Under the Patronage of the President of Kuwait University

16-18 March 2021

Abstract Book

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Organizing Committee

- Prof. Eiman Mokaddas, Vice Dean Research & Postgraduate Studies
- Prof. Syed Aljunid, Chairperson, Health Economics, Policy and Management, (FOPH)
- Prof. Kusum Kapila, Pathology
- Prof. Yunus Luqmani, Pharm Chem, FOP
- Dr. Mona Al-Ahmad, Microbiology
- Dr. Muddanna Rao, Anatomy
- Dr. Aisha Al-Jarallah, Biochemistry
- Dr. Ali Ziyab, Community Medicine
- Dr. Willias Masocha, Pharmacology & Therapeutics, FOP
- Dr. Jehad Al-Harmi, Obse & Gyne
- Dr. Laila Qadan, Medicine
- Dr. Fatma Khalil Ali, Medicine
- Dr. Issa Loutfi, Nuclear Medicine
- Dr. Maamoun Al-Aynati, Pathology
- Dr. Majeda Hammoud, Pediatrics
- Dr. Andreas Henkel, Physiology
- Dr. Mohammad Jamal, Surgery
- Dr. Leila Vali, MLS, FOAH
- Dr. Mohammad Ali, Diagnostics Sciences, FOD
- Dr. Janvier Gansana, Dept of Environmental & Occupational Health, FOPH
- Mr. Adel Mohahamed Al-Rebab, Administrative Manager
- Mr. Hussein Al-Tabtabaei, Acting Chairman, Dept of Finance

Conference Program

Inaugural Ceremony: Tuesday, 16th March 2021 **MS Teams Virtual Meeting Link: http://bit.ly/HSCPosterConference2021** **Moderator: Dr. Mona Ahmad**	
3:00 PM	***National Anthem, Recitation of Holy Quran***
3:05 PM	***Welcome Address & Opening of Poster Conference*** *Acting Vice-Dean for Research & Postgraduate Studies, Faculty of Medicine*
3:10 PM	***Virtual Opening of E- Poster Conference & e-poster viewing (ID 1-50)*** *President, Vice President for Research, HSC Vice President, Assistant Vice President for Research, HSC Deans and Vice-Deans, All Participants*
3:55 PM	***Introduction of Keynote Speaker: Professor Syed Aljunid*** *Chairman of Organizing Committee*
4:00 PM	***Keynote Lecture:* "Healthy Diets in the 21st Century: What are we talking about?"** **Prof. Carlos Augusto Monteiro** *Department of Nutrition, School of Public Health* *University of Sao Paulo, Brazil*
5.00 PM	***Announcement of Awards by Chief Judge***
5:30 – 6:15 PM	***Oral Presentation: Day 1*** *Oral Presenters : 15 minutes per each winner* *Oral -1 Best Young Researcher- Basic; Oral 2: Best Young Researcher- Clinical; Oral 3: Best Case Report for Young researcher*
17th March 2021	
4:00 – 5:00 PM	***E-poster viewing (ID 51-120)***
5:00 – 6:00 PM	***Oral Presentation: Day 2*** *15 minutes per each Oral Presenter winner* *Oral 4- PhD; Oral 5- Master's Program (MSc); Oral 6- Medical Resident*
18th March 2021	
4:00 – 5:00 PM	***E-poster viewing (ID 121 -187)***
5:00 – 6:00 PM	*Oral Presentation: Day 3* *15 minutes per each Oral Presenter winner* *Oral 7- Undergraduate; Oral 8- Undergraduate ; Oral 9- Undergraduate*
6:00 PM	***Vote of Thanks: Prof. Syed Aljunid***

Total Poster Presentations: 183

Original Research Posters: 151

Case Report Posters: 32

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

Photograph of Organizing Committee

Vice Dean for Research & Postgraduate Studies, FOM

 *Prof. Syed Al Junid, Chairperson Health Economics, Policy & Managment*	 *Prof Kusum Kapila, Pathology*
 *Prof. Yunus Luqmani, Pharmaceutical Chemistry*	Dr. Mona Al-Ahmad, Microbiology
 *Dr. Mudanna Rao, Anatomy*	 *Dr. Aisha Al-Jarallah, Biochemistry*
 Dr. Ali Ziyab, Community Medicine	Dr. Willias Masocha, Pharmacology & Therapeutics, FOP
Dr. Jehad Al-Harmi, Obse & Gyne	*Dr. Laila Qadan, Medicine*
Dr. Fatma Khalil Ali, Medicine	*Dr. Issa Loutfi, Nuclear Medicine*
Dr. Maamoun Al-Aynati, Pathology	*Dr. Majeda Hammoud, Pediatrics*
 *Dr. Mohammad Jamal, Surgery*	*Dr. Mohammad Ali, Diagnostics Sciences, FOD*

Dr. Janvier Gansana, Dept of Environmental & Occupational Health, FOPH

Mr. Adel Mohahamed Al-Rebab, Administrative Manager

Mr. Hussain Al-Tabtabaei
Acting Chairman, Finance & Purchasing

Centre for Research Support & Conferences

Dr. Nada Madi, Director

Ms. Teena Sadan
Senior Technician

Ms. Leya Sara Jacob
Senior Computer Engineer

Mrs. Rania Al-Mawlawi
Administrative Coordinator

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

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 23 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 Professor Carlos Augusto Monteiro from Department of Nutrition, School of Public Health, University of Sao Paulo, Brazil. Professor Carlos's keynote address titled "Healthy Diets in the 21st Century: What are we talking about?" promises to be an exciting way to start the poster conference. This year we have 187 poster abstracts and I have no doubt that the 25th HSC Poster Conference will be a great success. I thank Kuwait University for the continuing support and sponsorship of the Poster Conference and Prof. Carlos Augusto Monteiro 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 Eiman Mokadass
Vice-Dean for Research & Postgraduate Studies
Faculty of Medicine

Message from the Chairperson; 25th HSC Conference Committee

On behalf of the Organizing Committee of the 25th Health Science Center Poster Conference I would like to welcome all participants to this scientific conference. From its inception the Poster Conference became a forum for research networking, exchanging ideas, establishing collaborations and communicating scientific advancement. Started as a Poster Day, to meet the need for sharing information among basic and clinical scientists, residents, graduates and undergraduate students, the Poster Conference progressed to become an important venue for presentation of health-related research projects conducted in Kuwait and the Region. The past keynote speakers have included several Nobel Laureates, prominent academicians, scientists and clinicians from around the world speaking on a diverse range of subjects. This year we are honored to have Professor Carlos Augusto Monteiro from Department of Nutrition, School of Public Health, University of Sao Paulo, Brazil. Professor Carlos's keynote address titled "Healthy Diets in the 21st Century: What are we talking about?" promises to be an exciting way to start the poster conference. This topic is timely and highly relevant since most countries in the regions are facing high burden of chronic diseases related to poor diets. We look forward to the continuing enthusiastic participation of researchers from the faculties of the Health Sciences Center and others of Kuwait University as well as other institutions and hospital departments in Kuwait and abroad.

I believe that the 25th Health Science Center Poster Conference will build upon the successes of the previous meetings. I invite you all to join in making this year's poster conference a memorable one.

Prof. Syed Aljunid
Chairperson of 25th HSC Poster Conference

Keynote Speaker

Prof. Carlos Augusto Monteiro
Department of Nutrition, School of Public Health
University of Sao Paulo, Brazil

Carlos Monteiro, MD, PhD, is a Professor of Nutrition and Public Health at the School of Public Health, University of Sao Paulo, Brazil. He is the Head of the University of Sao Paulo Center for Epidemiological Studies in Health and Nutrition. His research lines include methods in population nutritional and food intake assessment, secular trends, biological, socioeconomic determinants of nutritional deficiencies, obesity, other nutrition-related chronic diseases, food processing in the food system and human health, food & nutrition programmes and policies evaluation. On these subjects, he has published more than 200 journal articles that had more than 10,000 citations in the Web of Science. He has served on numerous national and international nutrition expert panels and committees. At present, Professor Monteiro is a member of the WHO Nutrition Expert Advisory Group. In 2010, he received the PAHO Abraham Horwitz Award for Excellence in Leadership in Inter-American Health. In 2018, he was included in the Clarivate Analytics Global Highly Cited Researchers List.

Keynote Abstract

Healthy Diets in the 21st Century: What are we talking about?[1]

Carlos A. Monteiro[2]

Conventionally, healthy diets have been defined as those fulfilling human nutrients requirements and by this assuring normal function of human bodies, including growth and development, and minimizing the incidence of diseases. But in the age in which we all live now, where 1) the most widespread and increasing form of malnutrition – obesity – rather than linked to specific nutrients is caused by wholly obesogenic dietary patterns; 2) food processing main role is no longer increase duration of foods but rather to extract from a few of them cheap ingredients used with flavours, colorants and other cosmetic additives in the formulation of culturally void, energy-dense, hyper-palatable, aggressively marketed, habit forming, highly profitable ultra-processed food and drink products; and 3) an increasing globalized food system undermines genuine, diversified, long established dietary patterns, enlarges inequities and puts in danger natural resources and biodiversity, defining healthy diets based only on the fulfilment of nutrients requirements and limiting their aims to physical health and the prevention of specific diseases is too narrow. Healthy diets now should be seen as those associated with dietary patterns able to prevent all forms of malnutrition, to promote physical, mental and social dimensions of health, to reduce inequities and to preserve natural resources and protect biodiversity. In a phrase, healthy diets must nourish people, populations and the planet. All the evidence indicates that healthy diets in the twenty-first century are those based on a variety of whole or minimally processed foods, mostly plants, plus small amounts of processed culinary ingredients and of processed foods, all produced by social and environmental sustainable food systems, and freshly prepared dishes and meals made with these foods and enjoyed at regular times, in proper places and, whenever possible, in company. Increasingly produced and consumed ultra-processed food and drink products have no place in healthy diets.

[1] Abstract of a keynote lecture delivered at the 25TH HEALTH SCIENCES CENTER POSTER CONFERENCE, 10-12 March 2020, Health Sciences Auditorium, Jabriya

Kuwait University.

[2] Professor of Public Health Nutrition at the School of Public Health, University of Sao Paulo, Brazil.

Best Poster Award Winners: 24th HSC Poster Conference 2019

24th HSC Oral Presentation of Award Winners		
Poster No.	**Oral Presenter**	**Title**
Undergraduate		
96	Halimah Boloki	Investigation of Fusidic Acid Resistance Determinants in Methicillin-Resistant Staphylococcus aureus obtained in Kuwait Hospitals.
161	Amr Abdlekarim	The Prevalence of Burnout and its Associated Factors Among Surgical Specialists in Kuwait Ministry of Health Hospitals
41	Shurooq Zakariya Albaghdadi	In vitro characterization of biofilm formation in Prevotella species
Graduate MSc		
140	Fajer Al-Shamlan	Bradykinin sensitizes the cough reflex via a B2 receptor dependent activation of TRPV1 and TRPA1 channels through metabolites of cyclooxygenase and 12-lipoxygenase
2	Taiba Al-Arbeed	Anti-apoptotic and Neuroregenerative Effects of Soluble Protein Fraction of the Epidermal Secretion from the Arabian Gulf Catfish following Sciatic Nerve Crush Injury in Rats
Graduate Resident		
130	Maram Al-Wazzan	Assessment of the diagnostic impact of glioma reclassification based on the 2016 WHO integrated molecular/histological classification system
Graduate PhD		
141	Bashaier Al-Zaid	Hetero-dimerization of the Incretin Receptors
Young Researcher Clinical Sciences		
143	Afrah Aladwani	Does Regular Consumption of Beetroot Improve Chemotherapy-Induced Anaemia In Cancer Patients?
206	Ali Safar	An Unexpected Diagnosis: Multiple intra-abdominal abscesses secondary to Actinomycosis from an intrauterine contraceptive device
Young Researcher Basic Sciences		
55	Ahmad Al-Serri	An association between the common FTO gene polymorphism and obesity in Kuwaiti children: A cross-sectional study
3	Mohammed Al-Onaizi	Determining the Long-term Consequences of Type 2 Diabetes on Hippocampal Neuroinflammation and Synaptic Integrity: Implications for Alzheimer's Disease

Past Poster day Keynote Speakers and Lectures

2019

What it takes to become an academic surgeon; Prof. Sami Asfar, Professor, Department of Surgery, Faculty of Medicine, Health Sciences Centre, Kuwait University.

2018

The internal exposome – a global approach to a better understanding of human disease.
Professor Paolo Vineis, Chair in Environmental Epidemiology, Imperial College London, UK

2017

Vascular stiffness and systolic hypertension; Prof. Pierre Moreau, B. Pharm., Ph.D
Dean and Professor, Faculty of Pharmacy - Health Sciences Center, Kuwait University

2016

Chemokines: Key players in immune surveillance and agingProf. Bernhard Moser; Chair (Infection & Immunity), Institute of Infection and Immunity, Cardiff University, Heath Park, Cardiff, UK

2015

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

2014

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

2013

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

2012

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

2011

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

2010

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

2009

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

2008

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

2007

From Molecular Imaging to Molecular Medicine.
Prof. Henry N. Wagner, Jr. MD, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

2006

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

2005

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

2004

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

2003

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

2002

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

2001

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

2000

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

1999

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

1998

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

1997

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

Original Research Abstracts List by Subject Area

Allied Health

1

*Jomah A, Albanaw A, Al-Shammeri A: Hydrogen sulfide pregulates cyclooxygenase 1 in the spinal cord of Streptozotocin-induced Diabetic Rats

2

Matrah S*, Bakhiet M, AlFadhli S: Mitochondrial haplogroups reveals the genetic basis of diabetes mellitus type 2 comorbidity in psoriasis

Anatomy

3

Abd-El-Basset EM*, Rao MS, Najem A: dBcAMP Rescues Hippocampal Neurons and Enhances Neurogenesis in Kainic Acid Injury by Increasing BDNF Secretion

4

Alfarhan NW*, Rao MS: Dibutyryl cAMP Enhances Cognitive Functions, Neurogenesis, BDNF, VEGF in Diabetic Rats

5

Alfarhan MW*, Al-Hussaini H, Kilarkaje N: Role of peroxisome proliferator-activated receptor-gamma (PPAR-γ) in type 2 diabetes-induced testicular DNA damage and repair in leptin receptor-deficient obese mice

6

Al-Sarraf A *, Al-Duwailah M, Kazem F, Abdullah L, Rao MS, Kilarkaje N, Al-Onaizi MA: Spatial memory deficits and synaptic dysfunction in Type 2 Diabetes

7

Kazem F*, Al-Duwailah M, Al-Sarraf A, Abdullah L, Rao MS, Al-Onaizi MA: Determining the effects of Type 2 Diabetes on Learning, Memory, and Adult Hippocampal Neurogenesis: Implications for Alzheimer's Disease

8

Kittaneh R*, Al-Hussaini H, Kilarkaje N: Effects of Resveratrol on diabetes-induced up-regulation of mitogen-activated protein kinases signaling and apoptosis in retinal pigment epithelium of dark Agouti rats.

9

Yassin K*, Aref R, Nabulsi D, Al-Hussaini H, Kilarkaje N: Effects of Resveratrol on diabetes-induced apoptosis in retinal pigments epithelium in Wistar rats

Biochemistry

10

Abbas G*, AlEbrahim F, Kankouni R, AlBelushi S, Benov L: Effect of the metal center on the photoefficiency of porphyrin-based photosensitizers

11

*Al-Ansary M, Kunieda T, Quinlan RA : Newly Identified Tardigrades Chaperone Proteins with unique structural and chaperone activity compared with Human CRYAB

12

Alrefaee S*, Mohammed T, Abdulhakim E: Ferritin in dialysis patients

13

Alrefaee S, Subramanian S*: Renal stone formation and serum testing

14

Al-Habeeb M*, Benov L: Impact of Structural Symmetry and Metallation on Photosensitizer Photo-stability and Anticancer Activity

15
* Kavalakatt S, Khadir A, Madhu D, Koistinen HA, Al-Mulla F, Tuomilehto J, Abubaker J, Tiss A : Urocortin 3 overexpression reduces ER stress and heat shock response in 3T3-L1 adipocytes

16
Sina Kavalakatt*, Abdelkrim Khadir, Dhanya Madhu, Maha Hammad, Sriraman Devarajan, Jehad Abubaker, Fahd Al-Mulla, Ali Tiss: Urocortin 3 levels are impaired in overweight humans with and without type 2 diabetes and modulated by exercise

17
Thomas B*, Kandanath BM, Alkhalaf M: Determination of caffeine content in coffee using the Waters Analytical HPLC

Community Medicine

18
Abdullah L, Alkandari A, Aloufan L, Murad D, Alfahad M, Alfalah D, Muqaddam A, Alrashid M, *Nasri T, Al-sabah R: The Association of Cyberbullying with Self-esteem and Emotional and Behavioral Problems

19
Abdullah L*, Alkandari A, Aloufan L, Murad D, Alfahad M, Alfalah D, Muqaddam A, Alrashid M, Nasri T, Al-sabah R: The Prevalence and Associated Factors of Cyberbullying among Kuwait University Students

20
Alowayesh MS*, Aljunid SM, Alattar A, Aladsani A, Alessa T, Alroudhan D: Health related quality of life of patients with diabetes in Kuwait

21
*AlRashed M, Abbas G, AlBelushi S, Alkhatlan S, Alqarbah M, Alrushaid S, AlSharekh N, Bahbahani B, Khamissi F, Akhtar S: Prevalence and Factors Associated with Medical Trust in Healthcare Among Public Sector Employees in Kuwait

22
*Al-Baloul J, Al-Buraiki R, Al-Ebrahim F, Al-Enezi Z, Al-Fadhel N, Al-Hendal S, Kankouni R, Al-Moosawy N, Al-Sayegh A, Al-Shatti M, Longenecker J, Jacob S: Prevalence of Cardiovascular Risk Factors Among University Students in Kuwait

23
Almekhlef AM*, AlHuwais DH, Alsulaibi DJ, Al-Mojel M, Alomirah M, Alenazi NA, AlAmirah R, Snober S, Alawadhi TF, Albatineh AN: Fasting Plasma Glucose is Associated with Mild Cognitive Impairment Among Patients with Type II Diabetes Mellitus in Kuwait: A Population based Study

24
Alnajem A, Redha A, *Alroumi D, Alshammasi A, Ali M, Alhussaini M, Almutairi W, Esmaeil A, Ziyab A: Electronic cigarette use and secondhand aerosols exposure in relation to respiratory symptoms among adolescents in Kuwait: a cross-sectional study

25
Esmaeil A, Alshammasi A, *Almutairi W, Alnajem A, Alroumi D, Ali M, Redha A, Alhussaini M, Ziyab AH: Patterns of electronic cigarette, conventional cigarette, and hookah use and related passive exposure among adolescents in Kuwait: a cross-sectional study

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Kazem F, AlMaateeq B, AlAblani D, AlMashmoom S, AlDraiweesh H, AlSenin R, AlMandeel B, AlHaddad A, AlShahabi R, *AlDorai A, AlAjmi A, Shaban W : Burnout Among Physicians During COVID-19 Pandemic in Kuwait

27
*Lari F, Algharibah N, Alrashidi M, Aldhubaiei D, Alenezy W, Alenenzi M, Albdah H, Alotaibi N, Alhajri M, Akhanam R, Krisnan A, Akhtar S : Prevalence and determinants of SARS-COV-2 vaccine hesitancy among health-care workers in Kuwait

Cytology

28
Balakrishnan M*, Al Baloushi F, George SS, Mallik Mk, Kapila K: Atypical Glandular Cells of undetermined significance: Intraobserver reproducibility in cervical smears and Human papillomavirus testing.

Dentistry

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Abdelsalam G, Alkoot Y, Qudeimat M: Patients' Perception and Satisfaction with at-Home and in-Office Teeth Bleaching

30
Alhuwais M, Alkanderi A, Joseph B: Awareness and Behavior of Diabetic Patients in Kuwait Towards Their Oral Health

31
Alkandari S*,Bhardwaj RG, Al-Khabbaz A, Ellepola AN, Karched M: Isolation and characterization of extracellular vesicles from Granulicatella spp

32
Abdulrahman S*, Almosawi Z, Alhadher F, Bhardwaj RG, Al Khabbaz A, Karched M: Characterization of the Microbiota of Periimplantitis Patients

33
*Kareem FM, Al-Tannak NF, Alzoubi F, Novotny L : Determination of Endocrine Disruptor Bisphenol-A leakage from Five Different Matrices of Dental Resin-Based Composite Materials

34
Nazar H*, Shyama M, Ariga J, Alsumait A: Dental caries experience among adult employees in Kuwait

Diabetes

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Irshad M *, Taghadom E, Al-Ozairy E: Association between Serum Uric Acid and Glucose Levels in Healthy and Diabetic Individuals

Ethics

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Al-Mojel M*, Ashkanani H, AlFahad M, AlYaqoub E, AlZamel A, AlZaabi A, Eliwa Y, Bouhaimed M: Attitudes of Physicians Towards Incentives in Kuwait: Should Incentives Affect Quality of Healthcare?

Genetics

37
Ali H*, Al-Mulla F, Hussain N, Naim M, Esbeitah A, AlSahow A, AbuBaker J, Abu-Farha M, Ahmad S, Harris P: Customized targeted sequencing approach for genetic diagnosis of autosomal dominant polycystic kidney disease: Overcoming PKD1 pseudo-regions and facilitating clinical applications

38
Al-zayed N*, Mojiminiyi O, Shehab D, Al-Temaimi R: Vitamin D levels and vitamin D receptor common genetic variants in type-2 diabetes patients from Kuwait

39
*Dashti M, Alsaleh H, Eaaswarkhanth M, John SE, Nizam R, Melhem M, Hebbar P, Al-Mulla F, Thanaraj TA : Associations of Mitochondrial Variants and Haplogroups with Asthma in Kuwait

40
Dashti M, Alsaleh H*, Rodriguez-Flores JL, Eaaswarkhanth M, Al-Mulla F, Thanaraj TA: Mitochondrial haplogroup J associated with higher risk of obesity in the Middle East

41
Lari F*, Mojiminiyi O, Shehab D, Al-Temaimi R: Leptin genetic variant rs7799039 is associated with type-2-diabetes risk in a sampled Kuwaiti population

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*Marafi D, Zakkariah M, El-Anany E Fatih JM, Sites E, Kaiyrzhanov R, Alsaif HS, Al-Maraghi A, Al-Owain M, Guliyeva U, Guliyeva S, Alhashem AM, Danish E, Karageorgou V, Beetz C, Mitani T, Du H, Rosenfeld JA, Jhangiani SN, Coban Akdemir Z [16], Gibbs RA, Fakhro KA [17][18], Sutton VR [19], Pehlivan D [19][20], Maha S Zaki MS [21], Gleeson JG [22], Maroofian R, Houlden H, Alkuraya FS, Posey JE, Elsea SH and Lupski JR [19][23]: GeneMatcher facilitates the discovery of SLC38A3 as a cause for developmental and epileptic encephalopathy

Health Economics

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Boodai H*, Adel L, Al-Kanderi B, Al-Otaibi J, Sugunan B, Behzadi S, Menoun P, Amrizal MN, Aljunid SM: Cost Analysis and Economic Burden of Root Canal Treatment in School Oral Health Programme of Kuwait

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Odeh A*, Aljunid SM, Annaka M, Al-Wotayan R: Prescribing Patterns of Primary Healthcare Physicians in Kuwait: A Preliminary Analysis

45
Odeh A*, Buqammaz M, Almatrouk J, Abdulghafoor K, Aldousari A, Aljunid SM: Cost Analysis of the Management of Beta Thalassemia Major among Paediatric Cases at NBK Children's Hospital, Kuwait

Health Policy and Management

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Abdulghafoor K*, Aljunid SM: Assessment of Managerial Skills and Leadership Style of Managers in Public Hospitals in Kuwait: A Pilot Study

47
Al-Deaiji EA*, Aljunid SM: Health Seeking Behaviour of Low Back Pain Patients Attending Physiotherapy Outpatient Clinics in Kuwait Public Hospitals

Health Technology Assessment

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*Darawsheh B, Germeni E : Implementing HTA in Kuwait -A Qualitative Study Of Perceived Barriers And Facilitators

Medical Education

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Aburezq MT*, AlAlban FB, Alabdulrazzaq MS, Badr HE: Gestational Diabetes Mellitus in Kuwait: Prevalence, Risk Factors and the Role of Physical Activity.

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Eliwa J*, Jamal D, Alashqar A, Qadoura B, Bouhaimed M: Perception of Negative Teaching Approaches by Clinical Tutors in Kuwait

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Husain EH*, Al-Awadi A, Al-Qabandi W: Pediatrics for Medical Students: Comparing Results of Traditional Vs. COVID-19 Pandemic Teaching

Medical Statistics and Epidemiology

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*Al-Maosherji Sh, Al-Mutawa F, Al-Ramthan A : A Study Analysis of A New Vitiligo Treatment: VT Treatment

Medicine

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Al-Ali M*, Al-Jafar H: Liver severity based on SCD complications

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Al-Awadhi AM, *Haider MZ, Sukumaran J, Hasan EAH, Bartella YA: Lack of association between protein tyrosine phosphatase non-receptor type N22 gene functional variant R620W and rheumatoid arthritis in Kuwaiti patients

55
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Allied Health

1

Hydrogen sulfide pregulates cyclooxygenase 1 in the spinal cord of Streptozotocin-induced Diabetic Rats

*Jomah A [1], Albanaw A [1], Al-Shammeri A [2]
[1] Department of Medical laboratory science, Faculty of Allied Health Science, Kuwait University; [2] MSc. in Anatomy & Neuroscience, Faculty of Medicine, Kuwait University

Introduction:
Diabetes affects around 500 million patients worldwide, with an estimated rising trend, with prevalence of about 8.8% in adults. Diabetic neuropathy is the most common complication of diabetes. Cyclooxygenase-1 has been targeted for many nonsteroidal anti-inflammatory drugs. Hydrogen sulfide (H_2S) is an endogenous reducing agent, colorless, flammable and poisonous gas.

Methods:
Eight Sprague Dawley Male Rats (2-3 months of age, ~300-400 g) were obtained and divided into four groups (non-diabetic as control, non-diabetic with H_2S treatment, diabetic, diabetic with H_2S treatment). Diabetes was induced into the animals using STZ injection, and tissue was harvested after 28 days of the experiment. Samples of the spinal cord were processed histologically and stained using COX1 antibody.

Results:
The treated control tissue showed some scattered stain in both the white and grey matter of the spinal cord, the glial cells and connective tissue stained mildly as well. The diabetic tissue sample showed very intense staining in the glial and connective tissue of the grey area and the white, with no neuronal cell staining. The H_2S diabetic treated tissue showed mild staining pattern all over the section. The neurons of the H_2S treated diabetic tissue shows COX-1 positive reaction which appears darker due to the background hematoxylin staining. Previous investigations have shown a that COX-1 is involved in modulating inflammation that help to protect different tissues of the body. Our results confirm previous investigations and we were able to show that H_2S has increased the COX-1 expression in the damaged diabetic tissue, which is a sign of tissue regeneration and healing.

Conclusions:
This is the first time a study showed a positive outcome of H_2S in upregulates COX-1 in the spinal cord diabetic rats. In the future, further studies will be needed in order to study in detail the effect of H_2S in upregulates COX- 1 with the probability of using Western blot and RT-PCR.

Key Words: H[sub]2[endsub]S; Neuroprotection; Cyclooxygenase 1;

Funding Agency: None

Allied Health

2

Mitochondrial haplogroups reveals the genetic basis of diabetes mellitus type 2 comorbidity in psoriasis

Matrah S*[1], Bakhiet M[2], AlFadhli S[1]
[1] Medical Laboratory Sciences, Allied Health, Kuwait University; [2] Department of Molecular Medicine, College of Medical and Medicine Sciences, Arabian Gulf University, Kingdom of Bahrain

Introduction:
Accumulative published data showed a clear link between psoriasis (Ps) and the increasing prevalence of comorbid conditions, such as diabetes mellitus type 2 (DM2). The distribution in the mitochondria (Mt) system and the mitochondrial genomic haplogroups were involved in the pathogenesis of DM2.
Objective
In this study, for the first time, we studied the mitochondrial genomic haplogroup's role in the potential coexistence of Ps and DM2.

Methods:
Ninety-eight Kuwaiti individuals were recruited as 4 cohorts (20 Healthy Controls (HC), 15 DM2, 34 Ps, and 29Ps/DM2). Ion torrent was used to sequence Mitochondrial DNA (mtDNA) in all cohorts. Chi-square test (x 2) was used to assess differences in the distribution of each haplogroup between cases and controls ($P < 0.05$).

Results:
mtDNA haplogroups were analyzed in Ps, DM2 and PsDM2 patients, compared to HC. Haplogroups RO, U, J, T, N, L3, M, H, X, HV, R, and K were detected in the studied population. Haplogroup R0, U (OR 0.36, P=0.02) and K (OR 0.3, P=0.04) showed a significantly decreased risk of Ps. However, haplogroup M had a high risk for Ps (OR 4.0, P=0.003). Haplogroup R0 and J had decreased the risk of DM2(OR 0.28, P=0.007). While haplogroup T had a potential risk with DM2 patients (OR 2.25, P=0.04). In Ps/DM2, haplogroup R0 (OR 0.46, P=0.04), T and K (OR 0.32, P=0.04) had lower the risk.

Conclusions:
This is the first study that correlates mtDNA haplogroups with Ps/DM2. Our results indicated that mtDNA haplogroups may have the potential to contribute the pathogenesis of Ps as a disease and DM2 as a comorbidity of Ps. Also, we showed for the first time that the diabetes comorbidity in psoriasis patients is related to mitochondrial diabetes.

Key Words: Mitochondrial haplogroups ; Psoriasis; Mitochondrial diabetes;

Funding Agency: None

Anatomy

3

dBcAMP Rescues Hippocampal Neurons and Enhances Neurogenesis in Kainic Acid Injury by Increasing BDNF Secretion

Abd-El-Basset EM*, Rao MS, Najem A
Anatomy Dept, Faculty of Medicine, Kuwait University

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 neurogenesis in the hippocampal injury.

Methods:
A lesion was induced in the hippocampi of four months BALB/c male mice by one injection of 1µl kainic acid (0.25µg) into each 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 each 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. Total numbers of animals is 72 with N=6. Morphological studies using FluroJade-B and Cresyl violet staining to assess the degenerated neurons, immunostaining for NeuN (neuron) and for DCX and BrdU (neurogenesis) of brain sections were done. Another two sets of animals were used, one to estimate the expression of BDNF using ELISA and the second was treated with BDNF receptor inhibitor AZ-23. One way ANOVA was used for statistical analysis.

Results:
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 number of neurons. In addition, it was found that dBcAMP stimulated the expression of BDNF. Treatment with AZ-23, showed significant increase in the degenerating neurons suggesting the role of BDNF in neuroprotection.

Conclusions:
dBcAMP protects the hippocampal neuron from degeneration and enhances neurogenesis by increasing the expression of BDNF.

Key Words: dBcAMP; Hippocampus; Neurogensis;

Funding Agency: MA01/14

Anatomy

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Dibutyryl cAMP Enhances Cognitive Functions, Neurogenesis, BDNF, VEGF in Diabetic Rats

Alfarhan NW*, Rao MS
Department of Anatomy, Faculty of Medicine, Kuwait University

Introduction:
Dibutyryl cyclic adenosine monophosphate (dBcAMP) is a cell-permeable synthetic analog of cAMP, enhances differentiation and survival of newly generated neurons. Present study was aimed to investigate the effects of dBcAMP on learning, memory and adult neurogenesis in streptozotocin model of diabetes.

Methods:
Diabetes was induced in three months old male Wistar rats by single injecting streptozotocin (50mg/kg). Diabetic rats were divided into diabetic (D) and diabetic + dBcAMP (D+dBcAMP) groups. Age matched normal rats served as control (C) group (n=24/group, Total=96). D+dBcAMP group was treated with dBcAMP (10mg/kg) intraperitoneally for 10 days from 1st day of diabetes (experiment-1) or from 30 days after onset of diabetes (experiment-2). C and D groups were treated with PBS. All rats were injected with BrdU during dBcAMP/PBS treatment period (for 10days) to label the proliferating cells and were subjected to Morris water maze and passive avoidance tests to assess the cognitive function. Hippocampal neurogenesis (by immunostaining for doublecortin (DCX/BrdU), brain derived neurotrophic factor (BDNF) and Vascular endothelial growth factor (VEGF), (by ELISA) and DCX content (by Western blot) were analyzed.

Results:
Results showed a significant memory deficit, decreased neurogenesis, decreased neuronal differentiation, decreased BDNF, VEGF contents in diabetic rats compared to control rats ($p<0.01$-0.001, One way-ANOVA Bonferroni's multiple comparison test), in both experiments. Above deficits were alleviated by treatment with dBcAMP (D vs dBcAMP, $p<0.01$-0.001).

Conclusions:
We conclude that dBcAMP enhances hippocampal BDNF and VEGF contents and hence enhances neurogenesis and neuronal differentiation there by enhance cognitive functions in diabetic rats. This effect of dBcAMP is independent of duration of the diabetic condition. This work is supported by Kuwait University, Grant # YM02/17, OMICS # SRUL02/13
and ARC facility of HSC.

Key Words: Hippocampus; Diabetes; dBcAMP;

Funding Agency: Research Sector, CGS, Kuwait University, Grant No. YM-12/17

Anatomy

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Role of peroxisome proliferator-activated receptor-gamma (PPAR-γ) in type 2 diabetes-induced testicular DNA damage and repair in leptin receptor-deficient obese mice

Alfarhan MW*, Al-Hussaini H, Kilarkaje N
Department of Anatomy, Faculty of Medicine, Kuwait University

Introduction:
Hyperglycemia-mediated alterations in DNA damage repair mechanisms may form a basis for carcinogenesis. In this study, we investigated the role of peroxisome proliferator-activated receptor-gamma (PPARγ) in diabetes-induced alterations in DNA damage repair mechanism in the testis.

Methods:
Leptin receptor-deficient db-/db- male mice (7-week-old; n=10/group), a type 2 diabetes model, were treated for 84 days either with pioglitazone (PPARγ agonist), or 2-chloro-5-nitro-N-phenylbenzamide (PPARγ antagonist). Age-matched male lean non-diabetic (db+/db+) mice served as controls. Semi-quantification of 4-hydroxynonenal and 8-oxo-dG levels estimated the oxidative stress and the TUNEL assay quantified cell death. The base-excision repair (BER) pathway proteins- 8-oxoguanine glycosylases 1&2, apurinic/apyrimidinic endonuclease, DNA polymerase δ, poly (ADP-ribose) polymerase 1 and X-ray repair cross-complementing protein-1 were semi-quantified by Western blotting. The data were analysed using one way ANOVA and LSD test with the statistical significance set at $P<0.05$.

Results:
The diabetic mice showed increased oxidative stress and oxidative DNA damage, and PPARγ stimulation reduced only lipid peroxidation, and PPARγ inhibition inhibited both lipid peroxidation and oxidative DNA damage. In obese diabetic mice, BER was upregulated to repair the increased DNA damage. PPARγ stimulation inhibited BER indicating its detrimental effects, and PPARγ inhibition led to reduced BER pathway in conjunction with reduced oxidative DNA damage. However, regardless of PPARγ modulation, the obese mice showed comparable testicular apoptosis with the control.

Conclusions:
PPARγ activation in the absence of leptin signaling upregulates DNA damage and inhibits BER mechanisms in the testis. The inhibition of PPARγ in the absence of leptin signaling is more beneficial to the testes of diabetic mice.

Key Words: Diabetes mellitus; Pioglitazone; PPARγ;

Funding Agency: Research sector, College of Graduate Studies, Kuwait University YM05/17

Anatomy

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Spatial memory deficits and synaptic dysfunction in Type 2 Diabetes

Al-Sarraf A[1]*, Al-Duwailah M[1], Kazem F[1], Abdullah L[1], Rao MS[2], Kilarkaje N[2], Al-Onaizi MA[2]

[1]Undergraduate Medical Degree Program, Faculty of Medicine, Kuwait University; [2]Anatomy Department, Faculty of Medicine, Kuwait University

Introduction:
Type 2 diabetes mellitus (T2DM) has a prevalence of 14.7% in Kuwait. Many studies have linked long-term exposure to diabetes with neurodegenerative disease, which are characterized by synaptic loss and neuroinflammation. However, the mechanisms through which T2DM mediates these changes is unknown. This study investigates the effects of T2DM on spatial memory, hippocampal synaptic integrity and neuroinflammation.

Methods:
To test the effects of T2DM on spatial memory, T2DM (db/db) and lean control mice were tested on the Morris Water Maze (MWM) task. To study the effect of diabetes on synaptic integrity, hippocampal homogenates were assayed for PSD95 and synaptophysin. Because our previous findings showed a chronic inflammatory profile in T2DM animals, we then assessed the levels of different proinflammatory cytokines to identify specific cytokines that may underlie the neuropathology observed in T2DM.

Results:
In the 24hr probe trial, both lean and obese mice spent significantly more time in the platform quadrant compared to the other quadrants (2-way ANOVA shows a significant effect of quadrant, $F(3, 56)=18.7$, $p<0.0001$). Lean mice spent significantly more time in the target compared with the opposite quadrant (1-way ANOVA, $F(1,14)=7.79$, $p<0.05$), while T2DM mice did not (1-way ANOVA, $F(1, 14)=1.29$, $p=0.27$). T2DM mice had significantly lower levels of these synaptic markers compared with their lean counterparts. We report that db/db animals display a significantly elevated proinflammatory profile highlighted by high expression levels of IL-1β and IL-6 ($p<0.05$).

Conclusions:
T2DM leads to progressive loss of both post- and presynaptic integrity as indicated by the decreased PSD95 and synaptophysin levels. These findings are consistent with the impaired spatial memory observed in T2DM mice. Concurrent high levels of proinflammatory cytokines seen in diabetic mice might suggest neuroinflammation as an important player in mediating these changes.

Key Words: Diabetes; Memory; Synaptic Dysfunction;

Funding Agency: ZM03/16

Anatomy

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Determining the effects of Type 2 Diabetes on Learning, Memory, and Adult Hippocampal Neurogenesis: Implications for Alzheimer's Disease

Kazem F* [1], Al-Duwailah M [1], Al-Sarraf A[1], Abdullah L [1], Rao MS [2], Al-Onaizi MA [2]

[1] Undergraduate Medical Degree Program, Faculty of Medicine, Kuwait University;[2] Anatomy Department, Faculty of Medicine, Kuwait University

Introduction:
Diabetes Mellitus Type 2 (T2DM) is a major disease burden that continues to be on the rise in Kuwait. Cognitive decline and memory loss is recognized as a comorbidity in T2DM. Adult neurogenesis in the dentate gyrus of hippocampus plays a role in memory encoding, and its dysregulation is seen in Alzheimer's. However, whether adult hippocampal neurogenesis underlies cognitive decline in T2DM is unclear. This study aims to investigate the effects of T2DM on learning, memory and neurogenesis.

Methods:
To determine if altered hippocampal neurogenesis and cognitive function is disrupted in T2DM, 12 T2DM db/db (leptin receptor knockout) and 12 lean control (5 month old) mice were either injected with BrdU (Bromodeoxyuridine; cell proliferation marker) or a vehicle control (PBS). To assess cognitive function, the animals underwent the Morris Water Maze (MWM) learning sessions. After completion of behavioral analysis, animals were sacrificed and brain sections were immunolabeled for neurogenesis markers to evaluate the effect of T2DM on adult hippocampal neurogenesis.

Results:
In the MWM learning and relearning session test, diabetic animals group showed significantly greater latency to find the platform compared to their lean counterparts ($p<0.05$). In the memory retention tests, entry latency into the platform quadrant of the T2DM mice was significantly higher ($p<0.05$), and distance travelled in the platform quadrant was significantly lower ($p<0.05$) compared to controls. Moreover, preliminary data shows significantly reduced BrdU and DCX expression in diabetic mice compared to controls.

Conclusions:
T2DM animals display impaired spatial navigation and memory impairment, as demonstrated in the water maze findings. Neurogenesis markers in the T2DM mice showed decreased proliferation in the hippocampus of diabetic mice. Our findings suggest that T2DM impairs adult hippocampal neurogenesis, and may underlie the cognitive dysfunction.

Key Words: Diabetes; Neurogenesis; Memory;

Funding Agency: ZM03/16

Anatomy

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Effects of Resveratrol on diabetes-induced up-regulation of mitogen-activated protein kinases signaling and apoptosis in retinal pigment epithelium of dark Agouti rats.

Kittaneh R*, Al-Hussaini H, Kilarkaje N
Department of Anatomy, Faculty of Medicine, Kuwait University

Introduction:
Microvascular changes and retinal degeneration precede diabetic retinopathy. Oxidative stress alters several intracellular signalling pathways, including polyol pathway, advanced stress alters several intracellular signalling pathways, including polyol pathway, advanced glycated end products formation, mitogen-activated protein kinases (MAPKs), protein glycated end products formation, mitogen-activated protein kinases (MAPKs), protein kinase C, and inflammation, which form the basis of diabetic retinopathy. Many antioxidants kinase C, and inflammation, which form the basis of diabetic retinopathy. Many antioxidants have been investigated as possible preventive and therapeutic remedies for diabetic have been investigated as possible preventive and therapeutic remedies for diabetic retinopathy. The current study investigated the modulatory effects of Resveratrol on type 1 retinopathy. The current study investigated the modulatory effects of Resveratrol on type 1 diabetes-induced changes in MAPKs and apoptosis in retinal pigmented epithelium (RPE) diabetes-induced changes in MAPKs and apoptosis in retinal pigmented epithelium (RPE) of dark Agouti rats.

Methods:
Adult male rats (12-14 weeks, n=15) were segregated into normal control, Resveratrol-treated, streptozotocin-induced diabetic, and Resveratrol-treated diabetic groups (5mg/kg/d, po, from the day of confirmation of diabetes to the sample collection day). The RPE was collected on day 30 for RT-PCR and Western blotting analysis for apoptosis and MAPKs.

Results:
Resveratrol, when administered to normal rats, significantly increased gene expression of caspases-3, -8 and -9, Bax, Bcl2, p38MAPK, JNK, and p53 as compared to the control. On the other hand, diabetes significantly decreased gene expression of caspases-8, Erk, p38MAPK, and JNK. Resveratrol reversed the inhibited gene expression of caspase-8, Erk, JNK and p38MAPK to normal control levels in diabetic rats. After the induction of diabetes, Resveratrol normalized diabetes-induced upregulation of proteins- caspases-3 and -9, cytochrome-c, Bcl2 and ERK.

Conclusions:
Resveratrol when given to normal rats upregulates transcription of MAPKs and apoptosis genes; however, their protein levels do not increase suggesting the lack of induction of apoptosis and MAPK-mediated cell signalling, which might be due to posttranscriptional modifications. Resveratrol imparts its protective effects by normalizing apoptosis and MAPK signalling in diabetic rats, suggesting

Key Words: Diabetic retinopathy; Apoptosis; Resveratrol;

Funding Agency: YM 04/17

Anatomy

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Effects of Resveratrol on diabetes-induced apoptosis in retinal pigments epithelium in Wistar rats

Yassin K*, Aref R, Nabulsi D, Al-Hussaini H, Kilarkaje N
Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Oxidative stress-mediated retinal structural changes are one of the early pathological changes seen prior to the onset of diabetic retinopathy. Oxidative stress stimulates many signalling pathways eventually leading to inflammation and apoptosis of retinal cells. The present study investigated modulatory effects of Resveratrol, a natural antioxidant, on type 1 diabetes-induced retinal pigment epithelial (RPE) cell apoptosis in Wistar rats.

Methods:
Adult male rats (12-14-week-old, n=4) were made diabetic using single dose of streptozotocin (55mg/kg, ip) and treated with Resveratrol (5mg/kg/d, po) from the day of confirmation of diabetes to the sample collection day 90. The untreated control, resveratrol-treated control and untreated diabetic rats were maintained for comparison. The eyes were dissected, the neural retina was separated from RPE, and the eye cup containing RPE was flat-mounted for immunofluorescence for caspases-9 and -3, and cytochrome C. The number and location of labelled RPE cells were counted. The data were expressed as mean +_ SE for each group and analyzed for statistical significance by one-way ANOVA using non-parametric test for two independent samples (Mann-Whitney Test) with significance level set at $p<0.05$, using SPSS software Version 25.

Results:
Analysis of flat-mounted RPE layer showed clustering of apoptotic RPE cells, mainly at the centre of the RPE layer around the optic disc. Diabetes increased the number of caspases-9 and -3 labelled RPE cells and showed a trend in increasing the number of cytochrome C labelled RPE cells. When given to diabetic rats Resveratrol did not show any protective effects on apoptosis-related proteins.

Conclusions:
Diabetes in Wistar rats for 90 days increases the expression of pro-apoptotic proteins 'caspase 9 and 3' in the RPE, but gavage of 5mg/kg/d dose-level of Resveratrol does not prevent diabetes-induced apoptosis of RPE cells.

Key Words: Retinopathy; Resveratrol; Dabetes;

Funding Agency: RM01/16

Biochemistry

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Effect of the metal center on the photoefficiency of porphyrin-based photosensitizers

Abbas G*, AlEbrahim F, Kankouni R, AlBelushi S, Benov L
Department of Biochemistry, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Photodynamic therapy (PDT) is approved for treatment of various diseases. It kills unwanted cells by combining a photosensitizer (PS) and visible light. A medically applicable PS should have low dark toxicity, selective uptake, and high photoefficiency. Majority of clinically approved PSs are porphyrin-based. The metal chelated by the porphyrin ring affects the quantum yield of the PS, but its effect on PS interaction with cellular components and on PS photoefficiency is not known. The aim of this study was to investigate the effect of the metal center on photocytotoxicity of porphyrin-based PSs.

Methods:
Estrogen/tamoxifen resistant cell line pII was used as a model system. PS were produced by incorporating Zn, In, or Ag into a meso-tetrakis(N-alkylpyridinium -3-yl)porphyrin ring. PSs efficiency and dark toxicity were evaluated by determining the effects of PSs on viability and cell proliferation using MTT and SRB assays, respectively. Mechanisms of PS-induced cell damage was studied by flow cytometry. Activation of cell death pathways was assessed by Western blotting. All experiments were repeated 2 – 3 times with each sample run in triplicate. Results are presented as mean ±SD.

Results:
Viability assay demonstrated that replacing the butyl side chain attached to the porphyrin core with a 6-carbon aliphatic chain increased the photoefficiency. All tested hexyl derivatives blocked cell proliferation irrespective of the nature of the metal center. Flow cytometry analysis revealed that <2% of the cells underwent apoptotic death, a result that was confirmed by Western blot analysis of caspases activation.

Conclusions:
The metal chelated by the tetrapyrrole ring had little effect on the biological photoefficiency of the PSs. Factors like cellular uptake and subcellular distribution, which depend on substituents at the periphery of the tetrapyrrole ring, are the main determinants of PSs photoefficiency.

Key Words: Photodynamic therapy; Cancer; Singlet oxygen;

Funding Agency: MB01/18 Kuwait University

Biochemistry

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Newly Identified Tardigrades Chaperone Proteins with unique structural and chaperone activity compared with Human CRYAB

*Al-Ansary M [1], Kunieda T [2], Quinlan RA [3]
[1] Department of Biochemistry, Faculty of Medicine, Kuwait University, Kuwait; [2] Department of Biological Science, University of Tokyo, Japan; [3] Department of Biological and Biomedical Sciences, Durham University, UK

Introduction:
Small heat-shock proteins (HSPs) are the "paramedics" of the cell and they sustain the normal cellular functions, they have been used/targeted for therapeutics approaches and linked to a variety of medical conditions. Despite the efforts that have been made in identifying the different types of HSPs and their potential therapeutic approaches, there are still yet more to be discovered among different types and families of HSPs among different species and tissues. Ramazzottius varieornatus has remarkable capabilities to tolerate extreme stress condition among all living animals. The aim of this project is to recombinantly express and purify newly identified chaperones from Ramazzottius V. and compare their functions with a known human chaperone.

Methods:
Bioinformatics of Tardigrades DNA sequence homology showed what is believed to be a new HSPs family, PCR primers were designed to amplify the HSP gene regions with recombinant polymerase for pGEM-T ready ligation, Transformed bacterial-induced proteins were purified (Dialysis, SEC, IEC, HPLC and high-speed centrifugation fractionation). Purified protein fractions were used for TE Microscopy morphology analysis and chaperone assay kinetic analysis.

Results:
TEM images of a negatively stained purified sample show aggregates particles of different sizes (10-12nm, 30-40nm, >80nm) and protein Filaments. The newly identified proteins have higher chaperone activity compared with human HSP alpha B-crystallin. Heating cooling cycles showed some thermal hysteresis properties.

Conclusions:
Newly identified HSPs which has been named 20.3, 20.5 and 20.6 have been recombinantly expressed and purified. They showed enhanced chaperone activity compared with the Human CRYAB. Oligomerisation of each HSP20.3, 20.5 and HSP20.6 is different, with some similarities with CRYAB, HSPs 20.5 and 20.3 shows some filamentous structures with chaperone characteristics and have some thermal hysteresis properties.

Key Words: Biomedical sciences; Alpha B Crystalin; Recombinant DNA Technology;

Funding Agency: Kuwait University PhD Scholarship

Biochemistry

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Ferritin in dialysis patients

Alrefaee S*, Mohammed T, Abdulhakim E
Clinical Biochemistry Department, Clinical laboratories, J.A. Armed Forces Hospital, Ministry of Defense, Kuwait

Introduction:
Serum ferritin is a clinical biomarker widely used to estimate body iron status. At the same time it is considered a marker of chronic diseases and inflammation - infection processes where levels may increase independently of iron status. In this study we are going to study the relation between ferritin, thyroid hormones, PTH and micro-total protein (MTP) as a marker of clinical status in dialysis patients.

Methods:
This study is based on data collected during August 2016 to October 2019 at Biochemistry unit - J.A.Armed forces hospital, Kuwait. We included 769 participants attending dialysis unit for permanent washing cycles. Serum ferritin, free thyroxine (FT4), parathormone levels (PTH), and 24 hours urine collection for micro-total protein (MTP) were examined.

Results:
406 (52.8%) were males while 363(47.2%) were females. Median levels were: ferritin 9.95 ng/ml, FT4 0.4 pmol/l, PTH 2.6 pmol/l and median MTP 601.5 mg/day. Ferritin distribution was not the same across category of both sexes (p=0.001, Mann-Whitney). Spearman's correlation didn't show any significant association between ferritin and other markers used in the study (P>0.05). However, negative relations were noticed between ferritin, FT4 and MTP.

Conclusions:
Levels of ferritin and FT4 may give the impression about clinical status in dialysis patients, however. Further studies needed.

Key Words: ferittin ; dialysis; marker;

Funding Agency: None

Biochemistry

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Renal stone formation and serum testing

Alrefaee S, Subramanian S*
Clinical Biochemistry, Clinical laboratories, J.A.Aremd forces Hospital, Ministry of defense, Kuwait

Introduction:
Renal stones are formed in the kidneys when certain substances such as minerals or salts reach high levels in urine. Testing the composition of these stones provides information regarding forming substances and guide plans for future prevention of stones either by medication or dietary changes.

Methods:
We retrospectively reviewed stone analysis reports of 16 patients attended J.A armed forces hospital during the year 2019. Infrared spectroscopy (Bruker optics, Germany) was the method used for stone analysis. The connection between serum levels of calcium, phosphorus (inorganic phosphate), body urea nitrogen (BUN) & kidney stone were also reviewed.

Results:
5 females and 11 males were involved: 78.5% were Kuwaitis and rest were non- Kuwaitis' .12 cases were received from outpatient clinic compared to 4 cases received from ward1. Calcium oxalate (ca-ox) were the major components of 68.8% of stone while 18.8% were Calcium oxalate + carbonate (ca.ox+carb), 6.3% were Calcium oxalate+triglyceride (ca.ox+TG) & 6.3% were uric acid (UA) stones. 9 cases only had records for serum calcium (median 2.3 mmol/l) and body urea nitrogen (BUN) (median 4.8mmol/l), however, no records were found for serum phosphorus. The distribution of age (p= 0.09), BUN (p=0.8) & calcium (p=0.7) were the same across categories of stone composition (Kruskal-wallis test; SPSS).

Conclusions:
Further studies are needed to determine the connection between serum levels of calcium, phosphorus, BUN and renal stone formation

Key Words: renal stones; calcium ; BUN;

Funding Agency: None

Biochemistry

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Impact of Structural Symmetry and Metallation on Photosensitizer Photo-stability and Anticancer Activity

Al-Habeeb M*, Benov L
Department of Biochemistry, Kuwait University Faculty of Medicine

Introduction:
Photodynamic therapy (PDT) combines a light-sensitive medication, a photosensitizer (PS), and visible light for treatment of various disorders. Generation of singlet oxygen ($^1O_2$) (type II reaction) or radicals (type I processes) by a PS, are considered prominent mechanisms generating cell-damaging species. Because such species are short-lived, efficacy of PDT depends on quantum yield and cellular location of the PS. Additional, often overlooked factor, is the photo-stability of the PS. The aim of this study was to investigate how structural modifications and metallation affect photo-stability and PDT efficacy of porphyrin-based PSs.

Methods:
Hydrophilic and amphiphilic ZnP-based and metal-free PSs with different 3D shapes were used as model compounds. Rate of singlet oxygen generation and PSs photo-degradation were determined by UV-VIS spectroscopy. PDT efficacy of tested PSs was assessed on cancer cell cultures. Viability and cellular uptake were determined using MTT and confocal microscopy, respectively. Experiments were repeated at least twice, with data expressed as mean ±S.D.

Results:
In spite of significant differences in photo-efficiency among symmetrical ZnP, symmetrical and asymmetrical metal-free ligand PSs, they displayed insignificant variations in singlet oxygen quantum yield. The lowest photo-degradation rates were observed when testing hydrophilic metal-free analogs. An asymmetrical metal-free PS displayed higher photo-cytotoxicity compared to tested symmetrical hydrophilic ZnPs. Different patterns of cellular uptake were observed with symmetrical and asymmetrical metal-free and metal-based PSs.

Conclusions:
Incorporation of Zn^{2+} in the tetrapyrrole porphyrin ring decreases photo-stability of the PSs. 3D structure and lipophilicity, which dictate PSs ability to reach and damage critical cellular components, together with photo-stability, are key factors in determining the photo-efficiency of a PS.

Key Words: Photodynamic Therapy; Photo-stability; Photosensitizer;

Funding Agency: College of Graduate Studies and Research sector (Grant YM06/16) at Kuwait University

Biochemistry

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Urocortin 3 overexpression reduces ER stress and heat shock response in 3T3-L1 adipocytes

* Kavalakatt S [1], Khadir A [1], Madhu D [1], Koistinen HA [234], Al-Mulla F[5], Tuomilehto J[4][6], Abubaker J [1], Tiss A [1]

[1] Biochemistry and Molecular Biology department, Research Division, Dasman Diabetes Institute, Kuwait; [2] University of Helsinki and Department of Medicine, Helsinki University Central Hospital, Helsinki, Finland; [3] Minerva Foundation Institute for Medical Research, Helsinki, Finland; [4] Department of Public Health Solutions, Finnish Institute for Health and Welfare, Helsinki, Finland; [5] Research Division, Dasman Diabetes Institute, Kuwait; [6] Department of Public Health, University of Helsinki, Helsinki, Finland

Introduction:
The neuropeptide urocortin 3 (UCN3) has a beneficial effect on metabolic disorders, such as obesity, diabetes, and cardiovascular disease. It has been reported that UCN3 regulates insulin secretion and is dysregulated with increasing severity of obesity and diabetes. However, its function in the adipose tissue is unclear.

Methods:
We investigated the overexpression of UCN3 in 3T3-L1 preadipocytes and differentiated adipocytes and its effects on heat shock response, ER stress, inflammatory markers, in the presence of stress-inducing concentrations of palmitic acid (PA) by analyzing gene expression through RT PCR and protein expression through Western blotting. Glucose uptake was also assessed using Glucose uptake assays.

Results:
Results & Conclusion: UCN3 overexpression significantly downregulated heat shock proteins (HSP60, HSP72 and HSP90) and ER stress response markers (GRP78, PERK, ATF6, and IRE1□) and attenuated inflammation (TNF□) and apoptosis (CHOP). Moreover, enhanced glucose uptake was observed in both preadipocytes and mature adipocytes, which is associated with upregulated phosphorylation of AKT and ERK but reduced p-JNK. Moderate effects of UCN3 overexpression were also observed in the presence of 400 µM of PA, and macrophage conditioned medium dramatically decreased the UCN3 mRNA levels in differentiated 3T3-L1 cells.

Conclusions:
Novelty: We have for the first time shown that the beneficial effects of UCN3 in adipocytes are excreted, at least partially, by the improvement in cellular stress response and glucose uptake and attenuation of inflammation and apoptosis.

Key Words: Urocortin 3 ; Obesity; Diabetes;

Funding Agency: KFAS

Biochemistry

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Urocortin 3 levels are impaired in overweight humans with and without type 2 diabetes and modulated by exercise

Kavalakatt S[1,2]*, Abdelkrim Khadir[1], Dhanya Madhu[1], Maha Hammad[1], Sriraman Devarajan[2], Jehad Abubaker[1], Fahd Al-Mulla[2], Ali Tiss[1]

[1]Research Division, Dasman Diabetes Institute, Kuwait; [2] Doctoral Programme inBiomedicine, University of Helsinki, Kuwait

Introduction:
Urocortin3 (UCN3) regulates metabolic functions and is involved in cellular stress response. Although UCN3 is expressed in human adipose tissue, the association of UCN3 with obesity and diabetes remains unclear. This study investigated the effects of Type 2 diabetes (T2D) and increased body weight on the circulatory and subcutaneous adipose tissue (SAT) levels of UCN3 with its modulation by a regular physical exercise.

Methods:
Normal-weight (n=37) and overweight adults with and without T2D (n=98 and n=107, respectively) were enrolled in the study. A subset of the overweight subjects (n=39 for each group) underwent a supervised 3-month exercise program.UCN3 levels in SAT were measured by immunofluorescence and RT-PCR. Circulatory UCN3 in plasma was assessed by ELISA and was correlated with various clinical and metabolic markers.

Results:
Our data revealed that plasma UCN3 levels decreased in overweight subjects without T2D compared with normal-weight controls [median; 11.99(0.78-86.07) and 6.27(0.64 -77.04), respectively; $p<0.001$], whereas plasma UCN3 levels increased with concomitant T2D [median; 9.03(0.77-104.92) $p<0.001$]. UCN3 plasma levels were independently associated with glycemic index; fasting plasma glucose and hemoglobin A1c ($r=0.16$ and $r= 0.20$, $p<0.05$, respectively) and were significantly different between both overweight, with and without T2D, and normal-weight individuals (OR=2.11 [1.84–4.11, 95% CI] and OR=2.12 [1.59–3.10, 95% CI], $p<0.01$, respectively). Conversely, the UCN3 patterns observed in SAT were opposite to those in circulation; UCN3 levels were significantly increased with body weight and decreased with T2D. After a three-month supervised exercise protocol, UCN3 expression showed a significant reduction in SAT of both overweight groups (2.3 and 1.6-fold change; $p<0.01$, respectively).

Conclusions:
In conclusion, UCN levels are differentially dysregulated in obesity in a tissue-dependent manner and can be mitigated by regular moderate physical exercise.

Key Words: Urocrotin 3; Obesity; Diabetes;

Funding Agency: KFAS

Biochemistry

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Determination of caffeine content in coffee using the Waters Analytical HPLC

Thomas B*[1], Kandanath BM [1], Alkhalaf M [1]
OMICS Research Unit, Research Core Facility; [1] Health Sciences Center, Kuwait

Introduction:
Caffeine is a mild addicting drug though used for medicinal purposes, is also the active ingredient that makes tea, coffee and chocolates valuable to humans. In the recent years, the food and pharmaceutical industries is giving caffeine an increased attention, due to its pharmacological properties. The aim of this study is to determine the content of caffeine in two commonly used instant coffee brands (Nescafé Red Mug and Nescafé classic) using High Performance Liquid Chromatography (HPLC) with Photodiode array detector (PDA) from Waters.

Methods:
Nescafe samples were purchased from local stores. 2 gm of coffee samples were weighed and 100 ml of boiling distilled water was added and let to stand for five minutes with stirring, solution was cooled and filtered into conical flasks.1 ml of the filtrate were pipetted into 50 ml volumetric flask and made to mark with the mobile phase. The standards were run as duplicates and samples as six injections. The HPLC conditions are as following: Reverse phase, Column XTerra MS C18 3.5µm, 3.0 × 50 mm, flow rate-0.75 ml/min, PDA at 272nm, mobile phase, methanol-water (60:40) and 10ul injections volume. Caffeine standards were prepared from 100ppm (0.01mg/ml Caffeine Standard Waters). 10, 20,40,60 and 100 ppm caffeine working solutions were prepared. A calibration curve of peak areas versus concentration of the standards was plotted. The caffeine level of the various samples was calculated using the regression equation of the best line of fit using the Empower Software.

Results:
Nescafé Red Mug showed caffeine content around 45.68 ppm per 100ml and Nescafe Classic around 59.27 ppm.

Conclusions:
Quantitative analysis of caffeine levels in beverages and non-beverage products has been practiced by many researchers. A good analytical method is required to provide accuracy, selectivity, and speed. HPLC becomes one of the preferred methods because it meets these specifications, thereby making it a suitable analytical method.

Key Words: Caffeine; High Performance LIquid Chromatography (HPLC); Reverse

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

Community Medicine

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The Association of Cyberbullying with Self-esteem and Emotional and Behavioral Problems

Abdullah L, Alkandari A, Aloufan L, Murad D, Alfahad M, Alfalah D, Muqaddam A, Alrashid M, *Nasri T, Al-sabah R
Department of Community Medicine and Behavioral Science, Faculty of Medicine, Kuwait University

Introduction:
Background: Cyberbullying is a modern phenomenon with public health implications related to serious mental health consequences on youth self-esteem, emotional distress, substance use, and suicidal behavior. The objective of our study was to investigate the relationship of cyberbullying with self-esteem and behavioral and emotional problems among Kuwait University Students.

Methods:
The cross-sectional study was conducted in October 2019 in seven randomly selected colleges of Kuwait University. After obtaining written informed consent, 1252 students completed a self-administered questionnaire, which included 3 sections: Cyberbullying questions, Rosenberg Self-Esteem Scale, and Strengths and Difficulties Questionnaire (SDQ).

Results:
A statistically significant difference was found between those who were involved in any lifetime cyberbullying behaviors (victim+bully+bully-victim) and those who were not with respect to their scores on the Rosenberg Self-esteem scale. Regarding SDQ scales, there was a significant difference for most of the SDQ scales between students who endorsed any lifetime cyberbullying behaviors and those who did not. Additionally, a significant difference was found in the mean scores of the SDQ for lifetime involvement in cyberbullying behaviors between cyber-victims, cyberbullies, and bully-victims with regard to the conduct problem scale and prosocial scale. Adjusted logistic regression analysis revealed that being involved in any type of cyberbullying behaviors was related to student internalizing behaviors.

Conclusions:
Since emotional problems and self-esteem were significantly related to cyberbullying, university-wide public health promotion campaigns are encouraged to address the negative consequences of cyberbullying on students' psychological health.

Key Words: Cyberbullying; Self-esteem; SDQ;

Funding Agency: None

Community Medicine

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The Prevalence and Associated Factors of Cyberbullying among Kuwait University Students

Abdullah L*, Alkandari A, Aloufan L, Murad D, Alfahad M, Alfalah D, Muqaddam A, Alrashid M, Nasri T, Al-sabah R
Department of Community Medicine and Behavioral Science, Faculty of Medicine, Kuwait University

Introduction:
Cyberbullying is a modern phenomenon, the prevalence of which has increased with the rapid advancement of technology. The objectives of our study were to investigate the prevalence of cyberbullying among Kuwait University students and to explore the relationship between sociodemographic factors and cyberbullying behaviors.

Methods:
The cross-sectional study was conducted in October 2019 in seven randomly selected colleges of Kuwait University. After obtaining written informed consent, 1252 students completed a self-administered questionnaire, which included sociodemographic characteristics, cyberbullying questions, and the use of electronic devices.

Results:
The lifetime prevalence of cyber-victimization was 15.8% and cyberbullying was 6.8%. The most common offence was posting hurtful comments about other individuals as reported by victims and bullies with frequency of 31.1% and 30.8%, respectively. Posting mean names or comments about religion with a frequency of 31.1% was also the most common offence for the victims. The most common social media site where offenders cyberbullied others was Twitter (37.5%) while victims reported being cyberbullied on both Twitter and through cellphone text messages with percentage of 31.4% for each. After adjusting for possible confounding variables, logistic regression analysis showed that gender, mother's educational level and parents' marital status were significantly related to lifetime endorsement of any type of cyberbullying behaviors (victim, bully, bully-victim).

Conclusions:
The intent of our study was to contribute to the expanding knowledge of cyberbullying in post-secondary education. Although the prevalence of cyberbullying in the current study was justifiably lower than that found in other studies conducted on middle and high school students, we still found different significant associations. Hence, a need for further investigation of cyberbullying at the post-secondary level is encouraged.

Key Words: Cyberbullying; Prevalence; University students;

Funding Agency: None

Community Medicine

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Health related quality of life of patients with diabetes in Kuwait

Alowayesh MS* [1], Aljunid SM [2], Alattar A [3], Aladsani A [4], Alessa T[5], Alroudhan D[6]

[1] Department of pharmacy practice, School of Pharmacy, Kuwait University;[2] Department of health policy, School of Public Health, Kuwait University; [3] Endocrine Department, Alamiri Hospital, Ministry of Health; [4] Endocrine Department, Alsbah Hospital, Ministry of Health; [5] Endocrine Department, Jabir Hospital, Ministry of Health; [6] Endocrine Department, Mubarak Hospital, Ministry of Health

Introduction:
Diabetes is known to compromise health related quality of life (HRQoL). The prevalence of diabetes in Kuwait in 2014 was 18%. Given the high prevalence rate in Kuwait, understanding diabetes burden on patients is a must. The aim of this study is to assess the HRQoL of patients suffering from diabetes in Kuwait.

Methods:
This study was a cross-sectional study. It used a multi-stage cluster sampling. Patients were recruited from the six governorates of Kuwait. A hospital and two primary care centers from each governorate were included. Patients with diabetes (18-80 years) were included in the study. EuroQual five dimension five levels (EQ-5D-5L) instrument for measuring health related quality of life was used.

Results:
The study included 1182 patients from all over Kuwait. The mean age was 56.3 (±13.1). The majority were females and had type-2 diabetes, (65.3%, 89.5% respectively). Neuropathy was the most prevalent complication compared to the others (19.7%). The EQ-5D-Visual Analogue Scale (VAS), which reports the overall health of the patient in a scale of 0-100 on the day of the questionnaire from the patient perspective, had a mean of 74.7 (±19.6) for the study population. Patients with at least one comorbidity compared to patients with no comorbidites, and patients with at least one diabetes complication compared to patients with no diabetes complications, perceived their health to be lower, their VAS scores were significantly different ($p<0.001$). The highest domain that patient reported to have no problems in was self-care (84.4%). Older adults (>71 years of age) were the highest to have severe problem in mobility compared to all the other age group ($p<0.001$). Females were more likely to have severe problems in anxiety and depression than males ($p<0.006$).

Conclusions:
Diabetes has a high burden on the quality of life of patients. Patients who are older and with higher morbidity report to have more problems in health related quality of life.

Key Words: Diabetes; Quality of life; Kuwait;

Funding Agency: Kuwait University, PR 01/19

Community Medicine

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Prevalence and Factors Associated with Medical Trust in Healthcare Among Public Sector Employees in Kuwait

*AlRashed M, Abbas G, AlBelushi S, Alkhatlan S, Alqarbah M, Alrushaid S, AlSharekh N, Bahbahani B, Khamissi F, Akhtar S

Department of Community Medicine, Faculty of Medicine, Kuwait University

Introduction:
This cross-sectional study estimated the prevalence of medical trust in healthcare among public-sector employees in Kuwait and examined the factors associated with it.

Methods:
The study was on public-sector employees during December 2019. Employees of either gender and any nationality, aged 21 to 65 years, were enrolled from 13 ministries. A self-administered questionnaire and a validated scale was used to measure trust scores (range: 10- 50). Participants were categorized as either having medical trust (score ≥ 30) or not (score < 30). Prevalence of medical trust was computed and factors associated with it were evaluated using multivariable logistic regression.

Results:
1107 respondents indicated their consent and completed the questionnaire. Of these, 61.4% were female and 81.1% were Kuwaiti. The prevalence of medical trust was 67.4%. Education level was significant and medical trust was stronger among less educated participants (i.e. didn't complete high school, adjusted OR (aOR) = 2.1; 95% CI: 0.96-4.64; p = 0.067; university graduates, aOR = 1.62; 95% CI: 0.99-2.66; p = 0.54, compared to postgraduates). Furthermore, participants who never had a negative experience with healthcare were 3.23 times more likely to have medical trust (aOR = 3.23; 95% CI: 2.33 – 4.49). Moreover, those who do not think they know better about their illness were 2.22 times (aOR = 2.22; 95% CI: 1.69 – 2.91; p < 0.001) more likely to have medical trust.

Conclusions:
The level of medical trust among public sector employees is reasonably high. Factors influencing this were participant's education level, past experience with healthcare, and self-perceived knowledge about respondents' own illness. A study with a representative population sample is needed to verify these results and to derive appropriate recommendations for improvement of healthcare.

Key Words: Community Medicine ; Trust; Doctor-patient relationship ;

Funding Agency: NONE

Community Medicine

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Prevalence of Cardiovascular Risk Factors Among University Students in Kuwait

*Al-Baloul J, Al-Buraiki R, Al-Ebrahim F, Al-Enezi Z, Al-Fadhel N, Al-Hendal S, Kankouni R, Al-Moosawy N, Al-Sayegh A, Al-Shatti M, Longenecker J, Jacob S

Department of Medicine, Kuwait University

Introduction:
Cardiovascular disease (CVD) is the leading cause of death in Kuwait. This trend is linked to increases in cardiovascular risk factors, which are understudied in the younger population. This study aims to assess the prevalence of cardiovascular risk factors among university students in Kuwait.

Methods:
This cross-sectional study sampled 1078 students aged 17-24 years from Kuwait University (KU), Public Authority for Applied Education and Training (PAAET), and private universities. Information regarding cardiovascular risk factors, including smoking, hypertension, obesity, and physical activity were obtained through a questionnaire, in addition to measurements of blood pressure, weight and height. Multivariate logistic regression was used to adjust associations of cardiovascular risk factors (binary independent variables) and potential confounders.

Results:
The mean age was 20.1±1.8 years, 36.7% were male participants, and 63.3% were female participants. The prevalence of smoking was 43.5% and 2.2% among male and female participants, respectively. The prevalence of high blood pressure was 31.4% and 6.1% in male and female students, respectively. High blood pressure was significantly associated with age>22 years (OR=1.6; p=0.04), male gender (OR=6.6; p=<0.001), overweight (OR=1.6, reference group, BMI<25 kg/m 2; p=0.003) and obesity (OR=2.9; p=<0.001). The prevalence of overweight and obesity was significantly higher in male (52%) than female students (38.6%; p<0.001). Overweight/obesity were associated with age>22 (OR=1.7; p=0.001), male gender (OR=6.7; p=<0.001) and high blood pressure (OR=2.1 p=<0.001).

Conclusions:
A high burden of cardiovascular risk factors was observed among university students in Kuwait. Therefore, public health interventions and policies should be developed to reduce these risk factors in younger individuals in order to prevent future CVD events.

Key Words: Cardiovascular risk factors; University students ; Kuwait;

Funding Agency: NONE

Community Medicine

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Fasting Plasma Glucose is Associated with Mild Cognitive Impairment Among Patients with Type II Diabetes Mellitus in Kuwait: A Population based Study

Almekhlef AM*, AlHuwais DH, Alsulaibi DJ, Al-Mojel M, Alomirah M, Alenazi NA, AlAmirah R, Snober S, Alawadhi TF, Albatineh AN

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

Introduction:
Type 2 diabetes mellitus (T2DM) and mild cognitive impairment (MCI) are highly prevalent chronic conditions. Both are associated with social, medical, and economic burdens. The study aims to estimate the prevalence of MCI among patients with T2DM in Kuwait, and model the association between MCI in patients with T2DM and several risk factors like fasting blood glucose (FBG).

Methods:
A cross-sectional study was conducted and data were collected from 343 eligible patients with T2DM aged between 21 and 65 years. MCI as the primary outcome was measured by Montreal Cognitive Assessment (MoCA) tool. Covariates included socioeconomic and demographic, diabetes related and recent lab results. Poisson logistic regression with robust variance-covariance matrix was used to assess the relationship between MCI and an array of covariates.

Results:
The prevalence of uncontrolled diabetes was 52.8%. The prevalence of MCI among T2DM patients was 80.47%. In the adjusted model, FBG was significantly associated with MCI This means, for every one-unit increase in FBG, there was 2% increase in the risk of developing MCI among T2DM patients (APR=1.02, 95%CI: 1.00–1.04, PV=0.014). Current smokers (APR=1.36, 95% CI: 0.95–1.94, PV=0.096) and former smokers (APR=1.47, 95% CI: 1.02–2.13, PV=0.039) are at a higher risk to develop MCI compared to non-smokers. Contrary to our expectations, age and duration of T2DM onset were not significantly associated with MCI.

Conclusions:
The prevalence of MCI among T2DM patients is high in Kuwait. Results indicated that it is not age or duration of having T2DM but controlling blood sugar is key to reduce the risk of MCI. Our findings suggest that smokers and former smokers have higher risk of developing MCI compared to non-smokers. Better physician-patient discussion about importance of controlling blood glucose should be part of any future interventions or policy implementation.

Key Words: T2DM, Mild Cognitive Impairment; Montreal Cognitive Assessment; Fasting

Funding Agency: None

Community Medicine

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Electronic cigarette use and secondhand aerosols exposure in relation to respiratory symptoms among adolescents in Kuwait: a cross-sectional study

Alnajem A, Redha A, *Alroumi D, Alshammasi A, Ali M, Alhussaini M, Almutairi W, Esmaeil A, Ziyab A

Department of Community Medicine, Faculty of Medicine, Kuwait University

Introduction:
Objectives: Globally, a surge in electronic cigarette (e-cigarette) use has been observed in recent years, with youth being the most attracted group. However, respiratory health effects of e-cigarette use and exposure to secondhand aerosols (SHA) from e-cigarettes remain unclear. Hence, this study sought to assess associations between e-cigarettes use and household SHA exposure with respiratory symptoms among adolescents.

Methods:
A school-based cross-sectional study was conducted by enrolling high school students (n=1,565; aged 16-19 years). Participants self-completed a questionnaire on tobacco products use and respiratory symptoms. Current cigarette smoking and e-cigarette use were defined as any use in the past 30 days. Household exposure to SHA in the past 7 days was ascertained. Respiratory outcomes included current (past 12 months) wheezing, study-defined current asthma, and current symptoms of severe asthma. Associations were assessed using Poisson regression with robust variance estimation, and adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) were estimated.

Results:
Among the analytical study sample (n=1345), current e-cigarette use and cigarette smoking was reported by 369 (27.4%) and 358 (26.6%) participants, respectively. Compared to never e-cigarette users and never cigarette smokers, former/current e-cigarette users with no history of cigarette smoking had increased prevalence of current wheezing (aPR=1.49, 95% CI: 1.03-2.15) and study-defined current asthma (aPR=1.66, 95% CI: 1.03-2.68). Moreover, household SHA exposure demonstrated dose-dependent associations with respiratory symptoms.

Conclusions:
E-cigarette use and household SHA exposure were independently positively associated with respiratory symptoms. Such observations indicate that e-cigarette use and SHA exposure negatively impact respiratory health among adolescents; hence, public health strategies are needed to curb the ever increasing use of e-cigarettes.

Key Words: E-cigarette; Respiratory Outcome; Adolescents;

Funding Agency: None

Community Medicine

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Patterns of electronic cigarette, conventional cigarette, and hookah use and related passive exposure among adolescents in Kuwait: a cross-sectional study

Esmaeil A[1], Alshammasi A [1], *Almutairi W [1], Alnajem A [1], Alroumi D[1], Ali M[1], Redha A[1], Alhussaini M[1], Ziyab AH[2]
[1]Faculty of Medicine, Kuwait University, Kuwait City, Kuwait; [2] Department of Community Medicine and Behavioral Sciences, Faculty of Medicine, Kuwait

Introduction:
Use of tobacco products among adolescents is a major global public health concern. This study sought to estimate the prevalence and patterns of e-cigarette use, cigarette smoking, and hookah smoking among adolescents in Kuwait. Moreover, prevalence of exposure to environmental tobacco smoke (ETS) and secondhand aerosol (SHA) from e-cigarettes was estimated.

Methods:
This cross-sectional study enrolled students (n=1,525, aged 16–19 years) attending public high schools across Kuwait using stratified two-stage cluster sampling. Participants completed a questionnaire on tobacco product use. Prevalence estimates of current (past 30-day) use of e-cigarettes, conventional cigarettes, and hookah were assessed. The extent of current (past 7-day) exposure to ETS and SHA in households and public places was determined. Associations were evaluated using Poisson regression with robust variance estimation, and adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) were estimated.

Results:
Overall, 26.4%, 25.1%, and 20.9% of the study participants were current e-cigarette users, current cigarette smokers, and current hookah smokers, respectively. Current use of any tobacco product was reported by 35.1% of the total study participants. Moreover, among the study participants, 41.9% reported current exposure to household ETS, 32.0% reported current exposure to household SHA from e-cigarettes, and 62.2% reported current exposure to ETS and/or SHA in public places. Males were more likely than females to be current e-cigarette users (aPR=5.19, 95% CI: 4.09-6.57), current cigarette smokers (aPR=5.42, 95% CI: 4.26-6.90), and current hookah smokers (aPR=3.43, 95% CI: 2.72-4.32).

Conclusions:
The use of e-cigarettes, conventional cigarettes, and hookah among adolescents in Kuwait is high. The patterns of tobacco product use among adolescents in Kuwait follow international trends, where e-cigarettes are gaining substantial popularity among youth.

Key Words: Electronic cigarettes; Cigarettes; Adolescents;

Funding Agency: None

Community Medicine

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Burnout Among Physicians During COVID-19 Pandemic in Kuwait

Kazem F [1], AlMaateeq B [1], AlAblani D [1], AlMashmoom S [1], AlDraiweesh H [1], AlSenin R [1], AlMandeel B [1], AlHaddad A [1], AlShahabi R [1], *AlDorai A [1], AlAjmi A [1], Shaban W [23]

[1] Faculty of Medicine, Kuwait University; [2] Department of Community Medicine and Behavioral Sciences; [3] Ministry of Health, State of Kuwait

Introduction:
Background and Objectives: The outbreak of coronavirus disease 2019 (COVID-19) was rapidly presented as a worldwide threat. Healthcare workers, given that they are on the frontline facing this crisis, are not only at a higher risk of contracting the infection, but also of being psychologically afflicted. Burnout is a psychological syndrome characterized as a negative emotional reaction to one's job as a consequence of extended exposure to a stressful work environment. Studies show a correlation between physician-associated burnout and quality of life, which may result in poor performance and increased risk of committing medical errors. We aim to investigate the level of burnout among physicians in Kuwait during the COVID-19 pandemic and assess its predictors, as well as measure physicians' quality of life and perception of the quality of care they provide.

Methods:
This cross-sectional study was conducted through an online questionnaire. The survey assessed baseline characteristics and work-related conditions of physicians working in Kuwait. The validated Maslach Burnout Inventory (MBI) and Brunnsviken Brief Quality of Life scale (BBQs) were utilized. Data collected were analyzed using Kruskal-Wallis test, Mann-Whitney U test, and multinomial logistic regression model.

Results:
Responses from 638 participants showed that the median emotional exhaustion (EE), depersonalization (DP), and personal accomplishment (PA) score was 2.89, 1.40, and 4.00 respectively. Bivariate analysis showed a significant association between burnout and professional status, specialty, working hours, and quality of life. Higher burnout and lower quality of life were associated with lower perceived quality of care.

Conclusions:
High burnout was significantly associated with poor quality of life, low satisfaction with level of care provided, and high susceptibility to committing medical errors. Further studies should focus on providing resources and implementing measures to combat burnout.

Key Words: Burnout; Physicians; COVID-19;

Funding Agency: NONE

Community Medicine

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Prevalence and determinants of SARS-COV-2 vaccine hesitancy among health-care workers in Kuwait

*Lari F [1], Algharibah N [1], Alrashidi M [1], Aldhubaiei D [1], Alenezy W [1], Alenenzi M [1], Albdah H [1], Alotaibi N [1], Alhajri M [1], Akhanam R [1], Krisnan A[2], Akhtar S [2]

[1] Faculty of Medicine, Kuwait University; [2] Department of Community, Kuwait University

Introduction:
Objectives: This cross-sectional study aimed to i)assess the prevalence of SARS-CoV-2 vaccine hesitancy, ii)examine the determinants of the SARS-CoV-2 vaccine hesitancy among health care workers HCWs in Kuwait.

Methods:
An e-questionnaire was administered through social media and help of Kuwait Medical Association and 11 hospitals was solicited. The prevalence was computed and a multivariable logistic regression analysis was used to assess its determinants.

Results:
A total of 1057 HCWs responded, mainly Kuwaiti and female. The prevalence of hesitancy among the respondents was 51.7%. The predominant reason for hesitancy was concerns about safety and side effects of the vaccine. The multivariable logistic regression model showed that HCWs without the past year's history of having influenza virus vaccination and/or had no intention of influenza vaccine uptake this year were 4.64 times more likely to be hesitant to get vaccinated against SARS-CoV-2, compared to those who have had vaccinated against influenza virus during the past year and/or intend to have it this year. In comparison with HCWs who were ready to pay, HCWs who were unwilling to pay for this vaccine were 3.80 times more likely to be hesitant for SARS-CoV-2 vaccine uptake. They were also 23.0 times more likely to be hesitant intaking the vaccine, if the vaccination was not mandatory, compared with those who would take the vaccine, even if it was not mandatory. Furthermore, the hesitant respondents were 7.80 times more likely not to recommend the vaccine to others, compared to the non-hesitant respondents.

Conclusions:
This study showed a higher prevalence of SARS-CoV-2 vaccine hesitancy among HCWs in Kuwait. The hesitancy was higher among the HCWs who did not receive or are not planning to receive the influenza vaccine, those who are unwilling to pay for the vaccine, or take it if it was not mandatory, who were unlikely to recommend the vaccine to others, compared to their counterparts in reference categories.

Key Words: Prevalence Kuwait; SARS-CoV-2 vaccine hesitancy ; Health-care workers ;

Funding Agency: None

Cytology

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Atypical Glandular Cells of undetermined significance: Intraobserver reproducibility in cervical smears and Human papillomavirus testing.

Balakrishnan M* [1], Al Baloushi F [1], George SS[2], Mallik MK[1], Kapila K[1]
[1]Department of Cytopathology, Mubarak Al-Kabeer Hospital, Kuwait; [2] Department of Pathology, Faculty of Medicine, Kuwait University.

Introduction:
The diagnostic category of atypical glandular cells(AGC) continues to evolve and remains a diagnostic challenge for both clinicians and cytopathologists. The probable reason for this is that AGC encompasses cellular changes ranging from a variety of benign or reactive processes (75%) to preneoplastic or neoplastic pathology (25%), involving various cell types. The literature reports AGC as an uncommon interpretation in most laboratories, ranging from 0.18 to 0.74%. Our aim is to review the morphological diagnosis of AGC and compare with high risk HPV (HR-HPV) typing.

Methods:
Cases reported as AGC on liquid-based preparations in the cytology laboratory of Mubarak Al Kabeer Hospital were reviewed from August 2018 to July 2019. Two pathologists and a cytotechnician blindly reviewed 149 Papanicolaou smears reported as AGC and categorized them using The Bethesda system (2014) into negative for intraepithelial lesion or malignancy (NILM),Atypical squamous cells of undetermined significance (ASCUS), AGC, low-grade squamous intraepithelial lesions (LSIL) and high-grade squamous intraepithelial lesions (HSIL). Within the AGC category, reviewers tried to specify whether the cells were of endometrial / endocervical/ or glandular (Not Otherwise Specified) and also document whether they favored AGC reactive or neoplastic. The results of HR-HPV testing in these patients was correlated.

Results:
The review diagnosis in 149 reported cases of AGC was NILM in 13(8.7%), AGC in 101(67.7%), AGC-reactive in 29(19.4%), AGC-neoplastic in 1(0.6%), ASCUS with AGC in 4(2.6%) ,ASCUS with AGC -reactive in 1(0.6%). The original diagnosis of AGC was retained in 101(67.7%) cases.HR-HPV positivity was seen in 13 cases of AGC, 4 cases of AGC-reactive and in one case of ASCUS with AGC.

Conclusions:
Eighteen of 136 (13.2%) AGC cases had HR-HPV positivity. Out of the 18 cases, the most prevalent HPV genotype was the HPV viruses other than types 16, 18, 45.

Key Words: Cervical smears; AGC; HR-HPV;

Funding Agency: None

Dentistry

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Patients' Perception and Satisfaction with at-Home and in-Office Teeth Bleaching

Abdelsalam G[1], Alkoot Y[1], Qudeimat M[2]
[1] Faculty of Dentistry, Kuwait University; [2] Department of Developmental and Preventive Sciences, Faculty of Dentistry, Kuwait University

Introduction:
At-home chemical bleaching and in-office light activated bleaching are two methods performed to improve the shade of natural teeth. The aim of this prospective cross-sectional study was to compare at-home and in-office bleaching techniques with regards to satisfaction, teeth sensitivity, and gingival irritation among adults in Kuwait.

Methods:
A validated questionnaire testing patient's satisfaction with teeth color and side effects was distributed to a convenient sample of adult patients attending Kuwait University Dental Clinics, Private Clinics, and Governmental Clinics. Subjects underwent either at-home chemical bleaching or light activated in-office bleaching. The first part of the questionnaire was provided before dental bleaching, the second part two weeks post-bleaching, and the final part one-month post-bleaching. Satisfaction was measured using the Visual Analogue Scale (VAS).

Results:
The study enrolled subjects between the age range of 21 to 40 years with a total sample size of 102 participants. A total of 44(43%) subjects underwent at-home and 58(57%) underwent an in-office bleaching treatment. The satisfaction level increased in both groups at two weeks and one month post-bleaching. In the at-home bleaching group, the side effects were: 25(57%) patients with teeth sensitivity and 11(25%) with gingival irritation at two weeks post treatment compared to 11(25%) with teeth sensitivity and 5(11%) with gingival irritation at one month post bleaching. In the in-office bleaching group, the side effects were: 37(64%) patients with teeth sensitivity and 10(17%) with gingival irritation at two weeks post treatment compared to 19(33%) with teeth sensitivity and 6(10%) with gingival irritation at one month post bleaching.

Conclusions:
No significant differences were noted regarding the patient satisfaction, teeth sensitivity, and gingival irritation between the two bleaching methods when evaluated at baseline, two weeks, and one-month post- bleaching.

Key Words: Bleaching; Satisfaction; Sensitivity ;

Funding Agency: NONE

Dentistry

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Awareness and Behavior of Diabetic Patients in Kuwait Towards Their Oral Health

Alhuwais M[1], Alkanderi A[1], Joseph B[2]
[1] Faculty of Dentistry, Kuwait University, Kuwait; [2] Department of Diagnostic Sciences, Faculty of Dentistry, Kuwait University, Jabriya, Kuwait

Introduction:
The purpose of this study was to demonstrate the awareness and behavior of diabetic patients in Kuwait towards their oral health and to educate these patients to maintain a better oral health-related quality of life.

Methods:
This is a cross-sectional study done through an anonymous questionnaire randomly distributed to adult diabetic patients attending the Ministry of Health (MOH) diabetic clinics and Kuwait University Dental Center (KUDC). The questionnaire included socio-demographic characteristics, the patients' awareness about the relationship between diabetes and other systemic diseases, and the relationship between diabetes and oral health, as well as the patients' awareness towards oral health.

Results:
A total of 206 diabetic patients participated in this study. Results show that more than 75% of the patients were aware of the effect of diabetes on general health, whereas more than 60% were aware of the effect of diabetes on oral health. Regarding oral health behavior, more than 50% of the participants visit the dentist when in pain, the majority brush their teeth at least once a day, and most of them do not floss nor use mouthwash].

Conclusions:
Diabetic patients' level of knowledge about the effect of diabetes mellitus on their general and dental health was found to be good. However, general health awareness was higher than dental health awareness. Awareness and association between diabetes and oral health need to be improved in diabetic patients.

Key Words: Attitudes; Awareness; Diabetic Patients;

Funding Agency: None

Dentistry

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Isolation and characterization of extracellular vesicles from Granulicatella spp

Alkandari S*,Bhardwaj RG, Al-Khabbaz A, Ellepola AN, Karched M
Oral Microbiology Research Laboratory, Faculty of Dentistry, Kuwait University

Introduction:
Granulicatella species are non-motile, non-spore-forming, facultatively anaerobic Gram-positive cocci. They are part of the normal oral flora but cause serious infections such as infective endocarditis. When oral bacteria accidentally enter the bloodstream due to transient tissue damage during dental procedures, they have the potential to attach to the endocardium or an equivalent surface of an indwelling prosthesis and cause infection. Many bacterial species produce extracellular vesicles (EVs) as a virulence strategy. In this study, it is hypothesized that Granulicatella species produce EVs that may play a role in the pathogenesis of Granulicatella endocarditis. Therefore, the objective was to isolate and characterize EVs produced by these species.

Methods:
The reference strains G. adiacens CCUG 27809 and G. elegans CCUG 38949 were cultured on chocolate blood agar with 0.001% pyridoxal hydrochloride at 37 °C and 5% CO2 for 2 days. A loop full of colonies from the CBA plates was inoculated into 100 ml brucella broth supplemented with 0.001% pyridoxal hydrochloride for 2 days. The EVs were isolated using differential centrifugation and filtration protocol and then observed using electron scanning microscopy.

Results:
Vesicles of varying sizes (30-250 nm) were seen in the electron micrographs. For comparison, images of bacterial whole cells and the vesicle preparations were captured at the same magnification of ×10000. Vesicle shape and size was visualized better at a higher magnification of □40000. Currently, we are performing protemic analysis of the vesicle preparation by using mass spectrometry.

Conclusions:
To the best of our knowledge, this is the first research that presented evidence for the hypothesis that Granulicatella species release EVs. Characterization of the EVs may provide new insights into virulence mechanisms of Granulicatella.

Key Words: Membrane vesicles; Granulicatella; Proteomics;

Funding Agency: Kuwait University, Research Sector Grant SRUL 01/14, College of Graduate Studies supportive funding

Dentistry

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Characterization of the Microbiota of Periimplantitis Patients

Abdulrahman S*, Almosawi Z, Alhadher F, Bhardwaj RG, Al Khabbaz A, Karched M
Oral Microbiology Research Laboratory, Faculty of Dentistry, Kuwait University

Introduction:
Microbiota associated with periimplantitis is distinct from chronic periodontitis and is characterized by elevated levels of specific oral bacterial species. Periimplantitis is becoming an important oral infection in Kuwait. No knowledge is available of the microbiota of Kuwait patients with perimplantitis.

Methods:
After screening, a total of 24 subjects comprising 12 patients with peri-implantitis and 12 orally and systemically healthy control subjects were recruited in this study. Subgingival plaque samples were collected using sterile paper points. DNA was purified from the samples and the DNA concentrations were determined using Nanodrop spectrophotometer and qPCR. Targeting the V3-V4 variable region of the 16S rRNA gene, the DNA samples were subjected to metagenomics using the MiSeq NextGen sequencing platform by Illumina.

Results:
qPCR quantitation of the PCR amplicons showed intact 16S rRNA gene target. The libraries for sequencing were of expected size and yield for 16S rRNA gene V3-V4 region. Preliminary sequencing results revealed that the obtained Operational Taxonomic Units (OTUs) consisted of 16 phyla. Bacteroidetes, Firmicutes, Fusobacteria, Proteobacteria, Actinobacteria were the major phyla. Relative genera and species abundances between the periimplantitis and the healthy groups and Analysis of Similarity (ANOSIM) for the taxa is currently being done. Alpha diversity and beta diversity are being carried out on the OTU table. Principal Coordinate analysis based on unweighted Euclidean distances will be performed for beta diversity.

Conclusions:
Comprehensive analysis of the microbiota associated with peri-implantitis may improve our understanding of the role of particular bacterial species in the disease.

Key Words: Periimplantitis; Microbiota; metagenomics;

Funding Agency: Kuwait University, Research Sector Grant SRUL 01/14

Dentistry

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Determination of Endocrine Disruptor Bisphenol-A leakage from Five Different Matrices of Dental Resin-Based Composite Materials

*Kareem FM[1], Al-Tannak NF [2], Alzoubi F [3], Novotny L [2]
[1] Drug and food control-Pricing Department, Ministry of Health, Kuwait; [2] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University, Kuwait; [3] Department of General Dental Practice, Faculty of Dentistry, Kuwait University, Kuwait.

Introduction:
Bisphenol-A (BP-A) derivatives as resins, are common components in dental restorative materials and materials used for orthodontic treatment. However, they are a source for BP-A leakage, which can affect adult and child health as an endocrine disruptor.

Methods:
We have investigated the leaking of BP-A in four selected weights (0.1, 0.2, 0.3, 0.4 mg) of five different resin combinations with four selected weights used in dental restorative materials. The resin combinations were cured with light for 20 seconds and kept in 1 ml of acetonitrile and sonicated for 15 minutes. Samples were subsequently analyzed by UPLC-UV and LC-MS. BP-A was detected in all resin combinations, and in all selected sample weights.

Results:
BP-A was below the limit of quantification (LOQ) in all selected weights of Filtek Z350 XT Universal Restorative System. The results show that BP-A is still released from selected dental resin combinations available in the market despite the general concern about its potential adverse effects.

Conclusions:
The detected amounts of BP-A were within the acceptable levels indicated by the U.S. Environmental Protection Agency and the U.S. Department of Health and Human Services National Toxicology Program and represent a very small contribution to the total BP-A exposure.

Key Words: Bisphenol A (BP-A); UPLC-UV; Dental composites;

Funding Agency: Kuwait university

Dentistry

34

Dental caries experience among adult employees in Kuwait

Nazar H* [1], Shyama M [1], Ariga J [2], Alsumait A [3]
[1] Research and Survey Division, Dental Administration, Ministry of Health, Kuwait; [2]School Oral Health Program, Kuwait-Forsyth, Kuwait; [3] National Oral Health Program, Ministry of Health, Kuwait

Introduction:
The objective of this study was to determine the dental caries experience among adult employees in Kuwait.

Methods:
This cross-sectional study was done among adults working at the Ministries Complex and Housing Authority in Kuwait. A convenience sample (n=1294) of adults participated in this study. Six trained and calibrated dentists examined them. Oral examinations were performed using a mouth mirror and a periodontal probe. Dental caries was scored using WHO diagnostic criteria using the tooth based indices for decayed, missing and filled teeth.

Results:
The survey sample comprised of 1294 adult employees; in which 846 (65.4%) were Kuwaiti, 448 (34.6%) were from other nationalities. Their ages ranged from 19 to 77 years, the mean being 36.2 years, with the gender distribution of 67.6% males and 32.4% females. The mean DMFT in the adults was 10.3. The DMFT among 35 to 44-year-olds was 10.7. Caries experience was lowest in the 19-24 age group (7.8) and highest in the 65-77 age group (18.9) ($p<0.001$). Females had slightly higher caries experience (DMFT) (11.0) than males (10.1) ($p=0.021$) and Kuwaitis (11.1) higher than non-Kuwaitis (8.9) ($p<0.001$). The mean DMFT varied by the income level, dental visits and treatment urgency. The proportion of caries-free adults was 28%. Higher percentage of females; more than one-third (34.6%) were caries-free compared to a quarter of males (24.8%) ($p<0.001$). In multivariate analysis, adults with poor oral hygiene (OR=1.5), occurrence of oral pain (OR=1.4), those with intermediate school or lower level of education (OR=2.6), and those needing urgent dental care (OR=4.6), were significantly associated with caries risk.

Conclusions:
Adults in Kuwait were found to have moderate dental caries. Implementing Geriatric oral health programs is needed and efforts should be laid on introducing oral health promotion activities in workplaces promoting oral hygiene practices among adults in Kuwait.

Key Words: Dental caries; Adult employees; Kuwait;

Funding Agency: None

Diabetes

35

Association between Serum Uric Acid and Glucose Levels in Healthy and Diabetic Individuals

Irshad M [1]*, Taghadom E [1], Al-Ozairy E [12]
[1] Dasman Diabetes Institute, Kuwait; [2] Faculty of Medicine, Kuwait University,

Introduction:
Previous prospective studies of an association between serum uric acid (UA) concentration and diabetes risk are limited and their findings are inconsistent. This study aimed to examine the relationship between UA and fasting blood glucose (FBG) levels among healthy and people with Type 2 diabetes.

Methods:
Medical check-up data from 187 male and 89 females were examined, of them 143 (51.8%) were diagnosed for Type-2 diabetes. All participants were categorized into four quartiles based on UA concentrations and correlated with the FBG, HbA1C, blood urea nitrogen (BUN), creatinine and lipid profile. Independent t-test and Pearson correlation were performed for statistical analysis. P-value <0.050 is considered significant.

Results:
People with diabetes had a lower concentration [mean (± SD)] of UA [292.12 (75.35) µmol/L] compared to healthy [317.74 (± 73.47) µmol/L) individuals (p=0.005). In the correlation study, UA was positively associated with BUN, creatinine, and triglyceride, but negatively associated with FBG, HbA1C and HDL cholesterol concentration (p <0.007). The prevalence of diabetes was decreased with increasing concentration of UA across the quartiles.

Conclusions:
UA levels were high in healthy individuals but declined in people with diabetes with increasing HbA1C and FBG concentrations. An inverse significant association was observed between the levels of UA and the frequency of diabetes in the present study.

Key Words: Type 2 Diabetes; Uric acid; Blood glucose;

Funding Agency: None

Ethics

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Attitudes of Physicians Towards Incentives in Kuwait: Should Incentives Affect Quality of Healthcare?

Al-Mojel M* [1], Ashkanani H [1], AlFahad M [1], AlYaqoub E [1], AlZamel A [2], AlZaabi A [2], Eliwa Y [3], Bouhaimed M [4]

[1]Medical students, Faculty of Medicine, Kuwait University; [2] Trainee Doctors; [3]Assistant Registrar; [4] Department of Community Medicine, Faculty of Medicine, Kuwait University.

Introduction:
It has been hypothesized that incentives are an important factor that predicts the quality of healthcare in a country. Scarce literature is available regarding the attitudes of physicians towards the incentive system in their respective countries, and how incentives affect the quality of work and healthcare delivered to the patients. Objectives: This study aims to assess the current attitudes of physicians towards the salary system in Kuwait, and its relation to the motivation for work and quality of healthcare.

Methods:
This cross-sectional study was conducted amongst physicians across the various hospitals in Kuwait. The study sample included physicians from all general hospitals, as well as Al-Sabah Specialist Hospital. A validated questionnaire was used to collect the data from the physicians. All physicians were approached and the participants were all included as a part of the sample. We didn't use any statistical tests as this is a descriptive result of our exploratory study to highlight the need for thorough follow up with associated factors and larger study sample.

Results:
The acquired sample size was 200 physicians. Our findings suggest that as students, the majority of doctors (79%) were expecting to be paid more than what they are receiving as physicians. Moreover, the majority of doctors agreed (~ 85%) that they should be paid more for their on-call hours. The majority of the physicians (80%) also think that with more incentives, there will be an improvement in the medical research field in Kuwait, and that there will be an improvement in healthcare delivery and quality.

Conclusions:
This pilot study concluded that physicians in Kuwait are not content with their current incentives. Therefore, providing more incentives may improve the quality of healthcare, as well as the interest in research. However, this problem raises the ethical question of why incentives affect the quality of healthcare to begin with.

Key Words: Incentives; Physicians Attitude; Healthcare Quality;

Funding Agency: None

Genetics

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Customized targeted sequencing approach for genetic diagnosis of autosomal dominant polycystic kidney disease: Overcoming PKD1 pseudo-regions and facilitating clinical applications

Ali H*[1,2,3], Al-Mulla F [2], Hussain N [3], Naim M [3], Esbeitah A[4], AlSahow A[5], AbuBaker J[6], Abu-Farha M[6], Ahmad S[7], Harris P[8]

[1]Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, Health Sciences Center, Kuwait University, Kuwait, [2]Department of Genetics and Bioinformatics, Dasman Diabetes Institute [DDI], Dasman, Kuwait, [3]Division of Nephrology, Mubarak Al-Kabeer Hospital, Ministry of Health, Kuwait, [4] Department of Radiological Sciences, Faculty of Allied Health Sciences, Health Sciences Center, Kuwait University, Kuwait, [5] Division of Nephrology, Al-Jahra Hospital, Ministry of Health, Kuwait, [6] Department of Biochemistry and Molecular Biology, Dasman Diabetes Institute, DDI, Dasman, Kuwait, [7] Institute of Ophthalmology, University College London [UCL], London, United Kingdom, [8] Division of Nephrology and Hypertension, Mayo Clinic, Rochester, USA

Introduction:
Autosomal dominant polycystic kidney disease (ADPKD) is the most common renal hereditary disease and characterized by growth of bilateral multiple renal cysts & expansion of kidney size leading to impairment of kidney functions and end-stage renal disease. ADPKD is caused by mutations in PKD1, which accounts for 85% of genetically resolved cases, & PKD2. ADPKD genetic diagnosis is complicated by the fact that PKD1 lies in a segmentally duplicated region, where the first 32 exons are replicated 6 times proximal to PKD1 resulting in 6 pseudo-genes. While Whole Exome Sequencing (WES) technology is becoming more affordable and its use for diagnostic and research purposes more widespread, we have shown previously that such technology produced poor and unreliable results specially over the duplicated region of PKD1 in the form of poor mutation detection sensitivity (7.14%), significantly low reading depth & poor genotype quality score. Our objective is to develop & design a custom targeting approach to efficiently & specifically sequence all coding regions of PKD1 and facilitate clinical diagnostic applications.

Methods:
We developed and designed a PKD1 custom targeted approach to specifically target genuine PKD1 coding regions & avoid the pseudo-regions. We relied on the minor sequence differences between the genuine gene and its pseudogenes. Results from our custom approach were compared to the gold standard sanger sequencing and whole exome sequencing to determine its reliability.

Results:
Our custom targeted approach successfully identified various types of PKD1 mutations in ADPKD patients. Results indicated enhanced reading depth across the whole coding regions of PKD1 and improved genotype quality.

Conclusions:
Our PKD1 custom targeted approach overcame the major limitations observed previously in WES and provide a reliable Next generation sequencing (NGS) based alternative to sanger sequencing for the clinical genetic diagnosis of ADPKD.

Key Words: PKD1; ADPKD; NGS;

Funding Agency: Kuwait University Research Grant SRUL02/13, Kuwait Foundation for the Advancement of Science grant PR17-13MM-07 and Mayo PKD center DK090728.

Genetics

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Vitamin D levels and vitamin D receptor common genetic variants in type-2 diabetes patients from Kuwait

Al-zayed N*[1], Mojiminiyi O[2], Shehab D[3], Al-Temaimi R[2]
[1]Undergraduate Medical Program, Faculty of Medicine, Kuwait University; [2]Pathology Department, Faculty of Medicine, Kuwait University; [3]Medicine Department, Faculty of Medicine, Kuwait University

Introduction:
Introduction and Background: Vitamin D deficiency is associated with an array of chronic non-communicable disorders such as type-2 diabetes (T2D). Several common genetic variants in vitamin D receptor (VDR) gene are reported to influence vitamin D levels. Our aim was to investigate vitamin D levels and VDR genetic variants in T2D patients.

Methods:
In this cross-sectional case-control study two all Kuwaiti cohorts were included; a cohort of well-characterized T2D patients (n=79), and a cohort of healthy controls (n=138). Vitamin D levels were assessed using enzyme linked immunosorbent assay, and VDR genetic variants genotyping was conducted using four Taqman genotyping assays.

Results:
Vitamin D levels were categorized as deficient or sub-optimal in all of the cohorts, however vitamin D levels were significantly lower in the T2D patients (p= 0.012). HbAc1 levels were affected by vitamin D levels when adjusted for age (β= 0.081, 95%CI: 0.064 - 0.1, p <0.0001). Vitamin D levels were high in lower BMI individuals (p= 0.015) after adjusting for sex and age. None of the assessed VDR variants (rs731236, rs2228570, rs1544410, rs7975232) associated with T2D risk. However, low vitamin D levels were marginally influenced by VDR variant rs2228570A when adjusted for sex (p= 0.045) in the overall cohort.

Conclusions:
Vitamin D levels and VDR genetic variants are not associated with T2D risk, but appear to have a role in T2D progression and therefore may have a role in supportive therapy in T2D patients.

Key Words: Type-2 diabetes; Vitamin D; Genetic variant, Kuwait;

Funding Agency: Yes

Genetics

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Associations of Mitochondrial Variants and Haplogroups with Asthma in Kuwait

*Dashti M [1], Alsaleh H [2], Eaaswarkhanth M [1], John SE [1], Nizam R [1], Melhem M [1], Hebbar P [1], Al-Mulla F [1], Thanaraj TA [1]

[1] Genetics and Bioinformatics Department, Dasman Diabetes Institute, Kuwait City, Kuwait; [2] Kuwait Identification DNA Laboratory, General Department of Criminal Evidence, Ministry of Interior, Kuwait City, Kuwait

Introduction:
Asthma is chronic inflammation of the lungs that causes intermittent airflow obstruction which may results in irreversible patho-remodeling of the lungs airways. Asthma, a common and multifactorial disorder, has a prevalence of around 11% among Kuwaiti young adults and is characterised by strong predisposing factor especially from maternal side. In this study, we carried out association tests between maternally inherited mitochondrial haplogroups/variants and the disease status of asthma among asthmatic patients and controls in Kuwait.

Methods:
Indirect mitochondrial genomes of 287 subjects were extracted from exome sequencing data of unrelated native Arab individuals from Kuwait. Mitochondrial variants identification and haplogroup assignments were carried out with Genome Analysis Toolkit and HaploGrep2 tools, respectively. Statistical analysis was conducted to identified associated mitochondrial haplogroups and/or variants (after adjusting for age and sex) with bronchial asthma.

Results:
Maternal haplogroup M had 3-fold increased risk for developing bronchial asthma (OR/95% C.I = 3.371 /1.091-10.416; P = 0.035). 10 variants showed significant differences between asthmatic and control groups that mainly located within nicotinamide adenine dinucleotide dehydrogenase subunits genes and Cytochrome C oxidase genes which control respiratory metabolic system.

Conclusions:
The associated haplogroups and variants with risk of bronchial asthma, identified from the reported discovery cohort need to be replicated in a larger cohort from Kuwait.
NOVELTY OF FINDINGS: To the best of our knowledge, our study is the first to associated mitochondrial DNA variants with asthma in the Middle East.

Key Words: Mitochondrial; DNA; Asthma;

Funding Agency: NONE

Genetics

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Mitochondrial haplogroup J associated with higher risk of obesity in the Middle East

Dashti M[1], Alsaleh H[2]*, Rodriguez-Flores JL[3], Eaaswarkhanth M[1], Al-Mulla F[1], Thanaraj TA[1]

[1]Genetics and Bioinformatics Department, Dasman Diabetes Institute, Kuwait City, Kuwait; [2]Kuwait Identification DNA Laboratory, General Department of Criminal Evidence, Ministry of Interior, Kuwait City, Kuwait; [3]Department of Genetic Medicine, Weill Cornell Medicine, New York NY 10065

Introduction:
Obesity, a multifactorial disorder, is a major risk factor for cardiovascular disorders and diabetes. The Qatari population has a high prevalence of obesity. It has been recognized that maternal contribution to transmission of obesity traits to offspring can be large. In this study, we aim to delineate mitochondrial haplogroups and variants associated with obesity in Qatari population.

Methods:
Mitochondrial genomes of 864 Qatari individuals were extracted from whole exome sequencing data with an average coverage of 77X. Samples were distributed onto two sub-cohorts based on their body mass index (BMI); obese group: BMI ≥ 30 and non-obese group: BMI < 30. We carried out mitochondrial haplogroup profiling followed by testing for association signals for obesity involving mitochondrial haplogroups and mitochondrial variants. We used univariate and multivariate analyses that were adjusted for covariates.

Results:
Qatari individuals with the mitochondrial haplogroup J were found at increased (2-fold) risk for obesity (OR/95% C.I = 1.925 /1.234-3.002; P-value = 0.004), while individuals with mitochondrial X haplogroup were at low risk for obesity (OR/95% C.I = 0.387/0.175-0.857; P-value = 0.019). A set of 29 mitochondrial variants were found significantly associated with obesity even after adjusting for sex, obesity status and haplogroup.

Conclusions:
The study leads to identification of mitochondrial haplogroup of J to be associated with higher risk for obesity in Qatari population. In addition, potential association was also observed between the X haplogroup and low risk for obesity in Qatari population.

Key Words: Mitochondrial; DNA; Obesity;

Funding Agency: NONE

Genetics

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Leptin genetic variant rs7799039 is associated with type-2-diabetes risk in a sampled Kuwaiti population

Lari F*[1], Mojiminiyi O [2], Shehab D[3], Al-Temaimi R[2]
[1] Undergraduate Medical Program, Faculty of Medicine, Kuwait University; [2]Pathology Department, Faculty of Medicine, Kuwait University; [3] Medicine Department, Faculty of Medicine, Kuwait University

Introduction:
Leptin (LEP) is a hormone produced by fat cells and is involved in the regulation of energy balance by inhibiting hunger. Different variants in the leptin receptor gene have been associated with the development of metabolic disorders. Our objective here is to investigate the association of LEP genetic variant rs7799039 with the development of Type-2-diabetes (T2D) and its related clinical characteristics in a Kuwaiti population sample.

Methods:
This case-control study included 151 T2D patients and 100 healthy controls from Kuwait. Blood DNA extraction was carried out, followed by LEP rs7799039 Taqman real-time genotyping polymerase chain reaction.

Results:
LEP variant rs7799039 was found associated with T2D risk (OR: 1.75, 95%CI: 1.2-2.5; p = 0.002). The risk association of rs7799039A with T2D was in an autosomal recessive model (OR 3.09, 95%CI: 1.4 - 6.8; p = 0.004). Intra-T2D cohort analysis revealed that T2D patients of rs7799039AA genotype had higher serum cholesterol levels (5.1 mmol/L) than AG+GG genotypes T2D patients (4.6 mmol/L; β=0.35, 95%CI: 0.072 - 0.614; p = 0.011).

Conclusions:
LEP non-coding variant rs7799039 presents a high risk genetic factor for the development of T2D in the Kuwaiti population, and is associated with cholesterol levels in T2D patients.

Key Words: Type 2 Diabetes; Leptin; Genetic risk, Kuwait;

Funding Agency: None

Genetics

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GeneMatcher facilitates the discovery of SLC38A3 as a cause for developmental and epileptic encephalopathy

*Marafi D [1], Zakkariah M [2], El-Anany E [2] Fatih JM [3], Sites E [4], Kaiyrzhanov R [5], Alsaif HS [6], Al-Maraghi A [7], Al-Owain M [8][9], Guliyeva U [10], Guliyeva S [10], Alhashem AM [11], Danish E [12], Karageorgou V [13], Beetz C [13], Mitani T [3], Du H [3], Rosenfeld JA [3][14], Jhangiani SN [15], Coban Akdemir Z [3][16], Gibbs RA [3][15], Fakhro KA [7][17][18], Sutton VR [3][14][19], Pehlivan D [3][19][20], Maha S. Zaki MS [21], Gleeson JG [22], Maroofian R [5], Houlden H [5], Alkuraya FS [6][9], Posey JE [3], Elsea SH [3][14] and Lupski JR [3][15][19][23]

[1] Department of Pediatrics, Faculty of Medicine, Kuwait University, Kuwait; [2] Section of Child Neurology, Department of Pediatrics, Al-adan Hospital, Riqqa, Kuwait; [3] Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, USA; [4] Division of Molecular and Human Genetics, Nationwide Children's Hospital, Columbus, USA; [5] Department of Neuromuscular Disorders Institute of Neurology, University College London, UK; [6] Department of Genetics, King Faisal Specialist Hospital and Research Center, Saudi Arabia; [7] Department of Human Genetics, Sidra Medicine, Qatar; [8] Department of Anatomy and Cell Biology, College of Medicine, Saudi Arabia; [9] Department of Medical Genetics, King Faisal Specialist Hospital and Research Center, Saudi Arabia; [10] MediClub Hospital, Azerbaijan; [11] Davison of medical genetic and metabolic medicine, department of pediatric, Prince Sultan medical military city, Saudi Arabia; [12] Department of ophthalmology, King Fahad armed forces hospital, Saudi Arabia; [13] Centogene GmbH, Rostock, Germany; [14] Baylor Genetics Laboratory, Houston; [15] Human Genome Sequencing Center, Baylor College of Medicine, Houston, Texas,USA; [16] Human Genetics Center, University of Texas Health Science Center at Houston; [17] Department of Genetic Medicine, Weill Cornell Medical College, Qatar; [18] College pf Healthy and Life Sciences, Hamad Bin Khalifa University, Qatar; [19] Texas Children's Hospital, Houston, USA; [20] Section of Pediatric Neurology and Developmental Neuroscience, Department of Pediatrics, Baylor College of Medicine, USA; [21] Department of Clinical Genetics, Human Genetics and Genome Research Division, National Research Centre, Egypt; [22] Rady Children's Institute for Genomic Medicine, Howard Hughes Medical Institute, University of California, USA; [23] Department of Pediatrics, Baylor College of Medicine, Houston, USA

Introduction:
The solute carrier (SLC) family is a superfamily of more than 400 transmembrane transporters involved in the exchange of amino acids, nutrients, ions, metals, and neurotransmitters across biological membranes. SLCs are highly expressed in mammalian brain. Defects in close to 100 unique SLC-encoding Online Mendelian Inheritance in Man genes are associated with rare Mendelian disorders.

Methods:
Using exome sequencing and family-based rare variant analyses on a Kuwaiti family with two affected siblings with developmental and epileptic encephalopathy (DEE), we identified a shared deleterious homozygous splicing variant in SLC38A3, a sodium-coupled neutral amino acid transporter and a principal transporter of glutamine, the precursor for neurotransmitters GABA and glutamate. Six additional subjects from five unrelated families with biallelic deleterious SLC38A3 variants were identified through GeneMatcher and collaborations with clinical molecular laboratories. Untargeted metabolomic analysis was performed on cerebrospinal fluid (CSF) of one subject.

Results:
Molecular findings included one splicing, one stop-gain, one frameshift and four missense variants. All subjects had global developmental delay, absent speech, and severe axial hypotonia. Visual impairment, seizures and microcephaly were majority (7/8) of affected individuals. Brain imaging was normal in majority (7/8). Brain magnetic resonance spectroscopy showed elevated lactate peak in one subject and low glutamine/glutamate peak in her affected sibling. Metabolomic analysis of a CSF of sample revealed significantly elevated N-acetyl glutamine (Z-score: +3.65), potentially representing a metabolic marker of the disease.

Conclusions:
Our data support the contention that SLC38A3 is a novel disease gene for DEE, and emphasizes the importance of utilizing available international matchmaking tools such as GeneMatcher to facilitate novel disease gene discovery.

Key Words: Solute carrier (SLC); Developmental and epileptic encephalopathy (DEE);

Funding Agency: NHGRI and NHBLI to BHCMG (UM1 HG006542, J.R.L)

Health Economics

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Cost Analysis and Economic Burden of Root Canal Treatment in School Oral Health Programme of Kuwait

Boodai H*[1], Adel L[1], Al-Kanderi B[1], Al-Otaibi J[1], Sugunan B[2], Behzadi S[2], Menoun P [2], Amrizal MN [1], Aljunid SM[1]

[1]Department of Health Policy and Management, Faculty of Public Health, Kuwait University; [2]Capital Center of School Oral Health Program, Ministry of Health, Kuwait

Introduction:
Root canal treatment (RCT) or endodontic therapy involves a sequence of clinical procedures that includes the removal of infected pulp tissue and sealing of decontaminated areas of tooth from further bacterial invasion. The objective of the study is to conduct a cost analysis of RCT procedures and estimate the economic burden from provider's perspective.

Methods:
Cost analysis of RCT using activity-based approach was conducted on patients from Capital Centre of School Oral Health program (SOHP). Information regarding costs was collected through direct observations of patients and staff activities. Additional information was obtained from staff interviews and reviews of patients' medical records.

Results:
A total of 22 (12 males, 10 females) non-medically compromised patients were selected from 170 patients that received RCT from the Centre in October 2019. The mean cost of RCT per patient from MOH perspective was found to be 69.31 KD. The minimum and the maximum costs were found to be 63.80 and 85.60 KD. The highest component of the total cost is on consumables (49.7%), followed by human resources (36.4%), dental equipment (8.0%), sterilization (5.6%) and utility (0.3%). The annual economic burden of RCT in Kuwait, which was bases on the total number of RCTs performed in 2018 were estimated to be 1,995,296 KD. The best and worst-case scenario, bases on lowest and the highest cost per case, for the annual economic burden was estimated to be KD 1,836,674.4 and 2,464,252 KD, respectively.

Conclusions:
The cost of RCT is substantial and comparable with some non-communicable diseases. There is dire need for effective primary prevention and/or early detection and treatment of dental caries so that RCT becomes unnecessary.

Key Words: Cost Analysis; Root Canal Treatment; Economic Burden;

Funding Agency: None

Health Economics

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Prescribing Patterns of Primary Healthcare Physicians in Kuwait: A Preliminary Analysis

Odeh A*[1], Aljunid SM[1], Annaka M[2], Al-Wotayan R[2]
[1]Department of Health Policy and Management, Faculty of Public Health, Kuwait University; [2]Primary Care Department, Ministry of Health, Kuwait

Introduction:
According to the WHO, generic medications are the most common solution for bringing down pharmaceutical expenditures and costs for both the patients and the government. Efforts to increase uptake of generics include policies to support generic substitution and prescribing. This study aims to describe the prescribing habits among physicians in primary healthcare centers in Kuwait.

Methods:
500 hypertension patients who sought treatment at three Primary Care Centers (PHC) from Al Jahra governorate for the duration of October 2018 till December 2018 were randomly selected from the Primary Care Information System database. Only data from these three PHC were made available to the researchers.

Results:
Mean age of the 500 patients was 56.78 (SD=11.842). Out of the 500 patients, 57.2% were female, 63.4% were Kuwaitis and 24% were elderly (age more than 65). 11.6% (58 patients) had other chronic non-communicable comorbidities. The mean number of drugs per prescription was 2.14 (SD=1.515 Range 1 to 9 drugs). The total number of drugs prescribed was 1,072. Only 56 drugs were prescribed by generic name making the generic prescribing rate 5.22%.

Conclusions:
The generic prescribing rate is very low among primary care physicians in these PHC. Active interventions should be carried out to encourage generic prescribing among the physicians in these PHC in order to reduce the overall pharmaceutical expenditure.

Key Words: Prescribing pattern; Primary Healthcare Centres; Physicians;

Funding Agency: None

Health Economics

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Cost Analysis of the Management of Beta Thalassemia Major among Paediatric Cases at NBK Children's Hospital, Kuwait

Odeh A* [1], Buqammaz M [1], Almatrouk J [1], Abdulghafoor K [1], Aldousari A [2], Aljunid SM[1]

[1]Department of Health Policy and Management, Faculty of Public Health, Kuwait University; [2] NBK Hospital, Ministry of Health, Kuwait

Introduction:
Background: The life expectancy of beta Thalassemia Major patients increased with medical advances. Patients therefore, require lifelong blood transfusions and costly iron chelation therapy, the costs of which have never been studied in Kuwait. This study aims to analyse the cost of management of Beta Thalassemia major in paediatric patients in a tertiary level hospital to estimate the burden of management of Beta Thalassemia major.

Methods:
An economic evaluation using Activity-Based Costing approach was conducted in NBK Children's hospital by reviewing medical records of 22 patients receiving blood transfusion in the hospital. Costs were considered from provider's perspective.

Results:
The mean age for the 22 cases was 8.18 year (SD=5.07 years). Of the 22 patients, 13 (59.%) were females, 14 patients were Non-Kuwaitis (63.6%). The total cost per patient was estimated to be on average 1,657.68 KD annually. The cost ranged from 1,422.90 KD in the best-case scenario to 10,071.27 KD in the worst-case scenario annually. Significant components of cost were drugs, investigations, consumables and blood, representing 35.52%, 25.77% 14.88% and 11.69% of the total expenditure respectively. Other cost components were 8.58% administrative, 2.42% equipment and 1.14% for human resource. The economic burden of management of Beta Thalassemia major is estimated to cost on average 787,396.10 KD annually with 675,875.60 KD in the best case and 4,783,949.20 KD in the worst-case scenario.

Conclusions:
The study suggests that the management of Beta Thalassemia major in paediatric has a high economic burden. This study can be used as a basis for estimating the lifelong burden of treating a Beta Thalassemia major patient in Kuwait and be used by policymakers to guide cost containment measures.

Key Words: Cost analysis; Thallassemia; Activity-Based Costing;

Funding Agency: None

Health Policy and Management

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Assessment of Managerial Skills and Leadership Style of Managers in Public Hospitals in Kuwait: A Pilot Study

Abdulghafoor K*[1], Aljunid SM[1]
[1] Department of Health Policy and Management, Faculty of Public Health, Kuwait

Introduction:
Effective management and leadership in healthcare facilities are crucial in facing the current challenges in health systems. This pilot study aims to assess the managerial skills and leadership style of managers in public hospitals in Kuwait.

Methods:
A self-administrated questionnaire was developed and distributed to 60 participants from two public specialized hospitals in Kuwait. A total 34 respondents completed the questionnaire (57% response rate). The questionnaire consists of four parts: demographic characteristics information, service characteristics information, management skills assessment questions (15 questions), and leadership style assessment questions (12 questions). Based on the total score of management skills each category is classified into high management skills and low management skills. The same was done for transformational leadership each category is classified into Transformational and Non-Transformational leadership style.

Results:
Among the 34 responders, 16 (47.1) are males, 22 (64.7%) are first-line management and 27(79.4%) have more than 2 years of working experience as managers. Overall, 21(61.8% of them have high management skill and 18 (52.9%) practice Transformational Leadership style. Only 4 (11.8%) have attended formal training in management. Older managers tend to have higher management skills compared to the younger ones (mean score: 65.8 vs. 56.2; p= 0.034). Management skills are highly correlated with Transformational Leadership style (r=0.677; p <0.001). Gender, working experience and managerial level are not significantly related to management skills and leadership style.

Conclusions:
Kuwait's public hospitals managers have high managerial skills, practice transformational leadership style but most of them has no formal training in management.

Key Words: Management skills; Leadership style; Public hospitals;

Funding Agency: None

Health Policy and Management

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Health Seeking Behaviour of Low Back Pain Patients Attending Physiotherapy Outpatient Clinics in Kuwait Public Hospitals

Al-Deaiji EA*, Aljunid SM
Department of Health Policy and Management, Faculty of Public Health, Kuwait

Introduction:
Low back pain (LBP) is a common medical problem seen in primary care and hospital-based clinics in Kuwait. However, there is no published data on the Health Seeking Behaviour (HSB) and its related factors of patients with LPB either in the community-based or hospital-based settings in Kuwait. The study aimed to assess the health seeking behaviour of Low Back Pain patients attending physiotherapy clinics in Kuwait governmental hospitals.

Methods:
This is a cross sectional study on health seeking behaviour (HSB) among LBP patients attending physiotherapy outpatients clinics in seven Kuwait governmental hospitals. A total of 316 patients were randomly selected to participate in this study. The respondents were interviewed using a 74-item questionnaire that covers patients' socio-demographic data, and assessing patients' knowledge, Self-efficacy, patient's satisfaction on physiotherapy services, Health Seeking Behaviour (HSB), patients' perceptions, and patient's compliance based on Health Belief Model (HBM).

Results:
Most of the respondents were females (66.4%) and age 40 years and above (59.2%). Female patients are more likely to have poor knowledge on LBP than the males (95.7% vs. 84.9%; X2=15.29 p <0.0001). Most respondents have moderate (42.6%) and high self-efficacy (32.3%) on LBP. The perception of the respondents on LBP based on HBM was either low (32.9%) or moderate (57.3%). The overall satisfaction on physiotherapy services among the patients was high (60.1%). The perceived susceptibility related to LBP was moderate (35.4%) or high (55.7%). Females has higher level perceived susceptibility than males (63.8% vs. 39.6%; X2=20.233; p <0.001)

Conclusions:
Hospitals managers should plan and provide an effective health education programme especially among female patients with LBP in order to improve their knowledge and perceptions on this clinical condition.

Key Words: Low Back Pain; Health Seeking Behaviour; Health Belief Model;

Funding Agency: None

Health Technology Assessment

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Implementing HTA in Kuwait -A Qualitative Study Of Perceived Barriers And Facilitators

*Darawsheh B [1], Germeni E [1]
[1]Health Economics and Health Technology Assessment [HEHTA], Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK

Introduction:
Objectives. This study sought to explore main barriers and facilitators to implementing health technology assessment (HTA) in Kuwait from the perspective of key stakeholders.

Methods:
Semi-structured qualitative interviews were conducted with ten key stakeholders: seven healthcare providers working at various departments of the Kuwaiti Ministry of Health (MOH), and three academics with substantial experience in teaching HTA or related fields. Interviews were conducted face-to-face, audio-recorded, and transcribed verbatim. Data were analyzed using an inductive thematic approach.

Results:
Participating stakeholders reported several factors that might act as a barrier to building HTA in Kuwait: minimal awareness of HTA, lack of institutional and human capacity, a fragmented healthcare system, poor communication between researchers and policy makers,the country's wealth, politics, as well as data quality, availability, and sharing. Institutionalizing HTA as a politically empowered body, enforcing its recommendation by law, and benefiting from neighboring countries' experiences were suggested as possible ways to move forward.

Conclusions:
Studies exploring the unique challenges that high-income developing countries may face in implementing HTA are still scarce. The results of this study are consistent with evidence coming from other developing countries, while also suggesting that the abundance of financial resources in the country is a double-edged sword; it has the potential to facilitate the development of HTA capacity, but also hinders recognizing the need for it.

Key Words: Qualitative research; Health technology assessment; Developing country;

Funding Agency: NONE

Medical Education

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Gestational Diabetes Mellitus in Kuwait: Prevalence, Risk Factors and the Role of Physical Activity.

Aburezq MT*[1], AlAlban FB [1], Alabdulrazzaq MS [1], Badr HE [2]
[1]Department of Community Medicine and Behavioural Sciences, Faculty of Medicine, Kuwait University, Kuwait; [2]Faculty of Science, University of Prince Edward Island [UPEI], Canada

Introduction:
Gestational diabetes mellitus (GDM) causes serious complications affecting the mother and fetus. Physical activity (PA) during pregnancy has positive effects on the mother and fetus. The objectives of this study were to assess GMD prevalence in Kuwait, identify its risk factors, and to evaluate its association with PA.

Methods:
A cross-sectional study was conducted among a randomly selected 653 post-partum women from all public maternal centers and five private centers. An anonymous self-administered questionnaire was used to collect participants' socio-demographic data, medical and obstetric history. Pregnancy Physical Activity Questionnaire (PPAQ) was used to assess PA level. PPAQ generates total activity score and seven sub-scores of different types of physical activity.

Results:
Participants' mean age was 30.1±5.3. GMD was diagnosed among 14.1% of participants. Binary logistic regression revealed that poor income, having 2+ chronic diseases, past history of GDM, hypothyroidism, high systolic and diastolic blood pressure during pregnancy were independently correlated with presence of GDM. Overall, means of PPAQ total and sub-scores were low and only PPAQ sub-score -Vigorous Intensity Activity- was significantly higher amid women without GMD than those with. However, PPAQ mean scores showed significant positive correlation with women' BMI pre-pregnancy and birth weight; and a significant negative association with systolic and diastolic blood pressure during pregnancy.

Conclusions:
GDM prevalence was relatively high in Kuwait and correlated with social and medical factors. PA helped in improving gestational blood pressure and birth weight, hence, directing women in reproductive ages towards lifestyle changes programs to educate them about the importance of PA during pregnancy, along with establishing screening programs for early detection and management of GDM, might help reducing the risk of maternal and fetal complications.

Key Words: Gestational diabetes; Physical activity; Gestational hypertension;

Funding Agency: None

Medical Education

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Perception of Negative Teaching Approaches by Clinical Tutors in Kuwait

Eliwa J*[1], Jamal D [1], Alashqar A [1], Qadoura B [1], Bouhaimed M [2]
[1] Ministry of Health, Kuwait; [2] Department of Community Medicine, Faculty of Medicine, Kuwait University

Introduction:
There is abundant literature about the presence of humiliation, intimidation, harassment and even abuse in many medical education settings around the world. These "Negative teaching approaches" are not studied in Kuwait's medical education environment. This study aims to explore medical students' perceptions about negative clinical teaching approaches based on their personal experiences.

Methods:
A self-reporting questionnaire was distributed to a stratified random sample of 152 clinical year students in Kuwait University-Faculty of Medicine (KUFoM). The questionnaire assessed each student's socio-demographic, personal and witnessed experience with negative teaching practices.

Results:
Most students (71%) personally experienced negative teaching from a clinical tutor, including being asked questions intimidatingly (72%), spoken to rudely or with hostility (61%), belittled or humiliated (61%), and yelled at (54%). In addition, 82% of students witnessed other students experience negative teaching, including being yelled at (83%), spoken to rudely or with hostility (81%), asked questions intimidatingly (78%), belittled or humiliated (73%), and cursed or sworn at (32%). Also, 42% of students reported that clinical tutors in both medical and surgical departments used negative teaching equally. All in all, 94% of students wanted an end to these negative teaching approaches.

Conclusions:
Most students in KUFoM had experienced and/or witnessed negative teaching practices used by clinical tutors. Teaching by humiliation is unfortunately present explicitly or in subtler forms than previously thought. Our alarming findings shed light on many issues including and not limited to: undermining a professional and healthy learning environment, student's mental health, and effect on students' learning. Developing and improving a clinical teaching environment, including continuous training and professional development of clinical tutors is warranted.

Key Words: Medical education; Clinical teaching; Perceptions, negative teaching;

Funding Agency: None

Medical Education

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Pediatrics for Medical Students: Comparing Results of Traditional Vs. COVID-19 Pandemic Teaching

Husain EH*[1], Al-Awadi A[2], Al-Qabandi W[3]
Department of Pediatrics, Faculty of Medicine, Kuwait University.

Introduction:
with COVID-19 Pandemic, many medical schools were forced to adopt the online teaching. The traditional teaching of pediatrics consisted of 4-5 hours of bed side teaching in the morning. In the hospital, students were divided into two groups each consisting of 4-5 students. The theoretical and clinical reasoning were given during the afternoon sessions as problem-based learning (PBL) twice a week face to face. During the pandemic, the clinical teaching in hospitals was modified and students were divided in 4 small groups consisting of 2-3 students in each group for 2.5 hours. The problem-based learning (PBL), was conducted on Microsoft (MS) teams. Also, eight interactive tutorials were added online to the teaching activity to support the shorter hours of hospital clinical teaching. The objective of this study is to compare the final exam performance of the students in the traditional teaching and the pandemic teaching.

Methods:
during the academic year 2019-2021, all the sixth-year medical students (65 students in the traditional teaching group and 34 in the pandemic teaching group), had the same final theoretical multiple-choice question exam and OSCE exam (70%). Using IBM SPSS statistic data program v.25, the mean scores and grades of two groups were compared.

Results:
The mean score of the final exam was 56.17±4.8 for the traditional teaching and 58.13± 4.2 in the pandemic teaching (P=0.048). The grades of the students in the traditional teaching vs. pandemic teaching were as follows: A (9% vs. 15%), A- (18 vs. 30%), B+ (35 vs. 18%), B (18 vs 30%), B- (18 vs. 7%), C (2 vs. 0%) with no significant differences between them (P=0.155).

Conclusions:
The mean score of the final exam was higher in the pandemic teaching group which might reflect a more focused and effective teaching. Other studies are needed to investigate other factors that could have contributed to this difference.

Key Words: Pediatrics; COVID-19; Pandemic;

Funding Agency: none

Medical Statistics and Epidemiology

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A Study Analysis of A New Vitiligo Treatment: VT Treatment

*Al-Maosherji Sh [1], Al-Mutawa F [2], Al-Ramthan A [3].
[1] BBA, Department of Accounting, Gulf University for Science and Technology, Kuwait; [2] Ministry of Health-Kuwait; [3] Ministry of Health-Kuwait.

Introduction:
Patent WO20200588091A in vitiligo treatment/methodology is a two-phase patent methodology and compositions for leukoderma treatment, patented by HSC researchers at Kuwait University. It is a day-and-night natural based treatment that uses photosynthesizers followed by antioxidants and tyrosinase cofactors. The study aims to measure the effectiveness of the treatment.

Methods:
The data of this study was extracted from randomly selected patients who used the patented treatment through a questionnaire. The data covers the patient's demographics, vitiligo awareness, previous vitiligo conventional treatments, and the patented treatment evaluation.

Results:
Data collection showed 52% (52 individuals) Female and 48% (48 individuals) Male use the patented treatment in this study. Patients were respectively divided into six groups based on their ages "10-20YO" 15% (15 individuals), "21-30YO" 30% (30 individuals), "31-40YO" 30% (30 individuals), "41-50YO" 18% (18 individuals), "51-60YO" 6% (6 individuals), and "60+YO" 1% (an individual). 28% (28 individuals) were using only topical treatments (corticosteroids or/and tacrolimus), 10% (10 individuals) were using UV radiation therapy only, 10% (10 individuals) were using herbal medications only, 42% (42individuals) were using a combination of UV and conventional topical treatments, 10% (10 individuals) were not using any treatment. 3% (3 individuals) have not followed the prescribed procedure of the patented treatment. 96% (96 individuals) had improved repigmentation, and 4% (4 individuals) had no repigmentation. 12% (12 individuals) have a recurrence after abandoning the patented treatment.

Conclusions:
Patent WO20200588091A showed to be responsive among all age groups. 4% (4 individuals) did not have any repigmentation, and 12% (12 individuals) which had recurrence after abandoning the treatment.

Key Words: Dermatology, Medical Statistics, Epidemiology, Vit; VT Treatment. ; Patent

Funding Agency: NONE

Medicine

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Liver severity based on SCD complications

Al-Ali M* [1], Al-Jafar H [2]
[1] Department of Gastroentrology and liver, Amiri Hospital; [2] Department of Hematology, Amiri Hospital

Introduction:
Sickle Cell disease (SCD) is a congenital disorder. The abnormal haemoglobin S causes voso-oclusive crises that lead to microinfarctions in the liver and other organs. Liver complications in this study related to sickling process and blood transfusion 1.This classification designed to be applicable only for SCD patients to assess their hepatic status severity to provide the best prophylactic and treatment measures.

Aim: This study conducted to create a valid, simple and applicable hepatic severity classification for SCD patients.

Methods:
Diagnosis and confirmation of SCD done by complete blood count, High Performance Liquid Chromatography (HPLC), liver function test, coagulation profile, abdomen us, fibroscan. A score was designed to grade liver disease into mild, moderate and severe. Scoring based on deranged liver function test and liver imaging abnormalities. Classification of SCD hepatic complications severity based on, A- Deranged liver function biomarker, iron overload, virology status, B-Parynchmal imaging abnormality, C- Signs of liver failure, MELD stands for "model for end-stage liver disease." And PELD, for children younger than 12. A MELD score is a number that ranges from 6 to 40, based on lab tests. It ranks your degree of sickness, which shows how much you need a liver transplant.Aug 26, 2018

Results:
This study conducted over 3 years on 150 SCD patients. Normal findings (45) 30%, mild patients (35) 23 %, moderate (63) 42 % and sever (7) 5%. If the patient had liver transplant the patient reassessed based on MELD score. Each patient reassessed annually or whenever required for the incidental clinical situations.

Conclusions:
Liver severity in this study based on sickle cell disease complications. This classification is simple ready to use from the patient follow up investigations. This hepatic severity classification provide a good idea about the liver status for the treating physician.

Key Words: SCD; Liver; Severity;

Funding Agency: Kuwait Foundation For the Advancement of Sciences (KFAS) Funding contract No: P116-13MM-01

Medicine

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Lack of association between protein tyrosine phosphatase non-receptor type N22 gene functional variant R620W and rheumatoid arthritis in Kuwaiti patients

Al-Awadhi AM [1,2], *Haider MZ[3], Sukumaran J[3], Hasan EAH [2], Bartella YA[2]
[1]Department of Medicine, Faculty of Medicine, Kuwait University; [2] Rheumatic Disease Unit, Al-Amiri Hospital, Kuwait;
[3]Department of Pediatrics, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Rheumatoid arthritis (RA) is a chronic inflammatory disorder which is characterized by an inflammation of the synovial tissue of multiple joints leading to pain, deformities and reduced quality of life. Protein tyrosine phosphatase non-receptor type 22 (PTPN22) encodes for lymphoid specific phosphatase (LYP) which is a key negative regulator of T lymphocyte activation and has been associated with a number of autoimmune-related chronic diseases in different populations. The aim of this study was to investigate the association between PTPN22 gene functional variant R620W and rheumatoid arthritis (RA) by comparing its frequency in Kuwaiti RA patients and controls.

Methods:
The study included 175 Kuwaiti RA patients and 214 healthy controls. The diagnosis and classification of RA was based on that described by American College of Rheumatology. The genotypes of PTPN22 gene functional variant R620W were determined by PCR-RFLP and confirmed by DNA sequence analysis in both RA patients and the controls.

Results:
The TT genotype of PTPN22 gene functional variant C1858T was detected in 2/175 (1%) in RA patients compared to 2/214 (1%) in the controls ($p = 0.53$). In contrast, heterozygous CT genotype was detected in 2/175 (1%) RA patients compared to 32/214 (15%) in the controls. The CC genotype was detected in 171/175 (98%) RA patients while it was detected in 180/214 (84%) of the controls. The two RA patients who had the homozygous variant (TT) genotype were both positive for rheumatoid factor (RF) and did not show extra-articular manifestations.

Conclusions:
Our results did not find an association between the PTPN22 gene functional variant R620W and clinical manifestation of RA in Kuwaiti patients. This is in contrast to previous reports from a number of populations in which a positive association with genetic
susceptibility to RA has been reported.

Key Words: Rheumatoid arthritis; PTPN22 gene; Kuwait;

Funding Agency: None

Medicine

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Safety of IV Iron in Chronic Kidney Disease Patients (stages 3-5 ND) in Kuwait

Ali AlSahow*[1], Nawar H [1], Ali H [2], AlHelal B[3], AlQallaf A[4], Alyousef A[5], ElSharkawi Y[3]

[1]Nephrology Division, Jahra Hospital; [2]Department of Medical Laboratories, Faculty of Allied Health Sciences, Kuwait University; [3] Nephrology Division, Adan Hospital; [4] Nephrology Division, Mubarak Hospital, 5 Nephrology Division, Farwaniya Hospital

Introduction:
Iron deficiency is common in CKD pts stages (3-5 ND). IV iron is effective, however, evidence for safety in terms of hospitalization or CKD progression are conflicting. We present data on its use in our CKD pts.

Methods:
Retrospective data collection on CKD pts stages 1- 5 ND who received IV iron from 3 hospitals in Kuwait from Jan/2013 to Jan/2018 & followed changes in eGFR & Hgb over 12-month period.

Results:
Total of 950 CKD pts (stage 1 & 2 = 19%, 3 = 30%, 4 = 28%, 5 ND =20%). Pts were 63% women, 56% diabetics, 23% obese, 37% on RAAS blockers & 42% received ESA. Iron sucrose was used in 75% & ferric carboxymaltose in 25%. Indications were Hgb < 100 (g/L) &/or transferrin saturation (T-Sat) < 30%. During the 5 year period 20% received 2 or more doses of IV iron. Mean initial eGFR (ml/min/1.73) was higher for females (45 vs 31) but mean initial Hgb was lower (106 vs 109). Hgb increased significantly from mean of 107 to 117 in all, from mean of 111 to 121 in group 1 (CKD 1 & 2) & from mean of 104 to 114 in group 2 (CKD 3-5 ND). Initial T-Sat was 13% for group 1 & 16% for group 2. eGFR decline in both groups was nonsignificant (from mean of 41 to 39 in all & from mean of 25 to 24 in group 2). Mean comorbidity score was higher for group 2 (3.4 vs 2.1). No significant difference in change in eGFR & Hgb between groups 1 & 2, between types of IV iron used, between diabetics & non-diabetics & between men & women. eGFR decline in diabetics was nonsignificant (from mean of 30 to 28) & it did not change in non-diabetics (mean of 56). No associated mortality, & no allergic reactions, but, 30% of pts needed hospitalization during 12 months of follow up (6% needed 2 or more hospitalization). Hospitalized pts were older (55 vs 53), had higher mean comorbidity score (3.4 vs 3), lower initial eGFR (43 vs 47) & lower initial Hgb (103 vs 109).

Conclusions:
IV iron is effective in raising Hgb with neutral impact on eGFR, but possibly associated with higher hospitalization.

Key Words: IV Iron; CKD ND; Kuwait;

Funding Agency: None

Medicine

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GFR Decline, hospitalization, and Mortality with Intravenous Iron in CKD patients not on Dialysis

AlSahow A *[1], AlMuhaiteeb A [2], Nawar H [1], AlHelal B [3], AlYousef A [2], ElSharkawiY [3], AlQallaf A [4], AlRajab H [5], Abdallah E [3], Ali H [6][7]

[1] Nephrology Division, Jahra Hospital, Jahra, Kuwait; [2] Nephrology Division, Al-Amiri Hospital, Kuwait city, Kuwait; [3] Nephrology Division, Adan Hospital, Hadiya, Kuwait; [4] Nephrology Division, Mubarak Hospital, Jabriya, Kuwait; [5] Nephrology Division, Farwaniya Hospital, Sabah AlNasser, Kuwait; [6] Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, Health Sciences Center, Kuwait University, Kuwait; [7] Department of Genetics and Bioinformatics, Dasman Diabetes Institute, Kuwait

Introduction:
Iron deficiency is common in chronic kidney disease patients not on dialysis (CKD 1-5ND) and frequently treated with IV iron. However, there is conflicting evidence regarding its safety. We address this issue.

Methods:
Information on demographics, comorbidities, medications and laboratory results were collected for adult CKD 1-5ND patients who received IV iron from January 2013 to January 2018 in 3 public hospitals. Patients were divided into 2 groups. Group 1 had eGFR >60 mL/min and Group 2 had eGFR <60 mL/min. Endpoints were rates of hospitalization, mortality and eGFR changes over 12 months.

Results:
We analyzed 949 patients, 71% were females. Group 1 had 211 (22%) patients and Group 2 had 738 (78%) with mean age of 41 for group 1 and 57 for group 2. Group 2 had greater comorbidity burden. RAAS blockers were used in 67% of group 2 patients and in 33% of group1 patients. Mean IV iron dose was 906 g for group 1 and 1006 for group . Mean initial Hgb was 107g/L (113g/L for Group 1 and 106g/L Group 2; 106g/L for females and 110g/L for males) and improved to 117g/L in all (to 123g/L in group 1 and to 116g/L in group 2). Mean eGFR decreased from 43 mL/min to 41 mL/min (mean eGFR for group 2 decreased from 26 ml/min to 24 ml/min, statistically but not clinically significant). Hospitalization needed for 16% of group 1 versus 31% for group 2 with crude odds ratio for hospitalization 0.42 (95% CI 0.29–0.64) for Group 1 versus 2.33 (95% CI 1.56–3.47) for Group 2 ($p<0.001$). However, adjusted ratio for hospitalization for sex, age, initial eGFR, initial Hgb, and comorbidities was 1.8 (95% CI 0.62–5.36) and 0.55 (95% CI 0.19–1.61) for groups 1 and 2, respectively ($p=0.27$). No reported mortality in the 12-month follow-up.

Conclusions:
IV iron is safe and effective with no impact on eGFR and not association with higher mortality. Hospitalization after adjusting for confounders appears to be related to patients' medical condition (old age, low eGFR, comorbidities)

Key Words: Intravenous Iron; CKD non-dialysis; Hospitalization ;

Funding Agency: NONE

Medicine

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The introduction of the Ideal Family Medicine Clinic (IFMC) at Al-Yarmouk Primary Healthcare Center

Alduwaisan HS, Alhashemi MA, Al-Jareki TY, Alazemi MA, Johny S, *Al-Hilal ME Abdullah Alabdulhadi Primary Healthcare Center [Al-Yarmouk], Capital Governorate, Ministry of Health, Kuwait

Introduction:
All Primary Health Care Centers (PHCCs) in Kuwait provide services that are free of charge, have a walk-in service and are absent of an appointment system. This project focuses on the implementation of the Ideal Family Medicine Clinic (IFMC) model that works directly with an appointment system. This project aims to increase the consultation time (CT), reduce the waiting time (WT) at doctor's office, improve the patients electronic file (EF) and obtain patient and staff satisfaction. Both the Health Service Executive (HSE) model and CIPP (Context, Input, Process and Product) evaluation model were selected as a guide in order to
reach desired outcomes.

Methods:
Mixed methods were used in this project. A patient's satisfaction survey was given to all patients who attend the IFMC. A post-implementation staff survey was given to all the staff who were also involved directly in the current project. An EF audit was developed to check the percentage of completing patient's EFs. The EFs of all patients were analyzed to obtain average WT and CT.

Results:
At the end of the IFMC project, the average WT had decreased from 19.025 to 9.8 minutes. The CT had increased from 3.35 to 14.27 minutes. The percentage of completed EFs rose from 9.6% to 76.7%. Moreover, 95% of patient satisfaction was obtained. Besides those figures, 95.24% of the center's staff were satisfied with the IFMC.

Conclusions:
The IFMC is the first clinic of its kind in Kuwait. We have successfully achieved our objectives. In conclusion, we have shown the effectiveness of the IFMC and strongly recommend applying and evaluating it in other PHCC's.

Key Words: Appointment based clinic; Consultation time; Waiting time;

Funding Agency: None

Medicine

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Asthma patient's profile and perception of asthma control among primary care centers in Kuwait

Alhaddad S[1], Mohammed N[1], Almaateeq B[1], Khazem F[1], Almashmoom S[1], Alhenaidi M[1], Alkharqawi S[1], AlAjmi S[1], Almandeel B[1], Ali A[1], Al-Ahmad M[2]*

[1]Faculty of Medicine, Kuwait University; [2]Microbiology Department, Faculty of Medicine, Kuwait University

Introduction:
Asthma is a common chronic disease, with high morbidity and mortality

Methods:
A real-life, observational, questionnaire based study was conducted in 75 primary care centers in Kuwait, during the period of 2018-2019.The study included centers with chronic disease clinic (asthma clinic), among the six governorates in Kuwait. The questionnaire was distributed equally to GPs and family physicians practicing in each of these centers. Data related to asthma patients who were followed up at primary care centers, and were seen and evaluated up to 7 days earlier, were collected. Data included; demographics, duration of follow up, asthma control, investigations, and GINA (spell out) treatment. Furthermore, information related to treating physician's background and comfort in managing such patients were captured

Results:
Total of 465 patients were screened from 75 primary care centers from six governorates, both by GP and family medicine practitioners. Male patients predominated (56.5%).Patients were stratified as follows according to GINA treatment; (28%) in step 1,136(29%) in step 2,143 (30%) in step 3, 48(10%) in step 4, and 6(1.3%) in step 5. The highest number of severe asthma patients (step 4 and 5) GINA treatment were from Jahra and Farwaniya governorates. Unfortunately, majority of patients (69%) reported asthma exacerbation, 39% had 3 ≥ ER visits,13.5% had 2 ≥ hospital admissions, 46% had 2 ≥ courses of systemic corticosteroids, in the last 12 months. Comorbid conditions were common and 55% had associated allergic rhinitis, and 17% had atopic dermatitis. Spirometry was not available in 96% of cases. Asthma control test was not done in majority (79%) of patients. The majority of practicing physicians (62%) were GPs. None of severe asthma cases were offered referral to specialists

Conclusions:
There are unmet needs in asthma management and education,at primary care level. Proper diagnosis and access to investigational tools are required for proper asthma management

Key Words: Asthma; Primary care; Kuwait;

Funding Agency: None

Medicine

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Effect of Ramadan fasting on weight and Metabolic Parameters in Healthy subjects.

Al-Hilal ME*, Alduwaisan HS, Alhashemi MA, Mojiminiyi OA
[1] Medical Research Department, Abdullah Alabdulhadi Primary Health Center, Ministry of Health, Kuwait; [2] Department of Pathology, Faculty of Medicine, Kuwait University,

Introduction:
Background: Ramadan is the holiest month of the Islamic calendar. Depending on location, Ramadan fasting hours could range from 9 to 22 hours per day. There is tendency to consume special dishes that are high in carbohydrates. Studies in other populations showed that fasting is associated with beneficial effects on cardiovascular disease (CVD) risk factors. There is little evidence on the effect of fasting on health indicators and CVD risk factors among healthy subjects in Kuwait.
Aim: To study the effect of Ramadan fasting on weight and metabolic parameters in apparently healthy healthcare workers.

Methods:
This is an interventional study designed to compare the impact of Ramadan fasting on CVD risk factors. 57 of 145 healthcare workers at Yarmouk PHC participated in the study voluntary according to approved ethical guidelines. We measured height, weight, waist circumference, blood pressure, renal and liver function tests, complete blood count, C-reactive protein and full fasting lipid profile pre- and post- the fasting season. Information on age, gender, physical activity level (pre- during and post-fasting), marital status, level of education, nationality, smoking status, medical history or any medications intake were recorded. Paired samples t-test was performed to compare means of variables.

Results:
Ramadan fasting resulted in a significant ($p< 0.05$) decrease in body weight, (mean, (95% Confidence interval)) (-0.8 (-1.3 to -0.2), BMI (-0.3 (-0.5, to -0.1), Total Protein (-6.6 (-12.6, to -0.6), $p=0.03$), alkaline phosphatase (-4 (-6.1, to -1.9), and significant increase in phosphorus (0.07 (0.03 to 0.1). When stratified by gender, no significant changes were noted in glucose, lipid parameters, uric acid and urea in contrast to findings in other Kuwaitpopulations.

Conclusions:
Contrary to popular belief, fasting during the month of Ramadan has favorable effects on weight and BMI. A longer period study is required to demonstrate other metabolic benefits of fasting.

Key Words: Fasting Ramadan; CVD risk factors; Weight loss;

Funding Agency: None

Medicine

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Brain Severity Based On SCD Complications

Al-Mulla A[1], *Al-Qalaf[2], Al-Jafar H[3]
[1]Depatment of Neurology, Amiri Hospital; [2]Department of Neurology, Mubark Hospital; [3]Department of Hematology, Amiri Hospital

Introduction:
SCD is a congenital disorder, where the abnormal haemoglobin S causes voso-oclusions lead to microinfarction in the brain and other organs. Brain complications in this study based on compilations related only to sickling process 1. Aim: This study conducted to create a valid, simple and applicable brain severity classification for SCD patients.

Methods:
Diagnosis and confirmation of SCD done by complete blood count, High Performance Liquid Chromatography (HPLC). Brain MRI or CT performed for all patients. A score was designed to grade brain and CNS complications into mild, moderate and sever. Scoring based on brain MRI or CT imaging finding related to SCD. Classification of SCD brain complications severity in this study based on three parameters 1-Brain old infarction assigned as mild, 2-Brain apparent infarction assigned as moderate, 3-Cerebral haemorrhage, abscess, malfunction : assigned sever brain complication. The age, gender and the type of SCD implicated as a variant in this study. The degenerative changes not considered as SCD changes.

Results:
This study conducted on 110 SCD patients 65 had MRI and 45 had CT brain. Normal (91) 82% % mild patients (16) 15.3 %, moderate ()% and sever (3) 2.7 %, two of them required liver transplant one needs monthly exchange transfusion. The patients reassessed annually or whenever required for the incidental clinical situations.

Conclusions:
Brain complications severity in this study based on cerebral imaging related to SCD and clinical interview. This classification is simple, valid ready to use. SCD patients with moderate and sever brain complications are 18%, peering in mind that micro-infarcts could be microscopic. This finding requires autopsy histological study to detect the microscopic infarctions which are not visible by MRI nor by CT scan.

Key Words: SCD; Brain; Severity;

Funding Agency: Kuwait Foundation for the Advancement of Sciences (KFAS) Funding contract No: P116-13MM-01

Medicine

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Prevalence of Chronic Obstructive Pulmonary Disease in the Kuwaiti Population

Al-Mutairi S* [1], Ziyab A [2], Mojiminiyi OA [3], Issac JM [1], Alalawi A [4], Dewaysan H [5], Alyan SB [5]

[1] Department of Medicine, Faculty of Medicine, Kuwait University; [2] Department of Community Medicine, Faculty of Medicine, Kuwait University;[3] Department of Pathology, Faculty of Medicine, Kuwait University; [4] Al-Amiri hospital, MOH, Kuwait;

[5] Family Medicine, MOH, Kuwait.

Introduction:
Chronic obstructive pulmonary disease (COPD) is one of the most common respiratory diseases that involve mainly the airways, causing airflow obstruction. It is a progressive disease that is preventable and treatable. COPD is a leading cause of morbidity and mortality worldwide and results in a considerable economic and social burden. However, there are no epidemiologic data on disease burden that can aid health care planning in Kuwait. Therefore, this study sought to estimate the prevalence of COPD among the adult Kuwaiti population.

Methods:
A population-based cross-sectional study was conducted to enroll a random sample of the general Kuwaiti population, aged ≥35 years, using stratified cluster sampling method. COPD status was classified as "COPD population" (subjects fulfilling the symptoms/diagnosis and smoking criteria), "possible COPD" (subjects fulfilling either the symptoms/diagnosis criterion or the smoking criterion), and "no COPD" (subjects fulfilling neither criterion). Prevalence of COPD was estimated in the total study sample and according to sex and age. Chi-square tests were used to assess differences in proportions.

Results:
A total of 1,005 subjects were enrolled, of whom 663 (65.9%) were males. The mean age of the participants was 49.9 years (standard deviation: ±12.8). Of the total participants, 14 (1.4%) subjects fulfilled the criteria for the "COPD population" and 119 (11.8%) were identified as "possible COPD" cases. Male participants compared to female participants were more likely to be in "COPD population" (2.0% vs. 0.3%, p-value < 0.001) and "possible COPD" (16.8% vs. 2.3%, p-value < 0.001). Moreover, the prevalence of COPD showed an increasing trend as age increased.

Conclusions:
Prevalence of COPD among the adult Kuwaiti population is similar to the international estimates. Males and older adults are the mainly affected groups.

Key Words: COPD; prevalence; Kuwaiti;

Funding Agency: KFAS PR 17-13 MM-05

Medicine

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The Prevalence of Adult Congenital Heart disease among the general population in Kuwait

Ashkanani H*[1], Mohiyaldeen I [1], ELshenawy H [2], Alanbaei M [1,2]
[1] Kuwait University, Faculty of Medicine; [2] Department of Cardiology, Chest Diseases Hospital

Introduction:
Adult congenital heart disease (ACHD) is a highly underrepresented entity in medical literature, especially in the Middle Eastern region. This study assessed the prevalence of adult congenital heart disease among the population of Kuwait.

Methods:
A retrospective review of patients being followed up in the Chest Diseases Hospital, Kuwait, was conducted to assess the prevalence of adult congenital heart disease. Patients who fit the inclusion criteria were enrolled in the study. Using the classification system outlined by The American College of Cardiology Task Force 1 at the 32nd Bethesda conference, the severity of the patients' ACHD cases were divided into simple, moderate and complex.

Results:
A total of 611 patients were evaluated over a period of 18 months. The age distribution was similar in all classifications with no statistical difference and there were no statistically significant gender differences in all groups. During the assessment of those who underwent surgical and/or interventional repair, it was found that patients with a moderate classification tended to undergo complete repair more than those in the complex group. Almost 70% of patients with complex cardiac anomalies have undergone either partial or complete repair. The frequency of cardiac defects was also noted. The overall most prevalent cardiac defect was atrial septal defects (ASD). In the simple group, ventricular septal defects (VSD) and ASD were the most prevalent.VSD was still the most prevalent defect in the moderate group when associated with other cardiac lesions. The most prevalent anomaly in the complex group was double outlet right ventricle (DORV).

Conclusions:
Adult congenital heart disease is a large growing entity of heart disease due to advanced repair techniques. The most prevalent heart defect in our study was ASD with all its subtypes. VSD was the most prevalent defect in the moderate group; and DORV was the most prevalent in the complex group.

Key Words: Cardiology; Medicine; Kuwait;

Funding Agency: None

Medicine

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Endoscopic Internal Drainage of Laparoscopic Sleeve Gastrectomy Leaks - Experience With 20 Cases in Kuwait

Siddique I*[1,2]; Al-Sabah S[3,4]; Alazmi W[1,2]

[1] Department of Medicine, Faculty of Medicine, Kuwait University, Safat, Kuwait; [2] Thunayan Al-Ghanim Gastroenterology Center, Al-Amiri Hospital, Safat, Kuwait; [3] Department of Surgery, Faculty of Medicine, Kuwait University, Safat, Kuwait; [4] Department of Surgery, Al-Amiri Hospital, Safat, Kuwait

Introduction:
Leaks and fistulas after laparoscopic sleeve gastrectomy (LSG) are a major complication of bariatric surgery. The endoscopic management strategy for post LSG leaks has evolved from closure with covered self-expanding metallic stents (SEMS) to endoscopic internal drainage (EID). The aim of this study is to report our experience with the management of post LSG leaks treated with EID, either as primary therapy or after failure of closure therapy with SEMS.

Methods:
This retrospective study included all 20 patients treated for post LSG leaks with EID at our center over 30-months. EID was performed by deployment of double pigtail stents across the leak orifice, positioning one end inside the collection and the other end in the lumen of the stomach. The EID internally drains the collection and at the same time promotes leak healing.

Results:
There were 13 (65%) males and 7 (35%) females with a mean age of 34.2 ± 11.6 (range 17-57) years. EID was performed after a mean 62 days after LSG. Three patients had gastrobronchial fistula. 17 (85%) patients had failed some form of prior therapy for the leak. The mean duration of EID was 83 days and 17 (85%) patients had complete healing of the leak with a mean follow up of 16 months. There were 2 (10%) complications of EID and no mortalities.

Conclusions:
EID is an effective and safe endoscopic treatment of leaks following LSG. EID achieves complete drainage of perigastric collections and is well tolerated. It allows early feeding and has fewer complications than other techniques. Long term follow-up confirms good outcomes with no motility.

Key Words: Laparoscopic sleeve gastrectomy; Leak; Endoscopic internal drainage;

Funding Agency: None

Microbiology and Immunology

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Prevalence of Antimicrobial Resistance Among Gram-negative Clinical Isolates from a General Hospital in Kuwait

Alali W* [1], Alfouzan W [2,3], Dhar R [3]

[1]Department of Epidemiology & Biostatistics, Faculty of Public Health, Kuwait University; [2] Department of Microbiology, Faculty of Medicine, Kuwait University; [3]Microbiology Unit, Department of Laboratories, Farwania Hospital, Kuwait

Introduction:
The objective of this study was to determine the antimicrobial resistance profile (ARP) of clinical gram-negative bacterial (GNB) isolates originated from different samples and locations at a general hospital in Kuwait.

Methods:
A retrospective data of antimicrobial susceptibility testing (AST) of GNB from 2017–2018 were extracted from the microbiology laboratory. The data included the patient ID and location, specimen type, bacterial isolates (Acinetobacter spp., Enterobacter spp., E. coli, K. Pneumoniae, and P. aeruginosa), and the ARP. The AST was performed using Vitek 2 and MicroScan systems.

Results:
The ARP of 6,135 GNB isolates was obtained. High resistance (>50%) against ampicillin, aztreonam, ciprofloxacin, trimethoprim/sulfamethoxazole, ceftazidime, cefpodoxime, cefotaxime, and cefuroxime was observed. Low resistance (<10%) was observed against amikacin, amoxicillin/clavulanic acid, ertapenem, fosfomycin, nitrofurantoin, meropenem, piperacillin/tazobactam, and tigecycline. E. coli isolates from medical and surgical wards and P. aeruginosa isolates from pediatric ward had higher resistance prevalence to antibiotics compared to other locations. The highest overall resistance was detected in urine and wound samples. Prevalence of multi-drug resistance among E. coli, K. Pneumoniae, and P. aeruginosa was 50.3%, 51.3%, and 48.7%, respectively.

Conclusions:
Monitoring ASP of common GNB is vital to assess the status and trends of antibiotic resistance at hospital setting, to evaluate effective intervention strategies, and to select appropriate antibiotic treatment.

Key Words: Gram-negative bacteria ; Antimicrobial resistance ; Infections;

Funding Agency: None

Microbiology and Immunology

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Whole Genome Sequence Analysis of Klebsiella Pneumoniae Isolates Belonging to Sequnce Type 231 Harboring Rapidly Disseminating Blaoxa-232 Located on Colkp3 Plasmid in Kuwait

Al Fadhli A*, Jamal W, Rotimi VO
Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Background: Recently there has been a shift to OXA-48-like-producing strains such as OXA-181. OXA-232, another variant of OXA-48 carbapenemase have been reported elsewhere but not in Kuwait.
Objective: To determine the genetic backbone of K. pneumoniae, harboring blaOXA-232 gene, isolated from the rectal swabs of ICU patients in Mubarak Al Kabeer hospital.

Methods:
A total of 41 carbapenem-resistant K. pneumoniae were isolated from the rectal swabs of ICU patients during a period of 1 year. Identified by VITEK-2 and their susceptibility determined by E-test. DNA was extracted from 24-h-old culture using qiaamp DNA mini kit. Whole genome sequencing was carried out using an Illumina MiSeq Platform™. The genome was screened for the presence of insertion sequences, mobile genetics elements, plasmid replicons, resistance genes and Multi-locus Sequence typing using different software tools.

Results:
Two isolates (4.9%), designated MK-4 and MK-5, were OXA-232 producers and harbored several β-lactamase genes, including blaCTX-M-15, blaTEM-1b, blaSHV-100, blaOXA-232 in conjunction with many other resistance genes that confer resistance to aminoglycosides and/or fluoroquinolones. Seven replicon plasmid types namely Col (BS512), Col4401, ColKP3 that carried carbapenemase gene blaoxa-232, IncFIA, IncFIB (pQil), IncFII(K) and IncFII (pAMA1167-NDM-5), were detected in both isolates with one extra IncX4 in MK-5. Both isolates belonged to Sequence type ST231. Insertion sequence ISEcp1 present upstream and transposons, Tn903 and Tn3 were present. The blaoxa-232 plasmid was 100% identical to that of plasmid Pkp3-A bearing blaoxa-181.

Conclusions:
This is the first report of CRKP harboring blaoxa-232 in Kuwait. This gene, being carried on CoLKP3 plasmid, with insertion sequence ISEcp1 located upstream implies that there is the possibility of silent spread amongst the Enterobacteriaceae populations with consequent potentially serious clinical management challenge.

Key Words: Whole Genome Sequence ; Klebsiella Pneumoniae ; Plasmid;

Funding Agency: College of Graduate Studies. Project No YM07/17

Microbiology and Immunology

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Whole genome sequence analysis of non-carbapenemase-producing carbapenem-resistant Enterobacteriaceae isolates from intensive care unit patients in Kuwait

Al Fadhli A*, Jamal W, Rotimi VO
Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Reliance on the presence or absence of resistance genes to categorize strains by targeted PCR may fail to detect resistance associated with porin mutations, efflux pump systems, or de-repression of chromosomal β-lactamase genes.
Aim: To determine the genetic characterization of non-carbapenemase-producing carbapenem-resistant Enterobacteriaceae (CRE) isolated from rectal swabs of intensive care unit (ICU) patients of 4 major hospitals in Kuwait.

Methods:
Detection of genes encoding carbapenem resistance in the CRE isolates carried out by PCR assays and sequencing. The isolates with no detectable genes by PCR were subjected to WGS using an Illumina MiSeq platform.

Results:
Three isolates namely Escherichia coli MK17, Enterobacter cloacae MK176 and Proteus mirabilis Rz140 out of 88 confirmed CRE did not harbor any carbapenemase genes by PCR. WGS revealed that the following in MK17 strain: 2 plasmids, a large chromosome, IncFII plasmid carrying blaCTX-M-15, blaOXA-1 and blaTEM-1B that mediate β-lactam resistance, Acc(3)-lI-d, aadA2, aph(3′)-la, sul2, sul3, dfrA12, qnrS1, floR, cmlA1, tet(A), mph(A), mdf(A), Inu(F), 8 insertion sequences, including ISEcp1, and transposons Tn1000, Tn5403 and Tn1721; it belonged to ST4553. E. cloacae strain MK176, confirmed as ST50, carried a plasmid-mediated AmpC β-lactamase ACT-15 gene on its chromosome, concomitantly with chromosomally located fosA gene, a known mediator of intrinsic fosfomycin resistance. P. mirabilis Rz140 carried a gene mediating extended-spectrum β-lactamases (ESBLs) identified as TEM-1B with other acquired antimicrobial resistance genes.

Conclusions:
Genome mining of the resistant isolates identified previously uncharacterized gene clusters within the genomes of our sequenced strains. These findings should be helpful in determining the key roles of mobile genetic elements in the adaptive evolution and spread of antibiotic resistance.

Key Words: Whole genome sequence ; Enterobacteriaceae; Intensive care unit;

Funding Agency: College of Graduate Studies. Project No YM07/17

Microbiology and Immunology

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Elucidating the virulence genes harbored by carbapenemase- and non-carbapenemase-producing Klebsiella pneumoniae rectal isolates from patients admitted on the intensive care units using whole-genome sequencing.

Al Fadhli A, Rotimi VO, Jamal W*
Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Klebsiella pneumoniae is an opportunistic pathogen that causes severe community and hospital-associated infections. The relationship between resistance and virulence is a complex issue. Limited data is available on the virulence determinants carbapenem-resistant Enterobacteriaceae (CRE) in Kuwait. The purpose of this study was to investigate the virulence genes harbored by K. pneumoniae isolated from rectal swabs of ICU patients in 2 Kuwait teaching hospitals.

Methods:
Six isolates from patients on the ICUs of Al Razi and Mubarak hospitals, designated RZH144, RZH132 RZH108 and RZH173, and MKH381 and MKH347, respectively were subjected to whole genome sequencing (WGS) assays. RZH144 and RZH132 were non-carbapenemase-producing CRE (NCPE) isolates and the remaining 4, RZH108, RZH173, MKH381 and MKH347, were carbapenemase-producing (CPE) isolates. Analysis of the isolates' assembled contigs was carried out using Kleborate on https://pathogen.watch/.

Results:
A NCPE RZ132 K. pneumoniae isolate belonged to ST231-wzi104 and harbored gene clusters encoding the biosynthesis of siderophores aerobactin (iuc5) on 62-3LV. The capsular locus variants were KL51 and O locus O1v2. Another NCPE RZ144 isolate was confirmed as ST43-wzi412 and harbored KL61 and O1v1. Among our CPE, MKH381, MKH347 and RZH173 isolates, harbored 2 virulence loci: ybt14 and iuc5, encoding the siderophores yersiniabactin and aerobactin, respectively. They belonged to ST231-wzi104 and harbored yersiniabactin on ICEKp5. The sequence type of ybt was YbST145-1LV. Strain RZ108 was devoid of virulence loci. Its sequence type was ST15-wzi151 and harbored KL48 and O1V1. ST231 clonal lineage isolates shared common virulence plasmid variants.

Conclusions:
CPE K. pneumoniae ST231 had the highest virulence score and contained iuc5 which was found for the first time in ST231-CPKP isolates in Kuwait. In addition, ST231-CPKP harboring iuc5 has only been found in India, Thailand and Southeast Asia.

Key Words: ICU; Virulence genes ,WGS; Klebsiella pneumoniae ;

Funding Agency: College of Graduate Studies. Project No YM07/17

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Comparative delineation of clonal relatedness and genotypic characteristics of prevalent carbapenem-resistant K. pneumoniae ST231 isolated from patients in high dependency units in Kuwait major hospitals with those from other GCC countries using core genome multi-locus sequence type analysis (cgMLST)

Al Fadhli A*, Jamal W, Rotimi VO
Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Multidrug-resistant (MDR) K. pneumoniae ST231 clone is, until now, geographically confined to South-East Asia. The objective of this study was to investigate the clonal relatedness and genotypes of these isolates from Kuwait and compare with those prevalent in other GCC countries,

Methods:
Previously published method was used to determine the sequence types of the isolates based on whole genome sequence (WGS) data publicly available at www.cbs.dtu.dk/services/MLST. cgMLST was performed on 6 K. pneumoniae isolates obtained from rectal swabs of ICU patients in 2 teaching hospitals in Kuwait along with complete genomes of K. pneumoniae ST231 retrieved from National Center for Biotechnology Information (NCBI) Sequence Read Archive (SRA) with accession number PRJNA544438. A graph was generated using GrapeTree tool with MStree2 method. This Kuwaiti whole-genome project has been deposited at SRA submission /GenBank under accession number SUB7267389.

Results:
Thorough search of the NCBI yielded just one study reporting K. pneumoniae ST231 from Oman. Comparing their isolates with ours revealed that isolates in Cluster 1 from Kuwait were highly related to both OXA-232 producing K. pneumoniae ST231 reference genome to the extent that the isolates from Oman fitted into the cluster with only 24 locus differences. High genetic similarity was observed between 2 isolates originating from Al Razi hospital with 99% identity and an allelic distance of one.

Conclusions:
In this study, OXA-232 is the predominant variant of OXA48-like carbapenemase produced by K. pneumoniae ST231 in Kuwait. The cgMLST suggested similarities between our CRE isolates and the Oman isolates and that the ST231 clone encountered in Kuwait was a recent evolutionary event.

Key Words: cgMLST; WGS; K. pneumoniae ST231 ;

Funding Agency: College of Graduate Studies. Project No YM07/17

Microbiology and Immunology

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Surveillance and molecular characterization of rectal isolates of carbapenem-resistant Enterobacteriaceae (CRE) in Kuwait hospital ICU patients

Al Fadhli A*, Jamal W, Rotimi VO
Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Background: CRE are sometimes described as "nightmare bacteria" whose infections are difficult to treat with mortality rate that can be as high as 50%. Hospitalized patients whose care require support devices and are on prolonged courses of antimicrobial agents are most at risk. Emergence of CRE is now threating Kuwait, similar to many other countries. The objectives were to investigate the prevalence of rectal colonization of ICU patients by CRE and molecular epidemiology of the isolates.

Methods:
Rectal swabs were obtained from every consecutive patient admitted to 7 university hospital ICUs over a 3-year period and processed by standard methods. Susceptibility testing was performed by E-test. Genes encoding carbapenem resistance were detected by PCR and sequencing, clonal relationship was determined by MLST, resistance plasmids and horizontal resistance transfer were investigated by established methods.

Results:
A total of 1406 patients were studied. Ninety (6.4%) of these were confirmed as CRE-positive distributed as follows: Mubarak hospital (6.2%); Adan (4.8%); Al Razi (4.8%); Amiri (2.3%) and Ibn-Sina (1.1%) hospitals; Maternity and Sabah were negative. Of these, 81 (90%) harbored one or more of carbapenemase genes; 62 (76.5%) harbored one single carbapenemase gene and 19 (23.5%) harbored 2 carbapenemase genes. MLST analysis revealed that the K. pneumoniae and E. coli isolates belonged to 7 and 4 different sequence types (ST), respectively. Southern hybridization revealed the most prevalent gene, blaOXA-181, on a large plasmid of ~200 kb, blaNDM-5 gene on 80 kb plasmid. Genes mediating carbapenem resistance were successfully transferred from donors to competent recipients.

Conclusions:
Rectal CRE colonization rates were relatively high and new carbapenemases were present in isolates from Kuwait. The ICU patients seem to be a major reservoir of CRE.

Key Words: CRE ; ICU; MLST;

Funding Agency: College of Graduate Studies and University Research project (YM 07/17)

Microbiology and Immunology

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Whole Genome Sequencing of Clinical Isolates of Gram-negative Bacteria Showing Reduced Susceptibility to Ceftolozane/tazobactam

Alfouzan W* [1,2], Dhar R [2], Mokaddas E [1,3], Ali Abdullah A [4]

[1] Department of Microbiology, Faculty of Medicine, Kuwait University; [2]Microbiology Unit, Department of Laboratories, Farwania Hospital, Kuwait; [3]Microbiology Unit, Department of Laboratories, Ibn Sina Hospital, Kuwait; [4]Microbiology Unit, Department of Laboratories, Amiri Hospital, Kuwait

Introduction:
The treatment options for infections caused by multidrug-resistant (MDR) gram-negative bacteria (GNB) have been limited. Ceftolozane-tazobactam (C/T) has been developed for use against MDR GNB including P. aeruginosa, K. pneumoniae, and E. coli isolates. The purpose of this work was to investigate mechanisms of resistance to C/T utilizing a whole genome sequencing (WSG) approach.

Methods:
Clinical isolates of P. aeruginosa (n=124), E. coli (n=164) and K. pneumoniae (n=133) were tested against C/T and 14 other antibiotics. Strains with C/T MIC values ≥8 µg/mL were further examined by WSG. All analyses were carried out using CLC Genomics Workbench 11.0 (https://www.qiagenbioinformatics.com/).

Results:
Overall 31 strains showing reduced or complete resistance to C/T underwent WGS and analysis. Eight unique sequence types (STs) were identified by MLST for 25 P. aeruginosa isolates. The most frequently observed horizontally-transferred β-lactamases in P. aeruginosa were of class D (n=46) and class B (n=20). Genetic lesions which introduced a premature stop codon in oprD were identified frequently in 17 of 25 isolates. All 3 K. pneumoniae and 3 E. coli strains presented unique sequence types by MLST (n=6). Porin disruption gene lesion was present in ompC-like in one of K. pneumoniae isolates while no lesions were observed in any of E. coli strains. Insertions of amino acids in PBP3-ftsI were identified in all 3 E. coli isolates.

Conclusions:
The WGS of GNB isolates in this collection provided several clues to their mechanism of resistance to C/T. Among the P. aeruginosa isolates, 100% possessed a transmissible β-lactamase whereas in the Enterobacteriaceae C/T resistance could be explained by the presence of β-lactamases, lesions in the ompC-like porins and mutation in PBP3- ftsI. Reduced susceptibility to C/T in some of the isolates may have been caused by higher levels of β-lactamase production, which could have exceeded the available amount of tazobactam.

Key Words: Gram-negative bacteria; Antimicrobial resistance; Whole genome

Funding Agency: None

Microbiology and Immunology

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Evaluation Of In Vitro Antibacterial Activity of Ceftolozane-tazobactam And 15 Comparator Compounds Against A Collection of Gram-negative Bacterial Isolates

Alfouzan W* [1,2], Dhar R [2], Ali Abdullah A [3], Mokaddas E [2,4]

[1] Department of Microbiology, Faculty of Medicine, Kuwait University; [2] Microbiology Unit, Department of Laboratories, Farwania Hospital, Kuwait; [3] Microbiology Unit, Department of Laboratories, Amiri Hospital, Kuwait; [4] Microbiology Unit, Department of Laboratories, Ibn Sina Hospital, Kuwait.

Introduction:
Increasing resistance to antibiotics is seen as a threat to effective therapy in infections caused by Gram-negative bacteria (GNB). The emergence of extended-spectrum beta-lactamase (ESBL)-producing organisms and increasing rates of carbapenem-resistant GNB are often seen in the nososcomial setting resulting in high mortality. Recently developed antibiotic ceftolozane-tazobactam (C/T) has emerged as an effective drug with activity against MDR-GNB. In this study we compared in-vitro activity of C/T with 14 other antibiotics against clinical GNB isolates.

Methods:
A total of 510 isolates were included in the study. MIC values were determined by broth microdilution for amikacin (AN), aztreonam (AZ), cefepime (CEF), cefotaxime (CTX), cefoxitin (FOX), C/T, ceftazidime (CAZ), ceftriaxone (CRO), ciprofloxacin (CIP), colistin (COL), ertapenem (ERT), imipenem (IMP), levofloxacin (LEV), meropenem (MEM), and piperacillin-tazobactam (PIP/TAZ).

Results:
C/T inhibited 95.7% of E. coli compared to 100% susceptibility to MEM, AN and COL, and 90.9% susceptibility to (PIP/TAZ). C/T inhibited 85.7% of K. pneumoniae compared to 94.0%, 95.5%, 94.0% and 75.9% strains showing susceptibility to MEM, AN, COL, and PIP/TAZ, respectively. C/T inhibited 88.8% of other Enterobacteriaceae isolates compared to 97.8%, 98.9%, and 80.9% isolates being susceptible to MEM, AN, and PIP/TAZ, respectively. C/T inhibited 79.8% of P. aeruginosa compared to 59.7%, 78.2%, 66.1% and 68.7% isolates showing susceptibility to MEM, AN, CEF, and PIP/TAZ, respectively. COL was the most active compound tested, with 96.8% of the strains being susceptible.

Conclusions:
E. coli and K. pneumoniae isolates that showed susceptibility to C/T was higher than PIP/TAZ whereas MEM, AN and COL showed better activity. In contrast, C/T showed greater activity against P. aeruginosa strains than MEM, AN, CEF and PIP/TAZ. The only antibiotic that performed better than C/T was found to be COL.

Key Words: Gram-negative bacteria; Antimicrobial resistance; Ceftolozane/tazobactam;

Funding Agency: None

Microbiology and Immunology

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Epidemiology of Major Parasitic Infections in Kuwait

*Al-Awadhi MA [1], Iqbal J [1], Ahmad S [1]
[1] Department of Microbiology, Faculty of Medicine, Kuwait University

Introduction:
Although Kuwait is considered a non-endemic country for most parasitic infections, about 70% of nearly 4.5 million residents are expatriates from endemic Asian and African countries and pose a risk of infection transmission to the local population. Control and prevention measures require adequate surveillance of the prevalence, incidence and relevant demographic data related to parasitic infections. This study retrospectively investigated the epidemiology of five major parasitic infections in Kuwait.

Methods:
Patients' epidemiological data were extracted from the Parasitology Reference Laboratory, Faculty of Medicine, Kuwait University for cysticercosis, malaria, schistosomiasis, cystic echinococcosis (CE) and toxoplasmosis from January 2010 (2013 for malaria cases) to December 2018. Statistical analyses were performed and a P-value less than 0.05 was considered as significant.

Results:
Overall, 2786 of 12227 (22.8%) subjects referred for parasitic infection investigation tested positive. The prevalence rates of malaria (25.9%) and toxoplasmosis (23.9%) were significantly higher than for schistosomiasis (19.0%), cysticercosis (14.7%) or CE (5.8%) ($P<0.001$). Significantly higher prevalence ($P<0.05$) was seen in: 1) cysticercosis cases among younger Kuwaitis, Indians and Nepalis; 2) Plasmodium falciparum & Plasmodium vivax mixed malaria cases among Indian, Pakistani and Afghani males with increasing annual trend; 3) schistosomiasis cases among Egyptian males with decreasing annual trend; 4) CE cases among Syrians and 5) toxoplasmosis cases among female subjects in older age groups (>30 years) from Egypt and Lebanon.

Conclusions:
While toxoplasmosis infection occurs autochthonously in Kuwait, other parasitic infections such as malaria, schistosomiasis and cystic echinococcosis are imported from endemic countries. In addition, taeniasis carriers import the adult tapeworm and are the likely source of cysticercosis in Kuwait.

Key Words: Malaria; Toxoplasmosis; Epidemiology;

Funding Agency: Kuwait University's Research Sector grant no. YM06/14.

Microbiology and Immunology

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An ensemble learning model for rapid and accurate detection of COVID-19

*AlJame M [1], Imtiaz A [2], Ahmad I[1], Mohammed A[1]
[1] Computer Engineering Department, Kuwait University; [2] Faculty of Medicine, Kuwait University

Introduction:
The COVID-19 pandemic has been affecting everyone globally for many months. The current gold standard for diagnosis is the polymerase chain reaction. However, this test can be expensive and requires a swab, which is a procedure that is user dependent. It also requires specialized equipment and has a relatively long turn-around time. Machine learning has been being implemented in medicine for many years now, and the latest concept has been in detecting COVID-19. While many studies have been implementing machine learning to detect COVID-19 using radiological evidence, we wanted to study the ability to detect COVID-19 using simple blood tests.

Methods:
We used de-identified public COVID-19 patient data and fed it into a multilayer machine learning system. Some studies had run the data through only single layer classifier system, but we decided to run the data through two-layer of classifiers to hopefully improve accuracy. Most of the data (80%) was used to train the system what values in the blood tests to give more importance to, and some data (20%) was used to test the system accuracy.

Results:
The multilayer machine learning system had an accuracy of 99.88% when detecting COVID-19, a specificity of 99.99%, and a sensitivity of 98.72%. These values were much higher than if we used only a single layer machine learning system.

Conclusions:
Our system has considerable practicality and is easy to implement. Many countries such as Pakistan have already started using machine learning systems for the rapid and accurate detection of COVID-19 in all healthcare settings. Creating a system that only needs the values of a cheap, rapid, minimally invasive, and non-user dependent blood test means this system can be scaled to many settings, including primary care settings that do not have the availability of advanced imaging such as CT scans. Kuwait can benefit greatly by the implementation of such a system.

Key Words: COVID-19; Machine learning; Integrated diagnostics;

Funding Agency: NONE

Microbiology and Immunology

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Modified Screening Media For Candida Auris

*Alobaid K, Torres L
Microbiology Unit, Department of Medical Lboratories, Chest Diseases Hospital

Introduction:
Candia auris has emerged as a leading nosocomial pathogen characterized by being multidrug resistant and by causing hospital outbreaks. Screening patients and contacts by surveillance cultures is effective tool in controlling spread of this fungus. The aim of this study is to examine the performance of modified Sabouraud media in isolating C. auris as compared to other Candida species.

Methods:
The procedure of preparing the modified SAB salt media is as follows: the media consisted of dextrose 40 g/L, Agar 15 g/L, Mycological peptones 10 g/L and Sodium chloride 100 g/L (10%). 65 grams of medium and 100 grams sodium chloride were suspended in 1 liter of distilled water. It was autoclaved at 121 ℃ for 15 minutes, followed by Cooling down to 45 ℃. Two ml of Gentamicin (80 mg) and 2 ml of penicillin (0.6 g) were added before dispensing, the final pH was 6.0. The modified SAB media were inoculated with common bacterial pathogens: Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Staphylococcus aureus, Enterococcus faecium. The media were also inoculated with six Candida species: C. albicans, C. parapsilosis, C. glabrata, C. tropicalis, C. krusei and C. auris (15 strains each). Turbidity of bacterial and Candida suspensions was standardized to 0.5 McFarland standard using DensiCHEK device (Biomerieux,France).Inoculated media were incubated at 42 ℃ for 48 hours and read daily.

Results:
All bacterial strains failed to grow at 48 hours. All tested Candida species failed to grow at 48 hours incubation except C. auris and C. glabrata.

Conclusions:
Use of modified SAB was successful in preventing the growth of common bacterial pathogens and common Candida species without compromising the growth of C. auris.

Key Words: Candida auris; Nosocomial; Screening;

Funding Agency: none

Microbiology and Immunology

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External validation of a bedside prediction rule among candidemic patients

Alobaid K* [1], Chadha A [1], Alansari A [2]
[1] Microbiology unit, medical laboratory department, Mubarak Alkabeer hospital; [2] Medical department, Mubarak Alkabeer hospital

Introduction:
Candidemia is a recognized nosocomial infection associated with high morbidity and mortality. Diagnosis is difficult, given the low sensitivity and long turnaround time of blood cultures. Clinical prediction rules are attractive options since treatment decisions can be made at the bedside, and they may help clinicians use antifungals more wisely. Most studies on prediction rules were conducted on ICU patients, but none have been tried beyond ICU settings. The aim of this study is to examine the Ostrosky-Zeichner's rule (CPR) on predicting cases of candidemia among hospitalized patients in ICU and non-ICU settings.

Methods:
This is a prospective study on cases of candidemia from March 2017 till May 2018 in a secondary hospital. Another group of patients who developed bacteremia were included as a control group. The inclusion criteria for cases and controls are (1) positive blood culture in a patient with signs of infection, (2) hospital acquired infections. CPR was modified to include ICU and non-ICU patients (mCPR). The rule included presence of central line and/or broad spectrum antibiotic plus two of the following: steroids, immune suppressive agents, pancreatitis, major surgery, total parenteral nutrition or major surgery.

Results:
50 cases of candidemia were found. Two cases were excluded, as they represented contamination. The control group included 60 patients. The sensitivity, specificity, PPV, and NPV of modified CRP were 40.4%, 98.3%, 67%, and 95% respectively. AUC of the ROC is 0.69 (95 % CI is 0.62-0.76). Although 29 cases (59.6%) were not predicted by the rule, 6 patients (21%) among them had femoral catheters.

Conclusions:
Clinical prediction rules are helpful adjunctive tools to rationalize the use of antifungals. The modified CPR has a high negative predictive value that helps in minimizing unnecessary use of antifungals. The presence of femoral catheters in some candidemic patients deserves further evaluation to design a new predictive rule.

Key Words: candidemia ; clinical predictive rule; diagnosis ;

Funding Agency: None

Microbiology and Immunology

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Decreasing Trend in T. gondii Seroprevaloence among Pregnant Women in Kuwait

Alshammarri N*, Iqbal J
Department of Microbiology, Faculty of Medicine, Kuwait University

Introduction:
Background: Primary toxoplasmosis early in pregnancy may cause the development of variable fetal pathologies. Understanding and documenting serological epidemiology and associated risk factors towards T. gondii infection is crucial to offer appropriate
interventions to prevent such fetal pathologies. Aims: This study was carried out to determine the seroepidemiological status and the major risk factors associated with T. gondii infection among pregnant women in the State of Kuwait.

Methods:
This was an observational cross-sectional multi center descriptive study. Blood samples and sociodemographic information was collected from 280 pregnant women attending the antenatal clinics. The blood samples were screened with VIDAS Toxo-IgG/IgM and SERIONE IgG/IgM and IgG avidity assays to detect T. gondii-specific antibodies.

Results:
The overall seroprevalence of T. gondii-IgG and IgM antibodies detected among pregnant women was 12.5% and 2.1% respectively. Only two IgG positive women had low IgG avidity suggesting an acute infection status. No significant association was observed in our study group between seroprevalence and known risk factors for toxoplasma infection.

Conclusions:
This is the first study on T. gondii infection and its associated risk factors among pregnant women in Kuwait. We report a toxoplasma seroprevalence rate of 12.5%, which is one of the lowest in the Middle East. No significant association was observed between T. gondii seroprevalence and known risk factors, which may be due to a higher education level among pregnant women (>94%) that may have changed women's behavior during pregnany thus minimizing the transmission of toxoplasma infection.

Key Words: Toxoplasma gondii; Seroprevalence & risk factors; Pregnant women ;

Funding Agency: CGS & Research sector YM14/17

Microbiology and Immunology

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GM-CSF/Th1/Th2/Th17 cytokines secretion by neutrophils from healthy subjects.

Ashkanany H*[2], Essa S[1], Ali A [2], Al-Nakib W[1], Raghupathy R[1]
[1] Department of Microbiology, Faculty of Medicine, Kuwait University; [2] Medical students, Faculty of Medicine, Kuwait University

Introduction:
Neutrophils, serve as the first line of defense. The aim of this study is to investigate the cytokine production by human neutrophils. This knowledge could help us to know the precise role of neutrophils in sickness and health. This being said, the fact that a single neutrophil, per se, normally produces very little quantities of cytokines does not mean that neutrophil-derived cytokines are not significant. Actually, we should not overlook that neutrophils generally greatly outnumber mononuclear leucocytes in acute infection/inflammatory sites, which suggests that they could indeed command the progress of the following stages based on their secreted cytokine profiles.

Methods:
Seventy-five healthy subjects were enrolled in this study. Neutrophils were isolated by density gradient separation and peripheral blood mononuclear cells (PBMC) were isolated from whole blood by Ficoll-Hypaque density gradient centrifugation. Neutrophils and PBMC were stimulated with phytohaemagglutinin (PHA). After stimulation culture supernatants were collected and evaluated for levels of granulocyte-macrophage colony-stimulating factor (GM-CSF), IFN-α, IFN-γ, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12, IL-17A, and TNF-α cytokines by MACSPlex Cytokine 12, human kit.

Results:
Mean values of GM-CSF, Th1 cytokines (INF-gamma, IL-2, and TNF-α) and Th2 cytokines (IL-6, IL-9, IL-10) were produced by neutrophils at moderate quantities when compared to PBMC. Other Th1 (IFN-α and-12), Th2 (IL-4, IL-5, and IL-10) and Th17 (IL-17A) cytokines were produced at lower mean values by neutrophils when compared to PBMC.

Conclusions:
Our results could clearly identify and characterize cytokines that neutrophils produce. There is a growing interest in classifying and characterizing all the cytokines that neutrophils may produce during infection/inflammation, with the purpose of finding novel targets for therapeutic interventions.

Key Words: Neutrophils; Cytokines; Healthy subjects;

Funding Agency: None

Microbiology and Immunology

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Increase incidence of HIV-1 subtype CRF06_cpx in Kuwait

Chehadeh W*[1], Albaksami O[2], Al-Shammari S[1]
[1]Department of Microbiology, Faculty of Medicine, Kuwait University; [2] Infectious Diseases Hospital, Ministry of Health

Introduction:
Since the first reported case of HIV/AIDS in 1981, an increase in the number of HIV-1 cases has been reported in Kuwait and elsewhere. In previous studies, we reported the detection of more than 10 different HIV-1 subtypes, suggesting the heterogeneity of HIV epidemic in Kuwait. This study aims to provide the first quantitative evidence of the epidemiological evolution of different HIV-1 subtypes in Kuwait over an 8-year period.

Methods:
From January 2012, 375 HIV-1 plasma samples were received for routine HIV-1 genotyping and drug resistance testing. The HIV-1 Pol gene was amplified by RT-PCR, and directly sequenced using Sanger method. A phylogenetic and bootscan analyses were performed for HIV subtype assignment.

Results:
HIV-1 Pol gene sequencing was successful for 326 (87%) out of 375 samples. CRF01_AE was the most prevalent subtype (31.6%), followed by subtypes C (21.2%), B (14.4%), CRF02_AG (9.5%), A (5.2%), CRF06_cpx (4.9%), and CRF35_AD (2.4%). Additional pure subtypes and recombinant forms were detected at very low frequency (< 2%). The analysis of data over the considered period indicates a fluctuation in the incidence of infection with HIV-1 subtypes A, C, CRF01_AE, CRF02_AG, and CRF35_AD, while the incidence of infection with subtype B remained relatively stable. However, the Chi-square trend test results showed a significant increase ($p<0.001$) in the incidence of HIV-1 subtype CRF06_cpx that shares a strong sequence similarity with sequences from West Africa. Such a trend was mirrored by changes in the incidence of HIV-1 infection.

Conclusions:
This study provides the first quantitative estimates on the incidence of HIV-1 infection with different subtypes, thus allowing a comparison between years. Accordingly, there is a major rise in the incidence of infection with HIV-1 subtype CRF06_cpx in Kuwait, highlighting the need for a continuous HIV-1 genotyping for a proper management of the associated burden of disease.

Key Words: HIV-1; Genotyping; Incidence;

Funding Agency: None

Microbiology and Immunology

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Performance comparison of GenoTypeMTBDRsl Version 1 and Version 2 for rapid detection of resistance to fluoroquinolones and second-line injectable drugs among multidrug-resistant Mycobacterium tuberculosis in Kuwait

Al-Mutairi NM*, Ahmad S, Mokaddas EM
Department of Microbiology, Faculty of Medicine, Kuwait University, Jabriya, Kuwait

Introduction:
Fluoroquinolones (FQs) are potent antibiotics against multidrug-resistant Mycobacterium tuberculosis (MDR-TB) and resistance to FQs causes increased mortality. Rapid drug susceptibility testing (DST) against FQs and second-line injectable drugs (SLIDs) is essential for successful treatment of MDR-TB. This study compared the performance of GenoType MTBDRsl version 1.0 (gMTBDRslv1) and GenoType MTBDRsl version 2.0 (gMTBDRslv2) for detecting resistance to FQs and SLIDs among MDR-TB isolates in Kuwait.

Methods:
MDR-TB (n=102) and 50 pansusceptible M. tuberculosis isolates collected during 2006-2019 were tested. Phenotypic DST was performed by MGIT 960 system using SIRE drug kit. Resistance-conferring mutations in gyrA/gyrB for FQs and rrs/eis genes for SLIDs were detected by gMTBDRslv1, gMTBDRsl2 and/or PCR-sequencing of respective genes. Fingerprinting was performed by spoligotyping.

Results:
No mutations were detected in pansusceptible isolates. Among 102 MDR-TB strains, gMTBDRslv1 detected gyrA and rrs mutations in 12 and 8 isolates, respectively. Mutations in embB were also detected among 59 MDR-TB isolates by gMTBDRslv1. gMTBDRsl2 additionally detected gyrB mutations in two and eis mutation in one isolate. No isolate contained a mutation in gyrA/gyrB + rrs/eis genes. Frequency of mutations conferring resistance to FQs and SLIDs was significantly higher among isolates collected during 2013-2019 versus 2006-2012 and among isolates resistant to three/four SIRE drugs versus two drugs. Fingerprinting data showed that most isolates with gyrA/B mutation were distinct strains.

Conclusions:
Although XDR-TB was not detected, an increasing trend in the frequency of pre-XDR-TB was evident in Kuwait. gMTBDRslv2 detected resistance to FQs and/or SLIDs in three additional isolates while gMTBDRslv1 additionally detected resistance to ethambutol in 58% of MDR-TB isolates. Thus, application of both tests is warranted for proper management of MDR-TB patients in Kuwait.

Key Words: Mycobacterium tuberculosis; GenoTypeMTBDRsl; Fluoroquinolone resistance

Funding Agency: Kuwait University Research Sector (KURS), Grant MI 01/18

Microbiology and Immunology

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Epidemiology and microbiological profile of common hospital-acquired infections among patients in the intensive care unit of a general hospital in Kuwait: A retrospective observational study

Dhar R[1], *Alfouzan W [12], Abdo N [34], Al ali W [5]

[1] Microbiology Unit, Department of Laboratories; [2] Department of Microbiology, Faculty of Medicine; [3] Department of Infection Control, Farwania Hospital; [4] Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Zagazig University, Zagazig, Egypt; [5] Department of Epidemiology & Biostatistics, Faculty of Public Health, Kuwait University, Kuwait

Introduction:
Patients admitted to intensive care unit (ICU) are prone to develop nosocomial infections due often to multidrug-resistant (MDR) organisms. The present study was undertaken to explore the epidemiology, microbiology and resistance pattern of common ICU-acquired infections.

Methods:
Retrospective data of surveillance study on healthcare-associated infections for patients admitted to ICU of a secondary care general hospital. The study was carried out for two consecutive years viz. 2018&2019 and the data was recorded using the methods and definitions of the Kuwait National Healthcare-associated infections Surveillance System.

Results:
We analyzed data from 672 &736 patients, admitted to ICU for 3809 and 4113 days during 2018 and 2019, respectively. Of the 89 patients included in this study, 49 developed one HAI in the ICU while 26 and 2 patients presented with 2 & 3 HAIs during the two-year period. The HAIs included blood stream infections (BSI)-42.3%, pneumonia-28.8%, urinary tract infections (UTI)-15.3%, skin &skin structure infections (SSSI)-5.7% and Clostridium difficile infection-3.4%. The overall infection rate was 13.14 per 1000 patient days. The rates for device associated (DA)-HAIs were 6.27 for central line-associated BSI (CLABSI) per 1000 central line (CL)-days, 4.21 for ventilator-associated pneumonia (VAP) per 1000 mechanical ventilator (MV)-days and 1.91 catheter-associated UTI (CAUTI) per 1000 urinary catheter (UC)-days, respectively. Data showed that device use ratios (DUR) for CL, MV and UC were 0.81, 0.74, and 0.98, respectively. Acinetobacter baumannii and Klebsiella pneumoniae were the most common organisms with highest rates of antibiotic resistance.

Conclusions:
Among DA-HAIs CLABSI was found to be most common in our ICU, followed by VAP and CAUTI. Mostly these infections were caused by Gram-negative organisms with A. baumannii and K. pneumoniae being the leading causative agents with high antimicrobial resistance profile.

Key Words: Healthcare-associated infection; Central line-associated bloodstream

Funding Agency: NONE

Microbiology and Immunology

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Evaluation of CODEHOP-mediated PCR in HIV-1 Genotyping

Sarkhouh H A, Chehadeh W
Department of Microbiology, Faculty of Medicine, Kuwait University

Introduction:
Human immunodeficiency virus (HIV) drug resistance poses an important threat to the success of antiretroviral therapy (ART). HIV drug resistance testing is critical for the prevention and management of ART failure . HIV-1 genotyping was previously done by polymerase chain reaction (PCR) amplification prior to gene sequencing using consensus or degenerate oligonucleotide primers. However these primers may fail to detect all HIV-1 subtypes and CRFs described in different regions worldwide. In Kuwait, 18 different HIV-1 subtypes and CRFs were reported with predominance of subtypes B, C and CRF01_AE. It is therefore necessary to design one set of primers that can anneal all or most HIV-1 subtypes and CRFs. In this study, HIV-1 genotyping was assayed using consensus degenerate hybrid oligonucleotide primers (CODEHOPs)-mediated PCR.

Methods:
The nucleotide sequences of the pol region including protease, reverse transcriptase and integrase from 13 HIV-1 M group subtypes (A1, A2, A3, A4, B, C, D, F1, F2, G, H, J and K), and 96 CRFs were aligned using Mega X software. The J-CODEHOP software was used to design the CODEHOPs. The newly designed primers were tested in One-step and Two-step nested/seminested RT-PCR to genotype all HIV-1 subtypes and CRFs reported in Kuwait.

Results:
Two sets of CODEHOPs were designed, one for the amplification of protease and reverse transcriptase region and one for integrase region. Formamide was found to enhance PCR amplification and genotyping of HIV-1. The newly designed CODEHOPs could anneal all available HIV-1 subtypes and CRFs. Results of the direct sequencing of PCR products showed 100% concordance with the HIV-1 subtypes tested.

Conclusions:
Our findings indicate that CODEHOPs can be used in the HIV-1 genotyping. This approach looks easier, faster, cost effective compared to conventional PCR.

Key Words: CODEHOP; HIV-1; Genotyping;

Funding Agency: Kuwait University Research administration. grant number YM 01/19

Microbiology and Immunology

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Prevalence and molecular characterization of rectal carbapenem-resistant Enterobacteriaceae (CRE) isolates from food handlers and infected hospitalized patients in Kuwait.

Moghnai O*, Rotimi VO, Al-Sweih N
Department of Microbiology, Faculty of Medicine, Kuwait University

Introduction:
The emergence of carbapenem-resistant Enterobacteriaceae (CRE) in the community raises concern as little is known about the epidemiology of CRE in the community.

Methods:
Rectal swabs were collected from food handlers (FHs) working in the community (CFHs), healthcare settings (HCFHs) and infected patients and processed by standard methods. Isolates were identified by VITEK 2 and susceptibility testing performed using E-test. Genotypic characterization and clonal relatedness were determined by MLST and DiversiLab® (DL) as well as eBURST analysis.

Results:
A total of 405 FH participants and 92 infected patients were included in the study. Of these, 22 (5.4%) and 84 (91.3%) were colonized by CRE, respectively. The predominant CRE genes harbored by FHs and control isolates were: 19 (86.4%) and 26 (40%) blaKPC, 10 (45.5%) and 44 (67.7%) blaOXA, and 2 (9%) and 24 (36.9%) blaNDM, respectively. MLST analysis of the E. coli isolates from the CFHs and patients genotypically segregated them into distinct 5 and 4 sequence types (STs) and 2 novel STs assigned into 5 clonal complexes (CCs) and 2 novel STs assigned into 4 CCs, respectively. DL typing of Escherichia coli isolates revealed 2 similar isolates recovered from Indian HCFHs and Filipino CFHs. MLST analysis of Klebsiella pneumoniae isolates obtained from HCFHs detected 4 unique STs and 3 novel STs assigned into 5 CCs, the patients' isolates revealed 4 different STs, 2 identical STs and 1 novel ST assigned into 5 CCs. DL typing revealed 2 parent clones detected from Kuwaiti patients admitted into different hospitals.

Conclusions:
Our study revealed moderately and extremely high prevalence of CRE rectal colonizations among FHs and infected hospitalized patients, respectively. These isolates belonged to heterogenic genetic backgrounds suggesting that the isolates might have been imported from diverse geographical regions.

Key Words: Rectal colonization; CRE clonal relatedness; Food handlers and infected

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

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Virulence traits and antimicrobial resistance of Escherichia coli cultured from sewage in Kuwait.

Redha MA*, Al-Sweih N, Albert MJ
Department of Microbiology, Faculty of Medicine, Kuwait University.

Introduction:
Escherichia coli is a normal flora of the colon. Subsets of E. coli are pathogenic. They cause intestinal and extra-intestinal infections. A predominant flora of raw sewage is E. coli. Treated sewage (containing a reduced microbial count) discharged into the environment poses a health risk. The objective of the study was to determine the virulence traits and antimicrobial resistance of E. coli in raw sewage in Kuwait.

Methods:
Raw sewage was collected once every month for 12 months from May 2018 from three sites in Kuwait (Jabryia, Zahraa, and Hateen). A total of 36 samples were cultured on MFC agar. E. coli was identified by API-20E test and confirmed by a uspA PCR. E. coli was typed by the quadruplex phylotyping method of Clermont. Five categories of diarrheagenic E. coli (DEC) were sought by PCR assays. Extraintestinal pathogenic E. coli (ExPEC) was detected by PCR assays of Spurbeck et al and Johnson et al. Disk diffusion test was used to determine susceptibility to 15 classes of antibiotics. Genes mediating resistance to cephalosporins and carbapenems were detected by PCR.

Results:
140 isolates were E. coli. Phylotypes were: 65 (46.4%) group A, 35 (25%) group B1 (25%), 10 (7.1%) group B2, 3 (2.2%) group C, 15 (10.7%) group D, 4 (2.9%) group E (2.9%), and 8 (5.7%) group F (5.7%). 3 (2.1%) isolates were DEC while 57 (40.7%) isolates were ExPEC from group A (30%) and D (24.6%). 131 (93.6%) isolates were multiple drug resistant (MDR), 132 (94.3%) isolates were cephalosporin resistant, and 60 (42.9%) isolates were carbapenem resistant. Among 132 samples resistant to a cephalosporin, blaAmpC was found in all (100%), while blaTEM and blaCTX-M were positive in 53 (40.1%) and 22 (17%) isolates respectively. 9 (6.8%) strains harbored blaOXA-1 gene and 8 had blaCMY-2 (6.1%) gene. All samples were negative for carbapenemase genes.

Conclusions:
There was a high prevalence of ExPEC and MDR E. coli in sewage in Kuwait with the potential to cause human infection.

Key Words: E. coli; Sewage; Antimicrobial resistance;

Funding Agency: The study was funded by College of Graduate Studies, Kuwait University.

Microbiology and Immunology

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Effectiveness of Infection Control Measures on Environmental contamination and Colonization in Patients due to Candida auris in the High Dependency Unit of a Secondary Care Facility in Kuwait

Dhar R* [1], Alfouzan W [1,2], Al Merdasi N [1], Abdullah F [1], Abdo N [3,4], Al Rashidi M [5]

[1] Microbiology Unit, Department of Laboratories, Farwania Hospital; [2] Department of Microbiology, Faculty of Medicine, Kuwait University;[3] Department of Infection Control, Farwania Hospital; [4] 4Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Zagazig University, Zagazig, Egypt; [5] Administration, Farwania Hospital, Kuwait.

Introduction:
Objective: Candida auris is the rapidly emerging pathogenic yeast that can cause outbreaks in the hospital setting with high mortality rate. In this study we describe our approach and experience to control transmission during an outbreak due to C. auris.

Methods:
During a recent outbreak of C. auris infection and/or colonization in the high dependency unit (HDU) of our hospital strict infection and prevention control measures had to be implemented to control transmission. Among others measures, these included intensive screening program for new and in-patients in HDU and the environment of the affected cases and cleaning of patient room environment with detergent and water followed by disinfection with 0.1% bleach (daily and final cleaning).

Results:
Of 318 environmental samples screened from 26.12.2018 till 17.1.2019, 7 tested positive for C. auris. During the outbreak patients in the HDU were screened for colonization in nares, axilla and groin with C. auris from 1.1.2019 till 30.6.2019. Of a total of 624 patients screened 100 tested positive for C. auris with 48, 36 and 16 strains isolated from axilla, groin and nares, respectively. Following implementation of strict ICM and cleaning of environment with mops soaked in a solution containing 25 g of clorox, releasing 5000 ppm of chlorine, thrice in 24 h the repeat cultures of the positive environmental surveillance cultures yielded no growth of C. auris.

Conclusions:
Since there are no established patient decolonization or environmental cleaning methods in controlling C. auris transmission within healthcare facilities, many major health organizations have issued guidelines and recommendations for management of its spread. However, while we found the PAHO/WHO recommendation of cleaning with "soap and water followed by disinfection with 0.1% bleach effective for environmental surfaces, use of 2% chlorhexidine gluconate did not help in reducing the colonization rate among patients admitted in the HDU.

Key Words: Candida auris; Infection control; Environmental screening;

Funding Agency: None

Microbiology and Immunology

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Comparison of Molecular and Phenotypic Methods for Detection and Characterization of Antimicrobial Resistance in Selected Gram-negative Bacteria

Dhar R* [1], Alfouzan W [1,2], Sevilla M [1]

[1] Microbiology Unit, Department of Laboratories, Farwania Hospital, Kuwait; [2]Department of Microbiology, Faculty of Medicine, Kuwait University.

Introduction:
Objective: The aim of this study was to evaluate & compare the performance of 3 systems utilizing different methodology principles for identification of phenotypic and genotypic markers for extended-spectrum beta-lactamase (ESBL) and carbapenem resistance (CR) in selected Gram-negative bacteria (GNB).

Methods:
A total of 140 selected multidrug-resistant GNB isolates, which included P. aeruginosa (n=49), K. pneumoniae (n=40) & E. coli (n=51) were tested in parallel on 3 automated systems (Vitek 2, Phoenix, and MicroScan) for identification and antimicrobial susceptibility profile (ASP). These strains were examined for ESBL and CR associated genes e.g CTX-M, KPC, NDM, IMP, OXA-48-like, & VIM by three commercial molecular methods viz. GeneXpert, Easyplex & NG Biotech for NG-Test Carba 5, NG-Test CTX-M multi & NG-Test MCR-1, which are qualitative rapid immunoassay tests for detection of CR, ESBL & colistin resistance genes, respectively.

Results:
The ASP of these GNB isolates derived from Phoenix, Vitek 2, & MicroScan were comparable. Each of the phenotypic tests detected CR among 45, 17 and 3 P. aeruginosa, K. pneumoniae and E. coli isolates, respectively. ESBL was detected in 23 and 39 of K. pneumoniae and E. coli strains, respectively. Among 45 P. aeruginosa isolates Xpert detected VIM in 30, NDM in 3 & OXA-48 in 1 strain. In comparison only VIM was detected in 26 & 28 P. aeruginosa isolates by Easyplex & NG- Test Carba 5, respectively. Amplex & NG- Test CTX-M Multi detected CTX-M in 37 & 38 K. pneumoniae isolates, respectively. Among E. coli strains CTX-M was detected in 40 and 42 isolates by Amplex and NG- Test CTX-M Multi, respectively. None of the isolates tested positive for mcr-1 enzyme by NG-Test MCR-1.

Conclusions:
Although all phenotypic methods and genotypic assays were found to be comparable, the results would be more reliable if reference P. aeruginosa, K. pneumoniae and E. coli strains with known carbapnemase, CTX-M and mcr-1 genes were tested as controls.

Key Words: Gram-negative bacteria; Phenotypic identification; Genotypic assay;

Funding Agency: None

Microbiology and Immunology

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Three years retrospective epidemiological survey of community Urinary Tract Infections

Draghijeva EA*, Kostova EA
London Hospital, Kuwait

Introduction:
Urinary Tract Infections (UTIs) are common and the causative uropathogens exhibit changing resistance patterns.Adequate empirical antimicrobial treatment is possible only if resistance of the UTI pathogens in region is well established.The study was undertaken to determine the microbial etiology and antibiotic resistance of the uropathogens isolated from UTIs in one general hospital in Kuwait.

Methods:
During 2016-2019 epidemiological study involved 333 women, 50 men and 22 children with acute UTI.The identification of isolated bacteria performed with API system-BioMerieux and their antibiotic resistance-by Kirby-Bauer method.The results were interpreted according to CLSI guidelines.

Results:
405 urine isolates were collected. The first group of isolated bacteria was Enterobacteriaceae (73,09%), followed by Gram-positive cocci (22,72%), mixed cultures (2,23%) and Candida spp. (1,96%). The cumulative results of the uropathogenic bacteria and their resistance rates were represented.

Conclusions:
The main problem with uropathogens in our hospital is a high level of resistance to amoxicillin/clavulanate and trimethoprim/sulfamethoxazole. They should no longer be used as drugs of choice in the treatment of UTIs. The most effective antibiotics for the empirical treatment of acute community-acquired UTIs seems to be nitrofurantoin, cefaclor, aminoglycosides.

Key Words: Uropathogens; Empirical therapy; Antimicrobial resistance;

Funding Agency: None

Microbiology and Immunology

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Assessment of Immune Status against Measles, Mumps, and Rubella in Young Kuwaitis: MMR Vaccine Efficacy

Madi N*[1], Altawalah H[1], Alfouzan W[1], Al-Nakib W[1], Al-Roumi E[2], Jeragh A
[1] Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait; [2] Al-Jahra Hospital, Ministry of Health, Kuwait; [3] Al-Adan Hospital, Ministry of Health, Kuwait

Introduction:
Seroprevalence studies on measles, mumps and rubella IgG antibodies after the implementation of measles-mumps-rubella (MMR) vaccine are lacking in Kuwait. This research is an age-stratified serological study to assess the herd immunity to measles, mumps and rubella among the young Kuwaiti population to evaluate the effectiveness of the MMR vaccine.

Methods:
IgG antibody titers to mumps, measles, and rubella were determined with commercial immune-assay in serum samples of 1000 Kuwaitis aged 5-20 years.

Results:
The highest level of seropositivity was to measles (94.6%), which was significantly higher in females than in males. The highest seronegativity was for mumps (29%). The percentage of the young Kuwaiti population who were serologically positive for all the component of the MMR vaccine was 47%, and 2% of the individuals were without any protective antibodies to measles, mumps and rubella. Females aged 5-10 years were best protected to rubella; however, seronegativity in 8.2% of 11-20-year-old females makes them vulnerable to rubella virus infection and congenital complications during pregnancy.

Conclusions:
The study provided insight into the effect of the MMR vaccine on seroprevalence of antibodies against measles, mumps and rubella in Kuwait, which will contribute to the global knowledge base of vaccine coverage and help to inform elimination strategies. The findings strengthen the need for a third dose of MMR vaccine and catch-up campaigns for the young Kuwaiti population to increase vaccination coverage and prevent waning immunity, especially among those who received only one dose of the vaccine during childhood.

Key Words: Measles; mumps; rubella; MMR vaccine; Kuwait;

Funding Agency: Kuwait Foundation for the Advancement of Sciences (KFAS), project code: PR17-13MI-01

Microbiology and Immunology

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Analysis of whole-genome sequence data for characterization of Brucella melitensis isolates

Mustafa AS*[1], Khan MW [2]
[1] Department of Microbiology, Faculty of Medicine; [2] OMOCS Research Unit, Health Sciences Centre, Kuwait University, Jabriya, Kuwait

Introduction:
Brucellosis is present world-wide with high prevalence in Kuwait. The identification of Brucella genotypes is required to implement proper control measures. Analysis of whole-genome sequence data has shown its potential as an epidemiological typing tool. In this study, Kuwaiti Brucella melitensis isolates were analyzed using whole genome-based approaches for virulence factor, genotypes and the possible origin.

Methods:
The nucleotide fasta, amino acid fasta, and raw fastq files, corresponding to five Kuwaiti B. melitensis strains, were downloaded from NCBI repository. A nucleotide fasta file of 31 other strains of B. melitensis and one B. abortus were downloaded from NCBI genomes. In silico techniques were used to identify the sequences for virulence factors and genotypes using multi-locus sequence typing (MLST) and whole genome single nucleotide polymorphism (wgSNP).

Results:
All 58 virulence factors present in the database were found in the samples with at least 99 percent similarity with the standard B. melitensis 16M strain. Based on MLST, there was no particular type or subtype which was prevalent in the Mediterranean region, while the subtype 8 was most common among all the strains. Resolution of 21 genes MLST was better than 9 genes MLST. wgSNP analysis revealed that out of five Kuwaiti strains, four strains had close proximity with the strains of Iran, Iraq, Jordan, Afghanistan, and Turkmenistan, while one strain was found very close to Somali strain.

Conclusions:
The results show that whole-genome sequence data can be used to apply classical molecular techniques in silico for the rapid classification of Brucella into genotypes. Furthermore, wgSNP analysis can prove to be an effective tool in connecting the dots of missing information about B. melitensis infection.

Key Words: Brucella; Whole-genome sequnce; Analysis;

Funding Agency: Kuwait University Research Sector grants MI04/15 and SRUL02/13

Microbiology and Immunology

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Microbiological and clinical characteristics of sternal wound infections following cardiac surgery in a teaching hospital in Kuwait: A 5-year retrospective study

Nair D*[1], Singapurwala MF[2], Benwan KA[1,3]
[1]Department of Microbiology, Al-Amiri Hospital, Kuwait; [2]Department of Cardiac Surgery, SACC- Al-Amiri Hospital, Kuwait; [3] Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Sternal wound infections (SWI) following cardiac surgery form a fraction of surgical site infections (SSI) which are among the most common healthcare associated infections. Although the incidence is in the low range of 0.4-4%, the morbidity and mortality attributed to SWI are high.
Objective
To study incidence, microbial aetiology, risk factors and outcome of SWI that followed cardiac surgery in our hospital.

Methods:
A retrospective, single centre study involving 833 patients who underwent cardiac surgery from January 2012 to December 2016 was conducted in Al- Amiri hospital, Kuwait. Microbiological data were retrieved from laboratory computers, and clinical details from patient files. Cases were analysed with respect to age, sex, microbial aetiology, risk factors, and outcome. Statistical study was done using SPSS statistical package.

Results:
Incidence of SWI was 2.1%. Predominant micro-organisms isolated were Staphylococcus epidermidis (27.7%) and Pseudomonas aeruginosa (27.7%). Commonest risk factor was diabetes mellitus, 88.9% cases. 72.2% cases had a hospital stay for more than 10 days, median length of hospital stay following infection being 13.50 days. 30 day mortality outcome was zero.

Conclusions:
SWI leads to bacteremia, sepsis and extended hospital stay. Although incidence is low, morbidity due to SWI is high. Blood sugar control and weight reduction prior to surgery are very important. Infection control measures like nasal screen for Staphylococcus aureus, use of nasal mupirocin, and rectal screen for MDR gram negative bacilli can be considered preoperatively. In view of the most common organisms isolated, vancomycin with ceftazidime could be a better option for surgical antibiotic prophylaxis at our cardiac center.

Novelty of Findings
Multidrug resistant strain of Acinetobacter baumannii was one of the micro-organisms isolated from the sternal wound. Such strains pose a challenge to treatment, thereby signalling the significance of proper antibiotic stewardship and infection control practices.

Key Words: Infection, Sternal wound, Microbial aetiology, C; Sternal wound; Microbial

Funding Agency: None

Microbiology and Immunology

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Genomic characterisation of whole genome sequences of Acinetobacter baumannii isolates

Nasser K*[1], Al-Fouzan W[12], Dhar R[2], Purohit P[3], Al-Obaid I[3], Mustafa AS[1]
[1]Department of Microbiology, Faculty of Medicine, Kuwait University; [2]Department of Medical Microbiology, Al-Sabah Hospital, Kuwait; [3]Department of Medical Microbiology, Farwaniya Hospital, Kuwait

Introduction:
Whole genome sequencing (WGS) technologies are gradually replacing traditional polymerase chain reaction and DNA sequencing technologies in routine laboratories for the purposes of isolate identification, outbreak analyses, etc. Here, we describe a whole genome sequencing approach, along with analyses, for genomic characterisation of Acinetobacter baumannii strains isolated from two hospitals in Kuwait.

Methods:
Genomic DNA from sixty-seven phenotypically identified isolates received on blood agar was extracted by boiling, followed by purification using spin columns and quantitation by fluorometry. Whole genome sequencing was performed with Illumina MiSeq technology, following standard methods described by Illumina Nextera for 300 cycle kits. The sequence data were analysed using software and pipelines including BioNumerics, FASTQC, RASTtk, QUAST, and NCBI Prokaryotic Genome Annotation Pipeline.

Results:
Single nucleotide polymorphism (SNP) analysis resulted in the clustering of 5 genotypes, with 1,6,5,1, and 49 isolates per cluster. The discriminatory power of this characterisation at 98% similarity was 0.36. Of the 67 collected isolates, 36 were of adequate quality to undergo De novo assembly and annotation for submission to GenBank.

Conclusions:
Whole genome sequencing required much improvement in terms of standard bioinformatics processing, and data management, before it can be implemented as an outbreak surveillance and control tool. However, WGS remains a highly powerful method for identification and clustering of unknown strains, with much potential for routine laboratory investigations.

Key Words: Whole genome sequencing; De novo assembly; Acinetobacter baumannii;

Funding Agency: The College of Graduate Studies and Research Sector grants (YM07/16 and SRUL02/13).

Microbiology and Immunology

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Virulence traits and antimicrobial resistance of Escherichia coli cultured from sewage in Kuwait

Redha MA*, Al-Sweih N, Albert MJ
Department of Microbiology, Faculty of Medicine, Kuwait University

Introduction:
Escherichia coli is a normal flora of the colon. Subsets of E. coli are pathogenic. They cause intestinal and extra-intestinal infections. A predominant flora of raw sewage is E. coli. Treated sewage (containing a reduced microbial count) discharged into the environment poses a health risk. The objective of the study was to determine the virulence traits and antimicrobial resistance of E. coli in raw sewage in Kuwait.

Methods:
Raw sewage was collected once every month for 12 months from May 2018 from three sites in Kuwait (Jabryia, Zahraa, and Hateen). A total of 36 samples were cultured on MFC agar. E. coli was identified by API-20E test and confirmed by a uspA PCR. E. coli was typed by the quadruplex phylotyping method of Clermont. Five categories of diarrheagenic E. coli (DEC) were sought by PCR assays. Extraintestinal pathogenic E. coli (ExPEC) was detected by PCR assays of Spurbeck et al and Johnson et al. Disk diffusion test was used to determine susceptibility to 15 classes of antibiotics. Genes mediating resistance to cephalosporins and carbapenems were detected by PCR.

Results:
140 isolates were E. coli. Phylotypes were: 65 (46.4%) group A, 35 (25%) group B1 (25%), 10 (7.1%) group B2, 3 (2.2%) group C, 15 (10.7%) group D, 4 (2.9%) group E (2.9%), and 8 (5.7%) group F (5.7%). 3 (2.1%) isolates were DEC while 57(40.7%) isolates were ExPEC from group A (30%) and D (24.6%). 129 (92.1%) isolates were multiple drug resistant (MDR), 132 (94.3%) isolates were cephalosporin resistant, and 60 (42.9%) isolates were carbapenem resistant. Among 132 samples resistant to a cephalosporin, blaAmpC was found in all (100%), while blaTEM and blaCTX-M were positive in 53 (40.1%) and 22 (17%) isolates respectively. 9 (6.8%) strains harbored blaOXA-1 gene and 8 had blaCMY-2 (6.1%) gene. All samples were negative for carbapenemase genes.

Conclusions:
There was a high prevalence of ExPEC and MDR E. coli in sewage in Kuwait with the potential to cause human infection.

Key Words: Echerichia coli; Sewage; Antimicrobial resistance;

Funding Agency: The study was funded by College of Graduate Studies, Kuwait University.

Microbiology and Immunology

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Efficacy of chemical adjuvants, mycobacteria and a DNA vaccine vector for the induction of antigen-specific antibody responses to a major Mycobacterium tuberculosis-specific Th1 cell antigen Rv3619c

Safar HA[1], Mustafa AS*[1], Amoudy HA[1], El-Hashim A[2]
[1] Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait; [2] Department of Pharmacology & Therapeutics, Faculty of Pharmacy, Kuwait University, Kuwait

Introduction:
BCG, the currently available vaccine against tuberculosis, has shown limited efficacy in adults against pulmonary disease. Furthermore, BCG vaccine can't be used in immunocompromised people due to its ability to cause disease in them, and vaccination with BCG compromises the diagnostic potential of tuberculin due to the presence of crossreactive antigens. Therefore, efforts are being made to develop subunit vaccines using M. tuberculosis-specific antigens. Rv3619c is such an antigen and induces protective cellular (Th1-type) immune responses. However, recent studies have shown that antibodies also play a role in protection against TB. The aim of this study was to evaluate the ability of Rv3619c to induce antibody responses in mice by using different adjuvants and delivery systems.

Methods:
The gene of Rv3619c was cloned into three types of plasmids to create recombinant (r) plasmids. Two types of these rplasmids were used to transform Escherichia coli and mycobacteria (M. smegmatis and M. vaccae) and the third type served as a DNA vaccine construct. The rE. coli cells were used to express and purify rRv3619c. Mice (n = 5 for each group) were immunized and boosted with (1) rRv3619c adsorbed/emulsified with chemical adjuvants (Alum and Incomplete Freund's Adjuvant), (2) rM. smegmatis (3) rM. vaccae, and (4) the r-DNA vaccine. Four weeks after the last immunization, blood was collected from the immunized and non-immunized mice. Sera from the blood were tested for antigen-specific IgG antibodies using enzyme-linked immunosorbent assays.

Results:
Increased antigen (Rv3619c)-specific IgG responses were obtained in all groups of immunized mice, as compared to non-immunized controls. However, the increase in antigen-specific IgG antibodies was significant ($P < 0.05$) only with Alum and rM. smegmatis.

Conclusions:
The study suggests that Alum and rM. smegmatis are better adjuvants and delivery systems for the induction of antibody responses against Rv3619c.

Key Words: Rv3619c; Delivery Systems; Antibodies;

Funding Agency: Funded by Kuwait University (College of Graduate Studies, Research Sector grants YM06/15 and SRUL02/13) and KFAS Project CB1763MM03

Microbiology and Immunology

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Prevalence of carbapenemase-producing organisms at a tertiary care center in Kuwait

Shetty SA*[1], Abdullah AA[1], Behbehani A[1], Mokaddas E[1,2]
[1]Laboratory Department, Ibn Sina Hospital, [2]Department of microbiology, Faculty of Medicine, Kuwait University

Introduction:
The increasing burden of carbapenem resistance among Gram-negative isolates in our region and the difficulties confronted when treating those infections is of great concern.
Objectives
The study was done to evaluate the prevalance of carbapenemase - producing Gram- negative bacteria in a tertiary-care hospital in Kuwait.

Methods:
All Gram-negative isolates from different clinical specimens of patients from the Burns center, cancer center, renal transplant center and neurosurgery for the period between 1st of January, 2018 till 31st December, 2018 were included in the study done at Ibn Sina microbiology laboratory. Susceptibility testing was done by vitek 2 (Biomerieux) and carbapenem resistance for those isolates was confirmed by E-test for imipenem, meropenem and by IP/IPL (Etest® bioMérieux MIC Test Strip). Eazyplex(®) SuperBug CRE (Amplex) was done for all carbapenem -resistant isolates from blood to identify the type of resistance genes. This was confirmed by Xpert® Carba- R (Cepheid).

Results:
Out of a total of 3425 Gram- negative bacteria, 2149,1097 and 179 were Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter baumanni respectively. Sixty-six were isolated from blood, 214 from respiratory tract, 115 from urine and 222 from pus and other sites. The percentage of carbapenem resistance was 3.76% for Enterobacteriaceae, 48%for Acinetobacter baumanii and 41%for Pseudomonas aeruginosa. Of the 66 carbapenem resistant isolates from blood that were confirmed by Eazyplex and Xpert® Carba- R, NDM, OXA 48 and OXA 181 were the most common genes expressed by the Enterobacteriaceae isolates while OXA 23 and VIM were expressed by Acinetobacter baumanii and Pseudomonas aeruginosa respectively.

Conclusions:
The prevalence of CPOs at our center is considered high. Antimicrobial stewardship programme is urgently needed to control this problem.

Key Words: Carbapenemase-producing organisms; Resistance genes; Antimicrobial

Funding Agency: None

Nuclear Medicine and Radiology

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Bone Disease Severity Based On Sickle Cell Disease (SCD)

Al-Jafar H [1], *Alfeeli M [2], Alkhaldi S [1]
[1]Amiri Hospital, Ministry of Health; [2]Jaber Center for molecular imaging; [3]Mubark Hospital, Ministry of Health

Introduction:
SCD is a congenital disorder. The abnormal haemoglobin S in SCD causes vaso-oclusions which lead to microinfarction in the bone and other organs. Bone complications in this study are based on bone avascular necrosis related to sickling process. In the literature there have been no agreements for any organ on disease severity, so this classification designed to be applicable for SCD patients to assess their bone complication for prophylactic and treatment measures.

Methods:
1- Diagnosis and confirmation of SCD by laboratory blood tests. 2- imaging study by bone X-Ray, Bone scintigraphy, MRI for hips and shoulders having avascular necrosis which is detected by bone scan. By our preliminary, simple, clear and valid method, the AVN severity was graded as follow. one site AVN given 1, 2 sites given 2 and so on plus the summation of the scores of the affected joints .example AVN in one hip in grade 3 and one shoulder in grade 2 = 2 sites +3 (the hip score) +2 (the shoulder score) =7 From 1 up to 4 is mild, from 4-8 moderate, from 8-12 or more is sever

Results:
This study conducted on 150 SCD patients. (60) 40% have normal bone integrity, mild (46) 30% mild, moderate (30) 20% and (14) 10% sever.

Conclusions:
This study simplify assessing the severity of AVN which is the SCD complication in the bone. This classification simplify for the orthopaedic and hematology doctors to understand the severity of bone complication in SCD patients.

Key Words: SCD ; Bone ; Severity;

Funding Agency: Kuwait Foundation for the Advancement of Sciences (KFAS) Funding contract No: P116-13MM-01

Nuclear Medicine and Radiology

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Nuclear medicine and molecular imaging clinicians' attitudes towards the use of artificial intelligence and deep learning in nuclear medicine departments in Kuwait: A multi-center survey

Alhajeri M*[1], Assad S [1], Sarwar Shah SG[2]
[1] Jaber Alahmad Center for molecular Imaging, Kuwait City, KUWAIT; [2] NIHR Oxford Biomedical Research Centre, Oxford University Hospitals NHS Foundation Trust, John Radcliffe Hospital, Oxford, United Kingdom

Introduction:
Aim/Introduction: Artificial Intelligence (AI) is being increasingly applied in many fields including the health care. This study investigates the clinicians' vision and attitudes about the impact of AI and machine learning application in Kuwait nuclear medicine and molecular imaging departments and how it will support in the diagnosis and assessment in nuclear cardiology, neurology and oncology [1].

Methods:
This exploratory cross-sectional study involves a web-based questionnaire survey, which was designed using the Survey Monkey©. The survey was communicated using social media methods to a convenience sample (n=60) of clinicians working in specialized nuclear medicine (NM) and molecular imaging in six large government hospitals in Kuwait. Forty-One participants (n=41) completed the survey. Thus, the response rate was 68% (41 completed survey out of 60 invited). This study received ethics approval from the Ministry of Health, Kuwait.

Results:
The preliminary results showed that most participants (80 %) did not hear about AI applications such as machine learning, representation learning, and deep learning in diagnostic imaging. When testing AI acceptance among NM and MI physicians, the results showed a high rate of acceptance of using AI applications in diagnostic departments.

Conclusions:
Recent studies show that AI applications can improve diagnostic imaging practices. It plays an important role in nuclear medicine and molecular imaging field, especially in cardiology and oncology. Therefore, it will be a good solution for high income countries such as Kuwait. The outcome of this study will give recommendation for NM community and NM physicians to make decision for applying AI applications in Kuwait to improve nuclear medicine and molecular imaging workflow.
References: [1]. Hall, M. (2019) Artificial intelligence and nuclear medicine. Nuclear Medicine Communications; 40 (1): 1-2.

Key Words: Nuclear medicine; Artificial Intelligence ; Molecular imaging;

Funding Agency: None

Nuclear Medicine and Radiology

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Pattern of renal blood flow and reno-vascular parameters in sickle cell disease adult patients

Asbeutah A* [1], Adekile A [2], Almajran A [3], Asbeutah A [4] Naief A [5], Al-Jafar H [6]
[1]Department of Radiologic Sciences, Faculty of Allied Health Sciences, Kuwait University, P.O. Box 31470, 90805, Sulaibekhat, Kuwait; [2]Professor, Department of Pediatrics, Faculty of Medicine, P.O.Box 24923, Safat, Kuwait University, Kuwait;[3]Department of Community Medicine & Behavioral Sciences, Faculty of Medicine, Kuwait University, P.O. Box 24923, Safat-13110, Kuwait; [4]Department of Medicine, Beth Israel Deaconess Medical Centre, Harvard Medical School, 330 Brookline Ave, Boston, MA 02215, USA; [5]Department of Clinical Radiology, Al-Sabah Hospital, Ministry of Health, P.O. Box 5, Sulaibekhat, 1300, Jamal Abdel Nasser Street, Kuwait; [6]Department of Hematology, Al-Amiri Hospital, Ministry of Health, P.O. Box 5, Sulaibekhat, 1300, Jamal Abdel Nasser Street, Kuwait

Introduction:
To evaluate renal blood flow patterns and reno-vascular parameters in adult sickle cell disease (SCD) patients without laboratory evidence of renal impairment.

Methods:
Sixty-five steady-state adult patients with SCD (50 SS, 12 HbSβ0, and 3 SD), aged 32.89 ± 13.89 years and 30 age- and sex-matched healthy controls were studied. Kidney length, echo pattern, peak systolic velocity (PSV), end-diastolic velocity (EDV), renal-aortic ratio (RAR), resistive index (RI), acceleration time (AT), and renal vein velocity (RVV) were acquired, recorded, and analyzed using a curvilinear transducer of 1-5MHz through the abdomen.

Results:
The highest mean for ultrasound renal length and cortical thickness in the SCD and control groups were 11.78 ± 1.30cm and 11.27 ± 0.77cm, and 1.86 ± 0.41cm and 1.78 ± 0.28cm, respectively. The figures were significantly higher in the SCD patients group than the control group (P<0.05). Sixty (90.8%) patients had a mild diffuse increase in cortical echogenicity with preserved renal cortical thickness. The highest mean extra-renal PSV in the SCD and control groups were 138.46 ± 56.32cm/s and 101.75 ± 31.48 cm/s, respectively (P<.05). However, the highest intra-renal RI and AT in SCD and control groups were 0.69 ± 0.07 and 0.06 ± 0.02s and 0.63 ± 0.05 and 0.04 ± 0.01s, respectively (P<.05). There was no significant correlation between RI and AT and PSV among the patients with SCD (P>.05).

Conclusions:
Increased renal length and cortical echogenicity with elevated PSV and RI and AT values can serve as early sonographic changes in SCD adult patients without renal impairment.

Key Words: Sickle cell disease; Nephropathy; Renal artery duplex ultrasound;

Funding Agency: This study was supported by Kuwait Foundation for the Advancement of Sciences (KFAS) funding contract No. P116-13MM-01.

Nuclear Medicine and Radiology

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Tc-99m Myoview Stress & Rest Myocardial Perfusion Imaging Post Coronary Artery Stenting: Diagnostic and Prognostic Implications

Ashkanani H*[1], Malhas Z[1], Al-Ramzi R[1], Loutfi I [1,2]
Depts of Nuclear medicine, [1] Faculty of Medicine-Kuwait University; [2] Mubarak Al-Kabeer Hospital, Kuwait

Introduction:
Tc-99m Myoview gated-SPECT stress and rest myocardial perfusion imaging (MPI) has been widely used for non-invasive evaluation of ischemic heart disease (IHD) including diagnosis and risk stratification of patients affected by this condition. The aim is to study performance of MPI in patients who underwent revascularization procedures especially coronary angioplasty (PCI) and stenting in terms of presence of myocardial ischemia or scar and the prognostic implications of the findings.

Methods:
A total of 31 patients who had stress-rest Tc-99m Myoview gated-SPECT MPI over a period of 3 months were included in the study. All patients had revascularization procedures prior to the scan; mainly coronary angioplasty and stent placement. Risk factors for IHD were recorded including diabetes mellitus (DM), hypertension (HTN) dyslipidemia (DLP), obesity, smoking and a family history of IHD. The studies were scored as normal or abnormal and if abnormal showing ischemia or scar. Analysis included descriptive statistics for the demographics and the frequency of risk factors. The results of MPI were given as the frequency of normal or abnormal studies and whether ischemia or scar were present.

Results:
Mean age of the patients was 64.7 yr±9.49 with 22 males (71%), 21 patients (68%) had DM, 26 (84%) HTN, 25 (85%) DLP, 12 (39%) were obese. There were 7 (23%) smokers, 5 (16%) ex-smokers. Family history of IHD was positive in 5 (16%). There were 22 (71%) abnormal MPI studies. Of those, there were 19 (86%) showing ischemia, 10 (45%) scar and 7 (32%) with both ischemia and scar.

Conclusions:
Conclusions and Novelty of Findings: The high rate of abnormal MPI studies especially presence of ischemia post coronary artery stenting shown in this study would warrant close monitoring of the patients who had undergone this procedure to gauge its success objectively and to provide non-invasive long term follow up.

Key Words: Myocardial perfusion imaging; Coronary stenting; Ischemia;

Funding Agency: Research under KuMSA SCORE Scheme

Nuclear Medicine and Radiology

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Establishment of National Dose Reference Levels (DRL) for CT in Hybrid Imaging Studies "The First National Nuclear Medicine CT (PET/CT) Dose Audit for Kuwaiti Population - 2018"

Masoomi MA*[1], Al-Shammeri J[2], Elrahman H[1], Al-Shammeri I[1], Bradley D[3,4]
[1]Nuclear Medicine and Molecular Imaging, Adan Hospital, MOH, Kuwait; [2]Nuclear Medicine, Faculty of Medicine, Kuwait University, Kuwait; [3]Centre for Radiation Sciences, Sunway University, Malaysia University; [4] Faculty of Engineering and Physical Science, University of Surrey, UK

Introduction:
Dose characterization, optimisation, and reference levels based on the CT dose index (CTDI) concept have been well studied for diagnostic CT. Various organizations in the USA and Europe have established dose reference levels (DRL) for diagnostic CT based on the 75th percentile of CTDI values recorded from national surveys of different body regions. Unlike diagnostic CT, published DRL for Whole-Body/Half -Body CT used in PET/CT examinations are limited. This study proposes to establish a NDRL for CT part in Kuwait (KW), in support of optimisation and dose reduction.

Methods:
All KW PET/CT centers (N:7) participated in the study and only adult oncology data were collected due to the limited other studies. The CTDIvol, DLP and SL were recorded and the Median, Mean, SD, 75th, 25th percentiles as well as WB effective dose (ED) were calculated. Dose and scan length statistics for HB and WB scans (53% and 47% of total: 197) presented together with the proposed NDRLs and the Achievable doses.

Results:
There were variations in the proposed and achievable local DRL amongst 7 centers, highlighting the need for NDRL. Third quartile DLP (mGy x cm) and CTDIvol (mGy) values for the HB were (556, 5.5) which were higher than the UK NDRL (400, 4.3) but were lower than the Swiss NDRL (620, 6) and the France NDRL (762, 7.7). Comparatively, the Proposed NDRLs for (WB) were (677, 4.2) which were lower than Swiss National Data (720, 5.0). It is worth noting that, Swiss had about 5000 (HB) & 706 (WB), UK had 370 (HB) and France had 1000 (HB) entries. Calculated ED varied from 4.6 to 13 mSv, (mean values=8.4 mSv) for HB and from 4.5 to 8.4 mSv (mean value=5.6 mSv) for WB scans.

Conclusions:
There is currently variation in the radiation doses for CT of PET/CT imaging performed for the same clinical purpose in the NM departments. The study demonstrated the need for national CT DRLs for PET/CT as part of the state of the KW strategy for improving the national health services.

Key Words: PET/CT, NDRL; CTDvol, DLP; Molecular Imaging;

Funding Agency: KFAS - PR18-13MN¬01

Nuclear Medicine and Radiology

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Impact of 3D Volume Rendering Model and Pixelated Quantitative CT for Rapid Assessment of the Extent and the Severity of COVID-19 Lung

*Masoomi AM [1], Al-Kandari L[2], Al-Shammeri I[1], Elrahman MH [1], Ramsay S[2]
[1] NM Section, Medical Imaging Department, ADAN Hospital- MOH, KUWAIT;[2] Radiology Section, Medical Imaging Department, ADAN Hospital-MOH, KUWAIT

Introduction:
Coronavirus disease 2019 (COVID-19) has become an increasingly prevalent worldwide, declared a pandemic on March 2020 by WHO. Early diagnosis of novel COVID-19 is crucial to detect the disease at the early stage for treatment and control which has medical and economic impact. We are developing a combination of 3D visual model of COVID-19 lung and the quantitative CT (QCT) to better categorize the CT findings and to provide an objective approach to rapidly identify patients in need of hospital admission.

Methods:
We use a multistep Materialize Mimics Care Suite-3D to produce a 360 orientations of patient lung, where one can see through the lungs and the pattern of disease distributions in a virtual reality concept. In addition, we use DICOM file and MATLAB to generate a unique colour pixelated visual map and semi quantitative analysis of the CT of disease regions.

Results:
QCT map showed clearly various density levels of the infected lung region. The CT quantitative assessment of the lung CT scan was not subjective as per visual assessment. The generated 3D lung model showed distribution of the infected area in a virtual reality concept. A selected patient total lung volume was measured to be 4800 cc. The percentage infected volumes for the RT and LT lobes and the mean percentage were calculated to be 20.3%, 37.9% and 29.1% respectively. The initial results are promising and we are progressing to QCT analysis of further patients retrospectively in view of setting a reference volume level to categorize the COVID-19 infected lung as mild, moderate and severe, and in combination with laboratory tests achieve more rapid diagnosis.

Conclusions:
Combining 3D Modelling and QCT of COVIS-19 Lung can produce an accurate visualization of disease spread and its severity. It provides a new metrics of COVID-19 and is seen as the ideal tool that could predict which patient will need oxygenation soon or who no longer requires with significant impact on the Healthcare.

Key Words: COVID-19; 3D Modeling ; Quantitative CT ;

Funding Agency: KFAS [grant number: PN20-13NR-01]

Obstetrics and Gynecology

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High-Molecular Weight (HMW) Adiponectin and HMW/Total Adiponectin Ratio are Better Predictors of Polycystic Ovary Syndrome (PCOS) than total adiponectin

Al-Awadi AM*, Saleh LR, Al-Zaman E, Mahmoud N, Saldanha FL, Almawi WY
Departments of Medical Biochemistry and Obstetrics & Gynecology, Arabian Gulf University, Manama, Kingdom of Bahrain

Introduction:
Adiponectin is an adipocyte-secreted insulin-sensitizing adipokine, with anti-diabetic and anti-atherosclerotic properties. Adiponectin exists in plasma as three oligomeric isoforms, of which high molecular weight (HMW) is the most biologically active form of adiponectin in regulating glucose homeostasis.
Objective: We investigated whether decreased total and HMW-adiponectin, and altered HMW/total adiponectin ratio (HMWR) are independent predictors of polycystic ovary syndrome (PCOS).

Methods:
Study subjects included 122 PCOS women and 89 control women. PCOS was evaluated according to 2003 Rotterdam criteria. Plasma total and HMW adiponectin were measured by ELISA.

Results:
PCOS women had significantly reduced plasma total adiponectin, HMW adiponectin, and HMWR compared to controls. Logistic regression analysis revealed that HMW adiponectin levels and HMWR, more so than total adiponectin, were negatively associated with PCOS, after adjusting for age, BMI, WHR, and HOMA-IR. Receiver operator characteristic (ROC) area under the curve (AUC) for predicting PCOS were significantly larger for HMW adiponectin and HMWR, than total adiponectin. Categorizing levels of total adiponectin, HMW adiponectin, and HMWR in quartiles showed that PCOS was positively associated with low quartiles in HMW adiponectin and HMWR, but not total adiponectin. Logistic regression analysis confirmed the association of low HMW adiponectin and HMWR with PCOS. Serum HMW adiponectin and HMWR inversely correlated with age, BMI, hirsutism, fasting insulin, HOMA-IR, and positively correlated with serum LDL-cholesterol. On the other hand, total adiponectin was negatively correlated with waist-hip ratio and serum LH levels.

Conclusions:
Reduction in adiponectin secretion is an independent risk factor for PCOS. Our results demonstrate that changes in HMW adiponectin serum levels and HMWR are better predictors for the presence of PCOS when compared with total adiponectin serum levels.

Key Words: Adiponectin; Polycystic Ovary Syndrome; ELISA;

Funding Agency: None

Occupational health and safety

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Kuwait Oil Tanker Company (KOTC) Workplace HSE Standard Use Survey

AlQallaf M*, Gasana J [1], Al Obaid F [2]
[1] Faculty of Public Health, Kuwait University; [2]Kuwait Oil Tanker Company

Introduction:
KOTC is one of the Kuwait Petroleum Corporation (KPC) daughters. (KOTC) was first found in April 1957, by a group of Kuwaiti pioneer investors. They had a vision of the importance of oil transportations through the sea. When health, safety and environment (HSE) are mentioned, the oil industry will lead the discussion. All KOTC employees must know and practice those standards. The main obstacle is that most of the employees don't read those instructions, most of them don't attend the health and safety presentations and others don't check their mails regularly.
Objectives:
1. Explore KOTC workplace health, safety and environmental protection programs.
2. Find the best way to deliver HSE standards to all KOTC employees.

Methods:
A constructed questionnaire with 18 questions was used, starting with demographical questions down to the most appropriate way to deliver skills and knowledge. The questionnaire was sent to all KOTC employees by e-mail.

Results:
Results obtained from the pilot study survey administered to 10% (30 out of 300) KOTC head office staff showed the following:
• 100% (30) of KOTC employees are social media users,
• 70% (21) of KOTC employees like to receive health and safety tips in monthly basis,
• 80% (24) of KOTC head office employees like to receive health and safety tips by videos,
• 70% (21) of KOTC head office employees like to receive videos with duration of 1-3 minutes.

Conclusions:
KOTC staff must know and practice all health, safety and environmental protection standards in order to meet the market challenges. Most employees do not have a full knowledge and proper practices.By using a constructed questionnaire to 10% of KOTC head office staff, it is clear that most employees prefer 1-3 minute HSE videos.

Key Words: Kuwait; Occupational health; Safety;

Funding Agency: None

Ophthalmology

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Visual Impairment Registry of Kuwait 2018-2019 (KVIR)

Alomairah H* [1], Ali A [1], AlOtaibi A[1], Alabduljalil T [12], Almurjan J [1]
[1] Al-Bahar Eye Center,Ibn-Sina hospital, Ministry of Health of Kuwait; [2] Surgery Department, Faculty of Medicine, Kuwait University

Introduction:
Aim: To establish an easy access database about causes of visual impairment in Kuwait. This database will be a cornerstone for future visual promoting campaigns, healthcare delivery to community, and a research reference.

Methods:
A cross-sectional descriptive study was conducted in which 276 questionnaires that were randomly collected by interviewing patients who fit WHO criteria for visual impairment. This questionnaire included questions regarding sociodemographic factors (age, gender, marital status, etc.) patients best corrected visual acuity was measured and the cause of visual impairment was collected from previous records. Statistical analysis was performed by (Epi Info) program.

Results:
276 patients are registered in this visual impairment registry. Mean age of the sample was 53 years. Fifty four percent of patients were male. Al-Jahra governorate constituted of the largest bulk of patients (43 patients). Kuwaitis' presented more than 74% of the sample. According to WHO stratification of visual impairment: 37% of our patients in this registry were in level 1 (best corrected visual acuity in the better eye is between 20/70 and 20/200). The most common primary cause of visual impairment overall in the study was Diabetic Retinopathy (DR) presenting 31% of the total population followed by Cornea Related Conditions and Retinitis-Pigmentosa with 11% and 9.5% consecutively. Most common cause of visual impairment in male was Diabetic Retinopathy (27%) which is also the most common cause in female (35%)

Conclusions:
Most common cause of visual impairment in Kuwait was Diabetic Retinopathy in both males and females followed by Corneal Related conditions. Our perspective in this study is to focus more in prevention of progression to visual impairment caused by Diabetic Retinopathy by implicating measures to tightly control Blood glucose.

Key Words: Visual impairment; Diabetic retinopathy; Retinitis Pigmentosa ;

Funding Agency: None

Pathology

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A Replication Study of Variants Associated with Multiple Sclerosis Risk in the Kuwaiti Population

Ateyah K* [1], Dashti M [2], AlRoughani R[3], Al-Temaimi R[4]

[1] Undergraduate Medical Program, Faculty of Medicine, Kuwait University; [2] Genetics and Bioinformatics department, Dasman Diabetes Institute, Sharq, Kuwait City, Kuwait; [3] Neurology Clinic, Al-Amiri Hospital, Kuwait City, Kuwait; [4] Human Genetics Unit, Department of Pathology, Faculty of Medicine, Kuwait University, Jabriya, Kuwait

Introduction:
Multiple Sclerosis (MS) is a complex chronic neurodegenerative disorder resulting from an autoimmune reaction against myelin. So far, many genetic variants have been reported to associate with MS risk however their association is inconsistent across different populations. Here we investigated the association of the most consistently reported genetic MS risk variants in the Kuwaiti MS population in a case-control study designs.

Methods:
Fifty-six healthy Kuwaitis and 113 Kuwaiti MS patients were exome sequenced on Illumina's HiSeq2000 platform, and 404 healthy Arab control exomes from public databases were used. Bioinformatic analysis was used to mine for 94 MS related risk variants with ≥ 2 reports confirming MS risk association. Replication analysis was done on 170 MS patients and 311 healthy Kuwaitis using Taqman genotyping assays.

Results:
Of the 94 reported MS risk variants four variants showed MS risk association in Arabs exome analysis (EVI5 rs11808092 p=0.0002; TNFRSF1A rs1800693 p=0.00003; MTHFR rs1801131 p=0.038; and CD58 rs1414273 p=0.00007). Replication analysis in only Kuwaiti MS and healthy control samples confirmed EVI5 rs11808092A, TNFRSF1A rs1800693C, and MTHFR rs1801131G as MS risk genetic factors in the Kuwaiti population (OR: 1.6, 95%CI: 1.19 - 2.16, p=0.002; OR: 1.36, 95%CI: 1.04 - 1.78, p=0.025; and OR: 1.79, 95%CI: 1.3 - 2.36, p=0.001; respectively). CD58 rs1414273 did not sustain risk association (p=0.37).

Conclusions:
EVI5 rs11808092A, TNFRSF1A rs1800693C and MTHFR rs1801131G are MS risk factors in the Kuwaiti population. Further investigations into their roles in MS pathogenesis and progression are merited.

Key Words: Multiple sclerosis ; Exome sequencing ; Genetic risk;

Funding Agency: This work was funded by KFAS grant 2012-1302-02.

Patient safety

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Reducing Preanalytical Errors In Al Amiri Hospital Laboratories by Best Phlebotomy Practice Through Awareness And Extensive Training

Refaii TMK*, A Al Sallam SA, Al Failkawi Sh, A Al Wahid Abeer
Al Amiri Hospital, Departments of Clinical Laboratories and Nursing

Introduction:
Patient safety is the cornerstone of all healthcare settings.In laboratory medicine,patient safety is achieved by reducing errors in every step of the testing process. Pre-analytical errors constitute the majority of errors in the testing process(~60%).They include errors in patient verification, preparation, sample collection, transportation, preparation for analysis and/or storage of specimens.Such errors have a direct impact on patient safety.Hemolysis is responsible for most of those errors.Challenges in the preanalytical phase lie mainly in the diversity of staff involved.
Objectives:The aim of our initiative was to reduce pre-analytical errors focusing on hemolysis rate; reducing it from 0.58% to0.1% within two-years period starting from Jan.2017 to Jan.2019.

Methods:
A multidisciplinary team was formed of laboratory, nursing and phlebotomy staff as well as training & manager from BD Company (PAQC program).The team performed a gap analysis based on retrospective laboratory data .Data analysis was done to determine the commonest reasons for specimen rejection and locations with higher rates of preanalytical errors.A plan was designed to include an extensive training program,education and awareness of all sources of such errors over the two years.Site observations and collection of data were repeated semiannually.

Results:
Significant reduction was achieved in all the preanalytical errors and the hemolysis rate dropped from 0.58 to 0.084 and 0.37 to 0.182 percent in Biochemistry and haematology units respectively.Overall performance improved from 56 to 67%.

Conclusions:
Preanalytical errors; especially hemolyzed specimens constitute the majority of laboratory errors globally and have a negative impact on patient safety.Our applied program displayed significant improvement in error rates and we were able to achieve our target goal.We recommend the application of our initiative in other Ministry of Health organizations facing the same challenges.

Key Words: Pre-analytical errors; Patient safety; Hemolysis rate;

Funding Agency: None

Pediatrics

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Performance of bipolar steroid-eluting epicardial leads in the young- 12 years country experience

Alhamlan AW, Alhatlani NR, Elsayed MA, Lyubomudrov VG
Department of medicine, kuwait university

Introduction:
Post operative AV block and CAVB are main indicators for pacemaker implantation. The majority of congenital AVB is secondary to immune mediated injury of the conduction system, which occurs as a result of transplacental passage of maternal anti-SSA/Ro-SSB/La antibodies.
Objective: Review all patients that required epicardial pacemakers for isolated CAVB and post- operative AVB.

Methods:
Retrospective review conducted at chest diseases hospital (CDH) Inclusion: persistent post-operative advanced second or third-degree AVB and CCHB Exclusion: Patients with transvenous pacing system, SND, or pacemaker implantation (PMI) overseas

Results:
41 patients met the inclusion criteria:
26 patients undergone permanent PMI following intracardiac repair 15 patients born with CCHB
A total of 68 epicardial leads were implanted. 15 patients required pacing system reinterventions over the study period. Thirty patients (73%) underwent single-chamber pacing (ventricular), and eleven patients (27%) had dual-chamber system initially implanted. The mean follow-up time was 4.5 years ± 3 years. The mean weight and age at PMI were 6.4 kg ± 5.3 kg and 1.2 years ± 2. 1 years, respectively. All ventricular leads were placed on the anterior and diaphragmatic surface of the RV, except for 5 patients with LV apex placement. Three patients required system upgrade to biventricular pacing.The major causes for reoperations were due to lead failure, pacing system infection, and device upgrade.
Two patients died from heart failure due to subsequent DCM development.
Limitations: Small sample size and retrospective nature with the known risk for selection bias Incidence of lead failure was rather low over a relatively long follow-up period.

Conclusions:
For bipolar, steroid-eluting leads, the reported failure rate has significantly improved (7.5-11%)

Key Words: Pediatric ; Pacemaker; AV block;

Funding Agency: None

Pediatrics

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Early Pacemaker Implantation Post Congenital Heart Disease Surgical Repair– Tertiary Center Experience in Kuwait

Ebrahim M [1], Ashkanani H* [2], AlRamzi R [2], Malhas Z [2]
[1] Department of Pediatrics, Chest Diseases Hospital; [2] Faculty of Medicine, Kuwait University

Introduction:
Background: Atrioventricular block is a rare but serious complication following open-heart surgery in children with congenital heart diseases. Most patients with post-operative atrioventricular block will eventually require pacemaker implantation.
Aim of the study was to to document a single center experience of all patients with early pacemaker implantation secondary to post-operative atrioventricular block.

Methods:
A retrospective review of all patients with post-operative atrioventricular block requiring early pacemaker implantation over a period of 11 years was conducted from September 2008 till September 2019. All patients were identified through a surgical database. Mainly descriptive statistics were utilized.

Results:
Twenty-two patients met the inclusion criteria. Incidence rate of atrioventricular block requiring pacemaker implantation following open heart surgery was 1.7%. The median follow-up time was 4 years and 7 months The median weight, age, generator longevity and post-operative day of initial pacemaker implantation were 3.9 kilograms, 4 months, 4.7 years, and 10 days, respectively. The median cardiopulmonary bypass and aortic clamp time were 100 mins

Conclusions:
The incidence of atrioventricular block following open heart surgery was within previously published rate, with low pacemaker-associated morbidity. Epicardial pacemaker complications were rare. Battery longevity is as expected with such young cohort.

Key Words: Pediatrics; Cardiology; Pacemaker;

Funding Agency: None

Pediatrics

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Outcomes of Total Anomalous Pulmonary Venous Drainage and Predictors of Mortality Tertiary Center Experience

Ebrahim MA[1], Alsaqobi AK[2], *Alhajeri AA[2], Al-Bahrani M[3], Elsayed MA[4],Lyubomudrov VG[4]

[1]Department of Pediatrics, Kuwait University Faculty of Medicine, affiliated with Chest Diseases Hospital; [2] Medical Intern, Ministry of Health, Kuwait; [3] Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, Kuwait University; [4] Department of Pediatric Cardiac Surgery, Chest Diseases Hospital, Ministry of Health, Kuwait

Introduction:
Total anomalous pulmonary venous drainage (TAPVD) is a rare congenital anomaly associated with a high mortality rate, especially when associated with complex congenital heart disease (CHD).

Methods:
This is a retrospective study, conducted between 2011 to 2020, aiming to document outcomes and identify predictors for mortality.

Results:
A total of forty-nine patients were included. The mean follow-up time was 4.6 years (± 2.3). Thirty-four patients had isolated disease while 15 patients had complex TAPVD, 10 of which had single ventricle (SV) physiology. Pre- and postoperative pulmonary venous obstruction (PVO) were documented at 24.5% and 21%, respectively. The overall mortality rate was at 14% and highly associated with the complex group ($p < 0.001$). Multivariate analysis revealed SV physiology, cardiopulmonary bypass time, low rectal temperature and open chest as the only independent risk factors for early mortality. Conclusion: Outcomes were excellent in patients with the isolated type, but mortality remained high within the complex group. Death continues to be associated with previously identified risk factors along with low operative rectal temperatures and a postoperative open chest. PVO was not identified as a risk factor for death, except in univariate analysis, with good outcomes following secondary repair to relief the obstruction.

Conclusions:
Overall survival beyond hospital discharge offers excellent outcome.

Key Words: Total anomalous pulmonary venous drainage; Surgical outcomes; Predictors

Funding Agency: NONE

Pediatrics

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Teaching Pediatrics During COVID-19 Pandemic: Student's Satisfaction Survey

Husain EH [1], Al-Qabandi W [2]
Department of Pediatrics, Faculty of Medicine, Kuwait University

Introduction:
On March 11th, 2020 the World Health Organization (WHO) has declared the novel Corona virus (COVID-19) as a global pandemic. In Kuwait, all schools and Universities were closed from March 1st. The study at the faculty of Medicine, was resumed on the 9th of August 2020. At the department of Pediatrics, the clinical teaching in the hospitals was modified to decrease the chances of COVID-19 exposure. This included smaller groups (2-3 students) teaching instead of the regular groups of (4-5 students). The bed side teaching was made shorter and more intensified to 2.5 hours instead of 4-5 hours of regular clinical posting. The problem-based learning (PBL), was conducted on Microsoft (MS) teams. Also, interactive tutorials were added to the teaching activity to support the shorter hours of hospital clinical teaching. The objective of this study was to evaluate the satisfaction of sixth year medical students with the teaching of pediatrics during COVID-19 Pandemic.

Methods:
A self-administered questionnaire on MS forms was emailed to the students. The questionnaire evaluated the clinical hospital teaching, and E-learning. The responses were recorded on Likert scale.

Results:
The response rate was 88%. Thirty nine percent of the students agreed 2.5 hours of bed side teaching was adequate. Student rated the 2.5 hours of hospital teaching as: effective (90%), focused (97%), able to see and examine more patients (90%). All students agreed that small group teaching and E-learning were effective. The E-learning helped the students focus more (76%). The interactive E-tutorials were reported to add to the student clinical learning (83%). All the students preferred that the same teaching modality is applied in other clinical departments.

Conclusions:
The students were highly satisfied with the modifications of Pediatric teaching during COVID-19 pandemic.

Key Words: Pediatrics; Questionnaire ; Satisfaction;

Funding Agency: none

Pediatrics

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Pacemaker Implantation in Isolated Congenital Complete Heart Block – Tertiary Center Experience in Kuwait

Ibrahim M [12], Alsayegh H* [1], Alhamdan F [1]
[1] Faculty of Medicine, Kuwait University; [2] Chest Diseases Hospital, Ministry of Health

Introduction:
Congenital complete heart block (CCHB) is a rare but important disorder that carries significant morbidity and mortality. Most affected infants will inevitably need cardiac pacing. The objectives of this study are to present and review all patients that required pacemaker implantation due to isolated CCHB, along with long-term outcomes and compare the findings with other published studies.

Methods:
A retrospective study was conducted at the Chest Diseases Hospital and comprised of data of patients with CCHB that required pacing. All patient records were reviewed for patients' demographics, gestational age, age at diagnosis, echocardiographic findings, age and weight at pacemaker implantation, as well as electrocardiographic tracings. Indications for pacing, pacing mode, pacing complications and lead plus generator longevity were also obtained.

Results:
Sixteen (10 females and 6 males) live-born infants with CCHB were identified. and median birth weight and gestational age were 2.6 kilograms and 38 weeks, respectively. Five of affected infants were born to mothers with documented positive anti-SSA/Ro or anti-SSB/La antibodies. The majority of patients had CCHB at the time of pacemaker implantation. The median age at pacing requirement was 3.5 months. All patients were paced epicardially. The most predominant indication for pacing was severe bradycardia. Almost all implanted pacemakers were epicardial and were still functional to date. The median hospital stay per each intervention was 7 days. Complications of pacing included superficial infections, increased ventricular thresholds, chronic pain, pleural and pericardial effusion.

Conclusions:
CCHB is an uncommon disorder; however, it is associated with high morbidity and mortality in infancy. According to our study, the overall outcomes of infants with CCHB is good, although a significant number of infants needed pacing.

Key Words: Heart block; Congenital ; Pacemaker;

Funding Agency: None

Pharmacoeconomics

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Economic Impact of Waste in Prescribing, Dispensing, and Medication Consumption in the United States

Almanie SA*[1], Holdford DA[2], Carroll NV[2]
[1] Department of pharmacy practice, faculty of pharmacy, Kuwait University; [2] Department of pharmacotherapy and outcomes science, school of pharmacy, Virginia Commonwealth University

Introduction:
This research examines waste associated with the medication use process which consists of unfilled prescriptions, abandoned prescriptions, or unused prescription medications. The aim of this study is to quantify the direct medical costs of medication waste in delivery of care in the United States.

Methods:
A review of published literature and data from the 2012 Medical Expenditure Panel Survey was used to quantify the number of prescriptions wasted at different stages of the medication prescribing and use process and the associated costs were calculated.

Results:
In 2012, more than 26 million prescriptions were either unfilled or abandoned, and more than 225 million resulted in dispensed medications that were not used. The total cost of this waste was estimated at $30.4 billion.

Conclusions:
Patients who do not fulfill their role in the medication use process cause significant, avoidable costs to the health care system beyond the health outcomes not achieved.Novelty of the research: this is the first research that defines waste in terms of prescribing, dispensing, and unused medications. None of the existing studies has evaluated the cost of waste from these perspectives.

Key Words: Medication waste; Economic analysis; Unused medications;

Funding Agency: None

Pharmacology and Toxicology

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The Effect of the Hydrogen Sulfide Donor GYY4137 in Diabetes-Induced Vascular Dysfunction in Mesenteric Bed of STZ Diabetic Rats

AlShahwan H* [1], Chandrasekhar B [1], Anjilivilayil C [1], Qabazard B [2], Yousif MH
[1]Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University; [2] Department of Pharmacology & Therapeutics, Faculty of Pharmacy, Kuwait University.

Introduction:
Hydrogen sulfide (H2S) has been reported to have beneficial effects in different pathological conditions. A protective role of H2S against diabetes-associated vascular dysfunction is suggested. In this project, the effects of chronic treatment of diabetic rats with GYY4137 or NaHS (slow and fast H2S donors) on its downstream effectors endothelium nitric oxide synthase enzyme (eNOS), Extracellular signal-regulated protein kinases 1 and 2(ERK1/2), p38 MAP Kinase and H2S biosynthesizing enzymes (cystathionine-β-synthase (CBS), cystathionine-γ-lyase (CSE) have been investigated.

Methods:
Sprague Dawley male rats weighing 250g have been used according to National Institutes of Health Guide for Care and Use of Laboratory Animals. Animals have been divided into six groups: control [C], STZ-induced diabetes [STZ], control treated with GYY4137 (50mg/kg, ip daily, slow released H2S donor) [C+GYY1437], control treated with NaHS (3mg/kg every other day, fast released H2S donor) [C+NaHS], STZ-induced diabetes treated with GYY4137 [STZ+GYY4137], and STZ-induced diabetes treated with NaHS [STZ+NaHS]. Diabetes was induced by ip injection (55 mg/kg) of streptozotocin (STZ). After 28 days of diabetes induction and treatment, rats were sacrificed and mesenteric beds were isolated for biochemical studies. Western blotting was used to measure the expression of ERK1/2, p38, eNOS, and H2S biosynthesizing enzymes (CBS, CSE).

Results:
The biochemical studies showed significant reduction in the protein expression of ERK and p38 and significant increase in the expression of eNOS and H2S synthesizing enzymes (CSE & CBS) after treatment with GYY4137.

Conclusions:
Our findings indicate that GYY4137 may be a novel therapeutic tool to prevent diabetes-associated vascular dysfunction.

Key Words: Diabetes; Downstream Effectors; H2S Synthesizing Enzymes;

Funding Agency: project number: YM 06/18

Pharmacology and Toxicology

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Beta-caryophyllene, a CB2 Receptor-Selective Phytocannabinoid, Suppresses Mechanical Allodynia in a Mouse Model of Antiretroviral-Induced Neuropathic Pain

Aly E*, Khajah M, Masocha W
Department of Pharmacology and Therapeutics, Faculty of Pharmacy, Kuwait University

Introduction:
Neuropathic pain associated with nucleoside reverse transcriptase inhibitors (NRTIs), therapeutic agents for human immunodeficiency virus (HIV), responds poorly to available drugs. Cannabis, which activates cannabinoid type 1 (CB1) and CB2 receptors, relieved HIV-associated neuropathic pain in clinical trials. However, activation of CB1 receptors is associated with psychoactive adverse effects. Therefore, we investigated the effect of beta-caryophyllene (BCP), a CB2 selective phytocannabinoid, in a model of NRTI-induced neuropathy.

Methods:
The preventative and acute therapeutic effects of BCP on a model of 2′-3′-dideoxycytidine- (ddC-; NRTI) induced mechanical allodynia in female BALB/c mice were evaluated, as well as if CB1 or CB2 receptors mediate the acute antiallodynic effect of BCP. The expression of genes of proinflammatory cytokines (interleukin 1 beta, tumor necrosis factor α and interferon γ) was evaluated by real-time PCR in the brain and paw skin. The protein levels of astrocytes and microglia markers, glial fibrillary acidic protein (GFAP) and ionized calcium binding adaptor molecule 1 (Iba-1), and the phosphorylated levels of Erk1/2 and p38 MAPK in the brain were quantified using western blot.

Results:
Administration of ddC induced mechanical allodynia and increased the expression of cytokines mRNA and the phosphorylated level of Erk1/2 but did not alter either the phosphorylated level of p38 MAPK or the protein levels of GFAP and Iba-1. Treatment with BCP prevented the development of ddC-induced mechanical allodynia and attenuated established mechanical allodynia, through activation of CB2 but not CB1 receptors. Beta-caryophyllene prevented the ddC-induced increase in cytokines mRNA, and the phosphorylated level of Erk1/2.

Conclusions:
Beta-caryophyllene prevents the development of and alleviates NRTI-induced neuropathy through CB2 receptors. Therefore, BCP could be useful for the management of antiretroviral-induced neuropathy.

Key Words: Neuropathic pain; Mechanical allodynia.; Beta-caryophyllene;

Funding Agency: This study was supported by the College of Graduate Studies and by grant # YP03/18 from Kuwait University Research Sector

Pharmacology and Toxicology

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Disruption of GLP-1 Receptor Homodimerization Potentially Impairs Signalling Pathways

Al-Zaid B*, Al-Sabah S, Ezeamuzie C
Department of Pharmacology and Toxicology, Faculty of Medicine, Kuwait University,

Introduction:
Glucagon like peptide-1 is an important regulator of various aspects of metabolism, making its G protein-coupled receptor (GPCR); GLP-1R an attractive drug target. Receptor oligomerization is a well-recognized phenomenon within the GPCR superfamily. The objective of this project was to investigate the impact of disruption of GLP-1R homodimerization on different signalling pathways.

Methods:
Receptor dimerization was investigated using a bioluminescence resonance energy transfer (BRET) saturation assay. GLP-1R labelled at its C-terminus with either nano-luciferase (Nluc) or variant of yellow fluorescent protein (SYFP2) was expressed in Flip-In HEK-293 cells. Receptor dimerization was disrupted by substituting three amino acid residues in transmembrane helix 4 (TM4) with alanine (G252A, L256A, V259A). Dose dependent recruitment of G proteins and arrestin to GLP-1R were also monitored using BRET.

Results:
GLP-1R homodimerization resulted in an exponential curve consistent with a saturable BRET signal, whereas the mutated GLP-1R resulted in a straight line indicating a non-specific interaction. Recruitment of G alpha s and q to the mutated receptor were significantly reduced ($P<0.001$ & $P<0.01$ respectively, n=3) even though receptor expression was significantly increased ($P<0.01$ & $P<0.05$ respectively, n=3) compared to wild type. Arrestin recruitment to the mutated receptor was also significantly diminished ($P<0.0001$, n=4). However, in this case there was no significant reduction in receptor expression.

Conclusions:
These results confirm that GLP-1R forms a dimer and that mutation of residues in TM4 disrupts dimer formation. Furthermore, the mutated receptor exhibits impaired agonist dependent signalling at comparable or even greater levels of expression. This could be because GLP-1R requires dimer formation in order to interact with the signalling molecules tested or possibly due to a loss of high affinity agonist binding imparted by the dimer.

Key Words: GLP-1R; Dimerization; Signalling;

Funding Agency: College of Graduate Studies, Kuwait University.

Pharmacology and Toxicology

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PDIA1 regulates breast cancer cell immunorecognition in a manner dependent on oxidative stress

[1] Alhammad R, [2] Demonacos C
[1] Department of pharmacology and toxicology, Kuwait University; [2] Division of Pharmacy and Optometry, University of Manchester

Introduction:
The oxidoreductase protein disulphide isomerase A1 (PDIA1) is involved in the regulation of a variety of biological processes including the modulation of endoplasmic reticulum (ER) stress, unfolded protein response (UPR), ER-mitochondria communication and the balance between pro-survival and pro-death pathways.
Objective: To investigate the role of PDIA1 in regulating breast carcinogenesis under diverse types of stress.

Methods:
The role of PDIA1 in breast carcinogenesis was investigated by measuring ROS generation, mitochondrial membrane disruption, ATP production and HLA-G surface protein levels in the presence or absence of PDIA1. METABRIC dataset was used to assess the correlation of PDIA1/HLA-G ratio with overall survival and tumour stage.

Results:
The results showed that PDIA1 exerted pro-apoptotic effects in estrogen receptor (ERα)-positive breast cancer MCF-7 and pro-survival in triple negative breast cancer (TNBC) MDA-MB-231 cells. ATP generation was upregulated in PDIA1-silenced MCF-7 cells and downregulated in PDIA1-silenced MDA-MB-231 cells in a manner dependent on the cellular redox status. Furthermore, MCF-7 and MDA-MB-231 cells in the presence of PDIA1 expressed higher surface levels of the non-classical human leukocyte antigen (HLA-G) under oxidative stress conditions. METABRIC dataset showed that low PDIA1 and high HLA-G mRNA expression levels correlate with longer survival in both ERα-positive and ERα-negative stage 2 breast cancer patients.

Conclusions:
Taken together these results provide evidence supporting the view that PDIA1 is linked to several hallmarks of breast cancer pathways including the process of antigen processing and presentation and tumor immunorecognition.

Key Words: PDIA1; Oxidative stress; Breast cancer;

Funding Agency: NONE

Pharmacology and Toxicology

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Serotonin Type 3 Receptors are Involved in Mediating Serotonin-Induced Itching in Rats.

El Nebrisi E* [1,2], Howarth L [2], Lorke DE [3], Howarth FC [4], Oz M [5]
[1] Department of Pharmacology, Dubai Medical College, Dubai Medical University, Dubai, PO Box 20170, UAE; [2] Department of Pharmacology, College of Medicine and Health Sciences, UAE University; Al Ain, UAE; [3] Department of Anatomy and Cellular Biology, College of Medicine and Health Science Khalifa University, Abu Dhabi, UAE; [4] Department of Physiology, College of Medicine and Health Sciences, UAE University; Al Ain, UAE; [5] Department of Pharmacology and Therapeutics, Faculty of Pharmacy, Kuwait University, Safat 13110, Kuwait

Introduction:
Pruritus (itching) is among the most common dermatological complaints. It has been determined that some diseases, including cholestasis, polycythaemia vera, eczema, psoriasis and uremic disease, induce itch through the serotonergic pathway. Intradermal injection of serotonin (5-hydroxytryptamine; 5-HT) causes pruritus in humans and rodents. However, the mechanisms of action by which intradermal 5HT induces pruritus are not fully understood. In this study we hypothesized that activation of 5-HT subtype 3 (5-HT_3) receptors are involved in mediating 5-HT induced itching/scratching response in rats.

Methods:
5-HT, ondansteron, capsaicin, and menthol were injected intradermally (50 µl) into the rostral part of the back of male Wistar rats. The total number of scratching bouts was counted at 5 min intervals throughout the 60 min observation period to determine the time course of scratching using a digital video camcorder (Sony Handycam HDRXR500, Sony Corp., Tokyo, Japan).

Results:
Intradermal injection of 5-HT (0.1-1% w/V) induced scratching/itching response lasting up to 1 hour. Ten-minute pre-application of specific 5-HT_3 receptor antagonist, ondansetron (0.1% w/V), and noncompetitive 5-HT_3 receptor inhibitors such as capsaicin (0.1% w/V) or menthol (10% w/V) significantly decreased the cumulative numbers of scratching/itching responses recorded for 1 hour.

Conclusions:
The results, in agreement with earlier studies, indicate that 5-HT_3 receptors play a role in mediating 5-HT-induced itching/scratching response, and demonstrate for the first time that noncompetitive 5-HT_3 receptor antagonists, capsaicin and menthol, inhibit 5-HT-induced itching.Involvement of TRPV1 and TRPM8 channels by capsaicin and menthol, respectively, has been shown in different itching models. However, the results of this study suggest that menthol and capsaicin can also alleviate 5-HT- induced itching.

Key Words: Serotonin; 5-HT3 receptor; Pruritus ;

Funding Agency: The research in this study was supported partially by grants from CMHS, UAE University.

Pharmacology and Toxicology

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Noncompetitive Actions of Capsaicin on Ligand-Gated Ion

El Nebrisi E* [12], Alzaabi AH [2], Howarth L [2], Lorke DE [3], Yang KHS [4], Howarth FC [5], Oz M [6]

[1] Department of Pharmacology, Dubai Medical College, Dubai Medical University, Dubai, UAE; [2] Department of Pharmacology, College of Medicine and Health Sciences, UAE University; Al Ain, UAE; [3] Department of Anatomy and Cellular Biology, College of Medicine and Health Science, Khalifa University, Abu Dhabi, UAE; [4] Department of Biological Sciences, Schmid College of Science and Technology, Chapman University, One University Drive, Orange, CA 92866, USA; [5] Department of Physiology, College of Medicine and Health Sciences, UAE University; Al Ain, UAE; [6] Department of Pharmacology and Therapeutics, Faculty of Pharmacy, Kuwait University, Safat, Kuwait

Introduction:
Capsaicin, the main ingredient responsible for the hot pungent taste of Chili peppers, is a unique alkaloid found in the Capsicum family. Although TRPV1 is considered a major target mediating biological effects of capsaicin, the exact nature of the biological actions of capsaicin is currently unknown. In the present study, the effects of capsaicin were investigated on the functions of human nicotinic acetylcholine (α-nACh) receptor and human 5-hydroxytryptamine type 3 (5-HT3) receptors.

Methods:
Cloned cRNAs for human α7-nACh receptor and human 5-HT3 receptor were expressed in Xenopus oocytes and ion currents were recorded by two-electrode voltage-clamp technique. Radioligand binding experiments were conducted on oocytes membranes containing expressed α7-nACh or 5-HT3 receptor.

Results:
Currents evoked by 5-HT (1 μM) and ACh (100 μM) were reversibly inhibited by capsaicin in a concentration-dependent manner with IC50 values of 82 μM and 8.6 μM, respectively. The maximum inhibition observed for capsaicin was not reversed by increasing concentrations of 5-HT. Radioligand binding studies indicated that the specific binding of the 5-HT3 antagonist [^{3}H]GR65630 and α7-nACh antagonist [^{125}I] α-bungarotoxin were not altered in the presence of capsaicin.

Conclusions:
The results indicate, for the first time, that capsaicin acts as a noncompetitive inhibitor of the 5-HT3 and α7-nACh receptors.

Key Words: Serotonin; 5-HT3 receptor; Xenopus oocyte;

Funding Agency: The research in this study was supported partially by grants from CMHS, UAE University.

Pharmacology and Toxicology

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Signaling Mechanisms Mediating Tryptamine- and Beta-Phenylethylamine -Induced Increase in Perfusion Pressure of the Perfused Rat Kidney

*Jragh D, Yousif M, Oriowo MA, Chandrasekhar B
Department of Pharmacology and Toxicology, Faculty of Medicine, Kuwait University.

Introduction:
Trace amines such as tryptamine and Beta-Phenylethylamine (PEA) are endogenous compounds present in mammalian tissues at low concentrations. These compounds affect the cardiovascular system producing tachycardia, hypertension or hypotension depending on the dosage, species and experimental condition. It was believed that trace amines are indirectly acting sympathomimetic producing their effects through releasing noradrenaline from the nerve ending. Currently, trace amines can produce their actions through activation of surface G-protein coupled receptors (GPCRs) specific for trace amines. These receptors are generally referred to as trace amine-associated receptors (TAARs). The study was designed to examine the hypothesis that TAAR activation plays an important role in maintaining normal blood pressure.

Methods:
Male Wistar Kyoto age 12-14 weeks were used in this investigation (n=50). Animals left kidney was carefully isolated and placed in a temperature-controlled perfusion chamber and perfused with Krebs' solution using a channel masterflex peristaltic pump. Dose-response curves were established for tryptamine and PEA before and in the presence of indomethacin, nifedipine, ritanserin and prazosin. Changes in perfusion pressure were recorded through a transducer Lectromed.

Results:
Tryptamine and PEA-induced significant increase in perfusion pressure of kidney preparations from normotensive WKY rats ($p < 0.05$). Perfusion of the isolated kidney with indomethacin, nifedipine, and prazosin significantly reduced the vasoconstriction response to tryptamine and PEA in the perfused kidney.

Conclusions:
The results obtained suggest that 5-HT2A receptors, alpha-1 adrenoceptors and TAAR1 receptors are involved in tryptamine and PEA-induced response in the perfused kidney. The responses were also inhibited by indomethacin and nifedipine would also suggest that the responses involved products of arachidonic acid metabolism and influx of extracellular calcium.

Key Words: Trace amines-associated receptors; Tryptamine; Beta-phenylethylamine;

Funding Agency: NONE

Pharmacology and Toxicology

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A study of the Effect of Chronic Hydrogen Sulfide Treatment on the Corpus Cavernosum of Type-I Diabetic Rat Model

Qabazard B* [1], Yousef M [2], Mousa A [3], Phillips OA [4]

[1] Department of Pharmacology and Therapeutics, Faculty of Pharmacy, Kuwait University; [2] Department of Pharmacology and Toxicology, Faculty of Medicine, Kuwait University; [3] Department of Anatomy, Faculty of Medicine, Kuwait University; [4]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University

Introduction:
Erectile dysfunction (ED) is a diabetic complication.Current treatment involve phosphodiesterase inhibition (PDEi). Experimental evidence showed a role of hydrogen sulfide as a mediator of erection. Changes take place in the diabetic penile tissue, including inflammation,oxidative stress,and fibrosis of the corpus cavernosum(CC),the major erectile structure.Objectives:to investigate the role of hydrogen sulfide as a potential protective mediator against diabetes-induced structural/functional alterations in CC by examining if it:(1)enhances corporal relaxation following pharmacological stimulation,(2)attenuates fibromuscular changes in diabetic CC.

Methods:
Male SD rats (300-400g,n=12) were used according to the National Institutes of Health Guide for the Care and Use of Laboratory Animals.After diabetes induction by a single i.p.injection of55mg/kg streptozotocin(STZ),diabetic state was confirmed (fasting blood glucose>250mg/dL), and animals were divided into six groups:nondiabetic control, nondiabetic control+GYY4137 (25mg/kg or 50mg/kg,i.p.), diabetic control, diabetic+GYY4137 (25mg/kg or 50mg/kg, i.p.).Following 4-week daily treatment, animals were sacrificed and CC tissues were mounted on organ bath to examine tissue reactivity, or processed for histopathologic examination (Masson trichome stain), or biochemical assays (hydrogen sulfide level).

Results:
Chronic treatment with hydrogen sulfide donor GYY4137 produces improvement in the reactivity of the diabetic penile tissue in response to the contractile agonists. GYY4137 improved smooth muscle:collage ratio in CC of diabetic rats. Diabetes was accompanied by a reduction in plasma hydrogen sulfide level, which further supports a possible role for hydrogen sulfide in diabetes ED.

Conclusions:
The findings suggest a potential protective role for chronic GYY4137 treatment against the degenerative structural changes in diabetic penile tissue which could be effective in preventing ED.

Key Words: Hydrogen sulfide; Diabetes; Corpus cavernosum;

Funding Agency: Kuwait University, Research Administration, Grant No.

Pharmacology and Toxicology, Pharmaceutical chemis

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Synthesis and biological evaluation of Novel 5-(Hydroxamic acid)methyl oxazolidinone derivatives as 5-lipoxygenase inhibitors

Phillips OA [1], *Bosso MA [2], Ezeamuzie CI [2]

[1] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University; [2] Department of Pharmacology & Toxicology, Faculty of Medicine, Kuwait University

Introduction:
Biosynthesis of leukotrienes (LTs) from arachidonic acid (AA) is catalyzed by 5-lipoxygenase (5-LO). LTs are pro-inflammatory mediators implicated in several human inflammatory and allergic diseases. 5-LO is therefore a viable therapeutic target.

Methods:
Nineteen novel oxazolidinone hydroxamic acids were synthesized and evaluated for inhibitory activity against leukotriene (LT) biosynthesis in 3 in vitro cell-based systems: human whole blood, isolated human blood monocytes, LTC4 release from allergen-activated mouse bone marrow-derived mast cells (BMMC), and cell-free recombinant human 5-lipoxygenase (5-LO). Zileuton®, the only clinically available 5-LO inhibitor was used as a reference drug.

Results:
Thirteen of the 19 compounds tested were active with IC50 ≤ 10 uM in at least one of the test systems. Six compounds, PH-211, PH-239, PH-246, PH-247, PH-249, and PH251 were active in all the test systems. Increasing the length of the alkyl chain on the hydroxamic acid moiety increased activity, while the replacement of the morpholinyl heterocycle with N-acetyl-piperazinyl moiety resulted in the loss of activity. The IC50 values for the inhibitory activity in cell-based assay systems were comparable to those obtained in cell-free inhibition of 5-LO enzymatic activity confirming that the compounds are direct inhibitors of 5-LO. PH-249 (C6) was the most potent on whole blood (IC50 = 0.7 uM) comparable to that of zileuton (IC50 = 0.7 uM), while PH-251 (C7) was most active on mast cells (IC50 = 0.2 uM). In vivo activity was demonstrated in zymosan-induced peritonitis in mice - an inflammatory model with significant LT involvement.

Conclusions:
Conclusions and Novelty of Findings: The novel oxazolidinones are potent 5-LO inhibitors with potential applications as anti-allergic and anti-inflammatory agents.

Key Words: Oxazolidinone - hydroxamates, Hydroxamic acid deri; 5-lipoxygenase

Funding Agency: Kuwait University

Pharmacy

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Largazole is a Brain-Penetrant Class I HDAC Inhibitor with Extended Applicability to Glioblastoma and CNS Diseases

*Al-Awadhi FH [1], Salvador-Reyes LA [2], Elsadek LA [3], Ratnayake R [3], Chen QY [3], Luesch H [3]

[1] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University, Kuwait; [2] Marine Science Institute, College of Science, University of the Philippines, Diliman, Philippines; [3] Department of Medicinal Chemistry and Center for Natural Products, Drug Discovery and Development (CNPD3), University of Florida, United States

Introduction:
Largazole is a marine-derived potent class I selective HDAC inhibitor prodrug with anticancer activity against solid tumors in preclinical models. In addition to the validated role of HDAC inhibitors in cancer therapy, recent evidence points to their potential applications in CNS diseases owing to their neuroprotective and memory-enhancing effects. However, key challenges to their development include issues related to brain bioavailability and isoform selectivity. Here we describe the anticancer effects of largazole in GBM, brain bioavailability, and its potential neuroprotective effects.

Methods:
The anticancer activity of largazole was assessed by MTT assay. Transcript levels were assessed by RT-qPCR and RNA-seq. Analysis of largazole thiol in brains was performed using HPLC-MS.

Results:
Largazole possesses in vitro activity against GBM cells and sufficiently crosses the BBB based on measurement of the active species, largazole thiol, to achieve therapeutically relevant concentrations in the mouse brain. The effective dose resulted in pronounced functional responses on the transcript level, revealing desirable expression changes of genes related to neuroprotection, including Bdnf and Pax6 upregulation.

Conclusions:
Our data supports the therapeutic applications of largazole in brain cancer and potentially other CNS diseases, especially given the class I HDAC selectivity and superior brain penetration over other clinically used HDAC inhibitors. Although the development of BDNF enhancing drugs is still underway, the discovery of additional new putative targets for the therapeutic intervention of neurodegenerative disorders is equally important. Investigations of the impact of largazole on the global network of genes implicated in CNS diseases identified Pax6 and Oprm1 as other potential targets. Hence, these changes in gene expression illuminated potential repurposing opportunities of largazole, which warrants further investigations.

Key Words: Histone deacetylases; Brain cancer; Largazole;

Funding Agency: National Institutes of Health grants R01CA172310 and R01CA138544

Pharmacy

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Anti-Proliferative and Anti-Progressive Effects of A Series of Glycinyl and Alaninyl Triazolyl-oxazolidinones on Kelly Neuroblastoma Cell Line

Al-Hasawi NA, *Amine SA, Sharaf LH, Al-Awadhi F, Novotny L, Philips OA
Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University, Kuwait

Introduction:
Neuroblastoma (NB) is the most common extracranial malignant tumor in children and infants. Kelly cell line represents an in vitro model of the malignant neuroblastic phenotype. Oxazolidinones exhibit diverse biological activities including anticancer and CNS besides their original antibacterial and anticoagulation properties. The aim of this study is to evaluate the in vitro anti-proliferative properties of six selected triazolyl-oxazolidinones, PH-145, PH-189, PH-223D, PH-223L, PH-224D and PH-232L on Kelly cell line.

Methods:
The selected triazolyl-oxazolidinones were synthesized using previously established methods. Their anti-proliferative effects were evaluated and the concentrations that produced 50% growth inhibition (IC50, µM) were determined. The inhibition of adhesion and migration of Kelly cells by two oxazolidinone derivatives, PH-223D and PH-224D were investigated at selected non-cytotoxic doses.

Results:
Data from our results showed that these oxazolidinones showed inhibitory effects on proliferation, and some level of inhibitory effects on adhesion and migration of Kelly cells, at micro-molar levels. The 5-nitro-2-furoyl-glycinyl oxazolidinone derivative containing a 4-methyltriazolyl group, PH-145 was the most potent anti-proliferative agent (IC50=6.52 µM), while the 5-nitrothiophene-2-carbonyl-alaninyl derivative PH-232L (IC50=56.24 µM) was the least potent. PH-223D and PH-224D markedly decreased the adhesion of Kelly cells by 66.50 ± 20.98 % and 43.66 ± 5.50 %, respectively. Furthermore, both compounds inhibited the migration of Kelly cells by 29.14% and 14.16%, respectively, with a significant inhibitory effect for PH-223D.

Conclusions:
The study showed that triazolyl-oxazolidinones possess anti-proliferative effects against Kelly cells. Further studies are necessary to establish their effectiveness against neuroblastoma cells in vivo and to determine their detailed anti-proliferative mechanism of action in order to discover more potent compounds.

Key Words: Neuroblastoma; Kelly cell line; Oxazolidinones;

Funding Agency: Kuwait University, Research Sector, Research Grant # PC01/17 (NAH).

Pharmacy

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Antioxidative and Neurobehavioral Recovery of Allium cepa Different Polarity Fractions following Sciatic Nerve Crush Injury in Rat

*Almutairi AM[1], Renno WM[2], Orabi KY[13]
Department of Pharmaceutical Chemistry Faculty of Pharmacy[1]; Department of Anatomy, Faculty of Medicine, Kuwait University[2]

Introduction:
Allium cepa (onion) has a broad range of pharmacological effects. Recently, attention has been focused on its neuroprotective activity. These effects are mainly attributed to its nonpolar thiosulfinates and polar flavonoids including quercetin (QC).

Methods:
Onion bulbs were extracted in 80% ethanol. The extract was dried, dissolved in water and, then fractionated with n-hexane and ethyl acetate to obtain three fractions with different polarities; low (LPF), intermediate (IPF) and high polar fractions (HPF). Wistar rats were randomly assigned into six groups; Sham, Crush, Crush+LPF, Crush+IPF, Crush+HPF and Crush+QC, which underwent sciatic nerve injury, followed by treatment with 50mg/kg i.p. for 3 weeks, then sacrificed at the end of week 4. The neurobehavioral (motor and sensory) outcomes were assessed. Urine and serum samples were collected before the sacrifice to examine the oxidative stress markers; total antioxidant capacity (TAS), 8-isoprostane (8-IP), and total oxidant status (TOS).

Results:
Following sciatic nerve injury, all treatment groups produced a significant recovery in sensory and motor functions when compared to the crush group. The most significant improvement in hopping, foot position, toe spread, and rotarod tests was produced by HPF and QC groups. Additionally, the QC group showed the most significant recovery in hot plate, tail-flick and paw pressure tests. Also, sciatic nerve injury produced oxidative stress characterized by a decreased serum TAS and increased urine TOS and 8-IP. Treatments alleviated the crush-induced oxidative stress as compared to the crush group. QC and IPF groups produced the highest increase in TAS. The LPF and IPF groups produced the lowest 8-IP concentration and the QC group produced the lowest TOS.

Conclusions:
All Allium cepa fractions and QC reduced sensory and motor neurobehavioral impairments with the best results produced with HPF and QC. Also, treatments alleviated the crush-induced oxidative stress markers.

Key Words: Allium cepa; Quercetin; Thiosulfinates;

Funding Agency: CGS and Research Sector (YP05/18.

Pharmacy

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Search for New Leads from Marine Macrofauna: Building up a Marine-Derived Library with Therapeutic Potentials

Al-Shamali MA*, Al-Awadhi FH, Orabi KY
Department of Pharmacy, Kuwait University

Introduction:
The marine environment represents a vital infinitive resource of macro and microorganisms, which is largely unexplored and characterized by its unique diverse chemical structures and biological activities. The overall aim of the project is to build up a small focused marine natural products library, mainly from sponges collected from Kuwaiti Arabian Gulf coast, and subject the library to both chemical and biological profiling.

Methods:
Ten samples were collected from the Arabian Gulf coast around Qaruh and Umm al Maradim islands. Voucher samples, description sheets, and photographs were sent for taxonomic identification. The samples were processed, extracted, and fractionated using a standard protocol. The chemical profiling was performed via spectral analyses (NMR and QTOF-MS/MS). The growth inhibitory activity of the generated fractions was assessed against Gr +ve / -ve bacteria and MDA-MB-231 cells using MIC and MTT assays, respectively.

Results:
A library composed of nearly 100 fractions was generated from the samples and subsequently screened against MDA-MB-231 cells, S.aureus, and E.coli. Although no antibacterial effects were observed, profiling data identified several active fractions against MDA-MB-231 cells. These cytotoxic fractions were further prioritized based on their spectral profiles for future HPLC isolation and purification of cytotoxic compounds.

Conclusions:
The discovery of novel bioactive leads from natural sources has always played a dominant role in the drug discovery process. The search for new bioactive compounds is crucial due to the development of multidrug-resistant microbes and cancers as well. The systematic study of marine macroorganisms as a source for bioactive substances can be potentially promising for future drug development.

Key Words: Marine Natural Products; Macrofauna; Drug Discovery;

Funding Agency: Collage of Graduate Studies and Research Sector (YP01/20)

Pharmacy

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Determining Successful Factors in Intrprofessional Practice with Dynamic Teams

Alsane DM*[1], Lockeman K [2], Slattum P [3], Macys A [4], Dow A [5], Donohoe K [6], Kirakwood C [7]

[1] Department of Pharmacy Practice, Faculty of Pharmacy, Kuwait University; [2] Centre for Interprofessional Education & Collaborative Care, School of Medicine, Virginia Commonwealth University; [3] Professor Emeritus of Pharmacotherapy and Outcomes Science; [4] Department of Statistical Sciences and Operations Research, Virginia Commonwealth University; [5] Centre for Interprofessional Education & Collaborative Care, School of Medicine, Virginia Commonwealth University; [6] Department of Pharmacotherapy and Outcomes Science, School of Pharmacy, Virginia Commonwealth University; [7] Department of Pharmacotherapy and Outcomes Science, School of Pharmacy, Virginia Commonwealth University

Introduction:
Background: Understanding the important factors that predict dynamic team effectiveness helps health educators to establish team training models that focus on improving collaborative student performance that facilitates their transition to practice and helps to improve the health and system outcomes. Objectives: 1) Assess the student attitudes and knowledge toward interprofessional teamwork. 2) Evaluate predictors associated with team effectiveness among dynamic student teams participating in a practice IPE setting.

Methods:
This was an exploratory cross-sectional study using a multi-measures approach to evaluate dynamic student teams in a real-life environment. Measures include self-reported surveys, a knowledge test, video recording, and an assessment of team healthcare plans. Study participants consist of students and clients. Team effectiveness was assessed based on students, clients, observer, and faculty rating. Pre/post analyses were conducted to assess the students' learning outcomes. Regression analyses were conducted to assess predictors associated with team effectiveness.

Results:
The sample size was equal to 72 students and 48 clients who participated in 100 clinical sessions. Overall, there was a significant improvement in student attitudes and knowledge. Among the evaluation approaches, faculty and client ratings were robust to evaluate dynamic student team effectiveness. Significant predictors included student age, sex, prior healthcare experience and number of clients encountered; client age, race, education level and number of wellness visits; clinic site and faculty.

Conclusions:
Practice IPE models are an excellent opportunity for health professions students to improve their skills, knowledge, and attitudes toward interprofessional teamwork. The results of this study suggest that in practice IPE models faculty and client ratings can be used as an approach to evaluate dynamic student team effectiveness.

Key Words: Interrofessional education; Teamwork; Collaborative Practice

Funding Agency: None

Pharmacy

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Simulation for developing clinical skills: A mixed-method study exploring pharmacists' experiences and perspectives

Katoue MG*[1], Ker J[2]

[1] Department of Pharmacology and Therapeutics, Faculty of Pharmacy, Kuwait University, Kuwait; [2] University of Dundee, Ninewells Hospital, Dundee, Scotland, the United Kingdom.

Introduction:
Simulation has been integrated in pharmacy education in many developed countries to prepare students for pharmacy practice. Most of the evidence about simulation-based education comes from Western educational systems. This study aimed to explore pharmacists' experiences and perceptions about simulation use for learning clinical skills in Kuwait.

Methods:
This was an exploratory descriptive study of pharmacists' perceptions about simulation-based education. A mixed-method research design was employed whereby pharmacists working in different hospitals across Kuwait participated in focus groups and completed self-administered surveys. The focus group interviews were audio-recorded, transcribed verbatim and analysed using framework analysis. Descriptive statistics were used to describe characteristics of study participants and survey findings and data were analysed using SPSS, version 22.

Results:
A total of 110 pharmacists participated in the focus groups. Pharmacists had different experiences in relation to simulation use for learning, which included learning and assessment. They identified many benefits of simulation such as enhancing knowledge retention and allowing learners practice and rehearse skills in safe environments. Participants suggested that simulation can be used to train pharmacy students and pharmacists on pharmacy practice skills, communication and teamwork skills. Most participants expressed positive attitudes towards simulation and they welcomed more integration of simulation in pharmacists' education and training.

Conclusions:
Pharmacists in Kuwait have diverse educational experiences regarding simulation use for learning. Collaborative efforts between educational institutions and healthcare authorities are needed to standardize and expand simulation use in training pharmacy students, trainees and practitioners to equip them with the clinical skills essential for safe practice.

Key Words: Simulation; Clinical skills; Pharmacists;

Funding Agency: None

Pharmacy

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Activity of N-Substituted-Amino Acid Triazolyl-Oxazolidinone Derivatives Against Linezolid-Resistant Strains of Gram-positive Cocci

Sharaf LH*[1], Kollu V[1], Verghese T[2], Udo EE[2], Phillips OA[1]
[1] Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University, Kuwait; [2] Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Linezolid (LNZ) has established effectiveness against drug-resistant Gram-positive bacterial strains, including vancomycin-resistant Enterococcus faecium, Methicillin- and vancomycin-resistant Staphylococcus aureus and penicillin-resistant pneumococci. Although it is rare, cases of acquired LNZ-resistance have been reported in some clinical isolates of staphylococci and enterococci. The main objective of this study is to investigate the antibacterial activity of selected triazolyl oxazolidinones against LNZ-resistant clinical isolates from hospitals in Kuwait.

Methods:
Selected D/L alaninyl and glycinyl triazolyl oxazolidinones were synthesized. Their antibacterial activity was evaluated against standard reference strains (S. aureus ATCC25923, CNS and S. epidermidis ATCC12228, E. faecalis ATCC29212, S. pneumoniae ATCC49619), and clinical isolates of LNZ-susceptible MRSA, E. feacalis and S. pneumoniae and LNZ-resistant strains(MIC≥16µg/ml). Minimum inhibitory concentrations (MICs, µg/ml) were determined by agar dilution method under aerobic conditions for all the strains except for S. pneumonia anaerobically.

Results:
The 5-nitro-2-furoyl alaninyl derivatives PH-214L(MIC:4), PH-223D(MIC:0.25-4), PH-227L(MIC:2-8), the 5-nitrothiophene 2-carbonyl derivative PH-232L(MIC:0.5-2) and the 5-nitro-2-furoyl glycinyl derivatives PH-145(MIC:<0.5-1) and PH-189(MIC:<0.5-1) showed potent activity against four LNZ-resistant CNS strains. While the 5-nitro-2-furoyl derivatives PH-223D(MIC:4-8), PH-145(MIC:1-2) and PH-189(MIC:2-4) showed potent activity against two LNZ resistant E. feacalis strains. Overall, the 5-nitro-2-furoyl glycinyl derivatives were the most potent against both LNZ-resistant E. feacalis and CNS strains compared with the alaninyl substituted derivatives.

Conclusions:
Our findings are novel in the fact that some triazolyl oxazolidinones demonstrated potent activity against LNZ-resistant bacterial strains and there is need for further studies.

Key Words: Oxazolidinones; Agar dilution method; LNZ-resistant bacteria;

Funding Agency: Kuwait University, Research Sector, General Facilities Grants GS01/01, GS01/03 & GS01/05

Pharmacy

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Effects of the combination of indomethacin plus minocycline on bacterial endotoxin-induced expression of inflammatory molecules in the mouse brain

Yassin M*, Masocha W
Department of pharmacology and therapeutics, Faculty of Pharmacy, Kuwait University, Kuwait

Introduction:
Bacterial endotoxin lipopolysaccharide (LPS) can induce both pain and inflammation. Our laboratory reported that combining indomethacin with minocycline potentiates their antinociceptive effects against LPS–induced hyperalgesia. Minocycline inhibits, while indomethacin has been reported to exacerbate, LPS-induced neuroinflammation. In this study we investigated safety profile of the combination of indomethacin with minocycline in terms of LPS-induced neuroinflammation.

Methods:
Male BALB/c mice (8-12 weeks old) were treated intraperitoneally with minocycline, indomethacin or their combination for 3 days. On the third day mice were inoculated with LPS 1 mg/kg or its vehicle and sacrificed at 4 h post LPS inoculation. Brains were dissected out and the expression of proinflammatory cytokines (IL-1 beta and TNF-α) and inducible nitric oxide synthase (iNOS) quantified by real time PCR, western blotting or ELISA.

Results:
Minocycline significantly reduced LPS-induced Il1b and Tnf, but not Nos2, mRNA expression. It reduced LPS-induced IL-1 beta, but not TNF-α and iNOS, protein expression. On the other hand, indomethacin had no effect on either mRNA expression of Il1b and Tnf or the IL-1 beta and TNF-α protein expression, while it significantly increased iNOS protein expression and LPS-induced Nos2 mRNA expression. Co-treatment with minocycline and indomethacin had no effect on either LPS-induced Il1b, Tnf and Nos2 mRNA expression or IL-1 beta and TNF-α protein levels while it significantly increased iNOS protein levels.

Conclusions:
Minocycline had protective effect against indomethacin's deleterious effects of increasing Nos2 transcripts, but not iNOS protein. Whereas, minocycline's protective effect against neuroinflammation was annulled in the presence of indomethacin. Thus, the combination might have a slightly better safety profile than indomethacin alone in terms of neuroinflammation.

Key Words: Neuroinflammation; Minocycline; Indomethacin;

Funding Agency: KU Graduate Studies Grant # YP01/18

Pharmacy

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Levetiracetam Rectal Drug Delivery for Treatment of Paediatric Epileptic Seizure: Hollow Against Conventional Suppository Dosage Form

Zaghloul A* [1], Ghoneim A [2]
[1]Department of Pharmaceutics, Faculty of Pharmacy, Kuwait University, Kuwait; [2]Clinical Pharmacist at Hadi Clinic, Jabriya, Kuwait

Introduction:
Hollow-type (HT) suppositories contain a hollow cavity that can accommodate either solid, liquid or gel. HT suppositories have been reported to be advantageous over conventional ones for the treatment of some chronic diseases such as asthma. Epilepsy is a major public health concern with an estimated 4.7 million people in the Eastern Mediterranean Region. Levetiracetam (LEV) is the most frequently prescribed anti-epileptic drug for children with less side effects and superior to that with phenytoin and valproate administration. Unfortunately, LEV has intense bitter taste and extensive liver metabolism. The objectives of this study were to develop and characterize LEV conventional and HT rectal suppositories to improve bioavailability and patient compliance.

Methods:
Suppository fatty bases (Witepsol®, Massa® and BUB different grades) and hydrophilic bases (PEG, different grades with different proportions) were used to prepare 2 gm conventional and HT suppositories each containing 250 mg LEV by fusion method. The formulations were characterized for weight uniformity, mechanical strength, penetration time, content uniformity, extraction efficiency and drug release in distilled water using UV spectrophotometry at 209 nm.

Results:
The preparation method produced suppositories elegant in shape and free of physical deformities. The results of physical characterization were acceptable for both types of suppositories. HT suppositories, generally, showed higher drug release compared with the conventional ones. After 10 min., BUB base HT showed 97.62 % drug release compared with 77.2 conventional type. PEG bases, generally, showed better results in both types compared with fatty bases.

Conclusions:
LEV was successfully prepared as HT and conventional rectal suppositories. The drug was released within 10 min of dissolution time and drug incorporated in BUB, HT base could be used for paediatrics as a potential alternative to the oral tablets.

Key Words: Levetiracetam; Epileptic Seizure; Rectal Suppositories;

Funding Agency: Research Sector, Kuwait University. Project No. PP01/19

Physiology

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Prenatal exposure to dexamethasone alters the gene expression of cox-2 and pge2 receptors in the rat hippocampus and prefrontal cortex and enhances anxiety-like behavior in a sex-specific manner

Abul M, Al-Bader M, Mouihate A
[1] Department of Physiology, Faculty of Medicine, Kuwait University

Introduction:
Dexamethasone (DEX) is given to pregnant women at risk of preterm delivery to accelerate the maturation of fetal organs. However, prenatal DEX dampens neurogenesis, alters the processes of learning and memory and affects anxiety-like behaviors later in life. Maternal rise in glucocorticoids (GCs) increases cyclooxygenase-2 (COX-2) expression in adult offspring. COX-2 activity promotes PGE2 production which could alter hippocampal neurogenesis. Thus, we sought to explore the lasting impact of prenatal DEX on gene expression of cox-2 and receptors of its product PGE2 in neonatal brains.

Methods:
Pregnant dams (n=6 in each group) received daily intra-peritoneal injections of either DEX (0.2mg/kg) or saline from gestation day (GD) 14 until GD21. Gene expression of cox-2 and pge2 receptors (ep1 & ep3), in the prefrontal cortex (PFC) and the hippocampus at postnatal day (PND)5 were measured using rtPCR. Open field test was used to test anxiety-like behavior at PND30.

Results:
Prenatal DEX reduced maternal body weight and offspring body and brain weights at PND5. Prenatal DEX decreased cox-2 gene expression in the PFC of male and in the hippocampus of female offspring at PND5. It also decreased ep1 gene expression in the hippocampus of PND5 female without significant effect on ep3 gene expression. However, the expression of ep3 gene was lower in the PFC and hippocampi of female rats when compared to male rats. Prenatal DEX enhanced anxiety-like behavior in both male and female offspring at PND30. This effect was more pronounced in female rats.

Conclusions:
The sGC-dependent and sex-dependent gene expression of the two major receptors of PGE2 in two key brain areas (hippocampus and prefrontal cortex) suggests that the long-term effects of prenatal sGC could be attributed, at least in part, to altered brain sensitivity to PGE2.

Key Words: Prenatal synthetic glucocorticoid; Anxiety-like behavior; Cyclooxygenase-2

Funding Agency: College of Graduate Studies, and Research Sector Grant Supported by the CGS and RS grant YM11/17.

Physiology

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Comparison of the hypotensive effect of captopril and apocynin

Ghadhanfar EA*, Turcani M
Department of Physiology, Faculty of Medicine, Kuwait University

Introduction:
Increased production of reactive oxygen species by vascular NADPH-oxidase is postulated as a possible cause of essential hypertension. This hypothesis is based on experiments that demonstrated in-vitro vasodilatory effects of apocynin, which inhibits NADPH-oxidase and Rho-kinase. However, attempts to show the hypotensive effect of apocynin in-vivo brought contradictory results. The aim of this study was to verify the putative hypotensive effect of apocynin in SHR with non-invasive minimally stressful telemetric method of blood pressure measurement. An angiotensin-converting enzyme inhibitor captopril was used as a positive control.

Methods:
Male adult (20-week-old) spontaneously hypertensive rats (SHR, n = 16) were implanted with telemetric transmitters to monitor aortic blood pressure, ECG, body temperature and animal locomotor activity. Cardiac function (pre-ejection time) and respiratory rate were also recorded. SHR were treated orally (dissolved in drinking water) with apocynin (400 mg/L) or captopril (330 mg/L) for four weeks. Data are presented as mean (SD) and were analyzed with repeated measure ANOVA.

Results:
Before treatment, all rats had elevated systolic 210 (9) mmHg and diastolic 173 (7) mmHg aortic pressure. Administration of captopril significantly reduced blood pressure within 48 hours by 25% ($p < 0.05$) and remained stable after that. Apocynin alone or addition of apocynin to captopril had no effect on aortic pressure. The hypotensive effect of captopril was associated with a permanent increase in heart rate by 13% ($p < 0.05$). Indices of autonomic nervous system activity did not offer an explanation for captopril induced tachycardia.

Conclusions:
Despite the proven in vitro vasodilatory effect, apocynin was not lowering arterial blood pressure in SHR during the 4-week long treatment. Apocynin also had no additional effect on blood pressure reduction caused by captopril.

Key Words: Telemetry; Apocynin; Hypotension ;

Funding Agency: None

Primary Care

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Anexity and media exposure during covid19 in kuwait

Alasousi FA, Al hamouri SM, Albdulhadi SA
KIMS-Faculty of Primary Healthcare

Introduction:
The COVID19 pandemic outbreak has affected our lives by influencing a number of different life's aspects. The social isolation, economic collapse, and media has caused psychological distress among the general public. Media specifically has a major influence on mental health. (1) In this study, we evaluated the relationship between anxiety and media exposure among Kuwaiti individuals during the COVID19 outbreak.

Methods:
In a cross-sectional study, we studied Kuwaiti citizens aged between 23–55yrs . Inclusion and exclusion criteria applied .An online questionnaire was used to assess media exposure and anxiety using a "generalized anxiety disorder scale" (GAD-7). The questionnaire was pre-tested on a sample of 100 people. A snowball sampling technique was used. In total, 3428 participants participated in the survey, and after excluding participants who did not meet the criteria, a total of 1230 participants from all the governorates in Kuwait were included in the final study.

Results:
All data was statistically assessed using SPSS 25.0 (Statistical Package for Social Sciences). Logistic regression (univariable and multivariable) was applied to measure the significant effects of study independent variables on anxiety levels after adjusting for study confounders. The results show that respondents who followed the news of the spread of the coronavirus felt more anxious compared to those who did not. In addition, the results indicated that respondents who frequently followed the news over the last week were more likely to have anxiety compared to other respondents (OR=2.62; 95% CI: 2.01-3.43; $p<0.001$).

Conclusions:
The results of the study revealed a statistically noteworthy association between media exposure and anxiety. Therefore, government should fight misinformation either by filtering rumors or correcting them through a national platform. Family physicians need to collaborate with psychiatrists to develop a guidelines for anxiety screening.

Key Words: Anexity; COVID 19; Media;

Funding Agency: none

Psychiatry

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Psychological Impact and Effect of Road Traffic Accidents in Kuwait

*Awad S[1], Imtiaz A [2], Qureshi M[3], AlZaid S[4]
[1] Medical Student, Kuwait University; [2] Physician, Kuwait University; [3] Radiology Resident, KIMS; [4] Department of Surgery, Kuwait University; Center for Global Surgery, McGill University.

Introduction:
Physical trauma and road traffic accidents (RTA) are increasing in prevalence and severity worldwide. It is estimated that 12% of Posttraumatic Stress Disorder (PTSD) results from RTA. Several studies illustrate the prevalence of RTA in Kuwait; however, none evaluate the mental health outcomes. This study aimed to discover the impact of RTAs and other physical trauma on both the PTSD and non-PTSD population of Kuwait.

Methods:
Data was collected through an opt-in online survey via convenience and snowball sampling. Consent was taken and all data was collected anonymously. The survey consisted of a trauma screen and the Posttraumatic Diagnostic Scale for the DSM-5 test. The data was then cleaned and imported into SPSS for analysis. All analysis was conducted using frequency percentages and was done on both the general population and PTSD positive people to compare results.

Results:
The total number of participants were 204 with a 71% response rate. 51% of the sampled population in Kuwait experienced a trauma, with the most prevalent being RTA at 20.1%. Among those who experienced a trauma, the rate of RTA was doubled. However, among those PTSD positive, the majority of trauma was child and sexual abuse followed by RTA. RTAs explained 15.8% of the burden in PTSD patients which is higher than the 12% rate seen worldwide. Among the general population, the median count of trauma was 1, but was 2 among PTSD patients. Thus, anyone with an RTA and another lifetime concurrent trauma (47.1%) is at risk of developing PTSD.

Conclusions:
RTAs are one of the top 3 traumas causing PTSD in Kuwait, emphasizing its severity to cause mental distress. Implementation of screening tools to those who experienced an RTA is vital, as the presence of an additional trauma places them at increased risk of developing PTSD. Since it is difficult to raise awareness to eradicate child and sexual abuse, minimizing RTAs is an effective way to decrease the incidence of PTSD in Kuwait.

Key Words: Road traffic accidents; Physical trauma; Kuwait;

Funding Agency: NONE

Psychiatry

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A three-face model for higher depression in females in Kuwait

Imtiaz A[1], *AlAmiri B[2]
[1] Physician, Kuwait University; [2] Child Psychiatrist Consultant, AlManara Center

Introduction:
Depression is the occurrence of sadness or emptiness with other cognitive and somatic symptoms that impact the person's functional ability. The burden of depressive disorders on the global population has been increasing over the past thirty years. The global point prevalence of depression is 3.2-3.4%. The prevalence of depression in Kuwait has been recorded as high as 22-37%. No studies have been done to try and explain the model for this higher prevalence.

Methods:
PubMed, EMBASE, SCOPUS and the APA PsychNET databases were searched using the keywords "Kuwait" and various forms of "depression". Exclusion criteria were duplicates, only prevalence studies, only males, and COVID-19 studies. Eligibility criteria included peer-reviewed papers, papers in Arabic and English, and papers discussing factors in women associated with depression. 743 articles were found initially, 297 after duplicate removal, 97 after exclusion criteria, and 56 studies met the eligibility criteria. The main themes and associations were taken from the eligible articles to find which factors were most associated with the higher rates of depression in Kuwait.

Results:
The 3 main contributors found were: psychiatric comorbidities, cardiovascular risk factors, and obstetrical and gynecological causes. In each section respectively, 54%, 41% and 52% of women had factors associated with depression. 50% of women affected with a psychiatric, cardiovascular, or obstetrical and gynecological illness are prone to developing depression. In addition, these factors feed and link with each other causing a perpetuating cycle of worsening depressive symptoms.

Conclusions:
The model helps explain a lot of the higher prevalence of depression in women. The patient must be approached holistically. These factors must be kept in mind and managed concurrently when dealing with depressed females in Kuwait.

Key Words: Depression; Women; Kuwait;

Funding Agency: NONE

Psychiatry

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Why are we obsessed? A neurobiological review for OCD in the Middle East

*Imtiaz A[1], AlAmiri B[2]
[1] Physician, Kuwait University; [2] Child Psychiatrist Consultant, AlManara Center

Introduction:
Obsessive-Compulsive disorder (OCD) is a psychiatric condition that leads an individual to have intrusive thoughts or obsessions and urges or compulsions. This disease has considerable morbidity worldwide. The global prevalence of OCD is around 2%. The prevalence in the Middle East is in the 4.5-23.1% range, which is more than double the global value. The Middle East is greatly affected by this disease as well, but no neurobiological explanations are available.

Methods:
Some of the keywords were OCD, prevalence, factors, Middle East, genetics, consanguinity, and prefontal cortex. PubMed, EMBASE, SCOPUS, and the IDRAAC databases were searched, with a total of 95 articles found. Only peer-reviewed studies in English, French, or Arabic were accepted. We were interested in studying the neurobiological intersection hence any papers discussing other factors or COVID-19 were excluded.

Results:
12 studies were included in the review. A decreased orbitofrontal cortex gray matter volume was seen in populations with similar culture and is a possible strong contributor to the pathogenesis of OCD in the Middle East. This led to hyperactivity and local connectivity of synapses in this area, leading to higher OCD. This neuroanatomical difference is perpetuated due to consanguinity. Additionally, since OCD is comorbid with depression, the activation of the hypothalamus-pituitary-adrenal axis further increased severity of OCD, which leads to more depression.

Conclusions:
There is a perpetuating loop leading to increasing severity of OCD and depression that could be leading to the high morbidity and prevalence of OCD in the Middle East. This is perpetuated by a complex epigenetic system leading to neurobiological changes in the population due to high rates of consanguinity.

Key Words: OCD; Middle East; prefrontal cortex;

Funding Agency: NONE

Public Health

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Factors contributing to Physicians adoption and satisfaction of Electronic Health Records (EHR) in Kuwait Public Health Care: Case of Al-Jahra Hospital

Alotaibi J*, Tolma EL
Faculty of Public Health, Kuwait University

Introduction:
Electronic Health Records (EHR) is the backbone of the integration of various information tools to help physicians make effective decisions in patient care. Recent research has shown that the adoption rate of EHR among physicians worldwide remains low. The objective of the study is to identify the factors that contribute to the adoption and satisfaction of EHR at a government hospital in Kuwait.

Methods:
This cross-sectional study took place at Al-Jahra hospital after receiving approvals to conduct the study by the hospital administration. Out of the 503 physicians working at the hospital, 310 physicians were recruited through convenience sampling with a response rate of 95%. The survey was self-administered and it contained 48 questions/statements. The primary dependent variables were satisfaction with EHR and adoption of EHR. The main independent variables besides demographics were barriers of using the HER and perceived level of ease or difficulty for using EHR. There were also three moderating variables: a) satisfaction with technical support, b) preference to use EHR, and c) preference of going back to using paper records. Descriptive analysis, followed by bivariate, linear regression and moderation analyses were conducted by using SPSS v. 23 and at a 0.05 alpha level.

Results:
The study sample consisted of predominantly males (82%), non-Kuwait (84%), and between ages 30-39 (42%). Gender and past use of EHR had no significant impact on the physicians' adoption of EHR. Instead, barriers had the most significant impact on physicians' adoption of EHR (p-value = 0.000) and on EHR satisfaction (p-value = 0.000). Preference in using paper was not influential in the relationship between the demographics with neither satisfaction nor adoption of EHR.

Conclusions:
Removing the barriers the physicians face while using the EHR systems at Al-Jahra hospital can be an important factor to consider regarding EHR adoption and improved related satisfaction.

Key Words: Electronic Health Records; Patient decision making; Hospital

Funding Agency: None

Public Health

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Quality of Life of Adult Patients with Type 2 Diabetes Mellitus in Kuwait

Al-Matrouk J[1], Al-Sharbati M[1]
[12]Kuwait University, Faculty of Public Health, Department of Health Policy and Management

Introduction:
Diabetes Mellitus Type 2 (T2DM) is an adult chronic disease, accounts for 90% of diabetes cases. Inappropriate control of T2DM is associated with impaired patient's Quality of Life (QoL) and reduced self-management. T2DM is a significant public health issue causing social, financial, and treatment burden on patients, healthcare, and society. Kuwait ranks 20th among countries in the prevalence of diabetes among adults. About 22% of adults in Kuwait have diabetes, while 50% of both genders ≥ 50 years have diabetes. This study aimed to evaluate the QoL in Kuwaiti T2DM adult patients and identifying associated factors with low QoL.

Methods:
This is a cross-sectional study conducted on a random sample stratified by gender, collected from diabetic clinics, consisting of 604 Kuwaiti adult patients with T2DM, aged ≥ 45 years, diagnosed by physicians as diabetics for ≥ 6 months. A validated demographic and the WHOQOL-BREF questionnaires were used to assess the QoL.

Results:
The sample consisted of both gender with equal proportions, and the age of 46% of the sample was within 56-65 years class. Only 24% of the patients had completed high school, while 57% were retired, and 54% have income >1000 KD/month. The majority of patients (76%) were married, and the great majority 99% were living with their families. Obesity was reported in 54% of patients, 16% were smokers, and 45% had a moderate HbA1c level (7-8.99%). Only oral Antidiabetic drugs were used by 50% of patients, and 24% of the sample had complications, 11% of them developed retinopathy. A family history of diabetes was reported in 74% of patients, and 45% of them have a duration of diabetes >10 years.

Conclusions:
Regarding the QoL, the median score was 71, so around 77% of the sample has a good QoL. There is more need for public health action to control the disease, thus improving their QoL; this can be achieved by improving the patients' health status and maintaining their ability.

Key Words: Quality of Life; Type II diabetes; Diabetes complications;

Funding Agency: None

public health

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Assessing Bromate Levels in the Most Selling Bottled Drinking Water in Kuwait

* Al-Qallaf MA [1], Al-Ali W [2]
[1] Quality Health Safety of Work Environment Department, Kuwait Institution for Scientific Research; [2] Faculty of Public Health, Kuwait University

Introduction:
Kuwait located in a harsh region with high temperature, low annual rainfalls, and limited freshwater resources. Kuwait has a high demand of water due to fast population growth, promoting agricultural activities and industrial revolution. Kuwaiti population consumption of drinking bottled water has increased in the last three decades.

Methods:
For water safety, bromate presence and concentration in drinking bottled water in Kuwait was assessed. In this cross-sectional study, a total of 60 bottled water samples from the most two selling locally manufactured brands plus mineral water brand. In addition, two of the most selling imported brands were collected from the same co-operation society markets as the local brands. All samples were analyzed at the Research Sector Projects Unit laboratory at Kuwait University via IC-MS following the US-Environmental Protection Agency 300.1 procedures for analyzing and quality control. pH as bromate formation contributing factor was measured by METROHM-781 pH/Ion Meter.

Results:
The mean bromate concentration was 3.88 µg/L (95% CI 2.69 - 5.08) and pH mean average values found 7.36 (95% CI 7.14-7.26). Despite that, almost all water samples (local/imported) bromate concentrations were under the maximum contamination level. There was only one sample exceeded MCL (14.9 ppm) and considered as outlier. The study also show that mineral bottled water samples had less bromate traces than the distilled bottled water. The data revealed that all pH values were different from the manufacturer composition labels. The relationship between pH values and bromate concentration of positive samples was not significant (P = 0.069) based on simple linear regression model. Moreover, the relationship was not significant with stratification by water type (local/imported).

Conclusions:
Our findings suggest that bottled water in the chosen brands during the study period in Kuwait is bromide safe.

Key Words: Bromate, drinking water, Kuwait, bottled water, Oz; Bromide; pH;

Funding Agency: NONE

Public Health

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Diabetes Mellitus and its Risk Factors among Migrant Workers in Kuwait

*Anwar A[1], Alfajjam S[2], Gasana J[3]

[1] MPH student, Environmental and Occupational Health; [2] MD, PhD in Occupational medicine, Head of Shuaiba Industrial Medical Center; [3] MD, MPH, PhD, Assc. Prof and chair of Environmental and Occupational Department in FOPH.

Introduction:
The prevalence of Diabetes Mellitus (DM) is growing enormously worldwide. Actions are needed to minimize the burden of DM and its complications. Therefore, investigations should be carried out on DM and its associated risk factors, especially among vulnerable migrant workers as it has a significant impact on their quality of life, health and productivity. DM in this study is defined as the worker met one the following criteria for diabetes: either diagnosed by a physician or at least two elevated serum fasting glucose levels ≥ 7 mol/L in addition to elevated HbA1c ≥ 6.5, despite adhering to a calorie-restricted diet.

Methods:
Descriptive cross-sectional study of all migrant workers attending SIMC from January-December 2018 was analyzed through SPSS version 24. Summary statistics was generated. Chi square test was used to assess the relationship between the outcome and other covariates:BMI, age, hypertension, Nationality and smoking status. Logistic regression was used to adjust for potential confounders that may affect the studied outcome.

Results:
A total of 3477 participants presented in the dataset of 2018. 10.1% of the total participants had DM. Almost 49% of the participants were overweight. The largest age group were between 31 and 40 years of age. A small percentage diagnosed with hypertension at 11.8%. 76.1% reported themselves as non-smokers. Diabetes was positively associated with age, hypertension and nationalities. However, no association was found between BMI and smoking tobacco.

Conclusions:
This is the first study in SIMC to assess DM and its associated risk factor among migrant, since migrant workers are neglected subpopulation that need our focus and attention to achieve justice and fairness. The findings revealed that the prevalence of DM among our study population was considerably lower. However, Healthy lifestyle, including healthy diet and physically active, needed to be introduced to prevent any further damage.

Key Words: Public Health; Diabetes; Migrant worker;

Funding Agency: NONE

Public Health

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Noise-induced hearing loss among the migrant industrial workers who attend the Shuwaiba Industrial Medical Centre (SIMC) in Kuwait

Buqammaz MK[1], Gasana J[1]
[1] Kuwait University, Faculty of Public Health, Department of Environmental and Occupational Health

Introduction:
Laborers in diverse industries are exposed to noise that could result in various audiometric and non-audiometric effects. The association between noise and hearing loss is debated in occupational health. There is no extensive literature on hearing loss and noise among workers generally and migrant workers specifically. The study aimed at finding out the prevalence of noise-induced hearing loss (NIHL), occupational noise-induced hearing loss (ONIHL), and non-occupational noise-induced hearing loss (non-ONIHL) among industry migrant workers in Kuwait. Furthermore, the association between hearing loss and other covariates were assessed.

Methods:
Secondary data extracted from SIMC's records were analyzed using SPSS. All participants were subjected to pure tone audiometry (PTA) as part of SIMC medical examinations.

Results:
A total of 3474 workers were included in the study with a sample of 1308 workers that have NIHL, 712 with ONIHL, and 598 with non-ONIHL. NIHL, ONIHL, non-ONIHL overall prevalence among workers represented 37.7%, 20.4%, and 17.2%, respectively. The prevalence of mild NIHL in the right ear is 19.3% of NIHL cases, and moderate and severe NIHL represent 7.4% and 10.2% of cases, respectively. Multivariate analysis was conducted to investigate the significance of age, years of experience, nationality, job type, and industry type as factors associated with NIHL, ONIHL, and non-ONIHL by logistic regression. There is an association between NIHL with age, nationality, and exposure to noise. ONIHL and non- ONIHL are associated with age, nationality, exposure to noise, and years of experience.

Conclusions:
Conclusion NIHL prevalence among migrant industry workers in Kuwait attending SIMC calls for prevention using available measures that include hearing conservation programs, usage of hearing protection devices, and following national and international occupational health and safety laws.

Key Words: Noise Induced Hearing Loss ; Migrant Workers; Noise;

Funding Agency: None

Quality Improvement

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Blood pressure machine calibration at Yarmouk Primary Health

Alholy F*[1], Alduwaisan HS [2], Ashraf J [2], Alenezi M [2], Al-Hilal ME [2]
[1]Royal College Of Surgeons in Ireland, Ireland; [2]Abdullah Alabdulhadi Primary Healthcare Center [Al-Yarmouk], Capital Governorate, Ministry of Health, Kuwait

Introduction:
Background: In Yarmouk general, specialized clinics and nursing rooms we are aiming to increase correct and corresponding reading of blood pressure (BP) machines both manual and computerized in all treating rooms up to 90% of the BP machines available in Yarmouk Clinic. This can be achieved by monthly and regular monitoring of all BP machines within one year through implementation of local policy of BP maintenance program and Hypertension guidelines, offering training to staff (nurses and doctors), regular auditing of the process, raising awareness campaign, and updating BP machines and their maintenance program. The success rate of that process will then be improved to up to 95% within 18 months via dealing with challenges, overcoming barriers and obstacles. Aim: The aim of this research is to increase correct and same reading of all BP machines in Yarmouk Clinic to the level of 100% in a one-year period. Additionally, to investigate the success rate of this research in an actual clinical practice.

Methods:
The available BP machines' accuracy was being checked monthly and correct measurement policy was implemented. Additionally, all medical staff has been trained and awareness campaigns were conveyed. After that, a verification of the success rate of the implemented improvement strategies has been conducted by investigating BP readings of 50 patients in routine clinical practice with automated and manual reference machine.

Results:
The rate of matching readings of all BP machines has significantly increased to reach an optimal value (100%). Also, an investigation of 50 patients BP values on automated and manual machines demonstrated that the differences between the two machine's systolic values were clinically insignificant (p value= 0.879). Similarly, diastolic values of both machines show no clinical significance (p value= 0.363).

Conclusions:
This research showed that BP measurement accuracy can be improved by taking correct measurement criteria into consideration.

Key Words: Blood pressure; Quality Improvement ; Patient safety;

Funding Agency: None

Quality Improvement

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Improve Records in Patients Electronic Files at Yarmouk Primary Health Center

Galal TA*, Benthafari FA, Fouad MM, Al azemi MA, Al WAhaib H, Aljady N, Al-Hilal ME, Alduwaisan HS
Abdullah Alabdulhadi Primary Healthcare Center [Al-Yarmouk], Capital Governorate, Ministry of Health, Kuwait.

Introduction:
Background: Incomplete patient electronic files (EF) affects quality of healthcare services negatively. Inadequate information in sections on signs and symptoms, diagnosis, follow-up action plan and summary window in EFs maybe related to poor follow up especially in multiple comorbidities cases. As a result, patient's safety will be at risk for medication error and wrong diagnosis. This would lead to increased cost of service by repeating unnecessary tests, waste of time, loss of trust between patient and healthcare institution and consequently loss of follow-up.
Aim: To increase number of completed documentation of patients' EF for up to 70 %.

Methods:
A team member of 8 people with well-defined roles has been formed under the supervision of the head of quality improvement team. Awareness and motivation of staff was increased by highlighting importance of completing patient's EF. An official letter request to MoH was made to increase number of staff. A shift to ideal family medicine clinic (IFMC), which is an appointment based clinic assisted in giving more time to doctors to fill EF. A random sample of 200 files visiting general clinics from May 2016 to May 2017 were selected. Sections on signs and symptoms, diagnosis and filling summary window were checked. Repeated prescription and lab examination were excluded from the analysis.

Results:
It was possible to significantly increase number of completed EF from 9.6% to 76.7% (P=0.001). Stabilizing the process for documentation in EF led to consistency in care provided.

Conclusions:
Improvements in completion of patient's EF were possible but not an easy task. Main challenges were crowded clinic, shortage of staff and difficulty to generalize to other clinics due to bureaucracy. In 2017, the IFMC was introduced and was successful in improving completion of EF. The next steps will focus on improvement of the success rate to up to 95% by dealing with challenges and overcoming obstacles.

Key Words: Electronic file; Quality Improvement; Patient safety;

Funding Agency: None

Social

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Socioeconomic Severity Based On SCD complications

Al-Galaf B[1], Mulla A[2], *Al-Jafar H[3]
[1]The Public Authority for Applied Education and Training, College of Basic Education, Department of Special need and training; [2]Pediatric Department, Al-Watani Bank Hospital, Sabah Medical Area, Ministry Of Health, Kuwait; [3] Consultant Hematologist, Amiri Hospital, Ministry Of Health

Introduction:
Sickle cell disease (SCD) is an autosomal recessive blood disorder. Under certain circumstances haemoglobin S polymerizes and causes microinfarcts in a vaso-occlusive crises. The infarcts cause systemic multi-organs complications in the liver, kidney, brain, bone, and other systems all over the body.The socioeconomic problems is a hidden complication which could have a big effect on the patient. The treating physicians need to aware about this complication and should have a simple method to calculate its severity. There is no consensus in the literature about the severity of any disease, but there is an agreement in the literature for a methods with validation to assess the severity

Aim: This was study conducted to assess the socioeconomic severity based on SCD complications away from other diseases not related to SCD disease .

Methods:
SCD diagnosed and confirmed by complete blood count, high performance liquid chromatography (HPLC), reticulocytes count and liver function test. The patients was interviewed to set up the socioeconomic variables, age, gender, study or occupation burden, income, death of children, parents, partners due to SCD social withdrawal and psychiatric status. A questioner questionnaire survey conducted to confirm the severity of the variables.

Results:
The preliminary results revealed that all the 50 SCD patients have socioeconomic problems associated with their disease in one variable or another. The severity is spectrum from mild to severe was 37 % mild, 40 % moderate and 23 % have severe socioeconomic severity based on SCD complications .

Conclusions:
The socioeconomic severity of SCD reflect an important aspect of their systemic silent complications. This study highlights an important hidden complication which the treating physician may not be aware of, also we created a simple assessment method for the clinicians to assess the socioeconomic severity based on SCD social complications.

Key Words: Socioeconomic; SCD; Severity;

Funding Agency: Kuwait Foundation for the Advancement of Sciences (KFAS) Funding contract No: P116-13MM-01

Surgery

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Illustrating the lack of trauma surgery experience in the medical curriculum in Kuwait

*AlShatti R[1], Imtiaz A[1], AlZaid S[2]
[1] Physician, Kuwait University; [2] Department of Surgery, Kuwait University; Center for Global Surgery, McGill University

Introduction:
Trauma is considered one of the major causes of death worldwide. Nearly one quarter are the result of road traffic accidents. Trauma is highly prevalent in Kuwait as well, with the morbidity and mortality rising every year. The curriculum in Kuwait doesn't deliver a full course of trauma teaching for medical students. This might reflect on the way physicians deal with trauma in different specialties. We wanted to see if there was an association between future interests and the need for trauma experience in clinical years. Understanding student preferences may fill the gap between the curriculum and the clinical life.

Methods:
An anonymous self-administered survey was administered online through Google Forms. The data was then imported into SPSS for statistical analysis. Pearson Chi Square was done to test whether there was any association between the 2 categorical variables.

Results:
There was no association between future choices and the want for trauma surgery experience. From a sample of 337 medical students, 85% of them think there should be a dedicated training for trauma added to the curriculum. This suggests that the awareness of the problem doesn't correlate with what specialty they are thinking about. Broad clinical teaching and experiences should be provided during medical school.

Conclusions:
Trauma has a big impact on daily life. Although society awareness and laws should be implemented to alleviate this problem, we still have to engage the medical professionals in this matter to achieve a higher standard of care for trauma victims. This assumption is agreed about between medical students with different future goals, which means it is not a matter of future specialty. We would like to encourage medical schools to incorporate a whole encompassing approach to education, and not focus on teaching specialty-specific topics only to those interested. A feedback loop with the students is an essential part of medical education.

Key Words: Trauma surgery; Curriculum development; Kuwait;

Funding Agency: NONE

Surgery

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Uniportal video-assisted thoracoscopic surgery a novel approach in the Management of Penetrating Stab Injuries of the Chest

AlShimali HM*[1], AlOtaibi FS[1], AlGhunaim EM[1], Ayed AK[1,2], AlShehab D[1]
[1]Chest Diseases Hospital; [2] Department of Surgery, Faculty of Medicine, Kuwait University

Introduction:
Chest trauma accounts for 25% of trauma related mortality. Current ATLS guidelines advocate urgent thoracotomy in case of blood loss more than 1,500 mL at first or more than 200 mL/hour during the first 2–4 hours from chest tube placement. However, since the introduction of video assisted thoracoscopic surgery (VATS) little was done with this technique in the field of trauma surgery.
Objective: The aim of this study is to evaluate the feasibility and safety of uniportal VATS for the management of penetrating stab wounds of the chest in the emergency setting.

Methods:
A retrospective review of all uniportal VATS performed for the management of penetrating stab wounds of the chest. Inclusion criteria was: uniportal VATS approach for the management of hemodynamically stable patients with active bleeding after penetrating stab injuries to the chest outside the cardiac box with a chest drain output of more than 1500 cc of blood on chest tube insertion.

Results:
21 patients were enrolled to the study. From which, 19 met the inclusion criteria. 2 patients were excluded due to 1- injury within the cardiac box 2- hemodynamically unstable. Mean age of the enrolled patients was 26.4. Intraopeerative findings, Days on chest tube and hospital stay were 2.52 and 4 days respectively. The conversion rate to open thoracotomy or multi portal VATS was zero. 30-day survival rate post uniportal VATS was 100%.

Conclusions:
Uniportal VATS, in the experienced surgeon hands, is a safe and feasible approach in managing penetrating stab wounds of the chest in the hemodynamically stable patient. However, further research with larger sample size is required to confirm these results.

Key Words: Video-assisted thoracoscopic surgery; Uniportal technique; Chest Trauma;

Funding Agency: None

Surgery

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Single lingula biopsy verses multiple biopsies in the diagnosis of interstitial lung diseases: single blinded prospective randomized controlled trial

AlShimali HM*, AlGhunaim EM, Al-Shehab D
Thoracic and Forgut Surgery Unit, Chest Diseases Hospital

Introduction:
Video-assisted thoracoscopic lung biopsy is commonly performed for the diagnosis of interstitial lung disease. Current guidelines recommend performing multiple lung biopsies; however, no single randomized controlled trial available to prove the superiority of multiple biopsies over single biopsy (lingula). The Aim of this trial is to report the diagnostic benefit of multiple lung biopsies over single biopsy.

Methods:
This is a prospective single blinded randomized trial performed in Thoracic surgery unit - chest diseases hospital. 26 patients undergoing thoracoscopic lung biopsy for diffuse interstitial lung disease where included in the study between the period of March - September 2019. Comparison of the operative and postoperative data, diagnosis and complications were measured and statically analyzed using SPSS software.

Results:
The mean age of the patients was 53.7 years. No statistical difference in the operative time, pleural drainage, and hospital stay complications was found between the two groups. Two cases of pneumothorax were reported in the multiple biopsies group compared to single lung biopsy; however it was not statistically significant p-value =0.07. Multiple lung biopsies reported higher number of histological diagnosis compared to single lingula biopsy which was statically significant p-value <0.05.

Conclusions:
Video-assisted thoracoscopic surgery is an effective diagnostic procedure. Multiple lung biopsies has higher diagnostic yield compared to sing lung biopsy.

Key Words: Video-assisted thoracoscopic surgery; Interstitial lung disease; RCT;

Funding Agency: None

Surgery

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Knowledge of Local and Global Physical Trauma and Trauma Centers among Medical Students in Kuwait

*Khadadah N [1], Imtiaz A [2], AlShatti R[2], AlZaid S[3]
[1] Medical Student, Kuwait University; [2] Physician, Kuwait University; [3] Department of Surgery, Kuwait University; Center for Global Surgery, McGill University

Introduction:
The WHO Global Burden of Disease Study has been showing a rising trend in physical trauma morbidity and mortality worldwide. Physical trauma is also following a similar trend in Kuwait. It is expected of medical students to be aware and knowledgeable about local and global rising problems, as these may play a role in clinical practice once they graduate. Since trauma is increasing in Kuwait, we wanted to test how much the medical students in Kuwait knew about this crucial issue.

Methods:
An online survey was conducted anonymously which tested knowledge about local and global issues in trauma. All years of medical school were encouraged to answer the questions. The data was analyzed on SPSS.

Results:
The study clearly demonstrated inadequate knowledge, understanding, and confidence pertaining to both local and global trauma issues among medical students. Most students were aware of the most prevalent trauma in Kuwait, but were unsure of the number of trauma centers in Kuwait. Additionally, 68.2% of students underestimated or incorrectly answered the prevalence of trauma in Kuwait. A similar pattern was observed when testing global trauma awareness. When assessing the most common mechanism of trauma worldwide, most students responded accurately; however, they were 7 times less confident in answering the question compared to local mechanisms. Medical students also showed a lack of understanding in the logistical aspects regarding the departments and benefits involved in trauma centers globally.

Conclusions:
This study has emphasized the gap between medical student knowledge and reality of trauma practice in Kuwait and worldwide. If this gap is not filled, patient care may suffer leading to higher rates of morbidity and mortality, as well as less patient satisfaction when dealing with trauma issues in Kuwait. It is important to raise awareness and education in this surgical specialty which has increasing effects globally.

Key Words: Medical student; Physical trauma; Knowledge and awareness;

Funding Agency: NONE

Surgical science, OMFS, esthetics

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The perception of ideal facial aesthetics among middle eastern university dental students.

Al-Harbi AN, AL-Sanea SS, AL-Harbi HN, Kamal MA
[1] Student, KU-Faculty of Dentistry; [2] Student, KU-Faculty of Dentistry; [3] Student, KU-Faculty of Dentistry; [4] Surgical science Department, Faculty of Dentistry

Introduction:
The perception of facial aesthetics has been the subject of debate since ancient times and it is not considered to be absolute or fixed, rather relative. The dynamic relativity of facial aesthetics is thought to be affected by many factors, including but not limited to ethnicity, demographic variations, geographic locations, and other social backgrounds. The aim of this study was to assess the perception of ideal facial aesthetics among dental students in their preclinical and clinical years.

Methods:
A cross-sectional study included all dental students (n= 175 students) at Kuwait University, Faculty of Dentistry. A morphometric questionnaire of six computer-generated 3D avatar female models with various facial features were constructed by altering the facial units: jaw, chin, nose, mouth, and cheeks shapes, and facial profiles. Students were asked to choose the most and least preferred among the 6 avatar models.

Results:
A total of 149 questionnaires were completed by the students, with an overall response rate of 85.1%. The majority of students were female (92.6%). The preclinical and clinical students agreed on the most and least attractive facial model for all features except jaw shape. Students agreed that models with a broad jaw, moderately protruded chin with moderate height, short and less projected nose, prominent and full projected lips, prominent cheek bone with minimal buccal fat, and straight profile, were considered the most attractive facial features.

Conclusions:
The study showed that dental students at Kuwait University have a perception of the facial esthetics that is largely in accordance with the findings in previously published studies. Dental students must recognize the variations of facial units and the ideals of facial esthetics to better understand and meet the demands and wishes of their patients, and to optimize the treatment plan in order to achieve this goal.

Key Words: Esthetic; Facial canons; Gloden proportion;

Funding Agency: NONE

Surgery- Ophthalmology

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Magnitude and Determinants of Refractive Error among Preparatory Schoolchildren in Kuwait

Bouhaimed M*[1], Al-Taiar A[1], Al-Sabah R[1], Rahman A[2], Shaban L[2], Khandekar
[1] Department Community Medicine and Behavioural Sciences, Faculty of Medicine, Kuwait University; [2] Department of Food Science and Nutrition, College of Life Sciences, Kuwait University; [3]Ophthalmic Epidemiology and Low Vision services-Research Department, King Khalid Eye Specialist Hospital, KSA

Introduction:
The World Health Organization (WHO) estimates that 19 million young children have vision impairment (VI) secondary to refractive error (RE). As children grow, refractive error changes, thus requiring frequent reassessment and management. Unfortunately, if such children do not get timely assistance, their learning ability, academic performance, and personality may suffer. Therefore, the WHO recommends vision screening at ages 12–13 and 15–16, as well as the provision of refractive services. Objectives: To estimate the magnitude and determinants of refractive error and compliance of spectacle wear among preparatory schoolchildren in Kuwait.

Methods:
A cross-sectional study in seven randomly selected schools in five governorates of Kuwait. Schools were selected using a stratified multistage cluster random sampling with a probability proportional to size. Uncorrected visual acuity (UCVA), best corrected visual acuity (BCVA), and strabismus were assessed by an ophthalmologist. Refractive error (RE) was evaluated for each eye using an auto-refractor. Compliance of visual aids was noted during screening.

Results:
A total of 339 students were examined. The prevalence of RE was 26.3% (95% CI [18.9, 28.3]). Mild, moderate, and high myopia contributed 60%, 17.5%, and 5% of RE, respectively, while hyperopia and astigmatism contributed 15% and 2.5%, respectively. One child had amblyopia. Compliance of spectacle wear was 82.5% (95% CI [61.4, 100]). Females (OR = 3.9) and Kuwaiti (OR = 1.9) had higher rates of RE. The prevalence of strabismus was 0.9%. Family income was not significantly associated with compliance of spectacle wear.

Conclusions:
High prevalence of refractive error, especially myopia, in preparatory children in Kuwait is a matter of concern. Female gender and Kuwaiti nationality were risk factors for RE. High compliance of spectacle wear is worth noting. Periodic vision screening and provision of refractive services are recommended.

Key Words: Refractive Error; Visual acuity; Myopia;

Funding Agency: This work was supported and funded by Kuwait University Research Project No. WF02/13.

Virology

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Cytokine profiles of peripheral blood mononuclear cells and neutrophils isolated from chronically infected naïve HCV patients.

Essa S [1], Siddique I [23], Motaz Saad [4], Raghupathy R [1]

[1] Department of Microbiology, Faculty of Medicine, Kuwait University; [2] Department of Medicine, Faculty of Medicine, Kuwait University; [3] Thunayan Al-Ghanim Gastroenterology Center, Al-Amiri Hospital, [4] Hepatology and gastroenterology, Mubarak Al-Kabir Hospital

Introduction:
Cellular immune subsets combat viral infections by several immune mechanisms; which include phagocytosis, cytokines production, extracellular traps formation, and interactions with other immune cells. This study aims to investigate the influence of chronic HCV infection on the production of cytokines by peripheral blood mononuclear cells (PBMC) and neutrophils from chronically naïve HCV-infected patients and compare the results with sex and age-matched healthy controls (HC).

Methods:
Neutrophils and PBMC were isolated by density gradient separation procedures. Then, neutrophils and PBMC were stimulated with a mitogen, and the proliferation indices were assessed by using flow cytometric carboxyfluorescein succinimidyl ester incorporation assay. After stimulation the stimulation indices were calculated, culture supernatants were collected and evaluated for the levels of GM-CSF, IFN-α, IFN- γ, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12, IL-17A, and TNF-α cytokines by MACSPlex Cytokine kit.

Results:
Statistically significant lower mean values were identified in the cytokine profiles of PBMC for INF-γ, IL-2, IL-6, IL-9, IL-10, and TNF-α ($p < 0{\cdot}0001$) in HCV-infected patients when compared with HC. On the other hand, statistically higher mean values were identified for GM-CSF, IL-5, IL-17A, and TNF- α ($p < 0{\cdot}0001$). As for neutrophils statistically, significantly lower mean values were identified in the cytokine profiles of GM-CSF, INF-α, INF-γ, IL-2, IL-4, IL-6, IL-9, IL-10, and IL-17A ($p < 0{\cdot}0001$). In contrast, statistically higher mean values were identified in the cytokine profiles of neutrophils for IL-5, IL-12, and TNF- α ($p < 0{\cdot}0001$).

Conclusions:
The present findings indicate that HCV infection is associated with altered cytokine profiles for both PBMC and neutrophils in HCV-infected patients when compared with HC. These findings may contribute to the failure of HCV-infected patients to clear the virus.

Key Words: Hepatitis C virus; Neutrophils; Cytokines;

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Case Reports

Anatomy

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Erythematous Linear Lesion on the Course of Superficial Fibular Nerve after the Topical Application of Black Henna: A Case Report

* Alkandari AF [1][2], Alawadhi FA [1], Alawadhi AA [1], Mousa A [2], Madhyastha S [2]

[1] Department of Surgery, Adan Hospital, Ministry of Health, Kuwait; [2] Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait.

CASE REPORT

Background. Henna, a dried leaf of the Lawsonia Inermis plant, is used to dye hair, nails, and skin of palms and soles with an orange-brown color. It is often mixed with chemicals such as Para Phenylenediamine (PPD) to fasten the process of dyeing and produce a black color. PPD, however, has many allergic and toxic effects. As an oxidative dye, it is used to stain myelin sheaths in the histological preparation of nervous tissue. We present a case of henna-induced cutaneous nerve inflammation, which is not reported before.

Case Summary. A 27-year-old female presented to the Casualty Operation Theater at Al-Adan hospital, complaining of pain in her left great toe for one-day. The patient denied any recent trauma to the affected foot. Upon examination, the proximal nail fold of the left great toe was inflamed (eponychia). The nail plate showed normal morphology compared to the rest of the toes. However, the proximal nail folds of the other toes had blackish macules, which upon asking, they appeared to be remnants of black henna applied 15 days ago. Coincidentally, an erythematous non-palpable tender lesion, was noticed on the dorsum of the foot. The lesion had an inverted-Y shape that was confined to the course of the superficial fibular nerve. The patient had no fever or regional lymphadenopathy. There was no muscle weakness or pain upon plantar flexion. No paresthesia, hyperesthesia, or burning sensation as well. A final diagnosis could not be made with certainty since a skin biopsy was not done. Cutaneous nerve inflammation was favored after excluding all the anatomical structures in the region. The eponychia was drained, and the patient was discharged home.

Conclusion. Using black henna should be avoided since it contains PPD, which can be absorbed through the skin and affect the underlying cutaneous nerves. Further studies will be useful to consider PPD as a neuroinflammatory agent in producing peripheral nerve inflammation while designing animal study models.

Key Words: Black henna; Para Phenylene Diamine; Superficial fibular nerve;

Anatomy

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Diagnosing an Isolated Flexor Digitorum Profundus Tendon Injury in Flexor Zone II: A Report of Five Cases

* Alkandari AF[1][2], Alawadhi AA [1], Alawadhi FA [1], Renno WM[2]
[1] Department of Surgery, Al-Adan Hospital, Ministry of Health, Kuwait; [2] Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait.

CASE REPORT

Background. Traumatic hand injuries are common and account for 20% of all hospital visits to Emergency Departments (EDs). Injuries of the hand's flexor tendons carry a poor prognosis, mostly if they were in zone II. Zone II is called 'the critical zone' and "No man's Land" as it has the worst outcome among the other flexor zones. Physicians in the ED may not be aware of the detailed anatomy of the hand. Unplanned extension of the wounds, in turn, may adversely affect the outcome. Such injuries should be assessed by experienced physicians and managed by exceptional hand surgeons.

Case summary. We report five cases of an isolated Flexor Digitorum Profundus (FDP) tendon cut after traumatic injury to zone II. History taking revealed that sharp objects accidentally caused all injuries. In case I and II, the injury was caused by a knife's edge while cutting fruits and affected the middle three fingers of the non-dominant hand. In case III, it was induced by a knife's tip while separating frozen burger patty and affected the index finger of the non-dominant hand. In case IV and V, it was induced by an aluminum's edge and affected the little finger of the dominant hand. On examination, patients could flex their fingers at the proximal and distal interphalangeal (IP) joints. However, they could not flex the fingers' distal IP joint where FDP tendon was cut. Upon surgical exploration, FDS tendons were intact, while FDP tendons were found to be retracted. Accordingly, the wounds were sutured, and the patients were referred to a hand orthopedic surgery unit at Al-Razi hospital for further management and care.

Conclusion. Proper assessment of traumatic hand injuries in flexor zone II is essential to avoid misdiagnosing an isolated FDP tendon laceration. Understanding the mechanism of injury together with basic anatomical knowledge of flexor tendons of the hand should allow ED physicians to identify tendon injuries, anticipate complications, and provide effective healthcare.

Key Words: Traumatic hand injury; Flexor Digitorum Profundus Tendon; Flexor zone II;

Cytopathology

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Small Cell Carcinoma Metastatic to the Pancreas: A Report of Two Cases.

Pathan SK* [1], Mallik MK [1], Hashim AA [3], Kapila K [1,2]

[1] Department of Cytopathology, Mubarak Al-Kabeer Hospital; [2] Department of Pathology, Faculty of Medicine, Kuwait University; [3] Department of Gastroenterology, Mubarak Al-Kabeer Hospital.

CASE REPORT

Background:
Metastatic lesions of the pancreas are uncommon and account for approximately 2% of pancreatic malignancies. Small-cell carcinomas (SCC), a group of highly malignant tumors giving rise to early and widespread metastasis are rarely reported in the pancreas. Limited data are available concerning incidence, clinical picture, management and prognosis for pancreatic metastases of SCC. The prevalence of SCC is less than 1.5% of all endocrine neoplasms in pancreas. Our cases represent rare metastatic lesions in the pancreas from SCC, diagnosed by Endoscopic ultrasound (EUS) guided FNA cytology and immunocytochemical studies.

Case summary:
Case 1: A 70-year-old man presented with mediastinal lymphadenopathy, mixed-density lung mass and a mass in the body of pancreas. EUS guided FNA from the pancreatic mass showed small, round tumor cells with extensive nuclear molding. The cytomorphological diagnosis was metastatic SCC. Immunocytochemical (ICC) staining showed that a variable number of neoplastic cells were positive for pan-cytokeratin (CK), TTF-1, chromogranin A, synaptophysin and CD-56. Case 2: A 41-year old Woman, known case of cervical small cell carcinoma, presented with jaundice and mass in the head of pancreas. EUS guided FNA slides from the pancreatic mass showed small cells with extensive nuclear molding having stippled chromatin. The cytomorphological diagnosis was metastatic SCC. The cells were positive for pan-CK and synaptophysin.

Conclusion:
Pancreatic metastases are commonly seen from kidney, lung, breast and GIT and they can be an important cause of focal pancreatic lesions and may occasionally be discovered during CT staging. Use of immunocytochemistry, when available, may help to confirm a suspected diagnosis. In our cases, the clinical suspicion was SCC. Cytology and immunohistochemical studies also favored the primary tumor as SCC.

Key Words: EUS guided FNA; Pancreatic metastasis; Small cell carcinoma;

Dermatology

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Treatment of post-burn leucoderma by VT-treatment

*AlSomali H [1], AlHadad S [2], AlShuraian H [3], AlMattar R [4], AlAnsary M [5]
Students in the Health Science Center, Faculty of Medicine, Kuwait University

CASE REPORT

Background:
Post-burn leucoderma is a leucoderma (whitening of the skin) that is caused by destruction of the melanocytes due to a skin burn, a degree of burn that involves the destruction of the epidermis including the melanocytes, and part of the dermis causing redness, blistering, and fibrinous exudate may appear on the wound. “VT treatment”, is an invented methodology of two-phased separated topical treatment, a treatment patented by faculty of medicine researchers – Kuwait University (world intellectual property number: WO2020/058809A1) that has been used for treating vitiligo. In this case report we are using “VT treatment” on post-burn leucoderma of second-degree burn.

Case summery:
Case #1: A 32-year old Kuwaiti female with recent second-degree burn causing leucoderma. The patient was treated with the “VT treatment” a week after the burn.Case #2: A 43-year old Saudi female with 8 years old second-degree burn causing leucoderma.
The management of both cases is in these following steps:
“VT treatment” 1 is first applied, placed on skin for 15 minutes then washed with water, post to “VT treatment” 1, “VT treatment” 2 (also called skin regeneration) is applied after the VT treatment 1 for 15 minutes then washed with water. Daily treatment (once a day). If no sign of irritation is shown after treatment, we proceed with light therapy 5 minutes after each treatment application.

Conclusion:
Both the recent and the old post-burn leucoderma cases showed a complete repigmentation with “VT treatment”. The new burn case apparently showed almost a complete tissue healing.

Key Words: Dermatology, medicine, leucoderma ; Skin-burn ; Post-burn leucoderma

Dentistry

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A Complex Orthodontic-Periodontal Treatment in a Case of Generalized Aggressive Periodontitis. A 7 Year follow-up

Gregor - Georg Z* [1,2], Giorgio D[2], Oliver H[3]

[1] Faculty of dentistry, HSC, Kuwait University; [2] Faculty of Dentistry, Division of Periodontology, Catholic University, Rome, Italy; [3] School of Dentistry, Department of Periodontics, Loma Linda University, CA, USA

CASE REPORT

Background:
Generalized aggressive periodontitis (GAgP) encompasses a distinct type of periodontal disease exhibiting much more rapid periodontal tissue destruction than chronic periodontitis. The best method for management of GAgP may include the use of both regenerative periodontal techniques and the administration of systemic antibiotics.

Case Summary:
The treatment of a case of GAgP over a period of 6.7 years is presented in this case report. Initial periodontal therapy (week 1- 32) consisted of supragingival plaque control and three appointments of scaling and root planing (SRP). Based on the periodontal pathogens isolated (5 species), the patient also received metronidazole plus amoxicillin for 1 week, followed 10 weeks later by metronidazole plus amoxicillin/ clavulanate for 1 week. The patient was put on regular supportive periodontal therapy (SPT) thereafter. Orthodontic treatment was performed after completion of the initial therapy for 96 weeks. Clinical attachment level (CAL), bleeding on probing (BOP) and plaque index (PI) were obtained at every examination.

Conclusions and Novelty:
Antimicrobial and mechanical treatment resulted in eradication of all perio-pathogens and significantly improved all clinical parameters. During orthodontic treatment and active maintenance, there was no relapse of GAgP. The patient participated in SPT for 194 weeks and thereafter decided to discontinue SPT. Twenty-four months later a relapse of GAgP was diagnosed and all teeth had to be extracted. These results indicate that a combined mechanical and antimicrobial treatment approach can lead to consistent resolution of GAgP. Further studies including a larger number of cases are warranted to validitate these findings.

Key Words: Generalized Aggressive Periodontitis; Orthodontic Treatment; Periodontal Maintenance;

Endocrinology

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Mayer-Rokitansky-Kuster-Hauser Syndrome: a Case of Mullerian Agenesis

*Kazem F[1], AlMashmoom S[1], AlMaateeq B[1], AlMendeel B[1], AlNaemi T[2]
[1] Faculty of Medicine, Kuwait University; [2] Adan Hospital, Ministry of Health, State of Kuwait.

CASE REPORT

Background: Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a developmental anomaly of the müllerian duct system, consisting of congenital absence of the uterus and vagina. Patients typically present with primary amenorrhea, infertility, & normal secondary sexual characteristics. Type I MRKH syndrome is characterized by variable uretrovaginal agenesis, while type II also incorporates extragenital malformations, including vertebral, cardiac, urologic (upper tract), and otologic anomalies.

Case Summary: A 15-year-old girl was referred to the endocrine clinic with primary amenorrhea. Upon clinical examination, there were no secondary sexual characteristics. Blood investigations revealed low estradiol and high FSH and LH, indicating primary ovarian failure. Chromosomal analysis results showed 46XX, excluding karyotypic abnormalities. Ultrasound was inconclusive, showing a hypoplastic right ovary and absence of the left ovary. An MRI was then done, revealing absent ovaries, uterus, cervix, and upper vagina, in addition to left renal agenesis. Her symptoms point to Type II of MRKH. This type of syndrome is usually diagnosed in adolescence where the patient experiences amenorrhea with normal secondary characteristics and normal external genitalia. Patient also lacks ⅔ of the uterus and the upper part of the vegina. The patient was started on Progyluton (estrogen replacement), after which she started having regular menses and developing her secondary sexual characteristics.

Conclusion and Novelty of Findings: Besides the rareness of the syndrome itself, the patient had some uncommon and contradictive presenting symptoms. Normally, MRKH patients have normal ovarian function, while this patient had ovarian failure (repeatedly low estrogen and high FSH and LH). She also had no secondary sexual characteristics, unlike the typical presentation of primary amenorrhea with developed secondary sexual characteristics.

Key Words: MRKH; Primary amenorrhea; Uretrovaginal agenesis;

Genetics

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Atypical genetic cases of Cherubism: sporadic mutations and Reduced penetrance complicate proper disease diagnosis and management

AlAli AM*[1], Dashti H [2], Alyahya Y [3], Ali H[4,5]

[1] Dental Department, Abdulrahman Al-Zaid Health Center, Ministry of Health, Kuwait; [2] Department of Oral & Maxillofacial Pathology, Faculty of Dentistry, Health Sciences Center, Kuwait University, Kuwait; [3] Department of Oral & Maxillofacial Surgery, Al Jahra Specialized Dental Center, Ministry of Health, Kuwait; [4] Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, Health Sciences Center, Kuwait University, Jabriya, Kuwait; [5] Department of Genetics and Bioinformatics, Dasman Diabetes Institute, Dasman, Kuwait

CASE REPORT

Background:
Cherubism is a rare inherited disorder involving the jaws exclusively and mainly seen in the paediatric population. It has distinctive clinical features and shares radiographic and histopathologic characteristics with other fibro-osseous lesions. Cherubism is caused by a mutation in the SH3BP2 gene located on chromosome 4.

Cases Summary:
First Case: A 7 y/o male patient presented with bilateral swelling of the cheeks and soap bubble radiographic appearance on both the maxilla and the mandible. DNA sequence analysis of SH3BP2 revealed a point mutation c.12 53C>A in exon 9. This mutation showed reduced penetrance, as the father who is carrying the same mutation did not show any phenotypic features of cherubism. This suggests possible involvement of modifier genes on disease penetrance.

Second Case:
A 6 y/o male patient presented with bilateral mandibular angle swelling. CT scan showed bilateral large lytic lesions extending at the mandibular ramus, angle and part of the body. Both lesions contain non-erupted teeth and showing partial loss of lingual and buccal cortical plates. Histopathological examination showed multinucleated cells, scattered collagenous and vascularised fibrous connective tissue. Genetic analysis of SH3BP2 showed a point mutation c.1258G>A in exon 9. Surprisingly, genetic analysis of his parents proved to be negative for the mutation, hence the mutation of the child has occurred sporadically.

Conclusions:
Cherubism is a very rare disease with reported cases in literature of about 300. Although the disease seems to be a simple monogenic disease characterised by specific features, the atypical genetic presentation of some cases can complicate clinical diagnosis and management. Careful genetic testing and results interpretation is important to insure proper case management.

Key Words: Cherubism; Atypical Case; SH3BP2 Gene;

Hematology

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Pseudo Chediak-Hegashi lnclusions in Acute Lymphoblastic Leukemia: A Rare Entity

Gooda R*, Marouf R
Hematology Unit, Mubarak Al-Kabeer Hospital, Ministry of Health, Kuwait

CASE REPORT

Background:
Chediak-Hegashi syndrome (CHS) is a rare inherited immune disorder that usually occurs in childhood and is characterized by oculocutaneous albinism, immune deficiency with an increased susceptibility to infection. It is caused by a defect in lysosomal regulatory protein which results in abnormal vesicle transport and lysosomal fusion producing defects in phagocytosis. On blood smear, giant eosinophilic granules are seen in the cytoplasm of granulocytes. Electron microscopic studies suggest that these are formed by fusion of azouraphilic granules. Pseudo Chediak-Hegashi (PCH) granules are also giant cytoplasmic inclusions resembling those seen in inherited Chediak-Hegashi syndrome. PCH granules were observed in acute myeloid leukemia, chronic myeloid leukemia, myelodysplasia and mixed lineage leukemias. Two mechanisms have been suggested for the pathophysiology of PCH: fusion of Golgi-derived or primary granules, or fusion of granules with cell organelles forming a giant autophagic granule.

Case Summary:
A 20-year-old male was admitted with one week history of fever. On examination he was pale and had bilateral supraclavicular and cervical lymphadenopathy. His CBC showed bicytopenia and normal WBC count. The blood smear showed 50% blasts morphologically consistent with lymphoblasts. Bone marrow aspirate showed 80% blasts. Many blasts showed large eosinophilic inclusions in their cytoplasm that gave faint positivity for PAS stain and were negative with Myeloperoxidase stain. Flowcytometry of aspirated sample revealed HLA-DR, TdT, CD34, CD10, CD19, CD20, CD22 and CD 79a positivity. The blasts were negative for T-lymphoid and myeloid markers. Cytogenetic testing was negative for BCR-ABL and TCF3-PBX1. A final diagnosis of Acute B-Lymphoblastic Leukemia (Acute B-ALL) with PCH was made.

Conclusion:
Pseudo Chediak-Hegashi has been reported in only three cases of acute lymphoblastic leukemia (ALL). We report another case of this rare entity in ALL with PCH.

Key Words: Chediak-Hegashi syndrome; Pseudo Chediak-Hegashi; Acute B-Lymphoblastic Leukemia;

Hematology

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Abnormal presentation of Primary myelofibrosis with mastocytosis on bone marrow biopsy.

Gouda EF, Bahl S, Hassan ML
Hematology Unit, Laboratory Department, Al Jahra Hospital, MOH, Kuwait.

CASE REPORT

Background:
Primary myelofibrosis (PMF) is one of the myeloproliferative neoplasms (MPN) in which the vast majority of patients have a mutation in either the JAK2, CALR, or MPL genes. In addition to the major complications (eg, thrombosis, hemorrhage), patients with PMF also suffer from symptoms that may interfere with their quality of life as severe fatigue, abdominal fullness and plethora. Mastocytosis as an incidental finding on bone marrow (BM) biopsy showing MPN features should be differentiated from systemic mastocytosis with an associated clonal hematological non-mast cell lineage disease (SM-AHNMD).

Case report:
A 67year old male presented with body aches, weight loss and left leg pain. Inside the hospital, he developed fracture of left femur shaft. His x-rays showed multiple lytic lesions with a fracture left shaft femur. Abdominal CT showed huge splenomegaly with hepatomegaly. His blood picture showed leuko-erythroblastic picture with few tear drops, and absolute monocytosis without increase in its percentage. BM procedure done to rule out multiple myeloma, lymphoma or metastatic infiltration. The BM aspirate was dry but the trephine biopsy showed hypercellularity with megakaryocytic atypia and MF-3 fibrosis. A single collection of spindle shaped mastocytes (≥15) with positive CD117, CD2 and CD25 are seen. Serum tryptase was 24 µg/L. JAK2 mutation was positive and BCR-ABL1 was negative. Patient was diagnosed as PMF.

Conclusion:
MPN presenting as lytic lesions with pathological fracture is a rare occurrence. The collection of mast cells on the BM though not fulfilling the criteria of SM needs to be followed up with serial serum tryptase in order not to miss SM-AHNMD.

Key Words: Primary myelofibrosis; Mastocytosis; Serum tryptase;

Hematology

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Case report: Metastatic neuroblastoma: A rare case diagnosed from bone marrow.

Gouda EF, Omara N*
Hematology Unit, Laboratory Department, Al Jahra Hospital, MOH, Kuwait.

CASE REPORT

Background:
Neuroblastoma commonly refers to a spectrum of neuroblastic tumors that arise from primitive sympathetic ganglion cells. It has the capacity to synthesize and secrete catecholamines. Neuroblastoma is a common tumor in children, accounting for approximately 8% of all childhood cancers. Bone marrow involvement was usually present at the time of presentation in case where the primary tumor was located in the
adrenal gland. Work up by radiography, bone marrow (BM) examination and laboratory investigations (eg, catecholamines) are helpful in detecting early stage metastasis which is the essential factor for improving treatment of neuroblastoma tumors.

Case Summary:
A 5 years old boy was presented with fever, limping, abdominal pain and pallor. Clinical examination detected generalized lymphadenopathy with mild splenomegaly. Blood analysis showed mild anemia, no abnormal differential count, normal coagulation, elevated ferritin. Quantiferon TB test and brucella agglutination test: Negative. Urine and blood C/S: no growth, CRP: 30.6 mg/dl, PCT:1.3 ng/mL. Abdominal CT: generalized lymphadenopathy, mild splenomegaly and right para-vertebral soft tissue mass? cold abscess. BM examination was performed to exclude Haemophagocytic Lymphohistocytosis, atypical granuloma and anemia of unexplained etiology. BM showed clumps of small blue round cells arranged in rosettes with a granular central area. Marked elevated values of Normetanephrine and tissue biopsy confirmed a diagnosis of neuroblastoma.

Conclusion:
Symptoms as systemic illness, bone pain and limping in a child should raise suspicion of a malignant metastatic tumor. Neuroblastoma with metastases to bone marrow without pointing features to the primary site presents a diagnostic challenge.

Key Words: Neuroblastoma; Bone marrow; Rosette cells;

Hematology

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A rare case of desmin-positive malignant small round cell tumor (MSRCT) with bone marrow infiltration

Hassan M* [1], Rifaat A[2], Ali M [2], Elsherbiny Z[2]
Hematology [1]; Histopathology[2] Units, Laboratory Departments, Al Jahra Hospital, Ministry of Health, Kuwait.

CASE REPORT

Background:
Malignant small round cell tumors (MSRCT) is a term used for tumors composed of malignant round and relatively undifferentiated cells. Desmin is the intermediate filament protein associated with both smooth and skeletal muscle differentiation. Desmin-positive MSRCT includes rhabdomyosarcoma (embryonal, alveolar and pleomorphic), PNET/Ewing's sarcoma and desmoplastic round cell tumors. Embryonal rhabdomyosarcoma (ERMS) displays some degree of myogenic differentiation, including either MyoD1 or myogenin positivity with lack of PAX3-FOXO1 fusion oncogene commonly seen in alveolar rhabdomyosarcoma.

Case Summary:
A 21-year-old female admitted at ICU for acute DIC with severe vaginal bleeding and a history of fever for 3 weeks. On examination, there were multiple ecchymotic patches and cervical lymphadenopathy. Primary workup of fever of unknown origin (FUO) was negative. CBC: WBC= 14.89 109/ L, Hb= 51 g/L and PLT= 71 109/L. The PBF examination revealed a leukoerythroblastic reaction with few atypical cells. Bone marrow (BM) examination was advised that showed total infiltration by small rounded non-hematopoietic cells in a fibrous stroma. After that, a sloughed, necrotic mass passed through the vagina; Sections prepared from the mass revealed malignant round cells with occasional nested pattern in a necrotic background. CT scan and MRI of the abdomen and pelvis revealed unremarkable changes with no definite vaginal masses. An extended panel of IHC markers was performed on both BM trephine and vaginal mass sections; the malignant cells were strongly positive with vimentin and desmin while negative with CD45, CD34, Cytokeratin, CD56, CD99, SMA, myoglobin and myogenin; Myo D1 marker was not available. FOXO1 t(1;13) gene rearrangement by FISH was not detected. The final diagnosis was MSRCT, most probably ERMS.

Conclusions:
BM examination, as one of the diagnostic approach of FUO, may help in diagnosis of unexpected non-hematological malignancies.

Key Words: Embryonal Rhabdomyosarcoma; Bone Marrow; Desmin;

Medicine

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Generalized status epilepticus as a possible manifestation of COVID-19

Abdulsalam MA [1], *Abdulsalam AJ [2], Shehab D [3]
[1]Department of Internal Medicine, Mubarak Al-Kabeer Hospital, Jabriya, Kuwait; [2] Department of Physical Medicine and Rehabilitation, Physical Medicine and Rehabilitation Hospital, Andalous, Kuwait; [3] Health Science Center, Faculty of Medicine, Kuwait University, Jabriya, Kuwait

CASE REPORT

Background:
Status epilepticus without a prior history of seizure or epilepsy is rare, different neurological manifestations, including seizures, are increasingly being documented with COVID-19 infection.

Case Summary:
We report a case of generalized status epilepticus secondary to COVID-19 infection.

Conclusion and Novelty findings:
Despite the many faces of this disease, further research is needed to clearly elucidate the mechanism of neurological presentations in SARS-CoV-2 infection.

Key Words: COVID-19; Neurology; SARS;

Medicine

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Coxiella burnetii Endocarditis in a Patient with Systemic Lupus Erythematosus: A Case Report of a Diagnostic Challenge

Alqallaf A [1], Alhashim A [2], Alajmi M [3], Alsaqob A [4], Al-Adsani W[5]
[1] Division of Nephrology, Mubarak Al-Kabeer Hospital, Jabriya, Kuwait;[2] Aldabbous Cardiac Center, Adan Hospital, Hadiya, Kuwait;[3] Department of Internal Medicine, Jaber Al-Ahmed Armed Forces Hospital, Kuwait City, Kuwait; [4] Medical Intern, Ministry of Health, Kuwait; [5] Department of Internal Medicine, Mubarak Al-Kabeer Hospital, Jabriya, Kuwait

CASE REPORT

Introduction
There is a close association between Q fever and autoimmune disease, with some case reports in the litera- ture of Q fever presenting as systemic lupus erythematosus (SLE) and others documenting their coexistence. However, making the correct diagnosis remains challenging and Q fever often is overlooked. Therefore, it is es- sential to review such a rare presentation to help in accurate diagnosis in future cases. This report is of a case of endocarditis due to Coxiella burnetii in a patient with Q fever and a history of SLE.

Case description
We report the case of a 43-year-old man with a history of SLE and rheumatic heart disease, status post-valve replacement. The patient initially presented with an acute kidney injury in the setting of a history of full-house lupus membranous nephropathy, which was diagnosed on kidney biopsy. The patient had been on immuno-suppressive therapy for 2 years. Shortly after he was admitted, echocardiography was ordered because the pa-tient had progressive dyspnea, revealing infective endocarditis involving multiple valves. He underwent valve repair surgery and was placed on an extended course of antibiotic therapy. His symptoms gradually resolved, with normalization of his immunological markers. The patient's immunosuppressive regimen was eventually discontinued. He remains on lifelong antibiotic suppression therapy.

Conclusion
This case highlights the importance of awareness of infectious causes of endocarditis in patients with under- lying autoimmune diseases such as SLE. This rare case of C burnetii endocarditis may have been associated with underlying valvular SLE.

Key Words: Lupus Erythematosus, Systemic ; Endocarditis ; Q Fever;

Medicine

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A Preventable Misfortune: A Case of Total Anomalous Pulmonary Venous Drainage Repaired in Adulthood

Alsaqobi A [1]*, Alanbaie M [2], Uthaman B [2], Al- Qallaf A[1]
[1]Department of Internal Medicine, Mubarak Al-Kabeer Hospital, Jabriya, Kuwait; [2]Department of Cardiology, Chest Disease Hospital, Sabah, Kuwait

CASE REPORT

Background
Total anomalous pulmonary venous drainage (TAPVD) is one of the less common cyanotic congenital heart diseases. Most patients present early in the first year of life. It is quite rare for this condition to present in childhood and it is extremely rare for it to manifest in adulthood. Delay in presentation especially in adulthood can have irreversible consequences on the pulmonary vasculature with persistent symptoms even after repair. Therefore, it becomes evident that it is important to review such cases and address the reasons behind those delays, which has been a neglected aspect of this entity. In this report, we present a case of a 23 year old female with supracardiac TAPVD first diagnosed and repaired in adulthood.

Case presentation
A 23 year old female, with a history of uncorrected atrial septal defect (ASD), presented with progressive dyspnea, and fatigue for 1 and half year duration. Physical examination was positive for a right ventricular heave, a fixed splitting of S2 with a loud P2 component and a systolic ejection murmur. ECG and chest x-ray showed right ventricular enlargement and snowman sign, respectively. Echocardiography and cardiac catheterization confirmed the diagnosis of unobstructed supracardiac TAPVD with a large ASD complicated by mild pulmonary hypertension.

Conclusion
Missed TAPVD in newborns can have catastrophic consequences for patients who remain asymptomatic for a long period of time. Pulmonary hypertension is the endpoint, sometimes with persistent symptoms after repair. There is a need for a way to detect those cases earlier.

Key Words: Total anomalous pulmonary venous drainage; Adult congenital heart disease; repair;

Medicine

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Foot drop post body contouring surgery: The cost of a six-pack?

Gopinath B, Alkandari SA, Al-Oraify MB, *Abdulsalam AJ
Physical Medicine and Rehabilitation, Physical Medicine and Rehabilitation Hospital, Andalous, Kuwait

CASE REPORT

Introduction:
Given the growing number of abdominoplasties being performed, it is increasingly important for both physicians and patients to acknowledge the possiblecomplications of this procedure. A group of these complications include different nerve injuries due to incisional, or less commonly, positional consequences.

Case Summary:
We present a 25-year-old (otherwise healthy) male who developed left foot drop immediately after body contouring surgery (abdominoplasty and bilateral inner thigh lift).

Conclusions and Novelty of Findings:
We suggest avoiding combinations of surgeries that lead to having to adjust patients into multiple positions (e.g. frog and semi-recumbent) to decrease compression and complications, as discussed in the literature.

Key Words: Abdominoplasty; Complication; Obesity;

Medicine

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Sonographic Evaluation of Laser Therapy Efficacy In Treatment Of Dupuytrens Contracture

Shehab D [1], Ambardar R* [1], Dughbaj M[2]
Department of Physical medicine and Rehabilitation Mubarak Al-Kabeer Hospital Kuwait [1]; Physical medicine and Rehabilitation Hospital Kuwait[2]

CASE REPORT

BACKGROUND:
A 65 year old woman is seen in PMR clinic for management of Dupuytren's contracture of the right hand as it affects her hand function. She has type 2 diabetes mellitus, hypertension and ischemic heart disease with no history of trauma, fracture or infection.Clinical examination of the right hand showed thickening of the palmar fascia of the fourth finger, with palpable tender nodule at MCPJ with incomplete hand fist and incomplete ring finger extension. Pain score using visual analogue scale (VAS), Michigan Hand Outcome Questionnaire (MHQ) was recorded.

CASE SUMMARY:
After a diagnostic ultrasound the patient received a total of 6 sittings of Low Laser Treatment (LLT) for the right hand, two sittings per week Ultrasound examination of region of interest at 1 cm proximal and 1 cm distal to the MCPJ of right ring finger showed a hypoechoic nodule measuring 11.4 mm in length and 1.5 mm in thickness and a hypoechoic cord measuring 6.3 mm in length.

RESULTS:
She started to show improvement in VAS score from 8/10 to 4/10 and MHQ score Ultrasound evaluation after finishing Low laser treatment at week 6 showed sonographic improvement in nodule and cord measurements, nodule length 10.9 mm and thickness 0.96 mm and cord length 5.9 mm .

CONCLUSION:
To our knowledge it is the first study that combined the effect of LLT in improving pain, hand function combining clinical and US images evidence. Ultrasonography is safe and easy and can be of value in diagnosis and monitoring outcome of rehabilitation interventions for the treatment of Dupuytrens disease.

Key Words: DUPYTRENS DISEASE; LOW LEVEL LASER; SONOGRAPHIC EVALUATION;

Medicine

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Swollen shoulder in Rheumatoid Arthitis: (where) shall we inject?

Shehab D [1], *AL Jarallah K [1], Ambardar R[2], Ozcakar L[3]
[1]Medicine Department, Faculty of Medicine, Kuwait University, Kuwait; [2] Department of Physical and Rehabilitation Medicine, Ministry of Health, Kuwait; [3] Department of Physical and Rehabilitation Medicine, Hacettepe University

CASE REPORT

Shoulder involvement is frequent during the natural history of Rheumatoid Arthritis (RA).Several structures can be targeted by the disease;especially the glenohumeral joint (GH).Further,the involvement of the periarticular structures (due to synovitis, pannus, bursitis and tendonitis) also results in pain,functional loss and difficulties with daily activities. In certain cases, while the patient history and physical examination suggest rheumatoid involvement of the shoulder, evaluation using laboratory and imaging tools are sometimes necessary for prompt diagnosis. On the other hand, concomitant problems might cloud the clinical scenario. Likewise, presenting an interesting patient of ours, we caution physicians as regards such challenging conditions.We also highlight once again the role convenient ultrasound (US) imaging during daily practice.

Key Words: RHEUMATOID ARTHITIS; SWOLLEN SHOULDER; INTRAARTICULAR INJECTION;

Microbiology and Immunology

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CNS blastomycosis: The first reported case in a Kuwaiti graduate student from America.

Alobaid K*[1], Alhasawi A [2], Grover S [2]
[1] Medical laboratory department, Mubarak Alkabeer hospital; [2] Medical department, Infectious diseases hospital

CASE REPORT

Background:
Blastomycosis is a systemic fungal disease endemic in North America. Clinical presentation ranges from asymptomatic illness to severe disseminated disease. It can involve the lungs, skin, bone and central nervous system. Because infection is geographically restricted, many clinicians are unfamiliar with the disease. Laboratory diagnosis is based on microscopy, culture and serology. But in this part of the world, lack of lab experience and awareness are major barriers to reaching the diagnosis. The present case clearly illustrates the value of gene sequencing in the diagnosis of blastomycosis especially in non-endemic areas.

Case summary:
A 24-year-old Kuwaiti man was admitted with a history of generalized seizures. In 20[1,2], he travelled to Tennessee, USA, for graduate study and finished in 2018, a few months before this illness. During his hospital stay, he underwent various investigations including MRI brain which showed left temporal occipital lesion. It was round shaped on intensive contrast enhancement. He was started on albendazole and steroids on assumption of neurocysticercosis. To control his seizures, he was started on oral Phenytoin 300mg once daily. The patient had decided to travel to France for further management. As routine, microbiology and radiology investigations were not conclusive, a brain biopsy was done which was suggestive of an infectious origin. Gene sequencing revealed the etiologic agent which was Blastomyces dermatitidis. The patient was started on Voriconazole 300mg BD. He had an uncomplicated treatment course. He had completed a full 12-month-course of voriconazole with good resolution of the lesion.

Conclusions:
CNS blastomycosis is a life-threatening disease. The diagnosis requires high degree of suspicion with great emphasis on travel history to endemic areas. Beside conventional laboratory diagnostic methods, gene sequencing is an appropriate option for early and accurate diagnosis. Novelty: First reported case in Kuwait.

Key Words: Blastomycosis ; Gene sequencing ; Kuwait ;

Microbiology and Immunology

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Fatal Pulmonary Aspergillosis In A COVID-19 Infected Patient

*Alobaid K[1], Alsarraf A[2], Mazloum S[3]
[1] Mycology reference laboratory, Medical laboratory department, Mubarak Alkabeer hospital; [2] Department of Intensive care, Jaber Al-Ahmad hospital; [3] Microbiology unit, Medical laboratory department, Jaber Al-Ahmad hospital.

CASE REPORT

Background: Critically ill patients who are infected with SARS-CoV-2 are prone to secondary infections. Aspergillus species has become a successful secondary pathogen complicating the course of disease and leading to significant mortality rates. Lack of awareness of COVID-19 associated pulmonary aspergillosis (CAPA) results in missed diagnosis and hence poor outcome.

Case Summary:72 years old man who is known to have diabetes millitus and hyperlipidemia was infected with SARS-CoV-2 requiring hospitalization. Broad coverage of antibacterial regimen and dexamethasone were given, but he developed severe respiratory failure and required intubation and mechanical ventilation. Bronchoscopy revealed evidence of tracheobronchitis and BAL culture grew Aspergillus fumigatus. Despite voriconazole therapy and maximal intensive support, the patient died few days later.

Conclusions: COVID-19 infected patients are vulnerable to secondary invasive aspergillosis manifesting as tracheobronchitis and/or pulmonary infection, which can lead to considerable mortality. Increased awareness and specific mycological workup are essential and may help to improve the outcome.

Key Words: COVID-19; Aspergillus; ICU;

Pathology

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Multiple Pathologies in a Case Presenting with Intestinal Obstruction: Appendiceal 'Adenocarcinoma Ex Goblet Cell Carcinoid' Coexisting with Crohn's Disease and CMV Infection

Alabdulhadi N*, Al-Taleb A, Francis I Pathology Laboratory, Mubarak Al-Kabeer Hospital

CASE REPORT

BACKGROUND:
Goblet cell carcinoid/carcinoma (GCC) is a rare tumor incidentally found in specimens of appendicitis. Carcinoid tumors co-existing with inflammatory bowel disease (IBD) in the small bowel have been sporadically reported in the literature but it is unknown whether this association is fortuitous or causative. The so-called 'Adenocarcinoma ex-goblet cell carcinoid' is the high-grade version of GCC that is appendix-specific, occurring predominantly in women, and is associated with widespread intra-abdominal dissemination. Herein we report a case of appendiceal adenocarcinoma ex-GCC in a patient with Crohn's disease.

CASE SUMMARY:
A 38-year-old female presented to the emergency room with a clinical picture of intestinal obstruction. Four months prior to this she was diagnosed with IBD on endoscopic biopsy which proved to be unresponsive to steroid therapy. MR enterography showed thickening of the walls of the terminal ileum, cecum and appendix with dilation of bowel loops distally. Laparoscopic ileocecectomy was preformed 3 days after admission and was sent for histopathological examination. The diagnosis of IBD-Crohn's disease was confirmed but in addition to that a superimposed adenocarcinoma ex-GCC was detected, originating in the appendix and extending to terminal ileum and cecum with serosal implants (stage pT4N2). Moreover, histology showed evidence of cytomegalovirus (CMV) infection of bowel with the characteristic intranuclear inclusions, which was confirmed by immunohistochemistry. The patient opted to continue her treatment abroad.

CONCLUSION:
Both Crohn's disease and disseminated adenocarcinoma ex-GCC are potential causes of intestinal obstruction. Their co-existence in this case is an interesting finding that is rarely encountered. The presence of CMV infection may suggest viral reactivation following steroid therapy but some evidence also suggests that CMV itself may be a possible cause of steroid-resistant IBD.

Key Words: appendix; adenocarcinoma ex goblet cell carcinoid; Crohn's disease;

Pathology

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Pediatric Precursor B-cell Lymphoblastic Lymphoma presenting as destructive bone lesion: a report of two cases and review of literature.

Alath P*[1], Shaaban HM [1], El-Kabany MA[2], Al Kandari SR[3], Nouh MA [4], George SS[5], Al JassarA [1], Kapila K[5]

[1,2]Department of Cytology and Histopathology, Kuwait Cancer Control Center, Kuwait; [3]Department of Radiology, Al Razi Hospital, Kuwait; [4]Department of Pathology, National Cancer Institute, Cairo University and Children cancer Hospital; [5]Department of Pathology, Faculty of Medicine, Kuwait University

CASE REPORT

Background:

Primary bone lymphoma (PBL) is a rare clinical entity accounting for <1% of all lymphomas and 7% of all malignant bone tumours. Precursor B cell lymphoblastic lymphoma (PBLBL) accounts for only 3% of pediatric Non-Hodgkin's lymphoma and presentation with primary bone involvement is rarely reported in literature. PBLBL may mimic Ewing's sarcoma (ES) which is the most common round cell tumour involving the bone. It is of vital importance to distinguish PBLBL from ES as the clinical behavior, treatment and outcome differ significantly. We report two pediatric cases of PBLBL of bone reported on cytology and confirmed by biopsy.

Case Summary:

Case 1: A 6 year old Egyptian girl presented with an aggressive osteolytic lesion of proximal metaphysis of left tibia with periosteal reaction and intramedullary fluid collection seen by MRI. Core biopsy and needle rinses for cytology showed small round cell tumour with abundant necrosis. Immunohistochemistry done on cell block section was positive for TdT, CD10, CD79a and negative for NSE, Synaptophysin,CD99 favouring PBLB. Case 2: A 6 year old non Kuwaiti boy presented with an aggressive lesion of upper half of left ulna with cortical thickening, permeation and areas of cortical breakthrough seen by MRI. Core biopsy and needle rinses for cytology showed a round blue cell tumour. The tumour cells stained positive for CD99, CD10,TdT PAX 5,CD43,CD79a and negative for LCA, Synaptophysin,CD20,CD3.Based on this a diagnosis of B-acute lymphoblastic lymphoma was given.

Conclusion:

Primary PBLBL of bone is rare. Clinically and histologically it may be confused with other small round cell tumours. The curability of PBLBL in contrast to other malignancies of bone makes early and accurate diagnosis of paramount importance. Hence PBLBL must be considered in differential diagnosis when dealing with small round cell tumours of bone in children and adequate immunohistochemistry markers used to differentiate this entity.

Key Words: Pediatric; Lymphoblastic lymphoma; Bone lesion;

Pathology

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Metastatic renal cell carcinoma to the thyroid gland: Report of two cases and review of literature.

Amir T* [1], El Shazly N [1], Alath P [1], George S S[2], Al Jassar A [1], Kapila K[2]
[1]Department of Cytopathology, Kuwait Cancer Control Center; [2]Department of Pathology, Faculty of Medicine, Kuwait.

CASE REPORT

Background

Incidence of thyroid metastasis ranges from 0.1% to 6% of all thyroid malignancies. Thyroid metastasis commonly originates from kidney, lung or breast. Renal cell carcinoma(RCC) is common accounting for 48.1% of all metastatic thyroid malignancies. The mean interval between RCC diagnosis and metastasis to the thyroid ranges from 6 to 12.5 years. Diagnosing thyroid metastasis is challenging because metastatic nodules mimic benign masses in ultrasonography and most cases are asymptomatic. We wanted to evaluate the utility of Fine needle aspirates(FNA) in metastatic RCC to thyroid

Case 1:

A 52 year- old Brazilian female presented with back pain and thyroid swelling. She was diagnosed with RCC one year back. Thyroid ultrasound showed multiple mixed echogenic nodules (TIRADS 3). Ultrasound guided FNA(USG-FNA) of left thyroid nodule (1.8x1.7cm) showed sheets and clusters of cells with clear cytoplasm, round nuclei with prominent nucleoli. The cells stained positive for CD10, RCC antigen and negative for TTF1. A diagnosis of metastatic RCC was made.

Case 2:

A 61 year- old Kuwaiti male presented with thyroid swelling for two years. He had a right nephrectomy 10 years back for RCC followed by partial gastrectomy four months later for metastatic RCC. Thyroid ultrasound showed multiple hypoechoic nodules in both lobes with increased vascularity. USG-FNA of left thyroid nodule (4x3cm) showed sheets and clusters of cells with round nuclei, prominent nucleoli and occasional grooving. The cells stained positive for CD10, RCC antigen, CK19, Vimentin and negative for TTF1 and CK 7. A diagnosis of metastatic RCC was made.

Conclusion

Diagnosis of metastatic RCC is clinically challenging due to its indolent clinical course. FNA an accepted diagnostic tool for thyroid malignancies/metastases has a reported sensitivity of 73.7% - 94% and specificity upto 100%. PAX2, RCC marker, CD10, vimentin, and alpha-methylacyl-CoA racemase are useful diagnostic markers for RCC.

Key Words: Fine needle aspiration cytology; Metastatic renal cell carcinoma ;

Pathology

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Diagnosis of Chondroblastoma,Fine Needle Aspiration-Report of three cases.

Gupta R* [1], Shadi A H[2], Ghafoori M[2], AL Abdulghani R [1], AL Jassar A [1], Kapila K [3]

[1] Department of Pathology, Kuwait Cancer Control Center, Kuwait; [2] Department of Radiology and Imaging, Al Razi Hospital Kuwait; [3] Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait

CASE REPORT

Background:
Chondroblastoma is an uncommon osseous neoplasm that accounts for less than 1% of all bone tumors. It characteristically arises in the epiphysis and extend to metaphyseal region of long bones and has been reported to affect people of all ages with slight male predilection. We report the cytological features on fine-needle aspiration (FNA) of three cases of chondroblastoma which was further confirmed by histopathological examination.

Case summary:
Case-1 13 years old female presented with the epiphyseal osteolytic lesion of right femoral head. Cytomorphology was consistent with chondroblastoma showing cluster of cells with round to ovoid nuclei and fine chromatin showing frequent nuclear grooves and convolutions along with osteoclast like giant cells in the background. The diagnosis was confirmed by histopathology. Case 2: 15 years old male patient presented with lytic lesion in the lateral condyle of right femur. Cytomorphology was same as case 1. The diagnosis was also confirmed by histopathology. Case-3: 34 years old male patient presented with lytic lesion in the acetabulum.
Cytomorphology was reported as suggestive of chondroblastoma because of polygonal cells in solid nests having bland nuclei with grooving, chicken wire type calcification and osteoclast like giant cells in the background. Histopathology was reported as compatible with chondroblastoma.

Conclusion:
FNA with the radiological findings provides an accurate and rapid method to diagnose osseous neoplasms. It is becoming a valuable preoperative technique in the management of these patients. Individually lying chondroblasts with a distinct cell boundary, nuclear grooves, chondroid matrix and chicken-wire calcification are diagnostic cytological features of chondroblastoma and make FNA a prudent preoperative method in the management of these patients.

Key Words: Chondroblastoma; Fine Needle Aspiration; Histopathology;

Pathology

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Multiple myeloma involving the thyroid, a case report

Sharfudeen S* [1], Kunhikrishnan A [2], George S [3], Al Jassar [1], Kapila K [3]
[1] Department of Pathology, Kuwait cancer control center; [2] Department of Hematology and Bone marrow transplant, Kuwait cancer control center; [3] Department of Pathology, Faculty of Medicine, Kuwait University

CASE REPORT

Background
Metastases to the thyroid are unusual; approximately 7.5% of thyroid malignancies, although the gland has a rich vascular supply. Common sites of origin arise from the lungs, oesophagus, breasts, and kidneys. Monoclonal proliferations of plasma cell origin may be seen in extraosseous plasmacytoma or as a part of extramedullary disease (EMD) of multiple myeloma, the most frequent site being the skin. The involvement of thyroid in plasma cell malignancy is exceedingly rare. We report a case of Multiple myeloma involving the thyroid gland, associated with Ig G kappa monoclonal protein and diagnosed on fine needle aspiration cytology (FNAC).

Case Summary
A 73 year old woman presented with thyroid swelling associated with dysphagia for a month. She had history of hypertension, diabetes, ischemic heart disease and pathological fracture of the right humerus 2 years back. A bone marrow study (38% plasmocytosis), immunophenotyping and serum electrophoresis pointed to a diagnosis of Multiple myeloma; for which she was treated with chemo/ radiotherapy. Follow up, a year later by PET/CT scan revealed high uptake in the thyroid. Ultrasonography (U/S) of the neck showed a solitary hypoechoic nodule in the left lobe of thyroid. FNAC from the nodule showed cellular smears, comprised of plasmacytoid cells in sheets, having hyperchromatic nuclei with a perinuclear hoff mixed with clusters of benign thyroid follicular cells and Hurthle cells.

Conclusion:
Clinical history, imaging techniques and FNAC are key factors in the diagnosis of thyroid lesions. Distinction between metastasis and direct infiltration of the thyroid by locally aggressive disease will significantly change treatment decisions and outcomes. There is limited data on the incidence and biology of extramedullary disease (EMD) spread. Potential mechanisms include decreased expression of adhesion molecules, along with loss of CD56, facilitating disease dissemination.

Key Words: Multiple myeloma; Thyroid; Fine needle aspiration cytology (FNAC);

Pediatrics

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Acute Necrotizing Encephalitis: Emphasizing the Importance of the Flu Vaccine

Alnajem A*[1], Esmaeil A[1], Ashkanani H[1], Rashed K[2], Alraqeeb F [2], Habeeb Y [2], Haider E[2]

[1]Kuwait University, FOM; [2]Department of Pediatrics, Mubarak Al-Kabeer Hospital

CASE REPORT

Background:
Acute necrotizing encephalitis is a rare but distinctive type of acute encephalopathy with global distribution. It is a parainfectious disease that is triggered by viral infection, most commonly influenza A virus.

Case Summary:
A 9 year old previously healthy girl presented with a 1 day history of fever, headache, vomiting, and coryzal symptoms. In the emergency room, the patient suddenly became encephalitic and developed seizure. She was resuscitated and received midazolam until she was stable. A full septic work up was done, which was negative, then she was started on antibiotics and antivirals, and an urgent CT head was done. The patient was sent to the ward as she was encephalitic with a GCS of 10. On the next day, the patient was shifted to the pediatric ICU, where her GCS dropped to 8, and she was placed on CMV for 2 days and received IVIGs for 5 days.She had a positive nasopharyngeal swab for influenza A virus, and on CSF analysis, she had high proteins. Culture and staining was positive with coagulase negative staphylococcus, and virology for the influenza A was negative. On CT, patient had bilateral basal ganglia and thalami hypodensities. Further evaluation by MRI was highly suggestive of acute necrotizing encephalitis related to viral infection. The patient was managed by a multidisciplinary team including general pediatrics, pediatric neurology, gastroenterology, physiotherapy, and virology. She received oseltamivir and clarithromycin for 14 days. Also, she was kept on seizure prophylaxis by levetiracetam and was started on esomeprazole and macrogol.

Conclusion:
Acute necrotizing encephalitis is an encephalopathy triggered by viral infection, most commonly the Influenza A Virus. It is diagnosed by positive NPS, as well as MRI changes. Therefore, it is important to take the flu vaccine, as there are several rare complications that are arising, and these complications are leading to significant cognitive impairments and negative quality of life effects.

Key Words: Necrotizing encephalitis; Pediatrics; Flu vaccine;

Pediatrics

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Pancreatic pseudocyst in a child: A case report and review of literature

BinNakhi HA, Abd-Alqawi N*, Abdulrahman R
Paediatric Department, Al Adan Hospital, State of Kuwait

CASE REPORT

Background:
We report a 6-year-old Kuwaiti girl who presented with acute pancreatitis (AP) that was complicated with the development of pancreatic pseudocyst (PPC). Paediatric acute pancreatitis (PAP) is increasingly recognized and diagnosed. In children AP resolve spontaneously with supportive management. Nevertheless, in some cases children with AP need to be followed for local and systemic complications that may include the development of PPC. This paper will provide a practical approach to PPC management in children based on the latest available guidelines, emphasising the importance of individualizing the management according to the patient clinical condition.

Case summary:
A 6 year old Kuwaiti girl who is product of full term normal delivery and known to be completely previously healthy presented with sudden onset of severe abdominal pain that is associated with repeated vomiting. Surgical causes were ruled out. Serum amylase (2332 IU/L) and lipase (5611IU/L) were elevated. Patient was diagnosed with AP started on intravenous antibiotic, intravenous fluid, and stopped oral feed to rest the gut. Patient was discharged after 10 days with no abdominal pain on fat free diet. She was readmitted within 5 days with severe abdominal pain. Abdomen US/CT showed PPC measures 8.4cm x7.2cm x5.7 cm with elevated pancreatic enzymes. Patient was managed conservatively and needed total parenteral nutrition (TPN). No surgical intervention needed. The PPC resolved over 5 weeks of duration.

Conclusion:
In children PPC may complicate AP. Paediatric PPC management is a challenge. It requires multispecialty team approach that include paediatrician, gastroenterologist, surgeon, and nutritionist. Supportive medical therapy, with intravenous hydration, pain control, and bowel rest may allow some pseudocysts to resolve. TPN may be needed. Surgical intervention is indicated in case of large, persistent, and symptomatic PPC due to the risk of infection, and or rupture.

Key Words: Pediatric Acute Pancreatitis; Pancreatic pseudocyst; Management of pancreatic pseudocyst in children;

Pediatrics

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Caroli syndrome: A case report of two sisters from Kuwait

BinNakhi HA*, Abdelkawi N, Al Badrawi A
Al Adan Hospital, Paediatrics Department, State of Kuwait

CASE REPORT

Background:
Caroli syndrome is a rare inherited (autosomal recessive) disorder of the intrahepatic bile ducts. It is characterized by congenital dilatation of the intrahepatic biliary tree and congenital hepatic fibrosis. Caroli syndrome is often associated with polycystic kidney disease (PKD). This case report of two sisters diagnosed to have Caroli syndrome will emphasize the clinical presentation, natural history, and the genetic findings of this rare syndrome.

Case Report:
The index case presented at age of 4 years with recurrent abdominal pain and repeated vomiting. On examination was found to have abdominal distension with significant hepato-splenomegaly. She is a product of full term normal delivery to healthy first degree consanguineous parents. Abdominal ultrasound confirmed the hepatosplenomegaly with dilated intrahepatic bile ducts (IHBD). It also showed evidence of bilateral polycystic kidneys. Abdominal computer tomography (CT) demonstrated central dot sign. The younger sister presented at age of 4 months with hepatosplenomegaly. Abdominal ultrasound and CT findings were suggestive of hepatic fibrosis with early portal hypertention and PKD. Genetic testing was homozygous to autosomal recessive polycystic kidney disease (ARPKD) gene for both sisters while parents are heterozygous. Currently both girls are doing well with normal hepatorenal function admitted several times for urinary tract infection and/or cholingitis.

Conclusion:
Caroli syndrome should be considered in the differential diagnosis of patients with unexplained hepatosplenomegaly, recurrent abdominal pain, and cholestasis due to congenital intrahepatic bile duct dilatation. It is important to recognize this syndrome due to its association with recurrent cholengitis, liver abscess, liver cirrhosis, and cholangiocarcinoma. Family screening for ARPKD is also needed in these patients to clarify the associated renal abnormality and the mode of inheritance of this rare disease.

Key Words: Caroli syndrome; Congenital Dilatation of Intrahepatic Bile Duct, ; Polycystic kidney disease;

Pediatrics

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Lidocaine induced acute ischemic stroke following dental procedure

Farara NE*, Zakkiriah M
Department of Pediatrics, Adan Hospital, Ahmadi Health Region, Ministry of Health, Kuwait

CASE REPORT

Background:
Local anesthesia can lead to lethal complications if injected in highly vascularized area. This case report describes a girl who developed stroke after local lidocaine injection for dental procedure.

Case summary:
An eleven year-old girl with no history of medical problems was admitted to the pediatric intensive care unit (PICU) at the Adan Hospital with status epilepticus following local lidocaine injection which was administered for a dental procedure. The patient's seizure was preceded by fainting, dizziness and persistent vomiting. The patient was found to have generalized weakness with double hemiparesis and exaggerated reflexes on the left side with up-going plantar reflex. The thrombophilic screen and the metabolic work up were normal. The MRI showed multiple cortical infarcts in the fronto-parieto-occipital area on the right side and also on the left frontal area suggesting hypoxic ischemic insult. The EEG showed encephalopathic picture but echocardiography was normal. The case was diagnosed as acute ischemic stroke following lidocaine injection. The girl was continued on Levetiracetam for seizures plus physiotherapy with good response. MRI was repeated 2 months later and showed intracranial gliosis suggesting resolving infarcts. She is currently being followed up in an outpatient clinic and shows good recovery.

Conclusion:
Local anesthesia complications should be kept in mind during dental procedures. Proper management must be done promptly if complications occur.

Key Words: lidocaine; seizures; infarcts;

Pediatrics

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Infantile scurvy: a case report with an unusal presentation

Sadeq S, Abdulla A*, Othman R
Department of Paediatric, Al Adan hospital, state of Kuwait

CASE REPORT

Introduction:

Scurvy, severe vitamin C deficiency, is one of the oldest diseases known to mankind. Yet, currently it is rare. It commonly present with limping and weakness. In this report a one year old female presented with retropharyngeal tear and lower limb swelling proved by plain x-ray as scurvy. This unusual presentation will alert Pediatrician that scurvy is one of the causes of spontaneous retropharyngeal tear.

Case:

A one year old girl, product of full term normal delivery known to be previously healthy, admitted to the hospital with acute onset of fever, and cough noticed to have respiratory distress with a gurgling sound. She was unable to swallow. A hard lump was found on the right thigh. Lateral neck x-ray showed widening of retropharyngeal space with air. CT neck confirmed the diagnosis of retropharyngeal tear. X ray lower limb showed subperiosteal reaction affecting both femur and upper end of tibia encroaching upon growth plate, picture highly suggestive of hypovitaminosis C (scurvy). The patient needed assisted ventilation for one day. She was managed with parenteral nutrition and therapeutic dose of oral vitamin C (300mg/day). Patient was discharged within ten days with complete healing of the pharyngeal tear. Repeated x-ray lower limb 2 month later showed complete resolution.

Conclusion:

Since scurvy, being rare as compared to other nutritional deficiencies, it is seldom suspected and this frequently leads to delayed recognition of this disorder which can be potentially fatal. Awareness of this nutritional deficiency is needed as it is easily treatable condition with excellent prognosis.

Key Words: Scurvy; Vitamin c defecieny; Retropharyngeal air;

Surgery

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Inflammatory fibroid polyp; a rare tumor presenting as small bowel intussusception

Alshamali M [1], Sallam S [1], Al-Zuabi M [1], Kenawy M [1], Abdulraheem J [1], Alzaid D [1], Aleid Y [2], Mohammad K [1]

[1] General Surgery Department, AL-ADAN Hospital, Kuwait; [2] General Surgery Department, Kuwait Institute of Medical Specialization, Kuwait

CASE REPORT

BACKGROUND:
An Inflammatory fibroid polyp (IFP), also known as Vanek's tumor, is a rare benign mesenchymal lesion of the gastrointestinal tract. IFP can be found throughout the gastrointestinal tract but most frequently in the gastric antrum or ileum. The clinical presentation is usually asymptomatic, yet the symptoms depend on the location of the polyp.

CASE SUMMARY:
We report a case of a 30-year-old healthy male, who presented to the emergency department with symptoms of bowel obstruction. A computed tomography of the abdomen was done which demonstrated a small bowel obstruction due to an ileal intussusception. A laparotomy was performed which revealed an ileo-ileal intussusception. After manual reduction, a pedunculated intraluminal mass was found at the terminal ileum and an enterectomy was performed with a small bowel anastomosis.

CONCLUSION:
The postoperative course was unremarkable and the patient was discharged home. Histopathology examination revealed the tumor to be a benign inflammatory fibroid polyp. This case report presents a rare benign tumor originating in the ileum, presenting as a small bowel intussusception that was discovered incidentally during an exploratory laparotomy

Key Words: Vanek's Tumor; Inflammatory Fibroid Polyp; Intussusception;

Surgery

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Hyperbaric oxygen therapy; an adjunct to the treatment of necrotic laparotomy wound

Alshamali M, Kenawy M, Almazroui L, Al-Zoabi M, Alzaid D, Sallam S, Bulbul F, Abdulraheem J, Mohammad K

Department of Surgery, AL-ADAN Hospital, Kuwait.

CASE REPORT

BACKGROUBD:

Hyperbaric oxygen therapy (HBOT) is a treatment in which 100% oxygen at a pressure greater than one atmosphere is administered to the patient. It can be used as an adjunctive therapy in many wound care settings.

CASE SUMMARY

We present a 41-year-old female, who had a prolonged hospital stay with an open abdominal wall dehiscence and scarring with multiple enterocutaneous fistulas. After her revisional surgery to resect the fistula, the patient developed ulceration and breakdown of her laparotomy wound. Hyperbaric oxygen therapy was initiated in addition to intensive wound care to stop the ulcer progression and promote the formation of granulation tissue. Once therapy was completed, a split-thickness skin graft was performedon the granulation tissue to attain wound closure. Hyperbaric oxygen therapy exerts its effect mainly by adequate tissue perfusion and oxygenation. It also has a crucial role in neovascularization as well as activating signaling pathways to stimulate wound growth factors.

CONCLUSION

In this case report, a combination of HBOT, wound care, and adequate nutrition resulted in the formation of a healthy granulation tissue bed. Subsequently, this resulted in the successful adherence of the skin graft. In addition to proper wound care and optimal nutritional support, HBOT can possibly play a role in enhancing wound healing in select cases.

Key Words: Hyperbaric; Abdominal; wound; Fistula;

Medicine

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Bowel Transplant: Unexpected Journey, Lessons Learned, and Challenges—A Case Report

Alqallaf A [1], *Alsaqobi A[2], Abu-Elmagd K[3]
[1]Mubarak Al-Kabeer Hospital, Kuwait; [2]Faculty of Medicine, Kuwait University, Kuwait; [3]Cleveland Clinic, Cleveland, Ohio, United States

CASE REPORT

Background:
A small bowel transplant is one of the least commonly performed solid organ transplant procedure. Many physicians are unaware of this therapeutic option and/or are unable to deal with such patients optimally. This compromises patient quality of care and leads to avoidable morbidity and mortality. Early recognition and treatment of complications is paramount in those patients to preserve graft integrity and more importantly to preserve life. Few centers perform this procedure and are mostly located in North America. This poses a challenge in the care of transplant patients who are referred for the procedure. We report a life that has been lost due to disorganized care and lack of timely follow-up given the rarity of this type of transplant

Case Presentation:
A 35-year-old Kuwaiti male underwent sleeve gastrectomy for morbid obesity. This was complicated by thrombosis of the portal, splenic and superior mesenteric veins. This required extensive bowel resection and the patient developed short bowel syndrome with parenteral nutrition dependence. The patient was referred to the Cleveland Clinic, Ohio, USA in order to be evaluated for small bowel transplantation. He underwent isolated intestinal transplant in June 2015. The patient returned to Kuwait in April 2016, where he faced a disorganized situation without any proper follow-up plans. He was initially followed by his primary general surgeon, then by various specialties from different centers. There were delays in completing important follow- up investigations such as monthly colonoscopy with regular graft biopsies and drug levels. Moreover, there were delays in close follow- up appointments, and failure to find a specialized team in the field of bowel transplant that was needed to manage acute issues and emergencies.

Conclusion:
It is of utmost importance that physicians have basic knowledge about this therapeutic option and how to deal with complications as the consequences of delay in management can be grim.

Key Words: Bowel; Transplant; Complications;

Pharmacology and Toxicology

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Psychological Severity Related to Sickle Cell Disease and Opioids Consumption

Al-Jafar Y*[1], Shamsaldeen F[2], Al-Sayhegh A3, Al-jafar H[4]
[1]Faculty of Pharmacy, Kuwait University; [2]Kuwait Center for Mental Health, Ministry of Health; [3]Amiri Hospital, Ministry of Health

Introduction:
Sickle cell disease (SCD) is inherited as an autosomal recessive disorder, characterized by the sickling of hemoglobin S (HbS) [1]. Patients of SCD experience a wide spectrum of psychological symptoms; it contributes to sever pain with other complications associated with the vaso-occlusive crisis. Opioids medications used as pain killer are a big concern in addiction and psychological problems in SCD [2]. No agreements regarding the concept of any clinical severity for any disease [3]. This study conducted to assess SCD psychological severity complications caused by SCD disease based on assessing pain, opioids, and depression (POD) score.

Methods:
Diagnostic laboratory tests conducted on 150 subjects in this study and confirmed by CBC, reticulocytes, HPLC, liver function test for SCD in Amiri Hospital, Kuwait over the last year. Forty patients subjected to the assessment questionnaire. All candidates visited our SCA outpatient department; they are on daily contact with the main investigator. The psychology severity related to SCD assessed based on the known pain scale, depression scale, and on opioids consumption. A questionnaire was used for the assessment that covers the three SCD related psychology factors POD. The equations are: 1- How often you have sickle cell pain, 2-How often you use the opioids, 3- Do you feel you have depression because of the pain 4- Do you feel depression if you don't use the opioid drug 8- Can you live without opioids, 9- Do you have psychology disorders. The calculation method is the average of score 30 points, 10 points for pain, 10 points for depression, and the opioids are given 10 points according to the amount and frequency of using the opioids as daily, weekly or monthly

Results:
In this on going, 41 total patients aged 8- 66 years old, 21 female 19 adults and 2 children and 20 male, 16 adult and 4 children. Still, other SCD patients are submitting their answers, which based on the three POD parameters. The result up tell now reviled 17 % sever grade POD with a score more than 20, moderate 47 % have with a score between 20-10 and mild 36 % the POD score was below ten grades. The response is good as those patients are very will known to the main investigator for the last four years in SCD clinical classification project.

Conclusions:
No definition for the severity of any disease, but agreements were accepted in the literature for classification scoring with acceptable validity. According to this study, the psychological severity of sickle cell disease could be classified as mild, moderate, and sever based on the three assigned parameters pain, opioid-consumption, and depression score.

Key Words: SCD; Opioid; Depression;

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Anatomy

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Heavy Metal Contents In Herbal Products Sold In Kuwait

Al Ajimi RS*[1], Miskin B [1], Smitha S[2], Rao MS[2]
[1]7th year Medical students, Faculty of Medicine, Kuwait University, Kuwait; [2]Department of Anatomy, Faculty of Medicine, Kuwait University. Kuwait

Introduction:
Heavy metals such as lead(pb), Zinc(Zn), cadmium(Cd) are toxic to human systems. Ingestion of significant amount of cadmium, lead causes poisoning and damage to the brain, liver and the kidneys. Compounds containing cadmium are also carcinogenic. Studies have shown high levels of blood lead content in Kuwait population. The present study was aimed to investigate Pb, Zn, and Cd content in some of the herbal products used extensively in Kuwait. In addition, we also investigated the microminerals such as copper(Cu), manganese(Mn), selenium(Se) content in these herbal product.

Methods:
Herbal products such as Guava leaves, Ashrak leaves, Boswethia carterii, compound mixture of Salvia officinalis+chamomile+Anse+Fennel+Black seed, Myraa + kramesia + olive oil, Henna paste were collected from Kuwait market. A known amount of samples (500mg) were digested in 5ml Perchloric/Nitric acid mixture (1:5) on a shaker, overnight to insure complete dissociation. The samples were then heated on a hotplate to evaporate the Perchloric/Nitric acid mixture completely. White crystals remained at the bottom of the beaker was dissolved in 5ml 1% Nitric acid and analyzed for Pb, Zn, Cd, Cu, Se, and Mn by Inductively Coupled Plasma Mass Spectrometry (ICP-MS). Sample in triplicate were analyzed and mean data was calculated and analyzed.

Results:
In all samples analyzed we found significant amount of Pb and Zn. Cd was found in very small quantity. Microminerals such as copper (Cu) and manganese (Mn) are also found in all in a significant amount. The selenium (Se) content was very minimal in all samples.

Conclusions:
Heavy metal and micromineral were present in large amount in some of the herbal products extensively used in Kuwait. Consumption of the above product may lead to enhanced levels in blood, causing toxic damage to the kidney, liver and brain in particular.

Key Words: Lead; Zinc; Cadmium;

Funding Agency: nil

Anatomy

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Ferulic Acid Enhance Neuronal Differentiation in Hippocampal Stem Cells Derived Neurospheres

Amina AAAS AlSalmi*[1], Kandari MA[1] Smitha S[2], Rao MS[2]
[1]6th year medical students, Faculty of Medicine, Kuwait University, Kuwait; [2]Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait

Introduction:
Asafoetida is an oleo-gum-resin obtained from the exudates of the roots of the plant Ferula asafoetida. Ferulic acid (FA, 4-hydroxy-3-methoxycinnamic acid) is the active component in asafetida. FA has been shown to be neuro stimulant, enhance neuronal stem cells proliferation in the hippocampus. Objective of the present experiment was to investigate the effects of FA on neuronal differentiation of progenitor cells in the hippocampal stem cells derived neurospheres.

Methods:
Stem cell culture was made from embryonic day18 hippocampal cells. Neurospheres were grown for one week and were divided into control (C), and three ferulic acid treatment groups (FA-5µM, FA-10µM and FA-15µM), Control neurospheres remained without any further treatment, FA-5µM, FA-10µM and FA-15µM groups were treated with 5µM,10µM and 15µM ferulic acid respectively for one week. Triplicate cultures were maintained for each group. After treatment, the neurospheres were grown in differentiation media for one week. Cultures were terminated, and immunostaied for TuJ-1, (Neuronal marker), GFAP (astrocytic marker) to label the neurons and astrocytes. Number of neurons and astrocytes differentiated in each neurosphere were quantified. Data were expressed as mean±SEM analyzed with one-way ANOVA.

Results:
Number of differentiated neurons from the neurosphere that are treated with 10µM and 15µM ferulic acid are found to be significantly (30-40%, $p<0.01$) more compared to control group. 5µM ferulic acid had no effect on neuronal differentiation. Number of differentiated astrocytes from the neurosphere that are treated with 10µM and 15µM ferulic acid are also found to be marginally increased (10-20%, $p<0.05$) compared to control group. 5µM ferulic acid had no effect on astrocyte differentiation.

Conclusions:
These results suggest neuron and astrocytes stimulatory role of ferulic acid in neurosphere. It facilitates the differentiation of neurons and astrocytes in the neurosphere.

Key Words: Stem cells; Neurosphere; Ferulic acid;

Funding Agency: nil

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Contact: Centre for Research Support and Conferences; Office of the Vice Dean for Research and Post Graduate Studies; Faculty of Medicine, Kuwait University; Tel: +965 246 36418 /+965 246 36494; Fax: 18455 253 965+; Email: poster@hsc.edu.kw; Web: www.hsc.edu.kw/poster