ABSTRACT BOOK

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Conference Program

Inaugural Ceremony: Wednesday, 8th March 2023 **Venue: HSC Auditorium; Moderator: Dr. Dana Al-Tarrah**					
9:00 AM - 12:00 PM	***Poster viewing***				
1:00 PM	***National Anthem, Recitation of Holy Quran***				
1:05 PM	***Welcome Address, Opening of Poster Conference*** *Acting Vice-Dean for Research & Postgraduate Studies, College of Medicine*				
1.10 – 1.20 pm	***Announcement of Awards by Chief Judge: Prof. Ahmed El-Hashim*** ***Award Winner's Presentation: Day 1: Moderator: Dr. Shorouk Dannoon*** *10 minutes per each winner's presentation*				
1.20 -2.20 pm	*1.20 -1.30 pm*	*1.35 -1.45 pm*	*1.50 -2.00 pm*	*2.00 -2.10 pm*	*2.10 – 2.20 pm*
Slots	*Oral -1 Resident1*	*Oral 2: Case report*	*Oral 3: UG1*	*Oral 4- MSc1*	*Oral 5- PhD1*
2.20 – 2.30 PM	***Introduction of Keynote Speaker: Dr. Suleiman Al Sabah*** *Chairman of Organizing Committee*				
2.30 – 3:30 PM	***Keynote Lecture:* "Why can we expect a revolution in obesity treatment?"** ***Professor Carel le Roux; MBChB, MSc, FRCP, FRCPath, PhD*** *Co-Director Metabolic Medicine lab; Diabetes Complications Research Centre* *Conway Institute, University College Dublin*				
3:30 – 5:00 PM	***Opening of Poster Conference & poster viewing with refreshments*** *President, Vice President for Research, HSC Vice President, Assistant Vice President for Research, HSC Deans and Vice-Deans, All Participants*				
5.00 – 6.30 PM	***Debate - Organized by KuMSA***				
9th March 2023; Moderator: Dr. Fatemah Safar					
9:00 AM – 12:00 PM	***Poster viewing with Refreshments***				
1:00 – 1:30 PM	***Detailed Announcement of Awards by Chief Judge***				
1:30 – 2:30 PM	***Award Winners' Presentation: Day 2:*** *10 minutes per each presentation*				
1.30 -2.30 pm	*1.30 -1.40 pm*	*1.45 – 1.55 pm*	*2.00 – 2.10 pm*	*2.10 -2.20 pm*	*1.20 -2.30 pm*
Slots	*Oral 6- UG 2*	*Oral 7- Resident 2*	*Oral 8- UG3*	*Oral 9- MSc 2*	*Oral 10-PhD 2*
2:30 PM	***Honoring of Award winners, Committees & Judges*** ***Vote of Thanks: Dr. Suleiman Al Sabah***				
3.00 PM	***Social Events– Organized by KuMSA***				

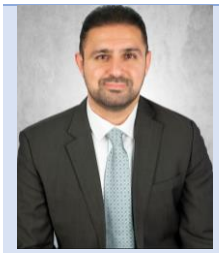
KIMS CME/CPED Credits: Category 1: 11 Credits; CME/CPED Reg. No. 04623/IME1/Mar23;
Online Registration for CME: https://bit.ly/PC2023Registration
Centre for Research Support and Conferences, Office of the Vice Dean for Research and Post Graduate Studies; College of Medicine, Kuwait University, Kuwait. Tel: +965 246 36418;
Email: poster.hsc@ku.edu.kw; Web: http://www.hsc.edu.kw/Poster/Main/Index.aspx

HSC Poster Conference Central Committee 2023

Dr. Heba Al Hussaini, Acting Vice Dean of Research & Postgraduate Studies

Dr. Sulaiman Al Sabah, Chairman of Organizing Committee, Pharmacology, COM

Prof Narayana Kilarkaje, Anatomy, COM



Prof. Maitham Khajah, Pharmacology & Therapeutics, COP

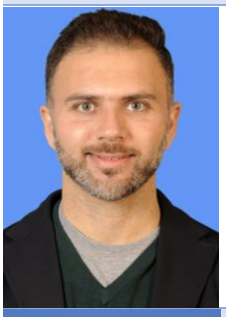
Prof. Ali Ziyab, Community Medicine, COM

Dr. Selma Alkafeef, Biochemistry, COM

Dr. Shorouk Dannoon, Nuclear Medicine, COM

Dr. Wassim Chehadeh, Microbiology, COM

Dr. Muath Alanbaei, Medicine, COM

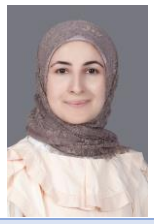


Dr. Ahmad Al Serri, Pathology, COM

Dr. Abdel Rahman Al Serri, Obse & Gyne, COM

Dr. Maysoon Al-Rushood, Pediatrics, COM

Dr. Munya Al-Fulaij, Pharmacology, COM

 *Dr. Fatemah Safar, Physiology, COM*	*Dr. Ghadeer Al Baloul, Radiological sciences, CAH*
 *Dr. Saud Al-Zaid, Surgery, COM*	 *Dr. Syed Saad bin Qasim, Bio-clinical Sciences, COD*
Dr. Dana Al-Tarrah, Social and Behavioral Sciences, COPH	*Ms. Latifa Salem Ben Farah, Finance Chairperson, COM*
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Centre for Research Support & Conferences

Dr. Selma Alkafeef, Director	
Ms. Teena Sadan *Senior Technician*	*Mrs. Rania Al-Mawlawi* *Administrative Coordinator*
Ms Yasmeen Al Bader	

Address of Vice-Dean for Research and Post-Graduate Studies, College of Medicine

A strong research culture is the keystone of any aspiring academic institution. It is with great pleasure that I invite you to our first in-person Health Sciences Center poster conference since the recent pandemic. The HSC poster conference has been an annual event since the first HSC conference was held at the College of Medicine in 1996. The HSC poster conference provides out staff and students with the opportunity to showcase their work in a wide range of academic disciplines within the field of Health Science, to engage in stimulating discussions and foster inter-disciplinary collaborations.

In the continuing tradition of inviting world-renowned scientists, whose work has a significant impact on human health, we are honored that Prof. Carel le Roux from the School of Medicine, University College Dublin, Ireland has agreed to deliver our keynote address entitled; "Why can we expect a revolution in obesity treatment?"

A total of 150 posters will be presented at this year's conference, and for the first time the winners of the poster competition will be delivering oral presentations in person on the day of the conference. I thank Kuwait University for the continuing support and sponsorship of the Poster Conference and the keynote speakers for accepting our invitation. I express my appreciation to the Vice-President Health Sciences Centre, the Deans of different Faculties of HSC for their encouragement and support, and all HSC technical and support staff who assisted in the organization and implementation of this meeting. I am especially very grateful to the Chairman of the 27th HSC Poster Conference and all members of the Organizing Committee and the Judging Committee for their commitment and efforts to make the conference a very successful event.

Dr. Heba Al Hussaini
Vice-Dean for Research & Postgraduate Studies, College of Medicine

Address by Chairman of the Organizing Committee

On behalf of the organizing committee, we are delighted to welcome you to the 27th Health Science Center Poster Conference. This annual event has always been an opportunity to exchange ideas, develop collaborations and showcase the work of our staff and students. After two years of being forced online by the recent global pandemic, we are especially pleased to interact in person once again. The format of the conference continues to evolve and this year we are excited to include oral presentations by the winners of the best poster awards in the main program. This change wouldn't be possible without the hard work of the judging committee to whom we are grateful. We also thank the HSC administration for their continuing support and of course, all of you who have submitted your abstracts.

We are honored that Professor Carel le Roux, University College Dublin, Ireland has accepted our invitation to deliver this year's keynote lecture entitled, "Why can we expect a revolution in obesity treatment?" This topic is relevant to all of us involved in understanding and improving human health as obesity is one of the leading causes of premature, preventable death worldwide; and Kuwait is no exception.

Wishing you all a productive and intellectually stimulating conference.

Dr. Suleiman Al-Sabah Ph.D.
Chairman, 27th HSC Poster Conference Organizing Committee

Keynote Speaker

Professor Carel Wynand le Roux
MBChB, MSc, FRCP, FRCPath, PhD
Experimental Pathology, School of Medicine,
University College Dublin And Metabolic Medicine,
Ulster University

Professor Carel le Roux (MBChB, MSC, FRCP, FRCPath, PhD) graduated from medical school in Pretoria South Africa, completed his Senior House Officer training at Barts and The London Hospital, his SpR training in metabolic medicine at the Hammersmith Hospitals and his PhD at Imperial College London. He was appointed as Senior Lecturer and promoted to Reader in 2009 at Imperial. He accepted a Chair as Head of Pathology at University College Dublin in 2011. He received the President of Ireland Young Researcher Award from Science Foundation Ireland, a Clinician Scientist Award from the National Institute Health Research in the UK and a Wellcome Trust Clinical Research Fellowship amongst others. A popular lecturer at undergraduate level, national and international conferences he has also supervised several MSc, MD and PhD students, many of whom have gone on to successful academic careers. After establishing a successful independent research group he published numerous high impact papers over the years that have influenced his field. In particular, his translational research on the understanding of the physiological role and pathological changes in appetite control and the impact of bariatric surgery on diabetes has been widely acknowledged. He has also been able to take up a variety of editorial positions of peer reviewed journals. Working within the Diabetes Complications Research Centre and the Section of Surgery and Surgical Specialities the focus of his research is primarily concerned with increased mortality and morbidity associated with obesity and diabetes. A better mechanistic understanding of how the "gut talks to the brain" will allow safer and more effective treatments to be used in future. To this end the role of gut hormones, bile acids and changes in food preference are areas of interest.

Keynote Address

Why can we expect a revolution in obesity treatment?

Prof Carel le Roux
Diabetes Complications Research Centre, University College Dublin, Ireland

Obesity is now recognised as a disease that is associated with serious morbidity and increased mortality. One of its main metabolic complications is type 2 diabetes, as the two conditions share key pathophysiological mechanisms. Weight loss is known to reverse the underlying metabolic abnormalities of type 2 diabetes and, as such, improve glucose control; loss of 15% or more of bodyweight can have a disease-modifying effect in people with type 2 diabetes, an outcome that is not attainable by any other glucose-lowering intervention. Furthermore, weight loss in this population exerts benefits that extend beyond glycaemic control to improve risk factors for cardiometabolic disease and quality of life. The evidence will be reviewed which supports the role of weight loss in the management of type 2 diabetes and propose that many patients with type 2 diabetes would benefit from having a primary weight-centric approach to diabetes treatment. The logistical challenges to implementing a new weight-centric primary treatment goal in people with type 2 diabetes will be discussed.

The new third-generation medications are however now facilitating a revolution. These medications appear to address many of the diseases leading to obesity at their origins. Treating obesity as a chronic disease with effective therapies allows the disease to come under control and remain under control as long as the therapies continue. The impact of effectively treating obesity will reduce the symptoms of obesity such as excessive appetitive behaviour, but it will also reduce the complications of obesity which will have far-reaching benefits for the individual, the healthcare system, and wider society.

150 Poster Presentations & 10 Award Winner Presentations

***Award Categories*:**

- Dr. Nael Al-Naqeeb Award for Best Undergraduate Research
- Graduate Research Award for Master's Program
- Graduate Research Award for PhD Program
- Graduate Research Award for Medical Residents
- Best Young Researcher Award for Basic Sciences
- Best Young Researcher Award for Clinical Sciences
- Best Case Report Award
- Award for Overseas Kuwaiti & GCC- HSC Student (NEW AWARD)

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Award Winners: 26th HSC Poster Conference 2022

Undergraduate: Dr. Nael Al-Naqeeb Award

- **Progesterone Limits the Increase in p53 caused by Dexamethasone Treatment in the Labyrinth Zone of Rat Placenta**
  Alkhabbaz A, Al-Naqeb A, Al-Abduljader F, Al-Salem Y, Al-Qaryyan M, Al-Awadhi M, Al-Bader M
  [1]Department of Physiology, College of Medicine, Kuwait University,[2] 6th year medical students, College of Medicine, Kuwait University.

- **Impact of the sugar alternative stevia on the expression of streptoccal genes involved in exopolysaccharide synthesis.**
  Alkanderi S, AlFreeh M, Bhardwaj RG, Karched M
  Oral Microbiology Research Laboratory, Faculty of Dentistry, Kuwait University

- **Cloning of partial and full LPL promoters into TOPO-TA and promoterless luciferase vectors**
  Mohamed AK*[1], Al-Barjas TA [2], Al-Bustan SA [2], Bastaki NK [2]
  [1] Undergraduate Molecular Biology program student, Department of Biological Sciences, Faculty of Science, Kuwait University, [2] Department of Biological Sciences, Faculty of Science, Kuwait University.

Medical Residents

- **Clinical Characteristics of Multisystem Inflammatory Syndrome in Children (MIS-C): Results From a National Pediatrics Registry**
  *Al-Shemmari SA[1], Al-Afasi KM[1], Othman FA[2], Al-Dihani AM[1], Atyani SM[3], Al-Kandari KH[4], Al-Furaij AK[1], Al-Kandari HM[1,2]
  [1]Department of Pediatrics, Farwaniya Hospital.[2]Population Health Department, Dasman Diabetes Institute, [3]Department of Pediatrics, Jaber Al-Ahmed Hospital,[4]Department of Pediatrics, Sabah Hospital

Young Residents Case Reports

- **Giant Cell-Rich Solitary Fibrous Tumor of the Lacrimal Gland with Prominent Angiomatoid Cystic Changes and an Underlying NAB2ex3-STAT6ex18 Fusion**
  Alsaadi KA*[1], Alwohaib M[1], Ali RH[2,3]
  [1] Al Bahar Eye Center, Ibn Sina Hospital, Sabah Medical District, Kuwait, [2] Cytogenetics Laboratory, Kuwait Cancer Control Center, [3] Department of Pathology, College of Medicine, Kuwait University

Young Researcher Clinical

- **Early Diagnosis of Classic Homocystinuria in Kuwait through Newborn Screening: A 6-Year Experience**
  Alsharhan H* [1]., Ahmed AA [2], Ramadan DG [3], Alsafi R [4], Al-Rushood M [2], Bastaki [2]
  [1]Department of Pediatrics, Health Sciences Centre, College of Medicine, Kuwait University, Kuwait, [2] Newborn Screening Laboratory, Kuwait Medical Genetics Center, Ministry of Health, Kuwait, [3]Department of Pediatrics, Al-Sabah Hospital, Ministry of Health, Kuwait, [4] Department of Pediatrics, Adan Hospital, Ministry of Health, Kuwait

Basic Sciences: Original Research MSc

- **Maternal Immune Activation Alters GABAergic Interneurons in the Offspring's Prefrontal Cortex: A Sex-Dependent Effect.**
  Alharbi RA*, Mouihate A
  Department of Physiology, College of Medicine, Kuwait University

- **Micro-RNA-146b-5p Modulation of the Cellular Stress Response in Papillary Thyroid Cancer**
  Al-Shammari BM* Al-Abdallah A, Kapila K
  Department of Pathology, College of Medicine, Kuwait University

- **The Role of The JAK1/Nrf2/Keap1 Pathway in The Regulation of Germ Cell Apoptosis**
  Alnajem AS* [1], Godwin Budadasari G [2], Al-Maghrebi M [2]
  [1]Department of Medicine; Farwaniya Hospital, Ministry of Health, Kuwait;[2] Department of Biochemistry; College of Medicine, Kuwait University, Kuwait

- **The role of TXNIP/NLRP3 inflammasome pathway in NADPH oxidase-induced ROS and germ cell apoptosis.**
  Almarzouq D*, Godwin Budadasari G, Al-Maghrebi M
  Department of Biochemistry; College of Medicine, Kuwait University, Kuwait

Original Research PhD

- **The Impact of GLP-1R-GIPR Hetero-dimerization on Cell Signalling**
  Al-Zaid B*, Al-Sabah S, Ezeamuzie CI
  Department of Pharmacology and Toxicology, College of Medicine, Kuwait University.

- **Alpha-2 Adrenoceptor Activation Attenuates Oxidative Stress, Inflammation and Neuropathic Pain in Type 1 Diabetes Mellitus.**
  Munawar N* [1], Masocha W [2], Bitar MS [1]
  [1]Department of Pharmacology and Toxicology, College of Medicine, Kuwait University; [2]Department of Pharmacology and Therapeutics, Faculty of Pharmacy, Kuwait University

Young Researcher Basic Scientist

- **Molecular Epidemiology and Genetic Characterization of SARS-CoV-2 in Kuwait**
  Safar HA [1], Madi N [2], Mustafa AS [2], Chehadeh W [2], Asadzadeh M [2], Sadeq M [3], Alawadhi E [4], Al-Muhaini A[4], Benthani F [5], Al-Adwani A [2]
  [1] Research Core Facility and OMICS Research Unit, College of Medicine, Kuwait University, Kuwait; [2]Department of Microbiology, College of Medicine, Kuwait University; [3] Jaber Al-Ahmad Armed Forces Hospital, Kuwait; [4] Jaber Al-Ahmad Hospital, Ministry of Health, Kuwait; [5] Johannes Kepler University, Centre for Medical Research, Austria

Past Poster Day Keynote Speakers and Lectures

2022

Human iPSC-NSC derived Extracellular Vesicle therapy for Alzheimer's Disease: Promise and Challenges; Prof. Ashok K. Shetty, Ph.D., Associate Director and Professor, Institute for Regenerative Medicine, Department of Molecular and Cellular Medicin College of Medicine, Texas A&M University

Biology or technology? Innovation is the Key; Prof. Pieter Doevendans MD, PhD, FESC, Director Netherlands Heart Institute, University Medical Center, Division Heart and Lungs, Department of Cardiology, The Netherlands

2021

Healthy Diets in the 21st Century: What are we talking about? Prof. Carlos A. Monteiro, Professor of Public Health Nutrition at the School of Public Health, University of Sao Paulo, Brazil.

2019

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

2009

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

2008

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

2007

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

2006

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

2005

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

2004

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

2003

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

2002

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

2001

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

2000

Molecular Mechanisms and Biomedical Implications of Apoptotic Cell Death Dr. Sten Orrenius, Professor and Chairman, Division of Toxicology, Institute of 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, the University of Florida USA.

Original Research Abstracts List by Subject Area

Allied Health

1
AlRashidi FT, Abdallah RW*, Alaazmi SM, Almenaye DA: High Serum Concentration Of Copper, But Not Cobalt Or Arsenic, Is Associated With Hyperglycemic Adults In Kuwait.

2
Asbeutah AM, Zahra AM, Al-Abboh H, AlMajran AA, Adekile A: Long-term transcranial Doppler ultrasound follow-up of Kuwaiti children with sickle cell disease

3
Kreedi FM*, Brown M, Marsh L: Nurse Educators Perception of Newly Graduated Registered Nurses Transition to Practice: A qualitative Study

4
Nambi G*, Alghadier M, Reddy RS, Khan F, Sirajudeen MS, Mani P Mohamed SP: The association between bio-psycho social factors and work-related musculoskeletal low back pain (WMS-LBP) among municipality sanitary workers in Saudi Arabia.

5
Osama Gheith*, Nashwa Othman, Torki Al-Otaibi, Tarek Said, Medhat A Halim, Faisal Al-Refaei, Nabil Elserwy, Fatma Mahmoud, Heba Abduo: Structured diabetes education: does it work in kidney transplant recipients with NODAT

Anatomy

6
Alkandari AF*, Madhyastha S, Rao MS: N-Acetylcysteine Amide ameliorates Aβ1-42 peptide-induced cognitive dysfunction by enhancing antioxidant defense in hippocampus and medial prefrontal cortex in rats

7
Alkandari AF*, Madhyastha S, Rao MS: Comparative study between polypropylene sutures, surgical staples, adhesive strips and adhesive glue in surgical wound closure in rats

8
Deema Alhubail *, Manal Alenezi, Hawraa Taher, Smitha S, Muddanna S Rao: Fresh Vegetables Contain Heavy Metals and Other Elements – A public health Concern

9
Hawraa Adel Ali *, Madhawi Majed Almutairi, Zahra Ahmed Abdullah, Shahad N Nasser Alajmi, Smitha S, Sampath Madhyastha, Muddanna S Rao: Neuroprotective effects of N-Acetylcysteine amide in In-Vitro STZ-model of Alzheimer's Disease

10
Madhawi Majed Almutairi *, Hawraa Adel Ali, Zahra Ahmed Abdullah, Shahad N Nasser Alajmi, Smitha S, Muddanna S Rao: Heavy Metals and Other Elements in Herbal products

11
Monirah Almutawa*, Muddanna S Rao: Thymoquinone improves cognitive functions, alleviates anxiety and decreases neuroinflammation in STZ-induced oxidative stress model

12
Nasser althefiri*, Majed al Mutari, Mohammed rakan, Mohammed Al mojel, Smitha S, Muddanna S Rao: Presence of Heavy Metals and Other Elements in Animal Food Products

Behavioral Sciences

13
AlAwadhi EB*, Albahar S, Tolma E, Longenecker J, Tawheed E, Al-Wotayan R: Disparities in the Uptake of Cervical Cancer Screening in Kuwait: A Cross-Sectional Analysis of the Nationwide STEPS Survey

Biochemistry

14

Al-Failakawi AT*, Al-Jarallah A, Rao MS, Khan I: NOB Reverses Experimental Colitis in Rats by Modulating Tight Junction Proteins and Inflammation

15

Al-Harban AA*, Tovmasyan A, Benov L: Newly Modified Tetrapyrrole Photosensitizers: Promising Photosensitizers for Photodynamic Treatment of Cancer

16

Al-Jarallah A, Babiker F: High Density Lipoprotein Reduces Blood Pressure and Protects Spontaneously Hypertensive Rats Against Myocardial Ischemia-Reperfusion Injury in an SR-BI Dependent Manner

Cardiology & Infectious Diseases

17

Asbeutah AA, Salem MH, Asbeutah SA*, Abu-Assi MA: The Role of an Antibiotic Envelope in the Prevention of Major Cardiac Implantable Electronic Device Infections

Cardiovascular Epidemiology

18

AlShammari Asmaa, Majdalani Rosemarie, Magdits Mariel, Jha Sapana, Devarajan Sriraman, Kurian Damian McCann Lily, Hughes Anna, Ionsecu Natalia PA-C, Raiszadeh Farbod: Worsening Renal Function in Patients Admitted with Congestive Heart Failure: Prevalence, Risk Profile, and Hospital Readmissions

Community Medicine

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Alhajri W*, Alrashidi S, Almutairi N, Almutairi G, Aladwani M, Alsanafi L, Almutairi S, Suresh A, Akhtar S: Exposure to tobacco smoke, concurrent morbidities and health services use among young adults in Kuwait

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Abueljebain H*, Aldooseri B, Alhajeri L, Aleisa F, Alibrahim A, Alajmi M, Alshemeri K, Al-Sabah R: Physical Activity and Mental Health among Kuwait University Students

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AlAli FA, AlHassawi MN, AlRagum FF, AlShammari NA, AlTarmoom MT*, AlShayji DW: Obesity Association with Uncontrolled Blood Glucose Levels in Type 2 Diabetes

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Al-Anazi SM, Al-Dhefeery NA*, Al-Hjaili RN, Al-Duwaihees AM, Al-Mutairi AS, Al-Saeedi RM, Al-Dhaen RS, Al-Rabiah SW, Sharaf-Alddin RA: Compliance With Hand Hygiene Practices Among Nursing Staff in Secondary Healthcare Hospitals in Kuwait.

23

Albatineh AN, Alajmi NK: Prevalence of Conspiracy Theory Ideation, COVID-19 Conspiracy, and their Association with COVID-19 Vaccination Status among adults in Kuwait: A Cross-Sectional Study

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AlHamlan AW, AlDhafiri DA, AlHajry NA, AlHouli AH, AlHubaida SM, AlJassar AM, AlMutairi NN*, AlRabeeh AS, Shaban WA, Al-Sultan AT: The Impact of Academic Stress on the Lifestyle of University Students in Kuwait

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Ali H Ziyab, Mohammad Almari, Anwar Mohammad, Abdullah Al-Taiar, Wilfried Karmaus: Sibship size and position in sibship in relation to lipid profile during adolescence: a cross-sectional study

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Almohaid S*, Akhtar S: A Case-Control Study of Risk Factors for Hepatocellular Carcinoma in Kuwait

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Aseel Alshalahi, Atheer Almathkour, Batoul Taqi, Maryam Alhashel, Maryam Alsamhan, Nawar Almuqatea Reem Almunaikh, Sadan Alhajeri, Zainah Alyaqout
Naif Almutawa, Abdullah AlMijren: The Prevalence of Irritable Bowel Syndrome Among Kuwait University Students: The Role of Anxiety, Depression, and Diet

29

Bughaith GA Alrashed DO Hussain HY Bouzubar LF* Alkandari FA Almaghrebi MY Alkandari ME Almousa Z: The Effect of the COVID-19 Pandemic on the Physical and Psychological Health of Elemantary School Children in Kuwait.

Cytopathology

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Sharfudeen S *, Abubakr A, Kapila K, Al-Jassar A: Primary Thyroid Lymphoma- A Review of 3 cases.

Dentistry

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Ali KM *, Bumpattarachai S, Savignano R, Kan J: Effects of Dental Chair Backrest Inclination on Virtual Interocclusal Record of Maximum Intercuspal Position: A Clinical Study

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Ali KM*, AlZaid A, Suprono M, Garbacea A, Savignano R, Kattadiyil M: Effect of Splinting Implant Scan Bodies Intraorally on The Trueness of Complete Arch Digital Impressions: A Clinical Study

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ALI KM: Applications of Artificial Intelligence in Prosthodontics

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Albahrani MM *, Alyahya A, Qudeimat MA, Toumba KJ: Salivary Fluoride Concentration Following Toothbrushing With and Without Rinsing: A Randomised Controlled Trial

35

Nazar H*, Ariga J, Shyama M: Oral Cancer Knowledge, Attitudes, and Practices among Newly Graduated Dentists in Kuwait

36

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Allied Health

1

High Serum Concentration of Copper, But Not Cobalt Or Arsenic, Is Associated With Hyperglycemic Adults In Kuwait.

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Introduction:
Diabetes mellitus (DM) is a chronic metabolic disease characterized by impaired functional β-cells, insulin resistance, and hyperglycemia. According to the latest IDF report, about a quarter of the adult Kuwaiti population are diabetic. Minerals are essential for a healthy body as they are vital for multiple physiological functions. Several studies have assessed the association between minerals imbalance and DM. For example, copper (Cu), which is essential for angiogenesis, is accumulated inside the cells of diabetic individuals, preventing the generation of new blood vessels and increasing the susceptibility to cardiovascular diseases (CVD). Cobalt (Co) and As concentrations imbalance are also associated with the development of DM. Yet, studies that measure Co and As levels in human diabetic patients still despair.
OBJECTIVES
To assess the association between mineral concentrations and hyperglycemia.

Methods:
Serum samples from 22 hyperglycemic and 22 matched non-diabetic control samples were collected. Following the WHO criteria, patients who had HbA1c ≥ 8 were considered hyperglycemic. Electrolytes such as Na, K, Ca, and P were measured using the automated AU5800 system. ICP-MS was used to determine serum samples' Cu, Co and As concentrations.

Results:
Cu level was significantly high in hyperglycemic patients. No change in the level of Co or As in hyperglycemic subjects has been observed. Additionally, there was a significant negative association between Cl and Na levels and hyperglycemia. There was no significant difference in serum Ca, P, or K levels in both studied groups.

Conclusions:
The data of this study demonstrate an elevated Cu level in the adult hyperglycemic population in Kuwait. Furthermore, the results showed significantly lower serum Cl and Na concentrations in the hyperglycemic group. Hypochloremia is an independent predictor of mortality in acute heart failure. Hence, both Cu and hypochloremia will be further investigated as predictive biomarkers for CVD. Furthermore, hyponatremia is independently associated with diabetic peripheral neuropathy. More investigation will be done into our hyperglycemic population. Our results could not find a significant association between serum Co, As, K, P or Ca concentrations and hyperglycemia. In conclusion, our results suggest that minerals can be used as independent predictive biomarkers for diabetic complications, particularly CVD complications.
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Ethical approval number 1001.

Key Words: Hyperglycemia; HbA1c; Trace elements;

Funding Agency: None

Allied Health

2

Long-term transcranial Doppler ultrasound follow-up of Kuwaiti children with sickle cell disease

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Introduction:
Transcranial Doppler imaging (TCDI) of the cerebral arteries is the method of choice to predict patients with sickle cell disease (SCD) who are at risk for stroke. The present study reports a 10-year TCDI follow-up of cerebral blood flow in Kuwaiti children with SCD.

Methods:
Twenty-one SCD pediatric patients (11 HbSS, 9 HbSβ0 Thal, and 1 HbSD), aged 16.0 ± 1.6 years were initially studied when they were aged 6.5 ± 1.2 years. TCDI scanning was carried out using a phased-array transducer of 1-3 MHz through the trans-temporal window. Peak systolic velocity (PSV), end diastolic velocity (EDV), time-averaged mean of the maximum velocity (TAMMV), resistive index (RI), and pulsatility index (PI) were obtained in the anterior and posterior Circle of Willis vessels.

Results:
In general, the values of the follow-up indices were lower than in the initial study although they remained within the normal range in all the intracerebral arteries. The normal TAMMV should be <170cm/s in all vessels. The average± SD between old (when there were 6.5 ± 1.2 years.) and follow-up (when there are16.0 ± 1.6) TAMMV were: 77.3 ± 20.9 and 71.6 ± 9.9 in the terminal internal carotid artery, 94.3 ± 25.8 and 82 ± 18.2 in the middle cerebral artery, 76.6 ± 25.6 and 70.6 ± 10.7 in the anterior cerebral artery, and 59.1 ± 15.8 and 63.9 ± 8.5 in the posterior cerebral artery respectively. The differences between the old and follow-up data for TAMMV was not significant (P>0.05). There was no overt stroke in any of the patients over the follow-up period.

Conclusions:
There was no neurological event in any of the patients and the TCDI mainly TAMMV values remained in the normal range at follow up. This indicates that the treatment protocol is well set.

Key Words: Sickle cell disease; Transcranial Doppler imaging; Ultrasound imaging;

Funding Agency: Kuwait Foundation for the Advancement of Science Grant No. CR 17-13MM-01.

Allied Health

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Nurse Educators Perception of Newly Graduated Registered Nurses Transition to Practice: A qualitative Study

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Introduction:
Feelings of stress related to unpreparedness for the role, lack of educational preparation, and lack of support are commonly described during this transition and could be a reason for Newly Graduated Registered Nurses (NGRNs) to leave the profession. There is a dearth of research linking Kuwaiti national NGRNs and their transition experiences from the perspective of Nurse Educators in Kuwait. This study aims to explore the views and experiences of transition from student nurse to Registered Nurse of Kuwaiti national NGRNs in their first post in clinical practice from the perspectives of Nurse Educators.

Methods:
This study used a qualitative method. six focus groups were conducted with Nurse Educators from the College of Nursing and the Nursing Institute of Kuwait. All focus groups were audio recorded and transcribed verbatim. The data were analyzed using Braun and Clarke's (2006) thematic analysis.

Results:
The findings provided four themes: (1) organizational Nursing support; (2) Education preparation; (3) Psychological well-being; and (4) Nursing professionalism. It was acknowledged that the lack of support provided to NGRNs throughout their clinical practice was a major element in the challenges they had throughout the transition, which is seen as a crucial cause of NGRN turnover. The negative social attitudes towards nurses in this study were another significant evidence for NGRN turnover in Kuwait. Furthermore, the short field-training periods are a concern for Nurse Educators and constitute a barrier to practice transition. There is a significant gap between nursing education and actual experience working in health care services, resulting in NGRNs having reality shock when they enter the field. Another significant barrier that may have an impact on NGRNs' retention is a lack of proficiency in the English language. Nurse Educators believed that some nursing students lacked punctuality, indicating a limited interest in the nursing profession and their careers.

Conclusions:
The study found that Kuwaiti national NGRNs received little organizational support, therefore, nursing stakeholders and policymakers in Kuwait need to develop a plan to enhance NGRNs' knowledge and skills in order to better align them with the roles and realities of actual nursing practice which might help in retention. It is necessary to improve Kuwaiti society's perception of nursing by highlighting the role that nurses play on the healthcare team. Funding: Kuwait Civil services commission

Key Words: Newly graduated registered nurse ; Transition ; Turnover ;

Funding Agency: Kuwait Civil services commission, 2018/782

Allied Health

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The association between bio-psycho social factors and work-related musculoskeletal low back pain (WMS-LBP) among municipality sanitary workers in Saudi Arabia.

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Introduction:
Work-related musculoskeletal disorders (WMSD) is common among municipality sanitary workers (MSW), in which low back pain (LBP) is the most common problem identified by recent surveys. The association between job-related biopsychosocial factors and work-related musculoskeletal - low back pain (WMS-LBP) in MSW is seldom studied in Saudi Arabia. Hence the study aimed to find the individual and multiple associations between biopsychosocial factors and WMS-LBP among municipality sanitary workers in Saudi Arabia.

Methods:
A cross-sectional study was conducted throughout all the regions of Saudi Arabia and data was collected from municipality sanitary workers working in thirteen different municipalities. Four Questionnaires were used to obtain information regarding demographic characteristics, biological (Body mass index (BMI) and physical health), psychological (psychological stress (The Kessler Psychological Distress Scale - K10) and mental health), social (job satisfaction (Job Descriptive Index) and social support (The 27-Item Social Support Questionnaire) factors and work-related musculoskeletal low back pain (WMS-LBP) intensity. Univariate analysis was performed for the individual analysis and hierarchical multivariate regression analysis was performed for finding the association between the variables.

Results:
A total of 2,182 sanitary workers completed the study and were included in the data analysis. Univariate analysis showed that there was a statistically significant relationship between biological, psychological, and social factors and musculoskeletal low back pain. In hierarchical multivariate regression analysis, physical health, psychological stress and job satisfaction showed a strong association with musculoskeletal low back pain. Body mass index and mental health was a moderate association with WMS-LBP and social support showed a mild association.

Conclusions:
Through this study, we concluded that physical health, psychological stress and job satisfaction plays important role in work-related musculoskeletal low back pain. However, other biopsychosocial factors such as body mass index and mental health should also be taken into consideration to control and prevent WMS-LBP. The reports of the study would be helpful for the clinicians and physiotherapists to take the right decision in controlling and preventing WMS-LBP among municipality sanitary workers in Saudi Arabia.

Key Words: Musculoskeletal; Low back pain; Bio-psycho social;

Funding Agency: None

Allied Health

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Structured diabetes education: does it work in kidney transplant recipients with NODAT

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Introduction:
Diabetes knowledge among kidney transplant recipients (KTR) with post-transplant diabetes (NODAT) is not fully evaluated. We aimed to evaluate the impact of structured diabetes education (SDE)on the development of diabetic vascular complications among kidney transplant recipients with NODAT.

Methods:
In this prospective randomized controlled trial, we categorized 210 KTR with NODAT into two groups. Group 1 (n=140) received structured diabetes education while group 2(n=70) received conventional education. We compared the 2 groups regarding clinical and metabolic parameters.

Results:
Most patients in the two groups (1&2) were Kuwaiti (60.7 vs. 58.6%), men (57.9 vs. 68.6%), with high school education levels (43.6vs.48.6%). The minority of patients were smokers (12.9 vs.8.7%), and chronic glomerulonephritis was the original disease in the two groups. Most of the enrolled patients (72.8 vs. 78.6%) underwent hemodialysis pre-transplant. Diabetic neuropathy was comparable in both groups (32.4 vs. 27.6% respectively) at the start of the study and after 24 months as follow up electromyography/nerve conduction did not show a significant difference between the studied groups. Similarly, diabetic retinopathy as per fundus imaging showing retinopathy was comparable in both groups ($p>0.05$). The percentage of patients with nephropathy decreased significantly in group 1 after 24 months of the study compared to group 2 and to the basal value in the same group($p=0.016$). Macroangiopathic events were higher in group 1 but did not rank to significance ($p>0.05$).

Conclusions:
SDE is recommended for all diabetic KTRs as it is associated with a significant reduction of diabetic nephropathy.

Key Words: Diabetes education; Renal transplant; Outcome;

Funding Agency: None

Anatomy

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N-Acetylcysteine Amide ameliorates Aβ1-42 peptide-induced cognitive dysfunction by enhancing antioxidant defense in hippocampus and medial prefrontal cortex in rats

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Introduction:
Oxidative stress is a key factor for many neurodegenerative disorders including Alzheimer's disease (AD). Among the inbuilt antioxidant defense in the brain, glutathione is one of the major antioxidants. N-Acetylcysteine (NAC), a glutathione precursor, provided neuroprotective effects in AD animal models. Its amide form, N-Acetylcysteine amide (NACA), has extended bioavailability compared to NAC. Objectives: We aimed to evaluate the neuroprotective effects of NACA against Aβ1-42 peptide-induced AD-like pathology in rats.

Methods:
Adult male Wistar rats (4 months old) were divided into five groups: Normal Control (NC), Sham (Sh), Aβ, Aβ+N, and N+Aβ+N (n=8 in all groups). AD-like pathology was induced in Aβ, Aβ+N, and N+Aβ+N groups by intraventricular infusion of Aβ1-42 peptide (5µg/ventricle) into each lateral ventricle. Treatment was given by intraperitoneal injection of NACA (75mg/kg) for 7 consecutive days after inducing AD-like pathology (Aβ+N group), or for 14 days before and after inducing the pathology (N+Aβ+N group). Learning and memory, antioxidant parameters, expression of AD pathology markers, and neurodegeneration were studied in all groups. All data were analyzed with the One-Way ANOVA test followed by Bonferroni's multiple comparison test.

Results:
Behavioral tests using the Morris water maze and passive avoidance tests showed significant cognitive recovery in NACA-treated groups compared to the Aβ group. Antioxidant effects by estimating lipid peroxidation, reduced glutathione, and total antioxidants in the hippocampus and prefrontal cortex showed significantly enhanced antioxidant defense in NACA-treated groups compared to the Aβ group. Western Blot analysis for Aβ, Tau, and Synaptophysin as well as histopathological evaluation of hippocampus and prefrontal cortex through immunostaining for neuronal proliferation, neuronal degeneration markers, expression of neurofibrillary tangles, β-amyloid expression, synaptophysin expression, and gliosis showed a neuroprotective effect in NACA-treated groups compared to Aβ group. All the above parameters were significantly decreased in the Aβ group compared to NC and Sh groups. There was no significant difference between NC and Sh groups in all parameters.

Conclusions:
This study demonstrates the neuroprotective effects of NACA against β-amyloid induced AD-like pathology by enhancing the antioxidant defense system in rat brains. It further suggests that NACA can be considered for future clinical trials.

Key Words: Oxidative stree; Antioxidants; N-Acetylcysteine amide;

Funding Agency: We thank the College of Graduate Studies and research sector, Kuwait University for funding this research through Grant No.: YM07/19

Anatomy

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Comparative study between polypropylene sutures, surgical staples, adhesive strips and adhesive glue in surgical wound closure in rats

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Introduction:
Surgical wound closure by sutures or staples usually results in scar formation. Alternatives, such as adhesive strips and adhesive glue may provide better cosmetic results since they do not leave marks. However, they are associated with an increased risk of improper wound healing because their application is limited to the epidermis layer of the skin only. In turn, improper wound healing will result in scar formation. A few comparative studies between different wound closure methods available in the literature are with contradicting conclusions. Objectives: This study aimed to compare polypropylene sutures, surgical staples, adhesive strips, and adhesive glue, the main four wound closure methods in terms of wound healing and scar formation in rats. Further, this study aimed to evaluate histologically the collagen fibers formation and inflammatory cells existence within the wounds two- and six- weeks after surgical wound closure.

Methods:
Three months old male Wistar rats were allocated into five groups (n= 8 in each group). A longitudinal full-skin thickness skin incision (approximately 5 cm in length) was created in the dorsal trunk region of rats. The wounds were kept open for 15 minutes and then were closed using polypropylene sutures (suture group), surgical staples (staple group), adhesive strips (strip group), or adhesive glue (glue group). The wounds were then covered with gauze and secured in place with sutures to avoid self-removal. No postoperative antibiotics were given. Each rat was then kept in a separate cage and the closure materials were removed seven days later. The rats were then exposed for gross and microscopic examination at two- and six weeks after surgery.

Results:
Results of the study showed that surgical wound closure with polypropylene sutures resulted in better wound healing and less scar formation than surgical wound closure by surgical staples > adhesive strips > adhesive glue. Hematoxylin and Eosin (H&E) stained sections taken across the healed wounds that were closed with polypropylene sutures showed fewer inflammatory cells at two weeks and adequate collagen fibers in the dermis at six weeks, contrary to that observed in staple, strip, and glue groups.

Conclusions:
Using polypropylene sutures in surgical wound closure is time-saving, cost-effective, and has better cosmetic results than all other alternatives.

Key Words: Polypropylene sutures; Wound closure; Wound healing;

Funding Agency: None

Anatomy

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Fresh Vegetables Contain Heavy Metals and Other Elements – A public health Concern

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Introduction:
Vegetables are significant component of our daily food. Recent studies show presence of toxic elements in the blood samples of Kuwait population. Source of such toxic elements is not known. No studies investigated the presence of heavy metals and other elements in the vegetables available in Kuwait. Objectives: The present study was aimed to determine the presence of heavy metals and other elements in different vegetables available in Kuwait.

Methods:
A total of 27 fresh vegetables were collected from different super markets in Kuwait. 50mg of each sample were processed for analysis of heavy metals and elements. Samples were digested in per chloric acid/ Nitric acid (1:5) solution and precipitate was dissolved in 5ml of 1% nitric acid. Inductively coupled plasma mass spectrometer (ICP-MS) was calibrated with low to high concentrations multi element standard solutions prepared from the commercial stock solution containing 29 known elements. From the standard curve, the concentration of various elements in the samples were determined by the system.

Results:
Results of the showed presence of Beryllium, Boron, Calcium, Iron, Titanium, Bismuth and Uranium in all 27 samples analyzed. Aluminum, Vanadium, Chromium, Copper, Zinc, Rubidium and Molybdenum are found in more than 80% of samples analyzed. Sodium, Calcium, Manganese, Potassium, Magnesium, Gallium, cadmium and barium are found in 30-80% of samples. Lithium, Sodium, cobalt and lead are found in 10-30% of samples. Arsenic and Lead are found in 2 - 10% of samples.

Conclusions:
This study demonstrates the presence of toxic heavy metals such as arsenic, lead, silver, aluminum, in the vegetables sold in Kuwait. Presence of significant amount of these heavy metals in a significant percentage of samples is of public health concern.

Key Words: Lead; Arsenic; Heavy metals;

Funding Agency: None

Anatomy

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Neuroprotective effects of N-Acetylcysteine amide in In-Vitro STZ-model of Alzheimer's Disease

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Introduction:
Initiation of Alzheimer's disease is claimed to be through oxidative stress (OS). Antioxidant therapy to alleviate the neurodegeneration in AD is most explored research area recently. N-Acetylcysteine amide (NACA), an antioxidant substance proved to be effective in neuroprotection in several neural injury models including AD. Recent findings suggest AD is an insulin resistant brain's state. Streptozotocin (STZ) is a glucosamine-nitrosourea compound commonly used to induce type-1 diabetes in rodents. Administration of STZ into rodent's cerebral ventricles or into neural culture has been shown to produce pathophysiological changes such as neuroinflammation, oxidative stress and biochemical changes as in AD. Hence, STZ-model of AD is one of the established animal models of AD. Neuroprotective effects of NACA in the in-vitro Aβ1-42 model of AD is well established but not in STZ-induced in-vitro model. Objectives: The present study was aimed to evaluate the neuroprotective effects of NACA against STZ-induced AD-like pathology in an in-vitro model.

Methods:
Primary culture of cerebral cortical tissue from E18 day fetus was done in advanced DMEM media containing 10% fetal calf serum, and 100 IU antibiotics. Cultures were grown for six days in a CO2 incubator maintained at 37oC, with 5% CO2. Cultures were then divided into Control, STZ-10µM, STZ-10µM + NACA-10µM, STZ-10µM+NACA-20µM groups and treated with 10µM STZ, 10 and 20µM NACA either for 24-hours or 72-hours duration. For all dose and duration triplicate culture were maintained. After treatment period, all cultures were fixed with 2% paraformaldehyde and immunostained with Tuj1 to stain the neurons and with GFAP to stain Astrocytes, Iba1 to stain the microglia. Number of neurons, their processes, number of astrocytes and number of microglia were quantified. Results were analyzed with One-way ANOVA, followed by Bonferroni's multiple comparison test.

Results:
STZ-decreased the neuronal size, number of processes, and neurite length compared to control group. STZ had minimal effect on astrocytes but increased reactive microglial cells. Treatment with NACA prevented neurons from degeneration at both doses, however effect was significant at 20µM concentration for 72hrs treatment. NACA also reduced the microgliosis in STZ treated culture.

Conclusions:
This study demonstrates the neuroprotective effects of NACA in the in-vitro STZ model of AD. This model may be used to study AD-pathology in in-vitro.

Key Words: N-Acetylcysteine amide; Alzheimer's disease; Streptozotocin;

Funding Agency: None

Anatomy

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Heavy Metals and Other Elements in Herbal products

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Introduction:
Heavy metal have a toxic effect on health. They gain the entry into the body through foods, soft drinks, water, and several herbal products commonly used in home remedy. Recent studies show presence of toxic elements in the blood samples of people who use herbal products and alternate medicines. The question whether the commonly used herbal products and medicines used in alternate medicine system do contain heavy metals and other elements is not answered. Objectives: The present study was aimed to determine the presence of the heavy metals and other elements in herbal products and alternate medicines available in Kuwait.

Methods:
A total of 23 herbal products and alternate medicines were collected from different stores in Kuwait. 50mg of each sample was processed for analysis of heavy metals and elements. Samples were digested in per chloric acid/ Nitric acid (1:5) solution and precipitate was dissolved in 5ml of 1% nitric acid. Inductively coupled plasma mass spectrometer (ICP-MS) was calibrated with low to high concentrations multi element standard solutions prepared from the commercial stock solution containing 29 known elements. From the standard curve, the concentration of various elements in the samples were determined by the system.

Results:
Results of the showed presence of Beryllium, Boron, Iron, Selenium, Molybdenum, Titanium, Titanium, Bismuth and Uranium in all 23 samples analyzed. Sodium, Magnesium, Aluminum, Calcium, Vanadium, Chromium, Manganese, Copper, Zinc, Strontium and Barium are found in more than 80% of the samples analyzed. Potassium and Rubidium are found in 30-80% of samples. Cobalt, Cadmium, and Lead are found in 10-30% of samples analyzed. Lithium, Nickel, Gallium, Arsenic and Silver and lead are found in 2 - 10% of samples. The concentration of above elements was highly variable ranging from 5-25µg/gram tissue or more in a few samples.

Conclusions:
This study demonstrates the presence of toxic heavy metals such as arsenic, lead, silver, aluminum, in the herbal products sold in Kuwait. Presence of significant amount of these heavy metals in a significant percentage of samples is health risk for individual who use such products.

Key Words: Heavy metals; ICP-MS; Lead;

Funding Agency: None

Anatomy

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Thymoquinone improves cognitive functions, alleviates anxiety and decreases neuroinflammation in STZ-induced oxidative stress model

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Introduction:
Neurodegenerative diseases such as Alzheimer's disease (AD) induce neuronal degeneration and cognitive decline. Among the several mechanisms of initiation of AD, oxidative stress (OS) is one. Preventing oxidative stress by taking natural products with lots of antioxidant properties such as thymoquinone (TQ) is investigated in several brain injury models. We aimed to assess the neuroprotective effects of thymoquinone (TQ), the main bioactive component of Nigella sativa seeds, against streptozotocin (STZ) induced oxidative stress in rats.

Methods:
Adult male Wistar rats were divided into i) Normal control (NC, n=6), ii) STZ induced oxidative stress (STZ-OS, n=6) and iii) STZ oxidative stress + TQ (STZ-OS+TQ, n=6). Oxidative stress was induced in rat brain by injecting single dose of STZ (50mg, i.p). These rats were either treated with TQ (10 mg/kg, i.p,); STZ-OS + TQ group) or saline (STZ-OS group). After treatment (7 days) rats in all groups were subjected to Morris water maze, elevated plus maze, passive avoidance, and open field behavioural tests. Rats were sacrificed for morphological studies on hippocampus. All data were analysed with One-way ANOVA followed by Bonferroni's multiple comparison test.

Results:
Morris water maze learning test revealed a significant learning deficit in STZ-OS group compared to NC group ($p<0.05$) and these parameters were significantly increased in TQ treated group ($p<0.05$). Probe test showed significant memory deficit in STZ-OS group compared to NC group ($p<0.5$), and deficit was significantly decreased in TQ treated group ($p<0.05$). STZ treatment resulted in significant passive avoidance memory impairment ($p<0.05$); TQ treatment significantly decreased such memory impairment ($p<0.05$). Elevated plus maze and open-field tests revealed significant anxiety like behaviour in STZ-OS group ($p<0.05$ in both tests). Treatment with TQ significantly decreased anxiety like behaviour ($p<0.05$). Morphological studies on hippocampus showed neuronal degeneration, increased astrocytes and microglia in STZ-OS group suggesting inflammatory process, where as in TQ treated group, neurodegeneration was minimal, with population of astrocytes and microglia in different subregions of the hippocampus, that are comparable to NC group.

Conclusions:
TQ with its anti-oxidative properties improves cognitive functions, decreases anxiety like behaviour, prevents neurodegeneration and suppresses the neuroinflammation in STZ-OS model.

Key Words: Hippocampus; Anti-oxidant; Thymoquinone;

Funding Agency: None

Anatomy

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Presence of Heavy Metals and Other Elements in Animal Food Products

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Introduction:
The quality of the food we ingest plays key role in heath and disease. Recent studies show presence of high amount of heavy metal lead in the blood samples of Kuwait population. No studies investigated the presence of heavy metals and other elements in the food such as meat and milk/milk products in Kuwait. Objectives: The present study was aimed to determine the presence of heavy metals and other elements in different meat and milk products sold in Kuwait.

Methods:
A total of 22 meat and milk products were collected from different super markets in Kuwait. 250mg of meat or 1.0 ml milk products were processed for analysis of heavy metals and elements using multi-element standard solution in an inductively coupled plasma mass spectrometer (ICP-MS). Samples were digested in per chloric acid/ Nitric acid (1:5) solution and precipitate was dissolved in 5ml of 1% nitric acid. Inductively coupled plasma mass spectrometer (ICP-MS) was calibrated with low to high concentrations multi element standard solutions prepared from the commercial stock solution containing 29 known elements. From the standard curve, the concentration of various elements in the samples were determined by the system.

Results:
Results showed the presence of Beryllium, Boron, Calcium, Titanium, Bismuth and Uranium in all 22 samples analyzed. Aluminum, Calcium, Manganese, Iron, Copper, selenium, Strontium and Molybdenum are found in more than 80% of the samples. Sodium, Magnesium, Vanadium, Chromium, Potassium, Zinc, Rubidium, Cadmium and Barium are found in 30-80% of samples. Lithium, Nickel, Cobalt, Gallium and Arsenic are found in 10-30% of samples. Silver and Lead are found in 2 - 10% of samples. The concentration of above elements was highly variable ranging from 10-30µg/gram tissue or more in a few samples.

Conclusions:
This study demonstrates the presence of toxic heavy metals such as lead, silver, aluminum, arsenic in the meat and milk products sold in Kuwait. Presence of significant amount of these heavy metals in a significant percentage of samples is of public health concern.

Key Words: Heavy metals; ICP-MS; Lead;

Funding Agency: None

Behavioral Sciences

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Disparities in the Uptake of Cervical Cancer Screening in Kuwait: A Cross-Sectional Analysis of the Nationwide STEPS Survey

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Introduction:
Cervical cancer is projected to increase by 48% in Kuwait by 2035. This is alarming considering that cervical cancer is now considered a preventable disease if detected early. With limited data in Kuwait, we aimed to investigate the prevalence of cervical cancer screening (CCS) using a representative sample of the Kuwaiti population and to assess the disparities in CCS uptake among Kuwaiti women.

Methods:
A representative sample of the Kuwaiti population (n= 3915) was obtained through the WHO's National Non-Communicable Risk Factors Survey (STEPSs 2014) conducted in Kuwait. Data on demographics, socioeconomic characteristics, and health status, were analyzed for women aged 18-69 years (n=2292), for which information on cervical cancer screening was available. Results were weighted to account for the age distribution of the female Kuwaiti population. Statistical analyses included descriptive statistics, bivariate analysis, and multivariable logistic regression adjusted for participants' sociodemographic factors and health status.

Results:
The weighted CCS prevalence was 15.2% (95% CI [13.7-16.7]). The odds of CSS were higher for older age, where women aged 60-69 were four times more likely to be screened than those aged 18-29 (OR 4.0 [2.6-9.4]). Higher odds of screening were also associated with being married (OR 5.0 [2.6-9.4]), divorced or widowed (OR 5.2 [2.6-11.3]), retired (OR 2.1 [1.3-3.5]), having a high school degree or higher (OR 2.7-2.8 [1.1-7.0]), and hypertension (OR 1.7 [1.1-2.4]). The odds of screening were 40% lower among women who were overweight or had diabetes (OR 0.6 [0.4-0.9]), and 60% lower among women who did not live in the Capital governorate (OR 0.4 [0.3-0.6]).

Conclusions:
The uptake of CCS among Kuwaiti women is minimal. Disparities occur in terms of age, area of residence, education level, marital status, employment status, in addition to the presence of health issues (such as hypertension). More efforts are needed to advocate CCS through organized, widely publicized, physician-endorsed screening programs that account for existing disparities as well as the country's distinctive social, religious, and cultural norms.

Key Words: Cancer; Cervical; Disparities;

Funding Agency: None

Biochemistry

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NOB Reverses Experimental Colitis in Rats by Modulating Tight Juction Proteins and Inflammation

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Introduction:
Ulcerative colitis (UC) is a relapsing inflammatory condition of the GI-tract involving mucosal inflammation in the rectum and proximal colon. UC is treated using highly toxic chemicals which are associated with serious side effects. Therefore, interest in natural product such as nobiletin (NOB), a citrus flavonoid as an adjunct treatment has also surged.

Objective:
In this study we examined the ameliorative effects of NOB on experimental colitis induced by dextran sulfate sodium (DSS) in drinking water in Sprague-Dawley male rats.

Methods:
Colitis was induced in SD male rats by DSS in drinking water for seven days. Animal were divided into 4 groups: 1. non-colitis control, 2. non-colitis control treated with NOB, 3. DSS colitis, and 4. DSS colitis treated with NOB. Animals were treated daily with NOB (60 mg/kg BW) starting from two days before the induction of colitis. Animals, 2hrs after receiving treatment with NOB, were sacrificed on day 7. Body weight and rectal bleeding were monitored throughout the experiment. Colitis was assessed by colon weight and length, myeloperoxidase activity (MPO) and histological analysis. Cytokines were measured using cytokine array and ELISA, confocal immunofluorescence was used to examine the expression of claudin proteins.

Results:
Non colitis animals gained weight of the test period while there was reduction in the wit gain the colitic animals which was reversed by the NOB treatment. There was a significant increase in MPO activity in colitis group compared to control. Hyperplasia, Goblet cell loss and epithelial tissue damage in colon tissue was measured for histological scoring. All these changes were reversed significantly in NOB treated group. Cytokines and chemokines that showed significant changes in their levels have a role in neutrophil migration, infiltration and survival (ICAM-1, LIX, CINC-1, L-selectin, GM-CSF, Fas ligand) and as inflammatory mediators (TNF-α, MMP-8, TIMP-1, IL-10, 1L-6, IL-4, IL-2, IL1α, IL-1R6). Claudin isoform-2 was increased while isoform 1 was decreased and these changes were reversed by nob treatment.

Conclusions:
Our results demonstrate development of colitis in the experimental animals which was reversed/ prevented by NOB treatment suggesting anti-inflammatory effects of Nobiletin which may be used as an adjunct treatment for UC. Claudin expression suggests leakiness in the colon which might cause hypersensitivity and inflammation in the colon.

Key Words: Colitis; Nobiletin; Cytokines;

Funding Agency: Kuwait University Research sector through a grant (YM 10/20), and partly by the College of Graduate Studies, KU. Research Core Facility (SRUL02/13), HSC for using the instrumentation.

Biochemistry

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Newly Modified Tetrapyrrole Photosensitizers: Promising Photosensitizers for Photodynamic Treatment of Cancer

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Introduction:
Photodynamic therapy (PDT) is based on the use of a light-absorbing photosensitizers (PS), and irradiation with visible light to destroy unwanted cells and tissues. In the presence of molecular oxygen, light activation of the PS leads to the local production of singlet oxygen, and other reactive species that kill the targeted cells. Because such species have short diffusion distances, only structures in close proximity to the PS are modified, which makes localization of a PS a key determinant of PDT outcome. Design of new, more selective and efficient PSs requires detailed knowledge about structure-activity relationship. The objective of this study was to investigate the effect of lipophilicity, position and number of positive charges on the PDT activity of specially designed PSs.

Methods:
PSs having identical tetrapyrrole core and varying peripheral substituents, carrying from one to three positive charges were studied on PII breast cancer cell line as a model system. Effect of PDT on cell viability was verified by MTT assay. Real time morphological changes were studied by live-cell imaging analysis using Incucyte, and effect on proliferation was determined by the sulforhodamine B assay. The cellular uptake of PSs was assessed spectrophotometrically. The type of cell death induced by the PSs was studied by flow cytometry. All experiments were repeated at least 3 times, each sample run in triplicate.

Results:
The number of charges, their position, and PS lipophilicity played a key role in cellular uptake, and photo-cytotoxicity of the compounds. The most lipophilic PS with 1+ charge had stronger PDT activity than the amphiphilic 2+ and the more hydrophilic 3+ charged PSs. A PS with 2+ charges at trans conformation was more potent than a PS with 2+ charges at cis position. Cellular uptake of the PSs revealed that a hydrophilic PS $^{3+}$ displayed the lowest cellular uptake while the amphiphilic cis and trans PSs with 2+ charges were taken up by cells more efficiently. The most lipophilic PS $^{+}$ displayed the highest cellular uptake, and the highest PDT activity, but exhibited dark toxicity. None of the other compounds displayed dark
toxicity at the tested concentrations.

Conclusions:
The structure-activity relationship revealed that the amphiphilic PS with 2+ charges at trans conformation combines low dark toxicity with the highest photo-efficiency, and can be considered as potent PS for future investigation.

Key Words: Photodynamic therapy; Photosensitizer; Breast cancer;

Funding Agency: College of Graduate Studies and Research sector (Grant YM08/20) and OMICSRU/RCF, projects SRUL02/13 & GM01/15, Kuwait University

Biochemistry

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High Density Lipoprotein Reduces Blood Pressure and Protects Spontaneously Hypertensive Rats Against Myocardial Ischemia-Reperfusion Injury in an SR-BI Dependent Manner

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Introduction:
Hypertension is a key risk factor in the development of cardiovascular diseases. Elevation in blood pressure alters high density lipoprotein (HDL) function and composition. The exact role of HDL in cardiovascular complications observed in hypertension is however not clearly understood. HDL protected against myocardial ischemia/reperfusion (I/R) injury in normotensive rats. Nonetheless, it's not clear if restoration of HDL function and/or composition protects against myocardial I/R injury in spontaneously hypertensive rats (SHR). Objectives: In this study we tested the effect of HDL treatment on I/R injury in Wistar Kyoto rats (WKY) and SHR and investigated the possible underlying mechanism(s).

Methods:
HDL (900 ng/kg/min) or vehicle were continuously administered to 11-week old WKY and SHR for one week (chronic treatment). Blood pressure was measured before and after treatment. Hearts were subjected to I/R injury using a modified Langendorff system. Another set of rats were treated with HDL administered at reperfusion (acute treatment) in the presence or absence of scavenger receptor class B type-I (SR-BI) blocking antibody. Cardiac hemodynamics were computed and cardiac enzyme release and infarct size were measured. Total cholesterol (TC) and HDL-cholesterol (HDL-C) were enzymatically assayed. Markers of autophagy and inflammation were detected by immunoblotting and ELISA, respectively.

Results:
HDL treatment did not increase TC or HDL-C levels in SHR or WKY, yet it significantly ($P<0.01$) reduced systolic and diastolic blood pressure in SHR. Chronic and acute HDL treatment significantly ($P<0.05$) protected WKY and SHR against myocardial I/R injury. Chronic HDL treatment was significantly ($P<0.05$) more protective in SHR whereas acute HDL treatment induced significantly ($P<0.05$) greater protection in WKY. The extent of HDL induced protection was proportional to the expression levels of cardiac SR-BI and blockage of SR-BI completely abolished HDL mediated protection in SHR. Chronic HDL treatment significantly ($P<0.05$) reduced markers of autophagy and inflammation including in hypertensive rats.

Conclusions:
We demonstrate a novel hypotensive and a cardioprotective effect of HDL against myocardial I/R injury in SHR, the magnitude of which is directly related to the expression levels of cardiac SR-BI. Mechanistically, chronic HDL treatment protected SHR hearts by reducing autophagy and inflammation.

Key Words: High density lipoprotein; Hypertension; SR-BI;

Funding Agency: Research Sector, MB03/16

Cardiology & Infectious Diseases

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The Role of an Antibiotic Envelope in the Prevention of Major Cardiac Implantable Electronic Device Infections

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Introduction:
Over the past decade, rates of cardiac implantable electronic device (CIED) related infections have increased and been associated with increased morbidity, mortality and financial burden on healthcare systems.

Methods:
To examine the effect of an antibacterial envelope in reducing major CIED related infections, we performed a systematic review and meta-analysis by searching PubMed/MEDLINE, CENTRAL, Google scholar and Clinicaltrials.gov for studies that examined the effect of an antibiotic envelope in reducing major related CIED infections, comprising of device-related endocarditis, systemic infection requiring systemic antibiotics and or device extraction, compared to control up till February 15th, 2020. A random- effects meta-analysis was conducted by calculating risk ratios (RR) and respective 95% confidence intervals (CI).

Results:
We include 6 studies that comprise of 11,897 patients, of which 5844 received an antibiotic envelope and 6053 did not. Compared with control, utilization of an antibiotic envelope at the time of procedure was associated with a significant 74% relative risk reduction in major CIED related infections among patients at high risk for infection (RR: 0.26 [95% CI, 0.08 –0.85]; P =.03), while no significant reduction was observed among patients enrolled from studies with any risk for infection (RR: 0.53 [95% CI, 0.06–4.52]; P=.56). Additionally, no reduction in mortality among patients that received an envelope compared to control was observed (RR: 1.15 [95% CI, 0.53–2.50]; P=.72).

Conclusions:
The utilization of an antibiotic envelope at the time of device implantation or upgrade reduces major CIED infections, especially if used in patients perceived to be at higher risk for infection.

Key Words: Antibacterial envelope ; Cardiac implantable electronic device ; Pacemaker ;

Funding Agency: None

Cardiovascular Epidemiology

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Worsening Renal Function in Patients Admitted with Congestive Heart Failure: Prevalence, Risk Profile, and Hospital Readmissions

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Introduction:
Renal function is often negatively impacted in patients with Congestive Heart Failure (CHF) due to the interplay between the heart and kidneys. Worsening Renal Function (WRF) has been associated with decreased survival, accelerated CHF progression, and higher hospitalization rate. Previous literature has thoroughly documented the effects of CHF on hospital readmissions; however, few studies have examined the impact of WRF on CHF during hospitalization.

Methods:
This was a retrospective chart review utilizing the data of 297 patients admitted to Harlem Hospital Center (HHC) for CHF from 2019 to 2020, either due to an exacerbation of symptoms or new-onset of disease. The analysis of our study centered around identifying the risk factors and 30-day hospital readmission rates of patients with WRF, defined as an increase in serum creatinine of ≥ 0.3 mg/dL from admission, in comparison to patients who did not develop WRF. The significance between the two groups was measured using Fisher's Exact test, Wilcoxon rank-sum, and chi-square analysis. A risk score calculated from the sum of point values assigned to each independent risk factor was created.

Results:
Data shows that 27% of hospitalized CHF patients developed WRF. Patients with WRF had a significantly longer hospital stay and a significantly higher increase in daily Creatinine values. We identified old age, overweight, type 2 diabetes (T2D), chronic kidney disease not on dialysis, and high Furosemide dose (oral and intravenous) as independent risk factors. Other independent risk factors include abnormally high serum levels of ProBNP (≥ 9,000 ng/dL), troponin T ≥ (0.04 ng/mm), and Creatinine (≥ 1.5 mg/dL). Based on this data, our point score reflected that patients with a 6+ risk score were four times more likely to develop WRF than patients with a risk score of 0. There was no association between WRF and higher 30-day readmissions.

Conclusions:
WRF is common in hospitalized CHF patients. Although WRF was not associated with an increased 30-day hospital readmission rate, it was associated with longer hospital length of stay and thus increased economic burden. Our results highlight the benefits of implementing changes at HHC to address the particular risk factors and clinical characteristics associated with WRF to identify patients at increased risk and prevent further progression of renal impairment in hospitalized HF patients.

Key Words: Congestive Heart Failure; Worsening Renal Function; Hospital Readmissions;

Funding Agency: None

Community Medicine

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Exposure to tobacco smoke, concurrent morbidities and health services use among young adults in Kuwait

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Introduction:
Tobacco smoking, resultant morbidities and related health-care utilization is a public health concern worldwide. This study i) assessed the prevalence of exposure to tobacco smoke among young adults, ii) assessed the self-rated and physician-diagnosed morbidities and iii) examined the association between exposure to tobacco smoke, related morbidities and health-care use during the past one year.

Methods:
During October 2022, a cross-sectional study design was implemented for data collection using a structured e-questionnaire. The participants were enrolled as a sample of convenience from among the undergraduate students of the Kuwait University. The prevalences (%) of exposure to tobacco smoke (1st-hand and/or 2nd-hand at home - one or both parents smoke vs. none), concurrent self-rated and physician-diagnosed morbidities, health-services use (one or more times vs. none) during the past one-year were computed. Multivariable logistic regression model was used to evaluate the association between sociodemographics, lifestyle factors, self-rated and physician-diagnosed morbidities and health-services use.

Results:
Of 1323 participants, 87.5% were Kuwaiti and 75.8% were females. The prevalence of 1st-hand and 2nd-hand smoking was 13.4% (177/1323) and 50.8% (672/1323) respectively. In this sample, self-rated respiratory morbidities were highly prevalent including shortness of breath (59.1%), cough (46.3%), chest pain (26.9%), and exercise difficulty (21.6%) along with physician-diagnosed morbidities including asthma (16.8%), eczema (11.2%) and COPD (1.4%). The morbidities significantly associated with the health-services use were cough (aOR =2.09; CI:1.66- 2.63; $p < 0.001$), shortness of breath (aOR=1.30; CI:1.01-1.67; $p = 0.042$), nausea/ vomiting (aOR = 2.62; 95% CI: 1.87-3.67; $p < 0.001$) and asthma (aOR = 1.88; 95% CI: 1.39-2.55; $p < 0.001$).

Conclusions:
This study recorded high prevalence of exposure to 1st-hand and 2nd-hand tobacco, related respiratory and allergic ailments among young adults. Focused intervention to minimize the exposure to tobacco smoke and resultant potential reduction in respiratory and allergic morbidities may reduce the health-services use among young adults in this and other similar settings. If implemented, future studies may look at the effects of such intervention.

Key Words: Tobacco smoke; Respiratory morbidity; Young adults;

Funding Agency: None

Community Medicine

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Physical Activity and Mental Health among Kuwait University Students

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Introduction:
Background and Objectives: Physical inactivity is a serious public health issue that affects all aspects of health. The aim of this study was to evaluate the intensity level of physical activity among Kuwait University students, to determine the association between physical activity level and mental health, and to explore the sociodemographic and lifestyle-related characteristics of the relationship between physical activity and mental health.

Methods:
This cross-sectional study surveyed 1371 students aged 18 years and older enrolled in eight randomly selected colleges of Kuwait University. The number of students selected from each college was proportionate to the total number of students in each college. Data were collected using a self-administered questionnaire that included four sections: sociodemographic characteristics, the International Physical Activity Questionnaire short form, physical activity-related questions, and the General Health Questionnaire-12. The response rate was 98.2%.

Results:
Of the surveyed students, 45.9% had low intensity levels of physical activity and 28.4% endorsed possible psychological distress. Univariate logistic regression analyses showed that all sociodemographic variables including physical activity intensity levels were significantly associated with general mental health. However, in multivariate logistic regression analysis, only age, gender, monthly income satisfaction, and doctor diagnosed medical conditions remained significant.

Conclusions:
Our study found that most students had low intensity levels of physical activity. Furthermore, the most reported motivator for engaging in physical activity was improving health, while the most reported barrier was the lack of time. Almost a third of our participants endorsed possible psychological distress. Acknowledgments: We would like to thank our supervisors, Dr. Reem Al-Sabah and Mr. Abdullah AlMajran, for their guidance. We would also like to acknowledge the Department of Community Medicine and Behavioral Science and the ethics committee for this opportunity. We would like to thank the Kuwait Ministry of Health, Ministry of Education, Deanship of each of the eight colleges, and the Dean of Admissions and Registration for providing us with valuable information. Finally, we would like to thank all 1407 students who completed our survey and allowed us to use their information to conduct our study and the professors who allowed us to distribute our survey during lectures.

Key Words: Physical Activity; Mental Health; Kuwait University Students

Funding Agency: None

Community Medicine

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Obesity Association with Uncontrolled Blood Glucose Levels in Type 2 Diabetes

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Introduction:
Background and objectives: Diabetes Mellitus is a chronic metabolic disorder characterized by abnormally high blood glucose levels. "Diabesity" refers to concurrent obesity and Type 2 Diabetes Mellitus (T2DM). The prevalence of obesity and diabetes are in parallel with each other; obesity was found to be associated with high morbidity and mortality of diabetes. Thus, the aim of this study is to assess the association between obesity and uncontrolled blood glucose levels in T2DM patients and compare the individual association between uncontrolled blood glucose levels with BMI and WC, among T2DM patients.

Methods:
A cross-sectional study was conducted in October 2022. An in person questionnaire was obtained from 252 T2DM Kuwaiti patients aged 18 years and above, of either gender. We computed the prevalence and frequency of sociodemographic variables, lifestyle factors, BMI, WC and HbA1c. Independent sample T-Test and Mann-Whitney U test analysis were obtained, to test the difference in BMI and WC across HbA1c categories (controlled <6.5%, uncontrolled ≥6.5%). Univariable logistic regression analysis was done to analyze the association between sociodemographic factors and uncontrolled Hb1Ac. A final multivariable regression analysis was carried to determine the adjusted odds ratios (OR) and their 95% confidence interval (CI) to interpret the final model.

Results:
Most of the participants were above 50 years and 52% were females. Most of the study population were obese (48.8%) with very high waist circumference (78.6%). Mann-Whitney U-test and independent sample T-test showed no significant difference in the anthropometric measurements across HbA1c categories. In the multivariable regression model, using insulin injections (adjusted OR=3.544. 95% CI: [1.414-8.884]) and not following a specific diet (adjusted OR=2.070. 95% CI: [1.081-3.966]) was significantly associated with uncontrolled HbA1c levels. No association was found between uncontrolled HbA1c levels and individual obesity measurements. However, a significant association was observed between uncontrolled HbA1c and a combined obesity risk category.

Conclusions:
In conclusion, individually, WC or BMI are not associated with uncontrolled T2DM. Yet, using an obesity risk category that considers both WC and BMI is a significant indicator for uncontrolled blood glucose levels in T2DM.
Acknowledgments: We would like to thank Dr. Anwar AlBaloul and Dr. Ahmad AlSultan for their guidance in this research.

Key Words: Type 2 Diabetes Mellitus; Wait circumference ; BMI;

Funding Agency: None

Community Medicine

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Compliance With Hand Hygiene Practices Among Nursing Staff in Secondary Healthcare Hospitals in Kuwait.

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Introduction:
Background: Hand hygiene (HH) among healthcare workers, especially nurses, is the main preventive measure to control healthcare associated infections but compliance with hand hygiene (CwHH) remains low in various settings including Kuwait. This study aimed to assess the knowledge of, attitudes towards, and CwHH among nursing staff in secondary care hospitals in Kuwait.

Methods:
A cross-sectional study was conducted on nursing staff in all six secondary care hospitals in Kuwait. Data on knowledge of, attitudes towards, and self-reported CwHH were collected through a self-administered question- naire that was developed based on WHO's questionnaire, while the data on actual compliance were objectively col- lected through direct observation of nurses during routine care by two independent observers using WHO's observa- tion form.

Results:
Of 829 nurses approached, 765 (92.2%) responded and participated. Of all participants, 524 (68.5%) were able to list "My Five Moments for Hand Hygiene" fully and appropriately. However, several misconceptions (e.g. air circulation in hospital is the main route of infection) about HH were found among the nurses. CwHH was (25.0%) by direct observation while self-reported compliance was (69.5%) each varied significantly ($p < 0.001$) between different hospitals. Female nurses compared to male nurses and non-Arab compared to Arab nationalities were more likely to report CwHH in multivariable analysis. Several items on knowledge of and attitudes towards HH were also associated with self-reported CwHH.

Conclusions:
Observed CwHH among nursing staff in secondary care hospitals in Kuwait was low, which highlights the need to make more efforts to improve HH practices. Interventions that have been used elsewhere and found to be effective may be tested in Kuwait. Despite the good overall knowledge on HH among nurses, there are several mis- conceptions that need to be corrected.

Acknowledgements: Not applicable.

Key Words: Hand hygiene; Compliance; Nurse;

Funding Agency: None

Community Medicine

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Prevalence of Conspiracy Theory Ideation, COVID-19 Conspiracy, and their Association with COVID-19 Vaccination Status among adults in Kuwait: A Cross-Sectional Study

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Introduction:
Background: Conspiracy theories influence people's compliance with preventive strategies and accepting vaccination, thus affecting the persistence of the pandemic and overall population health. A lack of knowledge about COVID-19 has led people to believe in conspiracy theories, their origin, and their purpose. This study aimed to investigate the association between COVID-19 vaccination status with conspiracy ideation and COVID-19 conspiracy ideation.

Methods:
In a cross-sectional study, data from 554 participants ≥18 years living in Kuwait were collected using a questionnaire distributed over social media platforms. Descriptive statistics and correlations were reported for continuous variables and associations were tested for categorical variables. To estimate and test the effect of exposure variables while accounting for potential confounders, multiple logistic regression modeling was implemented and odds ratios (OR) with their 95% confidence intervals (CI) were reported for some exposures.

Results:
The prevalence of generic conspiracy ideation, COVID-19 conspiracy belief and vaccination against COVID-19 were 33%, 28.3%, and 85.4%, respectively. After adjusting for potential confounders, results indicated that believers in conspiracy theories (aOR=6.04, 95%CI: 2.72 – 13.42), believers in COVID-19 conspiracy theories (aOR=3.34, 95%CI: 1.55 – 7.18), and those using sources of information other than TV/newspaper or official spokesman (aOR=9.5, 95%CI: 2.55 – 35.4) were significantly more likely to be unvaccinated.

Conclusions:
Belief in conspiracy theories, COVID-19 conspiracy theories, and obtaining main health information from sources other than official sources have a negative effect on vaccination status in Kuwait. Hence, this entails a negative effect on efforts to control and combat the spread of COVID-19 in the community. Therefore, health policymakers need to address this issue to promote better health for the population.
Acknowledgement: I would like to express my deep gratitude to Dr. Ahmed Albatineh, my research supervisor, for his patient guidance, enthusiastic encouragement and useful critiques of this research work. I would like to express my very great appreciation to my family who supported me during this journey, and I would like to extend my sincere thanks to every participant who participated in this study.

Key Words: Conspiracy ideation; COVID-19 conspiracy; Vaccination, Kuwait;

Funding Agency: None

Community Medicine

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The Impact of Academic Stress on the Lifestyle of University Students in Kuwait

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Introduction:
Stress is considered as a main health problem that leads to negative lifestyle habits. High academic stress is known to be one of the major factors that may contribute to higher level of stress. Therefore, our aim was to measure the impact of academic stress on the lifestyle factors, such as physical activity, eating habits, and quality of sleep of university students living in Kuwait.

Methods:
This cross-sectional study was conducted from December 2021 to January 2022 on students in different universities in Kuwait aged 18-25 years. An online questionnaire was sent to students on different platforms. This questionnaire involved questions about the sociodemographic data, academic stress, physical activity, eating habits and quality of sleep. Scales like ESSA, IPAQ-SF, CES, and quality of sleep scale were used.

Results:
There was a significant association between an increase in educational stress score and compulsive eating score ($p \leq 0.001$). Moreover, we found an inverse relation between the educational stress score and sleep quality ($p \leq 0.001$). Additionally, sleep quality score decreased significantly with higher coffee intake ($p \leq 0.001$) as well as with melatonin intake ($p \leq 0.001$). Furthermore, there is a statistically significant decrease in the trend of the stress score as physical activity levels increased ($p = 0.012$). Also, our study found statistically significant differences in median stress scale scores between males and females ($p \leq 0.001$), across the different university majors ($p = 0.013$), between different studying hours ($p \leq 0.001$), and across different GPA grades ($p \leq 0.001$).

Conclusions:
In conclusion, academic stress has a negative effect on physical activity, eating habits, and quality of sleep of university students in Kuwait. Therefore, these results must be taken into consideration, and action must be done to decrease academic stress. Acknowledgements: First and foremost, we would like to convey our gratitude to Dr.Wafaa Shaban, our academic adviser, for her invaluable assistance, knowledge, and support throughout the study process. We'd like to thank our project assistant, Dr.Ahmad AlSultan, for his fantastic job and for always being willing to help whenever we needed it. Finally, we'd want to express our gratitude to everyone who took the time to participate in this study.

Key Words: Academic Stress; Kuwait University; University Student's Lifestyle;

Funding Agency: None

Community Medicine

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Sibship size and position in sibship in relation to lipid profile during adolescence: a cross-sectional study

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Introduction:
Background. Epidemiologic studies have reported associations of sibship size and position of the child in the sibship with multiple health outcomes, including adiposity and diabetes. However, little is known about sibling effects on lipids. Hence, this study sought to evaluate associations of the number of total, older, and younger siblings with lipid profile among adolescents.

Methods:
In a cross-sectional study among high school students aged 14 to 19 years, lipid levels were measured in capillary blood. Parents reported the number of siblings (total, older, and younger). Geometric means of lipids were calculated, and linear regression was used to estimate the ratio of geometric means (RoGM) and 95% confidence intervals (CI). Analyses were sex-stratified.

Results:
Of the total study sample (n = 1,584), 758 (47.9%) were boys and 826 (52.1%) were girls, with median age of 16.0 years. Total cholesterol (TC) was lower by 8% (adjusted-RoGM = 0.92, 95% CI: 0.88–0.96) among boys with ≥3 older siblings compared to those with no older siblings. Similarly, boys with ≥3 younger sibling compared to those with no younger siblings had reduced TC by 7% (adjusted-RoGM = 0.93, 0.87–0.99). Moreover, an increased number of total siblings (≥4 vs. 0/1: adjusted-RoGM = 0.80, 0.67–97) and older siblings (≥3 vs. 0: adjusted-RoGM = 0.90, 0.82–0.98) were associated with reduced low-density lipoprotein cholesterol (LDL-C) among boys. Similarly, lower levels of triglycerides (TG) were seen among boys with ≥3 older siblings compared to those with no older siblings (adjusted-RoGM = 0.87, 0.78–0.96). A higher number of younger siblings was associated with increased high-density lipoprotein cholesterol (HDL-C) among boys (≥3 vs. 0: adjusted-RoGM = 1.08, 1.01–1.17). Sibship characteristics were not associated with lipids among girls.

Conclusions:
Increased number of total, older, and younger siblings were associated with favorable lipid profiles among adolescent boys, but not girls. Mechanisms underlying these associations need further investigations.

Key Words: Sibling effect; Lipid profile; Adolescent ;

Funding Agency: Full fund by (Kuwait National Guard), Partial fund by (College of Graduate Studies, Kuwait University), (Salman Abdullah Al Dabbous and Sons Company)

Community Medicine

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A Case-Control Study of Risk Factors for Hepatocellular Carcinoma in Kuwait

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Introduction:
Background: Hepatocellular Carcinoma (HCC) is one of the major types of primary liver cancer globally. There is scarcity of published data on the risk factors for HCC from the Middle Eastern countries specifically in Kuwait. Therefore, this case-control study sought to examine the risk factors associated with HCC in Kuwait.

Methods:
Fifty-three histopathologically confirmed HCC cases were recruited from Kuwait Cancer Control Center Registry. One hundred ninety-six controls (1:4 ratio) were selected from medical and/ or surgical outpatient's clinics at six general hospitals of Kuwait. A structured questionnaire was used to collect the data from cases and controls through face-to-face interview. Adjusted odds ratios (ORadj) and their 95% confidence intervals (CI) were estimated using a multivariable logistic regression model.

Results:
Multivariable logistic regression model showed that HCC cases compared to controls were 41.6 times more likely to have had history of non-alcoholic fatty liver disease (NAFLD) (ORadj = 41.6; 95% CI: 8.9 - 193.5; $p < 0.001$). History of non-steroid anti-inflammatory drugs (NSAIDs) use were significantly less common among HCC cases than controls (ORadj = 0.18; 95% CI: 0.04 - 0.7). cases compared with controls were more likely to have reported the history of regular consumption of the alcohol (ORadj = 14.2; 95% CI: 1.2 - 173.4; $p = 0.038$). Compared with controls, HCC cases reported to have had regularly used olive oil (ORadj = 0.17; 95% CI: 0.04 - 0.77). Furthermore, compared to controls, HCC cases tended to frequently consume milk and/or milk substitute (3 glass/ week) (ORadj 7.2; 95% CI: 1.2 - 43.4).

Conclusions:
Age, NAFLD, excessive consumption of milk and milk substitutes, excessive alcohol consumption, and butter consumption were associated with increased HCC risk. Conversely, use of NSAIDs or regular use of olive oil had protective effect against HCC risk. Overcoming pitfalls in dietary patterns and preventing/ treating NAFLD may help minimize HCC risk in Kuwait and other countries in the region. The results of this study may help plan an evidence-based educational program based on identified risk factors for HCC in Kuwait. Future studies may look at the impact of such efforts

Key Words: Hepatocellular Carcinoma; Risk Factors; Case-control study;

Funding Agency: None

Community Medicine

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The Prevalence of Irritable Bowel Syndrome Among Kuwait University Students: The Role of Anxiety, Depression, and Diet

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Introduction:
Background: Irritable Bowel Syndrome (IBS) is a clinically diagnosed multifactorial gastrointestinal disorder. Several studies demonstrated that psychological factors and dietary intake have a substantial effect on developing IBS. Thus, increasing its susceptibility in university students, due to their high workload, disturbed eating habits, and decreased quality of life.
Aim of the study: The aim of this study is to estimate the prevalence of IBS among Kuwait University students using Rome IV criteria and compare the results between different colleges. Furthermore, we will be identifying associated risk factors, including sociodemographic status, anxiety, depression, and diet.

Methods:
This cross-sectional study enrolled 758 Kuwait University students. Data collection was conducted using an online self-administered questionnaire, available in both Arabic and English. The survey consisted of 7 sections: (A.) Sociodemographic status, (B.) Godin Leisure Time Exercise Questionnaire, (C.) Food/Vegetable/Fiber Screener, (D.) Hospital, Anxiety, and Depression Scale, (E.) Rome IV criteria (F.) IBS ± Symptoms Severity Scale, and (G.) Red Flags.

Results:
Among 758 students in Kuwait university, 34.3% are diagnosed with IBS by Rome IV criteria. Before adjusting the data, the significant variables with IBS were year of college, anxiety, and depression. After adjustments, only anxiety (p-value<0.001), depression (p-value<0.001), and diet (p-value=0.017) were the associated predictors.

Conclusions:
Based on our results, we concluded that the prevalence of IBS among Kuwait University students was 34.4%. Our study determined that anxiety, depression, and diet are significant predictors. Further studies should be conducted to assess the temporality between risk factors and IBS.

Key Words: Irritable bowel syndrome; Depression ; Anxiety;

Funding Agency: None

Community Medicine

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The Effect of the COVID-19 Pandemic on the Physical and Psychological Health of Elemantary School Children in Kuwait.

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Introduction:
Background and Objectives: COVID-19 has negatively affected the physical and psychological health of children. This study aimed to assess the impact of the pandemic on elementary school children and find possible correlations between physical and psychological health and other behaviors.

Methods:
A cross-sectional study was performed using a web-based questionnaire that was distributed to parents or legal guardians of children in elementary school (ages 5 to 11 years) through social media platforms. A total of 1032 responses were received and used in our analysis. The Pediatric Symptom Checklist was included in the questionnaire to assess psychological health. Other questions were asked about changes in weight and weight related behaviors such as physical activity and diet.

Results:
The study showed that a higher proportion of children were overweight/obese compared to pre-pandemic. There were significant correlations between weight gain since the beginning of COVID-19 and decreased physical activity ($p<0.014$), not participating in sports activities online ($p=0.003$), increased screen time ($p<0.047$), and increased unhealthy eating habits, among other factors. A higher level of psychological impairment based on scores of the Pediatric Symptom Checklist was reported. These impairments were associated with decreased physical activity ($p=0.002$), increased screen time ($p<0.001$) and online gaming ($p<0.001$), and increased anxiety of the parent ($p=0.003$).

Conclusions:
The pandemic had a significant effect on the physical and psychological health of children in elementary school. A higher proportion of the sample was overweight or obese now compared to pre-pandemic. Additionally, the proportion of children that reported psychological impairments increased compared to pre-COVID.

Key Words: COVID-19; Children; Health;

Funding Agency: None

Cytopathology

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Primary Thyroid Lymphoma- A Review of 3 cases.

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Introduction:
Primary thyroid lymphomas (PTL) are a rare cause of extranodal lymphomas (about 2%) as well thyroid malignancies (0.5–5%). Its incidence is two per million persons and is more common in women than in men. Studies show that 98 percent of PTL are B-cell Non-Hodgkin lymphoma. This study was conducted over a two-year period; in which three cases were diagnosed as PTL by fine needle aspiration cytology (FNAC). The common clinical presentation, cyto-radiological findings and immunophenotypical findings of PTL have been analyzed and presented.

Methods:
This retrospective study was conducted in a tertiary care cancer hospital during a 2 year period between Oct 2020 to Oct 2022. A total of 1121 thyroid FNAC were done during this period, of which 121 thyroid malignancies were diagnosed and classified as VI by The Bethesda system of reporting thyroid cytology. Three out of 121 (2.4%) PTL cases were analyzed.

Results:
Two out of the 3 patients were females, and the mean age of presentation was 44 years. Common clinical findings which prompted patients to seek medical attention were, large rapidly growing neck mass, associated with dyspnea/ stridor, dysphagia and neck discomfort. Radiologically they were seen to be involving adjacent neck structures such as neck muscles, entrapping the blood vessels, encasing/involving the lymph nodes and forming large inseparable masses. One case also showed intracranial metastasis. Two of the 3 cases were B-cell Non-Hodgkin lymphoma and one case was Hodgkin lymphoma. Smears were highly cellular, consisting of monotonous population of lymphoid cells in Non-Hodgkin lymphoma, whereas, in the Hodgkin's lymphoma, typical Reed Sternberg cells were seen in a background of a polymorphous lymphoid population.

Conclusions:
This study highlights the need for a high level of suspicion, that is needed in patients presenting with rapidly enlarging neck mass and typical radiological findings. FNAC combined with immunophenotyping could give a precisive diagnosis of lymphoma. Accurate pre-operative diagnosis between Primary thyroid carcinoma versus Lymphoma as well as distinction between Primary and Secondary lymphoma is crucial due to the considerable difference in diagnostic tools, treatment modalities and prognosis.

Key Words: Primary thyroid lymphoma; Non-Hodgkin lymphoma; Fine needle aspiration

Funding Agency: None

Dentistry

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Effects of Dental Chair Backrest Inclination on Virtual Interocclusal Record of Maximum Intercuspal Position: A Clinical Study

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Introduction:
Digital dentistry enables taking virtual interocclusal records of teeth by scanning their buccal and labial surfaces while in Maximum Intercuspal Position (MIP). While virtual interocclusal records are commonly used to obtain MIP in an intraoral scanner, evidence for the best position to obtain them is limited. Objectives: To evaluate the influence of backrest inclination on the accuracy of virtual interocclusal record of MIP obtained with an intraoral scanner and compare it to conventional interocclusal record of the MIP obtained with a polyvinylsiloxane(PVS) record at 90 degrees, 120 degrees, and 180 degrees dental chair backrest inclination.

Methods:
A total of 10 dental students with fully-dentate volunteered to participate in this study(IRB approved). Each participant's maxillary and mandibular arches were scanned using Trios3 intraoral scanner to create STL files to enable fabrication of 10 printed maxillary models and 10 printed mandibular models used in this study. Virtual interocclusal records were obtained by scanning labial surfaces teeth while in MIP at 90 degrees, 120 degrees, and 180 degrees dental chair backrest inclination. All scans were saved as STL files. Conventional interocclusal records were obtained by using PVS while in MIP at 90 degrees, 120 degrees, and 180 degrees dental chair backrest inclination. For each participant, maxillary and mandibular printed models were mounted using conventional interocclusal record technique and then scanned with a desktop scanner. All STL files were exported and analyzed by using a best-fit algorithm of a professional engineering software program to determine the positional deviation. One-way ANOVA and two-way ANOVA were performed to compare virtual and conventional interocclusal records at different backrest inclination. Tukey HSD post hoc comparisons were performed at an alpha level of 0.05.

Results:
There is no statistically significant difference in mandibular MIP for virtual interocclusal record at different chair backrest inclinations. there is no statistically significant difference in mandibular MIP between virtual interocclusal and conventional interocclusal.

Conclusions:
Virtual interocclusal records are as accurate as conventional interocclusal records and can be taken at any dental chair backrest inclination position.
Acknowledgement: Dr. Jaime Lozada for facilitating the research in the implant department.

Key Words: Virtual; Dental; Position;

Funding Agency: None

Dentistry

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Effect of Splinting Implant Scan Bodies Intraorally on The Trueness of Complete Arch Digital Impressions: A Clinical Study

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Introduction:
Statement of the Problem: A predictable protocol for accurately scanning implants for a complete edentulous arch has not been established. Purpose: The purpose of this study was to investigate the effect of splinting scan bodies intraorally on the trueness and scan time of implant digital impressions of the edentulous arch.

Methods:
19 edentulous jaws undergoing fixed complete denture treatment with a minimum of 4 implants were selected for this study. Verified master casts of the patients' edentulous jaws were scanned with a desktop laboratory scanner and scan bodies to obtain a reference (control) scan for each patient. Intraoral scan bodies were hand tightened on all the implants in the edentulous arch and an intraoral scan was taken with an intraoral scanner for each jaw; these scans represented the first test group. The same scan bodies were splinted using floss and pattern resin and the edentulous arch was scanned again for all patients; these scans represented the second test group. All scans were conducted by one investigator. The scan time for the first and second scan of each patient was recorded. To compare the trueness of the un-splinted scan to the splinted scan, the STL files of the two scans were superimposed to the control scan and positional and angular deviation were analyzed using Geomagic software. One sample T test was used to compare each group's distance and angular deviation to the control. ANOVA test was conducted to examine the effect of the scan technique on trueness (distance deviation/angular deviation) and scan time (α=0.05 for all tests).

Results:
There was no statistically significant difference in 3-Dimensional global positional deviation (p = .493) or in the X (p = .794), Y (p = .435), and Z axes (p = .871) between the splinted and un-splinted scan groups. No statistically significant difference in angular deviation was found between the splinted and un-splinted experimental groups as well (p = .250). A statistically significant difference in mean scan time was found between un-splinted group and splinted group (p = .001). The fastest scan time was found with the splinted group with an average of 2-minute faster scan time.

Conclusions:
Splinting implant scan bodies intraorally does not affect the trueness of complete arch digital impressions but can reduce scan time.

Key Words: Digital; Scan; Implant;

Funding Agency: None

Dentistry

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Applications of Artificial Intelligence in Prosthodontics

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Introduction:
Prosthodonticsalso known as dental prosthetics or prosthetic dentistry, is the area of dentistry that focuses on dental prostheses. Artificial intelligence (AI) models have been applied in different dental specialties like prosthodontics, implant dentistry, endodontics, periodontics, radiology, and dental public health. AI models have been applied for different prosthodontics applications. The clinical applicability and technology maturation stage of AI applications in prosthodontics is paramount for AI implementation in mainstream dentistry.
Objective: The aim of this literature review is to assess the development, performance, and limitations of the AI models for prosthodontic purposes.

Methods:
A literature review of articles related to artificial intelligence in prosthodontics was completed.

Results:
Artificial intelligence can be used in the field of prosthodontics as follows:
1- Perform tooth shade selection and provide a recommended porcelain selection to accomplish shade matching.
2- Map the finishing line of tooth preparations.
3- Automated tooth anatomy design.
4- Estimate the optimal parameters for successful casting of a metal framework.
5- Recognize implant type from radiographs.
6- Predict implant success.

Conclusions:
Artificial intelligence models have shown the potential for providing a reliable diagnostic tool for tooth shade selection, automated restoration design, mapping the preparation finishing line, optimizing the manufacturing casting, and identifying unknown implants from radiographic examinations.

Key Words: Artificial; Intelligence; Prosthodontics;

Funding Agency: None

Dentistry

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Salivary Fluoride Concentration Following Toothbrushing With and Without Rinsing: A Randomised Controlled Trial

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Introduction:
Caries prevalence has declined since the introduction of fluoridated toothpaste. There have been several developments regarding specific active fluoride ingredients but not enough evidence to support one over the other. The purpose of this double-blind randomized controlled trial was to compare salivary fluoride concentrations of different fluoride formulations in the form of toothpaste with and without post-brushing water rinsing in adults.

Methods:
The study included 120 participants who were randomly assigned to one of 12 groups (10 participants/group). The toothpaste formulas investigated included fluoride-free (0 ppmF); sodium fluoride (1450 ppmF); sodium monofluorophosphate (1450 ppmF); sodium fluoride and monofluorophosphate combined (1450 ppmF); stannous fluoride and sodium fluoride combined (1450 ppmF); and amine fluoride (1400 ppmF). Block randomisation was used to assign each participant to groups. Participants brushed with 1.0 g of one of the six different toothpaste formulations either with or without post-brushing water rinsing. Saliva was collected at six different times (at 0, 1, 15, 30, 60, and 90 min/s post-brushing). Samples were analysed using a fluoride ion-specific sensitive electrode connected to an ion analyser.

Results:
The demographic of the participants were not significantly different among the groups($P > 0.05$). Time, toothpaste formulation, and post-brushing rinsing routines had significant effects on saliva fluoride retention($P < 0.05$). Amine fluoride toothpaste was the only formula that showed statistically significantly higher concentrations of salivary fluoride at 90 min in both the rinsing and non-rinsing groups. Sodium monofluorophosphate toothpaste did not result in a significant difference compared to the control group at any time point, in both rinsing and non-rinsing groups.

Conclusions:
Based on the results from this study, no rinsing after toothbrushing in adults can be recommended when sodium monofluorophosphate containing toothpaste formula is used. It also concludes that amine fluoride resulted in a significantly higher saliva fluoride concentration at 90 min in both the rinsing and non-rinsing groups compared to other fluoride toothpaste formulations. Registry: Protocol Registration and Results System (ClinicalTrials.gov= NCT02740803).
Acknowledgements
The authors thank Mrs. G. Dukanovic for her outstanding assistance during all clinical sessions. We appreciate all the participants in the current study.

Key Words: Fluoride toothpaste; Rinsing post-burshing; Amine fluoride;

Funding Agency: None

Dentistry

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Oral Cancer Knowledge, Attitudes, and Practices among Newly Graduated Dentists in Kuwait

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Introduction:
Oral cancer awareness among newly graduated dentists could have a substantial impact in the prevention and early detection of oral cancer. This survey was undertaken to assess the knowledge, opinion, attitudes, and practices on oral cancer among newly graduated dentists in Kuwait.

Methods:
In this cross-sectional study, self-reported questionnaire was distributed to the newly graduated dentists. Of the 310 dentists who participated, 171 (55.2%) were males and 139 (44.8%) were females. The questionnaire included 23- questions on oral cancer knowledge, opinion, attitudes, and practices.

Results:
The mean age of the dentists was 25.8 ± 2.4 years and their mean years of experience 1.5 ± 1.7 years. Overall, a great majority of dentists (95.8%) recognized tobacco use and alcohol consumption as very important risk factors for oral cancer occurrence. Almost all of participants were aware of the most common form of oral cancer (94.2%). Most of the dentists correctly identified the most common site of oral cancer (93.5%). Majority of the participants recognized the most commonly associated lesions with oral cancer (91.6%). While 37.4% of the dentists agreed that they were adequately trained in oral cancer screening, most (89.7%) believed that patients should have mandatory oral cancer screening at the clinics. Also, majority (95.8%) expressed their willingness to attend continuing education and training courses in cancer screening and prevention. Most of the dentists (81.9%) referred a patient with a suspicious lesion to a specialist.

Conclusions:
Majority of the dentists were aware and knowledgeable about various aspects of oral cancer. There is a need to emphasize and reinforce the training programs in oral cancer education mainly in prevention and early detection. Continuing education programs and workshops are highly recommended to raise awareness of the dentists on risk factors and diagnosis of oral cancer.

Key Words: Oral cancer; Knowledge; Opinion; Attitude; Practices; Newly graduated dentists;

Funding Agency: None

Dentistry

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Oral Health Related Quality of Life (OHRQoL) among Kuwait Adults during the COVID-19 Pandemic

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Introduction:
During the COVID-19 pandemic, the Ministry of Health in Kuwait restricted non-emergency dental procedures, including in the private sector, and only permitted emergency procedures. Changes in oral health-related quality of life (OHRQoL) over the COVID-19 period were the focus of this investigation. Aim: To assess the (OHRQoL) among adults during the COVID-19 pandemic

Methods:
This cross-sectional study was conducted during 2020. Randomly, adults were sent an online questionnaire, with a total of 32 questions, 17 questions of which were on OHRQoL. Consent was obtained from each participant and the survey was approved by the Research Committee of the Ministry of Health-KUWAIT. Data were analyzed as percentages.

Results:
Overall, 920 participated in this survey, and 67% (620) of them were non-Kuwaitis. Two thirds of participants were government employees. 93% (857) of participants were not infected with COVID-19. Two-thirds of the participants (548, 60%) assessed their oral health as excellent or very good, and the majority (803, 87%) were satisfied with their oral health. The majority of participants always enjoyed their food (660- 72%) and 40% (362) like their smile. Few individuals (132-14%) reported being unable to visit the dentist every six months due to the pandemic. Almost half of participants (415- 45%) feared becoming infected with COVID-19 during dental visits. The majority of participants (628-68%) completed daily oral hygiene. Social and psychological activities were not disrupted by the pandemic; only 5 (0.43%) individuals avoided conversation, 7 (0.65%) had poor sleep quality, and 15 (1.41%) had missed work due to tooth pain.

Conclusions:
Outcomes of this survey suggest that most of the participants were satisfied with their oral health and the COVID-19 did not have major impact on OHRQoL. Many of the participants felt that COVID-19 affected their regular dental visits, which might have affected their oral health status. More studies should be planned to measure oral health status among population during COVID-19 pandemic.

Key Words: OHRQoL; COVID-19; Oral health practices ;

Funding Agency: None

Dentistry

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Influence of Surface Treatment on CAD/CAM Lithium Silicate Ceramics'Topography and Bonding to Human Dentine

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Introduction:
Clinical success of ceramic restorations depends on the strength of their bond to the dental substrate. CAD/CAM zirconia-reinforced lithium silicate (ZLS) is a novel dental glass ceramic. Ceramic restorations conventionally require conditioning with hydrofluoric acid (HF) followed by silanization before cementation. A novel single-step ceramic primer (MEP) is marketed as an alternative to the multistep HF treatment. Limited data is available on the adhesive bonding of ZLS to dentin. This study evaluated the effects of surface treatment on ZLS surface topography and bonding to human dentin.

Methods:
Celtra Duo and Vita Suprinity® PC. CAD/CAM blocks were sectioned to produce ceramic slices that were randomly assigned to three groups according to the surface treatment: no treatment (Control); 5% HF and silane; MEP. Ceramic slices were cemented to flat dentin using two etch-and-rinse and two self-adhesive resin cements (24 groups; n=5). The bonded samples were sectioned into microspecimens 24 hours after water storage at 37°C. The microtensile bond strength (μTBS) was measured with a universal testing machine. Optical profilometry measured 3D surface roughness parameters and scanning electron microscopy (SEM) images allowed topographic evaluation. μTBS and roughness data were statistically analyzed by three-way ANOVA and Tukey's test, and by Kruskal-Wallis and Mann Whitney U tests, receptively (α=5%).

Results:
Bond strength was significantly influenced by the type of cement and the interaction between surface treatment and the type of cement ($p < 0.05$). Control groups failed during sectioning, whereas HF and MEP promoted similar bond strengths within same cement groups. Etch-and rinse cements demonstrated significantly higher mean μTBS than self-adhesive cements. For surface topography, both treated groups were significantly different than control group. HF promoted the highest roughness parameters and most prominent surface changes.

Conclusions:
Effective surface roughening and appropriate adhesives are pivotal for successful bonding of indirect ceramic restorations, and MEP might be used as an alternative to HF for ZLS conditioning.

Key Words: Zirconia-reinforced lithium silicate; Bond strength; Surface roughness;

Funding Agency: College of graduate studies, Kuwait University

Dermatology

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Systemic Nail Disorders: A Review

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Introduction:
Nail disorders are an important entity in dermatology. They represent 10% of dermatological disorders. This review article aims to discuss common nail disorders associated with systemic diseases.

Methods:
This study is conducted based on publications and guidelines obtained by selective review in PubMed, including Cochrane reviews and meta-analyses.

Results:
Several nail disorders are commonly associated with systemic disorders. Nail psoriasis can affect 80% to 90% of psoriatic patients throughout their lives. Nail lichen planus affects the fingernails more than the toenails, and it is mainly diagnosed clinically. Nail lichen striatus is mainly a pediatric disease, and the diagnosis is confirmed by histopathology. Alopecia areata can cause nail pitting and trachyonychia. Anonychia can be congenital or a part of a syndrome, such as Iso-Kikuchi syndrome. Tuberous sclerosis causes ungual fibromas. Darier-white disease causes red longitudinal streaks with a V-shaped notch at the nail margin. Infections, such as syphilis and Human Immunodeficiency Virus (HIV), can also affect the nail unit. Nail clubbing is associated with respiratory, cardiac, inflammatory, neoplastic, gastrointestinal, infectious, and endocrine diseases. Leukonychia has several types, each of which gives a clue to a possible systemic issue. Splinter hemorrhages are associated with trauma, drugs, atopic dermatitis, among other disorders.

Conclusions:
Proper knowledge and examination of nail disorders is an important diagnostic tool. Multiple systemic disorders should be suspected upon the detection of nail disorders. This will help in early diagnosis and proper management

Key Words: Nail Disorders; Congenital; Review;

Funding Agency: None

Dermatology

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Localized Nail Disorders: A Review

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Introduction:
Nails have an important role in finger functionality. Nail disorders may be localized, or they can be a part of a more systemic pathology. This review article aims to discuss local nail disorders.

Methods:
This study is conducted based on publications and guidelines obtained by selective review in PubMed, including Cochrane reviews and meta-analyses.

Results:
Local nail disorders can occur due to infectious, inflammatory, congenital, traumatic causes. Infectious causes include acute paronychia, which leads to a characteristic yellow-green nail appearance, as well as onychomycosis, which includes proximal subungual onychomycosis, superficial white onychomycosis, and distal and lateral onychomycosis. Other infections include Herpes Simplex Virus (HSV) and syphilis, as well as Human Papilloma Virus (HPV), which can cause subungual and periungual verrucae. Traumatic nail disorders include subungual hemorrhage, which can occur to major trauma or repetitive minor trauma, and ingrown nails, which causes a painful, draining, and foul-smelling lesion, with hypertrophy of the nail fold. Onychophagia, or nail biting, can affect 20 to 30% of the general population. Malignancies can affect the nail unit, and they include squamous cell carcinomas, which is the second most common skin malignancy. Other malignancies are melanomas, which usually start as longitudinal melanonychia.

Conclusions:
Proper knowledge and examination of localized nail disorders is important for physicians and dermatologists. This will aid in treatment and referral processes to improve patient outcomes.

Key Words: Nails; Kuwait; Localized;

Funding Agency: None

Genetics

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Molecular Genetics Analysis of Nonsyndromic Orofacial Clefts (NSOFCs) in Kuwait

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Introduction:
Non-syndromic orofacial clefts (NSOFCs) are complex congenital abnormalities where the influence of environmental factors and their interaction with various genes involved in embryogenesis play a significant role in their development. This study aimed to investigate the genetic association of specific genetic variants at different developmental gene loci with the development of NSOFCs in Kuwait.

Methods:
Four genetic variants (rs7552, rs3758249, rs3821949, and rs3917201) at four developmental gene loci (FAM49A, FOXE1, MSX1, and TGFB3) were genotyped in a total of 240 DNA samples (patients (n = 114) and random controls (n = 126)) using Real-Time PCR employing the TaqMan® allele discrimination assay after they met the inclusion criteria. Genotype, allelic frequencies, and Hardy-Weinberg Equilibrium were determined for each variant in the cohort. The Pearson chi-square test was used to compare the genotype distribution of NSOFC patients and controls. Univariate and multivariate logistic regression was used to examine the associations of the four selected variants with the risk of developing NSOFCSs.

Results:
Based on the significant differences in genotype distribution between cases and controls, rs7552, rs3821949, and rs3917201 were found to have a positive association with NSOFCs. After adjusting for gender, the GG genotype of the rs7552 variant, the AG genotype of the rs3821949 variant, and the CC genotype of the rs3917201 variant were found to be associated with an approximately two-fold increased risk of NSOFC ($p < 0.05$). There were no associations ($p > 0.05$) between the FOXE1 rs3758249 variant and NSOFCs.

Conclusions:
This study reports significant findings on the possible role and small effect of FAM49A rs7552 (OR = 2.29; 95% CI: 1.3-4.035; P = 0.004), MSX1 rs3821949 (OR = 2.072; 95% CI: 1.215-3.534; P = 0.007), and TGFB3 rs3917201 (OR = 2.462; 95% CI: 1.259-4.814; P = 0.008) in the increased risk of NSOFCs. The results of this study provide a better understanding of the molecular genetics and role of developmental genes in the etiology of NSOFCs in Kuwait. Funding/Acknowledgements: The authors would like to convey thanks for the financial support of the Research Sector and the College of Graduate Studies at Kuwait University: Grant# YS 01/18. This research project was also conducted on samples collected from project KFAS-PR17-13DS-01, and we would like to express our great appreciation to the clinics and hospitals that contributed to the research by allowing us to collect blood samples (Al-Amiri Orofacial and Cleft Clinic and Al- Babtain Center for Plastic Surgery) under the supervision of Dr. Lateefa AlKharafi, Cleft and Craniofacial Unit, Ministry of Health, Kuwait.

Key Words: Non-syndromic orofacial clefts, Polymorphism.; Etiology; Genetics;

Funding Agency: YS 01/18

Genetics

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ADAT3 -Related Intellectual Disability: A Retrospective Review of the Clinical, Radiological and Molecular Findings of Cases in Kuwait

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Introduction:
ADAT3-related intellectual disability is a recently described autosomal recessive (AR) disease and a recognizable cause of AR intellectual disability in the Arabic Peninsula . It has been reported in about 52 individuals, mainly are from Saudi Arabia, but also has been reported in a Emirati family and in non-Bedouin Palestinian families, due to a founder variant c.382G>A; (p.Val128Met) in ADAT3 gene, encoding a protein that functions in tRNA editing. This disorder is characterized by developmental delay, cognitive impairment, abnormal brain structure, strabismus, microcephaly and failure to thrive. This study aims to review and analyze all cases detected in Kuwait with ADAT3 pathogenic variants and describe their clinical manifestations.

Methods:
A retrospective analysis was conducted on the data registry in Kuwait Medical Genetics Center for individuals with pathogenic variants in ADAT3 detected in Kuwait.

Results:
We report eleven Kuwaiti individuals (3 males; 8 females) from nine consanguineous families from several unrelated Bedouin and non-Bedouin tribes with the homozygous pathogenic Saudi founder variant in ADAT3 (NM_001329533.2:c.382G>A;p.Val128Met). Nine of them were diagnosed based on targeted molecular testing while two were diagnosed based on exome sequencing. All individuals were diagnosed during childhood (9-month till 10-year of age) except one adult person was diagnosed at age 21-year. All eleven subjects presented with global developmental delay and intellectual disability. Additional features were detected in our cohort which include abnormal tone (10/11), dysmorphic features (9/11), microcephaly (7/11), failure to thrive (6/11), strabismus (4/11), and seizures (2/11). Neuroimaging findings included brain atrophy, agenesis of corpus callosum, colpocephaly, arachnoid cyst and white matter changes.

Conclusions:
This is the first study describing ADAT3-related intellectual disability in Kuwaiti individuals from different unrelated tribes increasing the number of reported cases to 63. All individuals reported here were homozygous for the founder Saudi variant in ADAT3, thus extending the geographical region for this ancient founder mutation to include Kuwait as well. Our cohort shares the same phenotypic characteristics previously described for this disorder. Increase awareness of this recognizable cause of AR intellectual disability in the Arabian Peninsula among pediatricians would help in identifying more affected individuals and reduce the diagnostic odyssey.

Key Words: ADAT3; Microcephaly; Intellectual disability;

Funding Agency: None

Genetics

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A Minimal Risk Score for the Prediction of Type-2 Diabetes Mellitus Risk in the Kuwaiti Population

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Introduction:
Kuwait has the highest prevalence of type 2 diabetes mellitus (T2DM) and obesity in the region. Despite growing interest in T2DM research in the region, reports are very limited on the genetic factors associated with T2DM in Kuwait. Our objective was to investigate the association of global T2DM genetic risk factors and incidence of T2DM in Kuwait.

Methods:
Four variants were genotyped in four genes (FTO rs9939609, TCF7L2 rs7903146, VDR rs731236, LEPR rs1137101) for their association with T2DM risk in 203 Kuwaiti T2DM patients and 162 Kuwaiti healthy controls (HCs).

Results:
FTO rs9939609 allelic distribution did not differ between T2DM and HCs, whereas its genotype frequencies were significantly different between the two cohorts ($p = 0.0016$). FTO variant associated with T2DM risk in an autosomal recessive model ($p = 0.007$). Moreover, TCF7L2 rs7903146 allelic and genotypic frequencies were significantly different between T2DM and HCs ($p < 0.0001$ for both), rs7903146T allele associated with T2DM risk among Kuwaitis ($p < 0.0001$). We computed weighted (Effect size or β) and unweighted (Allele counting) genetic risk scores (GRSs) and found VDR and TCF7L2 variants combined had the best association with T2DM risk in both unweighted ($p = 0.006$) and weighted ($p=0.0002$) GRSs. Furthermore, weighted GRS that included FTO rs9939609, TCF7L2 rs7903146 and VDR rs731236 had the best positive predictive value (61.4%) and accuracy (58.5%).

Conclusions:
Our findings support the inclusion of indicators of environmental (Vitamin D, Obesity) and genetic risk factors for the construction of a predictive T2DM risk score. Further investigations of other T2DM genetic risk factors should refine and further support the clinical utility of a minimal T2DM GRS in predicting T2DM risk among Kuwaitis.

Key Words: Type 2 diabetes mellitus; Kuwait; Genetic risk score;

Funding Agency: None

Genetics

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Mitochondrial haplogroup R is protective against obesity in Arabs from Gulf region

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Introduction:
Gulf Cooperation Council countries are marked by high prevalence of obesity, which is a major risk factor for many metabolic disorders. In our previous reports, we assessed the contributions of mitochondrial DNA haplotypes and variants to the risk of obesity in Kuwaiti population and in Qatari population separately. The aim of the current study is to investigate contribution of mitochondrial DNA to the risk of obesity in a large representative sample set from the Gulf region.

Methods:
The study cohort comprised 1,112 subjects of which 348 were Kuwaiti and 764 were Qatari native individuals. The cohort was divided into obese and non-obese groups based on body mass index (BMI); individuals with BMI $\geq$ 30 kg/m2 were grouped as obese. 667 individuals formed the obese group and 445 formed the non-obese group. Mitochondrial DNA variants were extracted from whole exome sequencing data of the individuals from the cohort.

Results:
Mitochondrial haplogroup association results pointed out that the R haplogroup is protective against developing obesity (OR = 0.69; P-value = 0.045). Even after adjusting the multivariate logistic regression model for age and sex, the P-value remained significant (OR [95% CI] = 0.694 [0.482-0.997]; P-value = 0.048).

Conclusions:
The current study demonstrated that the previously identified association of mitochondrial R haplogroup with protection against obesity in Kuwait generalizes to Arabs from Gulf Cooperation Council countries. In addition, the literature-reported obesity-associated maternal haplogroup J for individuals in Qatar and L haplogroup for individuals in Kuwait maintained similar frequencies in the merged dataset of Kuwait and Qatar, however, they were not significant. Finally, we identified a number of mitochondrial DNA variants that were correlated positively and/or negatively with the risk of obesity within genes involved in cell energy production.

Key Words: Mitochondria; Obesity; Haplogroups;

Funding Agency: Kuwait Foundation for Advancement in Sciences for the institutional funding (RA-HM-2019-025).

Genetics

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Differentially methylated and expressed genes in familial type 1 diabetes

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Introduction:
There has recently been a growing interest in examining the role of epigenetic modifications, such as DNA methylation, in the etiology of type 1 diabetes (T1D). This study aimed to delineate differences in methylation patterns between T1D-affected and healthy individuals by examining the genome-wide methylation of individuals from three Arab families from Kuwait with T1D-affected mono-/dizygotic twins and non-twinned siblings.

Methods:
Bisulfite sequencing of DNA from the peripheral blood of affected and healthy individuals from each of the three families was performed. Methylation profiles of the affected individuals were compared to those of healthy individuals. The principal component analysis on methylation profiling based on base-pair resolution clustered the T1D-affected twins together family-wide.

Results:
The sites/regions that were differentially methylated between the T1D and healthy samples harbored 84 genes, of which 18 were known to be differentially methylated in T1D individuals compared to healthy individuals in publicly available gene expression data resources. We further validated two of the 18 genes-namely ICA1 and DRAM1 that were hypermethylated in T1D samples compared to healthy samples-for upregulation in T1D samples from an extended study cohort of familial T1D.

Conclusions:
The study confirmed that the ICA1 and DRAM1 genes are differentially expressed and methylated in T1D samples compared to healthy samples.

Key Words: Methylation; Type 1 diabetes; Genetics;

Funding Agency: Kuwait Foundation for Advancement in Sciences for the institutional funding

Genetics

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Novel homozygous ELOVL4 exonic deletion in two families with neuro-ichthyosis from same Saudi-Kuwaiti tribe

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Introduction:
Very long chain fatty acids (VLCFAs) are composed of more than 20 carbon atoms. They play an important role in the biosynthesis of cell membranes in the brain, skin and retina. VLCFAs are catalyzed by a multiprotein elongation system of enzymes referred as the ELOVL group, particularly ELOVL4. Up to date, three different Mendelian disorders have been associated with ELOVL4 variants, including autosomal dominant Stargardt-like disease 3, characterized by progressive visual loss, autosomal dominant spinocerebellar ataxia, and autosomal recessive congenital ichthyosis, spastic quadriplegia and mental retardation (ISQMR; MIM #614457). ISQMR is the rarest and until now, only seven subjects from five unrelated families with ISQMR are reported. Here we report four new patients with ISQMR from two unrelated families originated from the same large Kuwaiti-Saudi tribe and having the same 645bp homozygous exonic deletion in ELOVL4.

Methods:
Clinical exome sequencing was performed on probands of both families. QPCR was performed on all available members from both families.

Results:
Clinical exome sequencing detected a homozygous exonic deletion encompassing exon 1 of the ELOVL4 (NM_022726.3) in the probands of both families. QPCR confirmed the variant and segregation with the disease in both families. All four patients from the two families had failure to thrive, profound developmental delay, axial hypotonia, peripheral hypertonia, and dry erythematous skin similar to the seven previously reported cases described. Delayed myelination, corpus callosum and cerebral atrophy were seen in the brain MRIs of two cases.

Conclusions:
We report two families from the same Kuwaiti-Saudi tribe harboring a novel homozygous ELOVL4 exonic deletion suggesting that this is a founder variant in the tribe. This specific ELOVL4 exon 1 deletion should be suspected in patients with neuro-ichthyosis from same tribe. Furthermore, our cases expand the phenotype and genotype of the disorder, thus adding global effort of understanding rare diseases.

Key Words: ELOVL4; KUWAIT; Neuroichthyosis;

Funding Agency: None

Medicine

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Association of Anemia with In-hospital Outcomes in STEMI Patients at KAMC

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Introduction:
ST-elevation myocardial infarction (STEMI) is considered a major cause of mortality worldwide. Anemia is observed to be more frequent in STEMI patients. However, it was not included in any risk stratification tools. The aim of the study is to assess association of anemia with in-hospital complications, length of stay, mortality rate in STEMI patients.

Methods:
This retrospective cohort study included consecutive STEMI patients in King Abdullah Medical City (KAMC) from 2019 to 2022. The data was extracted from the hospital information system into SPSS. Anemia was defined as hemoglobin less than 13 mg/dL in men or less than 12 mg/dL in women. Using a multiple logistic regression model, we studied the association of anemia (as a predictor) with a composite of in-hospital complications: heart failure, cardiogenic shock, cardiac arrest, further PCI or CABAG, LV thrombus, major bleeding, or death (as an outcome).

Results:
Out of 611 included STEMI patients, 205 (33.8%) were anemic at admission. The anemic cohort was older (58.3 vs. 53.2 years, P<0.001), and had a higher incidence of hypertension (57.6% vs. 45.6%, P=0.005). After adjustment for all variables using multivariate analysis, in-hospital complications rate and length of stay in anemic group were higher (31.7% vs. 21.2%; P<0.005)(10.9 vs. 8.1; P=0.003). There was no significant change in mortality rate between anemic and non anemic groups.

Conclusions:
Anemia is an independent predictor of in-hospital complications and length of stay in STEMI patients. However, there was no association between mortality rate and anemia.

Key Words: STEMI; Anemia; In hospital complications ;

Funding Agency: None

Medicine

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Artificial Intelligence for Adenoma and Polyp Detection during Colonoscopy: A Pilot Randomized-Controlled Trial

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Introduction:
Colorectal cancer (CRC) is the third leading cause of cancer death in Kuwait. Colonoscopy screening is performed to detect and remove precancerous lesions. The effectiveness of colonoscopy screening to prevent CRC is dependent on high adenoma detection rate (ADR). Computer-aided detection (CADe) can identify and characterize polyps in real-time and differentiate benign from neoplastic polyps. Studies performed in Western and Asian countries showed improved ADR with CADe, but no such study has been performed in the Middle East.

Methods:
This was a pilot randomized-controlled trial conducted at Mubarak Alkabeer hospital. Patients aged 40-80 years presenting for outpatient diagnostic or screening colonoscopy were enrolled. We excluded patients with a history of inflammatory bowel disease, familial polyposis syndrome, colon resection and poor bowel preparation. Patients were randomly assigned to either high-definition (HD) colonoscopy (standard of care) or HD-colonoscopy with CADe system. The primary outcome was ADR. The secondary outcomes included polyp detection rate (PDR), adenoma-per-colonoscopy (APC), polyp-per-colonoscopy (PPC) and accuracy of polyp characterization.

Results:
From July 1st to October 31st 2022, 64 patients were included and allocated to HD-colonoscopy (n=32) and CADe-group (n=32). The mean age was 52.2 years (SD 7.9) and males represented 46.9% of the cohort. The commonest indication for colonoscopy was screening (45.3%) followed by evaluation of abdominal pain (26.6%) and rectal bleeding (12.5%). ADR (primary outcome) was significantly higher in the CADe group compared to HD-colonoscopy group (53.1% vs. 28.1%, p=0.04). The PDR (secondary outcomes) was significantly higher in the CADe group (87.5% vs. 53.1%, p=0.003). Other secondary outcomes including APC, PPC and polyp characterization were similar in both groups. Withdrawal time was similar in both groups (CADe= 9.3 minutes vs. WL-colonoscopy= 8.7 minutes, p=0.3). No adverse events were reported.

Conclusions:
In this pilot RCT, CADe system was found to significantly improve adenoma and polyp detection among patients undergoing screening and diagnostic colonoscopy in Kuwait compared to HD-colonoscopy without prolonging the procedure. A larger multicenter study is planned to confirm these findings before routine use of AI can be recommended in routine clinical practice.

Key Words: Colon cancer; Artificial intelligence; Colonoscopy;

Funding Agency: None

Medicine

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TC-325 (HEMOSPRAY™) Alone is More Efficacious than Standard Endoscopic Hemostatic Modalities when Managing Patients Presenting with Malignant Gastrointestinal Bleeding: A Systematic Review and Meta-analysis of Randomized Controlled Studies

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Introduction:
Background and aims: Novel topical hemostatic agents have shown promising results in treating patients with non-variceal gastrointestinal bleeding. However, data are limited as to their role, especially in malignant bleeding. The aim of this study was to perform a highly comprehensive systematic review assessing the effectiveness of topical hemostatic agents in malignant gastrointestinal bleeding in different clinical settings.

Methods:
We performed a literature search of OVID MEDLINE, EMBASE, and ISI Web of Knowledge databases through November 2022. Keywords included 1) hemostatic agent/powder (including Hemospray, TC-325, Endoclot, Purastat, Nanopowder) and 2) gastrointestinal bleeding. Randomized controlled trials (RCT) assessing the efficacy of topical hemostatic agents in malignant bleeding were included. Main outcomes were immediate hemostasis and overall rebleeding.

Results:
A total of 1158 citations were identified and 3 RCTs with a total of 185 patients were included in the analysis; all assessed TC-325 (Hemospray™). TC-325 achieved immediate hemostasis more often than standard endoscopic modalities in the 2 studies with available data (n=126) (RR 1.54 (1.13; 2.09)). Although rebleeding risk was not significantly different overall in both groups (RR 0.44 (0.08; 2.39), high heterogeneity (12=78%)), this important outcome was significantly improved by TC-325 versus control interventions when excluding one RCT that included controls undergoing no immediate endoscopic treatment ((RR=0.27 (0.06; 0.77)). All other outcomes did not differ significantly between the two groups: overall mortality (RR=1.42 (0.80; 2.39)); bleeding related mortality RR=0.10 (0.01; 1.87); and technical success RR=1.00 (0.97; 1.03). Results did not differ when stratifying the analysis according to an upper or lower malignant GI bleeding source.

Conclusions:
TC-325 is efficacious in the initial management of patients presenting with malignant GI bleeding, resulting in improvements in clinically important outcomes when compared to conventional endoscopic modalities. Additional RCTs are needed to confirm these findings owing to the limited available high-quality evidence.

Key Words: Gastrointestinal bleeding; Gastrointestinal malignancy; Topical hemostatic agents;

Funding Agency: None

Medicine

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Fraction B From Catfish Skin Secretions Causes Recovery of Diabetic Cardiac Complications by Modulating the Apoptosis and Inflammation Pathways in Rats

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Introduction:
Diabetes Mellitus (DM) causes cardiovascular complications that lead to heart damage. DM-induced heart damage is more resistant to treatment than non-diabetic cardiovascular complications. There is a need for more effective therapies based on an increased understanding of underlying mechanisms of DM-induced cardiovascular complications. This study investigated the possible positive outcomes of treating diabetic hearts in STZ-induced diabetes rat model utilizing catfish skin derived Fraction B (FB).

Methods:
This study aimed to unravel the effects of FB on the heart of STZ-induced diabetic rats by assessing histopathological changes, cardiac enzymes, and biochemical markers. Male SD rats were employed into four groups: Normal control (NC), Normal control+FB (NC+FB), Diabetic control (DC), and Diabetic+FB (D+FB). Diabetes in rats was treated with a single intraperitoneal (IP) injection of STZ. Rats with blood glucose higher than 15 mmol/ml were considered diabetic and treated with once-a-day IP injection of 4.5 mg FB/kg for ten weeks. Multiple groups of data were compared using ANOVA, followed by Bonferroni comparisons and LSD tests. The SPSS Statistical Package was used and statistical significance was defined as $P>0.05$.

Results:
FB significantly ($p<0.05$) reduced blood glucose levels and increased rats' weight. The DC+FB significantly reduced serum CK and LDH concentrations compared to DC group. Light microscopic assessment showed remarkable recovery of heart tissue in D+FB compared to DC group. The EM ultrastructural features of DC+FB heart tissues showed normal appearance of Z discs and well-defined mitochondria compared to DC group. Biochemical and immunohistochemical analysis revealed that FB significantly ($p<0.05$) improved heart protein level. The positive effects of FB were associated with modulating apoptotic pathway and decreasing inflammatory markers using anti-CRP, anti-Gal-3, anti-GDF15, anti-Bax, anti-Bcl-2, anti-CASP3, and anti-Cytochrome c.

Conclusions:
Study proved for the first time the therapeutic effects of FB treatment on DM–induced heart damage and explored its possible curative mechanisms in the diabetic heart.

Acknowledgment: Study was supported by College of Graduate Studies and Kuwait University Research Administration Grant no. YM06/21. Rats were obtained from Kuwait University College of Medicine's Animal Resources Center after getting health sciences research ethics committee approval of animal studies on 18 of Feb 2021.

Key Words: Diabetes; Cardiovascular complications; FB;

Funding Agency: The study was supported by Collage of Graduate Studies, Kuwait University and research sector grant no. YM06/21

Medicine

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The feasibility and safety of Endoscopic Ultrasound (EUS)-guided liver biopsy to diagnose parenchymal liver disease: A retrospective cohort study

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Introduction:
Liver biopsy plays an essential role in the diagnosis and management of liver diseases. Conventionally, percutaneous and transjugular approaches have been used to obtain liver biopsies. Despite high diagnostic yield, these techniques are commonly associated with post-procedure pain and occasionally result in serious adverse events. Recently, endoscopic ultrasound-guided liver biopsy (EUS-LB) has emerged as a more convenient and safer alternative. Despite the potential advantages of using EUS-LB, limited data exists for this technique mostly from specialized tertiary-care North American and European centers. The aim of this study is to evaluate the histological yield and safety of EUS-LB in Kuwait.

Methods:
This was a retrospective study conducted at Mubarak Al-Kabeer hospital for patients who underwent EUS-LB to investigate parenchymal liver disease. Patients' medical records were reviewed to determine baseline information. The histological characteristics were obtained from the final pathology report. The primary outcome was histological adequacy which was defined as adequate tissue for histological diagnosis. Secondary outcome was the safety of EUS-guided liver biopsy. Factors associated with increased histological adequacy were explored.

Results:
From July 1st 2019 to November 30th 2022, 31 patients underwent EUS-LB and were included in the analysis. The mean age of patients was 45.1 years (SD 15.7) and 15 (48.4%) were males. Conscious sedation was used in 90.8% of cases. The most used needle was 19G fine aspiration needle (FNA) (83.9%) with a median of 4 passes/procedure (range 2-5) using no suction technique (80.7%). On average, 11.7 (SD 11.6) portal tracts were obtained per procedure with aggregate length of 7.2cm (SD 4.9). The overall histological adequacy was 87.1% and the most common diagnoses being non-alcoholic steatohepatitis (NASH) (22.7%), drug-induced liver injury (DILI) (19.4%) and autoimmune hepatitis (9.7%). Adverse events occurred in 1 patient (3.2%), namely bleeding requiring transfusion. Self-limited pain occurred in 6.4%. No procedure-related mortality was reported. Needle type, gauge and suction techniques did not affect the diagnostic adequacy.

Conclusions:
With a histological diagnosis rate of 87.1% and adverse event rate of 3.2%, EUS-LB appears to be both an effective and safe technique for liver biopsy. Future comparative studies are needed to compare the efficacy and safety of this technique with conventional techniques.

Key Words: Endoscopic ultrasound; Liver biopsy; Liver disease;

Funding Agency: None

Medicine

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Diagnostic Yield and Clinical Impact of Capsule Endoscopy in Diagnosing Small Bowel Disease: A Single-Center Experience from Kuwait

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Introduction:
Capsule endoscopy (CE) is an established non-invasive diagnostic modality for a variety of small bowel pathologies and has a significant position in altering the treatment course. The diagnostic yield of CE in the published literature varies widely between 45-75%. Furthermore, it is unclear if any patient-related factors predict higher diagnostic yield. The aim of this study is to describe the Kuwaiti experience with CE in diagnosing small bowel pathology and describe the diagnostic yield as well as any predictive factors for identifying significant pathology on CE.

Methods:
This was a retrospective study conducted at Mubarak Al-Kabeer hospital in Kuwait for patients who underwent CE between October 2013 to February 2022. All patients underwent upper and lower endoscopy prior to referral to CE. Patients' medical records were reviewed to determine CE indications, results, complications of CE. The significance of the CE findings was classified according to the Saurin system. A multivariate regression analysis was performed to characterize baseline predictors for identifying significant pathology on CE.

Results:
Overall, 210 patients underwent CE and were included in the analysis. The mean age was 57.9 years (SD 18.5), and 129 (61.4%) were males. The most common indication for CE was obscure occult GI bleed (75.7%), obscure overt GI bleed (28.6%) and investigating GI symptoms (7.6%). Adequate bowel preparation was achieved in most patients (88.1%), imaging of the entire small bowel was achieved in 194 patients (92.4%) and no adverse events were recorded. The most common findings were vascular lesions in small bowel (40.0%), small bowel ulcer (22.9%), and erosions (22.9). The results of CE altered the treatment in 147 (70.0%) patients by identifying high-risk lesions that required further medical, endoscopic or surgical interventions. On multivariate analysis (adjusted for age and sex), melena at baseline was significantly associated with increased odd of identifying high-risk lesion (Saurin class P2) (adjusted OR 2.1, 95%CI 1.03-4.30, p=0.04).

Conclusions:
Capsule endoscopy is an effective and safe tool for investigating small bowel pathology with its findings altering the management of 70% of carefully selected patients undergoing such test. Melena at baseline is the strongest predictor at identifying high-risk lesion and these patients should be prioritized for CE.

Key Words: Capsule endoscopy; Gastrointestinal bleeding; Small bowel;

Funding Agency: None

Medicine

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Socio-Economic and Ethnic differences and Acute Kidney Injury Management and Outcome

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Introduction:
Kuwait has a large expatriate community with a limited access public ministry of health care compared to Kuwaitis. We examined differences in demographics, management, and outcomes between Kuwaitis and non-Kuwaitis with acute kidney injury (AKI)

Methods:
Prospective observational multi-center study of clinical characteristics, and outcomes at 30 days for all nephrology consultations for AKI from January 1 to June 30, 2021

Results:
Total AKI referrals were 3749 (males: 59%; mean age: 63 years). Patients with baseline eGFR < 60 were older than patients with eGFR of ≥ 60, had lower mean initial hemoglobin (Hgb) and higher diabetes, hypertension, and cardiac disease. Non-Kuwaitis had statistically significant higher COVID-19 related AKI (9% vs 7% of AKI in Kuwaitis were COVID-19 related). Expatriates represent two thirds of Kuwait's total population; however, they accounted for 43% of AKI cases. They were youngerthan Kuwaitis (58 vs 67), had more male involvement (72% were men vs 50% men in Kuwaitis), had higher baseline eGFR (73 mL/min vs 62 mL/min for Kuwaitis), and higher baseline Hgb (10.8g/dL vs 10.3g/dL). More hospital acquired AKI than community acquired AKI in expatriates (54% vs 46%), and more AKI in the summer than the winter (62% in summer vs 38% in winter), but no seasonal difference for Kuwaitis. No difference in mechanical ventilation Significantly higher utilization of dialysis for expatriates (35% vs 32% for Kuwaitis). However, no difference at 30 days in percentage of patients still on dialysis. At 30 days, 41% of the total cohort died with significantly higher death rates in Kuwaitis (39% of expatriates vs 43% of Kuwaitis died). Kuwaitis who died were older (69 years vs 58 years for expatriates). Mean eGFR at 30 days for those who survived and off dialysis was 49 mL/min, and significantly higher for expatriates (54 mL/min vs 46 mL/min for Kuwaitis.

Conclusions:
Younger with higher baseline eGFR expatriates accounted for 43% of AKI cases. However, they had higher rates of AKI in Summer (probably due to lack of air conditioning where they work or live), higher COVID-19 related AKI (probably due to delayed vaccination compared to Kuwaitis) and higher need for dialysis. However, at 30 days, they had lower mortality, similar kidney recovery rates and higher final eGFR

Key Words: Acute Kidney Injury; Dialysis; Mortality;

Funding Agency: None

Medicine

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TGF-β1 C (+869) T, codon 10 gene polymorphism significantly associated with rates of novel coronavirus disease 2019 (SARS-CoV2) in kidney transplanted patients in Kuwait

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Introduction:
Coronavirus disease 2019 (COVID-19), which began in Wuhan, China, in December 2019, has caused a large global pandemic and poses a serious threat to public health. SARS-CoV-2 has Globally. As of 8 November 2022, a total of 12,885,748,541 vaccine doses have been administered. Some COVID-19 patients experience sudden and rapid deterioration with the onset of fatal cytokine storm syndrome (CSS), which has increased interest in CSS's mechanisms, diagnosis, and therapy. Although the prototypic concept of CSS was first proposed 116 years ago, we have only begun to study and understand CSS less than 30 years. A growing body of clinical data suggests that CSS Th1, Th2, Th3, and macrophage-origin cytokines impact CSS.
Aim: We aimed to study the impact of cytokine gene polymorphisms in the mechanisms of CSS and the progression of COVID-19 among kidney transplant recipients.

Methods:
We screened 309 patients who had undergone kidney transplantation in the Hamad Al Essa transplant center. During the period of February 2020 to February 2022, sixty-four (20.7 %) of patients developed COVID-19 infections. Their blood samples were screened for the key Th1, Th2, Th3, and macrophage cytokines gene polymorphisms.

Results:
Our results showed that except TGF-β C (+869) T, codon ten but neither of interferon -μ T (+874) A, IL-6 G (-174) C, IL-4C (-490) T showed to be significantly associated with the progression of COVID-19 and CSS mechanism, p=0.0004).

Conclusions:
The latter finding can be a profoundly important factor in the initiation of CSS and the progress of Covid-19.

Key Words: Kidney transplantation; SARS-CoV2; Polymorphism;

Funding Agency: None

Medicine

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The outcome of ICU COVID-19 Positive Kidney Transplants compared to non-transplant patients: single center experience

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Hamed Aleesa OTC

Introduction:
COVID-19 is an ongoing pandemic that has altered our lives, especially that of kidney transplant recipients (KTR). We aimed to compare the COVID-19-positive KTR with non-transplant-positive cases that were managed in the intensive care unit (ICU) during the pandemic.

Methods:
Out of 2000 KTRs that was followed up in Hamed Al-Essa Organ transplant center in Kuwait, we collected data from all COVID-19-positive KTRs (group 1, n=79) till the end of January 2021. Clinical features, management details, and both patient and renal outcomes were reported and compared with (group 2, n=445) non-transplant cases admitted during the same period in the ICU during the pandemic.

Results:
Most of the cases were males (74% vs.73%), aged 51.7±16 and 60.8± 14 years, respectively. Both groups were comparable regarding patients with diabetes mellitus (50.6 vs. 55.2%), hypertension (62% vs. 57.1%), ischemic heart disease (20% vs. 19.8%), and chronic kidney disease (1.3% vs. 1.6%). Fever, cough, body aches, and gastrointestinal symptoms were the most frequent presentation among KTR. Meanwhile, complicated cases with sepsis(qSOFA >2), volume depletion, shock, and ARDS predominated among the non-transplant group ($p<0.05$). Therapeutic management included anticoagulation (81 %) in both groups, while steroids and tocilizumab were used frequently among the non-transplant group (8.7%). Within 30 days of follow-up, in group 2, we found that acute kidney injury, respiratory failure requiring mechanical ventilation, and mortality rate were significantly higher.

Conclusions:
We reported better outcomes of ICU-admitted COVID-19-positive KTR compared with non-transplant patients, possibly due to younger age-modified immunosuppression.

Key Words: COVID-19; Renal transplant; Outcome;

Funding Agency: None

Medicine

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Increased the risk of mortality when acute kidney injury (AKI) developed among COVID-19 positive patients: single center experience.

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Hamed Alessa OTC

Introduction:
Despite the lungs being the major targets of COVID-19, other organs as the kidneys are affected.
Aim: We aimed to study the prevalence of acute kidney injury (AKI) among positive COVID-19 cases that were managed in the intensive care unit (ICU) in a single isolation hospital during the pandemic, and to explore its impact on patient outcome.

Methods:
This retrospective study included 616 patients with COVID-19 who were managed, from February to December 2020. Of the 616 patients, 40.2% developed AKI (group 1, n=248) and were compared with the patients without AKI (group 2, n=368). AKI was categorized according to KDIGO criteria.

Results:
Most of the cases in the 2 groups were males, aged (60.8± 14 vs. 51.7± 16 years) respectively. Some factors were significantly predominating among group 1 as diabetes mellitus (63.7 vs. 40.5%), hypertension (74.2% vs. 40.5%), ischemic heart disease (26.2% vs. 12.5%) ($p<0.05$). Sepsis, volume depletion, shock, arrhythmias, and ARDS predominated among the AKI group ($P<0.05$). The number of cases that were managed by therapeutic anticoagulation was significantly higher in AKI patients (89.9 % vs. 51.9%); also cases who received supportive vasopressors and convalescent plasma transfusion, as well as steroids, were significantly higher in the same group. We found that acute respiratory failure requiring mechanical ventilation was significant among the AKI group (66.8% vs. 29.4%), and the overall mortality rate was significantly higher in the same group (62.5%. vs. 32.8%).

Conclusions:
The prevalence of AKI in patients with COVID-19 was 40.2%, and it was associated with poor prognosis among ICU covid-19 positive cases.

Key Words: COVID-19; Mortality rsik; AKI;

Funding Agency: None

Medicine

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(PCSK-9) inhibition among kidney transplant patients with high cardiovascular risk

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Hamed Alessa OTC

Introduction:
Proprotein convertase subtilisin/Kexin type A(PCSK-9) inhibitors have not been evaluated among kidney transplant recipients (KTR) despite its favorable cardiovascular profile.
Aim of the study: To evaluate the safety and efficacy of evolocumab in reducing lipids and cardiovascular events among risky KTR.

Methods:
One hundred ninety-five KTR - who were followed up in Hamed Al-Essa organ transplant center with high cardiovascular risk score (>20)-were enrolled in this prospective randomized controlled study between June 2017 and June 2018. Patients who received statin and evolocumab (140mg/ 2 weeks, group1, n=97) while those maintained on statin alone comprised group 2(n=98). After 24 months, they were followed up clinically and by laboratory investigations.

Results:
The two groups had comparable demographics. Before enrollment in the study, we observed a higher prevalence of NODAT in group 2 and more smokers in group 1($p<0.05$). Basal graft function was significantly higher in group 1, while the type of immunosuppression was equivalent in both groups($p>0.05$). We found no significant differences between the two groups concerning cardiovascular events, and both graft and patient outcomes ($p>0.05$). Despite the comparable triglycerides levels, we found significantly higher basal cholesterol in group 1(5.5 vs. 4.7, $p<0.001$), which came down significantly in the same group after three months and thereafter ($p=0.031$) compared to group 2 and basal values ($p<0.001$). We reported 2 cases of acute MI and one atrial fibrillation in group2.

Conclusions:
Evolocumab is a promising lipid-lowering agent among risky KTR. Earlier cholesterol reduction was observed in group 1 without significant positive cardiovascular impact.

Key Words: Hyperlipidemia,; Renal transplant; Outcome;

Funding Agency: None

Medicine

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Study the Effect of Sodium-Glucose Cotransporter-2 Inhibition Versus Dipeptidyl peptidase-4 Inhibition in Diabetic Kidney Transplant Recipients.

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Hamed ALeesa OTC

Introduction:
Diabetes is the most common cause of chronic kidney disease (CKD) globally. The renal and cardio-vascular benefits of the new anti-diabetic agents are not assessed comprehensively.
Aim of the study:
We aimed to evaluate the short term renal and cardio-protective effects of Sodium-Glucose Cotransporter-2 Inhibition (SGLT2i) Vs. Dipeptidyl peptidase-4 Inhibition (DPP4i) among diabetic kidney transplant recipients.

Methods:
In this observational trial, 222 diabetic kidney transplants recipients (NODAT or type 2 diabetes) were enrolled and were categorized into two groups. Group 1 (n=99) received SGLT2i while group 2(n=123) received DPP4i as an add on antidiabetic medications. All patients in the two groups were followed up for 12 months.This study was approved by MOH ethical committee (1351/2020). Appropriate statistical tests used for categorical and numerical variables.

Results:
Most patients in the two groups (1&2) were men (59.6 vs. 61.7%, p=0.73) in their middle age (58.5±11.9 vs. 54.4±12.9, p=0.016) years respectively. The two groups were matched regarding their demographics especially the type of donor, type of immunosuppression (induction or maintenance), number of cardiovascular events before enrollment in the study and the number of patients who were maintained on ACEi or ARB($p>0.05$). The minority of patients were smokers (12.9 vs.8.7%), and chronic glomerulonephritis was the original disease in 36.4 vs. 35.4% in the two groups, respectively. Most of the enrolled patients (72.8 vs. 78.6%) underwent hemodialysis pre-transplant. During follow up period, patients in both groups were comparable regarding mean blood pressure, body weight, HbA1C, 24-hour urine protein, and graft function (represented by the mean serum creatinine) at different time intervals and compared to base line values($p>0.05$). However, the mean HbA1C was significantly higher in group 1 during the whole follow up period of the study ($p<0.05$) but it did not drop significantly compared to baseline values ($p>0.05$). We did not report any macroangiopathic events (cerebral stroke, acute myocardial infection, or peripheral arterial disease) in the two groups during the study.

Conclusions:
Both GLT2i and DPP-4 I are comparable regarding short term renal and cardio-vascular protection among diabetic kidney transplant recipients.

Key Words: DM; Renal protection; Kidney transplant;

Funding Agency: None

Medicine, Nutrition, Health

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Does four-week consecutive, dawn-to-sunset intermittent fasting during Ramadan affect cardiometabolic risk factors in healthy adults? A systematic review, meta-analysis, and meta-regression

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Introduction:
Aims: This study aimed to evaluate the effects of Ramadan diurnal intermittent fasting (RDIF; 29-30 days) on cardiometabolic risk factors (CMRF) in healthy adults, and examine the effect of various cofactors on the outcomes using sub-group meta-regression.

Methods:
Data synthesis: We conducted a systematic review and meta-analysis to measure the effect sizes of changes in CMRF in healthy adult Muslims observing RDIF. Ten scientific databases (EBSCOhost, CINAHL, Cochrane, EMBASE, PubMed/MEDLINE, Scopus, Google Scholar, ProQuest Medical, ScienceDirect, and Web of Science) were searched from the date of inception (1950) to the end of November 2020. The CMRF searched and analyzed were total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), diastolic blood pressure (DBP), and heart rate (HR). We identified 91 studies (4431 adults aged 18-85 years) conducted between 1982 and 2020 in 23 countries distributed over four continents. RDIF-induced effect sizes for CMRF were: TC (no. of studies K = 77, number of subjects N = 3705, Hedge's g = -0.092, 95% confidence interval (CI): -0.168, 0.016); TG (K = 74, N = 3591, Hedge's g = -0.127, 95% CI: -0.203, 0.051); HDL-C (K = 68, N = 3528, Hedge's g = 0.138, 95% CI: 0.051, 0.224); LDL-C (K = 65, N = 3354, Hedge's g = -0.115, 95% CI: -0.197, -0.034); VLDL-C (K = 13, N = 648, Hedge's g = -0.252, 95% CI: -0.431, 0.073), DBP (K = 32, N = 1716, Hedge's g = -0.255, 95% CI: -0.363, 0.147), and HR (K = 12, N = 674, Hedge's g = -0.082, 95% CI: -0.300, 0.136).

Results:
Meta-regression revealed that the age of fasting people was a significant moderator of changes in both HDL-C (P = 0.02) and VLDL-C (P = 0.01). Male sex was the only significant moderator of changes in LDL-C (P = 0.055). Fasting time duration was the only significant moderator of HDL-C (P = 0.001) at the end of Ramadan.

Conclusions:
Conclusions: RDIF positively impacts CMRF, which may confer short-term transient protection against cardiovascular disease among healthy people.

Key Words: Intermettent fasting; Cardiometabolic ; Nutrition;

Funding Agency: None

Microbiology and Immunology

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Cytokine Responses of Peripheral Blood Mononuclear Cells and Neutrophils from Individuals Vaccinated with Anti-SARS-CoV-2 Vaccines in Kuwait.

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Introduction:
SARS-CoV-2 vaccines (Pfizer and AstraZeneca) are protective against SARS-CoV-2 infection, yet cytokine production patterns after vaccination are incompletely understood. The aim of this study was to investigate cytokine production by peripheral blood mononuclear cells (PBMC) and neutrophils elicited by Pfizer and AstraZeneca vaccine.

Methods:
PBMC and neutrophils were isolated using commercial separation media. Cell culture supernatants from PHA-stimulated, and unstimulated neutrophils and PBMC from 50 vaccinated individuals and 50 unimmunized healthy controls were evaluated for levels of the granulocyte-macrophage colony-stimulating factor (GM-CSF), Interferon (IFN)-gamma (γ) and IFN- alpha (α), interleukin (IL)-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12, IL-17A and tumor necrosis factor (TNF)-α using anti-cytokine antibody MACSPlex capture beads.

Results:
Levels of GM-CSF, IL-5, IL-12, and IL-17A secreted by PBMC were significantly higher within 2 months after vaccination ($p < 0.0028$, <0.0001, <0.0001, <0.01, respectively), whereas INF-γ and IL-4 were significantly secreted 3-6 months after immunization ($p < 0.0063$, <0.024, respectively). The Pfizer vaccine had a significant effect on increasing the production of GM-CSF ($p < 0.0001$), IFN-γ ($p < 0.0016$), and IL-5 ($p < 0.0001$) by PBMC. On the other hand, the AstraZeneca vaccine significantly boosted the secretion of IFN-α ($p < 0.037$), IL-12, and IL-17A ($p < 0.0001$, $p < 0.0033$, respectively) by PBMC.

Conclusions:
A significant difference between the control and vaccinated groups was observed for some of the cytokines released by the neutrophils for GM-CSF, IFN-γ, IL-2, IL-6, IL-9, IL-10, IL17A, and TNF-α ($p < 0.05$). Cytokine production profiles and ratios of Th1: Th2 cytokines indicate that Pfizer and AstraZeneca vaccines significantly trigger cytokine production by PBMC and neutrophils.

Key Words: SARS-CoV-2; Cytokines; Pfizer AstraZeneca;

Funding Agency: College of graduate studies and Research Sector, Kuwait University. Project No. YM02/22

Microbiology and Immunology

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Profiling Approach for Potable-Water Isolated Pseudomonas aeruginosa Strains

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Introduction:
P. aeruginosa is a medically, ecologically, and scientifically important Gram-negative bacterium. The ability to analyse the highly complex community of P. aeruginosa can expedite the source tracking, monitoring and elimination of this pathogen. In fact, the diverse phenotypes/genotypes of P. aeruginosa result in the ubiquity of this bacterium which is the source of ambiguity in profiling this robust bacterium. The feasibility of using preliminary metabolomic data combined with phenotypic characteristics to profile fifty P. aeruginosa strains isolated from potable water samples collected from Kuwait City was investigated.

Methods:
Potable water samples were collected aseptically from six points in Kuwait City. Microbial contents of samples were analysed by standard filtration and subsequent plating on suitable media. Pure bacterial cultures were identified based on standard biochemical tests and subjected to standard biochemical analyses where change of colour or identification of end products were used to confirm presence/absence of enzymes/pathways in tested bacteria. In addition, pathogenic factors such as biofilm formation, hemolysin/lipase production, and resistance to antibiotics were determined using standard methods.

Results:
High significantly similar results of tests in particular those associated with carbohydrate metabolism and AST were demonstrated. However, analysis of protein associated tests demonstrated higher resolution and provided better profiling data. In addition, using rates of enzyme activity such as rate of hemolysin rather than traditional binomial presence/absence approaches provided better data for strains profiling. Based on total biochemical test analyses, strains of isolated P. aeruginosa were grouped into three phylotypes. However, based on protein associated tests combined with phenotypic analysis, six groups of P. aeruginosa were depicted.

Conclusions:
The combined phenotypic and biochemical tests analysis showed higher resolution for profiling strains of P. aeruginosa. Protein associated tests showed higher applicability for bacterial profiling compared to carbohydrates associated test

Key Words: Pseudomonas aeruginosa, Potable water; metabolism; Profiling;

Funding Agency: None

Microbiology and Immunology

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Trends in Device-Associated Hospital-Acquired Infections in a Combined Medical-Surgical Intensive Care Unit of a Secondary-Care Facility - Kuwait, 2017-2021

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Introduction:
Background: Around 5-10% of hospitalized patients develop hospital-acquired infections (HAIs). In the ICU, 25.6% of all HAIs are associated with the use of an invasive device such as central line-associated bloodstream infections (CLABSI), ventilator-associated events (VAE), & catheter-associated urinary tract infections (CAUTI). The objective of this study was to conduct surveillance for HAIs in the adult ICU and determine DA-HAI rates due to multidrug-resistant (MDR) pathogens from 2017 through 2021.

Methods:
Following the CDC definitions of HAI, relevant data was recorded on Kuwait National Nosocomial Infections Surveillance (KNNIS) forms for patients in ICU from 2017-2021. Overall patient infection rate was calculated as the number of all infections per 100 patients at risk, overall patient day (PD) rate as the number of all infections per 1000 PD and DA infection rates as the number of infections per 1000 device days (DD).

Results:
For an aggregate of 17,859 PD, there were 13,072 central line (CL)-days, 12,843 mechanical ventilator (MV)-days, and 17,356 urinary catheter (UC)-days. Total number of PD declined from 4292 (2017) to 2769 (2021), reducing overall infection rate from 12.78 to 7.5 per 1000 PD. CLABSI rates reduced from 4.05 to 2.83, CAUTI rates from 2.45 to 1.3, and VAE rates from 5.03 to 3.02 per 1000 DD. CLABSI was the most common DA-HAI (45.6%), followed by VAE (33.8%), and CAUTI (20.6%) with average device utilization ratio (DUR) being 3.6, 3.4, 4.5 for CL, MV, and UC, respectively. Common MDR pathogens included A. baumanii (42.4%), K. pneumoniae (30.3%), and P. aeruginosa (9.1%) among all resistant pathogens causing DA-HAIs.

Conclusions:
An unsatisfactory surveillance data outcome will put in effect immediate measures for infection control and revision of antimicrobial stewardship policies and programs. This study showed a decline in DA-HAI and DUR rates during 2020-2021, which coincided with COVID period when majority of the patients were being admitted to special wards instead of ICU. To reduce the rates of HAIs, stringent infection control practices and comprehensive education are required.

Key Words: Device-associated infections; Intensive care unit; Infection control;

Funding Agency: None

Microbiology and Immunology

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Application of Next-Generation Sequencing for Detection of Drug Resistance Mutations in Patients Infected with Chronic Viral Hepatitis B and C Diseases

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Introduction:
Next Generation Sequencing (NGS) is a high-throughput platform, which has been recently introduced into diagnostic virology laboratories. It is efficient in characterizing viral diversity and detecting minor mutants that constitute as little as 1% of the total viral population. NGS can perform analysis from multiple amplified genomic regions, characterize viral genetic diversity, and detect minor strains that cannot be detected by the Sanger sequencing method. Our objective was to optimize NGS for the detection of HBV and HCV genotypes and drug-resistance mutations especially low-abundance variants circulating in Kuwait.

Methods:
A total of 40 plasma samples (20 from HBV-infected and 20 from HCV- infected patients) were received for routine viral load testing from chronic hepatitis patients attending the Gastroenterology Clinic at Mubarak Al Kabeer Hospital, Kuwait. After viral load testing, the remaining samples were subjected to the NGS workflow, which included the following steps: (i) for HCV, RT-PCR-nested amplification for all HCV subtypes (1-6) based on NS3, NS5A, and NS5B-A genomic regions. (ii) for HBV, workflow depended on amplifying polymerase region in a one-round PCR to identify HBV genotypes and drug-resistance mutations of interest. All 40 samples (20 HCV and 20 HBV) were sequenced on two runs using the Ion-Torrent S5 NGS platform (ThermoFisher Scientific, USA). Sequenced data were analyzed using DeepCheck Analysis Software (Advanced Biological laboratories Group, France), which subjects the raw data to a filtering process, and performs phylogenetic classification using reference HCV and HBV genomes sequences from GenBank (USA). The identification of resistance-associated substitutions (RAS) and minority variants harboring RAS by the DeepCheck software makes it possible to predict the selection of specific direct-acting antivirals against HCV or HBV.

Results:
Genotyping results for HCV showed the maximum prevalence of genotype 4a, followed by 3a and 1a. Mutation frequency leading to drug-resistance varied with the different genotypes of HCV. In the case of HBV, all 20 samples contained genotype D and mutation detection revealed that the majority of samples had a susceptibility tendency to various anti-virals while 10% showed A181T mutation.

Conclusions:
NGS is a useful detection method for genotypes and low-abundance mutations with a direct impact on drug resistance.

Key Words: Next Generation Sequencing; Hepatitis Viruses; Chronic Liver Diseases;

Funding Agency: None

Microbiology and Immunology

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Detection of Low-Frequency Drug-Resistant Variants of HIV-1 using Whole Genome Sequencing

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Introduction:
Introduction & Objectives: Next-generation sequencing (NGS) technologies provide high-throughput approaches through the rapid acquisition of thousands to millions of short nucleotide sequences. Sequencing the HIV whole genome (WGS) simultaneously captures all resistant variants and removes the need to design and optimize PCR assays for the detection of resistance to new drugs. Our objective was to standardize the WGS for HIV-1 to detect circulating subtypes in Kuwait as well as putative novel drug-resistant variants which may predict changes to epitopes.

Methods:
A total of 10 HIV-1 serum samples were received for HIV-genotyping testing from chronic HIV patients. The WGS workflow included the following steps: (i) serum samples were extracted using MagnaPure LC 2.0 (ii) for PCR-amplification, 5 different sets of primers corresponding for 5 HIV-1 genes GAG, Pol, vif/vpr/vpu, Gp120/Gp41, and Nef Accessory proteins were used. (iii) All amplified genomic regions were subjected to next-generation sequencing (NGS) using the Ion-Torrent S5 platform (ThermoFisher Scientific, USA). Sequenced data were analysed using DeepCheck Analysis Software (Advanced Biological laboratories Group (ABL), France), which subjects the raw data to a filtering process, and performs phylogenetic classification using reference HIV genomes sequences from GenBank (USA).

Results:
Genotyping results for all HIV samples showed existing hybrid subtypes which couldn't be detected by Sanger sequencing. Low-frequency drug-resistant mutations were also detected at low threshold-3 and threshold-5 vs. sanger which could only detect broad-range mutations at threshold-10 and 20.

Conclusions:
the increasing number of HIV drugs in development that interact with different proteins encoded by viral genes scattered across the HIV genome, limited the chance to be missed out by Sanger sequencing and increases the chance of failure. Therefore, we proved that sequencing the whole HIV-1 genome simultaneously captured all resistant variants and removes the need to design and optimize PCR assays for the detection of resistance to new drugs.

Key Words: Next Generation Sequencing; HIV-1 Whole Genome Sequencing; Drug-resistant

Funding Agency: None

Microbiology and Immunology

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Audit of Antibiotic Prescription in Burn and Plastic Surgery Center in Kuwait

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Introduction:
Antimicrobial resistance is a global threat that should be addressed. The judicious use of antimicrobials is a fundamental element to minimize the emergence of resistance. Observation of antibiotic prescription through audits is one of the tools to control their misuse. Objectives: To monitor and analyze the daily prescription of antimicrobial agents in a burn and plastic surgery center in Kuwait.

Methods:
Antibiotic prescription audit was conducted from June to November 2022 among inpatients in Babtain Burn and Plastic Surgery Center in Kuwait. Information was collected through audit forms that were filled upon prescription. Data was analyzed by assigned clinical microbiologist as part of antimicrobial stewardship program (ASP) in the hospital.

Results:
Over a period of six months, the overall consumption of antibiotics was mainly for surgical prophylaxis (81%). Among surgical prophylaxis, cefuroxime and metronidazole were mostly used (49%), (48%) respectively. Major errors were noted in surgical prophylaxis, where compliance to local policy was met in (80%) in terms of timing, whereas the number of doses were as follows: 1 dose (32%), 2 doses (17%), 3 doses (32%) and 4 doses and above (18%).

Conclusions:
The overall compliance is acceptable; however, the number of doses f surgical prophylaxis could be targeted and improved. Better documentation of data, including reasons of extending duration is required for better judgment. Continuous audit and feed back is a key method to raise the awareness among prescribers and promote the appropriate use of antimicrobials.

Key Words: Audit; Antimicrobial prescription; Burn;

Funding Agency: None

Microbiology and Immunology

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Molecular genetic analyses and sterol profiles identify alterations in ERG2 as a major mechanism conferring reduced susceptibility to amphotericin B in Candida kefyr

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Introduction:
The spectrum of yeast species causing invasive infections is changing due to increasing use of antifungal prophylaxis and emergence of drug-resistant and multidrug-resistant (MDR) yeasts is a matter of great concern due to limited antifungal armamentarium. The molecular basis of reduced susceptibility to amphotericin B (rs-AMB) among rare yeasts is poorly defined. This study determined genetic alterations in major genes involved in ergosterol biosynthesis and their association with total cell sterols among clinical C. kefyr including rs-AMB isolates.

Methods:
C. kefyr isolates (n=88) obtained from 74 patients in Kuwait and identified by phenotypic and molecular methods were analyzed. Etest was initially used to identify isolates with rs-AMB. Specific mutations in ERG2 and ERG6 involved in ergosterol biosynthesis were detected by PCR-sequencing. Fourteen selected isolates were also tested by SensiTitre Yeast One (SYO), total cell sterols by gas chromatography-mass spectrometry and ERG3 and ERG11 sequencing.

Results:
Eleven isolates from eight patients showed rs-AMB by Etest including two isolates with additional resistance to fluconazole or to all four antifungals. SYO yielded concordant results for seven of nine rs-AMB isolates. A nonsynonymous mutation in ERG2 was detected in nine of 11 rs-AMB but also in three of 77 isolates with wild-type AMB pattern. One rs-AMB isolate contained a deletion (frame-shift) mutation in ERG2. One or more nonsynonymous mutation(s) were detected in ERG6 in 11/88 isolates with rs-AMB or wild-type AMB pattern. Four and two of 14 selected isolates contained a nonsynonymous mutation in ERG3 and ERG11, respectively. Ergosterol was undetectable in 8 of 9 rs-AMB isolates and the total cell sterol profiles were consistent with loss of ERG2 function in seven rs-AMB isolates and loss of ERG3 activity in another rs-AMB isolate.

Conclusions:
Our data show that ERG2 is a major target conferring rs-AMB in clinical C. kefyr isolates.

Key Words: Candida kefyr; Antifungal susceptibility testing; Amphotericin B resistance;

Funding Agency: KURS grant MI 02/20

Microbiology and Immunology

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Vibrio cholerae Non-O1/Non-O139 and Vibrio fluvialis Recovered From Blood Cultures

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Introduction:
Non-O1/non-O139 serogroups of Vibrio cholerae have been reported to cause extra-intestinal infections including bacteremia. This is usually seen in patients with comorbidity such as hepatic dysfunction. Non-choleragenic vibrios including Vibrio fluvialis are known to cause intestinal and extra-intestinal manifestations. We report here two cases of bacteremia - one caused by V. cholerae non-O1/non-O139 and the other by V. fluvialis.

Methods:
Case 1. A 49-year-old male presented with abdominal pain, fever, anorexia & abdominal distension. Laboratory tests revealed deranged liver functions and blood culture grew Gram-negative bacilli (GNB). The radiological investigation suggested perforated gangrenous cholecystitis with cirrhotic liver changes. Despite initiating treatment with meropenem and vancomycin, the patient died in <24 h after admission to the ICU. Case 2. A 38-year-old male suffering from diabetes mellitus, hypertension, and end-stage renal disease on hemodialysis for the past year through the permanent subclavian catheter, visited Nephrology dept. for his dialysis session. His pre-dialysis blood sample was collected, which grew GNB. Since the patient remained symptom-free, he was not recalled for treatment. Both bacterial isolates were identified to the species level by Vitek 2 and confirmed by MALDI-TOFMS. They were further tested for V. cholerae O1 and O139 by a multiplex PCR assay for detection of rfb and ctxA specific sequences. The isolate from case 2 was tested by a toxR gene-based PCR assay. Antibiotic susceptibility was tested utilizing Vitek2 AST-N417 susceptibility cards.

Results:
Vitek 2 and MALDI-TOF identified the isolate from case 1 as V. cholerae and from case 2 as V. fluvialis. Both isolates were susceptible to cefuroxime, ceftazidime, ciprofloxacin, pipracillin/tazobactam and cotrimoxazole. PCR assay failed to detect rfb and ctxA specific sequences in both isolates for serogroups O1 and O139 V. cholerae. V. fluvialis was positive in toxR gene-based PCR assay as it produced an amplicon of 217 bp.

Conclusions:
Although cases of severe sepsis caused by V. cholerae non O1 and non O139 have been reported previously, there is no report of asymptomatic bacteremia due to V. fluvialis. The second patient would have been an asymptomatic carrier of V. fluvialis which would have gained access to the blood stream from the intestinal tract or through exit site of subclavian hemodialysis catheter.

Key Words: Vibrio choleare; Vibrio fluvialis; Blood culture;

Funding Agency: None

Microbiology and Immunology

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Causative Agents and Antibiotic Susceptibility Patterns of Urinary Tract Infections in Maternity hospital in Kuwait

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Introduction:
The etiology of urinary tract infections (UTIs) and the antibiotic susceptibility of the causative uropathogens have been changing over the past years resulting in maternal and neonatal complications worldwide. Our aim was to determine the bacterial species distribution of uropathogens and the prevalence of antibiotic resistance patterns over a 5-year period.

Methods:
A retrospective study was conducted in the Maternity hospital from January 2017 to December 2021. Urine samples were analyzed for 785 inpatients, 772 outpatients, and 128 referred to the neonatal intensive care unit (NICU) and special care unit (SCU). All samples were identified by the VITEK-2 identification card system and antibiotic susceptibility testing by AST-N020 card.

Results:
Significant bacteriuria was detected in 1685 uropathogens in inpatients and outpatients, and age groups were as follows 0-19 y (15, 2), 20-29 y (144, 20), 30-39 y (402, 115), 40-49 y (179, 37), 50-59 y (27, 8), ≥60 y (18, 3). Inpatients Escherichia coli accounted for (529, 67.4%), followed by Klebsiella pneumoniae (189, 24%), Acinetobacter baumannii (15, 2%) and others (52, 6.6%). In outpatients, E. coli were found in (560, 73%); the second and third most prevalent isolates were K. pneumoniae (172, 22%), C. koseri (12, 1%) and others (28, 4%). In neonates K. pneumoniae (45, 35%), E. coli (42, 33%), Enterobacter cloacae (15, 12%) and others (26, 20%) were detected. High resistance rates were observed among Enterobacterials against ampicillin, cephalothin, cotrimoxazole, fosfomycin, cefuroxime and cefotaxime. Resistance rates among inpatients, outpatients, and neonates were detected against ampicillin in E. coli (406 (20.5%), 354 (23%), 34 (21.5%)) and K. pneumoniae (187 (22.7%), 171 (29%), 44 (19.6%)), respectively. Resistance against cephalothin among E. coli (258 (13%), 229 (14.9%), 26 (16.5%) and K. pneumoniae (88 (10.7%), 47 (8%), 21 (9.3%)), respectively. There was a notable decline in antibiotic resistance for E. coli (2017- 2021) (from 444 to 278), while there was a rise in K. pneumoniae (from 140 to 182).

Conclusions:
Uropathogens causing UTI among patients were highly resistant to the first- and second-line antibiotics for treating UTI. Comprehensive surveillance programs are demanded to track the emergence of resistant uropathogens.

Key Words: Urinary tract infection; Antibiotic resistance; Uropathogens;

Funding Agency: unfunded

Microbiology and Immunology

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Analysis of Viral Diversity in Stool Samples from Infants and Children with Acute Gastroenteritis in Kuwait using Metagenomics Approach

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Introduction:
Current molecular target-dependent methods are used to detect only known viruses. However, metagenomics based on next-generation sequencing (NGS) technique is a target-independent assay that enables simultaneous detection and genomic characterisation of all microorganisms present in a sample. In this study, we aimed to develop a metagenomics approach using NGS to identify and characterise viruses in stool samples from infants and children with Acute Gastroenteritis (AGE) in Kuwait.

Methods:
We have investigated 84 stool samples from infants and children aged one month to ten years old with signs and symptoms of gastroenteritis who attended Mubarak Al-Kabeer and Al-Amiri hospitals in Kuwait from January to December 2017. A metagenomics approach using NGS to characterise viruses in clinical samples was used.

Results:
Metagenomics analysis revealed an average of 280,768 reads in which 5% of the reads were derived from viruses. The analysis of viral sequences verified that single infection of human adenovirus was the leading cause of gastroenteritis among infants and children, which was detected in 23.2% of the patients, followed by a mixed infection of human adenovirus and other viruses, which was detected in 20.9% of patients. Also, the newly discovered viruses known to cause gastroenteritis were detected, such as astrovirus MLB2, primate bocaparvovirus-1, Aichivirus A, cardiovirus, parechovirus A, astrovirus VA4, cosavirus-F, and bufavirus-3. Our results showed 71% agreement (k=0.445, P=0.000) between multiplex Real-Time PCR, which is used as a routine diagnostic test and metagenomics approach in the detection of viruses causing gastroenteritis in clinical samples.

Conclusions:
Despite the difficulties in sample preparation and analysis process, we showed that metagenomics approach is a powerful and promising tool for the detection and characterisation of different viruses in clinical samples.
Aknowledgment/Funding: This project was funded by College of Graduate Studies and Research Sector, Kuwait University. Project Number YM10/17. Special thanks to Research Core Facility and OMICS Research Unit for their support and help in using the facilities provided in the Unit. We are also grateful to Mr. Mohammed Khan for his outstanding help in
the bioinformatics analysis of the data.

Key Words: Next-generation sequencing; Metagenomics approach; Viral gastroenteritis;

Funding Agency: College of Graduate Studies and Research Sector (Project Number: YM10/17)

Molecular Biology

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Comparison of Trityl On purification and the Trityl Off Purification Methods in MermadeTM DNA Synthesized Oligos Upto 25 Base Pairs.

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Introduction:
To identify the best method for the purification of synthetic oligonucleotides synthesized in MermadeTM DNA synthesizer.Crude synthetic oligo nucleotides are purified by either Trityl On or Off methodologies. In the trityl On practices the final 5'DMT protecting group is retained on the nucleoside and removed during purification. But in Trityl Off method the 5'protecting group is cleaved during the final cycle in the synthesis. While both trityl On and trityl Off techniques are compatible with serial liquid chromatography. An advantage feature of trityl On separation is the lipophilic properties of DMT group which can serve to enable discrimination between the protected full length sequence and unprotected ones. The trityl On purification heighten the risk of nucleic acid damage due to the potential of depurination..

Methods:
B actin primers (forward and reverse) are synthesized by Trityl On and Off method. The synthesized primers were deprotected and incubated. The primers were then purified accordingly with trityl On and off method protocols. Reverse phase OPCs are used which are equilibrated using Acetonitrile then loaded with trityl off oligonucleotide(free of organic solvents)then eluted using 20% Acetonitrile. For trityl On method after equilibration the synthesized crude primer is passed through the reverse column follwed by 5M NH4OH and then 2-5% of TFA is added in the syringe barrel and incubated for 5 minutes and flushed out. In 7500 ABI Real time PCR relative quantitation with Trityl Off and On primers were done with 4 different DNA samples in duplicates.

Results:
The trityl On and off synthesized and purified primers showed high concentration and acceptable purity. Inspite of the higher concentration and purity of trityl On synthesized oligos the Trityl off synthesized oligos showed a positive reaction with an average Ct of 19 in 0.2 threshold in the real time PCR assay. Trityl On synthesized primers showed an undetermined reaction.

Conclusions:
Trityl Off purification will be the best method for the stability of primers. The trityl on protocol require a balance of purine hydrolysis at the time of detritylation.

Key Words: Trityl off; DNA synthesiser; Mermade;

Funding Agency: Srul02/13

Molecular Biology

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Evaluation of de novo assembly and correction tools on the identification of genome characterization, drug resistance, and virulence factors of clinical isolates using ONT sequencing

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Introduction:
Oxford Nanopore sequencing technology (ONT), a third generation sequencing technology, is being more rapidly used due to its affordability, simplicity, and reliability. Despite the advantage ONT has over next-generation sequencing in detecting resistance genes in mobile genetic elements, its relatively high error rate (10-15%) is still a deterrent. Several bioinformatic tools are freely available for raw data processing and obtaining complete and more accurate genome assemblies. Aim: In this study, we evaluated the impact of using mixed-and-matched de novo read assembly (Flye, Canu, Wtdbg2, and NECAT) and read correction (Medaka, NextPolish and Racon) tools in generating complete and accurate genome assemblies, and downstream genomic analysis of nine clinical Escherichia coli isolates.

Methods:
DNA of nine clinical E. coli isolates was extracted using Monarch DNA purification kit. The extracted DNA was checked for quality and quantity using a spectrophotometer (Nanodrop), and a fluorometer (Qubit), respectively. Oxford Nanopore Ligation Sequencing kit with Native Barcoding Expansion kit were used for library preparation. The prepared library was sequenced on ONT Mk1C device. Raw ONT data was processed using de novo assembly (Flye, Canu, Wtdbg2, NECAT) and read correction (Medaka, NextPolish, Racon) tools. FastQC was used as a quality control step and then genome completeness was evaluated by QUAST, antimicrobial resistance gene detection and plasmid identification were evaluated using staramr, pan-genome was detected by roary, and virulence genes identification was evaluated using abricate.

Results:
Flye and Canu assemblers were most robust in genome assembly, and Medaka and Racon correction tools significantly improved assembly parameters. Flye functioned well in pan-genome analysis, while Medaka increased the number of core genes detected. Flye, Canu, and NECAT assembler functioned well in detecting antimicrobial resistance genes (AMR), while Wtdbg2 required correction tools for better detection. Flye was the best assembler to detect virulence genes and the location of AMR and virulence genes (i.e., chromosomal vs. plasmid).

Conclusions:
This study provides insight into the performance of several read assembly and read correction tools when only ONT reads are available for sequencing clinical isolates.

Key Words: WGS; Genome assembly; ONT;

Funding Agency: This research received no external funding and was funded internally by the Microbiology De-partment, Faculty of Medicine, Kuwait university, and funding was independent of the study design and delivery.

Neuropharmacology and Molecular Biology

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Sex Differences in Neuroimmunity in a Mouse Model of Antiretroviral-induced neuroinflammation

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Introduction:
Background: Nucleoside reverse transcriptase inhibitors (NRTIs), drugs used to treat HIV infection, can cause neuropathic pain (NP) and neuroinflammation. An NRTI, 2′-3′-dideoxycytidine (ddC), was found to induce mechanical allodynia and increase proinflammatory cytokines in brains of female mice. In some models of NP, microglia activation is important for NP pathophysiology in male mice, while T cells are important in female mice. Objective: The aim of this study was to assess whether there are sex-dependent differences in NRTI-induced neuroinflammation.

Methods:
Age-matched female and male mice (BALB/c strain) were treated intraperitoneally once daily with 25 mg/kg ddC, or its vehicle, for 5 consecutive days. The Ethical Committee for the Use of Laboratory Animals in Teaching and in Research, HSC approved the animal experimental work conducted for this study. Response to mechanical stimuli was measured using dynamic plantar aesthesiometer. The expression of markers of microglia (CD11b and Iba1), astrocytes (GFAP), T cells (CD3e), signaling molecules (ERK1/2 and p38 MAPK), molecules involved in immune cell modulation (CD200, CD200R1), pro- and anti-inflammatory cytokines (IL-1β, TNF-α and IL-10) was evaluated by RT-PCR and western blot in the spinal cords on day 7 after ddC treatment. The data were analyzed by unpaired student's t-test, Mann-Whitney test, or two-way ANOVA.

Results:
ddC induced mechanical allodynia in all mice and increased Cd11b, Cd3e, Cd200r1, Mapk1, Il1b, Tnf and Il10 mRNA levels in female ($p < 0.05$), but not male, mice compared to vehicle treatment, whereas it had no significant effects on Gfap, Cd200 and Mapk14 transcripts in both sex ($p > 0.05$). ddC increased the protein expression of CD11b and phospho-p38 MAPK in female ($p < 0.05$), but not male, mice, while it elevated Iba1 in male mice compared to vehicle treatment ($p < 0.05$). There was no change in the levels of GFAP, CD3e, CD200, CD200R1, and phospho-p44/42 in both sex ($p > 0.05$).

Conclusions:
This study shows that changes in neuroimmune cells and molecules in the spinal cords of BALB/c mice during NRTI-induced neuroinflammation are sex-dependent. Thus, female mice are more prone to NRTI-induced neuroimmune changes than male mice.
Funding/Acknowledgements: College of Graduate Studies and the Research Sector of Kuwait University (KU, Grant # YP01/21) funded this study. Thanks to the Animal Resources Centre, and Research core facility, HSC, KU through grants SRUL02/13 and GM01/15.

Key Words: Neuroinflammation; Antiretroviral drug ; Sex differences;

Funding Agency: College of Graduate Studies of Kuwait University and Kuwait University Research Sector Grant number YP01/21.

Nuclear Medicine and Radiology

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Establishing and Practicing an Effective Management of Benign Nontoxic Multinodular Goiter in Kuwait. Two Different Dose Levels of Recombinant Human TSH and Radioactive Iodine

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Introduction:
The efficacy of rhTSH-assisted radioiodine therapy of multinodular goiter is not fully known and only a few studies, with a limited number of patients, have evaluated the effect beyond 1 year. Currently, there is no effective and safe management of benign non-toxic (MNG), available in KW covering the impact of the past environmental events and the genetic relation. This study is focusing on the application and effect of multi-dose rhTSH-assisted radioiodine over 2 years.

Methods:
Patients with benign non-toxic goiter who had refused surgery, or the surgery was not an option, and who had fine needle aspiration to exclude cancer and toxicity were divided into the randomized G1 and G2 (N=50, ≥18 years old). They received 2 different single doses of rhTSH injections 24 hours prior to therapeutic radioactive iodine (131-I). All patients had CT scan, TSH, T3, T4,CBC and biomedical tests at a 6-months interval for 2 years period. The Volumetric application of GE 670 SPECT/CT and MATLAB used for quantitative measurement. An intravenous dose of 120 MBq (planar) and 185 MBq (SPECT) were administered followed by Static or SPECT/CT images, 20 min post injection as per SOP. All patients had 131-I uptake at baseline and 24 interval post single dose of 0.1mg or 0.3 mg of rhTSH followed by a therapeutic dose of 131-I. The ethical approval (M2019-1-29/351) was obtained.

Results:
The patients were 67.8 ±10.5 years old (30% male and 70% female). The G1had 24 hours' radioiodine 131-I uptake (RAIU) in the range of 11-19.7± 2.9%, before receiving a single dose (0.1 mg) of rhTSH, followed by an oral single therapeutic dose of I-131in the range of 25-29 mCi (mean value =28.2±1.79 mCi). The G2 had 24 hours RAIU measurements in the range of 18-31.2 ± 5.2 %. This group received a single dose (0.3 mg) of rhTSH followed by an oral therapy dose of I-131 in the range of 20-30 mCi (mean value = 24.86 ±3.5 mCi). Thyroid volume (TV) measurements suggested a noticeable reduction in TV in both groups post-therapy: from 114.9 ± 14.7 to 93.8 ±25.4 ml (mean %PD of 19.4 ± 17.26%) in G1 and from 126.7 ± 84.4 to 64.1± 28.4 ml (mean %PD of 42.7 ± 21.6%) in the G2.

±Conclusions:
The ideal treatment for MNG is controversial, partly due to the variation in the natural history of these goiters. The preliminary results are encouraging, considering the impact of dietary, genetic factors, environmental exposure experience and its follow up effects.

Key Words: Nuclear Medicine ; BNMG ; rhTSH;

Funding Agency: KFAS - Grant Number: PN20-13NR-01

Nuclear Medicine and Radiology

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A Developed Machine Learning (ML) Models to Predict Thyroid 131I Uptake Based on 99mTc Thyroid Scan

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Introduction:
Thyroid scintigraphy is an effective imaging method for assessing the functionality of thyroid lesions including the uptake function of part or all of the thyroid gland and now it is commonly used, acceptable and easier to perform. Radioactive iodine uptake (RAIU) testing is a useful diagnostic tool for assessing thyroid pathologies. We aimed to construct machine learning (ML) system to automatically predict the value of RAIU by using the value of ^{99m}Tc thyroid scintigraphy and thyroid function test results.

Methods:
We used 226 patients data who underwent a thyroid ^{99m}Tc pertechnetate scan while having ^{131}I thyroid uptake between January 2018 to April 2022. Medical records and biochemical thyroid function tests were reviewed and ^{99m}Tc pertechnetate thyroid uptake values were determined for each patient.

Results:
The statistical analysis and all patient data were imported, cleaned and visualized in python programming language (python 3.9), using Jupyter notebook as an editor. The range of the measured ^{131}I uptake for patients was 0.17 % to 96 % $\pm$ 21.7 %. The range of the measured ^{99m}Tc uptake for patients was 0.1 % to 36 $\pm$ 6.44 %. The values of coefficient of determination (R^2) and route mean squared error (RMSE) for linear regression model were 0.54 and 13.87 respectively. The values of R^2 and RMSE for polynomial regression model were 0.85 and 8.34 respectively.

Conclusions:
The developed model can improve thyroid uptake value of iodine 131.
Acknowledgment: The authors wish to thank the anonymous referees and editors of this special issue for their constructive comments.

Key Words: Thyroid scintigraphy; Machine learning; Regression;

Funding Agency: None

Nuclear Medicine and Radiology

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Potential Pitfalls of Steatopygia on Bone Scintigraphy and the Added Value of SPECT and SPECT/CT

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Introduction:
Objectives. A retrospective study of bone scintigraphy to assess the prevalence of steatopygia on bone scintigraphy of obese patients and evaluate its effect on the appearance of the lumbar spine, and the added benefit of SPECT and SPECT/CT in overcoming possible artifacts.

Methods:
Between 2016 and 2019, patients who underwent bone scintigraphy, BMI ≥ 30, were included. Three nuclear medicine consultants reviewed the studies to determine whether significant steatopygia is present, if it resulted in attenuation of underlying lumber spine and crease edge artifact. SPECT or SPECT/CT images were reviewed to evaluate their impact in diagnosis. Ethical approval was obtained from MOH ethical committee.

Results:
56 patients out of the 100 were noted with steatopygia on planar images. Among the group of 80 obese patients, 50% patients showed steatopygia, while in the group of 20 morbidly obese patients, 80% patients showed steatopygia. 32 patients of the 56 with steatopygia, had significant attenuation at the lower lumber vertebrae. Nine of these patients showed crease edge artifact. SPECT and SPECT/CT clarified the scintigraphic abnormalities noted in all patients including patients with edge artifact alleviating diagnostic difficulty. Among the nine patients with edge artifact, six patients showed normal appearance on SPECT/CT images while three showed true abnormalities.

Conclusions:
Steatopygia is common on bone scintigraphy of obese patients, higher in females and morbidly obese patients. Obesity related artifacts in bone scintigraphy, including attenuation effect and edge artifact, are common in this patient group. SPECT or SPECT/CT improves the diagnostic accuracy by overcoming the steatopygia effects seen on planar images. (1278)

Key Words: Steatopygia; Obesity; Bone scintigraphy artifact;

Funding Agency: None

Nuclear Medicine and Radiology

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Reducing Radiation Exposure from PET Patients

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Introduction:
With the recent development of many PET tracers, to date there is no clear guidelines for discharging patients from Nuclear Medicine Departments after undergoing diagnostic procedures. This study investigates simple methods to reduce the emitted radiation from patients who underwent PET scans before being discharged.

Methods:
The study included 83 patients, 63 [18F]FDG and 20 [18F]NaF. Emitted radiation from the patients' urinary bladder was measured with an ionization survey meter at a 1-meter distance, presuming the urinary bladder to be the primary source of radiation. The measurements were taken at different time points after PET image acquisition: immediate (pre-void 1), voided (post-void 1), after waiting 30 min in the uptake room while drinking 500 mL of water (pre-void 2) and voided again (post-void 2). MOH ethical approval # 2018/805

Results:
For [18F]FDG patients, the reduction of emitted radiation due to drinking water and voiding alone from pre-void 1 to decay corrected post void 2 was an average of 22.49 ± 7.48% (13.65 ± 3.42 µSv/h to 10.48 ± 2.37 µSv/h, $p < 0.001$). As for [18F]NaF patients, the reduction was an average of 25.80 ± 10.03% (9.83 ± 2.01 µSv/h to 7.23 ± 1.49 µSv/h, $p < 0.001$).

Conclusions:
In addition to the physical decay of the radiotracers, utilizing the biological clearance properties have resulted in a significant decrease of the emitted radiation in this study. Implementing additional water consumption to facilitate voiding with 30 minutes of wait time before discharging certain [18F]FDG and [18F]NaF patients that need to be in close contact with others such as elderly, caregivers and inpatients, might facilitate lowering their emitted radiation by an average of 22-25% due to voiding, not counting in the physical decay which should add an additional 17% reduction.

Key Words: PET/CT; Radiation Exposure; Public Safety;

Funding Agency: None

Nuclear Medicine and Radiology

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The Effect of Metal Artifact on Attenuation Correction Map (AC images) in Hybrid Imaging Techniques (SPECT/CT and PET/CT Modalities)

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Introduction:
SPECT/CT & PET/CT used for anatomical and functional assessments of diseases. Metal artifact degrades diagnostic value of computed tomography (CT) images and Attenuation Correction (AC) map in patients with metal implants Total knee replacment (TKR). The objective of this study is to investigate the effect of metal artifact on AC map using Jaszczak phantom with metal inserts.

Methods:
For SPECT/CT, the Jaszczak phantom with metal inserts to spheres was injected with 15 mCi of Tc-99m. For CT protocol fix mill ampere (mA) and variable kilo volt peak (KVp) and vice versa were used .region of interest (ROIs) over all spheres were selected, Back Ground and between the spheres to calculate counts. For PET/CT phantom Preparation and calculation carried out as SPECT/CT but with the injection of 2.5 mCi of F18.

Results:
Qualitative and Quantitative analysis of SPECT/CT images show major effect of metal artifact on AC map which led to two basic Artifacts. First, counts of AC images are 5 folds more than non attenuaion correction (NAC)images for high volume of metal and 4 folds in low volume of metal. Second, streak artifact from metal on CT led to decrease in the count which qualitatively appeared as a line between the spheres. The quantities count analysis appears decreased by 10% than background in AC images. PET/CT Images appear to have mild qualitative effect of metal artifact of AC images in which an increased count of AC images by factor of 8 folds in High and low metal volumes. There is no qualitative effect of streak line artifact in CT AC images, with difference count appeared as line area to background nearly 65 %.
Discussion: fixed mA, variable kVp for SPECT/CT Spheres with high thickness of metal, increased counts in AC images linearly with increasing kVp. 5 folds at maximum KVp (140), and 3 folds at KVp (80), compared to NAC images PET/CT images, Inverse relationship between KVp and count in AC images. Counts elevated by factor of 6 at KVp 80 and by the factor of 5 at 140 kVp, comparing to NAC. CT streaking artifact lead to decrease of counts in AC images appear as a line in BG in AC images between spheres. Counts in SPECT/CT and PET/CT decreased by 10% and 60% respectively. With fixed KVp and variable mA, SPECT/CT count increased in AC images 4 folds compared to NAC images, For PET/CT images Inverse relationship between mA and count of AC images.

Conclusions:
The effect of metal artifact in CT images have a major & significant effect (Qualitative & Quantitative) in SPECT/CT and PET/CT AC Images, as we observed increase of count in and around spheres which lead to over estimation of result (False positive result), with significant reduction of counts in the area between spheres.

Key Words: Metal Artifact; Attenuation Correction Map; SPECT/CT and PET/CT Modalities;

Funding Agency: None

Nuclear Medicine and Radiology

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Automated Diagnosing and Differentiating Lung Infections on Chest X- Ray Images Using a Developed Artificial Intelligent (AI) Technique

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Introduction:
Deep learning Techniques can process medical images and extract data at higher speeds with much more accuracy. This can help doctors to process data and analyze test results more thoroughly. The recent coronavirus (COVID 19) pandemic has put a lot of pressure on the health system all around the world. It is also necessary to develop an accurate, fast, and cost-effective tool for diagnosis of viral pneumonia. In this work we aim to classify chest X-ray images in three categories, normal, pneumonia and COVID-19 using a pre-trained deep learning model named AI-CXR.NET.

Methods:
We used 8,123 chest X-ray images and further strengthened our model by tuning hyper parameters to provide better generalization, during the model validation phase. The model that inputs chest X-ray images is capable of extracting radiographic patterns of CXR images, and turns them into valuable information and monitor structural differences in the lungs caused by the diseases.For the working of a deep Convolutional Neural Network (CNN), the input images from the dataset are converted to matrix format first, so that the image can be recognized by the computer and then be processed. The images in the matrices are labeled based on their relative difference. The model learns the effects of these differences on the label during the training phase and makes the required predictions on the testing image dataset. During the data-pre-processing step, all the CXR images from the image dataset were resized to 224 x 224 pixel prior to training of the model to mitigate commonly found embedded textual information in the CXR images. Deep learning (DL)models extract features from the images using convolutional layers; based on these features, these models also classify images. The initial layers of DL models extract edges, contours, etc., while later layers extract more detailed attributes of images.

Results:
Statistical analysis and graphing of data were performed using Python 3 software. The deep learning model AI-CXR.NET successfully classifies three categories that include normal, pneumonia and COVID-19 with an accuracy of 99.17 %, precision of 99.08 %, recall of 99.18 % and the F1 score of 99.13 %.

Conclusions:
It is feasible to build an accurate deep learning system for classification of CXR images into three categories, though further classifications can be incorporated for more specific diagnosis.
Acknowledgment: The data obtained from the “Kaggle” open source.

Key Words: Artificial Intelligent ; Lung Infections ; X- Ray Images ;

Funding Agency: None

Nuclear Medicine and Radiology

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Comparison of Different Theoretical Dose Estimation with Practical Patient Effective Dose in PET-CT Oncology Scanning

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Introduction:
Patients receive radiation doses from the radiopharmaceuticals and the CT scan during PET/CT exams. Radiopharmaceutical is administered to the patients via an automatic injector. Our goal is to determine patients effective dose (ED) from the autoinjector (Intego) database and to compare the Intego ED for each individual patient with ED standard values from software that is approved by the International Societies of Nuclear Medicine.

Methods:
The study was conducted by collecting 146 PET/CT oncology patients undergoing whole body (18F-FDG and 18F-NAF) exams in Adan Hospital. Administered radiopharmaceutical, activities and effective dose were collected from (Intego) database, and the absorbed radiation dose was calculated using ICRP 106 -V18 software for 18F-FDG and NUREG/CR-6345 for 18F-NaF. Radsis software and the SNMMI online radiation tool calculator were used to calculate effective Dose for comparison. The effective dose for CT was calculated using NCICT adopted software.

Results:
There were 106 female patients (BMI = 31.62 ± 6.24 kg/m2) and 39 male patients (BMI =27.37 ± 5.5 kg/m2). The mean injected activity from 18F-FDG and 18F-NaF for male patient imaging were 234.3 ± 56.6 and 210.1 ± 34.4 MBq respectively. The mean injected activity for female patients was 221.9 ± 49.6 and 241.8 ± 55.6 MBq respectively. According to the NCICT, the ED mean values from the CT scan for male and female patients were 4.82 + 1.67 and 5.77 + 2.24 mSv respectively. For the comparison, we used the 3 softwares to calculate the PET/CT exams ED. Using the (Intego) database the ED for 18F-FDG and 18F-NaF exams for male patients was 9.82 ±1.64 and 11.2 ± 3.44 mSv respectively, for female patients the ED was 10.4 ± 3.64 and 11.8 ± 3.84 mSv respectively. Comparatively, for the same male and female patients, using Radsis software, the ED for 18F-FDG and 18F-NaF exams for male was 9.2 ± 2.8 and 8.82 ± 2.37 mSv and for female was 9.97 ± 3.14 and 10.37 ± 3.34 mSv. For the SNMMI online calculator the ED was 9.32 ± 2.77 and 4.0± 0.7 mSv for male from 18F-FDG and 18F-NaF, and ED for female from 18F-FDG and 18F-NaF was 9.97 ± 3.14 and 8.91 ± 3.34 mSv.

Conclusions:
For the Whole Body PET/CT the total ED for male using(Intego) database for 18F-FDG was close to the ED for the two other softwares while the ED for 18F-NaF was higher. The ED for 18F-FDG and 18F-NaF for female using Intego was higher with compare with the other softwares.

Key Words: ED effective dose; mSv millisievert; BMI body mass index;

Funding Agency: None

Nuclear Medicine and Radiology

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Projection of F-18 FDG Uptake in the Brain onto the CT Slices in PET/CT Hybrid Imaging: A Functional Anatomical Correlative Study

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Introduction:
F-18 fluorodeoxyglucose (F-18 FDG) is a glucose analogue used for evaluating cerebral function and metabolism. F-18 FDG uptake in the brain reflects neuronal activity, therefore, pathological changes in neuronal function are reflected as alteration of F-18 FDG positron emission tomography (PET) distribution in the brain. Recently, the use of hybrid F-18 FDG PET/CT imaging has enabled correlation of functional abnormalities of F-18 FDG uptake in PET with structural changes on CT giving a more complete evaluation in certain disease conditions like dementia and tumors. The objective of the study is to correlate the pattern and intensity of F-18 FDG uptake in various brain regions with the corresponding CT slices in terms of anatomical structures seen: grey and white matter, basal nuclei, ventricles and Hounsfield unit (HU) values.

Methods:
Ten F-18 FDG PET/CT studies performed for various neurological conditions including memory impairment, epilepsy, altered behavior and dementia were reviewed. F-18 FDG PET/CT was done 60 min after IV injection of 0.1 mCi/kg body wt. PET/CT slices were reconstructed using a Hermes workstation. Analysis was done using the BRASS software and manually by drawing regions of interest for uptake of radioactivity in the frontal, parietal, occipital cortex and cerebellum. Also, the ratio of regional uptake to cerebellum was taken. This is in addition to measuring the thickness of the uptake in each region. The CT findings in the same regions were inspected visually and analyzed quantitatively by recording the HU values.

Results:
The average age of the patients was 69.2 yr. There were 5 males and 5 females. F-18 FDG PET images showed high uptake in the cerebral and cerebellar cortex and in the basal nuclei. There were 599 counts/voxel (ratio to cerebellum 1.15) in the frontal, 602 (1.15) occipital, 582 (1.12) parietal, 517 (1.0) cerebellum. The thickness of FDG uptake was: 20 mm in the frontal, 16 occipital, 34 parietal, and 32 cerebellum. The average HU value in the corresponding areas was frontal 47, parietal 43, Occipital 53, and cerebellum 73.

Conclusions:
Correlation of F-18 FDG PET uptake in the regions of the brain onto the CT slices showed projection of the F-18 FDG activity beyond anatomically defined regions by CT. The average thickness of the uptake regions are reported providing baseline values that could be useful for clinical evaluation of abnormalities involving F-18 FDG distribution in patients.

Key Words: F-18 FDG PET/CT; Brain; Dementia;

Funding Agency: None

Nutrition

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Dietary Knowledge and Eating Behavior among Adults Attending a Primary Health Care Facility in Kuwait and its relation to Metabolic Risk Factors

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Introduction:
The Nutritional knowledge (NK) and eating behavior (EB) among diabetic individuals (DI) plays an important role in optimizing their clinical outcomes, beside preventing and delaying future complications. Therefore, it is essential to explore such factors among DI. For the current study, two objectives were addressed. First one is to assess NK and EB among DI. Second one is to examine the association between NK and EB among the study participants.

Methods:
A cross-sectional study for a sample of 100 adults with diabetes (AWD) visiting a primary health care facility. A self-administered questionnaire was given for the participants and they were asked to respond to questions about sociodemographics, NK, and EB sections. Participants' anthropometric and metabolic parameters collected from their medical records. Participants' NK evaluated by using Kuwait Adult Nutritional Knowledge Questionnaire (KANKQ). Participants' EB evaluated by the Eating Behavior Inventory (EBI).

Results:
Participants' mean age was 59.75 (±8.26) years. Based on their BMI, 27% of them were overweight and 68% obese. Based on WC & WHtR, central obesity recorded in 85% & 99%, respectively. KANKQ median (IQR) score recorded as 15.00 (13.3–17), while EBI median (IQR) as 81.5 (76.3–87.0). Results showed no significant association between nutritional knowledge (KANKQ) and eating behavior (EBI) among the participants. But findings showed NK is significantly correlated with one metabolic measure "HDL" ($r=0.273$, $p=0.006$), and EB is significantly correlated with three anthropometric measures "Weight, WC & WHtR" as ($r=-0.197$, $p=0.049$), ($r= -0.283$, $p=0.004$) and ($r= -0.228$, $p=0.023$), respectively.

Conclusions:
Study findings showed no significant association between NK and EB among the diabetic participants. However, a significant correlation between NK and HDL was found. Also, EB was significantly correlated with "Weight, WC & WHtR".

Key Words: Nutrition; Eating Behavior; Diabetes;

Funding Agency: None.

Obstetrics and Gynecology

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Effect of Combined Oral Contraceptives and Vitamin E on Hormonal Functions and Oxidative Stress in Women with Polycystic Ovary Syndrome: An Open-Label, Pilot, Randomized Controlled Trial

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Introduction:
Polycystic ovary syndrome (PCOS) is an endocrine disorder which is common among reproductive aged women. Currently, a variety of treatment strategies are employed to manage or mitigate symptoms linked to PCOS.
Objective: This RCT intended to evaluate the efficiency of 4th generation combined oral contraceptives (COC) and vitamin E in PCOS patients, as well as analyze the impact of vitamin E in PCOS in adolescents.

Methods:
A pilot randomized controlled open label study (CTRI/2022/08/045004) was conducted on 58 women with PCOS which included adolescents. Patients were randomized either to control (DRSP) group (n=15), who received COC, drospirenone 3mg with ethinyl estradiol 20 µg orally once daily for 28 days (1 cycle) or DRSP+ E2 group (n=15), who received vitamin E 200mg once daily in addition to the previous regimen or DRSP+ E4 (n=15), who received vitamin E 400 mg once daily in addition to COC regimen for the period of 3 months. Adolescent group (n=13) was administered only with vitamin E 400mg for 3 months. The primary outcome was to regularize the ovulation rate and hormones such as total testosterone (TT), FSH, LH and progesterone levels in PCOS women and adolescents, while the secondary outcomes were hirsutism, acne, alopecia and oxidative stress biomarkers such as GSH and FRAP assay.

Results:
Ovulation rate (percentage of cycles during the entire follow-up period in which ovulation occurred) was accounted 26 (57.7%) out of 45 cycles in the DRSP group, 32 (71%) out of 45 cycles in the DRSP+ E2 group ($P<0.05$), 35 (79.5%) out of 44 cycles in DRSP +E4 group ($P<0.05$) and 29 (64.4%) out of 45 cycles in adolescent group ($P<0.05$) which significantly increased in the third cycle over the course of 3 months. There were also significant differences between TT, FSH, LH and progesterone values ($P<0.05$). Additionally, significant differences were witnessed in the oxidative stress biomarkers.

Conclusions:
In terms of hormonal balance and oxidative stress, drospirenone/ethinyl estradiol with vitamin E 200 mg and 400 mg (DRSP +E2/E4) is surpassing control (DRSP) group. Adolescents who use vitamin E can alleviate their acne and hirsutism- like symptoms while experiencing regular ovulation rates.
Acknowledgment: The authors acknowledge the physicians and supervisors of SRM Medical College Hospital and Research Centre and also, the professors from SRM College of Pharmacy, Kattankulathur, Tamil Nadu, India for their support and guidance during the research.

Key Words: Pilot randomized controlled trial; Vitamin E; Combined oral contraceptive;

Funding Agency: None

Oncology

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Can We Predict Cardiotoxicity Among Breast Cancer Patients Receiving Cardiotoxic Treatment Using Traditional Cardiovascular Risk Estimators? A Prospective Cohort Study.

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Introduction:
Cardiotoxicity is a serious complication of widely used drugs that are considered standard treatment for the management of HER-2 positive breast cancer. The risks depend upon individual patient characteristics, including advanced age, comorbidities, history of ischemic heart disease, and previous cumulative exposure to cardiotoxic treatments. Predicting patients at high risk of cardiotoxicity is still challenging. This study investigates the feasibility of applying traditional cardiovascular risk estimators in predicting patients at moderate-high risk of cancer treatment-related cardiotoxicity and compares the results between two age cohorts in the Kuwait Cancer Control Centre (KCCC)

Methods:
In a prospective comparative observational study, 93 newly diagnosed HER-2 positive breast cancer patients allocated for trastuzumab ± different chemotherapy protocols were included and divided based on age (<60 and ≥60 years old). The atherosclerotic cardiovascular disease (ASCVD) risk estimator was applied at baseline to identify patients at intermediate-high risk of cardiotoxicity. Event of cardiotoxicity was defined as ≥10% decline in the left ventricular ejection fraction (LVEF) from the baseline value or reaching a LVEF value below 50%. The baseline LVEF was assessed and monitored every three months during treatment. The individual decline in the LVEF from the baseline value was calculated and compared between the two age cohorts using the Chi-Square test.

Results:
At baseline, only 26.9% of patients were considered at an intermediate-high risk of cardiotoxicity, representing 76.7% of older and 3.17% of younger patients. Post-treatment, older patients had a significantly higher LVEF decline than younger patients (86.7% and 55.6%, respectively; p-value <0.001). Among older patients, the estimated cardiovascular risk was relatively higher, but not statistically significant, in patients who developed ≥10% decline LVEF compared to patients who developed <10% decline (p-value = 0.058). In contrast, the estimated cardiovascular risk was similar between younger patients who developed ≥10% decline in their LVEF and those who developed <10% decline (p-value = 0.48).

Conclusions:
The traditional ASCVD cardiovascular risk estimator underestimated the risk of treatment-related cardiotoxicity among breast cancer patients and is considered inadequate in assessing the patients, especially those aged less than 60 years.

Key Words: Trastuzumab, cardiotoxicity; Breast cancer, chemotherapy, age,; Cardiovascular

Funding Agency: None

Oncology

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Comparing Trastuzumab-Related Cardiotoxicity Between Elderly and Younger Patients with Breast Cancer: A Prospective Cohort Study.

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Introduction:
Trastuzumab is an HER-2 targeted humanized monoclonal antibody that significantly improves breast cancer outcomes. However, it is associated with an increased risk of cardiotoxicity ranging from a mild decline in the cardiac function to permanent cardiomyopathy. The aim of this study is to compare trastuzumab outcomes between two age cohorts in the Kuwait Cancer Control Centre.

Methods:
In a prospective observational study, 93 HER-2 breast cancer patients undergoing chemotherapy+ trastuzumab were divided into two cohorts (<60 and ≥60 years old). The baseline left ventricular ejection fraction (LVEF) was monitored every three months. Event of cardiotoxicity was defined as developing ≥10% decline in the LVEF. The lower accepted LVEF level was 50%. The individual LVEF decline from the baseline was calculated and compared. Logistic regression analysis was applied to correlate age, comorbidities, BMI, anthracycline, and baseline LVEF, with cardiotoxicity after adjusting for the disease stage.

Results:
The median baseline LVEF was 65% in both cohorts (IQR 8% and 9% for older and younger patients). Whereas the median LVEF post-trastuzumab was 51% and 55% in older and younger patients (IQR 8%; p-value = 0.22), even though older patients had significantly lower exposure to anthracyclines compared to younger patients (60% and 84.1%, respectively; p-value <0.001). 86.7% of older and 55.6% of younger patients developed ≥10% decline in their LVEF. Only 29% of older and 27% of younger patients reached LVEF value below 50%. Age was the only factor correlated with developing ≥10% decline in LVEF (OR 4; p-value <0.012), but it did not increase permanent trastuzumab discontinuation. Besides, a baseline LVEF value below 60% contributed to reaching LVEF value 50%.

Conclusions:
Breast cancer patients aged ≥60 years were at a 4-fold higher risk of developing ≥10% decline in their LVEF compared to younger patients during trastuzumab treatment. Exposure to anthracyclines and comorbidities were not correlated with cardiotoxicity risk.

Key Words: Breast Cancer; Trastuzumab; Cardiotoxicity;

Funding Agency: *-*

Oncology

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A New Paradigm for Epidermal Growth Factor Receptor (EGFR) Expression Exists in PTC and NIFTP Regulated by microRNAs

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Introduction:
Identification of molecular alterations associated with tumor behavior is necessary to guide clinical management. The 2022 WHO classification has organized the thyroid follicular cell-derived neoplasms into benign, low risk and high risk neoplasms, and emphasized the value of biomarkers that may provide differential diagnostic and prognostic information to avoid overtreatment of low risk neoplasms. Objectives: This work aims to study the epidermal growth factor receptor (EGFR) expression, functional and spatial dynamics in relation to specific miRNAs alterations in papillary thyroid cancer (PTC) and in non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) considered as models of high-risk and low-risk thyroid tumors respectively.

Methods:
Primary thyroid cultured cells were used for miRNA gain/loss of function and luciferase reporter assays. Paraffin embedded tissues were used for real time PCR, immuno-fluorescence stain and confocal microscopy experiments.

Results:
Our results showed that in PTC, EGFR mRNA is reduced as an effect of miR-146b-5p upregulation. The EGF expression is low and the ERK pathway is inhibited. The EGFR protein high cytoplasmic expression and colocalization with the endosomal/exosomal markers, ALIX and CD63, suggest the occurrence of stress-induced EGFR internalization, accumulation in endosomal vesicles and secretion via exosomes. In NIFTP EGFR transcription is increased in association with downregulation of miR-7-5p and the EGFR/ERK pathway is active indicating dependence on the canonical EGFR pathway for growth.

Conclusions:
Downregulation of transcript level along with cytoplasmic accumulation of undegraded protein is a new pattern of EGFR regulation associated with malignancy in thyroid. Further research is needed to elucidate the intracellular trafficking defects responsible for this specific EGFR dynamic in PTC. Funding/Acknowledgements: This work is funded by Kuwait University research grants # MG 04/19 and KFAS project # PN20-13MI-02. We acknowledge the help of Research Core Facility RCF project # GM01/15.

Key Words: Thyroid cancer; miRNA; EGFR;

Funding Agency: This work is funded by Kuwait University research grants # MG 04/19 and KFAS project # PN20-13MI-02

Pathology

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Correlation Between Cytological, Ultrasound and Clinical Findings of Patients With Malignant Thyroid Nodules: 2-year Experience in Kuwait Cancer Center.

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Introduction:
Thyroid nodules are common, being detected in up to 65% of the general population. Cytological evaluations together with clinical and radiological assessment are vital for the management of thyroid nodules.The study aims to improve the clinical practice and management of thyroid malignancies by establishing predictive correlations between clinical, radiological and cytological findings of malignant thyroid nodules.

Methods:
This retrospective study analyzes 1121 cases of thyroid FNAC over 2 years (October 2020 to October 2022), in Kuwait Cancer Center Cytology Department. A cyto-histo-radiological correlation for malignant thyroid nodules was studied and a total of 12 parameters were analyzed; Gender, age, nodule laterality, number of nodules, size of malignant nodule, presence of calcification, nodule echogenicity, nodule composition, nodule margin, TIRADS score, Bethesda classification and diagnosis.

Results:
A total of 121 out of 1121 patients, who underwent thyroid aspiration, were diagnosed with malignant thyroid nodules with a mean age of 46.5 and a mean nodule diameter of 1.9 cm. A female predominance was noticed. Ultrasonography evaluation of thyroid nodules showed that the majority of the studied malignant nodules were located in the left lobe and appeared to have micro-calcification, solid composition, mixed echogenic pattern and ill-defined/lobulated margin, some of which showed extra thyroid extension. With regards to number of nodules, 40.5% of patients had 3 or more nodules. The echogenicity of the nodules was evaluated by ultrasonography with majority of nodules showing mixed echogenic pattern. TIRADS scoring system was used in 89 of the 121 cases. TIRADS-3, TIRADS-4 and TIRADS-5 were seen in 23.6%, 55% and 19% of the cases, respectively. The Bethesda grading system of thyroid cytology was applied on all the cases included in this study, which were graded as Bethesda Category VI. Among the malignant nodules, papillary carcinoma is the most frequent diagnosis. Medullary thyroid carcinoma, poorly differentiated thyroid carcinoma and rare cases of lymphoma were also encountered.

Conclusions:
In the light of this data, it is essential for clinicians performing ultrasound of thyroid and guided FNAC to document their sonographic impression of the nodule in an objective fashion using the TIRADS classification and correlate with the clinical and standard cytology to improve the management and learning curve and to audit their results.

Key Words: Thyroid; Malignant; Cytology;

Funding Agency: None

Pathology

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Identification of Regulatory Lymphocytes and PlGF Expressing Lymphocytes in Papillary Thyroid Cancer Using Confocal Microscope

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Introduction:
Tumor microenvironment (TME) plays essential roles in tumor growth and development. Immune cells infiltration is a common clinical finding in papillary thyroid cancer (PTC). The significance of the immune cells presence in the TME and the mechanisms of immune evasion in PTC are not well understood. Regulatory T and B cells are part of the cellular component of TME and contribute to tumor immune evasion. New subtypes of regulatory T and B cells were recently reported in many cancers including CD4+VEGFR1+ T cells, and CD19+ TGF-β+ cells. These subtypes were found to suppress the normal proliferation and differentiation of CD4 and CD8 T cells, inhibit Th1 cytokine production, and enhance the suppressive function of macrophages. Placental growth factor (PlGF) is an angiogenic factor with multiple reported immunomodulatory functions. We have previously reported that PlGF protein is highly expressed in tumor cells in PTC. This work aims to assess the presence of CD4+VEGFR1+ and CD19+ TGF-β+ regulatory lymphocytes and the expression of PlGF protein by immune cells in PTC.

Methods:
Double immunofluorescence staining was performed on tissue sections of PTC and follicular nodular disease (FND) used as controls. Primary antibodies specific for CD4, CD19, CD8, CD68, VEGFR1, TGF-β, and PlGF were used followed by appropriate secondary antibodies. Confocal microscope (LSM 700) was used for acquiring and analysis of the images. Thresholds were set using single labelled controls.

Results:
CD4+VEGFR1+ T cells and CD19+ TGF-β+ cells were detected in the lymphoid follicles inside and outside the tumor in PTC cases. These regulatory cells were not detected in the benign tissues. PlGF is co-localized with CD4, CD8, CD19 and CD68 in lymphoid follicles inside and outside the tumor in PTC. FND tissues showed no co-localization between PlGF and lymphocytes markers.

Conclusions:
Regulatory lymphocytes and PlGF expressing lymphocytes and macrophages were found in PTC microenvironment but not in benign tissue which suggest their contribution in immune mechanisms associated with malignancy.

Acknowledgment
This work is supported by college of graduate studies and research sector post graduate project number YM05/21. We acknowledge the use of Research Core Facility RCF project SRUL 02/13.

Key Words: Thyroid cancer; CD4+VEGFR1+ T cells; PlGF;

Funding Agency: College of graduate studies and research sector post graduate project number YM05/21

Pathology

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The Prevalence of High Microsatellite Instability (MSI-H) In Different Tumor Types in Kuwait

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Introduction:
Microsatellite instability (MSI) is a molecular alteration and a pattern of hypermutation detected in many types of cancer, which results from a defective DNA mismatch repair system. Detection of MSI-High (MSI-H) tumors has both prognostic and therapeutic implications because MSI status helps to predict response to chemotherapy and immunotherapy. Additionally, presence of MSI-H aids in identification of patients with lynch syndrome for whom the risk of a second malignancy increases. Our study aims to detect the incidence of MSI-H in different tumor types in Kuwait, which helps to identify the population that may have different prognosis and may benefit from certain therapeutic options.

Methods:
A retrospective study was conducted between June 2020 to November 2022. All cancer cases for which microsatellite analysis was performed are identified and retrieved from the molecular pathology lab database at Kuwait Cancer Control Center. Microsatellite analysis was performed using real-time polymerase chain reaction (PCR) which is recognized as the gold standard for MSI detection.

Results:
A total of 672 cases with 21 different tumor types were included in the study. Of those, 6.99% (n=47) showed (MSI-H) status. Some tumor types had noticeably higher MSI-H prevalence than others. The MSI-H prevalence is 11.66% in endometrial tumors, 7.76% in colorectal tumors, 12.5% in cervical tumors, 14.2% in skin tumors, 4.65% in gastric tumors, whereas 1 out of 3 tested vaginal tumors was positive for MSI-H status. Other tumor types that were tested but none of them showed (MSI-H) status include esophageal (n=16), gallbladder (n=10), pancreatic (n=18), small bowel (n=5), kidney (n=3), urinary bladder (n=6), prostate (n=7), soft tissue (n=8), breast (n=2), thyroid (n=5), lung and pleura (n=7), vulva (n= 2), ovary (n=9), CNS (N=1) and larynx (n=1).

Conclusions:
Comparing the incidence of MSI-H status in different malignancies in Kuwait with other studies worldwide, we concluded that the overall MSI-H incidence among populations differs, while the types of tumors (endometrial, cervical, colorectal, skin and gastric) exhibiting MSI-H status in our study are concordant with the most commonly reported worldwide. The attributing factors to this difference among populations should be addressed and further studied to direct the clinical practice toward a better characterization of these tumors and guide therapeutic strategies.

Key Words: Microsatellite instability; Cancer; Prevalence;

Funding Agency: None

Pathology- Inflammation

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Profiling The Expression of Long Noncoding RNA MALAT1 In Osteoblast's Inflammatory Models from Osteoarthritis Patients.

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Introduction:

In the past 20 years the role of the epigenetic regulation of genes in the pathogenesis of different diseases was established including osteoarthritis (OA). Among these epigenetic gene regulators, long noncoding RNA has emerged as an epigenetic regulator in many diseases. Metastasis Associated Lung Adenocarcinoma Transcript-1 (MALAT1) is one of the long noncoding RNA associated with different cancers and a mediator of osteoblast function and bone homeostasis. MALAT1 upregulated expression was reported in lumber intervertebral disc degeneration. Furthermore, its knockdown resulted in the inhibition of the human osteoblast cell line hFOB1.19 proliferation. Do these data indicate a role for MALAT1 in the pathogenesis of OA bone? The answer for this question may enrich the missing area in research regarding the expression and functional role of MALAT1 in OA subchondral bone. As such, the aim for this research was to profile the expression of MALAT1 in the subchondral bone tissue of patients with either knee or hip OA, and to determine the relationship of MALAT1 expression to parameters of joint
damage.

Methods:

For this purpose, a total of 17 bone biopsies and whole blood were collected from the hip and knee joints of OA patients, and bone from neck of femur of 6 non-OA patients as a normal control. Multiplex assay ELISA was used to analysis cytokines, primary osteoblasts were stimulated with human recombinant IL-1β, and the expressed genes were detected with qRT-PCR.

Results:

Statistical analysis was done using Graph Pad Prism 9. ANOVA followed by post hoc analysis of Bonferroni and Pearson correlations. P-value < 0.05 was considered as significant. MALAT1 was expressed in OA subchondral bone and its expression correlated significantly with serum DKK1 and galectin1. Furthermore, MALAT1 showed significant expression in primary osteoblasts inflammatory models.

Conclusions:

In Conclusion, long noncoding RNA MALAT1 was significantly expressed in OA subchondral bone and its induction in primary osteoblasts upon inflammatory challenge may indicate a role for this lncRNA in the pathogenesis of OA. This paves the road in the future to study its functional role in modulating OA patient primary osteoblasts and its relation to OA pathogenesis in addition to its possible role in joint damage and pain. This research was partially funded by KFAS grant CB18-63mb-01.

Key Words: Long noncoding RNA; MALAT1; OA Osteoblasts;

Funding Agency: Partial Funding KFAS grant: CB18-63mb-01

Pediatric Dentistry

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Effectiveness of Various Fluoridated Products on Dentine Tubule Occlusion

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Introduction:
AIM: The aim of this in vitro study was to compare different fluoridated products used for the alleviation of tooth hypersensitivity by the assessment of occlusion of dentinal tubules.

Methods:
Twelve extracted single rooted human teeth were sectioned to provide 70 dentinal slabs with 10 slabs in each of seven groups to evaluate five commercial products used for treating tooth hypersensitivity: 1) fluoride slow-release device (FSRD), 2) 1400ppm Fluoridated toothpaste), 3) Sensodyne toothpaste (1450 ppm F), 4) fluoride mouth wash 0.05 % NaF, 5) fluoride varnish 22,000 ppm F and two control groups: 6) artificial saliva and 7) distilled water. The total test period was 21 days and the slabs were stored in artificial saliva (except for the distilled water group) in an incubator at 37 oC. Scanning Electron Microscopy (SEM) was used to visualise the crystal apatite formation and the occlusion of the dentinal tubules. The occlusion of the tubules was scored as either: no, partial or full occlusion. Differences between the groups were assessed using a paired t test and a p value of < 0.05 was accepted as statistically significant. The study was conducted at Leeds Dental Institute, which also provided ethical clearance for the study.

Results:
SEM images showed there was significant occlusion of the dentinal tubules for all groups that had application of fluoridated materials after 21 days, compared to controls. FSRD and Sensodyne toothpaste were significantly ($p<0.0001$) superior to the other fluoride groups. Both control groups did not show any occlusion of the dentinal tubules at all.

Conclusions:
The fluoride device and Sensodyne toothpaste had a beneficial effect on tooth hypersensitivity due to their ability to occlude the orifices of exposed dentinal tubules.

Key Words: Dentine Hypersensitivity; Fluoride; Fluoride Slow Release Device (FSRD);

Funding Agency: None

Pediatrics

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General Health Status and Adverse Psychological Impact of COVID19 pandemic on Children

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Introduction:
COVID-19 is an infectious disease that was declared as a pandemic and public health emergency in late 2019 and has impacted children's mental health worldwide. This study aimed to assess the general and mental health status of children during COVID-19 pandemic and to identify the associated factors.

Methods:
A cross-sectional study conducted on children aging 3 to 12 years in Kuwait during three different stages of COVID19 pandemic (pre-total curfew, during total curfew, and post-total curfew). The psychological status was reported by the primary caregiver of each participent and sassessed using the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders criteria.

Results:
Of 2157 children aging 3 to 12 years, 853 (39.5%) reported increased level of aggression, 789 (36.6%) over-crying, 749 (34.7%) sadness, 493 (22.9%) anxiety, 429 (19.9%) anhedonia, 383 (17.8%) confusion, 274 (12.7%) nightmares, 177 (8.2%) avoidance, 174 (8.1%) physical symptoms and 121 (5.6%) bedwetting during the pandemic. Anxiety and physical symptoms were significantly increasing throughout the pandemic (20.1% vs. 21.8% vs. 27.3%, p=0.022 and 6.3% vs. 9% vs. 9.4%, p=0.031, respectively). Nightmares (11.4% vs. 11.3% vs. 15.6%, p=0.004) and anhedonia (19% vs. 17.6% vs. 23.2%, p=0.051) were significantly higher in post-total curfew, while over-crying at the beginning of the pandemic (39.8% vs. 32.1% vs. 37%, p=0.044). Among 657 children aging 8 to 12 years, 77 (11.7%) had homicidal behaviors, while 25 children (3.8%) self-reported having suicidal ideation during the pandemic. General health status also revealed disturbed sleeping pattern (84.6%), altered appetite (50.9%) and weight changes (36.9%), mainly weight gain, during this pandemic. Risk factors included being non-national, as well as having lower parental educational level and lower socioeconomic status; while protective factors involved meeting classmates, indoor and outdoor activities, and less screen time.

Conclusions:
COVID19 crisis had drastic impact on children's mental and general health, requiring serious action regarding screening them, particularly those at higher risk, and intervening accordingly. Caregivers are also advised to seek early professional help before such a stress leads to further functional and developmental impairment. Further investigations and research evaluating long-term effect of COVID19 pandemic are required to lessen its consequences and protect our future generation.

Key Words: COVID19; Pandemic; Psychological impact;

Funding Agency: None; please note that for tNONE. [please note that for the first authorship, one is above 35yrs and the other one (who is the corresponding author) is below 35yrs].

Pediatrics

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Biotin-Thiamine Responsive Basal Ganglia Disease: A Retrospective Review of the Clinical, Radiological and Molecular Findings of Cases in Kuwait with Novel Variants

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Introduction:
Biotin-thiamine-responsive basal ganglia disease (BTRBGD) is an autosomal recessive disorder caused by biallelic pathogenic SLC19A3 variants, characterized by subacute encephalopathy associated with other neurological manifestations.

Methods:
Retrospective analysis on data registry in Kuwait Medical Genetics Center of confirmed cases with BTRBGD.

Results:
Eighteen individuals were diagnosed with BTRBGD in Kuwait, including 10 (56%) males and 8 (44%) females at age ranging from newborn to 32 years and average age of diagnosis 2-3 years. All were Kuwaiti nationals except for 2 individuals. Most cases (15/18, 83%) presented initially with dystonia, confusion, convulsions, or dysarthria, while 3 individuals (3/18, 17%) were diagnosed pre-symptomatically during familial genetic screening. Symptoms resolved within 2-week with no neurological sequalae in two-third the symptomatic cases (10/15, 67%) but progressed in some cases (5/15, 25%) to severe cogwheel rigidity, dystonia and quadriparesis. Neuroradiological findings included bilateral central necrosis of basal ganglia. Molecular diagnosis revealed a previously reported homozygous SLC19A3 variant, c.1264A>G p.(Thr422Ala) in 16 individuals and two novel homozygous missense variants, c.952G>A, p.(Ala318Thr) and c.175T>C, p.(Trp59Arg) in Kuwaiti and Jordanian individuals respectively. All cases are still alive at age of 2-36 years and receiving high doses of biotin and thiamine supplementations.

Conclusions:
We report 18 cases of BTRBGD and report two novel SLC19A3 variants. In addition to the previously reported Saudi founder variant. BTRBGD is rare but requires high level of suspicion to achieve early diagnosis and initiation of biotin and thiamine supplements as the progression is greatly affected by treatment initiation timing.

Key Words: Biotin; Thiamine; Basal Ganglia;

Funding Agency: None

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ATP8A2-Related Disorder with Novel Variant in Six Individuals from Kuwait and Literature Review

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Introduction:
ATP8A2, encoded by ATP8A2, is a member of the P4-ATPase family of proteins, that flips phosphatidylserine across membranes to generate and maintain transmembrane phospholipid asymmetry which is an essential property for neuronal cell survival. Biallelic pathogenic variants in ATP8A2 have been linked to the autosomal recessive cerebellar ataxia, mental retardation, and disequilibrium syndrome (CAMRQ4: OMIM# 615268) characterized by severe hypotonia and movement disorder as well as optic, cerebral and cerebellar atrophy. The aim of this research it to expand the clinical phenotype and genotype of ATP8A2-related disorder.

Methods:
A retrospective analysis was conducted on the data registry in Kuwait Medical Genetics Center for individuals with pathogenic variants in ATP8A2 detected in Kuwait.

Results:
We report six Kuwaiti individuals from same kindred with a novel pathogenic variant in ATP8A2 (NM_016529.6:c.2212-1G>C) and describe their phenotypic characteristics. All individuals presented during infancy with an age range (0-4 month) with global developmental delay, severe hypotonia, while some have microcephaly, choreoathetoid movements, optic atrophy, strabismus, feeding difficulties and failure to thrive with survival rate of 67%. The average age at diagnosis ranged from 3 months to 12 years. Abnormal neuroradiological findings were reported in 3/6 (50%) which included cerebral atrophy, white matter hyperintensity, and hypomyelination.

Conclusions:
This is the first study describing a novel pathogenic ATP8A2 variant in six individuals from Kuwait with CAMRQ4 to further expand the genotype of the disease. Additionally, we summarize the molecular and clinical data for the 41 previously reported individuals with ATP8A2-related disorder to describe the full phenotypic spectrum.

Key Words: ATP8A2; Consanguinity; Hypotonia;

Funding Agency: None

Pediatrics

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Eicosapentanoic acid downregulates Hyperglycemia-induced of VEGF function in vascular smooth muscle cells activation

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Introduction:
Childhood obesity and type 2 diabetes mellitus (T2DM) is associated with an elevated risk of cardiovascular complications due to insulin resistance and increased lipid deposition. Omega-3-fatty acids (OFA) have been reported to exert beneficial effects against hyperglycemia-mediated inflammation and atherosclerosis, however exact mechanisms remain unknown. We examined the effect of OFA on the growth promoting function of vascular endothelium derived growth factor (VEGF) in vascular smooth muscle cells under hyperglycemic condition.

Methods:
Primary cultures of rat aortic smooth muscle cells (SMCs) were set up using DMEM/F-12 medium and confluent cultures were treated with varying concentrations palmitic acid (PA) and eicosapentanoic acid, an OFA, in the presence / absence of VEGF and /or high glucose (25mM, HG)). DNA synthesis was measured by bromo-deoxyuridine (BrdU) incorporation and gene expression of VEGF and its receptor was studied using RT-PCR.

Results:
VEGF-induced DNA synthesis was significantly ($p < 0.001$) increased following treatment of SMCs with HG when compared with those cultured with normal glucose. Addition of PA to the cell cultures further enhanced the HG-dependent stimulation of VEGF-mediated DNA synthesis. HG and PA were observed to markedly increase the gene expression of VEGF and VEGFR, however the effect was more pronounced and statistically significant ($p < 0.05$) on VEGFR. Supplementation of culture medium with OFA significantly decreased ($p < 0.01$) the HG/PA-mediated enhancement in VEGF-induced DNA synthesis. Gene expression of VEGFR was markedly reduced by OFA in cells treated with HG and or PA without any significant effect on VEGF gene expression.

Conclusions:
Our results suggest that activation of VEGF function under obesity and/or hyperglycemic conditions might contribute toward cardiovascular pathology. Omega-3-fatty acids exert beneficial effect against hyperglycemia-mediated atherogenic activity, at least partly, through downregulation of VEGF receptor.

Key Words: Obesity ; Hyperglycemia; VEGF;

Funding Agency: (This study was supported by research project MK 01/20 from Research Sector, Kuwait University).

Pediatrics

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Enzymatic Testing for Mucopolysaccharidosis Type I in Kuwaiti Newborns: A Pilot Study Toward Newborn Screening

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Introduction:
Mucopolysaccharidosis type I (MPSI) is an autosomal recessive lysosomal storage disorder characterized by deficiency or absence of α-L-iduronidase (IDUA) enzyme due to pathogenic variants in IDUA gene. Early treatment with hematopoietic stem cell transplantation and/or enzyme replacement therapy is associated with improved outcomes in this progressive multisystem disease. The diagnosis is usually delayed due to late presentation and nonspecific symptoms resulting in high morbidity and mortality. The incidence of MPSI in US is estimated to be 0.26:100,000, however, it is unknown in Kuwait. This ongoing pilot study to screen MPSI involves all Kuwaiti neonates born in Farwaniya Hospital over a period of 12-months. This study is aimed to examine the incidence of MPSI in Kuwait for inclusion in our national newborn screening program to enable early detection and adequate treatment.

Methods:
All Kuwaiti neonates born at Farwaniya Hospital, Kuwait from December 2021 to October 2022, were screened for MPSI. The screening consisted of determining IDUA enzyme activity in dried blood spots (DBS)-derived samples by Tandem Mass Spectrometry. A follow-up genetic analysis of IDUA gene is planned to screen the cases with diminished IDUA enzyme activity as second-tier testing.

Results:
A total of 547 newborns, including 284 (52%) males and 263 (48%) females, were screened. Ten of them had deficient IDUA enzyme activity but negative genetic testing for IDUA. However, we have diagnosed one additional female baby with MPSI, who belongs to Farwaniya Hospital, but the parents chose to deliver in a private hospital. She presented at age three months with recurrent upper airway infections, snoring and extensive Mongolian spots. The molecular study revealed previously reported pathogenic nonsense variant in IDUA c.1882C>T; p.(Arg628Ter), associated with severe phenotype. That being included, MPSI is estimated to be about 0.5% among tested females and 0.2% of all screened cases in Kuwait.

Conclusions:
Our study is the first to evaluate the incidence of MPSI in Kuwait. Given the single site, small number of screened babies and the short study duration thus far, it is premature to calculate the incidence of MPSI. As the study continues and more infants are screened, we will be able to estimate the incidence of the disease in our population correctly. Further studies including screening newborns in all maternity hospitals in Kuwait are needed to better calculate the actual incidence of MPSI. Our data support including MPSI in national newborn screening program to allow early initiation of treatment and thus improve the outcome of the disease.
Funding Acknowledgement:
This work was supported by Kuwait University grant MK02/21.

Key Words: Newborn screening; Mucopolysaccharidosis; Dried blood spots;

Funding Agency: Kuwait University MK02/21

Pediatrics

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L-Glutamine mitigates Bile Acid-induced mitochondrial dysfunction and IGF-1 impairment in rat hepatocyte cultures

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Introduction:
Bile acids play a major role in many vital functions of the liver and several extrahepatic tissues, however their excessive amounts are known to exert hepatotoxic effects. We have examined the effect of Glycochenodeoxycholic acid (GCDC) on key mitochondrial enzymes and Insulin-like growth factor 1 (IGF-1) function, a vital growth factor produced by the liver.

Methods:
GCDC (0-100 µM) was added to primary hepatocyte cultures in the presence /absence of L- Glutamine (L-Gln, 0-5mM). IGF-1- induced DNA synthesis was measured by incorporation of Bromo-deoxy Uridine (BrdU) following 24 hrs treatment with GCDC / L-Gln. Enzyme activities of Palmitoyl CoA oxidase (PCO) and cytochrome c (COX) oxidase were assayed in cell homogenates, and gene expression of IGF-1 receptor and carnitine palmitoyltransferase-1 (CPT-1) was evaluated by RT-PCR.

Results:
GCDC was observed to significantly ($p < 0.01$) decrease the enzyme activities of PCO and COX. GCDC was further observed to significantly ($p < 0.01$) decrease the gene expression of CPT-1. IGF-1-induced DNA synthesis and gene expression of IGF-1 receptor were significantly decreased in hepatocytes following 24 hr treatment with GCDC. Addition of L-Glutamine to the hepatocyte cultures markedly reduced GCDC-induced impairment of COX enzyme activity without any marked effect on PCO activity and CPT-1 gene expression was restored to nearly normal levels. L-Gln was further observed to significantly ($p< 0.05$) increase the gene expression IGF-1 receptor in GCDC treated hepatocytes.

Conclusions:
This study demonstrates that GCDC-induced hepatotoxic effects are mediated through mitochondrial dysfunction and impairment of growth promoting IGF-1 activity. L-Glutamine has potential beneficial effects against bile acid-induced cytotoxicity through upregulation of CPT-1 and IGF-1 receptor gene expression.

Key Words: Hepatocytes; Bile Acids; L-Glutamine;

Funding Agency: This study was supported by Research Grant MK 01/18 from Research Sector, Kuwait University

Pharmacology and Toxicology

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MKP-2/DUSP4 Silencing Enhances the Sensitivity of Breast Cancer Cells to Doxorubicin

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Introduction:
Doxorubicin (Dox) has limited efficiency in breast cancer (BC) due to drug-acquired resistance. The epithelial–mesenchymal transition (EMT) plays a major role in the survival and drug resistance of cancer cells. DUSP4/or MKP-2, mitogen activated protein kinase phosphatase, was found to be highly expressed in BC. However, its functional significance is not yet fully understood. In the present study, the possible involvement of MKP-2 in Dox-induced EMT was investigated in breast cancer cells.

Methods:
The study was approved by the ethics committee of the Kuwait Ministry of Health (2017/538). 108 retrospective formalin-fixed paraffin-embedded invasive ductal and lobular BC samples were retrieved from Adan Hospital. MDA-MB-231 and MCF-12A cells were used for MKP-2 virus infection (Adv. MKP-2), MKP-2 siRNA transfection, and Doxorubicin (1uM) stimulation. Western blot analysis, cell viability assay and flow cytometry were performed. Also, scratch and invasion assays were used.

Results:
Immunohistochemistry revealed 71.3% of patient tissues stained positively for MKP-2 while only 28.7% stained negatively. However, MKP-2 protein expression exhibited no significant relationship between BC prognostic factors, such as histological grade ($p= 0.977$), histological type ($p = 0.928$), HER2 status ($p = 0.804$), PR ($p= 0.696$), and ER ($p= 0.499$), tumor size ($p= 0.446$) and Ki-67 ($p= 0.469$). MKP-2 showed a significant staining for patients aged ≤40 years ($p= 0.04$). In MDA-MB-231 cells, MKP-2 siRNA dramatically reduced cell viability while Adv. MKP-2 reversed Dox inhibition of MCF-12A viability ($p \leq 0.05$) when compared to Dox alone. MKP-2 siRNA significantly arrested cells in G0/G1 phase and subsequently reduced both p-Cdc2 and cyclin B1. Also, significantly enhanced apoptosis as Caspase-3 ($p \leq 0.01$) and PARP ($p \leq 0.01$) were elevated upon treatment with Dox compared to control cells. In contrast, Adv. MKP-2 significantly reduced apoptosis induced by Dox in MCF-12A cells. MKP-2 siRNA abrogated cell migration and invasion induced by Dox. A reduction in matrix metalloproteinase, MMP-2 and MMP-9 when compared to Dox alone ($p \leq 0.01$, and $p \leq 0.01$, respectively) were detected. Also, a reduction in the N-cadherin, vimentin, and Snail in MKP-2 deficient cells was observed.

Conclusions:
Silencing MKP-2 attenuated Dox-induced EMT and accelerated apoptosis. Acknowledgements: Kuwait University (grant NM01/14), Research Core Facility (grant SRUL02/13)

Key Words: Dhemoresistance; Doxorubicin; DUSP4;

Funding Agency: Kuwait University (grant NM01/14), Research Core Facility, Health Science Center (grant SRUL02/13)

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The C-terminal regions of the GLP-1 and GIP receptors are not the key determinant for their differential arrestin recruitment but modulate receptor endocytosis.

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Introduction:
Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are important regulators of metabolism and mediate the incretin effect. This glucose-dependent potentiation of insulin secretion is severely impaired in patients with type 2 diabetes mellitus. While pharmacological doses of GLP-1 can overcome this impairment the same is not true for GIP. The reasons for this are unclear, however differences in the signalling profiles of the GLP-1 and GIP receptors (GLP-1R and GIPR) may contribute. The GLP-1R and GIPR are closely related members of the secretin class of G protein-coupled receptor but while GIPR predominately couples to Gs, GLP-1R can also couple to Gq. GLP-1R is also a robust recruiter of arrestin whereas arrestin recruitment to GIPR is relatively poor. The aim of this study was to identify the role of the C-terminal region of the two receptors in their differing signaling behavior.

Methods:
Chimeric receptors, where the C-terminal tail of one receptor was replaced with that of the other were constructed. Bioluminescent Resonance Energy Transfer (BRET)-based assays were used to compare mini-Gs, Gq, and arrestin recruitment and internalization of the chimeric receptors with that of wild-type receptors expressed in HEK-293 cells.

Results:
Replacement of the C-terminal tail had no significant effect on either Gs or Gq coupling to either GLP-1R or GIPR. Furthermore, his substitution had no effect on arrestin recruitment to GLP-1R nor did it rescue arrestin recruitment to GIPR. In contrast, replacement of the C-terminal tail enhanced agonist-mediated internalization of GIPR but inhibited that of GLP-1R.

Conclusions:
The C-terminal region of GLP-1R and GIPR is not the key determinant of their differing ability to recruit arrestin but modulates receptor endocytosis.

Key Words: GLP-1R; GIPR; Signalling;

Funding Agency: Research Sector, Kuwait University. YM02/19.

Pharmacology and Toxicology

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Apigenin attenuates LPS-induced neurotoxicity and cognitive impairment in mice via promoting mitochondrial fusion/mitophagy: Role of SIRT3/PINK1/Parkin pathway

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Introduction:
Mitochondria are highly dynamic organelles and crucial for neuronal function and survival. However, mitochondria could not exert their function without the essential dynamic balance between mitochondrial fusion and fission, along with the selective elimination of damaged mitochondria through effective mitophagy. Mitochondrial fusion is a two-step process that necessitates the fusion of the outer and inner mitochondrial membranes, through the action of the mitofusin1/2 (MFN1, MFN2) and ocular atrophy 1 (OPA1). PINK1-Parkin mitophagy pathway is the most extensively studied. Under normal conditions, low levels of phosphatase and tensin homolog (PTEN)-induced putative kinase 1 (PINK1) are maintained through complex processing. In damaged mitochondria, PINK1 is stabilized on the outer mitochondrial membrane, with the consequent recruitment of Parkin, the E3 ubiquitin ligase. The latter translocates to the mitochondria from the cytosol and instigate the degradation process. Mitochondrial mitophagy and biogenesis play a pivotal role in governing cellular fate. Alteration of the NAD+ metabolic pathway is proposed to be implicated in lipopolysaccharide (LPS)-induced neurotoxicity and mitochondrial dysfunction in neurodegenerative diseases. Apigenin, a naturally-occurring favonoid, has been reported to maintain NAD+ levels and to preserve various metabolic functions.This study aimed to explore the effect of apigenin on mitochondrial SIRT3, a NAD+-dependent deacetylase, activity as a mediator through which it could modulate mitochondrial quality control and to protect against intracerebrovascular ICV/LPS-induced neurotoxicity.

Methods:
Seventy-two male Swiss albino mice received apigenin (40 mg/kg; p.o) for 7 consecutive days. One hour after the last dose, LPS (12 µg/kg, icv) was administered. Morris Water Maze and Y-maze test were used to assess behavioral and cognitive parameters. Protein expression of fusion markers (MFN2, OPA1), biogenesis markers (PCG-1, TFAM) and mitophagy markers (PINK1, Parkin LC3I and LC3II) were evaluated. Mitochondrial SIRT3 was measured fluorometrically and mitochondrial ATP was evaluated colorimetrically.

Results:
Data obtained from the current study revealed that apigenin administration significantly ($p<0.05$) guarded against neuronal degenerative changes and maintained a normal count of intact neurons in mice hippocampi verified using TEM. Consequently, it inhibited the deleterious effect of LPS on cognitive functions. Apigenin was effective ($p<0.05$) in preserving the NAD+/NADH ratio to boost mitochondrial sirtuin-3 (SIRT3), activity, and ATP production. It conserved normal mitochondrial features via induction of the master regulator of mitochondrial biogenesis, peroxisome proliferatoractivated receptor γ (PPARγ) coactivator-1α (PGC-1α), along with mitochondrial transcription factor A (TFAM) and the fusion proteins, mitofusin 2 (MFN2), and optic atrophy-1 (OPA1). Furthermore, it increased phosphatase and tensin homolog (PTEN)-induced putative kinase 1 (PINK1) and parkin expression as well as the microtubule-associated protein 1 light chain 3 II/I ratio (LC3II/I) to induce degradation of unhealthy mitochondria via mitophagy.

Conclusions:
These observations reveal the marked neuroprotective potential of apigenin against LPS-induced neurotoxicity through inhibition of NAD+ depletion and activation of SIRT3 to maintain adequate mitochondrial homeostasis and function.
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Funding Agency: None
Key Words: NAD+, SIRT3, Apigenin, Mitochondrial fusion, Mitop; ICV; LPS;

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Pharmacological Investigation of Vitamin E with Combined Oral Contraceptives on INHBA Gene against PCOS that Intricate through Melatonin Pathway

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Introduction:
The interaction of environmental and genetic risk factors plays a role in the aetiology of metabolic disease. The most prevalent endocrine and metabolic condition in women of reproductive age is polycystic ovarian syndrome (PCOS). Disruption of the circadian rhythm and melatonin is a significant risk factor for PCOS.Obj: To evaluate the effect of vitamin E in combination with combined oral contraceptive (COC) against continuous light induced PCOS through hormonal parameters, oxidative stress markers and inhibin beta-A (INHBA) gene targeting melatonin- protein kinase C (PKC) pathway.

Methods:
Binding affinity of INHBA with vitamin E and COC was predicted by an in-silico method using AutoDock vina software. For In-vivo study (IAEC/240/2021), female Sprague Dawley (SD) rats were placed in the light experiment box after being randomly divided into control and experimental groups. The control group followed a circadian rhythm of a 12-hour: 12-hour light/dark cycle (L/D group) whereas, the experimental groups (4) were subjected to a 12-hour: 12-hour light/light cycle (L/L group) for 8 weeks for PCOS induction which was confirmed by serum testosterone (4.82±1.07). For treatment, group 3 (DRSP) group was administered orally with Drospirenone (DRSP) (0.4 mg/ kg) + ethinyl estradiol (EE) (2.4 µg/ kg), group 4 was given vitamin E (25mg/kg) in addition to the previous regime and group 5 was administered with vitamin E 50mg/kg in addition to the DRSP group regime for the period of 2 months. Moreover, the hormonal parameters like serum testosterone, FSH, melatonin and oxidative stress was estimated by GSH and FRAP assay. INHBA gene expression was scrutinized to correlate the circadian rhythm and oxidative stress targeting melatonin PKC pathway. Res: According to in-silico study, vitamin E and drospirenone have a higher binding energy and a good affinity for the INHBA (-8.2 kcal/mol and -7.7 kcal/mol, resp). In vivo data demonstrated a significant decrease in the increased testosterone levels ($P<0.05$), as well as alterations in FSH ($P=0.78$) and melatonin ($P=0.13$) when compared to control group. IHNBA gene expression was also significantly elevated which activates FSH secretion in pituitary gland.

Results:
According to in-silico study, vitamin E and drospirenone have a higher binding energy and a good affinity for the INHBA (-8.2 kcal/mol and -7.7 kcal/mol, resp). In vivo data demonstrated a significant decrease in the increased testosterone levels ($P<0.05$), as well as alterations in FSH ($P=0.78$) and melatonin ($P=0.13$) when compared to control group. IHNBA gene expression was also significantly elevated which activates FSH secretion in pituitary gland.

Conclusions:
Supplementation of vitamin E combined with COC could be effective against PCOS as if influences oxidative stress which indistinctly influences circadian rhythm and melatonin PKC pathway.

Key Words: Polycystic ovary syndrome; Vitamin E; Melatonin;

Funding Agency: None

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Vasoconstriction Effect of TAAR-1 Agonists in the Isolated Perfused Rat Kidney: Signaling Pathways and the Effect of Hypertension

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Introduction:
Trace amines such as tryptamine and 3-iodothyronamine (T1AM) are endogenous compounds present in mammalian tissues. These compounds produce a variety of effects both centrally and peripherally. They activate specific surface G-protein coupled receptors (GPCRs), known as trace amine-associated receptors (TAARs). The objective of this study was to investigate the vasoconstrictor effect of TAAR1 agonists in normotensive and hypertensive rats, and the possible signaling mechanism involved.

Methods:
Male Wistar Kyoto (WKY, n=52) and Spontaneously Hypertensive Rats (SHR, n=52) age 12-14 weeks were used in this study. Animals were sacrificed and the kidneys were cannulated, and placed in perfusion chamber with Krebs' solution using a multichannel masterflex peristaltic pump. Dose-response curves were established for tryptamine and T1AM before and in the presence of nifedipine (1µM), Y-27632 (1µM), GF-109203X (1µM), and Tempo (0.1mM). Changes in perfusion pressure were recorded through a transducer connected to a Lectromed. The TAAR1 mRNA expression was assessed using real-time polymerase chain reaction (RT-PCR). Data were statistically analyzed by Student's t-test.

Results:
Tryptamine- and T1AM-induced significant increase in perfusion pressure of kidney preparations from WKY and SHR rats. The increase in perfusion pressure was significantly greater in preparation from SHRs ($p < 0.05$). Nifedipine (1µM), Y-27632 (1µM), and GF-109203X (1µM) significantly reduced the vasoconstriction response to tryptamine and T1AM in perfused kidney preparations from WKY and SHRs without differentiating between the two groups. Whereas, Tempo (0.1mM) were more effective in preparations from SHRs compared to WKY rats. TAAR1 expression was significantly greater in SHRs than in normotensive WKY rats.

Conclusions:
The results obtained from this study would suggest that TAAR1 receptors are involved in tryptamine- and T1AM-induced response in the WKY and SHR rats perfused kidney. The responses were also inhibited by nifedipine, Y-27632, GF-109203X, and Tempo. This suggest that these responses involved influx of extracellular calcium, Rho-kinase and PKC pathways of calcium sensitization, reactive oxygen species, and increased expression of TAAR1 in preparations from SHRs compared WKY rats. Funding/Acknowledgments: This study was supported by the College of Graduate Studies and the Research Sector (YM 02/21). Special thanks to Research Core Facility and the Animal Resource Center, Kuwait University.

Key Words: Trace amine-associated receptors ; Tryptamine ; 3-iodothyronamine;

Funding Agency: College of Graduate Studies and the Research Sector (Grant No. YM 02/21)

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Role of N-terminal residues of CCL19 and CCL21 in binding and activation of CCR7

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Introduction:
Chemokines are chemotactic cytokines which mediate cell trafficking and play a key role in mobilisation of leukocytes. More recently, chemokines and their cognate receptors have been shown to be key players in different aspects of cancer biology. In particular, chemokines CCL19 and CCL21, acting on their associated receptor CCR7, are postulated to be key drivers of tumour expansion in a number of malignancies including breast, colon, gastric, & thyroid cancers. For example, CCL21 mediates the recruitment and co-localization of naïve lymphocytes and antigen-stimulated dendritic cells (DC) into T-cell zone within lymph nodes. Therefore, CCL21 does play a critical role in boosting of immune response to tumours. It has been reported that the cleavage of the N-terminal residues of CCL21 (SDGGAQ) and of CCL19 (GTNDAE) renders both peptides incapable of activating CCR7. However, little is known about the nature of the interactions that occur between the N-terminal residues of CCL19 or CCL21 and the CCR7 receptor. The aim of this study is to investigate the role of the residues in the N-terminus of CCL19 and CCL21 in CCR7 activation and to use this information in the discovery of novel CCR7 agonists and antagonists.

Methods:
To achieve this, we used solid phase peptide synthesise to prepare a number of short (three to seven amino acids) peptides inspired by the seven N-terminal amino acid residues of CCL19 and CCL21. Then, using a number of in vitro assays such as calcium flux, Cell motility (scratch assay), trans-well (Boyden chamber), and Western blotting. we pharmacologically characterised their ability to activate CCR7 or block the activation of CCR7. Furthermore, we used computational modelling to rationalise and better understand the role of these short peptides in activation of CCR7.

Results:
Our results demonstrate that these peptides, as well as some analogous peptidomimetic small molecules are indeed capable of acting as agonists or antagonists of CCR7. Our observation is that SDG acts as an agonist of CCR7 albeit with a reduced potency. SDGGA and SDGGAQD also activate CCR7 and are agonists at the receptor, however, pharmacology of AQD appears complex. Its behaviour resembles that of an antagonist or similar to a reverse agonist or a self-inhibiting agonist. The potency of the peptides appears to be 100-fold less than CCL21 itself. SDG peptide was shown to be potent, the SDG analogues MDG, SNG and non-peptide molecule compound 71 do seem to have ability for blocking P-MAPK pathway strongly. This suggests our original hypothesis, that modification of serine can afford antagonists.

Conclusions:
These observations are on the whole confirmed through a number of in vitro functional assays and are confirmed to be through CCR7 since CCR7 knockdown abrogates cells response to the peptides. Future work is focused on demonstrating that these CCR7 agonists can attract DC, lymphocyte into tumour, thus improving the efficacy of immunotherapeutic antitumour agents.

Key Words: Chemokines; CCR7; Immunotherapeutic anti-tumour agents;

Funding Agency: None

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Guanfacine Normalizes the Overexpression of Presynaptic α-2A Adrenoceptor Signaling in a Chronic Animal Model of Type 1 Diabetes

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Introduction:
Uncontrolled type 1 diabetes mellitus (T1DM) is associated with several complications, including neuropathic pain, which is difficult to manage with currently available drugs. Descending noradrenergic (NAergic) neurons possess antinociceptive activity. We have recently shown that chronic administration of guanfacine (GF), a selective alpha-2A adrenoceptor agonist, ameliorates diabetic neuropathic pain. This study was aimed to investigate the hypothesis that the development of neuropathic pain stems from a defect in the peripheral and/or central NAergic system activity in T1DM and chronic administration of GF reverses the defect of the NAergic system.

Methods:
To infer the regulatory role of this system, male Wistar rats (two-three months old; 200-250 grams; n=110) were treated with streptozotocin (STZ) (55 mg/Kg, i.p.) or its vehicle. Guanfacine (0.6 mg/Kg) was administered i.p. daily for a period of two weeks after the development of thermal hyperalgesia and, cold and mechanical allodynia. The expression and localization of α-2A adrenoceptors in the dorsal root ganglia and key regions of the central nervous system, including pons and lumbar segment of the spinal cord were examined using qRT-PCR, Western blotting, and immunofluorescence-based techniques. Differences were considered significant at $p \leq 0.05$ (one/two-way analysis of variance).

Results:
The data revealed that the alpha-2A adrenoceptors were upregulated both at the mRNA and protein levels in the neuronal tissues of STZ-T1DM rats. Furthermore, presynaptic synaptosomal-associated protein-25-labeled alpha-2A adrenoceptors were upregulated in the spinal cord lumbar region of STZ-T1DM rats. Interestingly, the levels of postsynaptic density protein-95-labeled lumbospinal alpha-2A adrenoceptors remained unaltered as a function of T1DM. Chronically administered GF to T1DM animals downregulated the upregulation of neuronal alpha-2A adrenoceptors. Furthermore, chronic GF administration mitigated T1DM-induced upregulation of presynaptic α-2A adrenoceptors in the spinal cord lumbar region. However, this effect of the drug was not seen in the lumbospinal postsynaptic fraction.

Conclusions:
Together, these findings demonstrate that alpha-2A adrenoceptors, key component of the descending neuronal autoinhibitory pathway, may function as a potential therapeutic target in the treatment of diabetic neuropathic pain. A:KU: YM05/19, Animal Resources Center, and Research Core Facility: SRUL02/13 and GM01/13.

Key Words: Diabetic neuropathic pain; Alpha-2A adrenoceptors; Guanfacine;

Funding Agency: Kuwait University, YM 05/19

Pharmacology and Toxicology

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Targeting Canonical Wnt/beta Catenin Signaling Pathway as a Therapeutic for Alzheimer's Disease by Anthocyanins from Flower Bract of Musa acuminata. Colla.

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Introduction:
The current treatment for Alzheimer's Disease (AD) is far from adequate. It is critical to discover potent therapy from natural sources as they impart lesser neurologic side effects. Cyanidin (Cyn) is an anthocyanidin having antioxidant properties. Objective: To evaluate the efficacy of cyanidin isolated from outer flower bracts of Musa acuminata Colla (a banana plant species) and to decipher its mode of action in the Bisphenol-A(BPA) induced in-vitro AD model.

Methods:
Cyanidin was isolated from outer flower bracts of Musa acuminata Colla using Amberlite XAD-7HP column. In-silico (computational) study was done using Auto Dock-v software to evaluate the binding affinity of cyanidin identified in the extract of Musa acuminata Colla with 10 target proteins involved in wnt/β-catenin pathway. In-vitro studies were carried out using PC-12 cell lines. Dose-response study was done to determine the toxicity of the compound. PC-12 cell cultures were divided into four groups and were treated with vehicle (DMEM medium), BPA(50ng/ml), BPA(50ng/ml)+Cyn-10µg/ml or BPA(50ng/ml)+Cyn-90µg/ml for 24 hours. Acetylcholinesterase (AChE) enzyme inhibition assay, neurite outgrowth assay, intracellular reactive oxygen species (ROS) assay and quantitative gene expression were evaluated in all groups.

Results:
Cyanidin showed a remarkable binding affinity with all proteins involved in wnt/β-catenin pathway(≥-7.5kcal/mol), the highest binding affinity was with AChE(-10kcal/mol). IC50 value in cell viability assay for cyanidin was found to be 92.3µg/ml. Accordingly two gradient doses below this value (90µg/ml as high dose and 10µg/ml as low dose) were selected for further analysis. AChE inhibition potential of cyanidin was comparable to that of Donepezil (cyanidin: 24.82µg/ml vs Donepezil: 14.26µg/ml; p=0.0502). Statistically significant difference ($p<0.05$) was found in expression of genes involved wnt/β-catenin pathway. The neurite length was longest at 72 hours in cultures treated with cyanidin (90µg/ml) along with nerve growth factor (NGF, 50ng/ml), compared to cells treated with NGF alone (320±22.51µm Vs 223±22.70µm; $p<0.001$). The relative fluorescence in ROS assay was statistically significant between the cell groups(BPA-1796 vs BPA+Cyn-90µg/ml-2248;$p<0.0001$)

Conclusions:
Cyanidin isolated from bract of Musa acuminata Colla is an excellent anti-oxidant, enhance neurite outgrowth and provides neuroprotection in an in-vitro AD model by restoring wnt/β-catenin pathway aberrated by BPA exposure.

Key Words: Alzheimer's Disease; Bisphenol A; wnt/beta catenin signaling;

Funding Agency: None

Pharmacology and Toxicology

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Outpatient Psychotropic Drug Interactions in a Public Psychiatry Hospital in Bahrain: An Audit Study

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Introduction:
Background: Psychotropic polypharmacy is particularly common which puts psychiatric patients at high risk for developing drug-drug interactions.

Objective: We aimed to study potential interactions between psychotropic medications prescribed within the outpatient psychiatry setting.

Methods:
This was an audit study, which targeted a sample of outpatient prescriptions ordered within the outpatient clinics of the main psychiatry hospital in Bahrain over 2017. We studied the grade and correlates of interactions between psychotropic drugs.

Drug interactions analysis: The selected prescriptions were systematically and retrospectively examined for the presence and degree of drug interactions by using the Medscape Multi-drug Interaction Checker. Detected interactions were graded according to their clinical relevance as listed in Medscape into three categories: Minor, significant and serious. Interactions were graded to be minor if they were not found to be of clinical importance or significance, or if the effect of the interaction has not been established. Comparatively, interactions were labeled to be significant if they were expected to result in a significant interaction that necessitated close monitoring. However, an interaction was said to be serious if it could cause potentially serious or life-threatening interaction that needed to be monitored closely whilst using alternative drugs is recommended.

Results:
The total number of prescriptions in our sample was 992 (56.1% males, 43.9% females). Psychotropic polypharmacy was detected in 842 prescriptions (84.9%). Potential interactions between psychotropic drugs were observed in 550 prescriptions (56.4%). The degree of interaction was minor in 43 prescriptions (7.8%), significant in 419 prescriptions (76.2%) and serious in 88 prescriptions (16%). Schizoaffective disorder subjects were the most likely to suffer from interactions (64.6%) whereas prescriptions issued for those who had schizophrenia contained the least number of interactions (51.6%). The total number of interactions was strongly associated with polypharmacy ($p < .001$), and gender ($p < .01$), but not with age ($p > .05$) or diagnosis ($p > .05$).

Conclusions:
High prevalence of polypharmacy and interactions between psychotropic medications were observed in our sample, particularly of the significant grade.

Key Words: Drug-drug interactions; Plasma level; Polypharmacy;

Funding Agency: None

Pharmacy

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Knowledge and Practice of Foot Self-Care Among Patients with Diabetes Attending Primary Healthcare Centres in Kuwait: A cross-Sectional Study

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Introduction:
Diabetes mellitus (DM) is a major cause of morbidity and mortality worldwide. Many patients have one or more risk factors for diabetic foot diseases, such as diabetic peripheral neuropathy (DPN). Patients can overcome such complications through good knowledge and practice of foot self-care. This study aims to evaluate the knowledge and practice of foot care among DM patients and to identify those at risk for developing DPN.

Methods:
This is a cross-sectional study using a self-administered questionnaire. Adult patients with a diagnosis of DM for at least 1 year were randomly selected. Data were analysed using SPSS, version 26.

Results:
A total of 357 patients participated, giving a response rate of 87.3%. Most patients (n = 283, 79.3%) showed good knowledge. In comparison, less than one-third of patients (n = 110, 30.8%) practiced good foot care. Approximately 17.4% of the patients had a higher risk of developing DPN. University students had lower odds of having good knowledge about foot care [OR: 0.19 (95%CI: 0.04–0.86)]. On the other hand, patients who reported having diabetes for a long duration (10 years and above) [OR: 1.88 (95%CI: 1.11–3.18)] and patients who did not have any other comorbidities [OR: 0.49 (95%CI: 0.26–0.90)] had higher odds of having good foot care knowledge. Patients who were on oral hypoglycaemic agents (OHAs) only had lower odds [OR: 0.63 (95%CI: 0.39–1.00)] of practicing good foot care. Patients who were using combination therapy with OHAs and insulin had a higher risk [OR: 2.67 (95%CI: 1.11–6.41)] of developing DPN. On the other hand, patients who reported that they did not have a previous history of a foot ulcer had a lower risk of developing DPN [OR: 0.21 (95%CI: 0.09–0.47)].

Conclusions:
To improve the foot care knowledge and self-care practice of patients, healthcare providers (HCPs) need to support patients through educational programmes and appropriate training.

Key Words: Diabetes; Footcare; knowledge, Practice and attitude;

Funding Agency: None

Pharmacy

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Comparing Polypharmacy and Drug-Related Problems Between Elderly and Younger Patients With Breast Cancer In The Kuwait Cancer Control Centre (KCCC).

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The Kuwait Cancer Control Centre (KCCC)

Introduction:
Increased medication burden among cancer patients is expected to compromise patients' tolerance and the consequent therapeutic outcomes, especially among older patients with multiple chronic comorbidities. Polypharmacy and medication appropriateness are not usually assessed during the baseline assessment in the clinical practice of oncology. The current study compares the prevalence of polypharmacy and drug-related problems between two age cohorts in the Kuwait Cancer Control Centre (KCCC).

Methods:
In a comparative population-based cross-sectional study, 180 newly diagnosed breast cancer patients were included and divided into two cohorts based on their age (<60 and ≥60 years old). The baseline number of medications was documented. Drug-related problems were identified and compared between the two age cohorts using the Chi-Square test.

Results:
The median number of medications consumed by patients was 2.5 (range 0-13) and 0 (range 04) in older and younger patients, respectively (p-value <0.001). Only 20% of older patients versus none of younger patients were taking at least five medications. A higher prevalence of drug-related problems was detected among older patients than younger patients (38.3% versus 12.5% respectively; OR 5.48, pvalue <0.001). Uncontrolled conditions, mainly diabetes and hypertension, were the most documented drug-related problems in both age cohorts.

Conclusions:
Breast cancer patients aged 60 years and above were at a 5.48 higher risk of developing drug related problems at baseline compared to younger patients. This could be attributed to the higher comorbidity burden among older patients. Both age cohorts maintained similar drug-related problems prevalence, with uncontrolled diabetes and hypertension being the most common and adverse drug reactions being the least common.

Key Words: Breast cancer; KCCC; CANCER;

Funding Agency: None

Pharmacy

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Quality by Design Approach for a Multicomponent Quantification Using HPLC-PDA and HPLC-MS: Application to Dosage Form and Biological Body Fluids

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Introduction:
A multicomponent pharmaceutical that contains loratadine, paracetamol, and pseudoephedrine is commonly used as a treatment for common cold and allergic rhinitis. Objectives: To separate and quantify the three analytes in the dosage by using High performance liquid chromatography-photo diode array and High performance liquid chromatography - mass spectrometry

Methods:
A quality by design strategy was followed to achieve the challenging separation. Shimadzu Nexera-i LC-2040C 3D instrument was used for separation. Screening and optimization steps were carried out to investigate the effect of many factors on the studied responses with a minimum number of runs. A total of 100mg of standard and working solutions were prepared. An Inertsil C-18 was utilized as a stationary phase: gradient and isocratic elution modes were used for HPLC-PDA and SPE-HPLC-MS, respectively. LabSolutions and Design-ExpertR 11 software were used for data acquisition and statistical analyses, respectively. Validity of data was ensured in terms of linearity and range, accuracy, precision, limit of quantification and detection, robustness, recovery and matrix effect, selectivity and stability.

Results:
The ANOVA of the factorial model showed that only three factors were significant: the % acetonitrile (factor A), flow rate (factor B), and pH (factor C) were significant. The detection of the analytes' peaks was carried out using a PDA detector at 248nm for loratadine and paracetamol, and 214 nm for pseudoephedrine. The second method was SPE-HPLC-MS, where the three analytes and desloratadine, the active metabolite of loratadine, were quantified in spiked plasma and urine, using betamethasone valerate as an internal standard. The recovery of the analytes from body fluids was above 96%, and the LOQ was below 0.5 ng/mL. The validation of the developed HPLC-PDA method was achieved as per ICH guidelines, whereas the HPLC-MS method was validated according to FDA guidelines for bioanalytical method validation.

Conclusions:
The developed HPLC-PDA method could be used in quality control laboratories for separation of the mixtures, while the SPE-HPLC-MS method could be used in pharmacokinetic studies to detect and quantify the mentioned drugs in biological body fluids. Acknowledgments: The authors express their sincere gratitude to the Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Kuwait University, for providing the facilities and instruments used to accomplish this study.

Key Words: HPLC; MS; Quality by design;

Funding Agency: None

Pharmacy

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Analgesics Use in Elective Metabolic and Bariatric Surgery, A Single Center Experience in Kuwait

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Introduction:
Kuwait is considered one of the top countries in the prevalence of obesity. Inadequate pain management in surgical patients may result in delayed recovery and postoperative morbidity. To date, there are no local studies evaluating the peri-operative pain management practices in elective metabolic and bariatric surgeries (MBS). This study reviews the practice in elective MBS and its impact on post-operative pain management.

Methods:
A retrospective pre- and post-intervention design was adopted. This study was conducted in a single center in Kuwait from September 11 to December 15, 2022, and patients were divided into pre and post intervention groups. Inclusion criteria were patients undergoing MBS, aged 18 or above. Demographics, body measurements, medical history, medications, intraoperative, operative, and post operative data were collected anonymously. Analysis was performed using Excel software. The intervention consisted of educational seminar in line with best analgesics use practices conducted with oral presentation delivered by PharmD trainees. In addition, hard and digital copies of educational material was shared on surgical wards, operating room and post-anesthesia care unit (PACU).

Results:
A total of 50 patients were enrolled, 25 patients in the pre-intervention group, and 25 patients in the post-intervention group. Around 92% of the patients in the pre-intervention group and 72% in the post-intervention group had a BMI ≥ 40 (kg/m^2). About 92% of the patients enrolled in both the pre- and post-educational group, received a multimodal intraoperative analgesia comprising of paracetamol with either an NSAID or an opioid, or both. There was no difference between the number of patients who received a multimodal analgesic approach in both groups. Pain assessment was conducted in 32% (n= 8) of the patients who were reviewed after the educational seminar.

Conclusions:
This study evaluated the use of analgesics in patients undergoing MBS, including the choice and types of medications used in the perioperative periods. There was no difference seen in the number of patients who received a multimodal analgesic approach following the delivery of the tailored educational seminar. However, this study highlighted the need of incorporating pain assessment tools to current practices to assist in evaluating pain control postoperatively.

Key Words: Multimodal analgesia ; Laparoscopic bariatric surgery; Pain;

Funding Agency: None

Pharmacy

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Biotransformation of Vinpocetine by Cunninghamella echinulata

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Introduction:
Microorganisms such as bacteria, fungi and actinomycetes are known for being biocatalysts. In addition, microbial models may be used to predict metabolic pathways in mammals. Moreover, microbes are capable of giving an array of derivatives in adequate quantities that are difficult to obtain from mammals or synthesis.Vinpocetine (VPN) is a semisynthetic monoterpene indole alkaloid that is used as a nutraceutical in some countries. Vinpocetine is phosphodiesterase inhibitor (PDI), antioxidant and anti-inflammatory. In addition, vinpocetine is reported to have a protective effect against neurodegenerative disorders and to treat cerebrovascular disorders including strokes. Lately, vinpocetine is proven to have a neuroprotective effect in manganese-induced Parkinson's disease and considered the future adjuvant therapy in COVID-19 due to its anti-inflammatory effect which protects lung tissue against damage. This work aims at exploring the capability of the fungus Cunninghamella echinulata to metabolize vinpocetine and isolating and predicting the structures of its potential metabolites.

Methods:
Forty different species of fungi and actinomycetes were screened, following the two-stage screening protocol, for their ability to metabolize vinpocetine. Positive hits were, then, detected via chromatographic comparison with substrate and culture controls. Cunninghamella echinulata was selected as a definite hit for preparative-scale fermentation and isolation of the produced metabolites using different chromatographic techniques. Finally, isolated metabolites were identified using different spectroscopic techniques.

Results:
Cunninghamella echinulata gave 3 metabolites which were isolated and purified. Their structures were elucidated using different spectroscopic techniques including 1D and 2D-NMR and HRMS.

Conclusions:
Three metabolites of vinpocetine were produced and isolated from Cunninghamella echinulata culture. Biological activities evaluation of these metabolites is underway.Acknowledgement: Spectral analysis were done at RSPU facilities, College of Science, Kuwait University, supported by grants numbers GS01/01 and GS01/03.

Key Words: Vinpocetine; Microbial Biotransformation; Vinpocetine N-Oxide;

Funding Agency: Spectral analyses were done at RSPU facilities, College of Science, Kuwait University, supported by grants numbers GS01/01 and GS01/03.

Pharmacy

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Simulation for Continuing Pharmacy Education: Development and Implementation of a Simulation-Based Workshop on Medicines Reconciliation for Pharmacists

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Introduction:

Simulation has been increasingly used to train healthcare professionals on clinical skills. Little is published on simulation-based education in the context of continuing pharmacy education (CPE) of pharmacists. Medicines reconciliation is an essential clinical skill which involves preparing an accurate and updated list of patient's medications at each transition of care.

Objectives

To describe the development, implementation and evaluation of simulation-based workshop to train hospital pharmacists on medicines reconciliation in Kuwait. The study aimed to explore pharmacists' perceptions about simulation use in CPE. It also assessed the impact of the workshops on pharmacists' attitudes toward, knowledge and comfort level to apply medicines reconciliation.

Methods:

One hundred ten pharmacists attended eleven simulation-based workshops. Data were collected using focus groups and self-administered surveys in a mixed-method research design. Focus groups were audio-recorded, transcribed verbatim, and analyzed for content. Descriptive statistics were used to report surveys' findings.

Results:

The workshops were well-received by pharmacists. Few pharmacists recalled previous exposure to simulation in CPE activities. Pharmacists' perceived challenges to simulation integration into their professional training were the need for good preparation/setting, qualified faculty, well-trained simulated patients and time constrains. Participants felt that simulation enhanced their attitudes toward, knowledge and comfort level to apply medicines reconciliation. They rated their knowledge level as having increased by 62.3% and comfort level as having increased by 37.0%. They overwhelmingly welcomed more integration of simulation in CPE activities.

Conclusions:

A simulation-based continuing education workshop was well-received by pharmacists and enhanced their self-reported knowledge, comfort level and preparedness to apply medicines reconciliation. Efforts are needed to expand the use of simulation in CPE activities for the development, refinement and maintenance of the clinical skills of pharmacists in Kuwait.

Key Words: Simulation; Continuing pharmacy education;

Funding Agency: None

Physiology

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The Effect of Interleukin-6 On GABAergic Inhibitory Tone in the Hippocampus of Prenatally Immune Challenged Rats: A Sex-Dependent Effect.

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Introduction:
Experimental evidence suggests that maternal immune activation (MIA) with bacterial active ingredient lipopolysaccharide (LPS) leads to the reduction in the inhibitory tone of the GABA interneurons in the offspring's hippocampus. In this study we sought to assess whether IL-6 mediates the long-lasting impact of LPS on the reduced inhibitory tone-in the hippocampus in juvenile offspring.

Methods:
All experiments were approved by Kuwait University Health Sciences Centre Animal Ethics Committee. Pregnant Sprague Dawley rats were given daily intraperitoneal injections of either pyrogen-free saline or lipopolysaccharide (LPS, 100 µg/Kg) in the presence or the absence of an IL-6 neutralizing antibody (IL-6Ab, 10 µg/Kg), on gestation days (GD) 15, 17 and 19. Each rat group consists of 5-6 pregnant rats. On postnatal day (PND) 21, male and female pups were separated from their moms and housed 4 per cage. On PND 30, parvalbumin- and somatostatin-containing inhibitory interneurons, and markers of inhibitory synapses including the vesicular GABA transporter (VGAT) and the GABAergic synapse organizer (Gephyrin) were monitored in the hippocampus using fluorescent immunohistochemistry. All data were compared using two-way ANOVA followed by Student-Newman-Keuls post-hoc test. Statistical significance is declared when the p value was less than 0.05.

Results:
MIA did not induce alterations in the Gephyrin and VGAT density in the hippocampus. The maternal co-administration of IL-6Ab and LPS induced a significant increase in these inhibitory markers in the CA1 ($p=0.0298$ and $p=0.0255$, respectively) and inhibitory synapses in CA1 and CA2 regions of the hippocampus ($p=0.0121$ and $p=0.0206$, respectively) in female but not male rat offspring. However, prenatal LPS did not affect the cell density of either parvalbumin- or somatostatin-containing interneurons in the hippocampus of both male and female offspring.

Conclusions:
MIA had no significant effect on the density of either inhibitory synapses or that of inhibitory interneurons. Neutralizing LPS-induced IL6 during pregnancy led to an increase in inhibitory synapses, namely in the hippocampal regions CA1/CA2 of female rats. The physiological significance of these finding requires further exploration.

Key Words: GABA interneurons ; Inhibitory synapses ; Lipopolysaccharides ;

Funding Agency: College of Graduate Studies, Kuwait University. Research Sector: Grant No. YM04/21.

Physiology

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Resistance Exercise Exerts a Protective Functional Effect in Sciatic Nerve Crush Injured Rats

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Introduction:
Peripheral nerve injury can lead to disability due to motor and sensory deficits. Rehabilitative aerobic exercise has been shown to improve functional recovery after sciatic nerve injury. Our objective was to assess whether resistance exercise (RE) prior to sciatic nerve crush injury (SCI) is protective. For this, we assessed the impact of RE on the functional recovery and levels of myelin basic protein (MBP) after SCI.

Methods:
Sprague Dawley rats (n=20) were divided into control and RE (10/group) after the approval of the animal ethics committee, Kuwait University. The RE rats pulled progressively increasing loads tied to their tail in a tunnel (3x/week) for 10 weeks, while the control rats walked through the tunnel without pulling any load. After 10 weeks, the left leg of each rat was subjected to a moderate SCI using a micro-mosquito forceps, while the right leg was used as sham. Functional recovery was assessed by extensor postural thrust test (EPT), toe spread reflex test (TSR), and foot position (FP) test on the following time points: base (1 week pre-surgery), 2nd, 5th, 8th, and the 12th days post-surgery. The MBP levels from the injury site and sham (control and RT) were assessed 14 days post injury using western blot. The statistical analysis was done using repeated measure ANOVA followed by adjusted Bonferroni for the behavioural tests, and one way ANOVA followed by Bonferroni for the MBP levels (p-value <0.05).

Results:
All the behavioural tests showed a significant reduction in functional performances of the injured groups compared to the sham groups at all post-surgery time-points and the injured groups compared to the pre-injured ($p<0.0001$). RE resulted in a significant functional recovery in the EPT values on the 8th day ($p=0.038$) and the TSR values on the 8th and 12th days ($p<0.0001$ and $p=0.015$, respectively) when compared to the control. However, when compared to the control, RE did not have a significant effect in the FP test. Similarly, RE did not significantly affect the protein levels of MBP.

Conclusions:
We observed that 10 weeks of RE prior to SCI improved the functional recovery in the RE rats when compared to the control rats. This was shown through the functional tests (TSR and EPT). However, the RE did not significantly affect the expression levels of MBP protein.
Funding: College of Graduate Studies, Kuwait University and Research Sector (Grant Number: YM06/22).

Key Words: Resistance exercise; Sciatic Nerve injury; Functional recovery;

Funding Agency: CGS

Physiology

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Type-1 respiratory failure triggers a complex signaling responses and apoptosis in the rat brain.

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Kuwait University

Introduction:
Type-1 respiratory failure (T1RF) is caused by lung injury or low partial pressure of O2 (PO2) in air. It is associated with secondary acute brain injury (sABI), but the mechanisms behind it are not clear and could include primary hypoxic injuries, lung injury-triggered inflammation, or increased intracranial pressure due to hypoxemia or mechanical ventilation. This study aimed to elucidate the effects of T1RF-induced hypoxemia on the brain.

Methods:
This study was approved by the Ethical Committee, College of Medicine. SD rats (n=48) were exposed to 8%O2 in N2 for up to 48h. We have shown previously that this protocol caused large reduction in PO2 in the cerebral cortex (CC) and an increase in lactate concentration in the brain. In this study, using TUNEL assay, we assessed apoptosis in the CC, ependymal layer, and choroid plexuses (CPs) during the time course of hypoxemia. Cerebrospinal fluid (CSF) samples were collected during normoxia and after 24h and 48h hypoxemia; concentrations of 32 signaling molecules in these sample were estimated by multiplex assays. Expressions of 84 signaling molecules in CC at various time points during hypoxemia were explored by RT2-ProfilerTM PCR Array. Numerical values are presented as mean (SD). Data was compared with one-way ANOVA and the Kruskal-Wallis test. Fold changes in the expressions of mRNAs were estimated using GeneGlobe software. Statistical significance was set at $p<0.05$.

Results:
Hypoxemia exerted significant effect on the number of apoptotic cells in CC, ependymal layer and CPs ($p<0.01$); in CC the number of apoptotic cells was 5.63% (4.76) during normoxia, 20.48% (4.1) after 24h hypoxemia ($p<0.01$ vs. control) and 32.37% (6.5) after 48h hypoxemia ($p<0.01$ vs. control, $p<0.05$ vs. 24h hypoxemia). There was a significant effect of the duration of hypoxemia on the concentrations of the following cytokines in the CSF: IL15, IL17A, IP10, VEGF, EPO, FGF21, FSTL1, GDF8/Myostatin, LIF and SPARC. When compared to normoxia, the expression of 11 mRNAs, most of them for pro-inflammatory cytokines, were 2-2.5 folds lower after 6h hypoxemia; expression of mRNAs for VEGF and IL7 were 2 folds and 2-5 folds higher after 24h and 48h hypoxemia, respectively.

Conclusions:
Our findings revealed a complex response by the brain during T1RF-induced hypoxemia and suggest an association between TIRF-induced hypoxemia and sABI. Acknowledgement: The study was funded by Kuwait University grant no YM05/18.

Key Words: Type 1 Respiratory failure ; Hypoxia ; Cytokines ;

Funding Agency: Kuwait University grant no YM05/18.

Physiology

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Expression of Placental Estrogen Receptors alpha and beta in Dexamethasone-Induced Intrauterine Growth Restriction (IUGR) and the Modulatory Effects of Melatonin

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Introduction:
Placental growth and function are essential for proper fetal development. Exposure to high levels of glucocorticoids (GCs) can severely affect placental growth resulting in IUGR. Estrogens are required for normal placental growth, and they exert their effect by binding to their receptors (ER alpha and ER beta). Dexamethasone, a synthetic GC, administration increases the level of placental apoptosis in rats by affecting the expression of ER thus reducing placental and fetal growth. Melatonin, a neurohormone and antioxidant, has protective effects on offspring in pregnancies complicated by IUGR and may have an impact on ER expression. Hypothesis: We hypothesized that exposure to DEX leads to a reduction in ER gene expression resulting in IUGR, and that melatonin can reverse this effect.
Objectives: To investigate the molecular mechanism underlying IUGR in rat placenta by studying changes in gene expressions of ERs on 21days gestation (dg) in the labyrinth zone of DEX-induced IUGR placentas and the possible modulatory effect of melatonin.

Methods:
Pregnant Sprague Dawley rats (n= 6/group) were divided into 4 groups: saline group (control; C), DEX group (0.2 mg/kg; intraperitoneal injections of DEX starting from 15 until 20 dg), DEX and melatonin group (DEX+MEL; 0.01% melatonin in drinking water for the entire pregnancy period, until sacrifice) and melatonin group (MEL). Gene expression of ER levels was studied by ReT-PCR.

Results:
A significant decrease in both placental and fetal body weights was detected in both DEX and DEX+MEL groups compared to the C group ($p \leq 0.05$ and $p \leq 0.001$, respectively). There was a significant reduction in ER alpha expression in the DEX group compared to the C group and this was corrected by melatonin in the DEX+MEL group ($p \leq 0.001$and $p \leq 0.05$, respectively). A significant reduction in ER beta gene expression was also seen in the DEX group compared to the C group and this was reversed in the DEX+MEL group ($p \leq 0.05$).

Conclusions:
IUGR was successfully induced by DEX administration as placental and fetal body weights were decreased. Downregulation of ER could be a contributing factor in inducing placental apoptosis and eventually IUGR. Although melatonin reversed the effect of DEX in ER, it failed to prevent the decrease in placental and fetal body weights.
Acknowledgement: Research Sector (Project# YM03/17) for financial support and the Animal Resource Center.

Key Words: Intrauterine Growth Restriction ; Dexamethasone, Melatonin; Estrogen Receptors;

Funding Agency: Research Sector (Project # YM03/17

Psychiatry

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Lower Blood Vitamin D Levels Are Associated with Depressive Symptoms in a Population of Older Adults in Kuwait: A Cross-Sectional Study

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Introduction:
Depression is a leading cause of global disability and is associated with reduced productivity, increased mortality, and high healthcare costs. Moreover, depressive symptoms are common in older adults and especially among senior adults. The burden of depression later in life is expected to increase in Kuwait, as the proportion of its population who are aged 65 or over -currently at 4%- continues to grow at a rapid rate. This study aimed to examine the association between vitamin D deficiency and depression in adults aged 65 years and older.

Methods:
This cross-sectional study was conducted in seven primary healthcare centers across Kuwait (November 2020 to June 2021). The participants (n = 237) had their serum vitamin D 25-(OH)-D concentrations (analyzed by LC-MS) classified as sufficient, ≥75 nmol/L (30 ng/mL); insufficient, 50–75 nmol/L (20–30 ng/mL); or deficient, <50 nmol/L (20 ng/mL). Depressive symptoms were evaluated using the 15-Item Geriatric Depression Scale (15-item GDS).

Results:
The mean serum 25-OH-D levels (nmol/L) in participants with normal, mild, moderate, and severe depression were 100.0 ± 31.7, 71.2 ± 38.6, 58.6 ± 30.1 and 49.0 ± 6.93, respectively ($p < 0.001$). The participants in the vitamin D sufficiency group were significantly less likely to exhibit depressive symptoms (% 88.2) than patients with mild (36%) and moderate (21%) depression ($p < 0.001$). Ordinal logistic regression showed that vitamin D deficiency (OR = 19.7, 95% CI 5.60, 74.86, $p < 0.001$) and insufficiency (OR = 6.40, 95% CI 2.20, 19.91, $p < 0.001$) were associated with higher odds of having depressive symptoms.

Conclusions:
It was found that the symptoms and severity of depression, measured using the GDS-15 scale, were strongly inversely associated with serum 25-(OH)-D, even after adjustment for sex, physical activity, health status, and marital status. These findings could have significant public health implications for the identification and treatment of depressive symptoms among older adults. Well-designed randomized controlled trials (RCTs) investigating the administration of vitamin D for prevention and treatment of depression in older adults with a concurrent vitamin D deficiency < 50 nmol/L (20 ng/mL) who are depressed at baseline are key to this area of research. These trials should have dosing protocols, uniform assays, and an adequate control of confounders

Key Words: 25 hydroxy Vitamin D; Aging; Depressive Symptoms;

Funding Agency: KFAS-grant no.: CB20-63MM-01; Ethics: URCE 19/47; Kuwait Ministry approval: CB20-63MM-01

Psycology

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The Relationship Between Social Desirability Bias and Self-reports of Conscientiousness among Undergraduate Kuwaitis

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Introduction:
Personality assessment as screening procedure receives great interest from both researchers and practitioners. One key concern for selection specialists is represented by the social desirability response bias which may lead to inaccurate self-reports. The EPQ-R deals with the problem of response bias by including a Lie scale that measures general social desirability. Conscientiousness is one of the five personality traits defined as the propensity to follow socially prescribed norms for impulse control, to be goal directed, to plan, and be able to delay gratification. The present study examined the relationship between social desirability response bias and self-report of Conscientiousness among a sample of university students.

Methods:
The participants were 760 first year undergraduate Kuwaitis: 288 males (mean age = 20.85±1.20) and 472 females (mean age= 20.57±1.27). Males were significantly older in age ($t=3.03.19$, $p<.02$). The EPQ-R Lie Scale (Eysenck, Eysenck & Barrett, 1985) 21 items × 2 was used as a measure of social desirability. Using the median as a cut point the SD scale was dichotomized too high and low. The high socially desirable responses scored (14.22±2.04) significantly higher on EPQ-R Lie ($t=5.81$, $p<.01$) than low socially desirable responses (6.22±1.76). The 9-items BFI Conscientiousness scale (John, & Srivastava, 1999) were administered to participants in Arabic.

Results:
T-tests examined the association between levels of social desirability bias and dichotomous Conscientiousness. The results revealed significant group differences found in Conscientiousness whereby high socially desirable responses scored (30.05±0.91) significantly higher in Conscientiousness ($t=5.92$, $p<.01$) than low socially desirable responses (29.78±5.46).

Conclusions:
These findings suggest that social desirability bias is associated with the key Conscientiousness measure. Methods are needed to reduce social desirability bias, clearly defining the role of "participant" and assessing the motivations for socially desirable responses.

Key Words: Social Desirability ; Conscientiousness; Undergraduate Kuwaitis;

Funding Agency: None

Public Health

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Impact of COVID-19 pandemic on routine immunization in State of Kuwait: Short-term disruption with rebound in vaccination utilization

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Introduction:
On March 11, 2020, the World Health Organization declared an international state of emergency to control the spread of SARS CoV-2, which started in Wuhan, China in 2019.. The importation of the coronavirus in Kuwait was first discovered on February 24, 2020. Preventive measures to mitigate the risks of the pandemic focused on wearing masks, frequent hand washing, social distancing, quarantine procedures, stay-at-home orders, closedown of schools and religious places, working & studying from home, and prevention of gatherings. To explore the impact of COVID 19 pandemic on routine immunization along four abbreviated time frames: pre-pandemic in 2019, stay-at-home (March to May), and reopening (June to August) in 2020 and corresponding months 2021.

Methods:
Observational study with a retrospective secondary analysis of monthly immunization data available for children ≤24 months from the Public Health Department from January 2019 to August 2021. Vaccine uptake was analyzed in the following four time periods: March May 2019 (pre-pandemic), March May 2020 (lockdown or stay at home), June August 2020 (post-lockdown), and March May 2021 (acclimatization). All vaccines administered at 2, 3, 6, 12, 18, and 24 months of age were included in the study. Descriptive statistics including total, means, differences & percentages were calculated & tabulated. Bar charts and line graphs, were plotted to compare vaccination visits and trends of the coverage rates before, during and after the first lockdown in the country and announcement of COVID-19 pandemic and subsequent year 2021. To evaluate the change between different periods student's T test was used to compare means. Also, effect sizes Cohen's d was calculated.

Results:
Mean of total visits from March-May 2020 dropped (-28.9%) compared to March-May 2019, then increased during the reopening June-August 2020 (+31.8%). All vaccinations scheduled for children ≤24 months showed reduction. The greatest reduction detected at age 24 m -44.2%, followed by 18 m -36.5% then at 1 year -28.8%. Greater declines among Non-Kuwaiti children than Kuwaitis for all types of vaccines. Mean of total visits March-May 2021 increased (+15.4%) compared to same period in 2020. However, reduction of -16.0% still exists compared to baseline in 2019.

Conclusions:
Huge negative impact of the COVID-19 pandemic on childhood vaccinations has been reported, with unprecedented declines in vaccination visits and vaccination coverage rates in Kuwait. Recoveries were recorded in subsequent months, but they could not reach baseline levels in 2019. Therefore, the COVID-19 pandemic had negative effects beyond direct viral infection, including the jeopardization of EPI services. Prolonged lockdown and isolation unfortunately led to reluctance to commit to the immunization schedule.

Key Words: Covid-19, Routine Vaccination; Missed vaccination; Impact, Rebound;

Funding Agency: None

Public Health

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Characteristics Associated with Women Undergoing their First Mammography Screening at a Younger Age

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Introduction:
Breast cancer is the leading cause of cancer death among women globally. Among the Gulf Cooperation Countries (GCC) countries, Kuwait has the highest age-standardized incidence rate of breast cancer. The earlier the tumor is diagnosed the higher the survival is expected for breast cancer patients. The goal of mammography screening is to improve early diagnosis, however, in Kuwait uptake of screening is very poor. To improve participation, it is critical to understand participant characteristics regarding screening to enable the development of more tailored programs with greater outreach.

Methods:
A cross sectional study was carried out to identify the characteristics of women who had undergone mammography screening for the first time at the Kuwait National Mammography Screening Program (KNMSP). Characteristics associated with women undergoing mammography screening for the first time were described and factors associated with undergoing screening at a younger (40-49 years) versus older age (50+ years) were assessed. Secondary data were obtained from the KNMPS database, for women aged 40 and above who were screened at the KNMPS during the first five years: between 1st April 2014 to 31st March 2019.

Results:
Logistic regression was performed through stepwise backward elimination analysis to determine characteristics associated with screening at a younger age. A total of 5,242 records were included in the study, of which 64.9% were screened at a younger age and 35.0% were older. Our study found that having higher education, increased pregnancy frequency, undergoing clinical breast examination, using hormone replacement therapy, and having a normal BMI were significantly associated with increased odds of undergoing screening at a younger age ($p<0.05$).

Conclusions:
Our findings can assist in increasing the uptake of screening at a younger age in Kuwait, through creating more targeted interventions and strategies to influence screening.

Key Words: Mammography Screening, Women Characteristics, Brea; Mammography Screening;

Funding Agency: None

Public Health

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Prevalence of dietary supplements use, associated factors and reported adverse events among young adults in Kuwait

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Research supervised by Dr. Dana AlTarrah

Introduction:
Dietary supplements (DS) are products used to supplement the diet to treat nutritional deficiencies and improve overall health status. Several studies showed that DS use could improve an individual's nutritional status and prevent diet-related diseases. However, with the global rise in DS use, there is an increased risk of misuse and/or excessive use leading to toxicity and adverse events (AE). More research on DS use is needed in Kuwait, and to date, there is no study that investigated DS use among young adults. This study aimed to investigate the prevalence of DS use, associated factors, and reported adverse events among young adults in Kuwait.

Methods:
A cross-sectional study was carried out using an online self-administered questionnaire. Snowball and convenience sampling were used via multiple social media platforms. Dependent variables were DS use and reported AE, and independent variables were sociodemographic and lifestyle characteristics and health status. Logistic regression analysis was performed to assess the association between independent and dependent variables. Ethical approval was obtained from the Health Sciences Center Ethical Committee and the Ministry of Health Ethical Committee in Kuwait.

Results:
The prevalence of DS use was 68.24%, and it was statistically associated with age (odds ratio [OR] = 1.07, 95% confidence interval [CI] 1.03-1.13; p-value [p]=<0.001) and being a female (OR = 1.55, 95% CI 1.01-2.41; p=0.047). Most participants did not experience AE (80.56%) associated with DS use. However, experiencing adverse events was statistically associated with having asthma (OR = 2.09, 95% CI 1.07-4.05; p=0.029) and diseases of the digestive system (OR = 3.22, 95% CI 1.24-8.35; p=0.016). No associations were found with nationality, educational status, income, BMI, and smoking status.

Conclusions:
This is the first study in Kuwait that focuses on factors associated with DS use and related adverse events among young adults. The findings of the present study will help in understanding the current patterns of DS use, developing targeted interventions, and implementing regulations and policies to manage DS use in Kuwait.
Funding/Acknowledgment: This study was not funded. The authors would like to thank the College of Public Health, Kuwait University.

Key Words: Dietary Supplements ; Adverse Events; Young adults ;

Funding Agency: None

Public Health

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The Psychological and Social Impacts of Curfew during the COVID-19 Outbreak in Kuwait: A Cross-Sectional Study

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Introduction:
The Coronavirus (COVID-19) pandemic in Kuwait led to a nationwide curfew between 22 March and August 2020. The purpose of this study was to evaluate the psychological and social impact of the COVID-19 curfew during the pandemic on Kuwaiti citizens and residents.

Methods:
A cross-sectional survey was used to collect data between 18 June and 15 July 2020 from Kuwaiti residents over the age of 21 through an online questionnaire shared via social media, including WhatsApp and Facebook. Mental health was measured using the validated Depression, Anxiety, and Stress Scale (DASS-9). Descriptive statistics were conducted to describe sample characteristics; cross tabs chi-square test and independent-samples t-test were conducted to identify gender differences. Pearson's correlation coefficient analysis was performed to identify intercorrelation between dependent and independent variables. Binary logistic regression analysis was conducted to calculate the odds ratios for predicting mental health variables.

Results:
Data from 679 respondents (42.1% males; 67.7% Kuwaiti nationals) were analyzed. Symptoms of depression were reported among 59.8% of females and 51.0% of males, and extremely severe depression among 20.4% of females and 13.6% of males (p = 0.30). Extremely severe depression was associated with being female (OR = 2.00, 95% CI: 1.13, 3.55), aged 21–29 (OR = 4.56, 95% CI: 1.86, 11.22), experiencing tensions or violent behaviors from family members (OR = 2.88, 95% CI: 1.75, 4.76), being physically inactive (OR = 1.64 95% CI: 1.00, 2.71), smoking cigarettes (OR = 3.02, 95% CI: 1.58, 5.79), and having poor or very poor quality of sleep (OR = 1.07, 95% CI: 1.07, 2.86). Severe or extremely severe psychological distress was associated with being female (OR = 3.09, 95% CI: 1.54, 6.19), aged 21–49 (OR = 3.68, 95% CI: 1.37, 9.92), having ill-health conditions or diseases (OR = 1.83, 95% CI: 1.07, 3.32) experiencing tension or violent behaviors from family members (OR = 3.56, 95% CI: 2.06, 6.09), smoking cigarettes (OR = 3.06, 95% CI: 1.47, 6.36), and having poor or very poor quality of sleep (OR = 2.20, 95% CI: 1.28, 3.78).

Conclusions:
Findings support an urgent need for targeted interventions to improve health behaviors and social support, including coping mechanisms specific to COVID-19 related stress, family counseling systems, and the provision of accessible and acceptable services using telehealth.

Key Words: COVID-19; psychological effect; Depression; psychological distress; Quality

Funding Agency: This research was funded by the UNDP Kuwait and the APC was funded by the Kuwait Institute for Scientific Research (KISR).

Public Health

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Effects of COVID-19 Lockdown on Physical Activity and Dietary Behaviors in Kuwait: A Cross-Sectional Study

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Introduction:
The Coronavirus disease (COVID-19) pandemic has brought about drastic measures that have significantly altered the norms of daily living. These measures have affected human behaviors in considerable ways. This study seeks to understand the impact of the pandemic on physical activity and dietary behavior among adults living in Kuwait.

Methods:
A cross-sectional survey was conducted between 18 June and 15 July 2020, using a questionnaire disseminated through social media, including WhatsApp and Facebook. A 65-item questionnaire was used to assess demographic information, COVID-19 related perceptions and behaviors, dietary and physical activity behaviors, and related health behaviors utilizing previously used and validated measures. The target population was individuals aged 21 years or older living in the State of Kuwait. Descriptive statistics were conducted to describe sample characteristics; cross tabs Chi-square test and independent-samples t-test were conducted to identify gender differences; and Pearson's correlation analysis was performed to identify intercorrelation between dependent and independent variables.

Results:
The study included 679 respondents; 57.9% females, and 67.7% Kuwaiti nationals. Both genders reported an increased consumption of vegetables, fruits, and carbohydrates, and a decreased consumption of fish and sugary drinks. Compared to males, females reported eating more during the outbreak than their pre-pandemic eating behaviors (32.3% vs. 35.9%, $p < 0.05$). Approximately one-third of respondents (33.1%) reported performing less than 30 min of physical activity or exercise per week, and 36.4% of respondents rated their quality of sleep as 'poor' or 'very poor'. The prevalence of smoking cigarettes among males was significantly higher than in females (40.6% vs. 5.3%, $p < 0.001$). Physical activity was positively correlated with vegetable consumption and quality of sleep. Quality of sleep was negatively correlated with the consumption of sweets and snacks, and the consumption of vegetables was negatively correlated with the consumption of sugary drinks.

Conclusions:
This study found both favorable and unfavorable changes in health behaviors during the COVID-19 pandemic, revealing an opportunity for stakeholders to prioritize developing interventions targeting certain health behaviors for promoting overall positive health behaviors among the residents of Kuwait.

Key Words: COVID-19; Physical activity; Dietary behavior;

Funding Agency: This research was funded by the UNDP Kuwait and The APC was funded by the Kuwait Institute for Scientific Research (KISR).

Traumatic Brain Injury

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Neurobiochemical, Peptidomic, and Bioinformatic Approaches to Characterize Tauopathy Peptidome Biomarker Candidates in Experimental Mouse Model of Traumatic Brain Injury

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Introduction:
Traumatic brain injury (TBI) is a multidimensional damage, and currently, no FDA-approved medicine is available. Multiple pathways in the cell are triggered through a head injury (e.g., calpain and caspase activation), which truncate tau and generate variable fragment sizes (MW 400-45,000K).

Methods:
In this study, we used an open-head TBI mouse model generated by controlled cortical impact (CCI) and collected ipsilateral (IC) and contralateral (CC) mice htau brain cortices at one (D1) three (D3), seven (D7) days post-injury. We implemented immunological (antibody-based detection) and peptidomic approaches (nano-reversed-phase liquid chromatography/tandem mass spectrometry) to investigate proteolytic tau peptidome (low molecular weight (LMW) <10K)) and pathological phosphorylation sites (high-molecular-weight (HMW); >10K) derived from CCI-TBI animal models.

Results:
Our immunoblotting analysis verified tau hyperphosphorylation, HMW, and HMW breakdown products (HMW-BDP) formation of tau (e.g., pSer202, pThr181, pThr231, pSer396, and pSer404), following CCI-TBI. Peptidomic data revealed unique sequences of injury-dependent proteolytic peptides generated from human tau protein. Among the N-terminal tau peptides, EIPEGTTAEEAGIGDTPSLEDEAAGHVTQA (a.a. 96-125) and AQPHTEIPEGTTAEEAGIGDTPSLEDEAAGHVTQARM (a.a. 91-127). Examples of tau C-terminal peptides identified include NVSSTGSIDMVDSPQLATLADEVSASLAKQGL (a.a. 410-441), and QLATLADEVSASLAKQGL (a.a. 424-441). Our peptidomic bioinformatic tools showed the association of proteases, such as CAPN1, CAPN2, and CTSL, CASP1, MMP7 and MMP9, ELANE, GZMA, and MEP1A, in CCI-TBI tau peptidome.

Conclusions:
In clinical trials for novel TBI treatments, it might be useful to monitor a subset of tau peptidome as targets for biomarker utility and use them for a “theranostic" approach.

Statements & Declarations
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Author Contribution: HY, KKWW had substantial contribution to the concept, design of the article, acquisition, analysis, and interpretation of data for the article. FK, KKWW, and RY revised it critically for important intellectual content. HY, CJ, NP, MK, IT, and ZY did the experimental work. HY wrote the paper. RY provided expertise and guidance. R.Y. provided expertise in mass spectrometry. HY and KKWW secured funding; KKWW provided expertise in the Traumatic Brain Injury. FK provided expertise in proteomics. Competing Interests: The authors declare no potential conflicts of interest for this article's research, authorship and/or publication. Data Availability Data are available for the reader who makes a direct request to the corresponding
authors.

Key Words: TBI; Tauopathy; Peptidomics;

Funding Agency: None

Cytopathology

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Metastatic Prostate Carcinoma Presenting as a Mediastinal Mass Diagnosed on Fine Needle Aspiration Cytology: A Case Report and Review of the Literature.

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CASE REPORT

Background: Prostate carcinoma is the second most common malignant disease in men and it is the second leading cause of cancer-related deaths in the world. It can have a variety of presentations, including asymptomatic with normal or raised prostate-specific antigen (PSA) levels, local invasion and regional lymph node involvement or metastasis with systemic symptoms. It usually spreads by direct extension and metastasizes to bone and lymph nodes of pelvis. We present an unusual first manifestation of a metastatic prostate carcinoma as a mediastinal mass.

Case Summary: A 74-year-old man, chronic smoker presented with cough and difficulty in breathing. CT chest showed multiple pulmonary nodules with mediastinal lymphadenopathy. Endobronchial ultrasound (EBUS) guided fine needle aspiration cytology (FNAC) of the subcarinal mass was performed. On FNAC, the smears were cellular and showed variable isolated cells with decreased cell cohesion and micro glandular pattern. The cells had indistinct cell membranes with high nuclear to cytoplasmic ratio and minimal nuclear pleomorphism with prominent nucleoli. Reactive lymphoid cells were seen in the background. The tumor cells stained positive for CK-7, PSA, AMACR (Racemase) and CD-10 and negative for CK-20, synaptophysin, chromogranin, PAX-8 and inhibin. The possibility of metastatic prostate carcinoma was suggested. The patient was reexamined for genito-urinary system abnormalities including prostate examination, and was found to have high PSA levels and, enlarged prostate, which was confirmed by ultrasound examination of the abdomen and pelvis.

Conclusion: The main diagnostic challenge in this case was the initial presentation of prostate cancer as mediastinal mass in a patient with no urological symptoms. Prostate cancer is responsible for only 2% of all metastatic carcinomas in the mediastinum. It should be suspected in male patients above 50 years especially if urologic symptoms and elevated PSA levels are present.

Key Words: EBUS guided FNA; Mediastinal mass; Metastatic prostate carcinoma.;

Dentistry

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Dental Management of a Child with Glanzmann's Thrombasthenia: A Case Report

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CASE REPORT

Background: Glanzmann's Thrombasthenia (GT) is a rare congenital bleeding disorder caused by a defect and/or deficiency of a platelet integrin (αIIbβ3), which is essential for platelet aggregation and haemostasis. The estimated prevalence of GT is 1:1,000,000; however, in Kuwait, it is high as 1:100,000. Patients have lifelong bleeding episodes that involve the mucocutaneous membranes even with normal exfoliation of primary teeth. Therefore, liaison with the haematology team and excessive care should be taken during dental treatment of these patients.

Case Summary: A 9-year-old boy with a history of GT was presented in our clinic with a painful tooth 36. Intra-oral examination revealed mixed dentition stage with multiple carious lesions, defective restoration on 36, poor oral hygiene (OH) and generalized gingivitis.

After consultation with his haematologist, preventive care was provided followed by full oral rehabilitation under general anaesthesia, including restorations and extractions of the carious teeth. Patient was prepared for the surgery a day before with intravenous (IV) platelet transfusion, recombinant activated factor VII (rFVIIa) and tranexamic acid (TA). Despite the pre-operative blood management, localized uncontrollable bleeding occurred following extraction, however, few minutes later, haemostasis was achieved by administering IV TA and rFVIIa, in addition to the localized haemostasis measures.

FOLLOW-UP: Over a follow-up period of one year, his OH improved but needs a continued reinforcement.

Conclusion: This case has highlighted the importance of liaison with the haematologist to have a pre, peri, and post-operative bleeding plan, and consequently delivering a safe quality dental treatment for children with bleeding disorder.

Key Words: Glanzmann's Thrombasthenia; Bleeding disorder; Dental management;

Dentistry

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Improving the Quality of Life of a Paediatric Patient with Crohn's Disease and Dental Caries

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CASE REPORT

Background: Crohn's disease is a chronic, recurrent inflammatory bowel disease, affecting 1.53 per 100,000/year in Kuwait. The impact of Crohn's disease on oral health includes development of dental caries. The quality of life of children with either Crohn's disease or dental caries is reported to be poor compared to healthy individuals.

Case Summary: A 9-year-old boy with Crohn's disease was referred by his paediatrician requesting dental clearance prior to Bone marrow transplant. Examination revealed very anxious child with poor oral hygiene, and multiple caries in both dentitions. Following intensive prevention, comprehensive dental treatment was completed under general anaesthesia including restorations, pulp-therapy and extractions. Preoperatively, antibiotic prophylaxis and hydrocortisone were administered intravenously. Monthly recall is planned. On recall visits, oral hygiene is significantly improved; and the patient was happy and cooperative. Treatment objectives were to eliminate sources of pain or infection; and restore dental-health prior to Bone marrow transplant.

Discussion: Both Crohn's disease and dental caries negatively affect the children’s quality of life due to Crohn's disease symptoms and dental pain. Therefore, the removal of any source of pain or infection will positively impact their quality of life. Additionally, considering immunosuppression following Bone marrow transplant, any teeth with questionable prognosis require a more invasive approach.

Conclusion: Dental management plays an important role in improving the psychosocial well-being of children.

Key Words: Quality of life, dental caries, Crohn's disease; Dental caries; Crohn's disease;

Dentistry

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Dental Management of a Child with Cystic Fibrosis

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CASE REPORT

Background:
Cystic Fibrosis (CF) is a multi-system autosomal recessive disease caused by alteration of cystic fibrosis transmembrane conductance regulator protein (CFTR). Life quality and expectation are affected by the disease as it involves pulmonary, gastrointestinal, reproductive and endocrine systems.

Clinical report:
A 12-year-old boy with a history of CF was presented in our clinic seeking dental check-up before traveling abroad for treatment of CF. Examination revealed poor oral hygiene, hypoplastic teeth, enamel caries and uncomplicated crown fracture 21.

Treatment objectives:
Improving the quality of the patient life by achieving and maintaining aesthetics, mastication and function and eliminating any potential source of infection.

Treatment procedure:
After liaising with his paediatrician, patient received complete oral rehabilitation under local anaesthesia.

Treatment outcomes:
Patient is caries free now and placed under strict follow-up program

Discussion:
Close follow-up and maintenance of proper oral hygiene is crucial in these patients to prevent further infection which might deteriorate their medical condition.

Conclusion:
• Continuous reciprocal relation with the paediatrician is important to provide safe effective dental care for children with CF.
• Education and prevention is essential to maintain good oral health in those patients.

Key Words: Cystic Fibrosis ; Dental Management; Medically compromized;

Dentistry

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Fabrication of a CAD/CAM bone reduction and implant placement guide: A technique article

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CASE REPORT

Background: Guided implant surgery can be performed with computer-aided design and computer-aided manufacturing bone-supported guides. In situations where bone reduction is required prior to implant placement, the implant surgical/placement guide is usually designed to be stacked on top of the bone reduction guide. This may introduce errors in implant placement from an unstable surgical guide if bone reduction is not completed exactly as planned.

Case Summary: The technique presented in this article allows clinicians to design a bone-supported implant placement guide that is independent of bone reduction; The final implant placement guide is anchored in bone using guide pins; it is designed with guide tubes that are connected with the bone anchored portion of the guide by multiple support struts giving access and visibility to the clinician and potentially increasing accuracy.

Conclusion: Advances in CAD/CAM can help facilitate guided surgery for oral surgeons and make it convenient and accurate.

Key Words: Digital; Guided; Surgery;

Dentistry

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Dental Management of a Patient with Atypical Haemolytic Uremic Syndrome in Kuwait: A Case Report

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CASE REPORT

Background: Atypical Haemolytic Uremic Syndrome (aHUS) is an extremely rare disease that is characterized by the triad of microangiopathic haemolytic anaemia, thrombocytopenia, and acute renal failure. The incidence of HUS in Kuwait is estimated to be 0.4/100,000 child per year; ~40% of the cases had atypical form. Several precipitating factors have been associated with aHUS that might trigger its episodes such as infections. Therefore, it is very important to evaluate the oral health of these patients and provide intensive prevention and dental treatment promptly. To our knowledge there were no reports in the literature that have discussed the dental management of patients with aHUS.

Case Summary: A 7-year-old girl with a medical history of aHUS was referred to our dental clinic by her pediatrician concerning about her oral health. Clinical examination revealed poor oral hygiene (OH), multiple carious primary and permanent teeth and localized dental abscesses associated with teeth 54 and 64. The patient was slightly anxious in the dental chair but with utilization of variety of non-pharmacological behaviour management techniques she successfully completed her comprehensive dental care under local anesthesia that consisted of intensive prevention followed by restorations and extractions of the abscessed teeth.

Follow-Up: An intensive OH programme was undertaken. Over a follow up period of 6-months, her OH showed improvement, however, needs a continued reinforcement.

Conclusion: Preventive care and oral health stabilisation in patients with aHUS is of a high priority to prevent the risk of infection and the need for invasive dental treatment.

Key Words: Dental management; Atypical Haemolytic Uremic Syndrome; Kuwait;

Dermatology

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A Case of Orf Disease: Unusual Presentation

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CASE REPORT

Background: The Orf disease, also known as contagious ecthyma, is a zoonotic infection caused by a Orf virus, an epitheliotropic DNA virus from the Parapoxvirus group. The virus is endemic in sheep and goats worldwide and manifests as an acute contagious skin condition that can cause substantial morbidity. It is transmitted to humans through direct or indirect contact of damaged skin with infected animal. In humans, after a brief incubation period of 3 to 7 days, an orf lesion appears as a pruritic erythematous macule and then rises to form a papule, nodule or hemorrhagic bullae. Secondary bacterial infection seems to be the most common complication of Orf. The diagnosis may be confirmed by electron microscopy, conventional histopathology or by isolation of the virus by PCR. Because of the benign, self-limited nature of the disease, no treatment is usually required.

Case Summary: A 48 years old male represented in the dermatology clinic with one-month history of small painless lesion on his left little finger, which gradually increased in size and developed hemorrhagic crust on the top. He denied any contact with animals. However, he had been helping in preparing food to celebrate a festival for almost a month. On examination there was a 1.5 cm nodule with a definite border, which was reddish brown in color with crustation. It was soft fleshy in consistency and no regional lymph nodes were palpable.

Conclusion: Orf disease is an uncommon dermatosis resulting from cutaneous infection with sheep pox virus. It is generally a benign and self-limited condition. Early clinical recognition is paramount to avoid unnecessary surgical intervention or extensive diagnostic workup. Diagnosis is usually based on a clinically typical skin lesion, and a history of animal exposure.

Acknowledgment: This case report was prepared in collaboration with Prof Nawaf AlMutairi, dermatology department Farwaniya Hospital, Kuwait

Key Words: Orf disease; Parapoxvirus; Zoonotic infection;

Ethics

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Women Health in Detention in Kuwait: Utilizing SWOT Analysis in Ethics Education

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CASE REPORT

Background:
Reported studies in population health indicates that amongst the most underserved groups of society are people in detention and those with a history of incarceration worldwide. In addition, the "Prison systems are rarely gender sensitive" and gender-specific issues need to be taken into consideration whenever healthcare in detention is discussed. In order to address this professional gap and issues related to gender vulnerabilities in healthcare facilities at correctional centers, young healthcare professionals need to be aware of this to help them appreciate the potential role they can play in their communities.

Objectives:
- To present the first experience in an academic course on "Ethics of Public Health Practice & Research" at a graduate level focusing on issues related to women's health in detention.
- To present the utilization of a SWOT analysis model which aided students' reflection and analytical skills.

Case Summary
The standards used in this reflective educational exercise are the ones delineated in the United Nations rules for the 'Treatment of Women Prisoners and Non-Custodial Measures for Women Offenders' (The Bangkok Rules, UNODC 2010)*. The SWOT technique which was used for identifying strengths and weaknesses, and for examining the opportunities and threats facing the provision of healthcare to women in detention in this exercise showed that this model can be utilized in public health ethics education. It was utilized in this reflective exercise to explore healthcare services provided to women in prison in Kuwait, to encourage healthcare professionals in training to consider a career in providing healthcare in correctional facilities, and to drive a transparent discussion with stakeholders and decision makers.

Conclusion:
A SWOT analysis is a tool, employed generally in management and strategy conceptualization. It can however be utilized in teaching ethics and professionalism in medical and public health education to discover the demographic, technical, political, legal, cultural and social elements leading to Strengths, Weaknesses, Opportunities and Threats of a peculiar health care providing organization and delivery system; especially in those dealing with vulnerable populations.

Key Words: Detention; Women; Ethics;

Hematology

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Pseudo Gaucher cells in a splenectomised B-thalassemia patient

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CASE REPORT

Background: Gaucher disease (GD) is a rare genetic lipid storage disorder characterized by deposition of unprocessed glucocerebroside in macrophages due to deficiency of the enzyme glucocerebrosidase. GD is divided into 3 clinical types. Type 1 chronic, non-neuropathic, adult type accounts for about 99% of cases with median age at diagnosis of 40.4 years. Gaucher cells (GC) accumulate in the spleen, liver and bone marrow. Histologically they appear as macrophages engorged with lipid with crumpled-tissue-paper appearance and eccentric nuclei. Pseudo-Gaucher cells (PGC) are morphologically similar to GC that have been demonstrated in some haematological disorders other than GD.

Case summary: A 41-year-old male known to have B-thalassemia major since childhood on regular blood transfusion. In 2010 splenectomy was done that showed dramatic decrease in his transfusion requirement. In 2021 he presented with unexplained progressive anemia with increased demand for blood transfusion. Peripheral blood smear showed marked aniso-poikilocytosis seen in thalassemic patients' smears. Bone marrow aspirate showed marked erythroid hyperplasia that was admixed with many Gaucher like cells. Trephine biopsy was hypercellular. The majority of cells were erythroid series that occupied most of the inter trabecular spaces. Large and medium sized sheets of PGC were seen along the trephine biopsy. Residual normal granulocytic precursors were seen with no increase of immature cells as CD34 positive cells and no abnormal localization of immature precursors (ALIP) was noted. Megakaryocytes were adequate and morphologically normal with no evidence of dysplasia. B-GGlucocerbrosidase enzyme and acid sphingomyelinase levels were normal. Genetic testing was also done to exclude possibility of Gaucher disease that showed no pathogenic mutations.

Conclusion: Pseudo –Gaucher cells have been described in many hematological disorders with high cellular turnover related to malignant proliferation such as chronic myeloid leukemia, acute lymphoblastic leukemia, Hodgkin disease and non- Hodgkin lymphoma. They also have been reported in some cases associated with ineffective hematopoiesis as Thalassemia and Myelodysplastic Syndrome. The relation between splenectomy and enhanced macrophage proliferation in the bone marrow has to be highlighted in further studies.

Key Words: Pseudo-Gaucher cells; Thalassemia; Splenectomy;

Hematology

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Chronic Myelomonocytic Leukaemia (CMML) in a Young Patient with Immune Thrombocytopenia.

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CASE REPORT

Background: CMML is a clonal haematopoietic stem cell disorder with overlapping myelodysplastic and myeloproliferative features. It is a disease of the elderly (median age at diagnosis is 65-75 years) with male predominance. The diagnostic criteria of CMML undergo salient modifications in the last WHO update, 5th edition, 2022, which include lowering the cutoff for absolute monocytosis to ≥ 0.5 × 109/ L, dividing CMML into two subtypes: Myelodysplastic-CMML (WBC < 13 x 109/ L) and Myeloproliferative-CMML (WBC ≥ 13 x 109/L), and eliminating CMML-0 subgroup. Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by thrombocytopenia and a variable risk of bleeding. Some studies reported thrombocytopenia (CMML-induced thrombocytopenia) in approximately 40% of CMML patients, which is usually related to bone marrow (BM) defects resulting from cytotoxic drug use or CMML itself, and, in very rare cases, ITP (CMML-associated ITP) could be a complication of CMML. We present a case diagnosed as Myelodysplastic-CMML1 in a young-aged female patient after a long period of having chronic ITP.

Case Summary: A 23-year-old female patient with refractory ITP (she was on Revolade therapy for 8 years, although she was non-compliant with the treatment, and recently she was shifted to N-plate) was admitted to our hospital for marked thrombocytopenia. Reviewing her CBC history revealed persistent monocytosis. A comprehensive workup was done and included: PBF, BM examination, immunophenotyping (IPT), molecular analysis and abdominal ultrasonography. CBC and PBF: Leukoerythroblastic blood picture with absolute monocytosis: 4.6 x 109/L, WBCs: 12.4 x 109/L and 1% blast cells. BM: hypercellular with trilineage dysplasia, 8% blast cells and fibrosis 2/4. PB IPT defined 14% monocytes with abnormal partitioning (CD14+/CD16-: 95%), while BM IPT revealed 1% myeloblasts. Molecular study: KRAS- mutation; BCR/ABL1, JAK2, CALR, and MPL were negative. There was mild hepatosplenomegaly by abdominal U/S. These findings matched the WHO prerequisite and supporting CMML diagnostic criteria, and an MD-CMML1 final diagnosis was given.

Conclusion: The occurrence of thrombocytopenia with CMML is not uncommon. Nevertheless, CMML-associated ITP hardly ensues, and there is no clear aetiology behind this association; further research might declare this point. We recommend a thorough review and complete workup, including BM examination and molecular analysis, for all cases of refractory ITP.

Key Words: CMML: Chronic Myelomonocytic Leukaemia; ITP: Immune thrombocytopenia; IPT: Immunophenotyping;

Laboratory Haematology

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Azathioprine- Induced Myelodysplasia with RUNX1 Mutation in Patient with Crohn's Disease

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CASE REPORT

Background: Myeloid neoplasms post cytotoxic therapy (MN-pCT) includes AML, MDS, and MDS/MPN arising in patients exposed to cytotoxic (DNA-damaging) therapy for an unrelated condition. In 5th edition World Health Organization (WHO), exposure to PARP1 inhibitors is added as a qualifying criterion for MN-pCT, and methotrexate has been excluded, while others including thiopurines have been remained. It is recommended that specification of the type of myeloid neoplasm is made when possible, with the appendix "post cytotoxic therapy" appended, e.g. MDS post cytotoxic therapy. Azathioprine (AZA) is one of the thiopurines and is widely used in patients with autoimmune diseases. A recognized carcinogen, AZA is also associated with the development of therapy-related myelodysplastic syndrome and acute myeloid leukemia (t-MDS/AML). The duration and cumulative dosages of AZA preceding t-MDS/AML are variable. RUNX1 mutations in AML in the WHO 5th edition is not recognized as a distinct disease type due to lack of sufficient unifying characteristics, however, it is now considered as molecular abnormalities associated with MDS. Thiopurine methyltransferase (TPMT) is the enzyme responsible for inactivating toxic products of AZA metabolism. Patients with homozygous deficiency of this enzyme have no enzyme activity and ideally should not be given AZA.

Case Summary: A 33 years old female patient, is a known case of Crohn's disease, was on Imuran for two years and discontinue four months before bone marrow (BM). On admission, there was no fever, organomegaly or lymphadenopathy. Ferritin: 336 ng/ml, Vitamin B12: 149 pmol/l, C3 & C4: Normal. Virology screen (HBV, HCV, HIV): negative. CBC showed marked pancytopenia. Bone marrow examination revealed: Hypo-proliferative BM with trilineage dysplasia, blasts 10% (confirmed by immunophenotyping), reticulin fibrosis (2/3), and maturation arrest. BM molecular testing revealed RUNX1 mutation. TPMT enzyme assay was requested.

Conclusion: This case; being had RUNX1 mutation; is in need for additional work-up for germline predisposition. It will be prudent to review the need for AZA especially when it has been prescribed for long period and consider any persistent pancytopenia with history of AZA intake as it may be a clue for early diagnosis of Therapy related myeloid neoplasms. Finally, potentially life-threatening myeloid neoplasms induced by treatment for autoimmune disease are an emerging clinical phenomenon.

Key Words: Azathioprine; Myeloid neoplasms post cytotoxic therapy; RUNX1 mutation;

Medicine

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Pseudocirrhosis: A Diagnostic Dilemma of Liver Schistosomiasis Mimicking Cirrhosis

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CASE REPORT

Background: Schistosomiasis or bilharziasis, remains to be the third most prevailing devastating disease among tropical diseases in developing countries. Schistosoma affects the liver through deposition of eggs in the portal vein, inducing a granulomatous reaction that causes periportal fibrosis and liver cirrhosis. Here we present a unique case of schistosomiasis generating the illusion of liver cirrhosis in the absence of liver fibrosis creating a diagnostic dilemma.

Case Summary: a 32-year-old Egyptian male presented to the gastroenterology clinic to investigate elevated liver enzymes. He gave no history of hematuria, jaundice, hematemesis, or ascites. The patient was born and raised in upper Egypt and gave history of swimming in freshwater as a child. He was infected with schistosomiasis at the age of 14 which was treated. Liver enzymes were mildly elevated (AST 31 U/L, ALT 63 U/L) and ultrasound liver showed coarse liver suggestive of underlying cirrhosis but no signs of portal hypertension. Transiet elastrography (Fibroscan) confirmed fibrosis grade F4 (cirrhosis). His stool and urine tests for schistosoma were negative. The rest of the workup including viral and autoimmune markers was unremarkable. Given the uncertainty of the diagnosis, a liver biopsy was performed. The histological result delineated a focal schistosoma ova with surrounding eosinophil cell rich inflammation and granuloma with no fibrosis. The patient was diagnosed with liver schistosomiasis with no liver cirrhosis. He was prescribed praziquantel and completed a course of 3 doses with improvement in his liver enzymes during follow-up. He is scheduled to have repeat imaging and fibroscan to confirm resolution of the previously noted pseudocirrhosis abnormalities.

Conclusion: Pseudocirrhosis depicts morphological changes of the liver that resemble cirrhosis, without the usual histopathological changes seen in cirrhosis. Multiple conditions can mimic cirrhosis on imaging including metastatic malignancy and sarcoidosis. Although schistosomiasis can lead to cirrhosis, in this unique case it mimicked the architectural changes found in cirrhosis instead. This was achieved through the appearance of deposited schistosoma eggs on the surface of the liver giving the illusion of liver cirrhosis. Therefore it is imperative to consider schistosomiasis as a rare mimicker of cirrhosis when encountering a suspected case of liver cirrhosis in patients from endemic areas.

Key Words: Schistosomiasis; Pseudocirrhosis; Liver biopsy;

Medicine

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Phenotypic Heterogeneity in a Family with TECRL-related CPVT Type 3: 1st Case in Kuwait

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CASE REPORT

Background: An 11 yrs. old, previously healthy boy, collapsed suddenly while walking casually with family. He was found pulseless, requiring CPR and defibrillation therapy to convert from presumed polymorphic ventricular tachycardia (PMVT) into sinus rhythm with prolonged QT interval and unstable repolarization. He was briefly started on dobutamine before developing 2 episodes of PMVT despite being on lidocaine infusion. He had frequent polymorphic/bidirectional ventricular complex ectopy mainly during stressful periods. During his hospital stay, he had a normal echocardiogram and cardiac MRI. Moreover, he underwent electrophysiology study with easily inducible unstable PMVT requiring defibrillation. Furthermore, he underwent arrhythmia panel testing through a commercial laboratory, which was negative. Whole exome sequencing eventually confirmed the high clinical suspicion for homozygous TECRL (c.331+1G>A) through another commercial laboratory. He is a product of consanguineous marriage with no family history of concern. His oldest brother's phenotype was highly suggestive of CPVT during his screening sprint exercise stress test, however, without QT prolongation. He was confirmed for the same homozygous mutation. Segregation studies through Sanger sequencing confirmed the heterozygosity status for both parents and one sibling.

Case Summary: We report additional evidence of the pathogenicity of the previously described highly conserved TECRL (c.331+1G>A) splice site mutation, at chromosome 7p14-p22 in one other Sudanese family. This same mutation has been also reported in the setting of oligogenic inheritance in a Tunisian family. Furthermore, TECRL (c.331+1G>A) variant was not reported as single nucleotide polymorphism in the general population including Saudi Arabian individuals. Moreover, functional studies from a symptomatic patient of the same Sudanese family demonstrated increased susceptibility to triggered activity, exaggerated with noradrenaline. Luckily, Flecainide therapy had been shown to reduce the triggered activity specifically for TECRL (c.331+1G>A).

Conclusion: Based on our experience, and on what has been reported in the literature, we call for including TECRL in the arrhythmia panels that are commercially available worldwide.

Key Words: TECRL; CPVT; Novel;

Medicine

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Calciphylaxis: A Case Series and Review

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CASE REPORT

Background: Calciphylaxis is a rare fatal condition that mainly affects morbidly obese patients with chronic kidney disease (CKD) on long-term dialysis. It is characterized by calcifications in the subcutaneous arteries and infarction of the skin. Typically, patients present with skin lesions in the form of livedo reticularis-like plaques that progress to necrotic ulcers. These ulcers are more prone to infections due to poor healing secondary to diminished vascular supply. Usually, it is misdiagnosed and caught at a late stage, leading to difficulties in the management of the patients. High-risk patients include those with end-stage renal disease (ESRD), long-term dialysis, and calcium-phosphorus abnormalities. In patients with high risk, physicians should consider calciphylaxis when the patient develops a skin lesion, especially when it is refractory to treatments. Diagnosis is mostly clinical, but histopathology and bone scintigraphy also aid in the diagnosis. The main course of mortality in patients with calciphylaxis is sepsis. Thus, immediate management with sodium thiosulfate, intensive dialysis, cinacalcet, and wound care must be started.

Cases Summary: We describe our clinical experience with three ESRD patients on dialysis with calciphylaxis. The patients presented with a picture of refractory cutaneous lesions that were later revealed to be calciphylaxis lesions. They were diagnosed with clinically with the support of risk factor assessment and relevant laboratory and imaging tests, such as calcium and phosphorus levels and bone scintigraphy. Thereafter, full calciphylaxis management was started; sodium thiosulfate, cinacalcet, daily hemodialysis sessions, anticoagulation with unfractionated heparin, pain management, and wound care. Unfortunately, all the patients developed sepsis, which led to their decease.

Conclusion: Calciphylaxis is a rare condition that should not be taken haphazardly as it can be fatal. Physicians, specifically dermatologists, should consider this condition in patients with CKD/ESRD on dialysis, especially when it is accompanied by calcium and phosphorus imbalance. The condition is usually diagnosed clinically, but it can be confirmed with histopathology. Early diagnosis and management of calciphylaxis are pivotal in the outcome and prognosis of these patients. In our cases, the patients responded really well to the sodium thiosulfate; however, they eventually deteriorated and were demised due to their extensive comorbidities.

Key Words: Calciphylaxis; End-stage renal disease; Long-term dialysis;

Medicine

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Cerebral paradoxical embolism following recurrent idiopathic deep vein thrombosis and pulmonary embolism in a kidney transplant recipient

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Hamed ALeesa OTC

CASE REPORT

Background: Paradoxical embolism occurs when a thrombus crosses an intra-cardiac defect into the systemic circulation. Aim: We aimed to present the management of a 35-year-old male kidney transplant recipient with a paradoxical cerebral embolism associated with a spontaneous VTE.

Case Summary: Adult kidney transplant recipient with recurrent deep venous thrombosis and showering emboli to the lung and paradoxically to the brain through patent foramen ovale, who was managed successfully. The role of bubble echocardiography was essential in diagnosis to avoid contrast-induced nephropathy.

Conclusion: This is the first successfully managed kidney transplant recipient with recurrent idiopathic deep vein thrombosis, pulmonary embolism, and paradoxical cerebral embolism. Bubble echocardiography was an excellent alternative to contrasted angiography to avoid nephrotoxicity. Vitamin k antagonists are superior to direct oral anticoagulants, especially among non-compliant patients.

Key Words: Embolism; Paradoxical; Kidney transplant;

Microbiology and Immunology

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A rare case of Gymnascella ear infection

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CASE REPORT

Background: The number of mold species causing invasive infection continues to expand, with the addition of fungi once thought incapable of causing human infection. We report here the first case of ear infection by the thermotolerant ascomycete Gymnascella.

Case Summary: A 55 year old male patient was admitted to the Neurology ward of Ibn Sina hospital with headache, blurred vision, nausea and bilateral ear discharge. Patient is a known case of diabetes insipidus, ischemic heart disease and tuberculous pleural effusion. He underwent surgery for otitis media and bilateral tympanostomy tubes were inserted a year back. His present CT showed inflammatory lesions in CNS along with bilateral oto-mastoiditis and marked pansinusitis. His PET scan revealed ventriculitis, osteomyelitis of mastoid bone and bilateral hilar lymph nodes highly suggestive of sarcoidosis. Swabs taken from both ears were sent for bacterial and fungal culture to the microbiology lab of Ibn Sina hospital. Sabouraud plates showed heavy growth of a mold that appeared dull white with a slight brown tint. The same white mold grew on all other media except MacConkey. There was no bacterial growth. The plate was sent to the Mycology Reference Laboratory and was identified as Gymnascella species (environmental fungus). Because of the doubtful significance of this fungus, ear discharge swabs were repeated for culture, which again grew the same. A serum sample, submitted to the reference laboratory for serological studies, was reported as negative for antibodies to Aspergillus. Patient was started on liposomal Amphotericin B 5mg/kg IV once daily for 3 weeks. ENT examination done10 days later showed no discharge and the bilateral tympanostomy tubes were in place and dry. Repeat cultures could not be done as the patient left against medical advice.

Conclusion: This case highlights the role of low-virulence environmental molds as an emerging cause of breakthrough fungal infection.

Key Words: PET scan; Gymnascella; Ear infection;

Microbiology and Immunology

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Family Tourism: A risk of infection of schistosomiasis in Yemen

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CASE REPORT

Background: Schistosomiasis is an acute and chronic disease caused by Schistosomes, found mostly in low-income countries with the largest burden of disease in Middle East and North African regions. Here, we report on the clinical and laboratory findings in family travellers visited Sana'a, Yemen and took bath in a lake.

Case Summary: A family of six ranged between 5 – 45 years visited their relatives in Sana'a, Yemen on 27th June, 2022. All the family members took bath on September 1, 2022 only once in a local lake and came back to Kuwait on September 18, 2022. All have developed the symptoms of schistosomiasis except the head of the family after a month. The patients were referred from area clinic to Infectious Diseases Hospital on 27th October 2022 and admitted in the hospital. The most frequent clinical symptoms were abdominal pain, headache, fever, dry cough, and diarrhea and asthenia. The stool examination revealed the presence of Schistosoma mansoni eggs and Charcot-Leyden crystals. The level of C-reactive protein was also very high in all patients. All the patients were treated with praziquantel, 20 mg/kg orally 3 times a day for one day with Rocephin 100 mg/Kg body weight for 7 days. After six days the patients became asymptomatic, the hematological parameters became normal, and the stool was also free from ova.

Conclusion: Schistosomiasis remains a common infection in travelers and migrants from west and east Africa and Yemen. The travelers visiting these countries should be counseled intensively on the risk of schistosomiasis infection. Pre and post travel advice and its effectiveness must be provided to all travellers vising these countries.

Key Words: Schistosoma mansoni; Schistosomiasis; Tourism;

Microbiology and Immunology

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First isolation of azole-resistant Aspergillus fumigatus with TR46 /Y121F/T289A mutations in Kuwait and an update on azole resistance in the Middle East

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CASE REPORT

Background: Pulmonary aspergillosis (PA) is a leading cause of death in immunocompromised patients, particularly those receiving chemotherapy and bone marrow transplant recipients. Aspergillus fumigatus is one the most prevalent causative agent and voriconazole is first-line therapy for PA. Azole-resistant A. fumigatus containing TR34/L98H mutations has been isolated from the environment of many countries, including Kuwait. In this case report, we describe the first isolation of A. fumigatus harboring the TR46/Y121F/T289A mutations from a female patient in Kuwait, which confers high-level voriconazole resistance.

Case Summary: A 33-year-old near-term pregnant lady with Crohn's disease presented with fever and watery diarrhea. After admission (Day-0), she required inotropic support. Abdominal CT revealed signs of colitis and she received hydrocortisone, piperacillin/tazobactam, and metronidazole. On Day-3, her health improved and the clinician performed cesarean section for delivery. However, on Day-7, she developed tachycardia and hypotension and received vancomycin and caspofungin for suspected sepsis on Day-8 in ICU. Her chest CT revealed pleural effusion and lung collapse. On Day-11, a pigtail was inserted and oxygen therapy was given via nasal cannula. Bronchoscopy revealed mucus obstruction in left bronchial tree and BAL culture yielded Aspergillus fumigatus which was later found to have voriconazole resistance-associated TR46/Y121F/T289A mutations in cyp1A. On Day-18, caspofungin was replaced by voriconazole. She maintained optimal oxygen saturation on ambient air, was shifted back to the ward (Day-21) and was discharged 2 weeks later (Day-36).

Conclusion: Here, we report the first isolation of A. fumigatus carrying TR46/Y121F/T289A mutations from a pregnant lady in Kuwait who was successfully treated for a probable respiratory infection with caspofungin and voriconazole. Although literature review from PubMed has identified A. fumigatus with TR34/L98H mutations in the cyp51A from several Middle Eastern countries, isolates with TR46/Y121F/T289A mutations have previously been reported only from Iran.

Key Words: Triazole-resistant Aspergillus fumigatus; TR34/L98H, TR46/Y121F/T289A; Middle East;

Ophthalmology

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Superior Ophthalmic Vein Thrombosis: A Case Report in an MRSA Positive Patient Post Covid-19 Vaccine

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CASE REPORT

Background: Superior ophthalmic vein thrombosis (SOVT) is an extremely rare condition (incidence of 3 –4 cases/ million/year). In this report, we present a case of right SOVT in an aseptic patient with positive blood culture for Methicillin-resistant Staphylococcus aureus (MRSA) who was COVID-19 negative and received ChAdOx1 nCoV-19 vaccine.

Case Summary: Presenting History: A 38-year-old female, previously healthy, presented with two weeks history of worsening right sided headache. It was associated with photophobia, phonophobia and right-sided ear pain and tinnitus. The patient had no history of contact with COVID-19 infected patients had a negative nasopharyngeal swab for SARS-CoV-2. She received two doses of the ChAdOx1 nCoV-19 vaccine with the second one 8 months before presentation. Physical examination: The patient appeared well and stable, she was afebrile with normal neurological and physical examinations. Ocular examination: The visual acuity was 6/12 (right) and 6/6 (left) with no relative afferent pupillary defect. Slit-lamp examination showed right eyelid edema, conjunctival congestion, and clear cornea with normal intraocular pressure. The fundus examination showed raising of the hyperemic right optic disc with blurred margins and normal left optic disc. Extraocular motility was limited in all directions especially in the lateral gaze up with vertical diplopia. The patient was seen by ENT specialist and there were no signs of otitis media.
Laboratory results: Complete blood cell count and chemistry results were normal. The inflammatory markers ESR and CRP were elevated at 93 mm/h and 102 mg/L respectively, D-dimer level was borderline at 419 ng/ml. Blood cultures grew MRSA and the patient tested positive for ChAdOx1 nCoV-19 antibody IgG. Imaging results. A brain computed tomography (CT) angiography examination was unremarkable. Orbital CT examination showed periorbital and orbital cellulitis with superior ophthalmic vein thrombosis. Outcome of this case. The patient was started on Vancomycin (2 x1-1.5 g, based on Vancomycin trough level), Flagyl (3 x 500 mg) and anticoagulant therapy (Enoxaparin injection 1ml per kg). At one-month follow-up, the patient reported complete resolution of symptoms with no impairment of visual acuity.

Conclusion: Most of the SOVT cases in the literature reported complete recovery. Suspected cases of SOVT should trigger early imaging studies and urgent ophthalmology consultation to minimize detrimental complications.

Key Words: Superior Ophthalmic Veien Thrombosis; MRSA; Covid-19;

Ophthalmology

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Leber's Hereditary Optic Neuropathy: Update on Current Diagnosis and Treatment.

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CASE REPORT

Background: Leber's hereditary optic neuropathy (LHON) is a fairly prevalent mitochondrial disorder (1:50,000) arising from the dysfunction of the mitochondrial respiratory chain, which eventually leads to apoptosis of retinal ganglion cells.

Patient presentation: The usual presentation is that of a young male with a sequential reduction in visual acuity. OCT has been used to study the pattern of optic nerve involvement in LHON, showing early thickening of the inferior and superior retinal nerve fibre layer and ganglion cell layer thinning corresponding with the onset of symptoms. Of the three primary mutations for LHON, the m.14484T>C mutation has the best visual prognosis.

Current Management: Recent emerging therapeutic options for LHON include idebenone and the **Background** of genetic vector therapy, which is currently in phase III clinical trials. Screening of family members and adequate advice to avoid environmental triggers, such as smoking and alcohol consumption, are also cornerstones in the management of LHON.

Conclusion: LHON is a mitochondrial optic neuropathy that affects young males but is also not 327 uncommon in females. Recently, advancements have been made in understanding the 328 pathophysiology of LHON and developing new therapeutic strategies, such as gene therapy 329 through the use of viral vectors in clinical trials. However, further studies are required to 330 incorporate gene therapy as a universally approved treatment for LHON.

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Key Words: Leber's hereditary optic neuropathy; Idebenone; Mitochondrial disorder;

Pathology

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Elastofibromatouses Change In The Gastrointestinal Tract: A case Series Study Of Four Cases

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CASE REPORT

Background: The elastosis or elastofibromatous changes in the gastrointestinal tract are extremely rare lesions, which are thought to be under recognized rather than rare. There are a limited number of cases reported in the literature of elastofibromatouses changes in the gastrointestinal tract and other reported extra-intestinal locations. They usually present as a colonic polyp and are incidentally found during colonoscopy. The pathogenesis hypothesis remains unclear for these changes. Although the pathogenesis remains unclear, the convincing hypothesis that this lesion represents elastic degeneration of submucosal vessels by previous persistent vascular injury has been proposed. Histologically these lesions appear as finely granular and or fibrillar amorphilic material, often mistaken for amyloid but are negative for Congo red and strongly positive for elastin stain.

Case Summary: We report four cases of the large intestine and review the clinicopathological features. Three patients (62,75 male year-old males and 62 year-old female) were detected with polypoid lesions in the sigmoid colon (3 cases), and one patient (64 years old female) lesion found in the descending colon (1 case). All four lesions showed fundamentally the same histopathological features.Histologically composed of finely granular and or fibrillar pale, eosinophilic to grey tan amphophilic materials, occasionally with fibrous component (elastofibromatous change) with accumulation in the submucosa and/or muscularis mucosa. The histochemical nature was confirmed by positive Verhoff elastic stain and negativity by Congo Red stain.

Conclusion: Even though clinically inconsequential, Elastofibromatous changes can closely mimic amyloid deposition. Pathologist need to be aware of this entity to ensure accurate diagnosis.

Key Words: Elastofibromatouses Change ; Gastrointestinal Tract; Case Series;

Pathology

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Spiradenocarcinoma: A Case Report

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CASE REPORT

Background: Spiradenocarcinoma is a rare malignant neoplasm that arises from eccrine sweat glands with potential aggressive behavior. It affects adult males and females equally with a predilection for the head and neck area. A benign spiradenoma and cylindorma are considered to be the precursor lesions from which it arises, but it can also develop de novo. In addition, this tumor has an association with Brooke-Spiegler syndrome, an inherited autosomal dominant disease characterized by multiple skin and salivary gland tumors. Evaluation of tumor grade is essential for prognostic estimation.

Case Summary: A previously healthy 72-year-old male presented with a skin lesion in the left supraclavicular region that was clinically asymptomatic for 8 years. Computed tomography showed a cystic lesion that is of soft tissue component with thin septations and enhancing wall. The lesion was removed under local anesthesia in the Emergency Department as an out-patient procedure. Grossly, it was a single circumscribed piece of tissue. On opening, solid and cystic areas with hemorrhage are seen. The histological examination revealed an encapsulated tumor composed of atypical cells arranged in sheets and nests with focal glandular differentiation. The cells feature large nuclei, prominent nucleoli, and moderate amphophilic cytoplasm. Frequent atypical mitoses and necrosis are seen. A focus of bland epithelial ductal structures with surrounding myoepithelial cells and hyaline basement-membrane like material is noted. Immunohistochemical (IHC) profile showed positivity for CK7, P63, SOX-10, CEA, and TTF-1. The overall histologic features are in keeping with a low-grade spiradenocarcinoma supported by the presence of a rare focus of residual spiradenoma and the IHC profile.

Conclusions: Spiradenocarcinoma is a rare sweat gland carcinoma. It is often associated with a benign slow-growing spiradenoma that undergoes malignant transformation. Additionally, a genetic association with Brooke-Spiegler syndrome has been established. The diagnosis of spiradenocarcinoma is confirmed by histological examination after surgical removal of the lesion. Long-term follow up of patients is advised as this tumor has a potential for local recurrence and metastasis.
Acknowledgments: I am thankful to the Pathology Department in Farwaniya Hospital for giving me the opportunity to present this rare case.

Key Words: Spiradenocarcinoma; Spiradenoma ; Syndrome ;

Pathology

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A Large Angiomatoid Fibrous Histiocytoma on the Shoulder of a Young Man Accompanied by Systemic Symptoms

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CASE REPORT

Background: Angiomatoid fibrous histiocytoma (AFH) is a rare soft tissue neoplasm of uncertain histogenesis and intermediate malignant potential, usually arising in the extremities of children and young adults. Interestingly, it may be associated with systemic manifestations (e.g. fever, weight loss, malaise, and anemia) suggesting tumoral cytokine production. AFH may resemble a hematoma due to the presence of blood-filled angiomatoid spaces. Histologically, it shows a morphological spectrum posing a diagnostic difficulty, with a differential ranging from reactive to malignant sarcoma. In > 90% of cases, there is a t(2;22) (q33;q12) translocation resulting in EWSR1::CREB1 gene fusion serving as a useful confirmatory test.

Case Summary: A 17-year-old male presented with a gradually growing mass on the left shoulder for 4 months, accompanied by weight loss, severe anemia (Hb 5g/dL) and a significant rise in serum c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). MRI revealed a thick-walled cystic mass measuring 18 cm with a heterogenous content and internal septations but no specific radiological features. Fine needle aspiration and tru-cut needle biopsy yielded only blood. The mass was surgically removed revealing the same: cysts filled with fresh blood and clots suggestive of a hematoma or a vascular neoplasm. The pathologist performed extensive sampling of the cyst walls to find viable diagnostic tumor areas for microscopic evaluation. The histopathological picture was inconclusive; pseudo-angiomatous spaces lined by monomorphic ovoid to spindled tumor cells that, on immunohistochemistry, showed strong expression of desmin (muscle marker) and focal expression for EMA & CD99, while they lacked expression of vascular markers. The diagnosis of AFH was confirmed by fluorescence in-situ hybridization and targeted RNA-based sequencing, revealing an EWSR1 rearrangement and an EWSR1:CREB1 fusion transcript, respectively. Four months later, the patient relapsed presenting with abdominal pain, vomiting and fatigue, along with a drop in Hb, rising CRP, and a recurrent 3cm mass at the same site. CT scan showed enlarged axillary lymph nodes and abnormal lung infiltrates. The patient was lost to follow up.

Conclusion: AFH may pose a diagnostic dilemma. A large cystic mass resembling a hematoma on the extremity of a child or adolescent, +/- systemic symptoms, should prompt the consideration of AFH. Adequate excision and careful follow-up are needed.

Key Words: Angiomatoid fibrous histiocytoma; Sarcoma; Soft tissue;

Pathology

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Metastatic Perivascular epithelioid cell tumor (PEComa) to the lymph node diagnosed by fine needle aspiration A case report

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CASE REPORT

Background: Perivascular epithelioid cell tumor (PEComas) are a family of rare mesenchymal tumors. The diagnoses of PEComa is a challenge due to overlapping cytomorphology and immunohistochemical features to malignant melanoma and clear cell sarcoma. The primary diagnosis is completely dependent on histopathology and immunohistochemistry with expression of both myogenic as well as melanocytic differentiation. They have been associated with mutation of tumor suppressor genes TSC1 and TSC2 genes, which are seen in tuberous sclerosis complex (TSC), an inherited disorder.

Case summary: A 57-year-old Kuwaiti woman, a known case of breast cancer treated with wide local excision, radio and hormonal therapy presented 2 years later with rising serum calcium and on investigation had a parathyroid adenoma which was surgically excised. Six months later she developed a soft tissue lesion on shin of left leg. Core biopsy revealed a malignant soft tissue tumor possibly a malignant melanoma or clear cell sarcoma. However, as S100 was negative, a malignant PEComa was considered. Whole body PET scan showed ipsilateral inguinal and pelvic lymph nodal metastases, fronto-parietal skull lesions and diffuse axial and appendicular skeletal uptake. A sonar guided FNA was performed on suspicious left inguinal lymph node, which showed tumor cells, scant lymphoid cells, and few multinucleated giant cells in a necro-inflammatory background. The tumor cells had comparable cytomorphology to the histopathology of primary leg soft tissue tumor. Cells stained positive for MUM 1 and negative for S100 and CK. A diagnosis of metastatic PEComa was made. Molecular studies done showed no significant mutation.

Conclusion: PEComas are ubiquitous mesenchymal tumors, more often seen in women that display immunoreactivity for melanoma-associated markers, variable reactivity for muscular markers, and non-reactivity for epithelial markers. Occurrence of PEComa has been reported at various anatomical sites. Most patients have sporadic PEComas and a relationship with other tumors is rare.

Key Words: PEComa; Fine needle aspiration; Metastatic;

Pathology

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Inflammatory Myofibroblastic Tumor in Failed Renal Graft: Case Report

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CASE REPORT

Background: Inflammatory myofibroblastic tumor (IMT) is a mesenchymal neoplasm with myofibroblastic cell phenotype accompanied by stromal lymphoplasmacytic inflammatory infiltrate. It has an intermediate behaviour, with the capacity of metastasis and local recurrence. It shows a wide anatomic distribution, but renal IMT are generally rare. IMT has been reported following solid organ transplantation, including lung, liver, and kidney, as well as hematopoietic stem cell transplantation. We are reporting a case of IMT occurring in a failed renal allograft.

Case Summary: A 61- year- old man who was undergoing hemodialysis following renal allograft failure presented with a palpable mass in his allograft. Radioloical evaluation detected exophytic mass at upper pole of the transplanted kidney with significant heterogenous contrast enhancement, suggestive of a suspicious renal mass. The patient underwent graft nephrectomy revealing an exophytic mass (6.5 x 6.0 x5.0 cm) with multinodular firm cut surface, at the upper renal pole, extending into perirenal fat and renal sinus. Microscopy showed a well delineated unencapsulated lesion composed of spindle and stellate cells with small to medium oval nuclei, dispersed within loose myxoid to eosinophilic fibrillar stroma that shows areas of hypercellularity and hyalinization. Prominent lymphoplasmacytic infiltrate is seen. No atypia or mitosis were appreciated. By immunohistochemistry, tumor cells were positive for CD34 and H-Caldesmon, while negative for Alk-1, SMA, S100, Desmin, CK, CD117, CD99, BC1-2, and STAT-6. The case was subsequently signed out as inflammatory myofibroblastic tumor in a background of end stage renal disease in renal allograft.

Conclusion: Solid organ transplant recipients have a 2-fold increased risk for cancer as a consequence of the chronic immunosuppressive therapy required to prevent graft rejection. Inflammatory myofibroblastic tumors (IMT) are rare, mesenchymal tumors that can occur in solid organ transplant recipients. This is the third reported case of IMT in renal graft. Pathogenesis is not yet clear, but has been linked to immunosuppression and viral infections. Surgical excision is the definitive therapy for IMTs.

Further studies are recommended to identify the pathophysiology of IMT in transplant recipients.

Key Words: Inflammatory myofibroblastic tumor; Kidney Transplant; Post-Transplant Malignancy ;

Pathology

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Papillary Carcinoma of Thyroid arising in Thyroglossal Duct Cyst-A Case report

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CASE REPORT

Background: Thyroid anlage migrates down at the third week of gestation, from the posterior dorsal midline of the tongue, to the lower anterior part of the neck to form the thyroid gland. Persistence of this tract of migration can give rise to sinuses, cysts or fistulas. Thyroglossal duct anomalies are found in about 7 % of adults, two thirds of them present as cysts and one third as fistulas. Malignancy arising in them is a rare event, with papillary thyroid carcinoma being the commonest. Thyroglossal duct cyst (TGDC) carcinomas are usually asymptomatic and the diagnosis in most cases is incidental after surgical excision. The use of fine needle aspiration cytology may enhance the pre-operative diagnosis.

Case Summary: A 38-year-old man presented with longstanding anterior midline swelling. The swelling was moving with deglutition and protrusion of tongue. Clinically, it was diagnosed as a thyroglossal cyst. The thyroid profile report was within normal limit. Ultrasonography of the neck revealed a cystic lesion with partially calcified soft tissue component. The mass measured 29x23x23 mm with internal septations and irregularly thickened wall.
He underwent fine needle aspiration cytology (FNAC) which was reported as papillary thyroid carcinoma arising in thyroglossal duct cyst. Microscopic examination showed sheets of follicular epithelial cells with enlarged round to oval nuclei, powdery chromatin, occasional nuclear crowding and few intra-nuclear inclusions. After that he underwent total thyroidectomy and thyroglossal duct excision with right neck lymph node dissection. Histopathology revealed a cyst lined by flattened cuboidal epithelium and neoplastic component of papillary carcinoma of the thyroid characterized by papillae with lining of cuboidal epithelium exhibiting mild pleomorphism and ground-glass appearance of nuclei with nuclear grooving. Thyroidectomy was reported as papillary micro carcinoma with two lymph nodes metastasis. The patient had an uneventful post-operative period

Conclusion: TGDC carcinoma is rare, occurring in approximately 1% of all TGDC cases. And the presence of papillary carcinoma in a TGDC with synchronous occult papillary thyroid microcarcinoma is a unique feature. FNAC under ultrasound guidance can help in sampling the mural nodule associated with the cystic lesions.

Key Words: Thyroglossal duct cyst; Papillary carcinoma ; Thyroid ;

Pathology

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Dermatofibrosarcoma Protuberans Metastatic to the Lung – A Rare Presentation Diagnosed on Fine Needle Aspiration

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CASE REPORT

Background: Dermatofibrosarcoma protuberans (DFSP) are slow growing tumors that are commonly seen on trunk, extremities and head and neck regions. They are prone to multiple local recurrences. Patients are predominantly males between 20 and 50 years of age. The fibrosarcomatous variant of DFSPs has increased risk of local recurrences (29.8%) and metastasis (14.4%) to lungs, lymph nodes and bone. There are very few published cases of DFSPs with distant metastasis. We present a case of DFSP metastatic to the lung that was diagnosed on fine needle aspiration cytology (FNAC).

Case Summary: A 53 year old male, non-smoker presented with chronic cough, progressive nail changes and bilateral arthralgia involving extremities. He had a past history of renal cell carcinoma and an anterior abdominal wall spindle cell lesion compatible with DFSP. The CT chest showed a right lower lobe lung mass (10 x 7.5 x 6.8cm) obstructing the main bronchus along with multiple right lower lobe nodules. An endobronchial ultrasound (EBUS) guided fine needle aspiration (FNA) was performed on the right lung mass and from right subcarinal lymph node. The FNA smears from the lung mass showed sheets and clusters of spindle cells with oval to spindly nuclei and moderate amounts of cytoplasm. Similar cells arranged in whorls were seen on the cell block section where mitotic figures were also noted. The tumor cells were positive for CD34 and Vimentin but negative for CD10, CK7 and TTF1. The case was diagnosed as a spindle cell tumor, consistent with metastatic DFSP on FNAC. The transbronchial lung biopsy corroborated the cytological diagnosis. The patient was referred to a specialized cancer centre for cytogenetic/molecular testing.

Conclusion: DFSPs often recur locally, but rarely metastasize. Out of fourteen cases of DFSP in a series by Azgar et al (2021), eleven showed distant metastasis to the lungs (81.8%), bone (36.3%) and soft-tissue (27.3%). Ours is one of the few cases of DFSP metastatic to the lung that has been diagnosed through FNAC. The patient underwent surgery followed by adjuvant chemotherapy and is currently under follow-up.

Key Words: Dermatofibrosarcoma protuberans; Metastasis; EBUS guided FNA ;

Pediatrics

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LYRM7-Associated Mitochondrial Complex I Deficiency with Non-Cavitating Leukoencephalopathy and Stroke-Like Episode

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CASE REPORT

Background: Defects of complex III (CIII) respiratory chain, result in characteristic but rare mitochondrial disorders associated with distinct neuroradiological findings. The underlying molecular defects affecting mitochondrial CIII assembly factors are few and yet to be identified. LYRM7 assembly factor is required for proper CIII assembly where it acts as a chaperone for the Rieske iron-sulfur (UQCRFS1) protein in the mitochondrial matrix and stabilizing it. We present here the seventeenth individual with LYRM7-associated mitochondrial leukoencephalopathy secondary to a previously reported pathogenic homozygous LYRM 7 variant, c.2T>C, p.(p.Met1).

Case Summary: A 4-year-old male proband presented with recurrent metabolic and lactic acidosis, encephalopathy, and myopathy. Further, he has additional, previously unreported features, including acute stroke-like episode with bilateral central blindness and optic neuropathy, recurrent hyperglycemia and hypertension associated with metabolic crisis. However, he has no signs of psychomotor regression. He has been stable clinically with residual left-sided blindness, and no more metabolic crises for 2-year-period on a mitochondrial cocktail. Although the reported brain MRI findings in other affected individuals are homogenous, it is slightly different in our index, revealing evidence of bilateral almost symmetric multifocal periventricular T2 hyperintensities with hyperintensities of the optic nerves and the optic chiasm but with no cavitation or cystic changes.

Conclusion: This report describes new clinical and radiological findings of LYRM7-associated CIII deficiency. It also summarizes the clinical and molecular data of the previously reported individuals to describe the full phenotypic spectrum.

Key Words: Mitochondrial disease; Blindness ; Complex 3 deficiency, LYRM7;

Community Medicine

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Screen-based media use among mothers of children with autism spectrum disorder and their children

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CASE REPORT

Background: Study the Screen-Based Media (SBM) use among mothers with Autism Spectrum Disorders (ASD) children in comparison to their ASD children, in term of the device type and duration.
Cases: Ninety-seven (n=97) mothers of children diagnosed with ASD and attending Al Wafa and Al Rashad autism Centers constituted the sample. The Comparative group was children who's SBM was measured previously in a similar study used similar methodology (N=75). Special data collection sheet was designed for the study to collect information regarding cases demography, type of SBM devices used and duration per hour daily.

Case Summary: Mothers used smartphones more frequently in comparison to children with ASD (P=.00) while children with ASD used tablets more frequently (P=.000). Both mothers and children with ASD used television at the same rate (P = 0.924). Mother SBM was 5+ Hr per day and it matches with screen time used by children with ASD

Conclusion: Mothers' use is high and it is comparable to the SBM use by children with ASD. Clinical implications and future direction were discussed.

Key Words: Screen-based media use; Mothers-ASD; Bahrain;

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