that MBIC, MBIC/2 and MBIC/4 values of the test extract showed the average biofilm inhibition by 80.8%, 47.1%, and 17.8%. SEM analysis of the treated cells have shown pronounced shrinkage, and deformed cells with convoluted and irregular surfaces. In TEM analysis the treated cells exhibited several changes including rupturing of the cell wall and plasma membrane, undulating cell wall, and swelling of cell wall at many places.

Conclusions:
The test extract shows significant antibiofilm activity and eventually lead to damage of membrane and cell wall. These results taken together makes this extract eligible for further development.

Key Words: Paganum harmala; Candida albicans; Native plants;

Funding Agency: Kuwait Institute for Scientific Research. (P-KISR-05-06)

Pharmacology and Toxicology

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Effect of acute inhibition of Ca2+/calmodulin protein kinase II (CaMKII) on aging-induced abnormal vascular reactivity

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Introduction:
The importance of aging as a potential risk factor for cardiovascular diseases has been increasing in the developing countries. CaMKII is a Ser/Thr-directed protein kinase. Studies reported that inhibition of signal transduction of CaMKII prevents development of diabetes-induced vascular dysfunction. Objectives of this study were to test the: (1) reactivity to vasoactive agonists in renal and carotid arteries of aged rats, and (2) effect of acute incubation with CaMKII inhibitor, KN-93, on responses to vasoactive agonists.

Methods:
Two groups of Male SD rats were used. Group 1 control (10 wks.). Group 2 old animals (30 wks.) (n=45 rats/group). The study conforms to National Institutes of Health Guide for Care and Use of Laboratory Animals and is approved by Kuwait University. Rats were sacrificed under light ether anesthesia. Renal and carotid arteries from control or aged rats were isolated. The vessels were cut and mounted in organ-baths containing Krebs Henseleit solution. A pretension of 0.5 g or 1.0 g was applied to the renal and carotid artery, respectively. Concentration response curves were established for phenylephrine (PE), carbachol or Sodium nitroprusside(SNP). Contractile responses to PE were calculated as gm/gm tension. The relaxant responses to carbachol or SNP were expressed as percentage reduction of tension induced by pre-contraction with PE (3x10-7 M). Effect of ex vivo incubation with KN-93 (10−5M) for 30 min on the responses of the arteries to vasoactive agonists was examined. Data are presented as mean ± S.E.M. (n=8). ($p<0.05$).

Results:
PE-induced vasoconstriction in renal and carotid tissues was potentiated in aged animals, while vasodilator responses to carbachol were attenuated. Abnormal vascular reactivity to PE and carbachol were significantly corrected after acute incubation with KN-93

Conclusions:
Inhibition of CamKII signaling pathway may prevent or retard the functional abnormalities in the cardiovascular system that are induced by aging.

Key Words: KN-93; Vasoconstriction; Carbachol;

Funding Agency: Kuwait University, Research Administration, Project No. MR02/16

Pharmacy

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Neurotherapeutic Effects of *Ginkgo biloba* Extract and Its Isolated Ginkgolide B

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Introduction:
Ginkgo biloba is known to contain flavonoids and terpene trilactones. The plant extract (GBE) show neuroprotective effects on many neurological diseases such as Alzheimer's disease, cerebral insufficiency and schizophrenia. This study describes the extraction, purification and neuroprotective effect evaluation of ginkgolide B in the crush sciatic nerve injury rat model.

Methods:
Chromatographic purification of ginkgolide-B (G-B) was done using vacuum liquid chromatography and prep-HPLC techniques. The isolated terpene was identified, as G-B, based on its spectral data. Sixty Wistar male rats were randomly allocated into 6 groups: NAIVE (n=6), SHAM (n=12), CRUSH (n=12), CRUSH+ terpene trilactones-enriched extract (TEGBE), and G-B. TEGBE (n=12), CRUSH+G-B (n=12) and CRUSH+GBE (n=6). GBE (50 mg/kg), TEGBE (50 mg/kg) and G-B (10 mg/kg) in 0.9% normal saline were administered intraperitoneally 1 hr following nerve crush injury, then once daily for 14 days. Functional and sensory neurobehavioral tests, histomorphological and immunohistochemistry (Neu-N, GFAP, and GAP-43) analyses on spinal cord and sciatic nerve were performed at weeks 3 and 6.
Results:
G-B was isolated and identified. GBE, TEGBE and G-B were shown to enhance functional and sensory behavioral parameters and to protect the histological and the ultrastructural elements in the sciatic nerve. All treatments prevented spinal cord neurons from further deterioration and ameliorated astrogliosis with concomitant decease in GAP-43 protein following sciatic nerve injury. Results demonstrated that G-B has the most significant potential effects among other treatments, nearly comparable to SHAM and NAIVE values.

Conclusions:
GBE and G-B exhibit neurotherapeutic effects in the crush sciatic nerve injury model. Further, G-B treatment showed the most neuroprotective outcome compared to other constituents. More in-depth analysis of the neuroprotective mechanisms will be needed.

Key Words: Ginkgolide B; Crush sciatic injury; Neuroprotection;

Funding Agency: YP03/15

Pharmacy

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Structural Diversity and Selective Anticancer Activity of Marine-Derived Elastase Inhibitors: Key Features and Mechanisms Mediating the Antimetastatic Effects in Invasive Breast Cancer

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Introduction:
The implication of dysregulated protease activity in cancer progression highlights the importance of proteases as therapeutic targets. Human neutrophil elastase (HNE) has been shown to play a role in tumor progression leading to metastasis and is associated with poor prognosis. 3-amino-6-hydroxy-2-piperidone-containing cyclodepsipeptides are among the most predominant HNE inhibitors isolated from marine cyanobacteria; However, there are no rigorous studies describing their cellular effects in cancer. Herein, we describe the discovery of new members of this family and report their effects on breast cancer progression.

Methods:
Floridian marine cyanobacterium was freeze dried, extracted and fractionated. Pure compounds were purified by HPLC. Structures were elucidated using NMR spectroscopy and mass spectrometry. Biological evaluation involves protease inhibition assays, AlphaLisa, RT-qPCR, and migration assays.

Results:
Three new compounds named loggerpeptins A–C along with molassamide were discovered. Molassamide was the most potent and selective analogue against HNE. Molassamide inhibited the cleavage of the elastase substrate CD40 in biochemical assays and exhibited significant cellular activity. As CD40 processing culminates in NFKB activation, we assessed the effects on the expression of target genes, including ICAM-1. Molassamide attenuated both elastase-induced ICAM-1 gene expression and cleavage, revealing a potential dual effect on migration. Molassamide also inhibited the elastase-mediated migration of highly invasive breast cancer cells.

Conclusions:
The discovery of loggerpeptins A−C and molassamide add to the growing family of cyanobacterial elastase inhibitors. This class of compounds might be developed into probes to further investigate the biology of elastase mediated processes and serve as a starting point for the design and development of more potent and selective leads with therapeutic potential.

Key Words: Breast Cancer; Elastase; Marine Cyanobacteria;

Funding Agency: National Institutes of Health grant R01CA172310.

Pharmacy

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Self-management apps: barriers to adoption

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Introduction:
Managing chronic conditions requires high quality clinical care and effective self-management. Digital health tools such as mobile health apps can potentially support patients' self-management of their conditions, especially that mobile phones have a high rate of utilisation. However, the adoption of mobile apps as self-management tools remains low amongst patients. The aim of this review is to identify barriers to the adoption of self-management apps amongst patients with chronic conditions and provide recommendations to overcome the barriers to patients' engagement with this technology.

Methods:
A comprehensive literature search in Embase, Cochrane, Scopus, ScienceDirect, MEDLINE and Google Scholar was conducted to identify relevant publications. We included studies that examined the barriers to adoption of self-management mobile phone apps relating to management and/ or prevention of chronic conditions. Thematic analysis was used to highlight the barriers to adoption of the technology among patients.

Results:
We identified 23 main barriers to patient's adoption of self-management mobile apps. These can be patient barriers: health and technological illiteracy; technology access barriers: limited internet access; technology design barriers: lack of customization to patient's preference; provider barriers: low integration into provider work flow; and health system barriers: limited institutional support. In order to overcome these challenges, the following facilitators should be promoted; patient engagement, provider productivity, technology accessibility and high quality integrated health systems.

Conclusions:
This review highlights the factors affecting patients' adoption of self-management apps, and the potential opportunities to facilitate patients' engagement. Future research reports on successful large-scale rollouts of integrated self-management apps/ mHealth strategies could provide insights on how barriers have successfully been overcome.

Key Words: Mobile apps; Self-management; eHealth;

Funding Agency: None

Pharmacy

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Medicine use and medicine related problems in liver cirrhosis: A systematic review

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Introduction:
Liver cirrhosis is a chronic disease that is associated with complications and a complex treatment. Medicine-related problems (MRPs) involve any events that can adversely interfere with treatment outcomes. It can occur at any stage of the medicine use process, which considers patients and health care providers (HCPs) as key components. Objectives: To investigate the prevalence, causes, and risk factors of MRPs in cirrhotic patients and to explore factors influencing the medicine use from patients and HCPs perspectives.

Methods:
A comprehensive systematic review of both quantitative and qualitative studies was conducted using the following databases: PubMed, Scopus, CINAHL, and Web of Science. Search terms used were medicine related problems, medicine use, perceptions, and alternatives. Arabic and English studies from inception to 2017 were included. Quantitative studies were analysed descriptively after extracting relevant data. While thematic synthesis approach was adopted for qualitative data.

Results:
A total of 16 quantitative studies and 11 qualitative studies were obtained after following the search strategy and applying the inclusion criteria. Mean frequency of MRPs ranged from 14-23.4%. The most frequent causes of MRPs were drug interactions, inappropriate dosing and contraindicated drugs. Major risk factors were polypharmacy, the severity of liver disease, and length of hospital stay. Diuretics and analgesics were among the most implicated classes leading to MRPs. Thematic synthesis of qualitative data yielded three major themes.

Conclusions:
MRPs represent a major issue in managing liver cirrhosis. Efforts should be directed toward improving the healthcare in this population in order to ensure patient safety. The review highlighted the need for interventional strategies that could involve both training and educational programs. Future research should be directed toward interventions that target both the patients and healthcare providers.

Key Words: Medicine-related problems, adverse drug reactions; Medicine use; Liver

Funding Agency: none

Pharmacy

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A survey on the knowledge, perception and self-confidence of healthcare professionals towards application of pharmacogenetic testing in clinical practice in Kuwait.

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Introduction:
Pharmacogenetic testing helps to select appropriate drug therapy for special population. The aim of this study was to assess the knowledge, perception, and self-confidence of pharmacists and physicians, regarding pharmacogenetic testing, and the barriers towards its application in Kuwait.

Methods:
A descriptive, cross-sectional survey was conducted on pharmacists and physicians from six public hospitals in Kuwait. The survey questionnaire had two sections; the first section explored demographic information, perceived challenges, and the preferred education format. The second section assessed three domains; knowledge, perception, and self-confidence in pharmacogenetic testing. The questionnaire had good internal consistency (>0.6). Data were analyzed using SPSS.

Results:
The survey questionnaire was distributed to 379 (61%) physicians and 238 (39%) pharmacists, with a response rate of 98.6%. The overall mean knowledge score (%) of the respondents was low (45 ±24), and there was no difference between the mean scores for pharmacists or physicians. Pharmacists had significantly more positive perceptions towards pharmacogenetic testing than physicians. Respondents with more years of work experience, and training in pharmacogenetic testing, perceived more positively towards the application of pharmacogenetic testing. Both pharmacists and physicians highlighted the lack of training facilities and clinical guidelines as the key challenges towards application of pharmacogenetic testing in Kuwait.

Conclusions:
Despite the low level of knowledge, there was a positive perception towards pharmacogenetic testing. Pharmacists accepted greater responsibility, and were more confident in providing, and identifying sources of pharmacogenetic information.

Key Words: Pharmacogenetic, Pharmacists, Phyisicans; Perception; Self-confidence ;

Funding Agency: None

Pharmacy

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Adherence and satisfaction of multiple sclerosis (MS) patients to Disease Modifying therapies (DMTs) in Kuwait.

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Introduction:
Multiple sclerosis (MS) is the leading cause of neurological disability in young adults. To date, there is no cure for MS, but disease-modifying therapies (DMTs) aid in reducing the frequency of relapses, slow disease progression and delay the onset of disability. Poor adherence to DMTs can result in therapy failure. Thus, it is of great importance to assess adherence level and determine predictors of non-adherence. The current study aims to explore the level of both adherence and satisfaction of MS patients. Another objective of the study is to assess the link between adherence and satisfaction.

Methods:
A non-interventional descriptive cross-sectional study was conducted using a questionnaire. Adherence was measured using Morisky scale, while therapy satisfaction was measured using the Treatment Satisfaction Questionnaire for Medication (TSQM) scale.

Results:
There were a total of 263 patients who participated in current study. The mean age of the sample population was 35.7 (±10.3) years. According to Morisky scale results there were 41.1% with a low level of adherence (less than 6), almost half (50.6%) showed medium adherence (6-8 points) and only 8.3% of the patients belong to high adherence group (score = 8). The satisfaction level differed significantly between different DMTs (Natalizumab, alemtuzumab, rituximab, interferon B-1a, interferon, interferon B-1b, teriflunomide, fingolimod, and dimethyl fumarate) in measures of side-effects and convenience. Interferon B-1b had the highest global satisfaction. The patients with mild disability had the highest scores in both adherence and satisfaction rate. There was a significant positive relationship between age and satisfaction, however that was not found between adherence and age. There was a significant positive correlation between all satisfaction subscales and adherence score.

Conclusions:
The significant correlation between adherence and treatment satisfaction of MS patients reveals the necessity of improving patients' treatment satisfaction in an attempt to improve their adherence, which in turn can lead to improved clinical outcome.

Key Words: Multiple sclerosis; Adherence; Satisfaction;

Funding Agency: None

Pharmacy

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Dissolution Enhancement of Atorvastatin Calcium by cocrystallization

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Introduction:
Oral drug delivery remains the most favorable route of administration for patients. However, the oral bioavailability is often low and variable, since the process of drug absorption from the GIT depends on many factors such as drug solubility, dissolution, permeability, etc. The aim was to enhance the dissolution rate of the poorly soluble drug atorvastatin calcium (ATC) by cocrystallization with selected coformers; Glucosamine (GluN) and nicotinamide (NIC). Dissolution enhancement of ATC, Class II-BCS, is expected to enhance the drug bioavailability.

Methods:
The cocrystals were prepared by solvent drop grinding (SDG) and solvent evaporation (SE) method (1:1 to 1:10 drug-coformer molar ratios). The cocrystals were characterized by Fourier transform infrared (FT-IR), differential scanning calorimetry (DSC), powder X-ray diffraction (PXRD), mass spectroscopy (MS), Scanning electron microscopy (SEM), solubility, and dissolution rate studies. The cocrystal preparations, the physical mixtures and the raw ATC were subjected to stability testing at 40 ± 0.5˚C/75 ± 5%RH and at room temperature (RT) (22-25˚C) for 6-months. Experiments were run in triplicates and average ±SD were calculated and differences were statistically evaluated by t-test ($p < 0.05$).

Results:
SDG and SE improved the dissolution rate of ATC with both coformers. Drug: coformer ratio 1:3 was optimum.The results of saturation solubility indicated that the saturation solubility of the cocrystals was enhanced by 31.05 % in GL2 and 86.19 % in NL2 compared to untreated ATC. Solubility was increased from 26, 35 and 50 µg/ml for ATC, GluN-, and NIC-cocrystals. The dissolution rate from the cocrystals was >90% after 5min., compared to 41% (ATC). The physicochemical characterization suggested H-bonding as the main mechanism involved in enhancing drug solubility and dissolution.

Conclusions:
Cocrystallization significantly improved the solubility and dissolution, in comparison with the untreated ATC.

Key Words: Atorvastatin; Glucosamine; Nicotinamide;

Funding Agency: College of Graduate Studies and Research Sector, Kuwait University

Pharmacy

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Patient safety culture in hospitals of the Middle East: A systematic review

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Introduction:
Patient safety is an issue of worldwide concern. A healthcare system will not achieve patient safety and reduce the incident of harm, unless they develop a patient safety culture. Evidence from the literature shows an increasing concern on patient safety in developing countries and their provision of a safety culture. Measuring the safety culture of an organisation provides insight into the areas of strength and the areas in need for improvement. This study was conducted to assess the existing patient safety culture in hospitals of the Middle East region.

Methods:
A systematic review was conducted including English and Arabic language studies (published from November 2004 to May 2017). Studies conducted in hospitals of the Middle East utilising the Hospital Survey on Patient Safety Culture (HSOPSC) tool were included. The studies were retrieved by searching the following databases: PubMed, CINAHL, EMBASE, PsychINFO, and data were collected by searching with the following keywords: patient safety, patient safety culture and its combination with hospital (HSOPSC) and Middle East (or representing countries).

Results:
34 studies were identified from the Middle East. Two top areas of strength were identified: Organisational learning and continuous improvement and teamwork within units. Top areas in need for improvement were: Non-punitive response to error and staffing. The average percentage of positive responses from hospitals in the Middle East showed relatively lower results when compared with international benchmark scores.

Conclusions:
There is a need to enhance patient safety culture in both developed and developing countries. Based on our findings the culture of blame still exists in the Middle East. There is a need to create a non-punitive culture that supports open and honest communication. Further research is needed to develop interventions that would influence a positive patient safety culture.

Key Words: Patient safety culture; Middle East; Hospital survey on patient safety

Funding Agency: None

Pharmacy

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Self-nanoemulsifying Drug Delivery System of Lamotrigine: Design, Preparation and In-vitro Characterization

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Introduction:
Lamotrigine (LMG) is one of the newer antiepileptic drugs which belongs to class II according to Biopharmaceutics Classification System (BCS). Its low aqueous solubility (0.17mg/ml) limits its oral bioavailability and onset of action. The aim of this study was to enhance the solubility and dissolution of LMG using self-nanoemulsifying drug delivery systems (SNEDDS) which may lead to enhancing its oral bioavailability.

Methods:
Solubility of LMG in various oils, surfactants, and cosurfactants was determined to identify components of SNEDDS. Surfactants and cosurfactants were selected based on two parameters, their ability to solubilize LMG and their emulsification ability. Pseudoternary phase diagrams were constructed to identify self-emulsifying area. Different formulations were prepared using Capmul MCM, rose oil, Cremophor EL (CR EL), Tween 80, polyethylene glycol 400 (PEG 400) in various proportions. The prepared formulations were tested for self-emulsification properties, % transmittance, droplet size upon dilution with water, and in vitro drug release in 0.1 N HCL compared to the pure drug.

Results:
Capmul MCM showed maximum solubility for LMG followed by rose oil compared to other oils. CR EL, Tween 80, and PEG 400 were selected among other surfactants and cosurfactants due to their high ability to emulsify the selected oils. The formulation containing 30% rose oil, 46.67% CR EL, and 23.33 % Tween 80 showed the best results regarding spontaneity of emulsification, % transmittance, droplet size, and in vitro drug release. This formulation showed 99.9% transmittance, 16.3 nm ± 0.42 droplet size and 100% drug release after 5 minutes, which is significantly higher ($p < 0.05$) than the non-emulsified drug (35%).

Conclusions:
The results indicated that LMG-SNEDDS could be successfully prepared and evaluated. The optimized formulation could be a potential carrier for improving solubility, dissolution, and hence the bioavailability of LMG.

Key Words: Lamotrigine; Self-nanoemulsifying; Drug Delivery System;

Funding Agency: None

Pharmacy

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Molecular entrapment of Ketoprofen in Beta-Cyclodextrin toenhance drug solubility and dissolution rate

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Introduction:
Ketoprofen (KET), a widely used NSAID, but has extremely poor aqueous solubility. The objective of the present work was transformation of this hydrophobic drug into soluble amorphous form by molecular entrapment in a natural hydrophilic carrier, i.e. beta-cyclodextrin (BCD).

Methods:
Phase solubility study with increasing BCD concentrations was done to analyze its influence on drug solubility. Drug- BCD complexes in various molar ratios were prepared by lyophilisation technique. The complexes were compared with untreated drug and physical mixtures (PM) in the same ratio for saturation solubility, particle size and in-vitro dissolution. Fourier transform infrared spectroscopy (FTIR) study was performed to identify the physicochemical interaction between the drug and carrier.

Results:
KET solubility increased linearly with increasing BCD concentration depicting an A_L type of phase solubility curve. Intrinsic solubility of KET in water was found to be only 128.63 µgm/ml. Saturation solubility studies showed a 19 fold increase in drug solubility for 1:1M KET-BCD complex. Lyophilisation also resulted in transformation of the crystalline drug (particle size–4.64 µm) into amorphous nano-particles (particle size< 250 nanometer). There was significant improvement in the drug dissolution rate of the inclusion complexes as compared to the untreated drug. The optimized complex (1:1M) showed 100% drug release, whereas untreated drug showed only 11.7% release in 10 minutes. The FTIR spectra confirmed that the enhanced dissolution rate of KET from its inclusion complex could be due to its physical interaction with BCD.

Conclusions:
This study reveals the potential of formulating KET: BCD freeze dried complexes with improved solubility and dissolution rate. These factors can enhance the bioavailability of hydrophobic drugs, decrease gastric irritancy and improve patient safety.

Key Words: Ketoprofen; Beta-Cyclodextrin; Lyophilisation;

Funding Agency: None

Pharmacy

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Population pharmacokinetics of Topiramate in patients with

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Introduction:
Topiramate (TPM) is anti-epileptic with high inter-individual variability observed in the drug's pharmacokinetic profile. Thus, routine therapeutic drug monitoring (TDM) is required. To our knowledge, TPM population pharmacokinetics (PPK) has not yet been studied in Kuwait. The aim of this study was to establish a PPK model for TPM in patients with epilepsy using plasma levels obtained for routine TDM and explore the impact of covariates on TPM pharmacokinetic profile in epileptic patients in Kuwait.

Methods:
Data were collected retrospectively from Al-Amiri, Mubarak Al Kabeer and Ibn-Sina hospitals in Kuwait from 2009 to 2016 for patients with epilepsy and treated with oral TPM with at least 1 TPM plasma level. TPM plasma samples were quantified by LC-MS/MS method. The data were analyzed by non-parametric modeling algorithm (NPAG) using Pmetrics software. One and two compartment models were examined. Several covariates were assessed including patient's demographics, renal function, concomitant medications and nationality. The developed model was then validated internally using visual predictive check.

Results:
A total of 173 plasma samples from 73 adult patients and 35 pediatrics (ped) with age of 2 years and above were included. A one compartment model with first order elimination rate constant (ke) fitted the data well. Age did not influence TPM's ke, while renal function and co-administration with carbamazepine (CBZ) had the greatest impact with median value of 0.0187 h^{-1} (0.0097-0.402). On the other hand, age and gender were the significant covariates for volume of distribution (V) with a median value of 67.5 L (2.066-122). Visual predictive check demonstrated good predictive performance for the developed model.

Conclusions:
TPM elimination in epileptic patients was 31% higher in patients co-administered with CBZ and most likely require higher TPM doses. Furthermore, females had 34% lower V than males and might require lower TPM doses.

Key Words: Topiramate; Population Pharmacokinetics; Covariates;

Funding Agency: College of Graduate Studies

Pharmacy

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Role of the pharmacist in parenteral nutrition therapy: challenges and opportunities to implement pharmaceutical care in Kuwait

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Introduction:
Pharmacists can provide beneficial pharmaceutical care services to patients receiving Parenteral Nutrition (PN) therapy by working within Nutrition Support Teams (NSTs). This study was designed to explore pharmacists' role in PN therapy in hospitals of Kuwait, sources of PN-related information, opinions on NSTs, perceptions about the barriers to pharmaceutical care implementation and views on how to enhance their practices.

Methods:
Data were collected via face-to-face semi-structured interviews with the senior Total Parenteral Nutrition (TPN) pharmacists at seven hospitals which provide TPN preparation services in Kuwait. The interviews were audio-recorded, transcribed verbatim and analysed using thematic analysis. Descriptive statistics were used to describe pharmacists' demographic details.

Results:
The pharmacists mainly performed technical tasks such as TPN compounding with minimal role in providing direct patient care. They used different sources of TPN-related information to guide their practice. None of the hospitals had a functional NST. However, pharmacists expressed preference to work within NSTs to improve service. Pharmacists perceived several barriers to providing pharmaceutical care including lack of reliable sources of TPN-related information, lack of a standard operating procedure for TPN across hospitals, insufficient staff, time constraints and poor communication between TPN pharmacists. To overcome these barriers, they recommended fostering pharmacists' education on TPN, establishing national standards for TPN practices, provision of pharmacy staff, development of NSTs, enhancing TPN pharmacists' communication and conducting research.

Conclusions:
TPN pharmacists in Kuwait are confined to performing TPN manufacturing processes. Pharmacists' role in patient care can be improved by education and training to equip them with the clinical competencies needed to practise as nutrition support pharmacists with patient-centred roles.

Key Words: Parenteral nutrition; Pharmaceutical care; Qualitative research;

Funding Agency: None

Pharmacy

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H2S donor GYY4137 prevents and ameliorates thermal hyperalgesia, and cold and mechanical allodynia in a murine model of paclitaxel-induced neuropathic pain

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Introduction:
Paclitaxel is used for treating metastatic breast cancer and other solid tumors. However, it can cause painful peripheral neuropathy. Recently, a putative role for the gaseous mediator hydrogen sulfide (H2S) in nociception modulation was suggested. The objectives: to investigate the potential of a slow-release H2S donor, GYY4137, to prevent or alleviate hyperalgesia and allodynia in mice with paclitaxel-induced neuropathic pain.

Methods:
Female BALB/c mice were used according to the National Institutes of Health Guide for the Care and Use of Laboratory Animals. Paclitaxel (2mg/kg), or vehicle, was administered by intraperitoneal (i.p.) injection to mice once daily for 5days to induce painful peripheral neuropathy. GYY4137 (50 mg/kg, i.p.) was given concurrently with paclitaxel for 5 days to evaluate a potential protective effect against thermal hyperalgesia, cold allodynia and mechanical allodynia (prophylactic regimen). In a separate set of experiments, GYY4137 or gabapentin were given to paclitaxel-treated mice to evaluate the ability of GYY4137 to treat established paclitaxel-induced thermal hyperalgesia, which was assessed every 30 minutes for 3 hours (therapeutic regimen). The effect of GYY4137 on the antitumor activity of paclitaxel was also evaluated in vitro using breast cancer cell line (MCF-7), and plasma H2S levels were determined using zinc-trapping assay.

Results:
Daily administration of GYY4137 together with paclitaxel prevented the development of paclitaxel-induced neuropathic pain. GYY4137 dose-dependently raised the reaction latencies against thermal hyperalgesia. GYY4137 treatment did not interfere with the antitumor activity of paclitaxel; rather, synergistic cytotoxicity was observed.

Conclusions:
GYY4137 prevents paclitaxel-induced hyperalgesia and allodynia, and ameliorates hyperalgesia without reducing antitumor activity. GYY4137 may be a useful agent for the prevention and treatment of chemotherapy-induced neuropathy.

Key Words: GYY4137; Paclitaxel; Peripheral Neuropathy;

Funding Agency: Kuwait University, Research Administration, Grant No. PT04/16

Physiology

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The effect of progesterone on placental glucose transporters 1 and 3 in dexamethasone-induced intrauterine growth restriction

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Introduction:
Intrauterine growth restriction (IUGR) is defined as fetal growth that does not reach its full potential. In IUGR, placental glucose transporters (GLUT1 and GLUT3) are down regulated, concomitant with lower maternal plasma levels of progesterone (Prg). In the uterus, GLUTs are up-regulated by Prg during early pregnancy. Evidence shows that Prg improves fetal wellbeing in IUGR pregnancies. Therefore, the aim of this study is to evaluate the effect of Prg on the levels of placental GLUT1 and GLUT3 in dexamethasone- induced IUGR.

Methods:
Pregnant female Sprague Dawley rats were divided into four groups based on daily i.p. injections from 15 days of gestation (dg) until the day of sacrifice (19 or 21dg): Saline (Control), Dexamethasone (Dex, 0.2mg/kg/day), progesterone (Prg, 5 mg/kg/day), dexamethasone and progesterone (Dex-Prg). The gene and protein expressions of GLUT1 and GLUT3 were evaluated in the labyrinth and basal zones of the placenta by real time PCR and western blot, respectively. Maternal plasma levels of progesterone were measured using ELISA.

Results:
Dex induced a significant reduction in fetal body weight on 21dg (-15%, $p<0.05$) compared to controls. Dex induced a significant decrease in total placental and labyrinth zone weights on both 19 and 21dg. In addition, administration of Dex resulted in downregulation of the protein expression levels of GLUT1 and GLUT3 on 19dg. We observed a decrease in progesterone levels in the plasma of pregnant rats given Dex. Co-injection of Dex and Prg led to slight improvement in the fetal body weight gain (-6%, $p<0.06$) and a significant elevation in placental efficiency (+12.8%, $p<0.05$). Prg prevented the Dex-induced drop in labyrinth GLUT3 protein expression on 19dg rats.

Conclusions:
The results of this study suggest that Prg may improve fetal body weight in Dex-induced IUGR, most probably through increasing placental efficiency and expression of placental GLUT3.

Key Words: Glucose transporters; Dexamethasone; Progesterone;

Funding Agency: College of Graduete Study and Research Sector. grant no. YM11/15

Physiology

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Effect of Exercise during Ramadan Fast on Sleep, Anthropometric Measurements, and Blood Parameters in Females.

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Introduction:
Ramadan fasting is a safe annual activity for healthy individuals. Body weight, waist circumference, body composition, or cellular and biochemical elements of blood experienced decrease, increase, or show no change during Ramadan. Aim: Physical activity for female adults was our main concern to investigate the physiological changes during Ramadan with aerobic exercise intervention. Subjective and objective measures related to general health, female health and sleep was assessed.

Methods:
The subjective measures include consent forms, general health questionnaire, Epworth Scale. Objective measurements consist of general examination: height, weight, age. Anthropometric measurements: waist hip ratio, BMI, body composition, and blood tests including Complete Blood Count (CBC), general biochemistry profile, iron profile, vitamin B12. The study included three groups; EDR group (exercised during Ramadan), ENR group (exercised non-Ramadan month) and FDR group (fasted during Ramadan and had no exercise intervention).

Results:
Within groups' comparisons, subjects showed multiple trends of improvements in anthropometric measurements in EDR group and these improvements showed significance only in Fat Body Mass, Fat Percent with p-values<0.05. EDR group showed no significant changes in anthropometric parameters. Between groups comparisons showed a significant change in EDR group in comparison to FDR group in Fat Body Mass, with p-values<0.05 while it remained non significantly altered in other groups. Blood tests showed no changes in all the groups. Sleep duration or daytime sleepiness didn't show any major change in all groups except the expected shifts in sleep schedule during Ramadan.

Conclusions:
Exercising while fasting in Ramadan reduces the fat percent more than fasting alone or exercising alone. We found no changes on blood basic haematology, biochemical parameters and sleep duration and or day time sleepiness parameters.

Key Words: Fasting; Sleep; Ramadan;

Funding Agency: College of Graduate Studies, Kuwait University

Physiology

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Changes in Cardiopulmonary Fitness, Hormones, and Blood Components in Females Exercising during Ramadan Fasting

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Introduction:
Physical activity and its physiological changes in females is our main focus according to World Health Organization global recommendations. Ramadan is a holy month of the Islamic religion and fasting is mandatory obligation. Aim: This research aimed to investigate the physiological changes in females during Ramadan with aerobic exercise intervention.

Methods:
Subjective measures includes: consent forms, general health questionnaire, Kuwait Physical Activity Questionnaire (KPAQ). Objective measures consist of general examination, body composition, Cardiopulmonary Exercise Testing (CPET), and fitness related tests (Balance, Flexibility, Anaerobic Power, and Grip Strength). This research includes 3 groups: EDR group (Exercised during Ramadan), ENR group (Exercised in non-Ramadan month) and FDR group (Fasted during Ramadan and had no exercise intervention).

Results:
Within groups comparisons; subjects showed improvements in the cardiopulmonary at exercise peak parameters: Tidal Volume(VT), and Oxygen Uptake(VO2) with p-value<0.05 and Respiratory Frequency(Rf), Minute Ventilation(VE), Relative Oxygen Consumption(VO2/kg), Respiratory quotient(R), and Metabolic Equivalents(METs) with p-value≤0.01 in EDR group, whereas, EDR group had no significant changes. In between groups comparisons EDR group in comparison to FDR group showed better results in cardiopulmonary parameters: VE, 1st minute of Recovery Diastolic Blood Pressure(RDBP), and first minute of recovery VO2, and 5th min of Recovery VO2 with p-value≤0.05 and VT, VO2, VCO2, O2Exp, METs, and 1st min of Recovery Systolic Blood Pressure(RSBP) with p-value≤0.01. EDR group showed a significant change in comparison to ENR group in VE, 1st min RSBP and RDBP with p-values<0.05, ≤0.001, and≤0.01.

Conclusions:
Exercise training during Ramadan is rewarding for the wellbeing, health, and fitness of sedentary subjects. There were no negative effects of exercising during Ramadan fasting on females health and fitness.

Key Words: Fasting; Exercise; Ramadan;

Funding Agency: College of Graduate Studies, Kuwait University

Physiology

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The Effect of Progesterone Administration on the Expression of Metastasis Tumor Antigens (MTA1 and MTA3) in Placentas of Normal and Dexamethasone-Treated Rats

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Introduction:
Administration of Dexamethasone (DEX; glucocorticoid) between gestational days (dg) 13 and 20 induces intrauterine growth restriction (IUGR) in pregnant rats. IUGR occurs because of apoptosis of trophoblasts, which can be inhibited by progesterone administration. A group of genes called MTAs play a role in the proliferation and differentiation of trophoblasts. MTA1 upregulates trophoblasts, while MTA3 downregulates them. Our hypothesis is that during IUGR, MTA1 decreases and MTA3 increases in the placenta and this is reversed by administering progesterone.

Methods:
Sprague Dawley rats were maintained under controlled conditions. Rats were mated overnight and the morning at which sperms were detected via vaginal smear was considered as 0 dg. Rats (n=8) were then divided into 4 groups: control group (V), DEX-treated group (D), DEX- and progesterone-treated group (DP) and progesterone-treated group (P). All groups received daily intraperitoneal injections starting from 15 dg. Animal dissection was performed on 19 dg, at which the placenta has reached its maximum growth; and 21 dg, when fetal growth has reached its maximum. Protein content in both basal and labyrinth zone was done using Western blotting followed by immunodetection.

Results:
In the labyrinth zone both MTA1 and MTA3 proteins decreased significantly at 21 dg in all treatment groups ($p \leq 0.05$ – 0.001). There was no significant difference in MTA1 and MTA3 protein content at 19 dg between groups; however, in the D treated group at 21 dg there was a significant reduction in the content of MTA1 ($p \leq 0.05$) and an increase in MTA3 ($p \leq 0.001$; that was reversed by P administration). In the basal zone, although levels of MTA1 and MTA3 appeared lower at 21 dg compared to 19 dg, the levels were only significantly lower in the MTA1 control and P-treated groups.

Conclusions:
MTA1 decreases and MTA3 increases in labyrinth zone of DEX-induced IUGR placentas, this is reversed by progesterone.

Key Words: Progestrone; MTA; IUGR;

Funding Agency: none

Physiology

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Effect of thermal preconditioning on the sensitivity of baroreflex control of heart rate

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Introduction:
An episode of short-term elevation of core body temperature protects against heatstroke development. Improvement of the baroreflex sensitivity was postulated as a possible mechanism. To substantiate this postulate, we examined the evolution of baroreflex sensitivity of heart rate control after passive hyperthermia of 42.0°C (abdominal temperature) for 15 minutes. We also tested the ability to survive in the hot environment 24 and 72 hours after the thermal preconditioning.

Methods:
Wistar-Kyoto male rats (n = 30) were implanted with telemetric transmitters to monitor ECG, aortic pressure and body temperature. 20 rats were preconditioned in a climatic chamber at air temperature of 44.4°C. 24 and 72 hours after preconditioning, prolonged exposure to hot air was used to induce heatstroke in the preconditioned rats (n = 20) and in the controls (n = 10). Baroreflex sensitivity was estimated in 1s intervals with the spectral method in the low frequency band. Numerical data represent the mean (standard deviation).

Results:
Repeated measure ANOVA did not show significant effect of thermal preconditioning on the average baroreflex sensitivity of 1.17 (0.28) ms/mmHg. However, 4 hours after the preconditioning, the distribution of baroreflex sensitivity values was significantly (Kolmogorov-Smirnov 2-sample test) shifted to higher values. Yet, this distribution shift was only transitory; prevalence of lower baroreflex sensitivity values was significantly elevated 20 hours later. Changes in the distribution of baroreflex sensitivity values had no significant effect on heatstroke, which appeared 54.1 (6.8) minutes after animals were placed inside the climatic chamber (air temperature 44.4°C).

Conclusions:
Thermal preconditioning did not elevate sensitivity of baroreflex control of heart rate and did not delay the development of heatstroke.

Key Words: Baroreflex sensitivity; Thermal preconditioning; Heatstroke;

Funding Agency: Kuwait University research grant No. MY02/11

Physiology

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A novel mutation in KCNA1 discloses contributions of a conserved phenylalanine to gating properties of Kv1.1 channels and ataxia

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Introduction:
Channelopathy mutations provide valuable information on disease causing mechanisms while unraveling the molecular workings of the channels involved. We have identified a novel heterozygous mutation in the KCNA1 (Kv1.1) gene of a young proband displaying typical symptoms of Episodic Ataxia type 1 (EA1). This mutation results in the substitution of phenylalanine, located at position 303 within the S4 segment of the voltage-sensor of the Kv1.1 channel, to a valine (p.F303V). The contributions of F303 towards the channel's voltage gating are unclear. We have thus functionally characterized the new mutation and biophysically and structurally assessed the role of F303.

Methods:
The mutation was introduced by site-directed mutagenesis. Mutant and wild-type KCNJ10 constructs were heterologously expressed in Xenopus laevis oocytes, and whole cell K^+ currents were measured from oocytes using the Two-electrode voltage-clamp technique. Structural analysis was performed in silico using Kv1.2 coordinates as template.

Results:
Protein-homology analysis identified the phenylalanine at position 303 as highly evolutionary conserved. The mutation brought significant positive shifts of voltage-dependence, changes in the activation and deactivation kinetics, reduced window currents, and decreased amplitude of currents. Structural analysis revealed altered interactions between F303V and L339 and I335 of the S5 helix of a neighboring subunit.

Conclusions:
We report a new mutation in KCNA1, the substitution of an aromatic phenylalanine with an aliphatic valine within the voltage-sensor destabilizes the open state of the channel. F303 fine-tunes the Kv1.1 gating properties and contributes to the interactions between the S4 segment and neighboring alpha helixes. The resulting channel's loss of function validates the clinical relevance of the mutation for EA1 pathogenesis.

Key Words: Channelopathy; Episodic Ataxia 1; Potassium channel;

Funding Agency: MIUR-PRIN 20108WT59Y_004

Psychology

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Psychoticism and Big Five Model of Personality: A Facets-Level Correlation Analysis

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Introduction:
The term psychoticism is psychiatric in nature, while Eysenck's Psychoticism is described by characteristics such as aggressive, more ruthless, egocentric, insensitive, antisocial, impulsive and tough-minded. The Five Personality Factors Model received empirical attention in literature. This model is comprised of five factors: Neuroticism, Extraversion, and Openness to Experience, Agreeableness, and Conscientiousness. The extent to which these dimensions are not overlapping remains unresolved, nor is it clear how P correlates with Big five facets among university students. The present study investigates the relationship between Psychoticism and the big five facets among university students.

Methods:
The participants were 2109 first year undergraduate Kuwaitis: 900 males mean age = 22.77±4.57 and 1209 females; mean age = 19.61±2.59). The Arabic version of the EPQ-R Psychoticism Scale (Eysenck, Eysenck & Barrett, 1985) 32 items×2, and the revised NEO Personality Inventory (Costa & McCrae, 1992): The NEO-PI-R is a 240-item questionnaire answered on a 5- point scale format. The reliability, correlation and principal component analysis was used.

Results:
Internal consistency was satisfactory for the Psychoticism, Neuroticism, Extraversion, Openness to Experience, Agreeableness, and Conscientiousness, with subscales respectively (Cronbach's alpha = .70, .79, .73, .81, .70, .71) for males and females. The results revealed that no significant gender differences were found in Psychoticism. The PCA showed that a two-component solution explains 52.47% of the total variance for males and females. The P correlated with N (r =0.26), with E (r=0.04), with O (r=-0.04), with A (r=-0.33), and with C (r=-0.28).

Conclusions:
Overall the inter-correlation of all scales is similar to those reported in previous research. The results reported that the six personality dimensions were distinct. However, future research needs to replicate the current findings within clinical populations.

Key Words: psychoticism; Big five; university students;

Funding Agency: None.

Public Health

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Vitamin D status among adolescents in Kuwait

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Introduction:
In Kuwait as in many Arab states in the gulf region, there are limited data on the prevalence of vitamin D deficiency among healthy adolescents. This study aimed to estimate the prevalence of vitamin D deficiency in a nationally representative sample of adolescents and investigate factors associated with vitamin D status.

Methods:
Cross-sectional study was conducted on 1416 adolescents who were randomly selected from middle schools in all governorates of Kuwait. Data were collected from parents and adolescents; while vitamin D was measured using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Logistic regression was used to investigate the independent factors associated with vitamin D status.

Results:
The Prevalence of vitamin D deficiency was 1,150 (81.21%, 95%CI: 71.61-90.81) while severe deficiency was 559 (39.48%). Only 51 (3.60%) were vitamin D sufficient. Prevalence was significantly higher among females compared to males (91.69% vs. 70.32%; $p<0.001$). There was a significant inverse correlation between vitamin D and PTH (Spearman correlation=-0.35; $p<0.001$). In relation to vitamin D status, elevated PTH (secondary hyperparathyroidism PTH ≥65 ng/L.) was detected in 312 (55.81%), 185 (31.30%) and 59 (27.57%) of adolescents with vitamin D severe deficiency, deficiency and insufficiency, respectively. In the final model, gender, age, governorate, parental education, vitamin D supplement, body mass index and number of times walking to school per week were all significantly related to vitamin D deficiency.

Conclusions:
High prevalence of vitamin D deficiency was noted among adolescents in Kuwait despite the abundant sunshine which may reflect strong sun avoidance behavior. Adequate outdoor daytime activities should be encouraged especially for females. We call for locally tailored guidelines for supplement in which females should have a higher amount of vitamin D supplement compared to males.

Key Words: Vitamin D; Adolescents; Kuwait;

Funding Agency: Kuwait University, Research Sector (Project No. WF 02/13)

Quality & Accreditation

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'Nursing Perceptions in Quality Improvement and Accreditation: A Leadership Voice'

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Introduction:
Nursing staff play a great role in quality improvement within multidisciplinary teams in healthcare. Therefore, their views and concerns need to be recognized and acted upon. The aim of this study is to explore the impact of accreditation activities on quality of care as perceived by nursing staff in leadership positions at a hospital which underwent an accreditation cycle.

Methods:
A cross-sectional survey utilized a self-reporting questionnaire with 7 scales adapted from Shortell and Pomey. The scales focused on leadership, strategic planning, human resources utilization, quality management, quality of results, patient satisfaction, and accreditation impact. It also included questions on sociodemographics, professional and accreditation experiences. It was distributed to all 47 nurses who are in leadership positions in Farwania Hospital as identified by the nursing directorate in the Ministry of Health. Mean scores were rated on a five-point Likert scale with higher scores reflecting positive impact.

Results:
The response rate was 95.7%. Participants' reported their involvement in accreditation activities as minimal in (0%), intermediate (34.2%), and maximal by the majority (65.8%). The highest score of 4.45 (SD ± 0.54) was for the strategic quality planning scale. The lowest score of 3.82 (SD ± 0.68) was for the quality management scale. The highest individual item score of 4.44 (SD ± 0.66) was for "nurses play a key role in setting priorities for improving quality", while "Adequate time given to nurses to plan and test quality improvements" had the lowest item score of 3.48 (SD± 1.17).

Conclusions:
Nursing staff leaders in a hospital which recently went through accreditation cycle in Kuwait correctly identified that nurses play a key role in setting priorities for improving quality. However, they voiced their concern about the need to give nursing staff adequate time to plan and test quality improvement interventions and activities.

Key Words: Leadership; Accreditation; Quality Improvement;

Funding Agency: None

Surgery

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Female Physicians Leading Health Care in the Arab World

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Introduction:
A global trend in female leadership roles amongst the medical profession is on the rise. From the years 2004-2018 females have been taking up leadership roles in varying and increasing amounts. This research aims to identify changes in trends in the medical field in terms of gender in the last decade in Kuwait.

Methods:
A case study was conducted, in which data on leadership positions in Kuwait's governmental hospitals were obtained from hospital registries. Demographic data about female to male physicians was collected from statistical books published by the department of Manpower, Statistics, and Planning of the Kuwaiti Ministry of Health (MOH). In addition, statistics on medical graduates was obtained from the Faculty of Medicine (FOM), Kuwait University (KU).

Results:
In general, every governmental hospital in Kuwait has experienced an increase in leadership roles among females: In 2008, among all leadership positions in Kuwait's general hospitals, males occupy a majority of seats (60%); whereas in 2016, the male to female ratio was 1:1. The most change in gender trends was witnessed at Mubarak Al-Kabeer Hospital, where female leaders went from 38% in 2008 to 73% in 2016. The specialties that have the highest number of females in leadership positions across all hospitals from 2008-2016 were nuclear medicine, radiology and laboratory. In KU's FOM, female graduates outweighed male graduates, except in 2005-2006, where females reached a minimum of 48%. Since then, the percentage fluctuated between 51% and 68%. The number of female physicians has also increased from its lowest of 31% of the total number of physicians in 2004-2006, to 37% in 2015.

Conclusions:
Females are now occupying more leadership positions in Kuwait's governmental hospitals, even though males constitute the greater percentage of physicians amongst all nationalities. Many factors play a role in this trend, which was explored in this research paper.

Key Words: Female Physician; Leadership; Arabs;

Funding Agency: none

Surgery

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Anoplasty for post-hemorrhoidectomy anal stenosis: A new technique

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Introduction:
Background: Post-hemorrhoidectomy anal stenosis though rare is very disturbing and devastating complication. Despite good results of previous procedures, many complications can ensue like flap necrosis, mucosal ectropion, and restenosis.
Objective: We report a new simple technique for repair of severe/moderate anal stenosis which requires no extensive flap mobilization or many sutures.

Methods:
Design: A prospective single armed study.
Patients: This is a personal series of 65 patients treated over a period of 20 years.
Setting: Tertiary care teaching hospital.
Intervention: The procedure entails mobilizing the anal mucosa to the dentate line via a vertical incision and mobilizing the adjacent perianal skin and subcutaneous fat to allow a completely tension free approximation of the perianal skin and the anal mucosa which are sutured together transversely.
Main outcome: Correction of the anal stenosis and the ability to have normal defecation with no pain.

Results:
59 patients (90.8%) continued the 5 years follow up, and 6 patients left the country after 2 years of follow up. There was only one case of recurrence after 2 years, which was treated by a second anoplasty. Four patients (59-66 years old) developed transient urine retention after surgery. One patient developed partial dehiscence of the suture line which was treated conservatively. No mucosal ectropion or perianal skin necrosis was observed. Complete healing of the perianal tension-releasing wound was within 2-3 months. By the third week after surgery, all the patients discontinued use of stool softeners or laxatives and were able to defecate comfortably.
Limitations: Single armed study with no comparison with other procedures and it is a personal collection of patients with no independent assessment.

Conclusions:
This procedure is simple, requires little dissection and only a few sutures with minimal complications. It is suitable for low severe and moderate anal stenosis.

Key Words: Anal Stenosis; Post-hemorrhoidectomy complication; benign anorectal

Funding Agency: None

Surgery

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Long term remission of diabetes post sleeve

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Introduction:
Bariatric surgery has been shown to cause remission of type 2 diabetes for obese patients undergoing it in the short-term follow-up. The aim of this study was to assess the long term outcome of diabetes mellitus type 2 post laparoscopic sleeve gastrectomy (LSG).

Methods:
A retrospective observational study was conducted among 43 previously diagnosed pre-diabetic and Type 2 diabetic (T2D) patients who were being treated with oral hypoglycaemics and/or insulin therapy, and had undergone laparoscopic sleeve gastrectomy (LSG) at Amiri General Hospital, Kuwait.

Results:
Post-operatively, 25.6% of the patients had complete remission of their diabetes, and most patients stopped (46.5%) or reduced the dosage (37.2%) of their medication post LSG. Significant differences in hba1c compared to the pre-LSG value was noticed in the group of patients that were followed up for 3 (6.33 ± 1.18, p value, 0.039) and 5 years (6.72 ± 1.34, p value, 0.034).The group of patients that were followed up for 3 years had the highest percentage of complete remission of T2D (55.6%), while at 1 year of follow up none of the patients experienced complete remission. The largest number of patients that underwent partial remission was seen in those with a 1 year follow up. Patients that were followed for 2 (61.18%) and 3 years (62.77%) post-LSG reached the highest EWL%, while the lowest was 45.25% among patients followed for 1 year.

Conclusions:
LSG was effective in achieving substantial weight reduction in the 3 and 5 year follow up with improved glycemic control for obese diabetic patients. Although weight regain was possible with time, majority of patients could maintain sustainable weight loss and diabetes remission

Key Words: Long term remission; Post sleeve; Diabetes

Funding Agency: None

Surgery

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Comparison of different antibiotics in peritoneal lavage in severe fecal peritonitis rat experiment

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Introduction:
Fecal peritonitis is caused by perforation of the bowel and bacterial contamination by fecal material. A surgical approach is still a cornerstone of fecal peritonitis management, which includes control and alleviation of the source of infection. It has been controversial over the years, that peritoneal lavage with antibiotics or without as an essential step of fecal peritonitis management.

Methods:
A total of 25 healthy Sprague-Dawley rats were randomly divided into 5 groups. Cecal ligation and perforation were performed on all groups to establish fecal peritonitis. After a 6-hour period, relaparotomy was performed, and swab cultures were taken before and after peritoneal lavage. The peritoneum was lavaged with normal saline 0.9% in Group A, with Gentamycin in Group B, with gentamycin and clindamycin for Group C, with metrodanazol for Group D, and with ceftriaxone for Group E. None of the groups was given any intramuscular or intravenous antibiotics.

Results:
Microbiological examination results of the pre- and post-lavage cultures revealed no reduction in bacterial colonization in Group A and D, whereas significant reduction of bacterial contamination or no growth of bacteria in Group B, C, and E. However, the mortality rate of all groups was 100% in 24-48 hours.

Conclusions:
Peritoneal lavage with antibiotics can reduce bacterial contamination caused by bowel perforation. However, there is no effect on the mortality rate with peritoneal lavage with antibiotics alone. Further studies are needed to investigate peritoneal lavage with antibiotics.

Key Words: fecal peritonitis; antibiotic in peritoneal lavage; intraperitoneal antibiotic.;

Funding Agency: NONE

Surgery

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Intragastric Balloon for Adults: a 4-year follow-up

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Introduction:
Intragastric balloons are a bariatric method available for weight loss. Data pertaining to intragastric balloons in our region is scarce. Furthermore, the long-term effects of intragastric balloons are lacking. Thus, this study focused on the efficacy, safety, possible predictors of weight loss of fluid-filled balloons, and the 4-year follow-up.

Methods:
A retrospective analysis of data obtained from adults who underwent balloon insertion at Al-Amiri Hospital in Kuwait from June 2012 to June 2016 was conducted.

Results:
A total of 129 patients were studied, with an average age of 30.9 years. Starting weight and BMI was 92.6kg and 35.1 kg/m^2, respectively. This showed a drop to 81.4Kg and 30.8 kg/m^2 at the time of removal of the balloon, respectively. Mean weight loss was 11.0Kg, corresponding to a %EWL of 51.1%. 51.2% of the patients reported that they were satisfied with the procedures and would recommend it to others. The follow-up period ranged from 6 months up to 4 years; it proved that EWL % was not maintained as it dropped to 41.5729% in patients that were studied for 4 years. There was no proportionate relationship between duration and maintenance of EWL%, making intragastric balloons not a suitable long- term modality in adults.

Conclusions:
Intragastric balloons are efficacious methods of weight loss reduction for the population and rarely cause any complications. Long-term study of up to 4 years proved that fluid-filled balloons are effective in the short-run rather than the long-term period for weight maintenance.

Key Words: Efficacy; Intragastric Balloon; Adults;

Funding Agency: NONE

Surgery

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The Efficacy of Intragastric Balloon in the Adolescent Population

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Introduction:
Intragastric balloons are a bariatric method available for weight loss. Data pertaining to intragastric balloons concerning adolescents in our region is very scarce. Furthermore, the long-term effects of intragastric balloons are lacking. Thus, this study focused on the efficacy, safety, 6 month follow-up, and possible predictors of weight loss of fluid-filled balloons.

Methods:
A retrospective analysis of data obtained from young patients who underwent balloon insertion at Al-Amiri Hospital and Royale Hayat hospital in Kuwait from June 2012 to June 2016 was conducted.

Results:
A total of 38 patients were studied, with an average age of 17.4. Starting weight and BMI was 105.7kg and 38.7 kg/m^2, respectively. This showed a drop to 95.2Kg and 34.6 kg/m2 at the time of removal of the balloon, respectively. Mean weight loss was 9.9Kg, corresponding to a %EWL of 34.2%. 36% of the patients reported that they were satisfied with the procedures and would recommend it to others. Six-month follow-up showed a further decrease in the mean weight and BMI of 2.1Kg and 0.7Kg/m^2 respectively; this corresponded to a %EWL of 36.9%. In addition, the age group (13-15 years) with the least results immediately upon removal, had the best long outcomes after 6 months of follow up, and vice versa to the 19 year olds' age group.

Conclusions:
Intragastric balloons are efficacious methods of weight loss reduction for the younger population and rarely cause any complications. Long-term follow up proves that fluid-filled balloons are effective in weight maintenance.

Key Words: Efficacy; Intragastric Balloon; Adolescents;

Funding Agency: None

Surgery

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Long-term outcomes of laparoscopic sleeve gastrectomy: A Kuwaiti centre experience

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Introduction:
As obesity is on a continuous rise around the world, laparoscopic sleeve gastrectomy (LSG) has been established as an effective mean of weight loss for obese patients. Multiple studies report LSG as a cost-effective procedure with low peri-operative complications. However, the data regarding the long-term outcomes of LSG patients in Kuwait & the Middle East are lacking.

Methods:
This study is a retrospective analysis of prospectively collected data between December, 2008 & December, 2011 for morbidly obese patients treated with LSG as a primary bariatric surgery at Amiri General Surgery Department, Kuwait.

Results:
A total of 187 patients (53 males (28.4%), & 134 females (71.6%)) had undergone LSG. All patients were followed up after 5-8 years from the date of surgery. The mean age of the patients at the time of the surgery was 36.5 ± 10.3 years. Remission of type 2 diabetes & HTN occurred in 19.5% & 19.6% of patients, respectively. For OSA symptoms (snoring, tiredness, & choking) the remission was 11.2%, 1.6% & 2.1%, respectively. Only 2 patients out of 4 were still on CPAP post LSG. No morbidities or mortalities were reported. The only acute complication within 30 days of surgery was leakage in 2 patients (1.1%). Long term complications following LSG were, depression (2.1%), DVT (1.6%), musculoskeletal pain on medication (17.1%), gallstones (19.3%), & GERD (41.7%). 21 (11.2%) patients underwent revisional bariatric surgery post LSG. The mean pre-op weight was 126.3 ± 25.3 Kg & the mean pre-op BMI was 47.1 ± 8.3 kg/m 2. The post-op mean BMI decreased to 34.3 ± 7 kg/m 2 at 5-8 years after LSG. The recent mean weight is 91.6 ± 19.9 Kg after 5-8 years following LSG. The mean total weight loss is 34.5% ± 1.5%.

Conclusions:
LSG is an effective type of bariatric procedure with lesser complications rate and mortality. It is associated with improvement in obesity related comorbidities, as well as significant improvement in weight in the long term period.

Key Words: Long-term outcomes; Laparoscopic sleeve gastrectomy, LSG; Sleeve

Funding Agency: None

Surgery

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Improvement of obstructive sleep apnea syndrome after Laparoscopic sleeve gastrectomy: A retrospective study

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Introduction:
Obesity increases the risk of many chronic health conditions, including obstructive sleep apnea (OSA). Bariatric surgery (BS) provides a significant, sustained weight loss for morbidly obese patients, with resultant improvement in obesity-related comorbidities. This study aims to evaluate the change in symptoms of OSA & the use of CPAP after laparoscopic sleeve gastrectomy as a bariatric surgery, given that the data about this subject is lacking in the Gulf region.

Methods:
On July 2016, a retrospective analysis of 30 patients who underwent laparoscopic sleeve gastrectomy (LSG) and a sleep study in the period between November 2011 & November 2015, was conducted. Out of 30 eligible patients, 10 participants who couldn't be reached were excluded from the analysis. The patients were asked about pre and post-operative weight and OSA symptoms using STOP-Bang and Epworth Sleepiness Scale (ESS) questionnaires.

Results:
The mean age of the patients was 35.5 years & the females were (45%). There was statistically significant improvement in ESS, & STOP BANG Questionnaire ($p < 0.001$) showing a drop from 8.65 to 0.75, and 4.1 to 1.5, respectively. The mean BMI showed a decreasing trend from 71Kg/m2 (47.6-90.2) pre-operatively, to 40.1 Kg/m2 (29-81.6) post-op, ($p < 0.001$). Fifty-five percent of our patients were on CPAP before LSG; however, all the patients were off CPAP after the surgery. The percent excess body weight loss (EBWL) was 60.31% with a follow-up range after surgery of 9-56 months.

Conclusions:
In conclusion, LSG plays a major role in the improvement and resolution of OSA symptoms, with a significant reduction in the use of CPAP in morbidly obese patients.

Key Words: Obstructive sleep apnea syndrome, OSAS; Laparoscopic sleeve gastrectomy,

Funding Agency: None

Urology

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The impact of the "Optimized Surgical Journey" on robotic assisted radical prostatectomy patients: a prospective non-randomized longitudinal cohort study

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Introduction:
Prostate cancer is the most common cancer in Kuwaiti males since 2011. After acquiring the Da Vinci Si robot in 2013, a robot assisted radical prostatectomy (RARP) program was established. We examined the impact of a standardized post-operative algorithm on robotic prostatectomies performed at our center in Kuwait.

Methods:
We collected data prospectively on all robotic cases performed between February 2014 and December 2017. We used the Clavien-Dindo system to grade complications. Major complications were defined as Clavien grade ≥ 3. We examined recovery variables on all patients. Since April 2015, we adopted a standardized post-operative algorithm called the optimized surgical journey (OSJ) for managing our patients post-operatively.

Results:
Between February 2014 and December 2017, a single surgeon's robotic experience at Sabah Alahmad Urology Center (SAUC) includes a total of 127 cases (107 cases done as the main console surgeon and 20 cases done with an invited robotic proctor). Of these, 51 cases (44%) were RARP (45 cases as the main console surgeon and 6 cases with an invited robotic proctor). Mean age for RARP patient cohort was 62 years. Mean prostate volume was 50 grams. Five patients had positive surgical margins (10%).The initial 12 RARPs were managed with non-standardized post-operative orders yielding a mean hospital stay of 4.83 days. Since April 2015, 39 patients underwent the OSJ protocol reducing hospital stay by 2.33 days ($p<0.001$). Adjusting for age did not affect our results. We report only 4 minor complications with no significant association with the OSJ.

Conclusions:
Standardized post-operative pathways improve recovery of patients undergoing major surgical procedures like RARP. The OSJ decreased length of hospital stay without compromising surgical or oncologic outcomes. Our limitations are the small number of patients and lack of randomization as well as possible impact of the learning curve on the initial cases.

Key Words: Prostate Cancer; Prostatectomy; Robotic;

Funding Agency: NONE

Urology

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Robotic assisted partial nephrectomy: Initial experience from a single center

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Introduction:
Advances in urology have focused on minimizing the invasiveness of surgical procedures without compromising oncologic outcomes. We present Kuwait's initial experience and outcomes of robot assisted partial nephrectomy (RAPN) using the da Vinci Si robot.

Methods:
After IRB approval data was recorded for all patients who underwent robotic surgery at our center. Complications were graded using the Clavien-Dindo system, defining major complications as ≥ III.

Results:
Between February 2014 and December 2017, a single surgeon's robotic experience at Sabah Alahmad Urology Center (SAUC) includes a total of 127 cases (107 cases as the main console surgeon and 20 cases with an invited robotic proctor). Of these, 21 cases (17%) were RAPN (18 cases as the main console surgeon and 4 cases with an invited robotic proctor). Mean age for RAPN patients was 50.1 years. Mean size of renal masses was 3.3 cm. Mean RENAL Nephrometry score was 7.46. The most complex tumor had a score of 9 a+h. Eight tumors were posteriorly located. All patients were subjected to either warm or zero ischemia partial nephrectomy. There was one major and five minor complications. Median hospital stay was three days. Mean estimated blood loss was 287.5mls. Pathology included 21 malignant renal cell carcinomas with negative surgical margins and one benign tumor. No tumor recurrence occurred over a mean follow up of 15 months.

Conclusions:
Our center's initial experience with RAPN shows good patient and operative outcomes. Larger number of cases is required to draw a definite conclusion. Dedication of all members of the robotic team is crucial to ensure good patient outcomes.

Key Words: Renal Cancer; Nephrectomy; Robotic;

Funding Agency: None

CASE REPORTS

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Structured diabetes education is helpful in controlling post-transplant diabetes in recent renal transplant body builder.

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CASE REPORT

Background:
Post-transplant diabetes mellitus is a common complication of solid organ transplantation. We aimed to present the role of diabetes education in improvement of PTDM in kidney transplant body builder.

Case Summary:
Thirty-six year old body builder with medications abuse (anabolics, short-acting insulin and even growth hormone) to help in body building. He was non-diabetic, normotensive without the family history of diabetes. During his the international competitions, he developed some fatigue for which he was investigated. He was found to have reached end stage kidney disease that was seemingly triggered by excessive exercise induced myoglobinuria. Renal biopsy showed focal segmental glomerulosclerosis. He was dialyzed till live unrelated renal transplantation with thymoglobulin induction and he was maintained on steroid, tacrolimus and mycophenolate mofetil. Few weeks later, after transplant he developed polydipsia, polyuria, nausea, headaches, blurry vision and inability to complete his training course. PTDM was confirmed and his blood sugar was partially controlled by 3 oral agents. Therefore, intensive insulin therapy was tailored to control his blood sugar. His c-peptide was acceptable and anti-GAD antibody came negative. However, his blood sugar was not tightly controlled. In view of his high HbA1C, he was subjected to our structured diabetes education program. This program was created to cover different items related to diabetes control including diabetic diet, proper exercise, blood sugar monitoring, sick day management and pathophysiological role of diabetic medications. Within 4 months, his blood sugar became well controlled and his diabetes medications started to be minimized. Nowadays, he is enjoying stable graft function with HBA1c around 5.6 on only diet.

Conclusion:
Proper diabetes education program is recommended to help renal transplant recipients with early PTDM in controlling their diabetic state. Success requires close evaluation as well as a multidisciplinary approach.

Key Words: Renal transplant; PTDM; Diabetes education

Cytopathology

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FNAC of Mammary analog secretory carcinoma of the parotid gland: A case report.

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CASE REPORT

Background:
Mammary analogue secretory carcinoma (MASC) is a recently recognized tumor of salivary gland with characteristic t(12;15)(q13;q25) that results in ETV6-NTRK3 fusion product. Mammary analogue secretory carcinoma often mimics other salivary gland tumors because of the similarities in cytological features . We report a case of MASC which proved to be challenging.

Case Summary:
A 28-year-old male presented to Mubarak Al-Kabeer hospital, cytology department for a fine needle aspiration(FNA) of a non tender parotid swelling ,progressively increasing in size for the past 2 years. CT showed a well defined cystic lesion about 2x3.2x2.6 cm involving the left parotid gland. FNA showed several clusters of epithelial cells with intracytoplasmic vacuoles along with clusters of metaplastic squamous cells and numerous foamy macrophages in a mucinous background. A diagnosis of salivary gland neoplasm with possibility of a mucoepidermoid neoplasm or acinic cell neoplasm was entertained. Superficial parotidectomy revealed a MASC.

Conclusion:
MASC a newly recognized malignant salivary gland tumor that mimics the histology and genetics of secretory carcinoma of the breast. Differential diagnosis of MASC on FNA should be included in the differential diagnosis of mucinous salivary lesions with cystic changes on FNA as its cytologic features overlap considerably with those of other tumors, especially acinic cell carcinoma and mucoepidermoid carcinoma. However, histopathology is the best discriminator between MASC and other salivary gland tumors. Fluorescence in situ hybridization (FISH) studies for ETV6 translocation helps to confirm the diagnosis.

Key Words: Mammary analog secretory carcinoma; Mucoepidermoid carcinoma; Fine needle aspiration cytology;

Dentistry

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Radiation Caries: A Clinical Case

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CASE REPORT

Background:
With over 1.4 million new cases of cancer diagnosed each year and a shift to outpatient management, chances of a dentist seeing these patients has increased. Oral complications as the result of chemotherapy and radiotherapy during cancer treatment are common.One of the most common after effect of radiotherapy involving head and neck is “Radiation Caries” which is rampant decay of the cervical region of the tooth, incisal edge and cusp tips due to decreased saliva production. If this condition is not diagnosed and treated at an early stage this can drastically affect the quality of life of the patient.

Case Summary:
A 49 year old female Indian presented at the dental division of Kuwait Oil Company (KOC) Ahmadi hospital during May 2016. Patient was diagnosed with uterine cancer during September 2012. She had undergone chemotherapy after surgery during 2012 which was followed by radiotherapy. Radiotherapy regime was performed during August 2013 and March 2014. Intra oral examination revealed multiple caries lesions with typical appearance which is common among patients receiving radiotherapy. Comprehensive treatment plan was devised to restore the function as well as the esthetics. Patient was given clear instructions on the precautions to be taken in future.

Conclusions:
Patient who get radiation therapy near the head and neck region should have regular dental checkup before, during and after the radiation therapy. Proper diagnosis and prompt treatment of such cases plays a major role in improving the quality of life in such patients.

Key Words: Radiation Caries; Radiotherapy; Cancer;

Dentistry
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Full mouth rehabilitation in a highly anxious patient using multidisciplinary approach with behaviour management: A rare case report

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CASE REPORT

Background:
Cancer patients can suffer oral toxic effects secondary to antineoplastic therapy in the form of radiotherapy or chemotherapy. This risk is conditioned by range of factors, including the high cell turnover rate of oral mucosa, diversity and complexity of the oral microflora, and soft tissue trauma during normal oral function. Multiple carious teeth in such person can lead to emotional imbalance and near death of a person's confidence. The aim of this report is to present functional and aesthetic rehabilitation in a case of neglected oral care with multiple missing posterior teeth and grossly decayed remaining teeth using multidisciplinary approach.

Case summary:
A 65 year old male presented with multiple missing posterior teeth and extensive caries on all his remaining teeth. Patient has a medical history of lower oesophageal carcinoma and had been operated abroad upon by laparoscopic assisted oesophagogastrectomy preceded by neo-adjuvant chemotherapy 7 years ago. The patient was very anxious about seeking dental treatment, so he avoided going to dentist. As a result he had very poor oral health, loss of oral function and lowered quality of life. Treatments included root canal treatment, crown lengthening done for inadequate clinical crown heights and full coverage restorations. Later on the edentulous span were restored with flexible partial dentures.

Conclusion:
Dental problems are often multi-factorial, and may not be satisfactorily resolved by restorative treatment alone. Maintenance phase of treatment is the cornerstone of a successful practice that aims to provide good quality general dental care to achieve on-going oral health for patients. Treatment not only restored function and esthetic, but also showed a positive psychological impact and there by improved perceived quality of life of the patient.

Key Words: Oesophageal carcinoma,; Emotional imbalance; Aesthetic

Dermatology

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Natural Photosynthesizers followed by natural Antioxidant as a Vitiligo treatment protocol based on Oxidative stress theory

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CASE REPORT

Background

Vitiligo is a multigenetic and multifactorial disorder that results in depigmentation of the skin. Studies suggest that depigmentation may occur by the effect of autoimmune response towards melanocytes. Many treatments options depend on phototherapy by UV radiation to induce melanogenesis, but the response is variable, and the medical and surgical treatments are still challenging. Recent studies suggest that many vitiligo patients have a decrease natural antioxidant activity and an increase in reactive oxygen species (ROS), Which may be the reason of tyrosinase polymorphism. Our hypothesis suggest that during phototherapy vitiligo patients may have greater anti-oxidant imbalance and we are suggesting a new treatment protocol by UV radiation/sun exposure with topical treatment of photosensitive compounds (Psoralen 6.6%) followed by an immediate topical known peroxynitrite antioxidant (effective extract is Cassia tora root water extract) that may trigger melanogenesis without excess/cascade of ROS reactions during the phototherapy.

Case Summary

Eight patients ranging from 20 to 38-years-old of male and female gender with stable and progressive vitiligo. The cases were diagnosed with different subtypes of vitiligo: Segmental vitiligo (SV), non-segmental vitiligo (NSV), focal vitiligo and vitiligo vulgaris. The cases were not undergoing any treatments and they have normal thyroid function. Pictures were taken before treatment and 2 to 4 months post-treatment. All cases showed repigmentation with the new treatment protocol with no recurrence in the pigmented area for at least 6-months observation.

Conclusion

Based on the low anti-oxidant theory causing vitiligo, we have developed a new treatment protocol with UV therapy that used pulse topical photo synthesizer followed by topical natural anti-oxidants. This protocol results in repigmentation of different types of vitiligo with different progression status, suggesting a new treatment protocol option.

Key Words: Vitiligo; re-pigmentation; Mohammad Alansari;

Ethics

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This Patient is More Than RRCC, T2 N1M1: One Case Report and Many Questions in Ethics, Professionalism, Health Policy, Occupational Health and Medical Education

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CASE REPORT

Background:

Clinical ethics is the structured approach to identify, analyze and resolve ethical issues in health care.

Case Summary:

Mr. E, a 51 years presented with painless haematuria. Known HT, congestive heart failure and asthma on medication. He lives alone, married with 4 children, working in the same cement and construction materials factory for 25 years, salary 276 KD/month, and non smoker. An ultrasound showed solid mass in the right kidney. A CT scan (performed 3 months later! in October 2017) confirmed the diagnosis and showed pulmonary nodules with multiple enlarged lymph nodes. The patient was admitted for right radical nephrectomy. The surgery was cancelled as the risk of death on table or being ventilator dependent in ICU post operatively were high. The patient was discharged from hospital and travelled to his country soon after. Mr. E's case highlighted multiple ethical, professional, health policy, occupational health and medical education issues and recommendations: communication challenges; lack of formal translation services; confidentiality; how informed is the informed consent? diagnostic decisions and expensive investigations? Social justice and MOH decision No. 293/2017 regarding clinical fees for expats; truth-telling and end-of-life decision making; quality of life assessment; faith-based decisions; empathy versus sympathy; futility; taking occupational history; reporting occupational disease\risk to patient, MOH, employer, and insurance company? doctors paying for patient's care and professional boundaries; education and dying patients?; patient overly optimistic or in denial? does the duty of care end with discharge? formal ethics consultation and hospital accreditation.

Conclusion:

Medicine is the science of healing and art of communication. As an encounter between human beings, it is embedded in a moral, cultural and legal context that need to be taken in consideration. There are always lessons to be learnt and room for improvement.

Key Words: End of life decision; Ethics; Occupational Health;

Hematology

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A rare case where bone marrow biopsy was the sole modality for the diagnosis of tuberculosis

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CASE REPORT

Background:
In places where advanced modalities for diagnosis of tuberculosis like molecular methods (nucleic acid amplification – NAA) are not available, bone marrow biopsy does play a role when all other conventional tests are negative.

Case summary:
A 56 years old male patient was admitted to the intensive care unit with community acquired pneumonia, septic shock and DIC. He was cachectic with signs of respiratory failure. He had no lymphadenopathy or organomegaly.Chest x-ray showed acute respiratory distress syndrome (ARDS)like picture, while computerized tomography (CT) scan did not add to the diagnosis.Sputum and bronchoalveolar lavage (BAL) samples for detection of acid fast bacilli (AFB), and T- spot test were initially negative.Complete blood count (CBC) showed pancytopenia. Bone marrow aspiration and biopsy were performed and bone marrow cultures (aerobic, anaerobic and TB) were sent. Multiple caseating granulomas were detected in the bone marrow biopsy, however AFB could not be detected by Ziehl-Neelsen (ZN) stain on trephine biopsy sample. TB culture was later positive from the bone marrow aspiration sample. A repeat of BAL sample for TB testing, after bone arrow findings, showed presence of AFB with positive culture for TB. The patient was started an anti – tuberculous therapy which proved life saving.Though a number of newer molecular modalities like nucleic acid amplification (NAA) are available for diagnosis of TB, their outreach may be a problem for the majority of the hospitals. In cases of diagnostic difficulties with or without hematological abnormalities or in cases of PUO, bone marrow biopsy may be considered for diagnosis.Bone marrow tuberculous granuloma needs to be differentiated from other granulomatous diseases of the BM.

Conclusion:
In cases with diagnostic difficulty, with a high suspicion of TB, bone marrow examination may be considered in cases with or without hematological indicators and in cases of PUO as a last resort.

Key Words: Key words: Tuberculosis; Bone marrow biopsy; Nucleic acid; amplification;

Medicine
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Teriparatide induced hyperparathyroidism

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CASE REPORT

Background:
Teriparatide, a recombinant human parathyroid hormone (PTH), is an effective anti-osteoporosis agent for severe osteoporosis (T-score of -3.5 or below). The normal biochemical response to teriparatide is transient hypercalcemia usually 4-6 hours after PTH injection, with normal or slightly suppressed endogenous parathyroid hormone. Primary hyperparathyroidism leads to renal calcium reabsorption, phosphate excretion in urine, and increased bone resorption. These actions of increased PTH lead to hypercalcemia, hypophosphatemia, and loss of cortical bone. We report a case of a patient who has severe osteoporosis (T-score -3.6) and initially normal PTH, treated with teriparatide for osteoporosis and after 2 months presented with severe hyperparathyroidism with severe hypercalcemia that required admission to the hospital.

Case Summary:
A 68 years old lady presented to the ER with confusion, dysarthria, anorexia, and generalized body weakness. She is on teriparatide 20 mcg s.c. daily for severe osteoporosis. Her labs showed Ca:3.58(NR:2.18-2.68), phosphate: 0.67(NR:0.8-1.6), and PTH:11.9(NR:1.3-9.3). She was admitted under closed monitoring. CT brain, stool OB, parathyroid scan, and serum and urine for paraproteins were negative. After six days of in-hospital treatment of hypercalcemia, the patient's serum Ca and PTH returned to normal. The patient was discharge home, and to be on Alendronic acid tab 70 mg daily. Clinical follow up reveals that her serum levels of calcium and parathyroid hormone are within the normal range for one year after discharge.

Conclusion:
The patient reported here had no secondary causes of hyperparathyroidism. After teriparatide treatment, she developed hyperparathyroidism which lead to hypercalcemia. After stopping teriparatide for five days, her parathyroid hormone level came back to normal. We conclude that patients should be closely monitored for symptoms of hypercalcemia during teriparatide treatment for osteoporosis.

Key Words: Teriparatide; hyperparathyroidism; hypercalcemia;

Medicine
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Adenosine induced atrial fibrillation

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CASE REPORT

Introduction:
Paroxysmal supraventricular tachycardia is a syndrome that is characterized by regular tachycardia rhythm. Most common presentations are palpitations and dizziness. It can be easily diagnosed with an ECG, which shows a narrow QRS complex and regular tachycardia. PSVT is commonly treated with carotid massage and adenosine in hemodynamically stable patients, and cardioversion in hemodynamically unstable patient.
In this case we report a patient who developed atrial fibrillation after adenosine treatment for SVT.

Case Summary:
A 28 years old gentleman presented to the ER with the complaint of palpitations of 4 hours duration for the first time. He denies any shortness of breath, chest pain, dizziness, syncope or presyncope. There was no history of alcohol, smoking or recreational drugs use. He denied any history of weight loss, diarrhea, heat intolerance or family history of sudden death. He was alert and with stable vitals except for regular tachycardia of 138. ECG was done and showed a regular narrow complex tachycardia. After failed valsalva maneuver, the patient was given adenosine 6 mg for the SVT and 2 minutes later he developed AF. The patient was admitted to the CCU and urgent echocardiogram was done for him, which was normal. The patient was given flecanide 200 mg and reverted to sinus rhythm. His CHADS-VASs score for AF stroke risk was 0. The patient was discharge after 24 hours of closed observation.

Conclusions:
The patient reported here had no secondary causes of AF. He developed AF after the administration of adenosine. After reviewing the literature, there has been few case reports with patients developing AF following the administration of adenosine. We conclude that AF is a possible life threatening complication of adenosine treatment. Therefore, patients should be monitored closely after adenosine administration.

Key Words: Adenosine; Atrial Fibrillation; Supraventricular tachycardia;

Medicine

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Linear psoriasis: a rare presentation of psoriasis

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CASE REPORT

Background:

Linear psoriasis (LPs) is an exceedingly rare clinical presentation of psoriasis. It is characterized by linear lesions along the lines of Blaschko. LPs may occur as the only manifestation of psoriasis (the isolated type) or it may coexist with nonsegmental plaques of psoriasis vulgaris (superimposed LPs). A limited number of cases have been reported in the literature.

Case summary:

A 36-year-old male presented with sudden eruption of linear red scaly plaques on his right arm and right half of the back. The patient is known to have psoriasis for five years. Past medical history was not contributory and similar or other types of psoriasis were not observed in his family. Cutaneous examination showed erythematous, scaly, raised, confluent and discrete papules and plaques localized to a linear band-like area on the right side of the back. The plaques were distributed along the lines of Blaschko, with a marked midline demarcation. Auspitz sign was positive. Histopathological examination of the skin biopsy revealed an acanthotic epidermis composed of pale keratinocytes with absence of the granular layer. Parakeratosis and microabscesses of Munro were observed in the stratum corneum. The dermis showed elongated papillae with only a thin suprapapillary plate covering the tips of these papillae.

Conclusion:

In patients with linear erythematous and scaly plaques along the lines of Blaschko, the diagnosis of LPs should be kept in mind, especially in patients with asymptomatic lesions of late onset. The main disease to be considered in the differential diagnosis of LPs is ILVEN (inflammatory linear verrucous naevus). LPs lesions usually respond more poorly to topical and systemic antipsoriatic treatment than lesions of common plaque-type psoriasis but the response is more favourable than ILVEN to the treatments.

Key Words: linear psoriasis; ilven; blaschko;

Medicine

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Endoscopic management of bariatric surgery leaks with insertion of internal drainage

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CASE REPORT

Background:
Bariatric surgery is an effective treatment for morbid obesity. Laparoscopic sleeve gastrectomy (LSG) is the most common and an effective bariatric surgical procedure. The rate of leakage at the staple-line after LSG has been reported to be between 1.5% and 5%. Management of leaks after LSG is challenging and includes surgical revision and/or drainage, percutaneous drainage of intra-abdominal collections, enteral feeding and antibiotics. Endoscopic management includes of covered self-expanding metal stents (SEMS). In patients in whom SEMS fail or are not tolerated, internal drainage is an option with deployment of pigtail drains from the intra-abdominal collection/abscess into the gastrointestinal tract. We report here our experience with the management of post LSG leaks with internal drainage with placement of double pig tail stents.

Case Summaries:
There were a total of 5 patients who were treated with internal drainage of the intra-abdominal abscess/collections secondary to leak after LSG. Three of these patients were initially managed for the leak by placement of a fully covered SEMS, but eventually needed internal drainage because of persistent leak in 2 and recurrent leak in one. Two other patients were treated for the post LSG leak with only internal drainage and no SEMS were inserted in these patients. All 5 patients had good response to the placement of internal drainage catheters and all were able to tolerate oral diet and discharged from the hospital. The internal drains were removed in all 5 patients after 40-90 days. All of the patients continue to do well with no recurrence of the leak after 3-17 months of follow up.

Conclusions:
Internal drainage is a viable option for patients with post LSG leaks who either fail to respond to SEMS, or those who present with a chronic leak. However, the sequence and choice of endoscopic esophageal stenting and/or internal drainage should be individualized according to clinical presentation.

Key Words: Bariatric Surgery; Sleeve gastrectomy; Post-operative leak;

Medicine

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Neither here nor there: intra-cardiac thrombus in transit wedged in a patent foramen ovale

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CASE REPORT

Background:

Intra-cardiac thrombus in transit (TIT) wedged in a patent foramen ovale (PFO) is a rare finding associated with impending pulmonary and/or paradoxical emboli. Surgical extraction, systemic anticoagulation, and thrombolysis are potential therapeutic approaches with no consensus on optimal treatment strategy.

Case Summary:

An 89 year-old obese woman with hypertension, hyperlipidemia, and obstructive sleep apnea presented with shortness of breath and episodic light-headedness of 2 months duration. She was found to be in atrial flutter, started on diltiazem for rate control and apixaban for anticoagulation, and scheduled for an outpatient transesophageal echocardiography (TEE)-guided cardioversion. A 1.4 cm intra-cardiac mass wedged in the PFO and protruding into the left atrium was incidentally noted on TEE, with normal biventricular systolic function and no evidence of thrombus in the left atrial appendage or significant valvular disease. Neurologic status was intact on physical exam. Cardioversion was aborted and patient admitted to the hospital for further evaluation and management. Differential diagnosis of the intra-cardiac mass included TIT versus less likely myxoma. Cardiac surgery consultation was obtained and patient was deemed a high risk surgical candidate due to age and comorbidities. Bilateral lower extremity duplex ultrasound was negative for DVT. Apixaban was switched to intravenous unfractionated heparin per thrombophilia consult recommendation. Repeat TEE after three days showed persistent mass with no change in size. Patient was subsequently discharged on weight-based low molecular weight heparin with complete resolution of mass on repeat TEE at one month, confirming the diagnosis of an intra-cardiac TIT. Neurologic exam remained intact with no evidence of embolic sequelae.

Conclusion:

Outpatient low molecular weight heparin is both effective and safe for the treatment of high surgical risk patients with a TIT wedged in the PFO.

Key Words: Thrombus in transit; Patent foramen ovale; Anticoagulation;

Medicine

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A case report of simultaneous thyroid storm and diabetic ketoacidosis

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CASE REPORT

Background:
Thyroid storm and Diabetic Ketoacidosis are metabolic emergencies that occur in uncontrolled thyrotoxicosis and diabetes mellitus respectively. it is uncommon for both to occur simultaneously. However, in the literature there are few case reports of such a presentation.

Case Summary:
A 31 year old phillipino lady presented with one day history of abdominal pain, and vomiting, 3 months history of polyuria and polydipsia and 9 months history of unintentional weight loss and palpitation. Her past medical history was negative except for hypertension. On examination, the patient looked agitated but fully conscious and oriented. She was tachycardic with a regular, collapsing pulse of 160 to 180 bpm. Her blood pressure was 140/80 mmHg and she was tachypnic but afebrile. Head and neck examination revealed exophthalmos and diffuse neck swelling. ECG showed supraventricular tachycardia, that did not improve with adenosine. Random blood glucose was 20.9 mmol/L and arterial blood gas analysis revealed severe metabolic acidosis. Urinalysis showed positive ketones. A diagnosis of diabetic ketoacidosis was made and immediately IV fluid with potassium and insulin infusion were started. The tachycardia, exophthalmos and neck swelling triggered the suspicion of thyroid storm. A provisional diagnosis of thyroid storm was made based on Burch-Wartofsky score of 55 and thyrotoxicosis was confirmed by thyroid function test. She was started on propranolol, IV hydrocortisone, propylthiouracil, and lugol's iodine. The patient was admitted to the ICU and stayed there for one day during which she improved dramatically.

Conclusion:
Diagnosis of thyroid storm and DKA simultaneously is a challenge as it is rare. However, it is a fulminant medical emergency that can result in a fatal outcome unless recognized and managed promptly.

Key Words: Thyroid storm; Diabetic Ketoacidosis; Diabetes;

Medicine

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A case of severe metabolic acidosis requiring hemodialysis in a patient on Dapagliflozin

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CASE REPORT

Background
Sodium-Glucose Cotransporter 2 (SGLT-2) inhibitor, a recent class of antihyperglycemic agents, is known to be complicated with euglycemic ketoacidosis. According to the FDA, 73 cases were reported between March 2013 and June 2015.

Case Summary:
A 43-year-old male known case of diabetes mellitus type II presented during the month of Ramadan with one-day history of shortness of breath and vomiting. He was started recently on Dapagliflozin. Drug history includes Glimepiride, Sitagliptin and insulin Glargine. He stopped insulin few days ago as his blood glucose was well controlled on oral agents. On examination, he was fully conscious and oriented but in respiratory distress. He was tachycardic with a heart rate of 115 bpm. Systemic examination was unremarkable except for mild generalized abdominal tenderness. Arterial blood gas analysis (ABG) showed severe metabolic acidosis (pH 6.9). Urinalysis showed ketones. Serum glucose was 10 mmol/L which was not as high as expected in a case of diabetic ketoacidosis (DKA). He received IV fluid with potassium replacement and was admitted to ICU where bicarbonate infusion was started. Blood tests were sent to identify a possible cause of high anion gap metabolic acidosis. Serum lactate was normal and toxicology screen was negative. He did not improve on bicarbonate infusion. ABG showed persistent acidosis (pH 7.1). Possible causes of metabolic acidosis were excluded and dapagliflozin associated euglycemic DKA was diagnosed. The patient underwent hemodialysis after assessment by a nephrologist. He improved dramatically and ABG showed a pH of 7.3. He was maintained on IV fluid as per DKA protocol. His condition completely recovered and he was discharged from ICU on
day 3.

Conclusion:
Patients receiving SGLT2 inhibitor must be promptly evaluated for ketoacidosis if they present with nausea or vomiting.

Key Words: Dapagliflozin; SGLT2 inhibitor; Euglycemic Diabetic Ketoacidosis;

Microbiology and Immunology

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Intestinal schistosomiasis - an incidental finding in a life threatening scenario

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CASE REPORT

Background

Schistosomiasis is a water-borne infection caused by trematode helminths called schistosomes. Intestinal schistosomiasis is a chronic form of the debilitating infection, the severity of symptoms varying with the schistosomal species involved and the pathological changes induced by the deposition of the ova.

Case summary:

This case discusses a 43 year old Philippino lady admitted with massive lower gastrointestinal bleed and diagnosed with extensive diverticular disease of the colon on colonoscopy. Resuscitation and transfusion with packed RBCs on several episodes of bleeding failed. The patient later underwent total colectomy with end ileostomy. Histopathology examination of colon biopsy revealed diverticulosis and the presence of numerous schistosome ova. The morphology of the ova pointed to infection with Schistosoma (S)japonicum. Ziehl-Neelsen stain for the ova was positive. PCR to detect schistosome DNA was not available. Direct microscopy of repeated urine and stool samples were negative. Indirect haemagglutination test for schistosomal antibodies was also negative. S. japonicum is known to produce a large number of eggs, about 3000 eggs/day and as a result the inflammatory changes in the intestine produced by S. japonicum are often severe. The diverticulae could probably be due to the long standing pressure effects of the ova. The patient improved post operatively, with no further bleed. She was also treated with praziquantel at discharge.

Conclusions

Schistosomiasis due to S.japonicum is endemic in the Philippines. Intestinal schistosomiasis is one of the most widespread parasitic infections in tropical and subtropical countries, with potentially serious complications which are preventable, if diagnosed early. In endemic regions with high prevalence of the disease, active screening for schistosome ova with mass deworming and health education for the community are essential to control the infection and to prevent complications.

Key Words: Schistosoma; Diverticulosis; Ova;

Microbiology and Immunology

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Newly discovered rope worm infection in Kuwait: A case report

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CASE REPORT

Background
Rope worms are anaerobic worms that were reported in 2009 during the cleansing of colon by coffee enemas. They are rope-like meter-long intestinal parasites and look like twisted fibers of rope attaches to the intestines with suction cups/heads that develop from suction bubbles, twists like a corkscrew and may obstruct the intestine. The worm may cause non-specific symptoms, including weight gain or loss, food allergies, common colds, coughing, back pain, rashes, headaches, indigestion, hair loss. They produce slime with a distinct odor.

Case summary
A 57 year old Egyptian reported to the outpatient clinic of Infectious Diseases Hospital, Kuwait on 16th September 2017, complaining of abdominal pain, bloating, gases, indigestion, and constipation/diarrhea for the last two years. He is unable to pass the stool without water rectal enema. He brought the stool with a worm-like structure after enema and the stool sample was sent to Infectious Diseases Hospital Laboratory for ova and parasites investigation. The macroscopic examination of the stool specimen showed two feet long taenia like worm, irregular cylindrical and rope – like shape, slime in nature with off – putting odor. However, the microscopy of the worm does not show any taenia - like morphological features. All the characters of this worm are very similar to rope worm reported earlier. The patient was treated by physians from the area clinic with multiple courses of albendazol with no improvement of symptoms and passage of the worm.

Conclusion
We report a case of rope-worm infection in a 57 year old Egyptian who presented with vague abdominal symptoms of pain, bloating, gases, indigestion, constipation/diarrhea and obstruction of the intestine for the last two years. The microscopy of the worm showed characteristics of a rope-worm. The symptoms did not improve after several courses of albendazole.

Key Words: Rope worm; Enema; Obstruction;

Oncology

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Case report of mucoepidermoid carcinoma arising in an intraparotid lymph node

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CASE REPORT

Background:
Salivary gland tumors occasionally arise in heterotopic salivary tissue outside the major and minor salivary glands. The salivary gland neoplasm that most commonly originates in ectopic salivary tissue is the Warthin's tumor, which usually arises within intraparotid lymph nodes.

Case Summary:
This a 41- year- old male patient presented to the otolaryngology clinic complaining of a mass in the left side of the neck. The patient had first noted the lesion 6 months previously. On physical examination, a 1.5X 2 cm rubbery, nontender mass was found over the angle of the mandible. No facial nerve dysfunction was present. No other nodules or masses were palpated. Contrast enhanced CT neck revealed well defined reniform mass lesion partially exophytic from the superior pole of the superficial lobe of the left parotid gland measuring 15x18x28 mm with moderate homogenous post contrast enhancement suggestive of pathologic intraparotid lymph node. No other parotid masses could be detected with preserved related fat planes. Fine needle aspiration cytology (FNAC) was performed and suggested Warthin tumor and elective left superficial parotidectomy was advised and performed. In the surgical resection specimen the tumor was diagnosed as low-grade mucoepidermoid carcinoma (MEC), arising from ectopic salivary tissue within an intraparotid lymph node. The patient was noncompliant and planned for follow-up appointment to confirm he is disease-free.

Conclusion:
In the current report, we describe a well-differentiated mucoepidermoid carcinoma that was confined to, and apparently arose within, an intraparotid lymph node. This appears to be a rare occurrence; we have found only two other documented cases of a mucoepidermoid carcinoma that apparently arose within an intraparotid lymph node.

Key Words: Ecotopic salivary tissue; Mucoepidermoid carcinoma; Intraparotid lymph nodes;

Pathology

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Bone marrow biopsy under unique circumstances

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CASE REPORT

Back ground:

Bone marrow (BM) aspiration and biopsy are useful diagnostic tools. Many times the diagnosis is only made by BM examination. It is an invasive procedure, so it is always done as the last option in diagnosis. BM examination shows the intramedullary hemopoiesis, cellularity as well as the blood cells maturation and differentiation. Adequate hemostastatic mechanisms are important before performing the BM biopsy. The platelet count, bleeding time, INR and APTT must be checked in some cases before taking this invasive biopsy. Protein C deficiency is a rare autosomal recessive thrombogenic disease, requiring anticoagulants to prevent serious thrombosis. Hairy cell leukemia (HCL) is a rare malignant BM disease characterized by peripheral pancytopenia including severe thrombocytopenia.

Case summary:

35 years old gentleman, a known case of protein C disease, had recurrent DVT. He was on warfarin. He presented with rapidly progressive pancytopenia. He was bridged from warfarin to enoxaprin before the BM biopsy. He was allergic to FFP and platelet transfusion. His obscure pancytopenia required urgent BM biopsy for the diagnosis. Although he had 4 abnormal parameters for hemostasis - platelets count 39x109, INR 2.5, APTT 60 (27- 38), and bleeding time 5.1(1- 4), the bone marrow examination was undertaken successfully without any complication. [picture 1- 3]. A diagnosis of HCL was made from this BM investigation.

Conclusion:

This unique case demonstrates that urgent BM examination can be performed without complications in spite of abnormal hemostatic parameters. This needs to be confirmed by further controled studies. To our understanding, this is the first case report in the literature describing BM examination done under such serious hemostastatic abnormality but without complications.

Key Words: Bone marrow; Biopsy; Bleeding;

Pathology

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Osseous metaplasia of the cervix: a rare transformation can mimic a tumor

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CASE REPORT

Background:
Osseous metaplasia (OM) is benign transformation of nonosseous soft tissue into bone. It is a well-known phenomenon in different soft tissue organs including the colon, thyroid and adrenal glands. However, it is very rare to be reported in the uterine cervix. OM of the cervix can present with different symptoms including: dyspareunia, pelvic pain, leukorrhea, menstrual irregularities, and post coital bleeding. Rarely, OM can mimic a tumor formation. In this report, a case of cervical OM is reported mimicking a cervical tumor.

Case Summary:
A 23- year old nulligravida presented with irregular vaginal bleeding for one-month duration. The patient was also complaining of a foul-smelling discharge, abdominal pain and unusual sensation of a mass in her vagina. Speculum examination revealed a foul-smelling bloody purulent discharge, tender cervix and a brownish growth located at the posterior cervical lip. A punch biopsy of the growth was performed. Histological examination of the tissue revealed multiple bone fragments with necrosis and an inflammatory exudate. Because of the unusual findings, a repeat biopsy was performed and yielded the same findings confirming the diagnosis of osseous metaplasia of the cervix.

Conclusion:
Although osseous metaplasia is a known phenomenon in different soft tissues, it is extremely rare in the uterine cervix and can mimic malignancy. Therefore, clinicians should be aware of it.

Key Words: Osseous metaplasia; Mimic; Tumor;

Pathology

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HER2 Intratumoral Heterogeneity in Breast Cancer: Instructive Case

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CASE REPORT

Background:
Accurate determination of human epidermal growth factor receptor 2 (HER2) status in breast cancer is essential for predicting response to HER2-targeted agents, but the presence of intratumoral heterogeneity (ITH) may yield false negative results particularly on fluorescence in-situ hybridization (FISH). Genetically heterogeneous tumors show clusters of HER2-amplified cells admixed with clusters of non-amplified ones. Herein we report a case of invasive ductal carcinoma that showed ITH on immunohistochemistry (IHC) and FISH leading to discordant HER2 results between the biopsy and resection specimen.
Case Summary:
A 42-year-old woman with a breast mass underwent a needle core biopsy. The histologic diagnosis was a grade III invasive ductal carcinoma with focal mucinous features. On IHC, the majority of tumor cells showed 3+ HER2 expression, while the minor mucinous component was negative. This heterogeneous expression, however, was overlooked and was not communicated in the pathology report. A few months later the patient underwent surgery and the resection specimen revealed the same morphological features. HER2 IHC was "equivocal" and subsequent FISH testing turned out to be negative for amplification. Repeat FISH testing on a different block was carried out for verification, which came back as positive. In retrospect, and upon revision of the IHC findings in view of the morphological features, the source of the discordance in HER2 results was clarified. The HER2 status was then amended to "positive for HER2 amplification with intratumoral heterogeneity".

Conclusion:
ITH is a potential source of HER2 discordance between the core biopsy and surgical specimen, between blocks of the same tumor, and between IHC and FISH assays. A standardized approach for assessment of HER2 on both IHC and FISH is needed to avoid misinterpretation, taking into account any morphologically and immunophenotypically distinct tumor cell populations within the same
carcinoma.

Key Words: HER2; Intratumoral heterogeneity; Breast cancer;

Pathology

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Lymph node metastasis in alveolar rhabdomyosarcoma of head and neck region: A rare presentation diagnosed by fine-needle aspiration cytology and immunocytochemistry.

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CASE REPORT

Background:
Rhabdomyosarcoma (RMS) is an aggressive malignant soft tissue sarcoma that arises from primitive striated muscle cells (rhabdomyoblasts). It is the most common childhood sarcoma that occurs in the soft tissues of the head and neck, genitourinary system, and extremities. Within the head and neck region, embryonal RMS is the most common RMS, whereas alveolar and pleomorphic tumors are more common in the extremities. Alveolar RMS tends to occur in slightly older patients with a mean age of 15–20 years. Herein we present a case of metastatic alveolar RMS originating in the nasal sinus, diagnosed by FNA cytology and immunocytochemistry (ICC).

Case Summary:
A 26-yr-old man presented with complaints of left-sided nasal obstruction, headache and enlarged left submandibular lymph node of 2 months duration. FNA was performed on the left submandibular lymph node. Smears showed tumor cells arranged in clusters as well as dispersed singly with irregular lobulated nuclei having fine chromatin and small nucleoli. Cells showed moderate to abundant light blue to pink cytoplasm with fine cytoplasmic vacuolations. There was brisk mitotic activity. A few binucleated to multinucleated tumor giant cells and sprinkling of lymphocytes were noted in the background. Considering anaplastic large cell lymphoma (ALCL), melanoma and undifferentiated carcinoma in differential diagnosis, the smears/ cell block sections were stained for pan-CK, LCA, EMA, CD-30, HMB-45 and Alk1 which yielded negative results. Since alveolar RMS may also show lobulated nuclei, the sections were further stained for desmin and myogenin yielding positive results and thus confirming this diagnosis.

Conclusion:
Cytologically, the presence of multinucleated tumor giant cells, including the rosette forms, in the FNA smears should alert the cytopathologist to the possibilities of sarcoma and ALCL. FNAC aided by ICC played an important role in the diagnosis of lymph node metastasis in case of alveolar RMS.

Key Words: FNAC; Lymphnode metastasis; Aveolar rhabdomyosarcoma;

Pathology

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Langerhans cell histiocytosis in an Infant- a cytological diagnosis.

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CASE REPORT

Background:
Langerhans cell histiocytosis (LCH) is a rare, proliferative disorder with clonal expansion of dendritic cells. It occurs in 1:200,000 children, but any age group can be affected. It presents with a broad spectrum of manifestations, varying from solitary lesions to disseminated, multisystem, life-threatening disease. We present a case of an infant with extensive involvement of the skull by LCH; that was diagnosed on Fine needle aspiration cytology (FNAC).

Case summary:
A one year old male infant was brought for fine needle aspiration with a history of a localized bulge over the right mastoid region for one month which was slowly increasing in size. Radiological examination revealed an aggressive tumor with erosion of the temporal bone, external bony canal and floor of the middle cranial fossa. The possibilities on radiology were LCH or Rhabdomyosarcoma. FNAC revealed sheets of histiocytic cells admixed with eosinophils. These cells stained positive for CD 1a and S100.The patient underwent surgery 10 days later, and histopathological examination confirmed the diagnosis. The patient was planned for chemotherapy and steroids.

Conclusion:
The purpose of this paper is to enhance the understanding of the diverse clinical presentation of LCH that can easily be misdiagnosed or overlooked. It also stresses the importance of identification of this entity on cytological examination, which is an easy, non-invasive and reliable procedure. It is important to make an early diagnosis, as the time from presentation to diagnosis is of prognostic importance.

Key Words: Langerhans cell histiocytosis; Fine needle aspiration cytology; Immunohistochemistry

Pediatrics

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Infantile Systemic Hyalinosis: A case report from Kuwait

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CASE REPORT

Background:
Infantile systemic hyalinosis (ISH) is a rare autosomal recessive disorder characterized by widespread deposition of hyaline material in many tissues leading to hyperpigmented skin over bony prominences, painful skin bumps, gingival hypertrophy with progressive joint contractures and bone abnormalities that impair movement. Most affected individuals develop protein-losing enteropathy results in severe diarrhea, failure to thrive, and cachexia. The symptoms and signs of ISH are present at birth or develop within the first few months of life, mental development is typically normal; life span is typically short due to chronic diarrhea and recurrent infections. We are reporting a Kuwaiti patient with ISH to raise the awareness of this rare disease among general pediatricians.

Case Summary:
A baby boy, who is the first offspring to consanguineous Kuwaiti parents, presented at age of two months with stiff hyperpigmented painful joints and muscle wasting. Latter on he developed chronic diarrhea and failure to thrive. Investigations showed that he has protein loosing enteropathy leading to malabsorption. He had small mouth with progressive severe gum hypertrophy. He became TPN (Total Parental Nutrition) dependent but continued to be marasmic. He was repeatedly admitted for recurrent infections and malnutrition. In spite of his disease he was alert with reasonably normal mental development. Genetic study revealed mutation in the CMG2 gene confirming the diagnosis of ISH. The patient died with septicemia at three years of age.

Conclusion:
ISH is a rare fatal genetic disease that is being more reported in Arab countries known to have high rate of consanguinity such as Saudi Arabia and Kuwait. With the recent advances in molecular genetic testing, knowledge regarding ISH will enable general pediatrician to recognize and diagnose such a rare disease and so council the parents more efficiently.

Key Words: Infantile systemic hyalinosis; protein loosing enteropathy; CMG2

Pediatrics

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Zellweger Syndrome: When to suspect?

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CASE REPORT

Background:

Zellweger syndrome (ZWS, cerebrohepatorenal syndrome) is a rare autosomal-recessive disorder characterized by the absence of functional peroxisomes resulting in impairment of beta-oxidation of very long chain fatty acids (VLCFAs). In the neonatal period, the triad of distinctive facial features, pronounced hypotonia, and hepatorenal dysfunction is the typical ZWS presentation. ZWS is a fatal inherited inborn error of metabolism that should be included in the differential diagnosis of infantile hypotonia and dysmorphism.

Case Summary:
A male newborn product of full term CS (due to fetal bradycardia) to consanguineous parents was admitted at age of 20 hours to NICU with hypoactivity, hypothermia and cyanosis. The baby was found to have dysmorphic facial features in form of wide anterior fontanel with prominent forehead, low set ears, hypoplasia of the orbital area, small mandible, high arched palate, short neck, unilateral simean creses, and bilateral talipes equinovarus. The patient also had severe generalized hypotonia, poor suck, and jaundice. Liver was firm enlarged 3 cm below costal margin. There was an ejection systolic murmur all over the pericardium. Liver enzymes markedly elevated. Echo revealed ASD. Plasma VLCFA was clearly elevated concentration of C26:0 and elevated ratio C26:0/ C22:0 and C24:0/ C22:0 ratio. The baby continued to have persistent hypotonia and developed failure to thrive and UTI.

Conclusion:
This is the first reported case of ZWS from Kuwait. Recognition and early diagnosis of this syndrome is important since genetic counseling and prenatal diagnosis are crucial. This case report may raise the awareness of the symptoms, and signs of such a rare disease emphasizing the importance of genetic counseling and family support.

Key Words: Zellweger syndrome; Cerebro-hepato-renal syndrome; Peroxisomal disorders;

Pediatrics

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Infantile Botulism: A case report highlighting diagnosis and treatment

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CASE REPORT

Background:

Infantile botulism (IB) is a life-threatening condition caused by neurotoxins produced by the bacteria Clostridium botulinum (CB). Ingested CB spores (found in dirt, dust, and honey) colonize the large intestine and produce botulinum enteric neurotoxin. Patients with IB present with constipation, generalized hypotonia with cranial nerves involvement, hypoventilation and respiratory failure. We report a case of infantile botulism resulted from ingestion of infected honey to raise awareness of the symptoms and signs of this disease and to emphasize that a high degree of clinical suspicion is needed to make prompt diagnosis and start early management.

Case Summary:

A 9 month old indian boy presented to ER with an attack of hypoventilation, floppiness, impaired level of consciousness, and increased salivation. He was intubated and shifted to PICUB for mechanical ventilation. Mother gave history of chronic constipation of five month duration. He was receiving natural mountain honey as a home remedy treatment of cough. The patient was treated as a case of complex partial seizure but the clinical findings of ptosis with dilated reactive pupils, bilateral symmetrical facial nerve palsy, generalized hypotonia, and lack of movement in addition to the quick recovery after stopping the honey intake alerted physicion to the diagnosis of IB. Stool culture was negative to CB. Immunoassays for the toxin and PCR were not done. Patient was discharged within a week with no neurological sequela.

Conclusion:

IB is life threatening but preventable disease. It should be considered in any infant presenting with acute flaccid paralysis associated with hypoventilation. Public health measures such as parents' education to avoid feeding honey to infants in the first year of life should be stressed on. Botulism Immunoglobin (BIG-IV or Baby BIG) is available in Kuwait and can be lifesaving if the disease is promptly diagnosed.

Key Words: Clostridium botulinum; Infant Botulism; Botulism Immune Globulin (BIG);

Pediatrics

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MHC Class II Deficiency: A Report of two Cases from Al-Adan Hospital in Kuwait

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CASE REPORT

Background:

MHC class II deficiency is a rare autosomal recessive disease characterized by the absence of major histocompatibility complex (MHC) class II leading to a form of severe combined immunodeficiency (SCID). This condition leads to severe CD4+ T-cell dysfunction and thus recurrent bacterial, viral and protozoal infections. Approximately less than 200 patients with this disease have been reported worldwide. It was found that MHC class II deficiency accounts for 19 % of combined immune deficiency cases in the National Primary Immunodeficiency Disorders Registry in Kuwait. We hereby reporting our experience with two patients diagnosed to have MHC class II deficiency syndrome emphasizing the importance of considering this disease in the differential diagnosis of patients who are suspected to have immune deficiency with an initial benign clinical course.

Case Summary:
Case1:
A one year old Kuwaiti baby girl presented with failure to thrive and history of mild diarrhoea and recurrent respiratory infections. She is product of FTND with birth weight 3.5 kg, first baby to a young consanguineous couples. immunological investigations revealed very low serum immunoglobulins, CD4 dysfunction, and no expression of MHC class II.
Case 2:
A one and half year old Kuwaiti baby boy product of LCS to a consanguineous parents presented with chronic diarrhoea and failure to thrive. He is known to have wheezy chest with recurrent chest infection. Investigations revealed low immunoglobulins, normal CD3, low CD4, and MHC I normal but MHCII not expressed.

Conclusion:
MHC class II deficiency, though worldwide rare, is being increasingly reported in Kuwait. Advances in immunological laboratory evaluation and genetic mutation confirmation improve the knowledge about phenotypic clinical presentation of this disease and helps the general paediatrician to have high index of suspicion for these patients leading to an early diagnosis and better management with a longer life expectancy.

Key Words: MHC class II deficiency; Bare lymphocyte type II syndrome; Severe combined immunodeficiency (SCID);

Pharmacy

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Life Threatening Hypersensitivity Reaction to Trastuzumab Infusion in Breast Cancer Patients: A Case Report

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CASE REPORT

Background:

Trastuzumab is a humanized monoclonal antibody that targets the human epidermal growth factor receptor-2 (HER-2). Around 15-30% of breast cancer patients show overexpression of HER-2.Trastuzumab becomes a main therapy in neoadjuvant/adjuvant protocols of breast cancer management.Trastuzumab infusion precipitates an immediate hypersensitivity reaction in 0.6-5% of patients due to the release of cytokines. Trastuzumab infusion-related hypersensitivity symptoms include fever, dyspnea, chills and hypotension.

Case Summary:

A 47 year old female was diagnosed with breast cancer stage III. The tumour biopsy revealed invasive ductal carcinoma [hormonal negative and showed HER-2
overexpression].

Management Plan

Neoadjuvant chemotherapy

4 cycles of Doxorubicin/Cyclophosphamide every 2 weeks

Then 12 cycles of weekly Paclitaxel+[Trastuzumab+Pertuzumab] every 3weeks

Hypersensitivity reaction

Four cycles of Doxorubicin/Cyclophosphamide were completed with excellent tolerance and good clinical response.

During the first cycle of Paclitaxel+Trastuzumab+Pertuzumab, Pertuzumab was administered, and 20 minutes later Trastuzumab was started. After receiving the first 50ml, the patient had sudden tachycardia that reached 260bpm, rigors, shivering and cold extremities. Vital signs couldn't be recorded

Conclusion:

IV hydrocortisone 300mg+chlorphenamine 10mg+paracetamol 1g and oxygen 5L/min were administered. Vital signs were recorded HR 200bpm, SpO 80%, BP 100/70mmHg, Temp 36.4 deg C. The ICU team administered IV pethidine 50mg and another 100mg of IV hydrocortisone. Vitals were still unstable. A third dose of IV hydrocortisone 200mg was administered with normal saline 50ml/hr. The patient became vitally stable and admitted in the ICU under observation.

Plan: to continue neoadjuvant chemo Paclitaxel and Pertuzumab only

Key Words: Oncology; Clinical pharmacy; Herceptin hypersensitivity;

Public Health Ethics& Occupational Health

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HEMAYA Health WISE Audit: Perception of Healthcare Professionals' about their Occupational Safety and Health and the Current Standards in the National Accreditation for Hospitals in Kuwait

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CASE REPORT

Background:

Hemaya HealthWISE is a human right advocacy project focusing on healthcare professionals' occupational safety and health. It is a collaborative initiative between national NGO's and international UN agencies under the patronage of the Higher Council of Planning and Development in Kuwait.

Case Summary:

The first stage of this project collected 363 comments from healthcare professionals' regarding own health, safety and wellbeing during a 2 days' workshop in 2017 at Amiri Hospital. The comments were classified according to the (8) "Work Improvement in Health Services" categories of the International Labour Organization and the World Health Organization. OSH as it relates to recruitment, institutional support, management, retention (24%); Biological hazards and infection control (19%); Selecting, storing and managing equipment and supplies (18.7%); Controlling occupational hazards and improving workplace safety (15.4%); Tackling discrimination, harassment and violence at the workplace (10%); Musculoskeletal hazards and ergonomic solutions (6.9%); Working time and family- friendly measures (4.7%). No comments or concerns expressed 'towards a green and healthy workplace'. The second stage of the audit focused on the (OSH) requirements in the accreditation standards for hospitals in Kuwait. A total of 115 explicit and implicit standards were identified: Leadership: (10); Human Resources (9); Environment (25); Rehabilitation Services (4); Mental Health Services (7); Medical Care (4); Obstetrics & Gynecology (4); Emergency Services (7); Specialized /Intensive Care (3); Surgical Care (5); Laboratory Services (5); Addiction Treatment Services (8); Patient Care Generic (4); Diagnostic Imaging Services (8); Cancer Care Services (5); Pharmacy Services (7); Patient Safety Required Areas (3); Information Management (1).

Conclusion:

Hemaya HealthWISE is committed to a proactive approach to occupational safety and health focusing on the professionals and the employers.

Key Words: Healthcare Providers; Occupational Safety and Health; Accreditation;

Surgery

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Acinic cell carcinoma primarily arising in ectopic salivary gland tissue within a peri-parotid lymph node: a case report

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CASE REPORT

Background:

Acinic cell carcinoma (ACC) is a low-grade malignant tumor that is epithelial in origin. Although ACC is slow growing, it has been re-classified as a malignant tumor due to its tendencies to recur and metastasize. The most common presentation is a slow growing mass with mild to no pain. Fine needle aspiration biopsy confirms the diagnosis, and it is treated by surgical excision. ACCs rarely arise primarily in the peri-parotid lymph nodes (LN). There are only a few cases reported in the literature of this presentation.

Case summary:

A 38 year old Indian lady presented with upper neck swelling for 6 months. Physical examination revealed a mass over the left parotid gland. Ultrasound revealed an intraparanchymal parotid lesion that appeared benign in nature. Guided FNAC showed an acinar cell rich lesion. MRI confirmed a suspicious lesion. The patient underwent a left superficial parotidectomy. Histopathology demonstrated features of ACC within the periparotid LN, and the tumor has invaded through and was seen lying outside the capsule in one focus. Final histopathology assessment of the superficial lobe of the parotid did not show any features of ACC. It was difficult to determine whether the tumor had arisen from heterotopic salivary gland tissue in the LN or was a metastasis from the parotid gland. Therefore, she underwent a left total parotidectomy a month later. On histopathology, the entire specimen of the left parotid gland did not reveal any parotid ACC. Hence, it was concluded that it was highly likely that the previously excised ACC within the peri-parotid LN is a primary neoplasm arising from ectopic salivary tissue within the LN.

Conclusions:

ACC primarily arising in ectopic parotid gland tissue within the peri-parotid LNs is a very rare presentation that physicians should be aware of. This type of lesion should be managed aggressively, despite of its slow-growing nature, due to its malignant tendencies demonstrated by distant metastasis and recurrence.

Key Words: Acinic Cell Carcinoma; Ectopic parotid; Otolaryngology ;

Surgery

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MPNST ex. diffuse neurofibroma arising in the parotid gland of a patient with unknown history of NF1

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CASE REPORT

Background:

Malignant peripheral nerve sheath tumor (MPNST) is extremely rare in the parotid gland, and in most cases, the prognosis is grim. It usually develops in the setting of Neurofibromatosis type-1 (NF1), but can also develop sporadically. Herein, we report a rare case of MPNST of the parotid gland, in a patient with no previous history of NF1.

Case summary:

A 45 years old patient presented with a non-tender right parotid swelling of one-year duration. A sudden increase in the size of the parotid mass over the past two months alerted the surgeon to proceed to investigate the nature of the mass and the etiology of the sudden change in size. The patient's initial investigations, which included radiological-imaging studies of the swelling, were consistent with a benign pleomorphic adenoma of the parotid gland. FNA cytology was non-diagnostic due to sampling error of intra-parotid lymph node. However, during the surgery the dissection was difficult and the tumor appeared adherent to the surrounding tissue, which lead to a total parotidectomy, in piecemeal!

The histopathology revealed morphologic features of diffuse neurofibroma with focal areas of MPNST. The tumor has an infiltrative growth pattern, invading into and around salivary lobules and adjacent soft tissue structures. Positive S100 staining further support the neural origin of neoplasm.

The patient was also diagnosed with NF1 based on clinicopathologic correlation with a referral for confirmatory genetic testing. The patient underwent radiotherapy to continue his treatment following the resection of the tumor.

Conclusions:

We would like to aware clinicians that the diagnosis of MPNST should prompt investigations for NF1, which has important clinical and genetic implications for the patient and family. Repeat FNA cytology under image guidance and/or intraoperative frozen section consultation can help in further guiding clinical management of salivary gland tumors.

Key Words: Malignant peripheral nerve sheath tumor; Parotid gland tumour; Neurofibromatosis type 1;

Surgery

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Foreign body induced appendicitis

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CASE REPORT

Background:

Foreign body ingestion is very common among specific groups, especially children; however, appendicitis caused by foreign body is rare.

Case summary:

40 year old female presented with abdominal pain in the right lower quadrant of 10 days duration after accidentally ingesting a drilling bit during dental cleansing. She had right iliac fossa tenderness and rebound on physical examination. The X-ray showed a pointed long metal object in the right lower quadrant. A contrast-enhanced computed tomography scan of the abdomen revealed a pointed metal object in the pelvis inconclusive whether its intraluminal or extraluminal. Diagnostic laprascopy showed an inflamed appendix with tip of the metal object perforating it; so appendectomy was carried out. Histopathology showed an inflamed appendix. The patient recovered well, symptoms subsided during follow-up in surgical clinic.

Conclusion:

Foreign bodies that cause appendicitis are rare; however they may become lodged at any site of the gastrointestinal tract and cause inflammation, schema or perforation. This is a bizzar and one of a few cases that demonstrate a foreign body (drilling bit) induced appendicitis.

Key Words: Appendix; Foreign body; Drilling bit;

Surgery

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Gastrointestinal Stromal Tumor (GIST) present as a cystic epigastric mass: a case report.

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CASE REPORT

Background:

Case summary:
57 year old male presented with abdominal pain and mass in the epigastric area on physical examination. He had an abdominal ultrasound that showed an abdominal cystic lesion in the left upper quadrant 5x7 cm in size. A contrast-enhanced computed tomography scan of the abdomen revealed same finding with uncertain origin. MRCP and endoscopic ultrasound showed a cystic mass originating from the pancrease with possible malignancy. Fine needle aspiration showed gastrointestinal stromal tumor. The laparotomy demonstrated a pedunclated mass 8cm, arising from the posterior wall of the gastric body and resection of the mass was performed. Immunohistochemical study showed GIST grade 1, spindle cells and positive CD117 and CD34. The patient recovered well and no recurrence of the tumor was found in the follow-up.

Conclusion:
Gastrointestinal stromal tumors are commonly presented as a solid lesion and cystic appearance is rare and can be misdiagnosed as pancreatic psuodcyst or liver simple cyst. This case if one of the few case reports that demonstrate a GIST as cystic lesion.

Key Words: Gastrointestinal Stromal Tumors; Cystic mass; c-kit;

Urology

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Selective Embolization for Upper Tract Urothelial Carcinoma: A Case Report

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CASE REPORT

Background

Urothelial tumors of the renal pelvis are relatively rare, Renal transitional cell carcinoma (TCC), or renal urothelial carcinoma (UC), is a malignant tumor arising from the transitional (urothelial) epithelial cells lining the urinary tract from the renal calyces to the ureteral orifice, it accounts for approximately 10% of all renal tumors. It's a disease entity that has not been as extensively studied and reviewed as carcinoma of the bladder. 5% of all urothelial neoplasms occur in the kidneys and ureters, the gold standard of treatment for patients with upper tract urothelial neoplasms is radical nephroureterectomy with removal of a cuff of urinary bladder. However, what if we have a patient who is not fit for any surgical intervention? In this report, we present a case of recurrent haematuria caused by invasive upper tract urothelial carcinoma in a non-operative patient which was treated with renal embolization.

Case summary:
61-year-old male patient with multiple co-morbidity presented with painless frank hematuria, physical examination was unremarkable except for mildly enlarge prostate in digital rectal examination, Computed Tomography Urography, Magnetic Resonance urography, cystoscopy, right retrograde pyelography and cytology done, revealed right kidney high grade urothilial carcinoma. Because the patient was not fit for surgery, he underwent selective right renal angiography then super selective embolization of the upper pole segmental artery using microcoils, Post-embolization course was uneventful (no hematuria, no fever or pain).

Conclusion
Therapeutic renal artery embolization may be of value in controlling hematuria. And we can use it to delay the surgical intervention or symptomatic relief or as a palliative treatment.

Key Words: Upper tract urothelial carcinoma; Selective embolization; Hematuria;

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Reduction of Multiple Sclerosis Burden with specialised multiple sclerosis clinic

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Introduction:
Relapses are a common feature of relapsing-remitting multiple sclerosis (RRMS). Relapses are associated with high healthcare costs due to the use of corticosteroid injections and plasmapheresis and utilization of inpatient or emergency services. MS specialists prescribe the correct disease modifying therapy (DMT), potentially reducing the number of relapses, and hence, saving healthcare costs and disability burden. Our study aims to identify the impact of the establishment of a specialized MS clinic on the rate of relapses, Expanded Disability Status Scale (EDSS), and escalation therapy.

Methods:
A cross-sectional study investigated the rate of admission due to MS relapse in Ibn Sina Hospital.
The rate of admission due to relapses three years prior and three years after establishing the MS clinic was quantified from admission logbooks. Each patient's sociodemographic data (gender, nationality, age, and age of diagnosis), latest EDSS status, and treatment plan, was attained from Ibn Sina's online filing system.

Results:
We identified 1,246 patients with RRMS to our study, most of whom are females 867 (69.6%) with a mean age at diagnosis 26.54 ± 8.58. The mean admission rate due to MS relapse was significantly reduced from 24.54 ± 7.48 to 2.92±4.26, P<0.004 after establishing the MS clinic. Most patients (61%) had escalated therapy (mean duration till escalation: 7.4 years). MS specialists prescribed second line DMT for 600 patients (50.1%). Escalation therapy was significantly higher in patients who were seen by an MS specialist versus those who were seen by a general neurologist (66.6% vs 33.4%, P<0.0. Mean EDSS at latest visit to MS clinic was less than 3 in 1039 (83.3%), from 3-4 in 59 (4.7%) and more than 4 in in 148 (12.7%).
Conclusions:
Optimal therapy decisions for MS patients via a specialized MS clinic are associated with a significant decrease in relapse rate, disability, and hence, the economic burden of multiple sclerosis.

Key Words: Multiple sclerosis; Burden; MS clinic;

Funding Agency: None

**** Refers to presenting author where indicated***

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