ABSTRACT BOOK

Under the Patronage of the President of Kuwait University

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Conference Program

Tuesday 10/2/2026

Inauguration of
the Poster Conference
College of Medicine Lobby

10:00 am Registration and ID Collection of Presenters

10:30 - 11:45 am Poster Viewing & Discussion

12:15 - 1:45 pm Oral Presentations for finalists
Acknowledgement & Recognition Session
LT 1-44, COM

Wednesday 11/2/2026

HSC Auditorium

10:00 am

Opening Remarks

Dr. Maryam Al-Qabandi
Director of Center For Research Support and Conferences, COM
HSC Scientific Conference Moderator

10:10 am

Welcome Remarks

Dr. Heba Al Hussaini
Vice Dean of Research and Postgraduate Studies, COM

10:20 am

Keynote Lecture

Title: From the NMDA Receptor Paradox to a New Pharmacological Principle for the Treatment of Neurodegenerative Diseases

Keynote Speaker: Professor Hilmar Bading
Managing Director, Interdisciplinary Center for Neurosciences,
Chairman, Department of Neurobiology,
Institute of Neurobiology, Heidelberg University, Germany

11:20 am

Winner Announcement

Dr. Maryam Al-Qabandi

- Abstract Winners
- Art Competition Winners

12:00 pm

Closing Remarks & Event Adjournment

Prof. Zoran Redzic
Chariman of the HSC Scientific Conference

HSC Conference Central Committee 2026

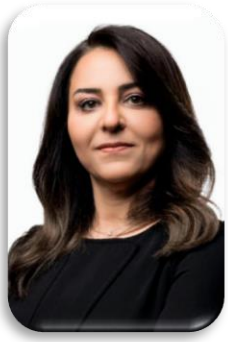
Central Committee

Dr. Heba Al Hussaini	Vice Dean for Research & Postgraduate Studies, College of Medicine
Dr Maryam Al-Qabandi	Director, Centre for Research Support and Conferences, COM
Ms. Rawabi Abdal	Chairperson, Centre for Research Support and Conferences, COM
Ms. Teena Sadan	Chief Medical Officer, Centre for Research Support and Conferences, COM
Ms. Kawther Fakhra	Administrative Coordinator, Centre for Research Support and Conferences, COM

Scientific Committee

Prof. Zoran Redzic	Chairman, Department of Physiology, College of Medicine
Dr. Fatemah Almarri	Department of Pharmacology, College of Medicine
Dr. Amenah Alrabeea	Department of Pharmacology, College of Medicine
Dr. Falah Alhajraf	Department of Pharmacology, College of Medicine
Dr. Abdulaziz Ali Karam	Department of Surgery, College of Medicine
Dr. Sarah Alyouha	Department of Surgery, College of Medicine
Dr. Fawaz Alnaqi	Department of Surgery, College of Medicine
Dr. Ali Jafar	Department of Surgery, College of Medicine
Dr. Ali Alali	Department of Medicine, College of Medicine
Dr. Yahuya Alansari	Department of Medicine, College of Medicine
Dr. Abdulhameed Alfaddagh	Department of Medicine, College of Medicine
Dr. Rashed Alrasheed	Department of Community Medicine, College of Medicine
Dr. Nadia Alnassar	Department of Community Medicine, College of Medicine
Dr. Hind Alsharhan	Department of Pediatrics, College of Medicine
Dr. Dana Marafi	Department of Pediatrics, College of Medicine Pediatrics
Dr. Mohammad Alansary	Department of Biochemistry, College of Medicine
Dr. Noor Alsabeeh	Department of Physiology, College of Medicine
Dr. Sarah Ahmed	Department of Microbiology, College of Medicine
Dr. Maitham Bahman	College of Pharmacy
Dr. Anwar Alawadhi	College of Allied Health
Dr. Fatima Al-Ghadban	College of Public Health
Dr. Muna Alsane	College of Dentistry
IT Support & Website	
Ms. Ashwaq Derie	DEPT. of Systems Development, Center of Information Systems, KU

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



It is with great pleasure to welcome you all to the 30th Health Science Center Conference, which has become a cornerstone of research innovation and knowledge dissemination in medical advances and health sciences.

This year, our conference has reached new heights, with an impressive total of 222 submitted abstracts. Among these, 173 showcase groundbreaking original research, while 49 are intriguing case reports.

We take immense pride in the awards presented at our conference, which have gained widespread recognition over the years. Each award is a testament to the dedication and brilliance of local and Gulf region researchers. The awards we present today acknowledge individual achievements and highlight the collective effort that drives our field forward.

As we gather here to celebrate excellence in research, let us not forget the core of our conference – the collaborative spirit that fuels advancements in clinical and health science research.

To all attendees, I extend my gratitude for your presence and participation. Let us engage in fruitful discussions, foster new collaborations, and share insights that will propel medicine and health sciences to greater achievements. Just as a final word and a humble reminder that the impact of our research extends far beyond this conference; it resonates in the lives of those we serve and it is through the exchange of ideas and knowledge that we can truly make a lasting impact on healthcare and our nation.

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

Address by Chairman of the Organizing Committee

Prof. Zoran Redzic
Chairman, 30th HSC Scientific Conference 2026

On behalf of the Organizing Committee, it is my great pleasure to welcome you to the jubilar 30th Health Science Center Conference. This annual event was established in the Faculty of Medicine under the leadership of Prof. Abdullatif Al-Bader in April 1996, with an aim to stimulate scientific research, critical thinking and analysis and exchange of ideas. The founders were aware that competent and strong scientific research is a prerequisite for academic excellence. The Conference was held annually and has grown progressively to involve all the faculties of the Health Sciences Center and contributions from other Faculties in Kuwait University, other life-sciences institutions in Kuwait and the Gulf region, and the Ministry of Health hospitals and centers. Over these 30 years, the number of institutions that do life-sciences and clinical scientific research in Kuwait and in the Gulf region has significantly increased. To address this change, this year we modified the eligibility criteria for the conference awards, so that other researchers outside the HSC and Kuwait University can also compete. We believe that increased competition will improve the quality.

We are honored to have Prof. Hilmar Bading, an outstanding neuroscientist at the Interdisciplinary Center for Neurosciences, University of Heidelberg, Germany, as a keynote speaker this year. Prof. Bading is a member of the German National Academy of Science Leopoldina and has been awarded several prestigious awards for his work, including Innovation Prize of the German BioRegions and Wolfgang-Paul-Prize of the Alexander von Humboldt Foundation. He kindly accepted to participate and present his work on the role of NMDA receptor in the treatment of neurodegenerative diseases.

This year we have a total of 222 submission that were accepted for the Conference, from which the selected few will be awarded. I want to sincerely thank members of the Scientific Committee, who carefully reviewed all submissions, and to members of the Judging Committee and Prof. Fawzi Babiker as a Chief Judge for selecting the best submission for the awards.

I want to especially thank Prof. Adnan Abul, Dean of the College of Medicine, and Dr. Heba Al-Hussaini, Vice-Dean for Research & Postgraduate Studies, College of Medicine for their continuous support. We are grateful to all HSC Colleges and the Kuwait University leadership for the support and sponsorship of the Conference. I would also like to express my appreciation to Ms. Teena Sadan and all HSC technical and support staff who assisted in the organization of the conference meeting.

We sincerely hope that this conference will be a pleasant, productive, and stimulating experience for all participants.

Prof. Zoran Redzic
Chairman, 30th HSC Scientific Conference 2026

Keynote Speaker

Professor Hilmar Bading, Managing Director,
Interdisciplinary Center for Neurosciences,
Chairman, Department of Neurobiology,
Heidelberg University, Germany.

Professor Hilmar Bading studied medicine (1978-1984) at Heidelberg University and did his MD Thesis at the Max Planck Institute for Medical Research. He received postdoctoral training at the Max Planck Institute for Molecular Genetics in Berlin and at Harvard Medical School, Boston. From 1993 to 2001, he was working at the MRC Laboratory of Molecular Biology, Cambridge, UK. Since 2001, he has been a professor of neurobiology and director of the Neurobiology Institute and the Interdisciplinary Center for Neurosciences at Heidelberg University. His research is focused on neuronal Ca++ signaling and gene regulation in the nervous system. He identified Ca++ as the principal second messenger in the coupling of neuronal activity to gene expression and explained the processes that mediate the dialogue between the synapse and the nucleus.

Keynote title:

From the NMDA receptor paradox to a new pharmacological principle for the treatment of neurodegenerative diseases.

Abstract

NMDA receptors are fundamental for both the physiology and the pathology of the mammalian central nervous system. They control plasticity-related events and adaptive processes in the nervous system, which include long-term potentiation (LTP), memory formation and the build-up of a neuroprotective shield. However, NMDA receptors can also bring about destruction and cell death. The discovery that the location of the NMDA receptor matters resolved the 'NMDA receptor paradox' and provided a unifying concept. NMDA receptors localized to the synapse and activated by synaptic inputs promote neuronal survival, gene expression and plasticity. In contrast, NMDA receptors that are located outside synaptic contacts - the so-called extrasynaptic NMDA receptors - couple to transcriptional shut-off and death signaling pathways. Increased extrasynaptic NMDA receptor signaling is now considered a key factor in disease progression of several human neurodegenerative disorders, including Amyotrophic Lateral Sclerosis, Huntington's disease, Alzheimer's disease, and stroke. Extrasynaptic NMDA receptors have become an important target for the development of therapeutic interventions. Based on new mechanistic insight into toxic extrasynaptic NMDA receptor signaling, which involves the formation of an extrasynaptic NMDA receptor/TRPM4 death complex, we are currently developing new types of broad-spectrum neuroprotectants.

KIMS CME/CPED Credited; **Reg. No. 008114 / Feb26**

Category 1: 5 Credits

Online Registration for CME Credits:

https://bit.ly/4kfCpcr

www.hsc.edu.kw/poster

Past HSC Poster Conference Keynote Lectures and Speakers

2025	Cancer Neuroscience of Brain Tumors: A New Hallmark of Cancer and a New Pillar of Therapy; **Prof. Dr. med. Frank Winkler**, MD, Department of Neurology, University Hospital Heidelberg & National Center for Tumor Diseases and Experimental Neurooncology Unit, German Cancer Research Center, Heidelberg, Germany
2024	The Candida Vaccine: From Bench to Bedside; **Professor Ashraf S Ibrahim**; Professor of Medicine, David Geffen School of Medicine at UCLA, Division of Infectious Diseases, Department of Medicine, Harbor-UCLA Medical Center
2023	Why can we expect a revolution in obesity treatment?; **Professor Carel le Roux**; Co-Director Metabolic Medicine lab; Diabetes Complications Research Centre, Conway Institute, University College Dublin
2022	**Keynote Lecture 1:** Human iPSC-NSC derived Extracellular Vesicle therapy for Alzheimer's Disease: Promise and Challenges; **Prof. Ashok K. Shetty**, Ph.D., Institute for Regenerative Medicine, Dept of Molecular and Cellular Medicine, College of Medicine, Texas A&M University **Keynote Lecture 2:** Biology or technology? Innovation is the key; **Prof. Pieter A. Doevendans**, Cardiologist UMCU, Utrecht, The Netherlands; Director Netherlands Heart Institute
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, Faculty of Medicine, Health Sciences Centre, Kuwait University.
2018	The internal exposome – a global approach to a better understanding of human disease. **Professor Paolo Vineis**, Chair in Environmental Epidemiology, Imperial College London, UK.
2017	Vascular stiffness and systolic hypertension; **Prof. Pierre Moreau**, B. Pharm., Ph.D, Dean and Professor, Faculty of Pharmacy - Health Sciences Center, Kuwait University.
2016	Chemokines: Key players in immune surveillance and aging. **Prof. Bernhard Moser**; Chair (Infection & Immunity), Institute of Infection and Immunity, Cardiff University, Heath Park, Cardiff, UK.
2015	The Future Healthcare: Personalized Medicine for Cancer Patients; **Prof. Ramzi M. Mohammad**, Ph.D., Director, GI-Cancer Research, Karmanos Cancer Institute, Michigan, Department of Immunology and Microbiology, Barbara Ann Karmanos Cancer Institute, Wayne State University, MI.
2014	Image-guided surgery – from bench to bedside; **Professor Samuel Achilefu**; Professor of Radiology, Mallinckrodt Institute of Radiology, Washington University School of Medicine.
2013	Stem Cells: Building and Rebuilding the Nervous System; **Professor Freda Miller**; Senior Scientist, Research Institute, Developmental & Stem Cell Biology, University of Toronto
2012	Cardiovascular health in the 21stcentury; **Professor Barry McGrath**, Professor of Vascular Medicine & Medicine, Southern Clinical School, Monash University, Australia.
2011	Cardiovascular Outcome Trials in Diabetes.; **Prof. Rury Holman**, Director of the University of Oxford Diabetes Trials Unit, University of Oxford, Canada.

2010	New mycobacterial vaccine candidates: from lab to clinical trials. **Prof. Abu Salim Mustafa**, PhD, FRC Path. Department of Microbiology, Faculty of Medicine, Kuwait University
2009	Evidence-Based Medicine and Knowledge Translation Research for Better Health Care.; **Prof. Brian Haynes**, Professor of Clinical Epidemiology and Medicine, Chief of the Health Information Research Unit at McMaster University, Hamilton Ontario, Canada.
2008	What Ails The World? How Do We Respond? **Prof. Abdallah S Daar, D.Phil** (Oxon), FRSC, FRCP (Lon), FRCS (Eng), FRCS (Ed), FRCS (C), Director of Ethics and Policy, McLaughlin Centre for Molecular Medicine, Professor of Public Health Sciences and Professor of Surgery, Senior scientist and Co-director, Program on Life Sciences, Ethics and Policy, McLaughlin Rotman Centre for Global Health, University of Toronto, Ontario, Canada.
2007	From Molecular Imaging to Molecular Medicine. **Prof. Henry N. Wagner**, Jr. MD, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA
2006	Stem cell research.; **Prof. Sir Martin Evans** FRS, DSc (Nobel Laureate), Director of the School of Biosciences and Professor of Mammalian Genetics at Cardiff University, UK.
2005	How Corticosteroids Work in inflammatory Diseases: New Molecular Insights.; **Prof. Peter Barnes** is of Thoracic Medicine at the National Heart and Lung Institute, Head of Respiratory Medicine at Imperial College and Honorary Consultant Physician at Royal Brompton Hospital, London, UK.
2004	The Nitric Oxide/Cyclic GMP Pathway: Targets for Drug Development; **Prof. Ferid Murad**, Nobel Prize recipient, Chairman, Department of Integrative Biology and Pharmacology, Director, Institute of Molecular Medicine, University of Texas Medical School, Houston, Texas, USA.
2003	The Post-Genomic Era: Global Impact on Medicine and Health Care Delivery; **Prof. Seyed E. Hasnain**, Director, Centre for DNA Fingerprinting & Diagnostics (CDFD) Hyderabad, India.
2002	Genetics and World Health: Fact or Fantasy; Prof.(Sir) David J Weatherall, Emeritus Professor, Weatherall Institute of Molecular Medicien, University of Oxford, UK.
2001	Genomic View of Human History; **Prof. Mary-Claire King**, American cancer Society Research Professor, Department of Medicine and Genetics, University of Washington, Seattle, Washington, USA.
2000	Molecular Mechanisms and Biomedical Implications of Apoptotic Cell Death; **Dr. Sten Orrenius**, Professor and Chairman, Division of Toxicology, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden
1999	Nutrition, Immunity and Infection: Basic Considerations and Public Health Significance; **Dr. Ranjit Kumar Chandra**, Professor & Director, Allergy, Asthma and Immunology Centre, Gurgaon, India.
1998	Futurology in Biomedical Research: From Crystallography to Crystal Gazing; **Prof. Jasbir S. Bajaj**, All India Institute of Medical Sciences, New Delhi, India.
1997	The Impact of Research on the Development of an Academician; **Dr. Elia Ayoub**, Distinguished Professor of Pediatrics, Department of Pediatrics, Pediatric Immunology and Infectious Diseases, College of Medicine, University of Florida USA.

Original Research Abstracts List by Subject Area

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Tahera Aleid, Nowall Al Sayegh, Sultan E Alsalah I, AbdulAziz Alhenaidi: Prevalence and risk factors of muscoskeletal pain among Kuwaiti pilgrims during hajj 2024

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Allied Health

1

Exploring Radiographers' Readiness for Artificial Intelligence in Kuwait: Insights and Applications

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Introduction:
There is a growing adoption of artificial intelligence (AI) in the field of medical imaging. AI can potentially enhance patient care, improve workflow, and analyze patient's medical data. This study aimed to explore radiographers' knowledge, perceptions, and expectations toward integrating AI into medical imaging and to highlight one of the available applications of AI by evaluating an AI-based software that generates chest reports.

Methods:
A cross-sectional survey was distributed to radiographers (n = 50) requesting information regarding demographics and knowledge of AI. In the retrospective part, chest radiographs were collected (n = 40), and an AI report was generated using Siemens AI software. A Likert scale was used by a radiologist to rate the report's accuracy. Ethical approval was obtained. Data are presented as mean ± SD.

Results:
The survey results showed that most participants agreed that radiographers must adapt the AI technology, and they showed interest in taking courses about AI within radiography (98%, 92%, n = 50). Participants' opinions on AI correlated with their perceptions of AI education ($p < 0.05$, $r = 0.307$). The findings from the retrospective study showed that the radiologist agreed with 53% of the AI-generated chest reports.

Conclusions:
The study findings identified a need for AI education and training for radiographers to increase their knowledge and improve their ability to use AI. Additionally, the study demonstrated that AI-powered tools are showing great promise in the field of medical imaging.

Key Words: Radiography; Artificial Intelligence; AI applications;

Funding Agency: None

Allied Health

2

Epidemiological Updates of Dermatophytosis in Kuwait: A Retrospective Study

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Introduction:
Dermatophytes are a group of fungi that infect keratinized tissues, including skin, scalp, and nails, causing dermatophytosis. Dermatophytes are categorized into three groups: anthropophilic, zoophilic, and geophilic. Anthropophilic dermatophytes cause mycosis primarily in humans; in comparison, zoophilic species are known to affect animals and can also affect humans. Geophilic dermatophytes are typically found in the wider environment and can be spread to both humans and animals. Only a few studies have explored the epidemiological and clinical characteristics of dermatophyte-related infections within the country.
Objectives: In this study, we explored the recent epidemiology of dermatophytosis at a national scale in Kuwait from January 2021 to December 2024.

Methods:
Data were obtained from the Reference Mycology Laboratory in Kuwait. Microsoft Excel was used to numerically code and label all data, and a statistical analysis was conducted using GraphPad Prism 10. A chi-square test was used to analyze the association between clinical specimens and age group in dermatophytosis. In addition, a chi-square test for independence was employed to determine the frequency of cases across the four seasons over the years. A P-value < 0.05 considered to indicate statistical significance. The study was approved by the Ministry of Health ethical committee (Approval Number: 2648, September 2024).

Results:
A total of 214 dermatophyte isolates from 211 patients were obtained from January 2021 to December 2024. The predominant dermatophytes were zoophilic species, accounting for 53% of cases, followed by anthropophilic species, accounting for 33%, 4% of cases involving geophilic dermatophytes, and 10.5% of cases involving unidentified species. The most frequently isolated dermatophyte was Trichophyton spp., with 132 (61.5%) cases, followed by 73 (34%) cases involving Microsporum spp. and 8 (4%) cases involving Nannizzia spp. Epidermophyton spp. were isolated in only 0.5% of cases. Molecular methods also detected seven cases of Trichophyton indotineae (3%) among all Trichophyton spp. Children under 10 years of age were the most frequently affected age group, accounting for 37% of cases ($X2 = 123.7$, $df = 18$, $P < 0.0001$). Dermatophytosis was slightly more prevalent in males than females in all age groups. Seasonal variation in the frequency of dermatophytosis across the years was statistically significant, with a P-value of 0.0087.

Conclusions:
The abundance of zoophilic dermatophytes was found to be higher than anthropophilic dermatophytes, which highlights the significant role of animal-to-human transmission. In addition, the emergence of T. indotineae cases in Kuwait calls for antifungal management in dermatological clinics, active surveillance of refractory recurring cases, and enhanced mycology diagnostic services. These data will assist in identifying causative agents to develop effective treatment and prevention strategies, especially considering the limited information on dermatophyte species distribution in Kuwait.

Key Words: Dermatophytes; Trichophyton indotineae; Epidemiology;

Funding Agency: None

Allied Health

3

Impact of Education on the level of Physical Activity among Pregnant Women in Kuwait: An Exploratory Study

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Introduction:
Pregnancy is a critical life stage characterized by physiological and psychological changes that can influence physical activity (PA). Moderate PA during pregnancy, as recommended by the World Health Organization, reduces complications and promotes maternal and fetal health. However, many women fail to achieve adequate PA levels, often due to insufficient knowledge and fear of adverse outcomes. This pilot study aimed to evaluate the impact of an educational intervention on PA levels among pregnant women in Kuwait.

Methods:
A quasi-experimental pre–post design was conducted with 20 pregnant women aged 18 years and above. Following ethical approval and informed consent, participants completed the Pregnancy Physical Activity Questionnaire (PPAQ) at baseline. They were then enrolled in a WhatsApp group and received a structured 3-week online educational program delivered by a certified prenatal instructor. The intervention included four live virtual sessions covering physiological changes during pregnancy, benefits of PA, exercise precautions and contraindications, and demonstrations of safe exercises. Daily motivational messages, educational videos, and reminders were shared to reinforce engagement. After completing the program, participants filled out the PPAQ again. Data were analyzed using permutation tests for non-parametric variables, with significance set at $p < 0.05$.

Results:
Post-intervention, PPAQ scores improved significantly. Moderate-intensity activity increased from a mean of 1.5 to 3.2 ($p = 0.004$), and sport/exercise activities rose from 0.5 to 2.0 ($p = 0.001$). The total PA score showed a mean difference of -28.68 (95% CI: -52.44 to -4.92, $p = 0.021$). Sedentary behaviors exhibited minimal change.

Conclusions:
This pilot study suggests that targeted education can enhance PA levels during pregnancy. However, findings should be interpreted cautiously due to methodological limitations, including small sample size, absence of a control group, and short intervention duration. Future research should employ larger, randomized samples and longer follow-up periods to confirm effectiveness and improve generalizability.

Acknowledgment:
We sincerely thank all participants who completed the educational sessions and contributed to this study.

Key Words: Pregnancy; Physical Activity; Education;

Funding Agency: None

Allied Health

4

EMMATKA trial: the effects of mobilization with movement following total knee arthroplasty in women: a single-blind randomized controlled trial

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Introduction:
Mobilization with Movement (MWM) is an examination and management approach for correcting the intra-articular translational and rotational movements to facilitate the active physiological movement. The study aimed to determine the effects of MWM on Total Knee Arthroplasty (TKA) using a randomized controlled trial (RCT) design.

Methods:
The trial is registered (ISRCTN ref: 13,028,992). A blinded examiner assessed patients at pre-surgical (before TKA), post-surgical (at 3-weeks post-TKA), 6-weeks and 6-months post-TKA. Participants were randomly assigned to receive MWM (six sessions, between 3 and 6 weeks post-TKA) plus standard rehabilitation (intervention group) or standard rehabilitation alone (control group) of outpatient rehabilitation including range of motion and strengthening exercises, cycling, gait and stair training. Outcome measures were range of motion (goniometer), pain (visual analogue scales), physical function (Timed Up and Go (TUG)), a 15-m walk test, and health status (Western Ontario and McMaster (WOMAC) Osteoarthritis Index). Change in outcome measures from post-surgical to 6 weeks and 6 months post-TKA were compared between groups. The primary outcome was change in knee flexion range of motion at 6 weeks.

Results:
84 women scheduled for TKA were randomly allocated to intervention (n = 42) or control (n = 42); mean ± (SD) age 65.1 ± 7.4 and 66.8 ± 8.9 years, respectively. The intervention group demonstrated significantly greater increase in knee flexion at both 6 weeks (median (IQR) + 10.000 (20.000) compared with + 2.500 (6.250) in the control group) and 6 months (+ 12.500 (15.000) and + 5.000 (10.000) respectively) (both $p < 0.05$). There were no differences between groups in secondary outcomes.

Conclusions:
Introducing MWM for TKA rehabilitation has greater benefits for women post-TKA in increasing knee joint flexion range of motion than the standard rehabilitation programs in the short and medium-term. This evidence-based approach offers a promising adjunctive intervention for optimizing recovery and rehabilitation process following TKA in women. Clinicians should consider including MWM approach in post-TKA rehabilitation programs.

Key Words: Knee Arthroplasty; Knee Pain; Rehabilitation;

Funding Agency: Kuwait Foundation for the Advancement of Sciences (KFAS)

Allied Health

5

Prevalence and risk factors of muscoskeletal pain among Kuwaiti pilgrims during hajj 2024

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MOH

Introduction:
Musculoskeletal pain (MSP) is a leading cause of disability worldwide and is frequently reported during the Muslim Hajj pilgrimage. However, the prevalence of MSP and factors associated with its occurrence among Kuwaiti pilgrims have not been previously investigated. This study aimed to determine the prevalence of MSP during Hajj 2024 and examine factors associated with MSP among Kuwaiti pilgrims.

Methods:
This retrospective cross-sectional study was conducted among Kuwaiti pilgrims during Hajj 2024. Pilgrims completed a structured survey assessing demographics, health status, lifestyle factors, and the presence of musculoskeletal pain. Associations between MSP and selected variables were examined using binomial generalized linear models with a log link.

Results:
A total of 557 participants were included, of whom 61% were women. Musculoskeletal pain was reported by 24% of participants. Female gender, short sleep duration (less than 6 hours), and smoking were significantly associated with MSP, while absence of hypertension was associated with a lower prevalence of MSP.

Conclusions:
This study, the first to focus on Kuwaiti pilgrims in this regard, showed that the reported prevalence of musculoskeletal pain (MSP) during Hajj was lower than that reported previously in studies of other nationalities. Several factors were found to be associated with MSP, including smoking, hypertension, poor sleep, and female gender. The findings of this study emphasize the need for a pre-Hajj screening programme and increased awareness of factors associated with the prevalence of MSP.
Musculoskeletal pain was prevalent among Kuwaiti pilgrims during Hajj 2024. Several demographic and lifestyle factors were found to be associated with MSP. Due to the retrospective cross-sectional design, causal relationships cannot be inferred. These findings highlight the importance of pre-Hajj screening and preventive strategies.

Key Words: Musculoskeletal pain; Hajj; Kuwait pilgrims;

Funding Agency: KAFS

Allied Health

6

Outcomes of Postmastectomy Lymphedema of Females Attending the Physiotherapy Department in Kuwait: A Five-year-Retrospective Study

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Introduction:
Postmastectomy lymphedema can result in poor functional recovery, chronic disability, and a reduced quality of life. One of the comprehensive conservative interventions is Complete Decongestive Therapy (CDT), which is delivered by a trained physical therapist and includes daily manual lymphatic drainage, multilayer compression bandaging, therapeutic exercises and skin care. Other conventional therapies (CT) combine machine-assisted lymphatic drainage with compression garments, exercise and skin care. The objective of this study is to compare the outcomes of postmastectomy lymphedema in female patients who received either CDT or CT.

Methods:
A chart review was conducted for female patients treated for postmastectomy upper-limb lymphedema at the physical therapy department between 2021 and 2025. Data extracted from medical records included: age, type of mastectomy, time elapsed since mastectomy, side of involvement, treatment type (CDT or CT), and degree of improvement in lymphedema based on changes in arm girth (pre-treatment girth minus post-treatment girth). Due to the retrospective design, data collection was limited to information available in existing records. Ethical approval was granted by the MOH Ethical committee (Study #2860/2025).

Results:
Data were collected from 214 female patients with a mean age of 57 years. 56% of the patients undergone a modified radical mastectomy. The time elapsed since mastectomy ranged from 1 to 28 years, and 52% of the procedures were performed on the left side. CDT was the treatment received by 58% of the patients. Both CDT and CT led to reductions in arm girth measures. The differences between the two treatments were not statistically significant. A significant correlation was found between patient age and the mean difference in outcomes in the two treatment groups at the 0.05 significance level, thus younger patients showed better outcomes.

Conclusions:
The findings suggest that both CDT and CT can be beneficial for managing postmastectomy lymphedema, offering comparable improvements in arm girth measurements. Given the lack of a significant difference between treatment types, clinicians may prioritize accessibility, patient preference, and resource availability when selecting a management strategy. Age-related differences in outcomes indicate that younger patients may be more likely to benefit from postmastectomy lymphedema treatments.

Key Words: Postmastectomy Lymphedema, Complete Decongestive T; words: Postmastectomy

Funding Agency: None

Anatomy

7

Are COVID-19 vaccines the primary cause of memory impairment?

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Introduction:
One day, COVID19 vaccine was the lifeline from a deadly, incurable novel pandemic. However, it quickly became a source of anxiety and fear for many due to its side effects. Although these side effects are rare, people have become overly concerned and refer any health issue such as memory impairment to the vaccine, ignoring their unhealthy daily habits that they began practicing recently in the post-vaccination period, which in turn cause brain fog. Here, we aimed to see the public opinion regarding the vaccine and its impact on memory, to study their habits in order to determine if the vaccine is the primary cause of memory impairment as well as to spread awareness among Kuwaiti society.

Methods:
An online questionnaire was randomly distributed to 300 individuals of Kuwait residents. They were asked about their vaccination status, opinion on the vaccine, health status, daily habits, how well they know about the vaccine and so on. Data were collected and analyzed on November 2025.

Results:
Out of 300 individuals, 242 complain of memory impairment in recent years. 81% of them believe that the vaccine is the primary cause of their memory problems. However, 54.3% of those who have memory problems are unvaccinated. Unfortunately, 70.4% of people who believe that their memory impairment is due to the vaccine, spend long continuous hours on the smart devices mainly on shorts, reels and social media. Moreover, most of the participants acquired unhealthy habits during the lock down and keep on them. Unreliable sources are the main references that most of individuals depend on to educate about the vaccine.

Conclusions:
Here we are not to say that COVID19 vaccines are totally safe in term of their effect on memory, but to draw the public attention to the habits that have invaded our life in the post-vaccination period which cause brain fog leading to memory impairment.

Key Words: COVID-19 vaccine; Memory impairment ; Brain fog;

Funding Agency: None

Anatomy

8

Effects of N-Acetylcysteine Amide and Thymoquinone on Inflammatory Cytokines in β-Amyloid (Aβ) Exposed Primary Cortical Neuronal Culture

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Introduction:
Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by neuroinflammation, synaptic degeneration, and neuronal death due to the accumulation of β-amyloid (Aβ) deposits, plaques, and neurofibrillary tangles within neurons. N-acetylcysteine amide (NACA) and thymoquinone (TQ) are recognized antioxidants with prospective therapeutic effects against oxidative stress in AD.

Methods:
This study was aimed to examine the impact of NACA and TQ on inflammatory cytokines and growth factors in cerebral cortical neural cultures exposed to Aβ1-42. The study was conducted after obtaining animal ethical approval from the animal ethical committee of the Health Sciences Center (HSC), Kuwait University. Primary cortical neural cultures were prepared from embryonic day 18 Wistar rat fetuses, grown for 10 days, and exposed to Aβ1-42 oligomers (10 μM), alone or in combination with NACA (10 μM) and/or TQ (12.5 μM), for five days. (n=6 cultures. Triplicate cultures were used for each study parameter). Cell viability was measured by MTT assay. Neurons, astrocytes, and microglial cells were quantified by counting the Tuj1- (neurons), GFAP- (astrocytes), and Iba1- (microglia) positive cells and measuring their protein levels by Western blotting method. Pro-inflammatory cytokines (IL-1α, IL-1β, IL-6, and TNF-α), anti-inflammatory cytokines (IL-4, IL-10, and IFN), and growth factors (CNTF, NGF, and VEGF) were assayed by multiplex cytokine array method. Data were analyzed with one way ANOVA followed by Bonferroni's multiple comparison test.

Results:
Aβ1-42 exposure significantly reduced cell viability ($p<0.05$), neuronal, astrocyte, and microglial populations ($p<0.05$), anti-inflammatory cytokine (IL-4, IL-10, and IFN-γ) levels ($p<0.05$), and growth factor (NGF, VEGF, and CNTF) levels ($p<0.05$), while increasing pro-inflammatory cytokine (IL-1α, IL-1β, IL-6, and TNF-α) levels ($p<0.05$). Treatment with NACA, TQ, or their combination effectively restored cell survival, reduced inflammation, and enhanced neurotrophic factor expression, with the NACA+TQ combination showing the strongest neuroprotective effect.

Conclusions:
Our study highlights that combining NACA and TQ may offer synergistic protection against Aβ-induced oxidative stress, inflammation, and neuronal damage.
Acknowledgments: This study was supported by Research sector, Kuwait University, Grant No. YM-07/22 and RCF, RU project # GM01/15.

Key Words: Alzheimer's disease; N-acetylcysteine amide; thymoquinone;

Funding Agency: Research sector, Kuwait University, Grant No. YM-07/22

Anatomy

9

Double-Mutant 5xFAD × db/db Mice Exhibit Markedly Increased Anxiety-Like Behavior Across Standard Behavioral Tests

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Introduction:
Alzheimer's disease (AD) and type 2 diabetes mellitus (T2DM) share overlapping mechanisms involving metabolic dysfunction, insulin resistance, and neuroinflammation. Combining the 5XFAD AD model with the db/db diabetic model enables investigation of how severe metabolic disease influences AD-related behavioral phenotypes. This study aimed to generate and characterize mice carrying both 5XFAD and db mutations to establish a dual-phenotype platform for future mechanistic analyses.

Methods:
Mice carrying 5XFAD transgenes and db alleles were bred using controlled crossing strategies to obtain wild-type, db/+, db/db, 5XFAD/+;db/+, and 5XFAD/+;db/db genotypes. Genotyping was performed using PCR amplification of APP, PSEN1, and Lepr loci followed by agarose gel electrophoresis to confirm allele distribution. All mice completed a standardized behavioral battery consisting of the Forced Swim Test (to assess depression-like immobility behavior), the Open Field Test (to evaluate locomotor activity and exploratory behavior through total distance traveled and center-periphery patterns), and the Elevated Plus Maze (to measure anxiety-related behavior via open- and closed-arm exploration). All tests were conducted under controlled lighting, timing, and habituation protocols to ensure consistency across genotypes. Ethical approval was obtained for mice work through HSC animal ethical committee.

Results:
Across all three behavioral assays—OFT, EPM, and FST—the double-mutant 5xFAD × db/db mice displayed the most pronounced anxiety-like phenotype. Relative to wild-type, db/db, and 5xFAD groups, the double mutants spent the least time in the center zone in the OFT, showed the greatest avoidance of the open arms in the EPM, and demonstrated the highest immobility duration in the FST. Together, these findings indicate that combining the metabolic deficit (db/db) with the neurodegenerative background (5xFAD) markedly exacerbates anxiety-related behavior beyond that observed in either single-mutant model.

Conclusions:
Future Prospects: Dual-phenotype 5XFAD/db/db mice provide a valuable model for probing interactions between metabolic dysfunction and AD-related behavior. Future work will incorporate cognitive testing and neuropathological analysis to define how diabetes accelerates or modifies AD progression.

Key Words: OFT, FST, EPM, ; insulin resistance, 5XFAD; diabetes alzhemirs;

Funding Agency: We thank the Animal Resources Centre and Research Core facility (SRUL02/13; GM01/15) at Kuwait University. Work was supported by grant RM01/19 and RM01/23 to MAO through KU.

Anatomy

10

High-Fat Diet Influences the Progression of Amyloid Pathology in 5XFAD Mouse Model

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Introduction:
Alzheimer's disease (AD) is a neurodegenerative disorder characterized by amyloid plaques accumulation and neurofibrillary tangles. Metabolic dysfunction induced by high-fat diet (HFD) has been linked to severe cognitive deficits in AD models. However, the extent of these effects and the molecular mechanisms by which HFD influences amyloid pathology remain unclear. This study investigated the impact of HFD-induced metabolic dysregulation on amyloid pathology, cognitive function, and synaptic integrity using the 5XFAD early-onset AD mouse model.

Methods:
Five- to six-month-old male 5XFAD and their age-matched wild-type (WT) mice were assigned to normal chow diet (NCD) or HFD (60% fat). Baseline phenotypic assessments included FDG-PET imaging, behavioral tests, and metabolic profiling. Mice were then fed with either NCD or HFD for 18 weeks, followed by same tests (n=11/ group). Cortical RNA sequencing was conducted across groups. Confocal microscopy was used to assess plaque load and microglial activation. For statistical analyses, unpaired t-tests and two-way ANOVA were used (mean ± SEM). Ethical Approval: MF-23-02.

Results:
At baseline, 5XFAD mice showed normal metabolic profiles with lower body weight compared to WT, likely due to hyperactivity ($P<0.01$). They also displayed altered anxiety-like behavior and impaired working memory. HFD feeding induces weight gain in both genotypes; however, this gain plateaued after week 6 in 5XFAD mice. HFD-fed 5XFAD developed hyperglycemia, glucose intolerance and insulin resistance compared to NCD-fed 5XFAD. Although HFD didn't alter brain glucose uptake in 5XFAD mice, a trend toward reduced plaques load was observed particularly in the hippocampus. Cortical RNA-seq revealed a significant upregulation of genes involved in neuroinflammation (Cst7, trem2), neuronal activity (Erg1, Erg2, Arc), and synaptic integrity (Homer1) in HFD-fed 5XFAD mice.

Conclusions:
Our results suggest that HFD-induced metabolic dysfunction influences the progression of amyloid pathology in 5XFAD mice. This may contribute to synaptic remodeling, cognitive impairment and identifying potential pathways linking metabolic dysfunction to AD progression.

Key Words: Alzheimer's Disease; Metabolic Dysfunction; Diet-induced obesity;

Funding Agency: Grant no. RM01/19 and RM01/23 to Dr. Mohammed Al-Onaizi through Kuwait University

Anatomy

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Tempol Attenuates Oxidative Stress and Neurodegeneration by Modulating Retinal Gene Expression in Diabetes

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Introduction:
Diabetic retinopathy, a leading cause of blindness worldwide, develops because of chronic hyperglycemia that triggers oxidative stress, inflammation, and neurodegeneration in the retina. Oxidative stress plays a pivotal role in early neuronal dysfunction. Tempol, a superoxide dismutase mimetic antioxidant, has shown protective effects in diabetic tissues, but its impact on retinal gene expression remains unclear. We investigated the modulatory effect of Tempol on diabetes-induced transcriptomic alterations in the neural retina, with a focus on oxidative stress and neuroprotection.

Methods:
Twelve-week-old male Wistar rats (n=5 per group) were divided into four groups: control, control + Tempol (25 mg/kg/day), diabetic (STZ 50 mg/kg), and diabetic + Tempol. Body weight and random blood glucose levels were recorded weekly. Post 12 weeks, neural retinas were dissected, total RNA was extracted, and microarray analysis was performed to assess the expression of over 22,000 genes. qPCR was performed to confirm microarray results for Stat1, Txnip, GFAP, Iba1, Prkca and Opn1sw. Ethical clearance was obtained for protocols related to animal work from HSC Animal Ethical Committee.

Results:
Diabetic rats exhibited progressive weight loss and sustained hyperglycemia throughout the 12-week period, and Tempol treatment did not alter these systemic parameters. Transcriptomic profiling revealed 494 diabetes-induced differentially expressed genes (353 upregulated, 141 downregulated), primarily linked to oxidative stress, immune activation, and visual system dysfunction. Tempol markedly reduced this number to 230 (50 upregulated, 180 downregulated), indicating partial normalization of the diabetic transcriptome. Key oxidative stress genes (TXNIP, Cat, Aldh1a1, Mt1/2) and gliosis-related markers (GFAP, Vim, Aif1, Lcn2) were upregulated in diabetic retinas, while neuronal and photoreceptor markers (Rcvrn, Opn1sw, Prkca, Prox1, Gad1, Nefl) were downregulated. Tempol attenuated these alterations, restoring antioxidant balance and preserving retinal cell-specific gene expression.

Conclusions:
Tempol mitigates diabetes-induced oxidative and inflammatory stress, and preserves retinal cell-type-specific gene expression. These results provide strong transcriptomic evidence supporting therapeutic potential of Tempol in the early stages of diabetic retinopathy.

Acknowledgements
We thank the Animal Resources Centre, RCF (SRUL02/13; GM01/15); and Dr. Josely George for technical help.

Key Words: Diabetic retinopathy; oxidative stress; neuroinflammation;

Funding Agency: Funding Agency: RM01/20 and MA01/22 to HAH through KU.

Anatomy

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Metabolic Dysfunction and Tau Pathology in Diabetes-Associated Dementia: Insights from Genetic and Diet-Induced Mouse Models and Human Brain Tissue

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Introduction:
Diabetes related dementia is associated with Alzheimer's disease-like pathology, characterized by tau hyperphosphorylation and aggregation. We investigated the effect of metabolic dysfunction on Tau pathology in mice using a genetic model of diabetes and a high fat diet (HFDc) induced model of insulin resistance. We further explored the effect of diabetes on Tau pathology in the human brain.

Methods:
The diabetes mouse model db/db was compared with age matched controls and grouped as young (5 months) and aged (12 months). For diet induced model, C57BL/6J mice were randomly assigned to be fed normal chow diet or commercial high fat diet. for short-term (12 weeks) and long-term (27 weeks). Cortical tissue was used to perform western blot analysis against Tau, PhosphoTau (T217, T231, S202/T205, S396), □-Actin and GAPDH. Band intensities were quantified and statistical analysis was performed using the unpaired Student's t-test. Only male mice were used in the study and n□3 for all groups. Ethical approval was obtained for both mouse and human samples through the HSC ethical committee.

Results:
Tau is hyperphosphorylated at S396 and T217 in the cortex and hippocampus of young db/db mice. Additionally, aged db/db mice display hyperphosphorylation at T231 and S202/T205 in the cortex. HFDc-fed mice displayed hyperphosphorylation in the cortex at T231, only when they developed insulin resistance. Binding of total Tau antibodies- Tau5 and BT2 is significantly impaired in all models when Tau is hyperphosphorylated. Initial analysis revealed a significant decrease in PP2Ac activity in db/db mice. To further explore how kinome-phosphatome expression is affected by T2DM, we used RNA-sequencing and identified 11 kinases that are upregulated in the hippocampus, including SGK1. Additionally, we characterized the expression of PHF1 and MC1 in the superior frontal gyrus of patients who suffered from T2DM or T2DM with Alzheimer's disease.

Conclusions:
Our findings highlight the impact of metabolic dysfunction on Tau pathology. Impaired dephosphorylation, complemented by an increase in kinase transcripts seems to be a key mechanism of tau hyperphosphorylation. These findings are useful for potential therapeutic targets against tau pathology in diabetes-related dementia.

Acknowledgements:
We thank the Animal Resources Centre and RCF (SRUL02/13; GM01/15). PHF1 and MC1 antibodies were obtained from the laboratory of the late Dr. Peter Davies. We also thank Dr. Rola Ali.

Key Words: Diabetes associated Dementia; Tau pathology; Metabolic dysfunction;

Funding Agency: Funding Agency - Kuwait University, Grant numbers RM01/19 and RM01/23

Anatomy

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Impaired Glucose Metabolism as an Amplifier of Neurodegenerative Features: Microtubule-Related Mechanisms

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Introduction:
Neurons rely on a network of microtubules to maintain their structural integrity and axonal transport. However, when this system deteriorates, as frequently seen in Alzheimer's disease, the breakdown in support and transport contributes to broader neuronal failure. Recent studies suggest that glucose impairment may cause similar microtubule damage, but the link remains unclear. Because metabolic stress is a major risk factor for dementia, it is important to clarify whether glucose dysregulation directly destabilizes the microtubule system in the brain. Thus, this study aims to elucidate how impaired glucose regulation might drive neurodegeneration by altering the microtubule skeleton.

Methods:
C57BL/6J-db/db mice at early and aged stages were used to model hyperglycemia, high-fat diet mice to assess diet-induced metabolic stress, and 5XFAD/+ mice to validate Alzheimer's-like pathology, with each group analyzed alongside its control (n=3 per group). Tau hyperphosphorylation was examined by phospho-tau S396 Immunofluorescence, microtubule stability by Western blotting for total and acetylated alpha-tubulin, and forebrain transcriptome via high-throughput sequencing for differential gene expression and pathway enrichment. Data were analyzed using an unpaired t-test, and all animal procedures were approved by the Animal Ethics Committee at Kuwait University

Results:
Tau phosphorylation was elevated in both the cortex and hippocampus of the db/db model. Moreover, the alpha-tubulin protein level was significantly reduced in mouse models of Alzheimer's disease, diabetes, and obesity, while the level of acetylated alpha-tubulin was significantly increased ($p < 0.05$). Transcriptomic analysis revealed differential expression of microtubule-associated genes in response to hyperglycemia and dietary metabolic stress.

Conclusions:
Our findings suggest that impaired glucose metabolism plays a role in weakening the microtubule network by altering gene expression, promoting tau phosphorylation, and reducing tubulin availability. The increase in acetylated tubulin levels might indicate a neuron's compensatory mechanism against a compromised microtubule structure. These results highlight a mechanistic link between diabetes-induced cognitive decline and neurodegenerative conditions like Alzheimer's disease
Acknowledgments: We thank the College of Graduate Studies, Animal Resource Center (MF-23-02), and the Research Core facility (SRUL02/13; GM01/15).

Key Words: Alzheimer's disease; metabolic stress; Microtubules ;

Funding Agency: College of Graduate Studies and RS Grant number RM01/19 and RM01/23

Anatomy

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Korean red Ginseng Extract Enhances Hippocampal BDNF, VEGF and Neurogenesis in Rats.

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Introduction:
Roots of Ginseng plant had been used as medicine and food supplement for centuries. Korean ginseng (Panax ginseng) is known for its medicinal benefits. Extracts of the Ginseng roots was proved to enhance adult hippocampal neurogenesis. Several different food supplements of Ginseng such as Korean Red Ginseng (KRG) extract are available in market. Present study was aimed to study KRG extract formulation on adult neurogenesis in Wistar rats.

Methods:
Present study was conducted after obtaining animal ethical approval from the animal ethical committee of Health Sciences Center (HSC), Kuwait University. Adult (3 months old) male and female Wistar rats were divided into Normal Control [NC, (n=12 (6 male, and female)], and Ginseng treatment [GT, n=12, (6 male+ 6 female)] groups. Rats in GT group were treated with KRG extract (50mg/kg, oral) for three weeks. KRG was purchased from local market. Rats in NC group were treated with 0.5ml saline for the same duration. After treatment, all rats were either perfused with 4% paraformaldehyde to collect the fixed brain tissues for morphological studies or perfused with cold saline to collect the fresh hippocampal tissue for biochemical studies. Sections of the brain were immunostained for doublecortion (DCX-marker for new neurons), GFAP (for astrocytes) and Iba1 (for microglia). DCX content in the hippocampus was quantitated by Western blot analysis. BDNF and VEGF were measured in the fresh hippocampal tissue by ELISA method. Data were analyzed with Student's t-test. Since in all parameters, there was no significant difference between male and female rats, data was clubbed and analyzed.

Results:
Immunostaining for DCX showed a significant increase in new neurons in the hippocampal dentate gyrus in GT group compared to NC group ($p<0.05$). This was confirmed by western blot analysis for DCX protein in the hippocampus. Immunostaining for astrocytes and microglia showed marginal increase ($p<0.05$) in their population in GT group. Analysis of BDNF and VEGF showed significant increase in BDNF ($p<0.05$) and VEGF in the hippocampal tissue in GT group compared to NC group.

Conclusions:
We conclude that KRG extract enhances the adult hippocampal neurogenesis by enhancing the BDNF and VEGF secretion by enhanced microglia and astrocytes.

Acknowledgments: We acknowledge research core facility, RU project # GM01/15.

Key Words: Hippocampus; Neurogenesis; Ginseng;

Funding Agency: Nil

Anatomy

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Ashwagandha Root Powder Enhances Hippocampal BDNF, VEGF and Neurogenesis in Rats.

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Introduction:
Ashwagandha is an herbal plant belonging to the Solanaceae family. Its root extract has been well studied. It has been used as anti-microbial, anti-inflammatory, anti-stress, anti-tumor, and neuroprotective agents. Several different food supplements containing Ashwagandha root powder (ARP) are available in market. Present study was aimed to study ARP formulation on Hippocampal neurogenesis in Wistar rats.

Methods:
Prior approval from Animal ethical committee of Health Sciences Center (HSC), Kuwait University was obtained before commencing the experiment. Male and Female Wistar rats (3 months old) were divided into Normal Control [NC, (n=12 (6 male, and female)], and Ashwagandha treatment [AT, n=12, (6 male and 6 female) groups]. Rats in NC group were treated with 0.5ml saline for three weeks. Rats in AT group were treated with Ashwagandha root powder (50mg/kg, oral) for three weeks. ARP was purchased from local market. After treatment, rats were perfused with cold saline to collect the fresh hippocampal tissue for biochemical studies on doublecortin (DCX-marker for new neurons), BDNF and VEGF. DCX was quantitated in the hippocampal tissue by Western blot analysis. BDNF and VEGF were measured in the fresh hippocampal tissue by ELISA method. A subgroup of rats was perfused with 4% paraformaldehyde to collect the fixed brain tissues for immunostaining for new neurons (DCX), astrocytes (GFAP) and microglia (Iba1). Since in all parameters, there was no significant difference between male and female rats, data was clubbed and analyzed with Student's t-test.

Results:
Analysis of BDNF and VEGF showed significant increase in BDNF ($p<0.05$) and VEGF in the hippocampal tissue in AT group compared to NC group. Immunostaining for doublecortin (DCX-marker for neurogenesis) showed significant increase in new neurons in the hippocampal dentate gyrus in AT group compared to NC group ($p<0.05$). This was confirmed by western blot analysis for DCX protein in the hippocampus. Immunostaining for astrocytes and microglia showed marginal increase ($p<0.05$) in their population in AT group compared to control group.

Conclusions:
It was concluded that ARP enhances the neurogenesis in the hippocampal dentate gyrus. This enhancement of neurogenesis is by enhancing the BDNF and VEGF secretion by enhanced microglia and astrocytes in the hippocampus.

Acknowledgments: We acknowledge research core facility, RU project # GM01/15).

Key Words: Hippocampus; Neurogenesis; Ashwagandha;

Funding Agency: Nil

Anatomy

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Beyond Blue Light: Metabolic Dysregulation and Multi-Organ Alterations Induced by Chronic Blue Light Exposure in Mice.

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Introduction:
Artificial light, especially blue LED light (450–470 nm), affects the biological system due to its short wavelength and high energy. Previously, we showed that 6-month-old mice exposed to blue light gained weight within a week and developed serum cytokines alteration and anxiety-like behavior after 8 weeks. Our present study aims to investigate the effects of prolonged blue light exposure on body weight, food intake, metabolic function, adipose tissue, liver and kidney morphology, testis and sperm quality.

Methods:
Three-month-old male C57BL/6 mice divided into control under normal light (n=19) and experimental under 450 nm LED (n=16) for 5 hrs /day for 40 weeks with ethical approval from Kuwait University. Food intake and body weight were recorded twice weekly, and fasting blood glucose was measured every two weeks. Metabolic assessments, (OGTT) and (ITT), were performed at weeks 0, 4, 8, 20, 32, and 40. At week 40, adipose tissues (EWAT, SWAT, BAT) along with the heart, liver, testis, and kidneys were collected and weighed. Histology included PAS (liver, kidney), Oil Red O (liver), Masson's trichrome (testis), and H&E (sperm). ALT assay in liver, and UCP1 protein expression in BAT by Western blot. Data were analyzed using GraphPad Prism (mean ± SEM), with Student's t-test (*$p < 0.05$, **$p < 0.01$) and Mann–Whitney for ALT

Results:
After 14 weeks, body weight increased by 17% despite decreased food intake; normalized intake was lower in LED mice (1 g/g) than controls (1.2 g/g). From week 8, LED mice showed impaired glucose tolerance and reduced insulin sensitivity, persisting until week 32; glucose intolerance remained at week 40 despite recovery of insulin resistance. The weight of sWAT and eWAT increased, while BAT and testis were unchanged. However, Liver, kidney, and heart weight decreased. Histology revealed cellular degeneration in the liver and kidney. Testis exhibited less sperm in seminiferous tubules, reduced spermatogonia with unclear nuclei, low germ cell numbers, and more abnormal sperm heads. ALT levels indicated no liver damage, and UCP1 expression in BAT was unchanged, suggesting no effect on thermogenesis.

Conclusions:
Chronic blue light exposure induces metabolic dysregulation and structural changes
Acknowledgment: We thank Kuwait University (Grant MA01/22) and the Research Core Facility SRUL 02/13&GM01/15 and Animal Resources Center staff, including Dr. Josely George, Maria Joji, and Bara Abed, for technical support.

Key Words: organ dysfunction; Fat accumulation; metabolic changes ;

Funding Agency: Kuwait University MA01/22

Antimicrobial and infectious diseases

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Colistin Prescriptions and Outcomes in Kuwait Public Hospitals

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Introduction:
Objectives: To describe the prescribing patterns of colistin, its efficacy and safety.

Methods:
This multicentre, retrospective, observational study collected data from five hospitals in Kuwait. Logistic regression models were used to assess treatment outcomes.

Results:
Overall, 205 patients administered colistin were included, of whom 117 were in the intensive care unit (ICU) and 88 in the non-ICU were administered colistin. Clinical cure was achieved in 145 patients; ICU patients had the lowest response rates (P=0.001). Nephrotoxicity occurred in 50 patients, with a similar incidence in ICU and non-ICU patients (P=0.72). Death occurred in 47 patients and was more common in ICU patients (P=0.001). Neurotoxicity was reported in 11 patients, with a higher incidence in non-ICU patients (P=0.001). The colistin loading dose did not affect the clinical cure rate, incidence of nephrotoxicity, or mortality. Patients on a high maintenance dose of colistin showed higher cure rates (odds ratio [OR], 2.67; 95% confidence interval [CI], 1.13-6.32) and were less likely to die (OR, 0.29; 95% CI, 0.11-0.76) than who received a low daily maintenance dose; however, they were more likely to develop acute kidney injury (OR, 3.32; 95% CI, 1.52-7.62).

Conclusions:
Administration of high maintenance doses of colistin improved cure rates but caused nephrotoxicity.

Key Words: Colistin; loading dose; gram-negative bacteria;

Funding Agency: Kuwait University Research Grant No. [PR01/17].

Behavioral Sciences

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Stress comping mechanisms among Kuwait University students: perceptions and practice

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Introduction:
Stress is the situations in which humans perceive them as challenges, and this lead to physiological and behavioral responses aimed aimed at coping with them, and stress perception is how demands are viewed. Stress coping strategies are the efforts and strategies that used to adapt and improve the overall wellbeing of humans. Previous literature has demonstrated significant associations between perceived stress, coping strategies, and adverse mental health outcomes, including psychological distress and suicidal ideation.

Methods:
This cross-sectional study included 2,130 Kuwait University students. Stress perception was measured by the Perceived Stress Scale (PSS-10), using a 5-point likert scale distributed as an online survey among Kuwait University students from all campuses except the college of Graduate studies. While stress coping strategies, such as turning to work, emotional support, getting help and advice, were assessed using a modified Brief-COPE scale, no direct mental health disorders were evaluated in this study. Descriptive analysis was conducted using frequencies and percentages. Differences across sociodemographic variables were measured using the Mann-Whitney U and Kruskal-Wallis H tests. A linear regression was used to determine the relationship between sociodemographic factors and the sum of stress coping scores. Logistic regression was applied to assess the effect of sociodemographic factors and the coping score on stress perception score among the participants, who were mainly Kuwaiti (88.5%) and female (83.3) students aged 18 and above.

Results:
As the data were not normally distributed, results are presented as medians: the median stress perception score was 24 (IQR 7), and the median coping score was 66 (IQR 16). The student's college was significantly associated with total stress coping score and confirmed by linear regression scientific collage (95% CI :0.22- 3.062) and art and literature collage (95% CI: 0.22 to 3.046) . Additionally, a significant difference was observed across college groups and perception. Also, a significant difference was noticed across residence and total coping score. Logistic regression showed a significant association between stress coping and perception (95% CI: 1.062-1.081) .

Conclusions:
The study found a significant association between total stress coping scores and college groups. Stress coping score was a significant predictor of stress perception. Our study highlights the need for Kuwait University to offer coping skills workshops and improve psychological services to support students' well-being.

Key Words: Stress coping mechanisms ; Stress perception ; Kuwait university students;

Funding Agency: None

Biochemistry

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Significance of nano transition metal complexes as anticancer and antibacterial therapeutic agents.

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Introduction:
Metal complexes have been utilized in medicine for thousands of years in various ways, with positive benefits. They are well recognized as delivery and diagnostic agents with anti-infective, antimicrobial, antidiabetic, and neurological properties.

Methods:
Based on this, Co, Zn, and Cu complexes were synthesized using a Schiff base reaction and were fully characterized by LC-MS, NMR, FTIR, elemental analysis, TGA, DSC, SEM, and DLS techniques. The complexes were then assessed using breast cancer cell line (MDA-MB-453).

Results:
The data show that the Cu–ligand complex was the most potent anticancer agent, fol lowed by the Zn complex, and then the Co complex. HEK293 cells were used as our control. This result is supported by DFT theoretical calculations. In addition, the complexes were tested for their biological activities against both Gram-positive (Basilus sabtilus) and Gram-negative bacteria (E. Coli), and the data reveal that Cu had a strong inhibitory effect on the growth of both types of bacteria.

Conclusions:
In summary, the copper complex proved to be a potent anticancer and antibacterial agent, and it can be considered for utilization in future therapies

Key Words: metal complexes; synthesis, characterization; biological evaluation;

Funding Agency: College of graduate Studies

Biochemistry

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Photophysical Properties of Fluorinated Porphyrin Photosensitizers

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Introduction:
Background/Objectives: Fluorination is a widely used approach to modulate the photophysical properties of porphyrin photosensitizers in photodynamic therapy. This study evaluated how increasing numbers of pentafluorophenyl substituents, ranging from non-fluorinated to tetra-fluorinated derivatives, influence electronic structure, fluorescence, singlet oxygen generation, and solubility. The aim was to identify the level of fluorination that provides optimal photophysical performance without compromising formulation behaviour.

Methods:
Methods and Ethical Approval: Non-fluorinated, mono-fluorinated, cis- and trans-difluorinated, tri-fluorinated, and tetra-fluorinated porphyrins were synthesized and characterized using UV–visible absorption spectroscopy, steady-state fluorescence spectroscopy, time-resolved fluorescence lifetime measurements, and singlet oxygen quantum yield determination performed on an Edinburgh Instruments FLS980. Absorption, emission, fluorescence lifetimes, and singlet oxygen quantum yields were measured in DMSO and aqueous media. Triton X-100 micelles were used to improve solubility of the highly fluorinated derivatives. No human or animal subjects were involved, therefore ethical approval was not required.

Results:
Increasing fluorination produced progressive blue shifts in absorption and enhanced fluorescence quantum yields and lifetimes. Singlet oxygen generation reached a maximum for the trans-difluorinated porphyrin, while the tri- and tetra-fluorinated derivatives showed reduced ΦΔ despite appearing monomeric in DMSO. In aqueous media, higher degrees of fluorination promoted extensive aggregation and strong fluorescence quenching. Micellar encapsulation restored monomer-like spectral characteristics for the tri- and tetra-fluorinated porphyrins and partially recovered their absorption and emission intensities.

Conclusions:
Moderate fluorination provided the best balance between improved photophysical properties and acceptable solubility. Excessive fluorination increased hydrophobicity, enhanced aggregation, and reduced triplet-state efficiency, resulting in lower singlet oxygen production. Formulation strategies such as micellar encapsulation are necessary to maximize the performance of highly fluorinated porphyrins in biological environments.

Key Words: Photodynamic therapy; fluorinated porphyrins; singlet oxygen generation;

Funding Agency: grant YM08/20 from Kuwait University

Biochemistry

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Synthesis and Anticancer Evaluation of Novel Pyridine Carbonitrile Derivatives with Selective Cytotoxicity Against Breast Cancer Cells

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Introduction:
Breast cancer and leukemia remain major therapeutic challenges due to limited selectivity of many chemotherapeutic agents. Pyridine carbonitrile scaffolds have shown potential anticancer activity. This study aimed to synthesize new pyridine carbonitrile derivatives and evaluate their cytotoxicity toward selected cancer cell lines, with emphasis on identifying compounds that demonstrate high potency together with selectivity toward malignant cells.

Methods:
Sixteen derivatives were synthesized and fully characterized using IR, NMR, 2D NMR, and high resolution mass spectrometry. The structure of compound 10 was confirmed by single crystal X ray analysis. Cytotoxicity was assessed using MTT assay against normal skin fibroblasts, K562 leukemia cells, MCF7 breast cancer cells, and HCT116 colorectal carcinoma cells. IC50 values and selectivity ratios were calculated. This study used only established human cell lines. No human participants, primary human tissues, or animal subjects were involved. Ethical approval was not required according to institutional guidelines.

Results:
Structural analysis of compound 10 confirmed a 2 methoxypyridine 3 carbonitrile core with furan and chlorothiophene substituents. Screening identified two active compounds. Compound 11 showed moderate cytotoxicity against K562 and MCF7 cells. Compound 1 demonstrated potent and highly selective activity toward MCF7 cells with an IC50 of 1.7 ± 0.3 µM and a selectivity ratio of 19.3 compared with normal fibroblasts. At 3 µM, compound 1 showed minimal toxicity to normal cells while maintaining strong activity against breast cancer cells.

Conclusions:
Compound 1 represents a promising anticancer lead with exceptional selectivity toward breast cancer cells, suggesting potential for reduced off target toxicity. Compound 11 displayed broader activity warranting additional study. These results support further mechanistic investigations and future in vivo evaluation of pyridine carbonitrile derivatives as selective anticancer agents.

Key Words: Pyridine carbonitrile derivatives; selective anticancer activity; breast cancer cells;

Funding Agency: Kuwait Foundation for the Advancement of Sciences grant CN22 15SC 1583

Biochemistry

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Bioactive Compounds of Marine Algae and Their Potential Health and Nutraceutical Applications

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Introduction:
Marine natural products are a biosynthetically diverse source of bioactive metabolites, some with unique mechanisms of action. Seaweeds are easily collected and contain compounds with pharmacological potential, including anti-obesity, antidiabetic, antioxidant, anti-inflammatory, anticancer, anti-HIV, and antitumor properties. Untargeted metabolomics allows qualitative or semi-quantitative analysis of diverse metabolites using techniques such as LC-MS, NMR, and GC-MS. This approach provides a global view of chemical components with minimal sample manipulation, aiding in metabolite annotation and comparison among species. The aim of this study was to perform untargeted metabolomic profiling of Kuwaiti green algae to identify and annotate bioactive metabolites with potential pharmacological applications.

Methods:
Dried and homogenized seaweed extracts were reconstituted in methanol, filtered, and analyzed using HPLC-QTOF-MS/MS. Chromatographic separation used a C18 reverse-phase column under a gradient elution. Mass spectra were acquired in both positive and negative ion modes with auto-MS/MS fragmentation. Metabolites were annotated based on accurate mass, retention time, and MS/MS fragmentation by matching to publicly available databases.

Results:
Many identified compounds are reported to have cytotoxic properties. Isodecortinol [1] and decortinol [2] are C29 sterols previously isolated from Codium decorticatum and Cladophora sp. The sterol 24-R-stigmasta-4,25-diene-3β,6β-diol [3] from Codium divaricatum and 29-hydroxy-stigmasta-5,24(28)-dien-3β-ol [4] from Chaetomorpha basiretorsa exhibited cytotoxic activity. (20S)-3β,20-dihydroxyergosta-5,24(28)-dien-16-one [5] from Cystophora brownii and 2-(3-methyl-2-butenyl)-2,3-epoxy-1,4-naphthalenedione 4,4-dimethyl ketal (6) from Landsburgia quercifolia were active against P-388 leukemia cells (IC50 0.6 µg/ml) and showed antifungal properties. Compounds 7 and 8 from Sargassum carpophyllum caused morphological abnormalities in Pyricularia oryzae and exhibited cytotoxic activity. Diterpenes 9 and 10 from Dictyota divaricata, and Dictyol A (11) from Dictyota volubilis, were also detected. Most identified peaks were terpenes. C29H49O2 (m/z 429.3719) was present in most seaweeds, while the ion m/z 429.3724 was unique to C. papillatum and C. vagabunda.

Conclusions:
Overall, Kuwaiti green algae contain structurally diverse sterols and terpenes with significant cytotoxic and antifungal activities, highlighting their potential as sources of bioactive compounds. Species-specific metabolites suggest unique chemotaxonomic markers, supporting their use in future drug discovery and marine natural product research. These findings underscore the importance of untargeted metabolomics in identifying novel therapeutic candidates from marine resources.

Key Words: LCMS; natural products ; macroalgae;

Funding Agency: kisr FM144C

Biochemistry

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HDL attenuates Ang II-AT1R-EGFR signaling and reverses vascular remodeling in spontaneously hypertensive rats

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Introduction:
Angiotensin II (Ang II) signaling via angiotensin II type 1 receptor (AT1R) and transactivation of epidermal growth factor receptor (EGFR) enhances vascular smooth muscle cell (VSMC) proliferation and contributes to vascular remodeling evident in spontaneously hypertensive rats (SHR) aorta. Although high-density lipoprotein (HDL) has been shown to lower blood pressure in SHR, the underlying mechanism(s) remain incompletely understood. We propose that HDL attenuates Ang II-AT1R-EGFR signaling and reverses vascular remodeling in SHR.

Methods:
Wistar Kyoto rats (WKY) and SHR were treated with HDL for 1 week. Vascular remodeling was histologically examined. VSMC proliferation and the expression levels of AT1R, EGFR, extracellular signal regulated kinases 1/2 (ERK1/2), scavenger receptor class B type-I (SR-BI) and its adaptor protein PDZK1 were examined by immunofluorescence. VSMC proliferation was further examined in vitro. All procedures involving animals were approved by the Health Sciences Research Ethics Committee (Approval ID: 5094, Approval Date: 18-09-2016).

Results:
HDL treatment reduced blood pressure, increased the production of nitric oxide, increased aortic lumen diameter, reduced media thickness to lumen diameter ratio, decreased collagen contents in SHR. Furthermore, HDL treatment decreased the number of proliferating VSMCs and α-smooth muscle actin, reduced the expression of AT1R and EGFR and increased the expression of SR-BI adaptor protein, PDZK1, in SHR aortas (n = 7-8 rats per treatment). In isolated VSMCs, HDL attenuated Ang II-induced proliferation by reducing AT1R expression and decreasing Ang II-induced transactivation of EGFR. HDL effects were SR-BI dependent and were mimicked by different HDL subpopulations, reconstituted HDL, and lipid free apolipoprotein A-I.

Conclusions:
HDL attenuates Ang II-AT1R-EGFR signaling, reduces VSMC proliferation, and reverses vascular remodeling in SHR. HDL modulation of vascular remodeling could be one mechanism by which HDL reduces blood pressure in SHR.

Key Words: Hyspertension ; High-density lipoprotein ; Aorta;

Funding Agency: This project was funded by the Research Administration, Kuwait University, Grant No. MB02/16.

Biochemistry

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The Effect of Phenotypic State on the Photodynamic Inactivation of Candida albicans

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Introduction:
The opportunistic pathogen Candida albicans is known to undergo a phenotypic switch from typical 'white' cells to mating-competent 'opaque' cells, which also display a preference for oxidative metabolism and skin colonization These characteristics make the opaque phenotype an interesting target for antimicrobial photodynamic inactivation (PDI)—the killing of microorganisms with compounds called photosensitizers that produce reactive oxygen species in response to light. Therapeutic PDI can be used to treat mucocutaneous infections and may provide a solution to antimicrobial resistance.The photosensitizer used in this study is Zn(II) meso-tetrakis(N-n-hexylpyridinium-2-yl)porphyrin, referred to as ZnTnHex-2-PyP. This amphiphilic compound has been shown to be effective against C. albicans and is thus a good candidate to investigate the effects of PDI on the different phenotypes.

Methods:
Phase-locked white and opaque C. albicans cells were incubated with different concentrations of ZnTnHex-2-PyP and then illuminated with an appropriate light source. Cell viability assays were performed in triplicate and measured by plating on solid media and counting the resulting colony forming units (CFU). Photosensitizer uptake and localization were assessed by confocal microscopy.

Results:
Dose-dependent inactivation was achieved in both phenotypes, with greater killing observed in opaque cultures compared to white, with 2.0-micromolar ZnTnHex-2-PyP resulting in 71% and 90% reduction in CFU/mL compared to controls for white and opaque cells, respectively. Confocal microscopy revealed intracellular accumulation in the cytoplasm and in vacuoles in both phenotypes.

Conclusions:
Here we show that PDI can be used to effectively kill opaque phase cells, the phenotype responsible for C. albicans skin colonization, supporting the potential use of photodynamic therapy to effectively treat cutaneous candidiasis. While both white and opaque cells were susceptible to photodynamic inactivation by the photosensitizer ZnTnHex-2-PyP, opaque cells showed higher sensitivity despite the similar subcellular localization observed in both cell types. It would be of clinical interest to extend these investigations to the hyphal and biofilm forms of C. albicans as well. This study supports the idea that phenotypic state can alter microbial sensitivity to treatment and sheds light on the mechanisms by which antimicrobial photodynamic therapy may be used to treat cutaneous candidiasis.

Key Words: Candida albicans; antimicrobial photodynamic inactivation; photosensitizers;

Funding Agency: Kuwait University grant MB01/18

Brain and Behaviour

25

Behavioral Profiling Reveals Cognitive Impairment and Heightened Anxiety in Female 5xFAD Mice

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Introduction:
Alzheimer's disease (AD) is the most prevalent neurodegenerative disease and the leading cause of dementia worldwide. One of the hallmarks of the disease, amyloid-β plaque accumulation, has been readily studied using the transgenic 5xFAD mouse model for the past decade. However, there remains to be a wide gap when it comes to female 5xFAD mice. This is concerning, especially considering that most patients diagnosed with AD are females; therefore, characterizing sex-specific drivers of disease progression is ever so important.

Methods:
In this study, four- to six-month-old female hemizygous (HEM)(n=5), and homozygous 5xFAD (MUT) (n= 16) mice were used and compared to wild type (WT) (n=17) as controls. To investigate behavioral, cognitive and motor performance, multiple behavioral tests were conducted. Open field test (OFT) was used to assess locomotor activity and anxiety-like behavior, Y-maze (YM) to evaluate working memory, and elevated plus maze (EPM) was used for anxiety and risk assessment. Motor function was assessed using wire-hang test (WHT) and tail suspension test (TST). For statistical analyses, one-way ANOVA was used, and data were presented as mean ± SEM. The ethical approval number for this project is MF-23-02.

Results:
Homozygous female 5xFAD mice exhibited severe anxiety-like behavior reflected by a significantly reduced percentage of distance traveled in the central zone of the open field test compared to hemizygous ($p<0.001$) and WT mice ($p<0.0001$). Both hemizygous and homozygous mice showed impaired risk assessment relative to WT mice. Lastly, homozygous mice demonstrated deficits in working memory and impaired motor function.

Conclusions:
These findings highlight a genotype-dependent effect of amyloid-β pathology, resulting in marked cognitive and behavioral deficits in female 5xFAD mice. By linking genotype-associated plaque severity with behavioral and cognitive decline in females, this work aids in addressing the existing gap in knowledge when it comes to characterizing female 5xFAD mice, which further strengthens the translational relevance of this mouse model for studying sex-specific vulnerability and disease progression in AD pathology.

Acknowledgments:
This work was supported by grant No. RM01/19 and RM01/23 provided to MAO through KU. We thank the Animal Resources Center and Research Core Facility (SRUL02/13; GM01/15) at KU for their support.

Key Words: 5xFAD, Alzheimer's Disease; Behaviour ; Animal Models;

Funding Agency: Grant No. RM01/19 and RM01/23 provided to MAO through KU.

Cancer Epidemiology

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Predicting Stage at Diagnosis in Breast Cancer Patients Using Machine Learning Approaches: A Nationwide 20-Year Analysis

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Introduction:
Breast cancer is the most prevalent cancer among women in Kuwait, and late-stage diagnosis remains a major barrier to early detection and timely treatment. Machine learning has shown strong capabilities in disease prediction by capturing nonlinear relationships across multiple predictors. Population-based cancer registries provide an important opportunity to identify factors associated with stage at diagnosis; however, machine learning has not previously been applied to registry data in Kuwait. To our knowledge, this is the first national study to implement machine learning models using the Kuwait Cancer Registry. This study aimed to develop and compare multiple machine learning models to predict stage at diagnosis using demographic, lifestyle, and tumor characteristics, and to provide a reference framework for improving early detection of breast cancer.

Methods:
We analyzed Kuwait Cancer Registry data (2000–2019) retrospectively, including 8,429 breast cancer cases after cleaning and preprocessing. Missing tumor characteristics (T, N, Mp, Mc, grade, morphology) were imputed using a K-nearest neighbors algorithm with treatment and histologic variables as predictors. Sociodemographic and tumor characteristics were used to train and evaluate eleven machine learning algorithms, including logistic regression (LR), random forest (RF), support vector classification (SVC), extreme gradient boosting (XGBoost), gradient boosting decision tree (GBDT), decision tree, multilayer perceptron (MLP), linear discriminant analysis (LDA), adaptive boosting (AdaBoost), Gaussian naive Bayes (GaussianNB), and light gradient boosting machine (LightGBM). Model performance was assessed using ROC-AUC (one-vs-rest), accuracy, sensitivity, and F1-score. Ethical approval is currently under review.

Results:
XGBoost demonstrated the strongest overall performance (AUC=0.902, accuracy=0.705, Kappa=0.586, sensitivity=0.696, F1=0.711), followed by LightGBM (AUC=0.898, accuracy=0.695) and Gradient Boosting (AUC=0.896). The Support Vector Classifier achieved the highest accuracy (0.710) with competitive sensitivity and F1-score (AUC=0.875, F1=0.711). Key predictors of stage at diagnosis included tumor grade, T-stage, N-stage, metastasis status, and age. Model performance was consistent across imputed and non-imputed datasets, indicating stability and balanced classification across stage categories.

Conclusions:
XGBoost achieved the best performance in predicting breast cancer stage using Kuwait's population-based registry data. Machine learning-assisted modeling of cancer registry data can support risk stratification to identify women at higher risk of late-stage diagnosis and strengthen early detection and prevention strategies in Kuwait.

Key Words: Breast Cancer, Machine Learning; Population-Based Registry, Predictive Modeling;

Funding Agency: Kuwait University - Project no. BE01/25

Chemistry, Biology, Biological Activities, Environ

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SYNTHESIS OF 4-PHENYL-N-ARYL-2-AMINOTHIAZOLE DERIVATIVES IN AQUEOUS MEDIA USING PEGYLATED RESORCIN[4]ARENE CAVITAND: BIOACTIVITY STUDIES

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Introduction:
2-Amino-1,3-thiazoles are an attractive moiety in medicinal chemistry. Biological importance of thiazoles has led researchers to explore this heterocyclic ring as a suitable core in designing and developing innovative therapeutic agents. Structural modifications around the thiazole ring structure have been exploited for its role as an important pharmacophore in many clinically used drugs. These heterocycle substrates are normally achieved from the chemical reaction in organic solvents. However, their synthesis in an ideal reaction media, i.e., water, has been limited. Water, in general, is cheap, reusable, non-toxic, eco-, and environmentally friendly. Accordingly, designing a micro-reactor capable of improving organic transformations in water is of a great interest. This research focuses on the synthesis of 2-amino-1,3-thiazoles in water using a spatially directional PEGylated resorcin[4]arene cavitand. The multiple PEG arms based on the macrocyclic upper rim provides a host-guest environment suitable for catalyzing aminothiazoles formation in water as a green approach in organic synthesis. As well to this, the biological activity of some of the prepared 1,3-thiazoles has been investigated against gram-positive and gram-negative bacteria, E. coli ATCC 8739, S. aureus ATCC 25923, P. aeruginosa ATCC 27853, and K. pneumoniae ATCC 13853.

Methods:
The catalytic structure [5], was constructed in five steps; (i) synthesis of resorcin[4]arene [1], (ii) synthesis of cavitand [2], (iii) synthesis of tetra-bromo cavitand [3], (iv) synthesis of tetra-propargyl cavitand [4], and (v) synthesis of PEGylated catalysts [5]. All prepared compounds were characterized from their respective spectroscopic data including NMR, FT-IR, and HRMS. Strains of both gram-positive and gram-negative bacteria were cultivated in nutritional broth and incubated at 37 0C for the entire night. Mueller-Hinton agar was streaked with a swab of the overnight culture. The streaked agar was covered with a 5, 2.5, or 1.25 µg solution of the tested thiazole chemical, and the plates were incubated at 37 0C overnight. It reports the zones of growth inhibition.

Results:
Notably, results revealed that the novel PEG-catalyst was capable to enhance the formation of aminothiazole derivatives (A-E) in water with >80% yields as compared to the catalyst-free (<20% yields). Also, the biological activity of the obtained aminothiazoles were investigated against E. coli ATCC 8739, P. aeruginosa ATCC 27853, and K. pneumoniae ATCC 13853 microorganisms, and results were considerable. Compound E exhibited the strongest activity against all tested microorganisms compared to the other compounds, likely due to the presence of two thiazolyl groups, whereas the others contain only one thiazole ring. Additionally, compounds C and D demonstrated greater efficacy than A and B, which may be attributed to the azine ring present in both C and D.

Conclusions:
In conclusion, a novel water-soluble PEG–resorcin arene cavitand has been successfully synthesized and its utility as a catalyst toward N-aryl-2-amino-1,3-thiazole formation in aqueous media has been examined. Also, the biological activity of the attained thiazole substrates (A-E) has been investigated against E. Coli ATCC 8739, P. aeruginosa ATCC 27853, and K. pneumoniae ATCC 13853. From these findings, our aim in the future is to design a new host-guest materials based on resorcin arene macrocycles for different type of applications associated to host-guest chemistry, supramolecular chemistry, medicinal chemistry and material science.

Key Words: Organic synthesis and catalysis in water; Environmental Chemistry ; Biological
Funding Agency: SC02/23

Clinical Neuropharmacology

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Acetylcholine energises movement, without improving reward sensitivity in patients with parkinsonism.

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Introduction:
Background: Lewy body diseases (LBD), including Parkinson's disease (PD) and dementia with Lewy bodies (DLB), involve both motor deficits (e.g. bradykinesia) and motivational deficits (e.g. apathy). While dopaminergic loss contributes to both, cholinergic therapies such as rivastigmine may improve cognition and apathy but can worsen tremor, creating a therapeutic dilemma. It remains unclear whether cholinergic enhancement improves motor vigour, reward sensitivity, or both.
Objective: To determine the effects of rivastigmine on motor vigour and reward sensitivity using saccadic and pupillometric measures in LBD.

Methods:
Twenty-four patients with LBD (16 PD, 8 DLB) prescribed rivastigmine and 31 healthy controls (HC) performed a reward-incentivised prosaccade task with eye-tracking and pupillometry. Patients were tested ON and OFF rivastigmine in a counterbalanced within-subject design (OFF: withheld overnight; ON: taken as usual). An auditory cue signalled potential reward (0p/10p/50p) before a speeded saccade to a peripheral target. Primary outcomes were saccadic peak velocity (and velocity residuals controlling for amplitude), amplitude, reaction time, and cue-evoked pupil dilation. Trial-wise linear mixed-effects models tested fixed effects of Drug and Reward and their interaction, with participant as a random effect. PD and DLB patients were analysed together as a single LBD group for primary analyses. HC were analysed separately for reward sensitivity. The study was approved by the National Research Ethics Service (NRES ref 18/LO/2152), and all participants gave written informed consent.

Results:
Rivastigmine significantly increased saccadic peak velocity and amplitude and reduced reaction time in LBD, indicating enhanced motor vigour and faster motor initiation. There was no Drug × Reward interaction for saccadic or pupillary measures, showing that rivastigmine did not enhance reward sensitivity. HC showed robust pupillary reward sensitivity, which was attenuated in LBD.

Conclusions:
Rivastigmine energised movement without improving reward sensitivity, suggesting cholinergic enhancement preferentially benefits motor initiation and movement vigour rather than reward processing in LBD.

Key Words: Parkinson's Disease; Cholinesterase Inhibitors; Eye Movements;

Funding Agency: None

Clinical Neuropharmacology

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Comparative Efficacy and Safety of Pharmacological Cognitive Treatments in Parkinson's Disease and Dementia with Lewy Bodies: Systematic Review & Network Meta-analysis

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Introduction:
Background: Treating cognitive impairment in Parkinson's disease dementia (PDD) and dementia with Lewy bodies (DLB) continues to pose a significant challenge to clinicians due to several factors. These include limited treatment options, refractory side effects, inconsistent daily variability in response to treatment and the lack of precise objective assessments.
Objectives: The aim of this study is to evaluate, compare and rank the current available pharmacological cognitive treatments based on their efficacy, safety and tolerability.

Methods:
We searched PubMed, PsycINFO, Embase and trials registries until January 2024 to identify Randomized Controlled Trials that assessed cognitive treatments in PDD or DLB. Network Meta-analysis was conducted using the netmeta package in R, and the primary outcome measures were global cognitive, neuropsychiatric and safety measures. GRADE and RoB 2 were used to assess the risk of bias in the studies.

Results:
22 out of 2045 studies identified met the inclusion criteria, comprising over 3300 PDD and DLB patients. The network meta-analysis showed that Rivastigmine capsules and Donepezil significantly improved global cognitive outcome measures in comparison to placebo (Standardised Mean Difference (SMD)= 0.36 [0.14; 0.57], 0.33 [0.12; 0.54] 95% CI respectively). Rivastigmine in both formulations (capsules and patches) improved global neuropsychiatric outcome measures significantly when compared to placebo (SMD= 0.21 [0.05; 0.38], 0.37[0.13,0.60] 95% CI respectively). Safety measures indicated that while Rivastigmine capsules result in a significantly higher rate of dropouts due to adverse events compared to placebo, there was no significant difference in the incidence of serious adverse events when compared to other medications and placebo. Rivastigmine was ranked first in both efficacy outcome measures. No differences were noted between its two formulations.

Conclusions:
Rivastigmine is likely to offer the highest cognitive, and neuropsychiatric benefits in PDD and DLB patients compared to the other cognitive treatments. Despite its efficacy, it was less tolerable, and Donepezil offers a more favorable overall benefit/risk profile. Prescribing cognitive enhancers requires a balanced consideration of the potential benefits against possible risks, tailored to the patient's individual symptoms and tolerance for side effects. More large head-to-head randomized controlled trials are needed for better evaluation and enhancement of our current treatment protocols.

Key Words: Parkinson's Disease Dementia; Dementia with Lewy Bodies; Network Meta-analysis;

Funding Agency: None

Community Medicine

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Factors Affecting Patients' Trust of the Treating Physician and Compliance to the Care Plan

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Introduction:
Background: Previous studies have shown that patient trust is a key determinant of healthcare utilization and adherence to treatment recommendations, with variations reported across healthcare systems and patient characteristics. However, data from Kuwait remain limited. This study aimed to identify factors influencing patients' trust in their treating physicians and its association with compliance to the recommended care plan in Kuwait.

Methods:
A cross-sectional study was conducted using a self-administered online questionnaire (Google Forms) distributed to adults aged ≥18 years across several ministries in Kuwait (including the Ministries of Education and Higher Education, Electricity and Water, Health, and Religious Endowment and Islamic Affairs) between October 15 and 19, 2023. The questionnaire was available in both Arabic and English and included sociodemographic items and the Wake Forest Trust in Physicians Scale (WFPTS), a validated 10-item Likert scale (1–5) assessing domains of fidelity, competence, honesty, confidentiality, and global trust, with total scores ranging from 10 to 50. Of 651 responses received, 649 valid responses (99.7%) were analyzed. Data were analyzed using SPSS version 28. Independent t-tests, one-way ANOVA, and chi-square tests were used to assess associations between demographical variables, trust level and compliance. Participants who did not consent or were under 18 years were excluded.

Results:
The sample consisted predominantly of females (82.4%), with a mean age concentrated in the 18–29-year group (52.2%), and most participants held a bachelor's degree (58.8%). Higher trust scores were observed among respondents with higher educational levels ($p = 0.047$) and those with health insurance ($p = 0.006$). Trust was significantly higher among participants who preferred conventional medicine (medical doctors, hospitals, clinics, pharmacies) compared with those favoring alternative medicine (herbs, natural supplements, cupping) ($p < 0.001$). About 57% trusted physicians in public and private hospitals equally, while 27% trusted private physicians more. Using ANOVA, higher trust levels were significantly associated with better compliance to the care plan ($p < 0.001$). The most frequently reported factors enhancing compliance were physicians treating patients with care and concern (25.6%) and taking patients' problems seriously (22%).

Conclusions:
Patients' trust in physicians was significantly associated with self-reported compliance to the recommended care plan, as demonstrated by ANOVA analysis. Higher trust scores were observed among participants with higher educational levels, those with health insurance, and those who preferred conventional medicine. Factors related to patient-centered care, including physicians treating patients with care and concern and taking their problems seriously, were frequently reported as enhancing compliance. These findings suggest that fostering empathy, attentiveness, and clear communication may strengthen physician–patient relationships and improve adherence to care plans in the Kuwaiti healthcare setting.

Key Words: Patient trust; Physician-patient relationship; Compliance to care plan;

Funding Agency: None

Community Medicine

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Multiple Tobacco Product Use and Perceived Cognitive Function among Young Adults: A Cross-Sectional Study

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Introduction:
Polytobacco use is a rapidly emerging global public health threat. Epidemiological data regarding the effect of polytobacco use on cognitive function is scarce. Thus, this study aimed to assess the association between polytobacco use and perceived cognitive functioning (PCF) difficulties among
young adults.

Methods:
A cross-sectional study enrolled university students (aged 18–30 years) in Kuwait. Participants self-reported current (past 30-day) use of e-cigarettes, conventional cigarettes, hookah, and heated tobacco products. We created a composite variable to classify tobacco use patterns as: no use, single use, dual use, or poly use (≥3 products). PCF difficulties were assessed using a validated scale and categorized in two ways: (i) as a binary variable ('within normal limits' vs. 'mild-to-severe' difficulties) and (ii) as an ordinal variable ('within normal limits,' 'mild,' 'moderate,' or 'severe' difficulties). Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were estimated using logistic regression models. The study was approved by the Health Sciences Center Ethics Committee for Student Research at Kuwait University (Ref. 1015/2025).

Results:
Data from 1,323 participants were analyzed (805 female participants). A total of 101 (7.6%) participants reported single tobacco product use, 108 (8.2%) reported dual tobacco product use, and 189 (14.3%) reported polytobacco product use (≥3 products). Mild, moderate, and severe PCF difficulties were reported by 208 (15.7%), 165 (12.5%), and 90 (6.8%) participants, respectively, with 463 (35.0%) participants collectively reporting 'mild-to-severe' PCF difficulties. Compared to 'no use,' current polytobacco use (≥3 products) was associated with increased odds of reporting 'mild-to-severe' PCF difficulties (aOR: 1.96, 95% CI: 1.30–2.97). Specifically, polytobacco use (≥3 products) was associated with increased odds of 'moderate' (aOR: 2.01, 95% CI: 1.14–3.54) and 'severe' (aOR: 3.29, 95% CI: 1.49–7.26) PCF difficulties.

Conclusions:
Polytobacco use is prevalent among young adults in Kuwait and is associated with increased odds of perceived cognitive difficulties. These findings highlight the need for targeted public health interventions to curb the uptake of multiple tobacco products and mitigate potential cognitive impairment.

Key Words: Tobacco, polytobacco use, multiple tobacco use; Cognitive function, cognition;

Funding Agency: None

Community Medicine

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Knowledge and Awareness of Diabetes among University Students in Kuwait

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Introduction:
Diabetes is a major public health concern in Kuwait, yet limited data exist on university students' diabetes knowledge and attitudes. This study assessed diabetes knowledge and perceptions among students across public and private universities in Kuwait.

Methods:
A cross-sectional study was conducted among 1,491 university students using a self-administered online questionnaire comprising validated tools: the Diabetes Knowledge Questionnaire (DKQ-24) and the Diabetes Attitude Scale (DAS-3). Diabetes knowledge was categorized as low (≤13), moderate (14–19), or adequate (≥20) based on DKQ-24 scores. Data were analyzed using non-parametric tests and multivariable logistic regression to identify factors independently associated with adequate diabetes knowledge.

Results:
Overall, 31.3% of students had low knowledge, 52.9% had moderate knowledge, and 15.8% had adequate knowledge. Median scores for the DAS-3 seriousness of type 2 diabetes and patient autonomy subscales were 22 and 30, respectively. After adjustment for confounders, adequate diabetes knowledge was significantly associated with older age (aOR = 1.28, 95% CI: 1.16–1.41), female gender (aOR = 1.84, 95% CI: 1.13–2.99), enrollment in Health Sciences compared to Arts and Humanities (aOR = 0.27, 95% CI: 0.16–0.47), advanced academic year (Year 5: aOR = 6.85, 95% CI: 3.81–12.34), and personal history of type 1 diabetes (aOR = 3.55, 95% CI: 1.91–6.60).

Conclusions:
Although most students demonstrated moderate diabetes knowledge, substantial gaps remain, particularly among non-medical and early-year students. Strengthening diabetes education through university-based health promotion and targeted awareness initiatives is essential to improve preventive behaviors in young adults.
Ethical Considerations:
Ethical approval was obtained from the Health Sciences Center Ethics Committee at Kuwait University. Electronic informed consent was obtained from all participants prior to data collection.

Key Words: Diabetes mellitus, Diabetes knowledge, Diabetes at; Diabetes awareness, DKQ-24,

Funding Agency: None

Community Medicine

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Medication Adherence in Adult Diabetic Patients in Kuwait

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Introduction:
Kuwait has one of the highest prevalence of diabetes in the world/globally, making medication adherence crucial for glycemic control and prevention of complications. This study aimed to measure medication adherence among diabetic adults, assess barriers and facilitators, and identify sociodemographic and clinical factors associated with non-adherence.

Methods:
A cross-sectional study was conducted among 828 adults with diabetes recruited from five randomly selected government ministries in Kuwait in October 2025. Data were collected using a bilingual (Arabic/English) online questionnaire covering sociodemographic characteristics, diabetes history, the 11-item Adherence to Refills and Medications Scale for Diabetes (ARMS-D), and perceived barriers and facilitators. Poor adherence was defined as ARMS-D score ≥16. Data were analyzed using descriptive statistics, non-parametric tests, and multivariate logistic regression. Ethical approval was obtained from the Health Sciences Center Ethics Committee for Student Research, Kuwait University (Ref: CM Project #5, 05 October 2025). Participation was anonymous and voluntary.

Results:
The median ARMS-D score was 14 (IQR 4); 35.9% demonstrated poor adherence. Refill planning failures (52.8%) and forgetfulness (44.6%) were the most reported behaviors. Median HbA1c was 7.0% (IQR 2.3). In multivariate analysis, increasing age independently predicted better adherence (AOR 1.027, p=0.043). Patients with double diabetes had significantly worse adherence (AOR 0.146, p<0.001). The strongest barrier was psychological stress (AOR 0.209, p<0.001), while self-motivation was the strongest facilitator (AOR 2.433, p<0.001). Other significant barriers included medication side effects, regimen complexity, family or schedule interference, religious fasting, and poor physician communication.

Conclusions:
Over one-third of adults with diabetes had poor medication adherence, primarily due to refill planning failures and forgetfulness. Psychological stress and low self-motivation emerged as key factors. System-level improvements (automated refills, extended clinic hours) and patient-centered strategies (reminder systems, motivational interviewing, mental health screening) tailored to Kuwait's sociocultural context could increase adherence and guide future interventions. Funding/Acknowledgements: We thank Kuwait University Faculty of Medicine, the Health Sciences Center, and ministry staff for their support.

Key Words: Medication adherence, ARMS-D; Diabetes mellitus; Kuwait;

Funding Agency: None

Community Medicine

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Attention Deficit Hyperactivity Disorders (ADHD) among Medical Students in Kuwait: Prevalence and Associated Risk Factors

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Introduction:
Attention deficit hyperactivity disorder (ADHD) is defined as a complex developmental disorder characterized by predominantly inattentive, disorganized, and/or hyperactive symptoms that can persist into adulthood and impair academic and emotional functioning. This cross-sectional study aimed to determine the prevalence of self-reported ADHD among medical students in Kuwait and explore its association with the sociodemographic, academic, behavioral, health- related, psychological, and other factors.

Methods:
A cross-sectional study was conducted among 660 medical students at Kuwait University between April 6 and 10, 2025. Data were collected through an online questionnaire incorporating validated tools, including the Adult ADHD Self-Report Scale version 5 (ASRS-5), Patient Health Questionnaire-2 (PHQ-2), Perceived Stress Scale-4 (PSS-4), Generalized Anxiety Disorder-2 (GAD-2), and Insomnia Severity Index (ISI). Univariable and multivariable logistic regression analyses were used to evaluate unadjusted and fully adjusted association between ADHD and above-mentioned risk factors. Ethical approval was obtained from the Joint Ethics Committee of the Health Sciences Center at Kuwait University, and all participants provided electronic informed consent.

Results:
The median age of the 660 participants was 20 years old. The majority were Kuwaiti (93%), female (75%), and single (98%). The prevalence of self-reported ADHD was 21%. The final multivariable logistic regression model revealed significant positive association of self-reported ADHD with age (OR=1.21, p<0.001), family history of psychiatric illnesses (OR=1.92, p=0.008), perceived stress (OR=1.25, p<0.001), generalized anxiety disorder (OR=1.28, p<0.001), and insomnia (OR=1.07, p<0.001). Smoking showed a significant negative association with self-reported ADHD (OR=0.62, p=0.038).

Conclusions:
A substantial proportion of medical students in Kuwait screened positive for ADHD symptoms. Significant associations with stress, anxiety, insomnia, and family psychiatric history highlight the need for awareness, early screening, and mental-health support within medical education to enhance student well-being and academic performance.
Acknowledgments:
This study was supported by the Faculty of Medicine, Kuwait University. The authors would like to thank Dr. Areej Al Ali, Mr. Abdullah Al Majran, the Saudi ADHD Society, and all participating students for their valuable contributions.

Key Words: ADHD; Medical Students; Risk Factors;

Funding Agency: None

Community Medicine

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The Prevalence and Burden of Musculoskeletal Disorders Among Health Sciences Center

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Introduction:
Musculoskeletal disorders (MSDs) are increasingly recognized among young adults, particularly healthcare students, due to prolonged sedentary behavior and academic stress. Despite their growing global prevalence, data from Kuwait remain limited. This study aims to assess the overall prevalence and burden of MSDs among students at Kuwait University's Health Sciences Center (HSC) and to identify associated risk factors.

Methods:
A descriptive cross-sectional study was conducted between April 6 and April 10, 2025, involving 503 students from various HSC colleges. Data were collected through a self-administered online questionnaire consisting of six sections including four validated questionnaires: demographics, study habits, physical activity (IPAQ), musculoskeletal symptoms (NMQ), stress levels (PSS-10), and spinal-related disability (ODI). Descriptive statistics, chi-square tests, Mann-Whitney U tests, and logistic regression analyses were used.

Results:
MSDs were highly prevalent, with 66.4% of students reporting pain in both upper and lower body regions. The most commonly affected areas were the lower back (63%), neck (61.2%), and shoulders (60%). MSDs were significantly associated with female gender ($p= 0.048$) and low physical activity levels ($p= 0.035$). Additionally, high perceived stress ($p<0.001$) and history of medical conditions ($p<0.001$) were linked to greater functional disability. Logistic regression analysis showed that high spine-related disability (ODI >20%) was consistently associated with increased odds of MSK pain across all body regions.

Conclusions:
is study highlights a significant burden of MSDs among HSC students in Kuwait, largely driven by modifiable factors such as study posture, stress, and physical inactivity. These findings emphasize the need for preventive strategies and awareness initiatives targeting ergonomic practices, mental well-being, and active lifestyles to reduce the risk of MSDs in student populations.

Key Words: Musculoskeletal Disorders (MSDs); Health Sciences Students; Prevalence;

Funding Agency: None

Community Medicine

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Knowledge of Risk Factors and Prevention Associated with Cardiovascular Diseases among the General Population in Kuwait

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Introduction:
Cardiovascular diseases (CVDs) are the leading cause of death globally by 32% and represent 46% of all mortalities in Kuwait. Many patients are not aware of CVDs risk factors, which causes a barrier to preventative methods and early treatment. This cross-sectional study aims to assess CVDs knowledge and intention to change behavior related to CVDs in the general population aged 18 and above in Kuwait.

Methods:
This study included 523 participants from the general population of Kuwait, aged 18 and above. The CVDs knowledge assessment questionnaire included 39 questions, adopted from two validated CVDs questionnaires. Multiple linear regression analysis was used to determine the association between individuals' CVDs knowledge score and their sociodemographic factors and lifestyle. The Mann-Whitney U test was used to determine the relationship between the individuals' CVDs knowledge score and their intention to change behavior. Ethical approval was obtained from the Ministry of Health's Standing Committee for Coordination of Health and Medical Research, and informed consent was obtained electronically from all participants.

Results:
The CVDs knowledge score was between zero and 17 points, with a median of 10. The most identified risk factors are obesity, physical inactivity, secondhand smoke, and stress levels.This study indicates that females exhibit greater knowledge. Age is positively associated with CVDs knowledge score. Engagement in prior discussions with a physician regarding CVD risk factors was associated with higher levels of CVD-related knowledge, whereas individuals with a previous CVD diagnosis exhibited comparatively lower CVD knowledge scores.

Conclusions:
There was considerable variability in participant's awareness, and many demonstrated knowledge of World Health Organization-identified CVD risk factors, including obesity, physical inactivity, exposure to secondhand smoke, and stress.Females and older individuals exhibited higher levels of knowledge. Despite this, many participants reported a lack of motivation to adopt healthier behaviors, although a willingness to increase physical activity was noted. Proactive discussions between healthcare providers and patients, particularly those with a family history of CVDs are essential for enhancing understanding and encouraging the adoption of effectivepreventive measures.

Acknowledgments:
We thank Dr. Anwar Al-Baloul and Dr. Ahmad Al-Sultan for their guidance and support. We also acknowledge the Department of Community Medicine and all participants for their valuable contributions.

Key Words: Cardiovascular diseases (CVDs); Knowledge ; Risk factors ;

Funding Agency: None

Community Medicine

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Obsessive Compulsive Symptoms among Health Science Center Students in Kuwait: Prevalence and its Associated Risk Factors

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Introduction:
Obsessive-compulsive symptoms (OCS) are common psychological phenomenon, particularly among early-adulthood college students (Vergara et al., 2023). OCS can significantly disrupt daily functioning in affected individuals (Vergara et al., 2023). This cross-sectional study aims to determine the prevalence of probable OCS among Health Science Center (HSC) students in Kuwait and to investigate its association with potential socio-demographic, academic, psychological, and other risk factors.

Methods:
An electronic questionnaire incorporating the Obsessive-Compulsive Inventory–Revised (OCI-R) scale, a screening tool assessing symptom domains that are consistent with the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria, was distributed to Health Science Center (HSC) students over five days (October 19–23). Prevalence of probable self-reported OCS was estimated using the OCI-R, defining OCS as symptom clusters meeting or exceeding the validated cutoff rather than individual symptoms alone. Chi-square test, t-test, and Mann-Whitney U test were used to assess the variation in OCS across socio-demographic, academic, behavioral, health-related, psychological, and other factors. Univariable and multivariable logistic regression analysis was used to evaluate the unadjusted and fully adjusted association between OCS and the above-mentioned risk factors.

Results:
The median age of the 1,202 participants was 20 years old. The majority were Kuwaiti (87%), female (83%), and medical students (42%). The overall prevalence of self-reported OCS was 54%. The final multivariable logistic regression model revealed significant association of self-reported OCS and year of study (7th year vs. 1st year: OR=0.27, 95% CI:0.12, 0.64), family income (>3000 KD vs. <1000 KD: OR=0.57, 95% CI:0.35, 0.95), perceived stress (OR=1.18, 95% CI: 1.12, 1.25), and depressive symptoms (OR=1.28, 95% CI: 1.17, 1.42).

Conclusions:
This study reveals a significant association between year of study, monthly family income, perceived stress, and depressive symptoms with self-reported OCS. Given the high prevalence of self-reported OCS, increasing awareness and developing targeted support strategies for this population are essential.

Key Words: OCS; Prevalence; Students;

Funding Agency: None

Community Medicine

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Knowledge, Attitudes, and Practices of Health Sciences Center (HSC) Studentsat Kuwait University Regarding Vitamin D Deficiency and Its Health Implications

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Introduction:
Vitamin D is a vital nutrient essential for bone health and overall well-being, with deficiencies linked to various health issues such as inflammation, infections, and depression. This study aims to assess the knowledge, attitudes, and practices of Health Sciences Center (HSC) students at Kuwait University regarding vitamin D deficiency and its health implications.

Methods:
A stratified cross-sectional study was conducted January-April 2025, targeting 1,000 HSC students aged 18 years and older from years 1-4. Data collection was carried out through randomly selected classes from each of the first 4 years of college. A self-administered online questionnaire available in English and Arabic was used to gather data on students' vitamin D knowledge, attitudes, and practices. This research study was reviewed and approved by HSC Ethics Committee for Student Research.

Results:
The total sample included 1395 students distributed proportionally from the five colleges of the HSC. Overall, general knowledge of vitamin D was moderate at best, as only 11.9% achieved high knowledge scores, 31% moderate, and 57.1% low scores. In the univariable logistic regression analysis, significant predictors of high knowledge scores (≥80%) including age, academic year, and college enrollment. In the multivariable analysis, college group (Medicine/Dentistry/Pharmacy vs. Allied Health/Public Health), academic year, and 2 practice-related factors were identified as significant independent predictors of high knowledge scores, after adjusting for all significant factors in the univariable analyses.

Conclusions:
The study showed significant gaps in knowledge and inconsistent practices related to vitamin D among HSC students at Kuwait University, despite their enrollment in healthcare fields of study. Due to the vital role HSC students will play as future healthcare professionals and given the published high prevalence of vitamin D deficiency in Kuwait, there is a clear need for targeted educational interventions to improve vitamin D knowledge and encourage healthier lifestyle behaviors that increase vitamin D levels.
Acknowledgments: We would like to sincerely thank Dr. Reem Al-Sabah and Mr. Abdullah Al-Majran for their valuable support and guidance for the entire duration of our study. We also thank the HSC deans for permitting access to lecture theatres for data collection and the faculty members and students for their cooperation.

Key Words: Vitamin D deficiency; Vitamin D knowledge; HSC students;

Funding Agency: Nonet Applicable

Community Medicine

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Knowledge and awareness of breast cancer symptoms, risk factors, and screening barriers among women in Kuwait: a cross-sectional study

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Introduction:
Breast cancer (BC) is the most diagnosed cancer globally and the second leading cause of cancer-related mortality across all demographics. In Kuwait, the incidence is 50 cases per 100,000 person-years. Delayed detection, often linked to limited awareness of BC symptoms and risk factors, contributes significantly to morbidity and mortality. This study aimed to assess BC knowledge, awareness of symptoms and risk factors, and perceived barriers to screening among women in Kuwait.

Methods:
A cross-sectional survey was conducted among 490 employed women aged 18 years and older across Kuwait using an online structured questionnaire. Participants' awareness of BC symptoms, knowledge of risk factors, and perceived barriers to screening were assessed. Composite scores were calculated for symptom awareness, risk factor knowledge, and screening barriers. Multiple linear regression was used to identify demographic predictors associated with each score.

Results:
The median participant age was 35 years, with 66.1% holding a bachelor's degree. Higher education levels were significantly associated with greater BC symptoms identification ($p = 0.013$ for bachelor's degree; $p = 0.009$ for postgraduate degree). Participants with a family history of BC demonstrated significantly greater knowledge of both BC symptoms and risk factors ($p < 0.001$). The most recognised symptom was a breast lump or thickening (72.0%), followed by bleeding or discharge from the nipple and pain in one of the breasts or armpits (65.1% each), while other symptoms, such as rash on/around the nipple (34.9%), or dimpling (29.2%) were less frequently identified. Regarding risk factors, having a close relative with BC was most frequently recognized (64.5%), while awareness of other risk factors, including obesity (29.7%), hormone therapy use (27.6%), and early menarche (10.6%), was limited. Taken together, these findings indicate moderate awareness of BC symptoms and risk factors. The most frequently cited barrier to screening was concern about pain or discomfort (57.8%).

Conclusions:
While women in Kuwait have moderate awareness of key BC symptoms and risk factors, knowledge gaps and screening barriers persist, particularly regarding lesser-known warning signs and screening apprehension. Public health strategies should prioritise targeted education initiatives, including workplace wellness programs and culturally tailored awareness campaigns, to improve early detection and reduce the BC burden in the region.

Acknowledgements
We acknowledge the help and time of the study subjects, also COM, KU to do data analysis.

Key Words: Breast cancer ; Awareness ; Barriers ;

Funding Agency: None

Community Medicine

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Public Use and Trust in ChatGPT for Medical Advice in Kuwait: A Cross-Sectional Survey

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Introduction:
Artificial intelligence (AI) tools such as ChatGPT are increasingly used for medical information, yet patterns of use, trust, and safety perceptions in Kuwait remain unclear. Understanding these behaviors is essential for future public-health guidance. At study initiation, the project was classified as exempt from ethical approval; however, we were later informed that submission was required. The necessary documents were immediately completed and submitted, and the study proceeded anonymously.

Methods:
A cross-sectional online survey was distributed via social media to adults aged ≥18 years living in Kuwait. Participation was voluntary and anonymous. Of 144 responses, 138 provided consent and were analyzed. The questionnaire assessed AI usage patterns, trust, perceived accuracy, safety concerns, and attitudes toward regulation. Data collection is ongoing, and additional responses aim to be gathered pending approval.

Results:
Most respondents were 25–44 years old, with a predominance of female participants. Approximately 80% reported using AI for medical or health information, with ChatGPT being the most commonly used platform. Perceived accuracy was generally slight to moderate. Trust was balanced: one-third trusted AI, one-third did not, and one-third trusted it "sometimes." Many participants had followed AI medical advice at least once, though most reported double-checking information with a doctor or online sources. Key concerns included misinformation, incorrect diagnoses, and replacing physician evaluation, while fewer cited privacy issues. Notably, nearly 80% supported establishing official national guidelines in Kuwait for safe AI use in healthcare.

Conclusions:
Adults in Kuwait frequently use ChatGPT for medical information but approach it cautiously. Strong public support for official guidance highlights the need for national education and regulatory frameworks. No identifying data were collected, and ethical approval was later confirmed as required and submitted accordingly.

Key Words: MEDICAL ADVICE; TRUST; AI;

Funding Agency: None

Community Medicine

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Awareness and Consumption Patterns of Pre-workout Supplements and Energy Drinks Among University Students in Kuwait

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Introduction:
The consumption of multi-ingredient pre-workout supplements (MIPS) and energy drinks (EDs) has become increasingly prevalent among young adults, yet limited studies have been done to assess patterns, reasons, knowledge, and reported side effects in Kuwait. Therefore, a cross-sectional study was conducted on university students in Kuwait to explore the prevalence of consumption and identify associated factors.

Methods:
A cross-sectional study was conducted in October 2025 and included university students in Kuwait aged 18 years and older. A self-administered electronic questionnaire was distributed through college visits, where QR codes were displayed for students to scan. Students were also asked to share the survey link with their peers via WhatsApp. Using two validated questionnaires, the survey was designed in both Arabic and English. Chi-square tests and logistic regression using SPSS were employed to analyze the associations between consumption and various factors. Ethical approval was obtained from the HSC Ethics Committee for Student Research and the Standing Committee for the Coordination of Health and Medical Research.

Results:
Among 765 participants, 27.7% used MIPS and 50.3% used EDs. MIPS were mainly consumed to enhance workout performance (88.2%) while EDs for studying (67.5%). Health concerns were the main reason for discontinuation or avoidance in both products. Most obtained information about MIPS and EDs from the internet (87.7% and 79.5%, respectively) and showed moderate knowledge of the constituents. The most frequently reported side effect for MIPS users was nausea (67.0%), whereas ED users reported heart problems (51.9%). Logistic regression showed that MIPS consumption was significantly associated (p-value < 0.001) with perceiving these products as safe (aOR = 2.554), knowledge of the ingredients (aOR = 2.415), and reading nutritional labels (aOR = 2.246). ED consumption was significantly associated with smoking (aOR = 2.832, p-value < 0.001) and university type (aOR = 1.995, p-value = 0.023).

Conclusions:
MIPS and ED use is increasing among university students in Kuwait, with different consumption patterns, motivations, knowledge, side effects, and factors influencing their use.

Key Words: Pre-workout supplements (MIPS); Energy drinks (EDs); University students

Funding Agency: None

Community medicine

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Prevalence of Computer Vision Syndrome and Associated Risk Factors among Kuwait University students

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Introduction:
Background and Objective: Computer vision syndrome (CVS), or digital eye strain, is a group of visual and ocular symptoms that results from extensive use of digital screens. This study aimed to determine the prevalence of computer vision syndrome among Kuwait University students and to highlight the contributing behavioral risk factors.

Methods:
A cross-sectional study was conducted among 1,176 undergraduates from 16 colleges at Kuwait University. An electronic self-administered questionnaire was distributed to participants. CVS-Smart Questionnaire, a valid and reliable tool for assessing CVS prevalence, was used covering five diagnostic criteria: visual symptoms, ocular surface symptoms and extra-ocular symptoms, frequency and screen-associated. ethical approval was obtained from Health Sciences Center Ethics Committee for Student Research, at Kuwait University (no. 1012/ Dated: October 12, 2025).

Results:
Data were analyzed using IBM SPSS statistics, Version 29. Chi-square and binary logistic regression were used to assess associations between CVS and potential risk factors. The study found that the prevalence of CVS among Kuwait University students was 69.0%. The factors that were significantly associated with CVS after adjustment included gender ($p<0.001$), prolonged screen time in a dark room ($p = 0.024$), screen illumination level ($p = 0.022$), use of glasses or contact lenses ($p<0.001$), details about objects seen after prolonged digital screen use ($p<0.001$) and the effect of digital screens on eye health and lifestyle |($p <0.01$) .

Conclusions:
This study provides a valuable insight into CVS prevalence and contributing factors among Kuwait University students, highlighting on the importance of increasing awareness and implementing proper preventative measures to control this rising health burden.

Acknowledgment: The authors are grateful for the support of the Department of Community Medicine and thank Dr. Ahmad Alsultan for his mentorship. Special thanks are extended to all participants who took part in the survey, making this research possible

Key Words: Computer Vision Syndrome ; Digital eyestrain ; Screen time;

Funding Agency: None

Community Medicine

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Prevalence and Risk Factors Associated with Eating Disorders Among College Students in Kuwait

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Introduction:
Eating disorders (EDs) are psychiatric conditions characterized by abnormal eating behaviors aimed at controlling body weight and shape. They have significant psychological and physical consequences, particularly among young adults. This study aimed to determine the prevalence of eating disorders and identify associated risk factors among Kuwait University students.

Methods:
A cross-sectional study was conducted in October 2023 among 756 undergraduate students aged 18–30 years from 15 colleges across Kuwait University, including both health sciences and non–health sciences campuses. Data were collected using a self-administered bilingual (Arabic and English) questionnaire. Eating disorder risk was assessed using the Eating Disorder Examination Questionnaire–Short (EDE-QS), a validated screening tool that measures eating disorder psychopathology rather than specific DSM diagnoses. A total score ≥15 indicated a high risk of an eating disorder. Additional questionnaire items assessed potential risk factors, including sociodemographic, co-morbid psychological disorders, lifestyle, social factors, anthropometric measurements, and medical history. Associations were examined using chi-square tests and multiple logistic regression.

Results:
The mean age of participants was 21.6 years, and 74.2% were female. The prevalence of high risk for eating disorders was 34.5% (n = 261). Eating disorder risk was significantly associated with negative body image perception, adherence to weight-loss diets, agreement with the belief that "the thinner, the better," experiences of weight-related bullying, higher exposure to social media and television body ideals, and having a close relative with an eating disorder. After adjustment, no sociodemographic factors were significantly associated with eating disorders risk. The strongest predictors of disordered eating risk were body image dissa3sfac3on (AOR = 4.36, p = 0.011) and exposure to media body ideals (AOR = 2.88, p < 0.001).

Conclusions:
Disordered eating risk was common among Kuwait University students, particularly among those exposed to sociocultural pressures related to body image. These findings underscore the need for targeted awareness initiatives, early screening programs, and preventive strategies within university settings.

Key Words: Eating Disorder; body image; media effect ;

Funding Agency: Nonen

Community Medicine - Epidemiology - MPH

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Assessment Of Health-Related Quality of Life Among Patients with Multiple Sclerosis: Role of Age at the Diagnosis, Comorbidities and Receipt of Therapeutic Rehabilitation Interventions In Kuwait

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Introduction:
Background: Multiple sclerosis (MS) is an autoimmune disease of the central nervous system with a rising trend both globally and in Kuwait. MS has adverse effects on patients' health-related quality of life (HRQoL). Limited published data exist on the effect of age at diagnosis, comorbidities, and therapeutic rehabilitation interventions on the HRQoL of patients with MS (pwMS) in Kuwait. This cross-sectional study aimed to assess the HRQoL and examine associated factors among pwMS in Kuwait.

Methods:
Between May and October 2025, a cross-sectional study enrolled 185 pwMS registered with Kuwait Multiple Sclerosis Association following HSC ethical committee approval. Inclusion criteria were MS diagnosis for ≥1 year and aged ≥21 years. Exclusion criteria were history of other neurological disorders, cognitive impairments or disabilities before MS. Data were collected using
an online, self-administered questionnaire, which included the MusiQol tool designed for MS. The MusiQoL index global score and 9 subscores were computed. Comorbidities were self-reported from a predefined list of diagnosed conditions, counted and categorized as 0, 1, 2-3, or ≥4. A multivariable linear regression model was employed to identify significant HRQoL predictors. The adjusted regressions coefficients ("β" ˆ) and corresponding 95% confidence intervals (CI) were used to interpret the final model.

Results:
Of the total 185 participants, 155 (83.8%) provided complete responses with valid MusiQol scores. Among these, the majority were female (58.9%), Kuwaiti nationals (68.6%), and aged 40-49 years (38.4%). The mean (SD) MusiQoL global index score was 51.8 (16.1). The significant predictors of HRQoL were reported as "β" ˆ(95% CI: lower-upper): being divorced "β" ˆ= -10.6 (- 18.6, - 2.6); family income (KD/mo) [1,000-2,000: "β" ˆ= 5.5 (0.6, 10.5); ≥2,001: "β" ˆ= 7.9 (0.6, 15.1)]; age at diagnosis [>20 years: "β" ˆ= - 15.0 (- 27.7, - 2.4); 20-29 years: "β" ˆ= - 12.7 (- 24.6, - 0.8); 40-49 years: "β" ˆ= - 19.4(- 32.5, - 6.3)]; secondary progressive MS "β" ˆ= - 7.6 (- 14.4, - 0.8); ≥4 comorbidities "β" ˆ= - 13.5 (- 20.3, - 6.6), and therapeutic rehabilitation "β" ˆ= - 5.5 (- 10.1, - 0.1).

Conclusions:
Overall mean MusiQoL global index score indicated moderate HRQoL level in this population. The significant predictors of HRQoL were marital status, family income, age at diagnosis, MS type, comorbidities and therapeutic rehabilitation. Clinical services should consider these predictors to improve HRQoL in pwMS.

Key Words: Multiple Sclerosis; Health-related quality of life; Kuwait;

Funding Agency: None

Dentistry

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Salivary Microbiome Signatures in Children With Type 1 Diabetes in Kuwait

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Introduction:
Emerging evidence suggests that the oral microbiome plays a critical role in systemic diseases, including Type 1 Diabetes Mellitus (T1D). While gut microbiome dysbiosis has been widely studied in T1D, less is known about how the oral microbial community differs between children with and without the disease. This study aimed to characterize the salivary microbiome in children with T1D and healthy controls and evaluate its discriminatory potential.

Methods:
We conducted a cross-sectional study involving 57 children diagnosed with T1D and age-matched healthy controls from Kuwait. Saliva samples were collected and analyzed using 16S rRNA gene sequencing. Microbial composition was compared across groups at multiple taxonomic levels. Differential abundance was assessed using Linear Discriminant Analysis Effect Size (LEfSe), and Random Forest modeling was applied to identify microbial biomarkers predictive of T1D status. Receiver Operating Characteristic (ROC) analysis was used to evaluate classification performance.

Results:
Although overall phylum-level composition was similar between groups, LEfSe analysis revealed significant differences. T1D samples showed enrichment of Kingella oralis, Fusobacterium sp., and Leptotrichia wadei, while Veillonella parvula was more prevalent in controls. Random Forest classification based on microbial features achieved high accuracy, with an area under the curve (AUC) of 0.91 in the validation set. Several taxa emerged as key discriminators between T1D and non-diabetic subjects.

Conclusions:
This study highlights distinct oral microbiome signatures associated with T1D in children. Salivary microbial profiling demonstrates strong discriminatory power and may serve as a promising non-invasive tool for future risk assessment and disease monitoring. However, the cross-sectional design, small sample size, and single-site recruitment limit generalizability. Longitudinal, multi-site studies are needed to validate these findings and explore mechanistic links between oral dysbiosis and T1D pathogenesis.

Key Words: Type 1 Diabetes; Saliva; Microbiome;

Funding Agency: Dasman Diabetes Institute

Dentistry

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The difference between Zirconia and Titanium Implant Preload Efficiency: Preliminary In Vitro Study.

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Introduction:
Objective: To investigate the effect of implant material on screw joint stability by comparing Reverse Torque Values (RTV) after 20 minutes (RTV1) to initial torque value (ITV).

Methods:
The study design considered the requirements of the International Organization for Standardization (ISO) 14801:2016 dynamic fatigue test for endosseous dental implants. A total of 24 implants (N=24) were utilized, divided into two groups of 12 implants each (n=12): Control Group (Titanium): 12 titanium implants; Test Group (Zirconia): 12 zirconia implants. Both groups received titanium screws to connect the titanium bases to the implants. The crowns were standardized in dimensions, material, fabrication technique), and were cemented with the same auto polymerizing composite resin cement. Implants were embedded in printed resin models through standard manufacturer osteotomy protocol, leaving 1.5 mm of threads exposed to simulate worst case scenario. Crowns were milled from 3Y-TZP zirconia. A new torque-limiting device (TLD) connected to a digital torque device (Mark-10, MGT50) was used for measurements. Specimens were initially tightened to the manufacturer-recommended Initial Torque Values (ITV1) were recorded. Reverse torque values (RTV1) were recorded after 20 minutes to account for embedment relaxation. Mann-Whitney U test was used to compare differences in ITVs, Preload Efficiency (defined as RTV1/ITV), Ethical clearance was not needed as this was an in vitro study.

Results:
Preload Efficiency (RTV1): Preload efficiency was calculated as the RTV1 divided by the applied torque, expressed as a percentage.

- The mean preload efficiency for Titanium was approximately 90.42%. The mean preload efficiency for Zirconia was approximately 97.27%.

Statistical Significance:

- The analysis found a statistically significant difference between the groups ($p \approx 0.022$).
- Zirconia exhibited significantly higher preload efficiency than Titanium after adjusting for the different tightening torque thresholds.
- This indicates that Zirconia abutment screws retained a greater fraction of preload 20 minutes after tightening, relative to their specified applied torques, compared with Titanium. The effect magnitude was determined to be moderate (Cohen's $d \approx 0.616$).

Conclusions:
The initial findings regarding short-term stability (RTV1) suggest that, when accounting for the different manufacturer-recommended torques, Zirconia implants exhibited significantly greater preload efficiency than Titanium implants.

Key Words: implant; zirconia; titanium;

Funding Agency: Kuwait University. DR02/23

Dentistry

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Dental professionals' Awareness, Attitude, and Barriers Towards Artificial Intelligence Application in the Kuwait Dental Field: A Survey

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Introduction:
Objectives The primary purpose of this study was to assess the awareness, attitude, and barriers toward AI application among dental professionals in Kuwait. T

Methods:
This research utilized a cross-sectional survey methodology. A digital questionnaire, consisting of 27 questions across five domains (demographics, knowledge and awareness, clinical practice, attitude towards AI, and barriers and concerns), was distributed to dental care providers over the age of 18 practicing in both the private and government sectors in Kuwait. The survey was available for 12 months (November 2023 to November 2024). A total of 300 responses were received, with 290 completed responses included in the final analysis. Categorical data comparisons were conducted using the Chi-square test or Fisher's exact test. A p-value of <0.05 was considered statistically significant, with an 80% test power. Data were stratified and analyzed based on variables including gender, specialty, undergraduate education location (categorized as 'Top 10 countries' or 'Other'), and years of work experience. Beliefs were categorized as Low (0-4), Moderate (5-7), and High (8-9). please note that ethical clearance was obtained from Kuwait University Health Science Centre Ethical committee.

Results:
The null hypothesis was rejected, indicating a difference among different dental professionals concerning their knowledge, attitude, barriers, or applications of AI. Analysis of beliefs demonstrated significant demographic differences:
1. Gender: Males were more likely to possess high beliefs (44.7%) compared to their female counterparts (26.3%).
2. Specialty: Prosthodontists were the most optimistic, with half (50.0%) holding high beliefs.
Regression analysis indicated that general dentists (p=0.023) and prosthodontists (p<0.001) were the only specialities found to possess a statistically significant influence on higher beliefs in AI adoption.
3. Work Sector: Dentists working in private practice were the most optimistic (40.6% high beliefs), while those in academia (41.7% moderate beliefs) or the government sector (38.3% moderate beliefs) primarily held moderate beliefs. 4. Education/Experience: Years of experience did not lead to drastic differences in results. Those who received undergraduate education in 'Top 10 countries' had equal majorities of moderate and high beliefs (37.1% each).

Conclusions:
The survey reinforces that AI holds the potential to revolutionise dental care by enhancing clinical workflows and decision-making. However, challenges remain, particularly related to ethical concerns and trust in AI technology.

Key Words: artificial intelligence; dentist; awareness;

Funding Agency: None

Dentistry

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Prevalence of Depression in Patients with Halitosis – A Single Center Cross-Sectional Study in Kuwait

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Introduction:
Halitosis, or chronic bad breath, is known to adversely affect social interactions and psychological health. Despite its impact, there is limited data on the prevalence of depressive symptoms among patients suffering from halitosis. This study aimed to assess the prevalence and severity of depression in patients with halitosis.

Methods:
A cross-sectional study was conducted over four months involving 49 patients diagnosed with halitosis. The patients were recruited from Abdulrahman AlZaid West Mishref Clinic. Each participant completed the Patient Health Questionnaire-9 (PHQ-9), a validated tool for screening depressive symptoms. Paper questionnaires in both Arabic and English were used. Depression severity was classified based on PHQ-9 scoring criteria into minimal, mild, moderate, moderately severe, and severe categories.Descriptive statistics were used to quantify the prevalence of depression severity levels.

Results:
Among the 49 patients surveyed 20 were males and 29 were females. The mean age was 42. The PHQ-9 is categorized according to score; 1-4 indicating minimal depression, 5-9 mild, 10-14 moderate, 15-19 moderately severe, and 20-27 severe depression. 39% exhibited minimal depressive symptoms, 35% mild symptoms, 14% moderate symptoms, 6% moderately severe symptoms, and 6% severe depressive symptoms. These findings indicate a presence of depressive symptoms in the halitosis patient cohort.

Conclusions:
The study reveals a presence of depressive symptoms among patients with halitosis, emphasizing the need for clinicians to consider depression screening, psychoeducation and referral to mental health services when needed.Although further studies are need on the possible association between halitosis and depression, an integrated approach, addressing both oral health and mental well-being may be important to improve patient outcomes. Routine depression screening via tools like the PHQ-9 may be beneficial in managing these patients holistically.

Key Words: Halitosis; Depression; Prevalence;

Funding Agency: None

Dentistry

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Symphyseal Distraction Techniques to Widen the Mandible and Advance the Chin

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Introduction:
Symphyseal distraction offers an alternative to genioplasty, effectively widening congenitally narrow mandibles transversely and lengthening chins anteroposteriorly. The potential for new bone creation via distraction osteogenesis is theoretically limitless, depending on distractor design. This study details the use of custom symphyseal distractors tailored for various applications.

Methods:
For transverse distraction, the Burlington transverse analysis helped distinguish between a narrow mandible and a wide maxilla, guiding surgical correction. Custom Guerrero symphyseal distractors, crafted from RPE screws attached to mandibular canine bands and mandibular border screws, utilized 3D-printed symphysis models to bend arms for bone screw engagement. An osteotomy lateral to the mid-symphyseal suture created a transport disk, with a distraction rate of 1 mm/day.For anteroposterior distraction, a screw embedded in an acrylic splint, fixed with circummandibular wires, connected to a plate and transcutaneous wires, facilitated chin lengthening along the occlusal plane. Surgical plates stabilized segments if early distractor removal was needed.

Results:
The Guerrero distractor successfully widened the mandible, resolving dental crowding from a narrow base, though adjacent teeth might drift into new bone, closing gaps. Anteroposterior distraction eliminated the bony step typical of genioplasties, though lengthening was constrained by the screw.

Conclusions:
This proof-of-concept design effectively lengthened chins and enhanced profiles, proving valuable for severe micrognathia and narrow mandible cases.

Key Words: Distraction osteogenesis; Craniofacial;, Orthodontics;

Funding Agency: None

Dentistry

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Salivary Oral Microbiota in Patients Undergoing Intragastric Balloon Placement.

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Introduction:
Obesity and type 2 diabetes mellitus (T2DM) are prevalent health concerns in Kuwait and have been linked to alterations in the oral microbiota. Intragastric balloon (IGB) therapy offers a minimally invasive method for weight loss in obese individuals, but its impact on the salivary microbiome remains poorly understood. This study aimed to evaluate changes in the salivary microbiota composition before and after IGB treatment.

Methods:
Saliva samples were collected from 22 obese patients undergoing IGB therapy at a private clinic in Kuwait, with 20 completing the study. Samples were obtained at baseline and six weeks post-procedure. DNA was extracted and analyzed using 16S rRNA gene sequencing, focusing on the V1–V3 regions. Microbial diversity and composition were assessed using QIIME2 and the Phyloseq R package, and statistical comparisons were made using the Mann–Whitney U-test.

Results:
Results showed no significant changes in alpha diversity (observed species, Shannon, Simpson indices) or beta diversity (PCoA, NMDS based on Bray-Curti's dissimilarity) between baseline and follow-up ($p > 0.05$), suggesting overall microbial stability. However, significant shifts in the relative abundance of specific taxa were observed, including changes in Veillonella, Porphyromonas, Neisseria, and species like Veillonella atypica, Streptococcus infantis, and Prevotella pasteri.

Conclusions:
These findings suggest that IGB therapy induces minor shifts in certain microbial taxa without disrupting overall salivary microbiota diversity. The results underscore the resilience of the oral microbiome and highlight the less disruptive nature of IGB compared to more invasive bariatric procedures. Ethical approval was obtained from Kuwait University Health Sciences Center Ethics Committee, and written informed consent was obtained from all participants prior to sample collection.

Key Words: Salivary microbiota; Intragastric balloon; Type 2 diabetes mellitus;

Funding Agency: Self-funded

Dermatology

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Knowledge and awareness about the harmful effects of sun exposure on the skin and sun safety methods used in the adult Kuwaiti population: A questionnaire-based study

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Introduction:
Objective
This study aimed to evaluate the awareness level about sun harmful effects on the skin of adult Kuwaitis and to study their attitudes and practices of using sun-protective methods.

Methods:
Study design and setting
Observational multicenter cross-sectional questionnaire-based study was conducted on both males and females who attended primary health care centers in the six governmental areas. From each governorate, one major city was selected. Data collection 2023 to 2024.

Data collection
Self-completed surveys were distributed to primary health care outpatients who were visiting the clinics for various purposes. The questionnaire utilised for data collection was evaluated on a pilot group of 15 individuals in order to determine the approximate completion time. The concluding analysis did not include these questionnaires. Cognitive testing of the questionnaire was performed to assess its validity and understandability. Skin phototype was determined through a self-reported six-category classification, in which participants selected their skin type from the following predefined options: very fair, fair, light brown, brown, dark brown, or black. Although skin phototype was self-reported rather than clinically evaluated, this method is frequently utilised in population-based surveys and was considered compatible with the objectives of the study.

Study sample
In 2023, the population of Kuwaiti above 18 years of age was 1,033,808 Kuwaitis living in the six governorates. To estimate sample size of 35% of population with a sample error of ±3% and 95% confidence level, at least 971 individuals needed to be interviewed. The sample excluded those non-Kuwaiti and those younger than 18.

Data analysis
The data were entered into Excel for descriptive analysis. Quantitative data were analyzed using the mean and standard deviation, while qualitative data were analyzed using descriptive statistics in the form of frequency and percentage. Inferential analysis was performed applying multivariable logistic regression models to determine independent predictors of sunscreen use beyond descriptive statistics. This method was chosen to enable control for potential confounding variables and to facilitate a more comprehensive evaluation of related factors.

Results:
A total of 723 persons consented to participate in the survey, resulting in a response rate of 74.5%. The suboptimal response rate may be attributed to the characteristics of the primary health care clinic environment, where time limitations and high number of patients may restrict participants' interest to stay longer to complete questionnaires. Although the reached sample size was smaller than initially projected, it was adequate for descriptive analysis. The mean age was 36 years. Two-thirds of the participants were females. Almost two-thirds of respondents were both mindful of the association between sun exposure and skin aging and pigmentation, while minority reported no side effects. 39% respondents were aware of the association between skin cancer and solar exposure. Females and lighter skin type demonstrated a higher level of using sunscreens. Only 27% of the participants were using sunscreens regularly and almost half of those who did not use it stated that it is not important to apply sunscreen.
Conclusions:
Participants demonstrated a general awareness of the effects of sun exposure; however, this awareness did not extend to adequate recognition of skin cancer risk or consis

Key Words: awareness; knowledge; skin cancer;

Funding Agency: None

Dermatology

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Efficacy and Safety of Ionic Contra-Viral Therapy (Digoxin/Furosemide) for Cutaneous Warts: A Systematic Review and Meta-Analysis of Randomized Controlled Trials Runing title: ICVT for cutaneous warts

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Introduction:
Background: Cutaneous warts, caused by Human Papillomavirus (HPV), are common and often difficult to treat due to high recurrence rates and side effects associated with standard therapies. Ionic Contra-Viral Therapy (ICVT), a combination of digoxin+furosemide, has emerged as a novel approach, though its efficacy remains uncertain. This is the first systematic review and meta-analysis on the topic.

Methods:
A systematic search of five databases was conducted for randomized controlled trials (RCTs) up to October 2025. Primary outcomes were clinical and dermoscopic responses; secondary outcomes included recurrence, wart size and number changes, and adverse events. Pooled analyses were conducted using risk ratios (RR) and mean differences (MD) with 95% confidence intervals.

Results:
Eight RCTs involving 456 patients were included. Compared to placebo, ICVT significantly improved complete clinical response (RR: 9.27, $p<0.001$), reduced recurrence (RR: 0.05, $p=0.01$), and decreased wart size (MD: -1.67, $p<0.001$). Against active controls, ICVT showed comparable efficacy in complete response (RR: 0.98, $p=0.95$) and recurrence ($p=0.56$). Fewer pigmentation changes (RR: 0.15, $p=0.01$) and hemorrhagic bullae (RR: 0.07, $p=0.01$) were observed with ICVT.

Conclusions:
ICVT shows promise as an effective and safer treatment for cutaneous warts. Further large-scale RCTs are needed to confirm these findings and guide clinical use.

Key Words: Cutaneous warts, Ionic Contra-Viral Therapy (ICVT); Digoxin and furosemide,

Funding Agency: None

Diabetes

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Retinal Thickness Across Diabetic Retinopathy Severity Levels: An Optical Coherence Tomography–Based Clinical Study

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Introduction:
Diabetic retinopathy (DR) is a common microvascular complication of diabetes and a leading cause of vision loss. Optical coherence tomography (OCT) enables precise assessment of retinal structural changes, supporting early detection of macular pathology. This study compared macular retinal thickness among people with diabetes with and without DR.

Methods:
This retrospective study analyzed the most recent OCT-based Early Treatment Diabetic Retinopathy Study (ETDRS) grid of people with diabetes attending the Dasman Diabetes Institute after the ethical approval. OCT parameters included central foveal, parafoveal, and perifoveal thickness across DR severity categories. Differences across DR severity groups were assessed using ANOVA. The analyses were performed using SPSS software (version 29).

Results:
A total of 1922 people with diabetes were included (48.9% male). DR was present in 77.3% of participants, comprising mild non-proliferative DR (NPDR, 47.8%), moderate NPDR (19.4%), and proliferative DR (PDR, 6.9%). Macular edema (ME) was observed in 3.9%. Central foveal thickness was significantly higher in NPDR with ME (mean difference: −56.6 µm; $p < 0.001$) and in PDR (−14.3 µm; $p < 0.001$) compared with no DR. Parafoveal thickness was significantly elevated in NPDR with ME (−14.3 µm; $p < 0.001$), while NPDR and PDR without ME showed no significant differences. Perifoveal thickness similarly increased in NPDR with ME (−22.0 µm; $p < 0.001$). Average retinal thickness and total macular volume were significantly higher only in NPDR with ME (−18.3 µm and −0.51 mm^3, respectively; $p < 0.001$).

Conclusions:
Macular retinal thickness, particularly in the central and para/perifoveal regions, is significantly increased in eyes with DR complicated by macular edema. These findings reinforce the value of OCT-derived retinal thickness mapping for early detection of diabetic macular edema and assessment of DR severity in clinical practice.

Key Words: Diabetes; Optical Coherence Tomography; Diabetic Retinopathy;

Funding Agency: None

Diabetes & Cardiometabolic Risk Factors

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Sex Differences in Cardiometabolic Risk Factors among People with Type 1 Diabetes

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Introduction:
Sex-related differences in cardiometabolic risk factors among people with type 1 diabetes (T1D) may influence complication risk and disease management. This study aimed to compare biochemical, cardiovascular, and anthropometric parameters between males and females with T1D.

Methods:
This study included 249 people with T1D (122 males and 127 females) who partcipitated in ethically approved research project (RAHM-2020-18) at Dasman Diabetes Institute. Parameters included glycemic indices, lipid profile, liver and renal function markers, anthropometric measures, and blood pressure. Sex differences were evaluated using mean differences with 95% confidence intervals (CI) and two-sided p-values.

Results:
No significant sex-related differences were observed in BMI, glycemic control (glucose, HbA1c). Males exhibited significantly higher levels of gamma-glutamyl transferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT) (all $p \leq 0.001$), triglycerides ($p < 0.001$), and serum creatinine ($p < 0.001$). In contrast, females had higher total cholesterol ($p = 0.002$), and HDL cholesterol ($p < 0.001$). Blood pressure was consistently higher in males, with mean systolic and diastolic differences of +5.9 mmHg and +2.6 mmHg, respectively. Additionally, males had a significantly higher waist-to-height ratio compared to females ($p = 0.045$).

Conclusions:
Males with T1D demonstrated a more adverse cardiometabolic profile, higher blood pressure, increased waist-to-height ratio, and lower HDL compared to females, despite comparable BMI and glycemic control. These findings highlight the need for sex-specific approaches into clinical monitoring, risk assessment, and management strategies for people with type 1 diabetes in Kuwait.

Acknowledgments:
Authors gratefully acknowledge the Dasman Diabetes Institute.

Key Words: Type 1 diabetes; Cardiometabolic risk factors; Sex Differences;

Funding Agency: None

Genetics

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Congenital Disorders of Glycosylation in Kuwait: First National Dataset Reveals Genetic and Phenotypic Diversity across 13 Subtypes

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Introduction:
Congenital disorders of glycosylation (CDGs) comprise nearly 200 monogenic diseases characterized by defects in the biosynthesis of oligosaccharides from monosaccharide precursors. Disruptions of glycosylation significantly impacts human physiology and embryonic development, resulting in a wide spectrum of clinical manifestations. Each CDG subtype is defined by mutations in a specific gene that impairs glycosylation, leading to variable multisystem involvement and severity.
Ojectives:
This study aims to establish the first national dataset on CDGs in Kuwait, identify the most prevalent CDG subtypes, and provide epidemiological data that may inform the development of future premarital genetic screening panels.

Methods:
A retrospective review was conducted at the Kuwait Medical Genetics Center. Patients were included if they had a genetically confirmed diagnosis of CDG. Cases lacking molecular confirmation or complete clinical documentation were excluded. Clinical and molecular data were extracted from medical records. The distribution of clinical features and CDG subtypes in the Kuwaiti cohort was descriptively compared with published regional CDG data, including a single-center study summarizing molecularly characterized CDG cases in Arab populations, selected GCC case reports, and reports from Saudi Arabia, to contextualize molecular subtypes and phenotypic presentation. No formal statistical testing was performed.

Results:
Twenty-five individuals (13 females,12 males) with confirmed CDG diagnoses were included. Most presented during infancy or early childhood, typically within the first year of life. Genetic diagnoses were made primarily through whole exome sequencing (WES) and targeted gene panels. Patients were classified into 13 distinct CDG subtypes: COG6 (7 patients, 28%), POMGNT1 (4 patients, 16%), ALG3 (4 patients, 16%), ALG8 (1 patient, 4%), ALG11 (1 patient, 4%), ALG13 (1 patient, 4%), ALG14 (1 patient, 4%), COG5 (1 patient, 4%), GALNT2 (1 patient, 4%), MGAT2 (1 patient, 4%), NGLY1 (1 patient, 4%), PGM1 (1 patient, 4%) and POMT1 (1 patient, 4%). Standardized documentation captured clinical and genetic data. Phenotypically, the most predominant clinical features were hypotonia (14 patients, 56%), followed by visual impairment and dysmorphic features (11 each, 44%). Seizures and microcephaly were observed in 9 patients (36%). Developmental delay and intellectual disability were reported in 7 patients (28%), while brain anomalies were identified in 4 patients (16%). COG6 was the most frequent gene affected (28%), followed by ALG3 and POMGNT1 (each 16%). Consanguinity was present in approximately 70% of families.

Conclusions:
This study presents the first national dataset of CDG cases in Kuwait, revealing significant genetic and phenotypic diversity across 13 subtypes. COG6, POMGNT1, and ALG3 emerged as the most frequently implicated genes, consistent with findings from neighboring countries. Clinical manifestations were heterogenous but frequently included hypotonia, visual impairment, dysmorphism, and neurological involvement. The findings emphasize the importance of early diagnosis, genetic counseling, and the utility of whole exome sequencing as a diagnostic tool.

Acknowledgements: We sincerely thank Dr. Hind AlSharhan for her guidance throughout the research process. We would also like to thank and appreciate Kuwait Medical Genetics Center for their cooperation.

Key Words: CDG; Congenital ; Kuwait;

Funding Agency: None

Genetics

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Evaluating Pharmacogenetics Implementation in Kuwait: Validation and Implications for Tier 1 Alleles in Over 3,000 Local and Resident Patients

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Introduction:
The Kuwait Cancer Control Center (KCCC) is pioneering the integration of genetic testing services centered on personalized medicine within the Middle East. The Association for Molecular Pathology (AMP) Pharmacogenomics Working Group has established recommendations aimed at standardizing pharmacogenetic (PGx) testing across clinical laboratories, ensuring that testing includes the most clinically relevant variants. A key aspect of these guidelines is the tier 1 panel of variant alleles, characterized by functional significance and a minor allele frequency greater than 0.1% in specific populations. The primary aim of this study is to evaluate the benefits of PGx-guided therapy through a comprehensive, population-based analysis of Kuwaiti individuals. Conducting research within extensive cohorts is essential for assessing the influence of PGx variants before clinical implementation. Furthermore, this study seeks to identify pharmacogenomic variants unique to the Kuwaiti population in comparison to other populations, and to investigate their potential clinical significance in gene-drug and genotype-phenotype associations.

Methods:
In this study, participants provided informed consent, and samples were primarily collected through Next-Generation Sequencing (NGS) for an inherited cancer panel. Genotyping was performed using the Express 120 Panel and the QuantStudio 12K Flex Real-Time PCR System, with CYP2D6 copy number assessed via the TaqMan copy number assay for Exon 9. Genetic variability was analyzed by comparing genotypes to data from the 1000 Genomes Project using Pairwise FST. Principal Component Analysis (PCA) was employed to evaluate genetic differentiation. Statistical analyses included the χ^2 test to assess Hardy–Weinberg equilibrium and multivariate analysis of variance (MANOVA) for comparison of allele frequencies.

Results:
The results suggest that Kuwait's population is genetically admixed, exhibiting significant variations in pharmacogenomic profiles that could impact drug metabolism. By emphasizing AMP PGx Tier 1 variants associated with drug responses, the study enhances clinical decision-making, enabling precise dosing and improved therapeutic outcomes. Accurate genotyping methodologies, such as real-time PCR, have further validated these findings.

Conclusions:
This research, based on a substantial sample of 3,000 patients, underscores KCCC's leadership in the field of precision medicine. It establishes a robust foundation for future research initiatives aimed at improving healthcare outcomes for Kuwait's diverse populations by integrating pharmacogenomic insights into clinical practice.

Key Words: Pharmacogenetics; Population genetics; Precision medicine;

Funding Agency: None

Genetics

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Ginger Extract Ameliorates the Diabetic-Induced Changes In the Retina of Diabetic Retinopathy Rats

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Introduction:
Diabetic retinopathy (DR) is a major complication of diabetes and a leading cause of blindness. In DR, retinal neuron degeneration takes place even before the retinal microvascular damage develops. Available treatments, such as anti-vascular endothelial growth factor and laser photocoagulation, are only effective at late stages of DR, and there is no protective treatment for DR to date. Ginger is an affordable natural herb with antioxidant and anti-inflammatory properties. This study aims to study the effect of ginger extracts on retinal structure in a type 1 diabetic (T1D) rat model of DR.

Methods:
T1D was induced in Sprague Dawley male rats by streptozotocin injection (60 mg/Kg). Rats (n=3/group) were divided into normal control (NC), diabetic control (DC), and diabetic rats treated daily with oral ginger extract for eight weeks (DG; 500 mg/Kg). Eyes were processed with and without the lens for section quality optimization. Retinal tissues were stained with Hematoxylin and Eosin (H&E). Total retinal thickness, individual layer thickness, and ganglion cell counts were quantified using ImageJ. Data was analyzed by ANOVA in GraphPad Prism ($P<0.05$). All procedures were approved by the Ethics Committee for the Use of Laboratory Animals (ECULA) at Kuwait University (SCI-IRB-2025/4/0490).

Results:
Retinal sections with the lens showed an artifact space within the retinal outer plexiform layer and preserved attachment of retinal pigmented epithelium layer (RPE) whereas sections without the lens were more intact but had RPE detachment. Diabetic retina showed disrupted retinal organization and vacuolization in ganglion cell layer (GCL) and photoreceptor layer. Total retinal thickness was significantly increased in DC compared with NC, while ginger treatment reduced this thickening. GCL thickness was significantly higher in both DC and DG compared with NC. Ganglion cell count was higher in DG than in DC. The increased GCL thickness in DG may reflect higher ganglion cell count numbers, whereas the increase in DC is likely due to cell vacuolization.

Conclusions:
The observed structural alterations in diabetic retina demonstrate the damaging effect of hyperglycemia on retinal neuronal integrity. Ginger treatment ameliorated the diabetic induced retinal changes, suggesting its potential role in promoting retinal neuron regeneration. Further molecular analysis is required to investigate the potential protective effect of ginger in DR.

Key Words: Diabetic Retinopathy; Ginger, natural herbal ; Retina ;

Funding Agency: This work is funded by the College of Graduate Studies and the Research Sector (project No. YS03/24) at Kuwait University

Genetics

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Mitochondrial Haplogroup H Is Linked to Lower Type 2 Diabetes Risk in Gulf Arabs

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Introduction:
Numerous studies have linked mitochondrial dysfunction to the development of type 2 diabetes (T2D) by affecting glucose-stimulated insulin secretion in pancreatic beta cells and reducing oxidative phosphorylation in insulin-responsive tissues. Given the strong genetic underpinnings of T2D, research has explored the connection between mitochondrial DNA haplogroups, specific variants, and the risk and comorbidities of T2D. For example, haplogroups F, D, M9, and N9a have been linked to an elevated risk of T2D across various populations. Additionally, specific mitochondrial DNA variants, such as the rare mtDNA 3243 A>G and the more prevalent mtDNA 16189 T>C, have also been implicated in heightened T2D risk. Notably, these associations vary among different populations. Given the high incidence of T2D in the Gulf Cooperation Council countries, this study investigates the correlation between T2D and mitochondrial haplogroups and variants in Arab populations from the Gulf region.

Methods:
This analysis involved mitochondrial haplogroup and variant testing in a cohort of 1,112 native Kuwaiti and Qatari individuals, comprising 685 T2D patients and 427 controls. Complete mitochondrial genomes were derived from whole exome sequencing data to examine the associations between T2D and haplogroups and mitochondrial DNA variants.

Results:
The analysis revealed a significant protective effect of haplogroup H against T2D (odds ratio [OR] = 0.65; P = 0.022). This protective association persisted when adjusted for age, sex, body mass index (BMI) and population group, with an OR of 0.607 (P = 0.021). Furthermore, specific mitochondrial variants showed significant associations with T2D risk after adjustment for relevant covariates, and some variants were exclusively found in T2D patients.

Conclusions:
Our findings confirm that the maternal haplogroup H, previously identified as protective against obesity in Kuwaiti Arabs, also serves as a protective factor against T2D in Arabs from the Gulf region. The study also identifies mitochondrial DNA variants that either increase or decrease the risk of T2D, underscoring their role in cellular energy metabolism.

Key Words: Mitochondria; Type 2 diabetes; Haplogroups;

Funding Agency: KFAS - Kuwait Foundation for the Advancement of Sciences

Genetics

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

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Introduction:
ADAT3-related intellectual disability (ADAT3-related ID) is a rare autosomal recessive disorder caused by biallelic variants in ADAT3, a gene essential for tRNA editing found on chromosome 19. The Saudi Founder variant c382G>A (Val128Met) results in the loss of an essential hook on the surface of the ADAT3 protein. This has since been demonstarted to be a cause of an intellectual disability syndrome known as ADAT3 related ID. While approximately 44 cases, predominantly from the Arabian Peninsula, have been previously described, data from Kuwait has not been reported. This study aims to characterize ADAT3-related ID in Kuwait.

Methods:
A retrospective analysis was conducted on the data registry in Kuwait Medical Genetics Center for individuals with pathogenic variants in ADAT3. This study was ethically approved by the institutional review board of the MOH and KMGC (2193/2022), in January 2023.

Results:
We identified 28 individuals from Kuwait, carrying a homozygous pathogenic Saudi founder variant in ADAT3 founder variant c.430G>A p. (Val144Met) (NM_138422.4). Most cases were diagnosed during childhood (6 months–15 years), while five were diagnosed in adulthood. Universal features included developmental delay and intellectual disability. Additional findings included abnormal muscle tone (20/28), dysmorphic facial features (15/28), microcephaly (16/28), strabismus (16/28), musculoskeletal abnormalities (13/28), short stature (10/28), spasticity (10/28), seizures (8/28), failure to thrive (8/28), and cardiac defects (5/28). Distinctive features of our cohort included chest wall deformities (5/28) and scoliosis (4/28). Neuroimaging demonstrated brain atrophy, corpus callosum agenesis, colpocephaly, arachnoid cysts, and pituitary hypoplasia, as previously reported in the literature. Limitations of this study include a small sample size, challenges with patient follow up, as well as limited comparative data in the literature on this condition.

Conclusions:
This is the first study to describe ADAT3-related intellectual disability in Kuwaiti individuals from diverse tribal backgrounds. All individuals were homozygous for the founder Saudi variant, suggesting it may also be considered a founder mutation in Kuwait. Raising awareness among clinicians about this identifiable cause of intellectual disability may enhance patient care through early recognition and pre-implantation genetic testing offered to those at risk

Key Words: ADAT3; Intellectual Disability ; Founder mutation ;

Funding Agency: None funding

Genetics

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An Association Study of Type 2 Diabetes Mellitus Genetic Risk Factors in the Kuwaiti Population

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Introduction:
T2DM is a chronic metabolic disease that results from a complex interaction between environmental and genetic factors. The heritability of type 2 diabetes mellitus (T2DM) is estimated to be 25–80% based on family and twin studies. To date, over 200 T2DM genetic risk variants have been reported in various populations. Despite Kuwait's high T2DM prevalence, replication studies of T2DM genetic risk factors remain limited. Objectives: To determine the association of the 10 commonly reported T2DM genetic risk factors in a T2DM population sample from Kuwait and design a genetic risk score (GRS) model specific to Kuwait.

Methods:
Genotyping of ADRB2 rs1042714, CCND2 rs76895963, CDKAL1 rs7754840, CDKN2A/B rs10811661, FTO rs1421085, IGF2BP2 rs7633675, KCNQ1 rs2237897, PPARG rs1801282 TCF7L2 rs7903146, and VDR rs731236 was performed using Taqman assays in 200 Kuwaiti T2DM patients and 160 Kuwaiti healthy controls. Unweighted and weighted GRSs were computed. Sample collection was according to the protocol approved by the ethics committees of the Faculty of Medicine, Kuwait University, following Helsinki Declaration guidelines (VDR/JC/87)

Results:
Three variants associated with T2DM risk in Kuwaitis (TCF7L2 rs7903146T: β=0.133, 95%CI: 0.066–0.199, p<0.001; VDR rs731236G: β=0.102, 95%CI: 0.033–0.17, p=0.004; and IGF2BP2 rs7633675G: β=0.075, 95%CI: 0.008–0.142, p=0.028). Some variants associated with risk of diabetes comorbidities (Retinopathy: CDKAL1 rs7754840C β=0.123, 95%CI: 0.034–0.213, p=0.007 and ADRB2 rs1042714G β=0.125, 95%CI: 0.024–0.226, p=0.016; Neuropathy: TCF7L2 rs7903146T β=0.284, 95%CI: 0.195–0.373, p<0.001 and VDR β=0.288, 95%CI: 0.194–0.382, p<0.001; Myocardial infarction: TCF7L2 rs7903146T β=0.065, 95%CI: 0.002–0.128, p=0.034. The best model performance was observed for the weighted GRS, including the six variants showing a positive effect toward T2DM risk despite their significance together with age and BMI (82.9% Accuracy; 66.3% Sensitivity; 91.1% Specificity; β=100.617, 95%CI: 10.097-1002.692, p<0.001).

Conclusions:
Reported T2DM genetic risk factors do not consistently associate with T2DM risk among Kuwaitis, but including these variants in a T2DM prediction GRS model may refine its performance. Including established T2DM risk factors like age and BMI enhances models' performance. A T2DM early screening GRS for Kuwaitis could enhance early interventions, curbing the T2DM burden on Kuwait's healthcare system.

Key Words: Type 2 diabetes mellitus; Genetic risk score; genetic variant;

Funding Agency: This study was funded by the College of Graduate Studies, Kuwait University

Genetics

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Age-related Distribution of Aneuploidy Types: Lessons from 100 Non-Invasive Prenatal Screens

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Introduction:
Non-invasive prenatal testing (NIPT) is frequently used to screen chromosomal abnormalities for prenatal diagnosis. Aneuploidy is one of the leading factors limiting embryo development in pregnancies. Maternal age, especially advanced maternal age, is known to increase aneuploidy risk. However, the distribution of specific aneuploidy types across age groups is not fully characterized.

Objectives: Here, we aimed to assess this characterization by evaluating how maternal age influences the frequency and pattern of aneuploidy types in suspected pregnancies.

Methods:
We retrospectively analyzed the chromosomes of 100 fetuses using Next-Generation Sequencing (NGS) based NIPT. Embryos were categorized by maternal age: below 30, 30-34, 35-37, 38-40, and above 40. Aneuploidy types included whole chromosome trisomy, monosomy, and sex chromosome abnormalities. A z-score was calculated to each chromosome and these values indicated the presence of chromosomal abnormalities.

Results:
Aneuploidy rates increased significantly with maternal age, rising from 8% in women below the age of 30, to 27% in women above the age of 40. The whole-chromosome monosomy was detected in none of the 100 fetuses, since NIPT is performed on pregnancies with a gestational age above 10 weeks and such abnormalities do not usually develop to that gestational age. Chromosomes 18 and 21 exhibited the steepest age-related increases.

Conclusions:
In conclusion, maternal age strongly influences both the rate and type of embryonic aneuploidy. However, NIPT performs poorly in comparison with invasive testing and thus, further testing is needed to confirm NIPT results.

Key Words: Non invasive prenatal testing (NIPT); Aneuploidy; Fetal fraction;

Funding Agency: Ministry of Health

Immunology

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Epigenetic H3K9/K18 Acetylation Sustains TNF-α Expression and Promotes Metabolic Dysfunction in Obesity

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Introduction:
Background/Objectives: Obesity-induced metabolic inflammation is a major contributor to insulin resistance, liver steatosis, and other metabolic disorders. While TNF is known to play a central role in these complications, the chromatin-level mechanisms that promote and sustain TNF transcription during obesity remain incompletely understood. This study aimed to define the epigenetic regulatory program driving TNF expression in diet-induced obesity (DIO), with a focus on histone H3K9/K18 acetylation.

Methods:
Animal experimental procedures were performed following the approval by the Dasman Diabetes Institute Animal Care and Ethics Committee. Male C57BL/6J mice were fed high fat diet (HFD) or chow diet (CD) for 16 weeks. Body weight gain was assessed on weekly basis. TNF expression and histone acetylation levels were evaluated in adipose tissue and liver. Chromatin Immunoprecipitation followed by qPCR (ChIP-qPCR) was used to quantify H3K9 and H3K18 acetylation at the TNF promoter. Oil Red O staining was performed for steatosis. OGTT and ITT were performed for glucose homeostasis assessment.

Results:
Compared with CD-fed mice, those with DIO exhibited significantly elevated TNF expression and increased global levels of H3K9/K18 acetylation in adipose tissue and liver. ChIP-qPCR analysis showed enriched H3K9/K18ac marks at the TNF promoter in both tissues of obese mice, indicating a transcription-permissive chromatin state. These epigenetic changes were positively associated with body weight gain, insulin resistance, and hepatic steatosis, linking TNF promoter specific acetylation with metabolic impairment.

Conclusions:
Conclusions: Diet induced obesity creates a permissive chromatin state that maintains TNF transcription by increasing H3K9/K18 acetylation at its promoter. This epigenetic remodeling contributes to metabolic dysfunction and may identify H3K9/K18 acetylation as a potential prognostic marker for metabolic impairment and liver steatosis in obesity.

Key Words: TNF; obesity; H3K9/K18 acetylation ;

Funding Agency: KFAS

Infection Prevention and Control

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Ten Years of Surveillance on Sharps Injuries in Kuwait: Trends, Contamination Patterns, and Predictors

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Introduction:
Sharps injuries are a preventable occupational hazard for health-care workers, with risk of transmitting blood-borne pathogens. Evidence on trends, contamination patterns, and the role of safety-engineered devices (SED) in Kuwait is limited.

Methods:
We conducted a repeated cross-sectional analysis of 3,374 reported sharps injuries among healthcare workers in Kuwait from 2014 to 2024 using the national occupational surveillance system. Outcomes were the contamination status of sharps and availability of SED. Descriptive statistics, Chi-square tests, and multivariable logistic regression were used to identify predictors of contaminated injuries and SED availability, reporting adjusted odds ratios (aORs) with 95% confidence intervals (CIs). The study used anonymized secondary data from the Ministry of Health occupational surveillance system, with no direct participant contact. Ethical approval was obtained from the Health Sciences Center, Kuwait University, and the Ministry of Health Ethical Committee, Kuwait (Approval No: 2024/2773).

Results:
Overall, 93.7% of reported injuries involved contaminated sharps. Contamination status did not differ by gender or nationality but varied by facility and department. Wards (95.2%) and the emergency & critical care department (95.0%) reported higher contamination compared with diagnostic and laboratory services (88.7%, p <0.001). Nurses were more than twice as likely to sustain contaminated injuries compared with physicians (aOR = 2.45, 95% CI: 1.57–3.80). Having an identifiable source patient increased the odds of contamination (aOR = 1.65, 95% CI: 1.10–2.49). Of 2,388 cases with SED data, 50.4% occurred when SED were not available. Availability differed by department and occupation; outpatient clinics had lower odds of SED presence compared with emergency and critical care (aOR = 0.59, 95% CI: 0.37–0.93). Activation of protective mechanisms strongly predicted SED use (aOR = 1.91, 95% CI: 1.38–2.64). Reported injuries increased over the study period, with peaks in 2017 and 2023–2024.

Conclusions:
Sharps injuries in Kuwait remain frequent, highly contaminated, and unevenly preventable across worker groups and settings. Nurses and ward staff face the greatest risks, while gaps in SED deployment and activation persist. Strengthening procurement systems, expanding competency-based training, and fostering non-punitive reporting are needed to reduce occupational exposure and protect the health workforce.

Key Words: Sharps injuries, safety-engineered devices, occupa; healthcare workers; Kuwait;

Funding Agency: None

Internal Medicine

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Efficacy and Safety of Antihypertensive Drugs Deprescribing in Older Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Introduction:
While antihypertensive treatment is beneficial, aggressive therapy in frail, multimorbid older adults carries significant risks, including falls and hypotension. Deprescribing has emerged as a strategy to mitigate these risks, but robust evidence on its safety and efficacy has been lacking. This systematic review and meta-analysis of randomized controlled trials (RCTs) aimed to evaluate the clinical outcomes of deprescribing antihypertensive drugs in older adults.

Methods:
A comprehensive search of PubMed, Scopus, CENTRAL, and Web of Science was conducted for RCTs up to October 2025. The primary outcomes were all-cause mortality, cardiovascular mortality, and all-cause hospitalizations. Secondary outcomes included major adverse cardiovascular events (MACE), serious adverse events (SAEs), and falls. Risk ratios (RR) were pooled using a random-effects model, using Stata SE v. 19.5.

Results:
Four RCTs involving 2,173 patients were included. The analysis found no significant difference between the deprescribing strategy and usual care for all-cause mortality (RR: 1.02, 95% CI [0.93, 1.12]; p = 0.62), cardiovascular mortality (RR: 1.11, 95% CI [0.80, 1.55]; p = 0.53), or all-cause hospitalizations (RR: 0.95, 95% CI [0.85, 1.05]; p = 0.33). Similarly, there were no significant differences in the incidence of MACE (RR: 1.09, 95% CI [0.90, 1.33]; p = 0.38), MI (RR: 0.76, 95% CI [0.42, 1.38]; p = 0.37), stroke (RR: 1.12, 95% CI [0.66, 1.89]; p = 0.68), SAEs (RR: 1.08, 95% CI [0.90, 1.30]; p = 0.41), or falls (RR: 1.00, 95% CI [0.89, 1.13]; p = 0.95).

Conclusions:
In older adults, a strategy of deprescribing antihypertensive drugs was not associated with an increased risk of mortality, MACE, or other SAEs compared to usual care. These findings may provide reassuring evidence on deprescribing strategies; however, further research is still required before widespread clinical endorsement.

Key Words: blood Pressure; Frail; nursing homes;

Funding Agency: None

Machine Learning

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Forecasting Hospital Workload with AI: A Hybrid Review and Case Study from Kuwait Cancer Control Center (KCCC)

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Introduction:
Accurate forecasting of hospital workload is essential for optimizing resource allocation, improving operational efficiency, and strengthening healthcare system resilience.

Methods:
This study uses a hybrid design, combining a focused literature review on predictive models for hospital workload with a case study evaluating three forecasting algorithms - Seasonal Autoregressive Integrated Moving Average (SARIMA), XGBoost, and Prophet - using monthly admission data from the Kuwait Cancer Control Center (KCCC).

Results:
All hospital outpatient clinic visits recorded between January 2021 and December 2024 were included and aggregated into monthly counts for model development and evaluation, yielding a total of 7,491 visits. SARIMA, Prophet, and XGBoost models were trained on 36 months of data (January 2021 - December 2023) and used to forecast monthly admissions for 2024, with performance assessed using Mean Absolute Error (MAE), Root Mean Squared Error (RMSE), and Mean Absolute Percentage Error (MAPE). XGBoost achieved the lowest errors (MAE 22.67, RMSE 25.92, MAPE 11.20), Prophet showed intermediate performance (MAE 30.08, RMSE 35.21, MAPE 14.51), and SARIMA had the highest errors (MAE 78.25, RMSE 81.97, MAPE 37.75). Diebold–Mariano tests showed that both XGBoost and Prophet were significantly more accurate than SARIMA ($p < 0.01$), whereas the difference between XGBoost and Prophet was not statistically significant at the 5% level ($p = 0.08$).

Conclusions:
These findings suggest that machine learning models, particularly XGBoost, may better capture complex, non-linear admission patterns than traditional statistical time series models in this context; however, the use of a single-center dataset with a relatively small sample size, absence of external validation, and focus on only three AI models limit the generalizability of these results. Larger multi-center studies, external validation across diverse hospital settings, and benchmarking against a wider range of AI architectures are needed to confirm these findings and to translate forecasting gains into measurable operational benefits such as improved staffing, bed management, and cost containment.

Key Words: Predictive Modeling; Hospital Visit Forecast; Machine Learning;

Funding Agency: None

Medical Education

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Public Perception on AI-Generated Health Information

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Introduction:
Artificial intelligence (AI) tools are widely used by the public to access health information. Although AI has demonstrated effectiveness in diagnostics and patient education, concerns remain regarding trust, accuracy, and ethical use, particularly in Kuwait where digital health adoption is expanding and AI may reduce pressure on healthcare services while supporting technological advancement. This study aimed to evaluate public perception and trust toward AI-generated health information, assess its accuracy, and identify influencing factors.

Methods:
A cross-sectional mixed-methods study was conducted using an anonymised online survey distributed via Instagram and personal networks in Kuwait between March and April 2025. Convenience sampling was used. Inclusion criteria were adults aged 18 years or older with recent access to health information. The survey instrument consisted of quantitative closed-ended Likert-scale questions assessing awareness, willingness to engage, and trust in AI-generated health information alongside open-ended questions exploring reasons for trust or concerns. Quantitative data were analysed using frequencies and percentages, while qualitative responses were analysed using thematic analysis. ChatGPT was used for accuracy assessment by generating ten health-related queries, which were cross-verified against established clinical guidelines. Ethical approval was obtained from the Research Ethics Committee, King's College London.

Results:
The survey recorded 75 participant responses. 75% were aware of AI generating health information. 65.8% expressed willingness to read this information, and 83.3% reported concerns regarding trust and accuracy. Reported concerns included accuracy (83.3%), algorithmic biases (73.3%), and data privacy (31.7%). Younger participants demonstrated higher acceptance of AI-generated health information versus older age groups. Analysis of open-ended responses identified three dominant qualitative themes: perceived convenience and accessibility, accuracy doubts (AI hallucinations), and the importance of clinical verification and governmental endorsement. Accuracy verification demonstrated that AI-generated responses were generally clinically accurate but lacked detail (crucial for healthcare-related decision-making).

Conclusions:
AI-generated health information may improve access to health education in Kuwait; however, challenges related to trust, accuracy, and ethics remain. Addressing these through clinical oversight and transparent governance may strengthen public trust and support safe AI integration into a technologically advanced healthcare system.

Key Words: N/A; N/A; N/A;

Funding Agency: None

Medical Education

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Insights into the Prophage Islands of Indigenous Gram-positive Bacteria

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Introduction:
Bacterial genomes frequently harbor integrated viral sequences (prophages) that significantly influence host phenotype, evolution, and virulence. This study comprehensively characterized prophage islands within the Bacillus velezensisALH8 genome.

Methods:
Whole genome of the sea sediment bacterium Bacillus velezensis ALH8 was sequenced. Then, prophage regions in the genome were analyzed using integrative bioinformatics and comparative genomics approaches.

Results:
Five distinct prophage regions spanning 259 kb (6.1% of chromosome) were identified in the bacterial genome (4.24 Mbp), comprising 184 phage-related genes organized into functional modules. Among these, three regions (199 kb, 77%) represent active prophages with intact induction and lytic capabilities, while one region (47 kb) is defective/dormant and another (28 kb) represents remnant fossilized sequences. Phylogenetic analysis reveals mosaic origins with contributions from Bacillus, Listeria, Bordetella, and Thermus phages, including a φ105-like temperate phage. Functional annotation indicates diverse phenotypic impacts including potential biofilm modulation, stress response enhancement, and antibacterial peptide production.

Conclusions:
These findings reveal the vast genetic reservoir carried by phages in Bacillus and offer insights into how prophage content can shape the bacterium's capacity to synthesize beneficial compounds, endure stress, and engage in ecological interactions.

Key Words: Prophage; Indigenous Gram-positive Bacteria ; Insights;

Funding Agency: Kuwait University

Medicine

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Efficacy and safety of oral ivermectin versus benzyl benzoate for the treatment of scabies: a systematic review and meta-analysis of randomized controlled trials

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Introduction:
Oral ivermectin and topical benzyl benzoate are two common treatment options for scabies, but there is ongoing discussion regarding their relative safety and efficacy. A thorough synthesis of the available evidence is required to inform treatment decisions because of the clinical debate caused by the contradictory findings from current randomized controlled trials (RCTs).

Methods:
A systematic review and meta-analysis were conducted on evidence retrieved from PubMed, Scopus, Web of Science, and CENTRAL for RCTs up to August 2025. The primary outcome was the cure rate. Secondary outcomes included pruritus improvement and the incidence of adverse events. Stata MP v. 18 was used to pool outcomes.

Results:
Ten RCTs involving 1,105 patients were included. Cure rates showed no significant difference between ivermectin and benzyl benzoate at 1 week (RR: 1.07, 95% CI [0.88, 1.30], $p = 0.51$), 2–4 weeks (RR: 0.99, 95% CI [0.88, 1.12], $p = 0.91$), or after more than 4 weeks (RR: 1.16, 95% CI [0.95, 1.43], $p = 0.15$). The overall pooled result confirmed no difference (RR: 1.04, 95% CI [0.95, 1.14], $p = 0.37$). For pruritus, no significant differences were observed at 1 week (RR: 1.07, 95% CI [0.80, 1.43], $p = 0.66$), 2–4 weeks (RR: 1.19, 95% CI [0.97, 1.46], $p = 0.09$), or beyond 4 weeks (RR: 1.10, 95% CI [0.89, 1.37], $p = 0.38$); overall RR: 1.13, 95% CI [0.99, 1.29], $p = 0.07$. Ivermectin showed significantly fewer adverse events (RR: 0.27, 95% CI [0.16, 0.46], $p < 0.001$), particularly less burning/stinging (RR: 0.07, 95% CI [0.02, 0.20], $p < 0.001$). Gastrointestinal (GI) events were not significantly different (RR: 1.47, 95% CI [0.67, 3.22], $p = 0.34$).

Conclusions:
Oral ivermectin and topical benzyl benzoate exhibit comparable efficacy for the treatment of scabies. However, ivermectin's significantly better safety and tolerability, combined with the practical advantage of oral administration, establish it as a valuable and often preferable therapeutic choice.

Key Words: itch, scabies, ivermectin, benzyl benzoate, meta-a; itch, scabies, ivermectin, benzyl

Funding Agency: 2418782

Medicine

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Knowledge and Awareness of Bowel Cancer Among Kuwait University Students

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Introduction:
Colorectal cancer (CRC) ranks as the third most common cancer globally and the second leading cause of cancer-related mortality. In Kuwait, it accounts for 10.2% of all cancers, yet public awareness remains limited. This study aimed to assess the knowledge and awareness of bowel cancer among Kuwait University students and to identify factors associated with their knowledge levels.

Methods:
A cross-sectional study was conducted among 555 Kuwait University students from various faculties between December 2024 and January 2025. Participants completed a 39-item self-administered questionnaire derived from the validated Cancer Awareness Measure (CAM) toolkit. Knowledge scores were developed for risk factors (0–11) and signs/symptoms (0–9). Statistical analysis was performed using SPSS v29, employing Mann-Whitney and Kruskal-Wallis tests, linear regression for risk factor scores, and logistic regression for signs/symptoms. Ethical approval was obtained from the Health Sciences Center Ethics Committee at Kuwait University.

Results:
Most participants were female (83.2%) and Kuwaiti (88.5%), with a median age of 21 years. The most recognized risk factors were alcohol consumption (59.5%) and smoking (55.9%), whereas HPV infection (22%) and childhood sunburn (20.4%) were least recognized. “Blood in stool” (53.9%) and “unexplained weight loss” (51.5%) were the most identified symptoms. Knowledge scores were significantly higher among medical students ($p<0.001$), participants familiar with bowel cancer ($p<0.001$), and those with a family history of cancer ($p<0.005$). Lower knowledge was noted among students from non-health faculties and residents of certain governorates.

Conclusions:
Significant disparities in bowel cancer knowledge exist among university students, with non-medical and less-exposed groups showing limited awareness. Educational interventions and targeted public health campaigns are warranted to improve recognition of lesser-known risk factors and promote early screening behaviors in the community.

Acknowledgements:
We extend our gratitude to Dr. Anwar Albaloul for her guidance and to Dr. Ahmad Alsultan for his assistance. We also thank all participating students for their contributions.

Key Words: colorectal cancer, bowel cancer, cancer education, cancer awareness, university

Funding Agency: None

Medicine

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β-Caryophyllene as a Multi-Target Therapeutic in Diabetes: Mechanistic Insights, Safety Profile, and Clinical Translation Potential

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Introduction:
Caryophyllene (BCP) is a natural sesquiterpene that selectively activates cannabinoid receptor 2 (CB_2R) and modulates PPAR-γ and ACE2/MasR pathways. Pre-clinical studies suggest it can simultaneously target hyperglycaemia, chronic inflammation and oxidative stress core defects of type 2 diabetes mellitus and its complications. This review aimed to compile pre-clinical evidence of BCP's efficacy in T1DM and T2DM models, clarify the molecular mechanisms underlying its metabolic benefits, and evaluate translational prospects and research gaps.

Methods:
This PRISMA-adapted narrative review systematically searched PubMed, Scopus, Web of Science and Google Scholar for studies published between 2000–2025 using the terms β-caryophyllene, diabetes, CB_2R, PPAR-γ and Nrf2.Preclinical (in vivo/in vitro) and clinical/observational studies evaluating BCP in diabetes or its complications were included if they reported glycaemic, inflammatory, oxidative, or organ-specific outcomes. Reviews, editorials, commentaries, patents,and non-original articles were excluded. Data extraction followed PRISMA-adapted guidelines. No experiments were conducted, so ethical approval was not required.

Results:
Across 62 pre-clinical and clinical investigations, BCP consistently lowered fasting glucose by 20-30 % and reduced HbA_1c by 0.5 % in streptozotocin-induced and high-fat-diet models. Neuroprotective effects included a 35-40 % improvement in neuropathic pain scores. Pharmacokinetic studies showed oral bioavailability with nanoemulsion formulations and blood-brain-barrier penetration of 60 %.Toxicology demonstrated a wide safety margin and FDA GRAS status with no adverse effects at therapeutic doses. Human data are limited to small, non-randomised pilots reporting modest glucose reductions, 0.3-0.5 % HbA_1c declines and 10-15 % CRP decreases, underscoring a translational gap.

Conclusions:
BCP demonstrates promising anti-hyperglycaemic, anti-inflammatory, and neuroprotective effects across robust preclinical models, supported by favourable pharmacokinetics and a wide safety margin. However, the current evidence base is limited by the scarcity of well-designed human studies. Phase II randomised controlled trials are needed to establish its clinical utility, particularly as an adjunct to standard therapies such as metformin or GLP-1 receptor agonists.If validated in clinical settings, BCP may represent a cost-effective, non-psychoactive therapeutic strategy for improving glycaemic control and preventing diabetes-related complications

Key Words: β-caryophyllene; diabetes; CB_2R;

Funding Agency: None

Medicine

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Beyond the Clinic: Mapping the Sarcopenia Crisis in Kuwait and Charting a Path Forward

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Introduction:
Sarcopenia, characterized by the progressive loss of muscle mass, strength, and function associated with aging, is widely recognized as a significant global health problem, particularly among the elderly. It is a geriatric syndrome linked to adverse outcomes such as reduced quality of life, increased risk of falls and fractures, and higher mortality rates Kuwait's rapidly aging population (5.3% ≥60 years) faces a confluence of risk factors—including high rates of vitamin D deficiency, diabetes, and obesity—that predispose them to sarcopenia, a debilitating loss of muscle mass and function. This underdiagnosed condition represents a silent geriatric health emergency threatening healthy aging.

Objective: This pilot study aimed to conduct the first community-based screening for sarcopenia among Kuwaiti elderly using the Asian Working Group for Sarcopenia (AWGS) criteria and suggest the appropriate public health strategy.

Methods:
An unfunded, cross-sectional pilot study was conducted in Al Asimah Governorate. Sixty-one (n=61) community-dwelling Kuwaiti nationals aged ≥60 years were recruited via random phone calls. Assessments included anthropometry, bioelectrical impedance analysis (BIA), handgrip dynamometry, the Short Physical Performance Battery (SPPB), and the SarQoL questionnaire, using AWGS diagnostic cut-offs.

Results:
The study revealed a high overall frequency of sarcopenia at 54.1% as determined through assessments using the Asian Working Group for Sarcopenia (AWGS) criteria, which included handgrip strength measurements via a dynamometer and gait speed evaluations using the Short Physical Performance Battery (SPPB). A steep age gradient was observed: 18.8% among those aged 60-69 years (P=<0.003), 43.5% among those aged 70-79 years (P=<0.303), and a staggering 90.9% in individuals aged 80 years and older (P=<0.001). Notably, gender disparities emerged, with 61% of those affected being female compared to 39% male (P=<0.012). This disparity may reflect cultural and lifestyle factors influencing physical activity and nutrition.

Conclusions:
This pilot study provides community-based evidence of potential silent a sarcopenia epidemic in Kuwait, revealing critically high frequency rates and a stark gender inequality. Despite limitations like a small sample size, the findings are powerful signal for an urgent public health response. Immediate action is required to validate these results with a national study and implement a multi-tiered strategic plan involving screening, public awareness, targeted interventions, and long-term policy changes to mitigate this crisis.

Key Words: Sarcopenia, Kuwait, Aging, ; Public Health, Prevalence, Geriatrics; Muscle

Funding Agency: None

Medicine

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Association Between Choroidal Thickness and Diabetes Mellitus: A Systematic Review

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Introduction:
This systematic review aimed to evaluate the association between diabetes mellitus (types 1 and 2) and choroidal thickness (CT) as measured by optical coherence tomography (OCT).

Methods:
A systematic literature search was conducted across PubMed, Embase, Web of Science, Scopus, and the Cochrane Library for observational studies published from 2010 to 2025, following PRISMA guidelines. Due to heterogeneity in study designs and outcome measures, a narrative synthesis was performed. Studies evaluating CT in diabetic patients were included, with or without comparisons to non-diabetic controls. After removing duplicates, 24 studies met the inclusion criteria. Data were extracted regarding study design, sample size, country of origin, type of diabetes, presence or severity of diabetic retinopathy (DR), OCT modality used, anatomical region examined, and CT outcomes.

Results:
A total of 24 eligible observational studies were included. Choroidal thinning was reported in 11 studies, while 8 demonstrated thickening, often in early disease stages or in association with diabetic macular edema (DME). Five studies found no significant change in CT, although some reported reductions in the choroidal vascularity index despite stable thickness. Considerable variability was observed across study designs, imaging protocols, and patient populations. Studies using swept-source OCT (SS-OCT) more consistently identified choroidal thinning compared to those using spectral-domain OCT (SD-OCT).

Conclusions:
Choroidal thickness appears reduced in patients with diabetes, particularly with DR progression, supporting its potential role as a non-invasive biomarker of diabetic choroidopathy. However, the variability in findings underscores the need for standardized OCT imaging protocols and further longitudinal research to clarify the temporal relationship between CT alterations and diabetic disease progression.

Key Words: Ophthalmology; Choroidal Thickness; Daibetes Mellitus;

Funding Agency: None

Medicine

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Relationship between Irritable Bowel Syndrome and Anxiety in Kuwait's General Population: A Cross-sectional Study

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Introduction:
Irritable bowel syndrome, or IBS, is a chronic condition characterized by recurrent abdominal pain with changes in bowel habit. There are many causes of IBS, one of which is dysregulation of the gut-brain axis, often influenced by mental disorders. Anxiety is a psychiatric disorder with a high prevalence across Kuwait. The aim of this study was to determine the prevalence of IBS and anxiety in Kuwait and to examine the association between them.

Methods:
A cross-sectional study was conducted using convenience sampling among Kuwait's general population. Data was collected from 326 individuals using ROME IV criteria and Beck Anxiety Inventory (BAI) through an online questionnaire shared on multiple online platforms accessible to the general population. Comparison between groups were performed using the Mann–Whitney U and Kruskal–Wallis tests where applicable. After assessing data normality, Shapiro-Wilk was used. Moreover, categorical variables were compared by Chi-square. Logistic regression was used to assess the association between anxiety level and IBS. We considered a p-value < 0.05 to be statistically significant.

Results:
Out of 326 total responses collected from the general population, 43% was found to have IBS. Our study revealed no significant association between IBS and sociodemographic factors, including age, gender, or nationality. According to the BAI-10 score, 165 of people were classified under low anxiety level group, 100 under moderate anxiety level group, and 61 under high anxiety level group. Logistic regression analysis demonstrated a significant association between anxiety levels and IBS. Participants with moderate anxiety had significantly higher odds of having IBS compared to those with low anxiety (OR = 2.76, 95% CI). Participants with high anxiety had an even greater likelihood of IBS (OR = 4.87, 95% CI).

Conclusions:
This study demonstrated a clear link between anxiety and IBS, further supporting the role of gut-brain axis in the pathophysiology of IBS. Further longitudinal studies in Kuwait is needed to be conducted in order to explore causality.

Key Words: Irritable Bowel Syndrome; Anxiety; Kuwait;

Funding Agency: None

Medicine

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Comparative Efficacy and Safety of Pudendal Nerve Block versus Caudal Block in Pediatric Hypospadias Surgery: A Systematic Review and Meta-Analysis

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Introduction:
Caudal block (CB), the conventional approach of analgesia used in hypospadias surgeries among children, has demonstrated short postoperative pain relief as well as perioperative complications, including immobilization and blood pressure changes. Pudendal Nerve Block (PNB) has recently shown superiority over CB regarding the analgesic dose and postoperative outcomes.Objective: To evaluate the efficacy and safety outcomes of PNB compared to CB for children undergoing hypospadias surgeries.

Methods:
Four databases, PubMed, Medline, Scopus, Web of Science, and Cochrane Library, were searched for relevant articles comparing the two interventions of interest. Primary outcomes were postoperative pain scores at 1, 2, 6, and 24 hours, while secondary outcomes included 24-hour analgesic consumption and safety outcomes. Continuous outcomes were analyzed using standardized mean difference (SMD), and dichotomous outcomes using risk ratio (RR), applying a random-effects model.

Results:
Ten comparative studies met the inclusion criteria (eight clinical trial studies and two observational studies), with a total population of 639. PNB showed lower postoperative pain than CB, with effects becoming clinically and statistically significant from 6 hours onward (SMDs = −0.75 to −2.05 through 24 hours). PNB also reduced 24-hour analgesic consumption (SMD = −2.29) and prolonged time to first rescue analgesia by 9.5 hours. Hemodynamic measures at 24 hours complication rates were similar between the two interventions. Sensitivity analyses suggested early time-point pain effects were less robust, whereas key secondary outcomes remained stable.

Conclusions:
PNB provides longer and stronger postoperative pain relief than CB in children undergoing hypospadias surgery, with reduced analgesic use and similar safety and hemodynamic profiles.

Key Words: Hypospadias; Pudendal Nerve Block, Caudal Block; Meta-analysis;

Funding Agency: None

Medicine

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Bioinformatics Identification of TRIM28 as Potential Prognostic Biomarker for Worse Prognosis in ERα-Positive Breast Cancer

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Introduction:
Background: Tripartite motif-containing 28 (TRIM28) overexpression promotes proliferation and metastasis in several cancers (e.g., lung, prostate, and gastric). Its prognostic role in ERα-positive breast cancer remains unclear.

Methods:
Gene expression and clinical data were retrieved from METABRIC (cBioPortal; study ID: brca_metabric) and TCGA-BRCA (Genomic Data Commons/cBioPortal; study ID: brca_tcga) cohorts. TRIM28 mRNA levels were evaluated in ERα-positive cases. Kaplan–Meier Plotter assessed associations with overall survival (OS) and distant metastasis-free survival (DMFS). Pathway analysis used Gene Set Cancer Analysis (GSCA). Statistical tests (Mann–Whitney U for two groups; Kruskal–Wallis for >2 groups) were performed in GraphPad Prism 9; $P < 0.05$ was significant.

Results:
TRIM28 mRNA was significantly upregulated in breast cancer versus normal tissue (median $\log_2$: 8.159 ± 0.5 vs. 7.7 ± 0.2; $P < 0.0001$). In ERα-positive patients, high TRIM28 expression (>75th percentile) predicted poorer prognosis: median OS 66 vs. 151 months ($P < 0.005$) and DMFS 78 vs. 150 months ($P < 0.01$) compared to low expression (≤75th percentile). TRIM28 positively correlated with tumor size (median 28 vs. 25 mm; $P < 0.001$) and Nottingham Prognostic Index (3.95 vs. 3.75; $P < 0.01$) in high vs. low groups. Pathway analysis revealed that genes significantly correlated with TRIM28 expression in ERα-positive breast cancer patients were primarily involved in the activation of cell cycle progression and DNA damage response pathways, concomitant with suppression of RAS/MAPK and receptor tyrosine kinase (RTK) signaling pathways.

Conclusions:
TRIM28 likely drives proliferation and metastasis in ERα-positive breast cancer, possibly via DNA damage response and cell cycle activation while suppressing RAS/MAPK and RTK pathways. Functional studies are needed to confirm its mechanisms. Overall, TRIM28 emerges as a promising prognostic biomarker for worse outcomes in ERα-positive breast cancer.
Key Words: TRIM28; bioinformatics; breast cancer;

Funding Agency: N/A

Medicine

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Successful Control of Some Challenging Cases in Late Adult and Elderly Onset Atopic Dermatitis

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Introduction:
Atopic dermatitis (AD), historically regarded as a pediatric disease, is increasingly recognized in older adults and the elderly. This subgroup often presents with atypical morphologies, intense pruritus, and frequent comorbidities, complicating both diagnosis and management. Data on biologic therapy in elderly-onset AD remain scarce. We aimed to evaluate the safety and efficacy of dupilumab in Kuwaiti patients with late-adult and elderly-onset AD.

Methods:
This single-center prospective pilot study enrolled 10 patients (≥50 years) with clinically confirmed AD of late-adult or elderly onset. Diagnosis was based on chronic eczematous morphology, persistent pruritus for ≥6 months, and exclusion of mimickers (e.g., cutaneous T-cell lymphoma, bullous pemphigoid, contact dermatitis). Patients received dupilumab (600 mg loading dose, then 300 mg every 2 weeks) for 24 weeks, with continued follow-up for up to 3 years. Severity was assessed with SCORAD and quality of life with DLQI at baseline and serial intervals. Ethical approval was obtained from the Kuwait Ministry of Health, and written informed consent was secured from all participants.

Results:
Participants (5 females, 5 males; mean age 71 ± 8 years) had a mean disease duration of 4.6 years. Nine patients had de novo senile-onset AD, and one had childhood-onset disease with late relapse. All patients demonstrated rapid and sustained improvement: SCORAD and DLQI scores decreased markedly by week 2, with continued decline through week 16 and durable control maintained during long-term follow-up. Pruritus improved dramatically, with parallel gains in quality of life. No patient experienced relapse during treatment continuation. Dupilumab was well tolerated; no serious adverse events occurred. One additional patient, excluded after enrollment, developed acute hypersensitivity following the first loading dose and recovered with supportive care.

Conclusions:
Dupilumab demonstrated rapid, sustained, and safe disease control in elderly AD patients, addressing a major therapeutic gap in this population. This case series highlights the importance of recognizing senile-onset AD, distinguishing it from clinical mimics, and considering targeted biologic therapy even in patients with comorbidities. Larger controlled studies are warranted to establish treatment guidelines for this under-represented population group.

Acknowledgments: We thank the patients and staff of As'ad Al-Hamad Dermatology Center for their collaboration and support.

Key Words: Atopic dermatitis; Biologics; Dupilumab;

Funding Agency: N/A

Medicine (Cardiology)

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An investigation into the accuracy of visual estimation of vessel diameter during coronary angiography using optical coherence tomography.

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Introduction:
Accurate visual assessment of coronary anatomy is essential in percutaneous coronary intervention (PCI) to determine optimal stent or balloon sizing. However, traditional angiographic estimation of diseased vessel diameter and lesion length is inherently subjective and prone to interobserver variability. Optical Coherence Tomography (OCT) is an intravascular imaging modality that provides objective and reproducible measurements. This study aims to evaluate the accuracy of visual estimation during coronary angiography (CAG) using OCT as the reference standard and to assess interobserver variability between operators.

Methods:
This single-center retrospective diagnostic accuracy study included 56 patients who underwent coronary angiography with OCT at a tertiary cardiac center. Two interventional cardiologists independently reviewed the angiograms and recorded subjective estimates of vessel stenosis percentage, stent diameter, and stent length. OCT measurements were used as the reference standard. The Wilcoxon signed-rank test was used to compare visual estimations with OCT measurements. Bland-Altman analysis assessed agreement and systematic bias. Interobserver variability was evaluated using Pearson correlation.

Results:
Visual estimation of stenosis percentage showed no statistically significant difference compared to OCT ($p > 0.2$). In contrast, estimated stent diameter differed significantly from OCT for both observers, C1 and C2 (C1: $p < 1\times10\text{-}7$; C2: $p = 0.0034$). C1 also significantly underestimated stent length ($p = 0.0043$), whereas C2's length estimates did not differ significantly from OCT. Bland-Altman analysis revealed systematic underestimation of diameter and length, more pronounced in C1. Interobserver agreement was moderate across all parameters (diameter $r = 0.69$; stenosis $r = 0.64$; length $r = 0.64$; all $p < 1\times10\text{-}5$). Chi-square testing demonstrated a significant association between C1 and C2 accuracy ($p = 0.005$).

Conclusions:
Visual estimation during CAG showed significant differences from OCT, particularly in stent diameter and length. Traditional CAG was associated with underestimation of vessel diameter however visual stenosis percentage estimates were more accurate. Moderate interobserver agreement was observed across all parameters, indicating consistency in visual assessment. These findings support the use of OCT to improve precision and reduce subjectivity in stent sizing and PCI planning.

Key Words: Coronary angiography; OCT, Optical Coherence Tomography ; Interventional

Funding Agency: None

Microbiology and Immunology

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Discovering Native Plants Microbiome for Medical Applications

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Introduction:
Kuwait is considered a harsh environment where native plants can survive. These plants contain endophytic bacteria, which are increasingly recognised as promising sources of novel therapeutic natural compounds. These endophytes can produce bioactive metabolites with inflammatory and antimicrobial activities, which need to be studied in the medical field due to increasing antimicrobial resistance and the global demand for new natural drugs. This study investigates the endophytic microbiomes of Limonium Lobatum (LL) and Cyprus Conglomeratus (CC), focusing on their identification, characterisation and evaluation of their potential to produce natural products with medical relevance.

Methods:
both rhizosphere and bulk soil samples were collected and analysed using USDA-NRCS procedures. Fatty acid methyl esters were examined by using gas chromatography with a flame ionisation detector. The endophytic bacteria from plant tissues were sterilised through washing steps and plated on different media followed by incubation. The DNA for isolated bacteria extracted, amplified, sequenced and subjected to phylogenetic analysis to determine the bacterial diversity associated with the native plants.

Results:
Rhizosphere soils associated with LL and CC differed significantly in several physiochemical properties, including pH, field moisture, Olsen P, SAR, $SO4_2$-, and $CaCO^3$ equivalents as determined by one-way ANOVA using SigmaPlot v16 (P-value < 0.05;). Fatty acid profiling showed clear species separation with LL and CC forming distinct clusters. Sequencing revealed the highest microbial diversity in bulk soil. LL showed firm compartment-specific microbial shifts, while CC showed more broadly distributed microbial patterns across tissues.

Conclusions:
In conclusion, the combination of soil physicochemical analyses, fatty acid profiling and microbiome analyses for both LL and CC demonstrates species-specific strategies for these plants to adapt to harsh environments including high salinity and temperature. The observed ecological and metabolic differences along with compartment-specific microbial shifts suggest that these plants may host unique microbial consortia capable of influencing the production of bioactive metabolites. Therefore, these metabolites could include antimicrobial, anti-inflammatory or any other therapeutically relevant compounds. These findings provide a foundation for future studies aimed at identifying novel natural molecules with potential medical applications.

Acknowledgement: This work was funded by the Kuwait Institute for Scientific Research (KISR).

Key Words: Microbiome, bioactive molecules, natural compounds, antimicrobial

Funding Agency: KISR

Microbiology and Immunology

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High Sucrose Limits TLR4 Targeted Protection Against High Fat Diet Induced Metabolic Dysfunction

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Introduction:
Toll-like receptor 4 (TLR4) is a key component of the innate immune system, activated by bacterial lipopolysaccharides (LPS) and free fatty acids (FFAs). Chronic stimulation of TLR4 promotes sustained inflammation and oxidative stress, both hallmarks of insulin resistance and obesity. TLR4 knockout (KO) mice are largely protected from metabolic disorders, including hyperglycemia, hyperlipidemia, obesity and insulin resistance when exposed to a high fat diet (HFD). Although TLR4 KO mice remain protected on a HFD with normal sucrose (HFD+NS), it is unknown whether this protection endures on a HFD with high sucrose (HFD+HS). This study examines whether excess sucrose can negate this TLR4 linked protection.

Methods:
3T3-L1 adipocytes were differentiated under control or metabolic-stress conditions (palmitate 100 µM; ± glucose: 50 mM high or 5.55 mM low), then stained (Nile Red O/BODIPY) for imaging and processed for RT-PCR. Preadipocytes were isolated from subcutaneous adipose tissue of C57BL/6 WT and TLR4-KO mice (N=3), expanded, and differentiated under the same treatments. Further, WT and TLR4-KO mice (N=5) were maintained on chow, HFD+NS, or HFD+HS diets for 14 weeks, ITT/OGTT were performed before sacrifice. Adipose tissue was collected for H&E histology and RT-PCR.

Results:
Ex vivo, differentiated preadipocytes from WT and TLR4-KO mice (n=3) exhibited greater lipid accumulation with high palmitate (100 µM) plus high glucose (50 mM) than with palmitate alone, reflected by increased BODIPY fluorescence ($p<0.001$). In vivo, TLR4 KO mice lose metabolic protection when they are exposed to a HFD with high-sucrose (HS, 16.84%). H&E-stained visceral adipose tissue (VAT) sections revealed diet-dependent adipocyte hypertrophy and crown-like structures, with inflammation increasing from chow to HFD+NS and HFD+HS. Importantly, TLR4 KO mice showed significantly smaller inflammatory areas than WT on both HFD+NS and HFD+HS ($p<0.001$, $p<0.01$). Consistently, macrophage/chemokine and pro-inflammatory genes (Mgl2, Ccl2, Adgre1/F4/80, TNF-α) were upregulated in WT with both HFDs but were blunted in TLR4 KO mice.

Conclusions:
Excess sucrose in a high-fat diet weakens the metabolic protection typically associated with TLR4 deficiency. These results underscore the critical role of diet composition and indicate that TLR4 inhibition alone may not be sufficient to prevent metabolic dysfunction induced by high-fat, high-sugar diets common in humans.

Key Words: Obesity; TLR4; Inflammation;

Funding Agency: RA AM 2020-007, KFAS

Microbiology and Immunology

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Emergence of Candida auris as a major bloodstream yeast pathogen in Kuwait, 2020-2023

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Introduction:
Background and Objectives: Invasive fungal infections (IFIs) are associated with high morbidity and mortality rates and mostly affect patients with compromised/suppressed immunity. Candida and other yeast infections represent a major component of IFIs and candidemia represents nearly 75% of all invasive Candida infections. The spectrum of Candida/yeast causing IFIs is changing due to changes in clinical practice. This study, approved by the HSC Ethical Committee, determined the epidemiological characteristics of candidemia/fungemia during a 10-year period (2014-2023) in Kuwait.

Methods:
Bloodstream yeast isolates submitted from all major hospitals to the Mycology Reference Laboratory during 2014-2023 were included. The isolates were identified by phenotypic characteristics, MALDI-TOF MS and/or by PCR/PCR-sequencing of rDNA. Susceptibility testing was performed by Etest and resistance of Candida auris to echinocandins was confirmed by PCR-sequencing of FKS1.

Results:
Of 2107 bloodstream yeast isolates analyzed, 490 C. albicans, 485 C. parapsilosis, 267 C. tropicalis, 208 C. glabrata, 530 C. auris and 127 other yeast spp. isolates were obtained. Although C. parapsilosis (2014-2016) or C. albicans (2017-2019) were the dominant yeast species during the first six years, C. auris became the most common bloodstream yeast pathogen during 2020-2023 with outbreaks reported from several major (Al-Sabah, Mubarak, Farwaniya and Adan) hospitals. Individual hospital-derived data from 3 hospitals also showed that C. auris has become the most common bloodstream yeast pathogen during 2020-2023. Persistent fungemia was noted in 46 patients with its duration varying from 2 weeks to more than 3 months. Although C. auris isolates were generally susceptible to caspofungin, 3 of 358 isolates were resistant (MIC of 32 mg/L) and contained a resistance-conferring mutation in FKS1 gene while the initial isolate from the same patient was echinocandin-susceptible with wild-type FKS1.

Conclusions:
Nationwide candidemia/fungemia data showed that C. auris has emerged as a major bloodstream fungal pathogen in Kuwait since 2020 causing outbreaks in several major hospitals. The data also highlight the limitations of currently available infection control measures to contain the spread of C. auris in healthcare facilities in Kuwait.

Key Words: Epidemiology of candidemia; Emergence of C. auris; Major pathogen in Kuwait;

Funding Agency: None

Microbiology and Immunology

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Global warming and the emergence of novel fungal pathogens: Molecular identification of rare filamentous fungi isolated from clinical specimens in Kuwait during 2020-2024

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Introduction:
The hypothesis that global warming may lead to the emergence of novel fungal pathogens as they adapt to withstand higher temperatures, a key human defense mechanism against fungi, has gained momentum with the emergence and global spreading of multidrug-resistant Candida auris in healthcare facilities. It is expected that plant pathogenic fungi may emerge as novel human pathogens if they develop thermotolerance and undergo other genetic changes triggered by hotter climate to become more virulent. Rapid and accurate identification of pathogenic fungi is critical for proper patient management. This study, approved by HSC Ethical Committee (VDR/EC/386 dated May 31, 2023), applied PCR-sequencing of ribosomal DNA (rDNA) as the universal barcode for rapid and accurate identification of rare filamentous fungi isolated in Kuwait during 2020-2024 which could not be identified by routine mycological techniques.

Methods:
Filamentous fungi (n=36) cultured from human clinical specimens as part of routine patient care were tested. rDNA was amplified with panfungal (ITS1 and CTS1R or NL1 and NL4) primers. Both strands of purified amplicons were sequenced and sequence data were used for homology searches with available archived data from GenBank by using BLAST. Sequence identity of more than 99% was used for species-specific identification.

Results:
rDNA was successfully amplified and sequenced from all 36 samples. BLAST searches identified one or more species of filamentous fungi belonging to 20 different genera including Acrophialophora, Albifimbria, Aspergillus, Cephalotricum, Chaetomium, Cladosporium, Diaporthe, Medicopsis, Microascus, Microsporum, Myrmecridium, Nectria, Neocucurbitaria, Ochroconis, Penicillium, Phaeosphaeria, Phecoacrimonium, Thermoascus, Trechispora and Trichophyton. Some of these organisms are known agents of onychomycosis or skin infections while others are emerging fungal pathogens capable of causing respiratory or other invasive infections, particularly in immunocompromised patients.

Conclusions:
Molecular detection of several genera of rare filamentous fungi in clinical specimens of patients with skin, respiratory or other infections in Kuwait supports the global warming hypothesis and the emergence of novel fungal pathogens. Rapid species-specific identification will greatly help in proper management of infections by rare filamentous fungi in Kuwait and will also increase awareness of their presence in the region.

Key Words: Rare filamentous fungi; Emerging pathogens ; Kuwait 2020-2024;

Funding Agency: None

Microbiology and Immunology

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Airborne Bacillus isolated from Kuwaiti Sandstorm as a New Source of Antimicrobials

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Introduction:
Sandstorms in Kuwait transport diverse airborne bacteria, yet their biosynthetic potential remains largely unknown. This study investigated five Bacillus strains—AD12 (B. stratosphericus), AD13 (B. safensis), and AD14–AD16 (B. subtilis)—isolated from outdoor air during a major sandstorm. This research represents the first integrated genomic–functional screening of sandstorm-derived Bacillus in Kuwait for antimicrobial and surfactant biosynthesis.

Methods:
Whole-genome sequences were analyzed using antiSMASH 7.0 to identify biosynthetic gene clusters (BGCs). Cluster diversity and predicted products were compared across strains. Antimicrobial activity was assessed using colony-on-lawn assays against MDR pathogens, while biosurfactant production was evaluated using the drop-collapse assay.

Results:
All strains contained multiple BGCs, including high-confidence clusters for bacilysin, bacillibactin, surfactin, fengycin, lichenysin, pulcherriminic acid, subtilosin A, and bacillaene. AD14–AD16 (B. subtilis) showed extensive BGC diversity, including uncommon carbapenem-like T3PKS clusters and hybrid PKS–NRPS signatures. AD13 (B. safensis) uniquely harbored a zwittermicin-like hybrid cluster, rarely reported in this species. Phenotypically, several strains demonstrated inhibition of MDR bacteria, including colistin-resistant Klebsiella pneumoniae, and strong surfactant activity, indicating previously unreported functional expression of these pathways in airborne isolates of these species.

Conclusions:

Sandstorm-derived Bacillus species possess novel and underexplored biosynthetic capabilities, highlighting aerosolized microbes as a promising reservoir for antibiotic and biosurfactant discovery.

Key Words: MDR; surfactants; antimicrobials;

Funding Agency: None

Microbiology and Immunology

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Bacteriological Profile and Antimicrobial Susceptibility Pattern of Isolates from Ocular Infections at a tertiary care hospital in Kuwait. A Four Year Study

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Introduction:
Ocular infections are one of the major causes of visual impairment around the world. Infections manifest commonly in the form of blepharitis, conjunctivitis, keratitis, endophthalmitis, orbital cellulitis and dacryocystitis. The purpose of this study is to identify bacterial pathogens causing ocular infection and to determine their in-vitro susceptibility to commonly used antibacterial agents in clinical practice.

Methods:
This four year retrospective study was done at Ibn-Sina Microbiology laboratory from the year 2021 to 2024. All the patients attending the Al Bahar ophthalmology department with ocular infections were included in the study. Specimens included conjunctival swabs, corneal scrapings, lens solutions, aqueous and vitreous tap. All positive cultures were processed by Vitek 2 (Biomerieux, France) for identification and antimicrobial susceptibility. E-test was done when required.

Results:
Out of a total of 557 isolates evaluated over the study period, 417 (75%) and 140 (25%) were Gram-positive and Gram-negative bacteria, respectively. Staphylococcus aureus accounted for most of the Gram-positive infections (37%) of which 50% were methicillin resistant Staphylococcus aureus (MRSA) followed by coagulase negative Staphylococcus (33%). Of the Gram-negative isolates, 55% belonged to Enterobacterales and 19% of those were Extended spectrum Beta- lactamase (ESBL) producers. Pseudomonas aeruginosa was the next common Gram-negative isolate accounting for 26% of the isolates. Flouroquinolones showed a decline in susceptibilty from 61% in 2021 to 53% in 2024 among MRSA isolates and from 57% to 51% among the coagulase negative Staphylococci. Aminoglycosides and vancomycin retained good efficiency. All the Gram- negative isolates displayed good and sustained susceptibility to quinolones, aminoglycosides, chloramphenicol and carbapenems over the four years.

Conclusions:
Understanding the bacteriological profile and antibiotic susceptibility trends helps guide effective therapy and reduce antimicrobial resistance. Continuous surveillance of ocular bacterial isolates and their antimicrobial profiles is crucial.

Key Words: Ocular; Gram Positive; Gram Negative;

Funding Agency: None

Microbiology and Immunology

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Prevalence of Multidrug-Resistant bacteria in hospital and outdoor environment during sandstorms in Kuwait

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Introduction:
Antibiotic resistance poses a growing global threat, with environmental reservoirs playing an increasingly recognized role in the emergence and dissemination of resistant bacteria. Kuwait's frequent sandstorms and shifting desert climate provide unique conditions that may facilitate airborne transmission of antimicrobial-resistant organisms.

Methods:
This study investigated the presence and resistance profiles of clinically relevant bacteria isolated from ambient air during sandstorms, alongside indoor hospital air in two major Kuwaiti healthcare facilities. Air sampling was conducted using SKC BioStage™ impactors across intensive care units, operating theatres, and corresponding outdoor dust-storm environments. A total of 84 isolates were recovered and identified by 16S rRNA sequencing.

Results:
Hospital air commonly yielded Staphylococcus aureus, coagulase-negative staphylococci, Bacillus spp., and Acinetobacter spp., whereas outdoor samples predominantly contained Pseudomonas and Staphylococcus species. Resistance testing revealed high multidrug resistance across isolates. Notably, 6.5% of S. aureus carried the mecA gene. Staphylococci exhibited high resistance to trimethoprim–sulfamethoxazole (73%) and erythromycin (50%), while Bacillus spp. showed substantial oxacillin resistance (63%). Acinetobacter baumannii isolates (80%) displayed extensive carbapenem resistance, and Pseudomonas spp. demonstrated imipenem resistance (70%) and multidrug resistance (55%).

Conclusions:
These findings highlight airborne dust as a potential environmental reservoir contributing to AMR transmission in Kuwait, underscoring the need for expanded environmental surveillance and targeted infection-control strategies.

Key Words: Airborne; Sandstorm microbiology; antimicrobial resistance;

Funding Agency: None

Microbiology and Immunology

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Deadly Convergence: Pan-Drug Resistance and Hypervirulence in Genetically Diverse Klebsiella pneumoniae

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Introduction:
Klebsiella pneumoniae is a leading cause of nosocomial infections, with hypervirulent strains (hvKp) posing heightened clinical concern due to their enhanced pathogenicity and rising multidrug resistance.

Methods:
This study investigated clinical K. pneumoniae isolates recovered from fifteen patients in a surgical ward in Kuwait. Species identification and antimicrobial susceptibility testing were performed using Vitek2, conventional biochemical assays, E-test, and broth microdilution. Three representative isolates (KpC87, KpC90, and KpC92) underwent whole genome sequencing using the Illumina HiSeq platform, and genomes were analyzed for virulence, resistance determinants, and plasmid content.

Results:
All three isolates exhibited a hypervirulent genotype, harboring multiple siderophore, fimbrial, and immune-evasion genes. Sequence typing revealed marked diversity: KpC87 (ST5523, KL28), KpC90 (ST1777, KL111), and KpC92 (ST231, KL51). KpC92 carried a rich plasmid repertoire, including IncFIA, IncFIB, IncFII(K), IncFII (pAMA1167-NDM-5), ColKP3, Col4401, and ColBS512. A broad array of antimicrobial resistance genes was detected, including bla_CTX-M-15, bla_SHV, bla_TEM-1B, bla_OXA-232, qnrS1, mph(A), aac(6')-Ib-cr, and notably a putative novel NDM-like carbapenemase on an IncFII plasmid.

Conclusions:
These findings highlight the emergence of pan-drug-resistant hvKp in Kuwait and emphasize the urgent need for enhanced genomic surveillance and strict infection-control measures to curb further spread in healthcare settings.

Key Words: Hypervirulent Klebsiella pneumoniae; Carbapenem resistance; Whole genome

Funding Agency: None

Microbiology and Immunology

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Evaluation of the genomic diversity of antibiotic resistance status of Klebsiella pneumoniae clinical isolates sourced from Farwaniya Hospital in Kuwait

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Introduction:
Antimicrobial agents are crucial for treating bacterial infections. Despite high efficacies in the 20th century, the emergence of drug-resistant strains has transformed their success into a World Health Organization (WHO) challenge. The aim of this study was to identify the markers of drug resistance in Klebsiella pneumoniae isolates from Farwaniya Hospital, Kuwait, using whole genome sequencing in comparison to the phenotypic susceptibility patterns.

Methods:
Methods and Ethical Approval: The study was approved by the Ministry of Health, Kuwait (Research number 1211/2019). A total of 35 K. pneumoniae isolates were collected from different clinical specimens from patients in Farwaniya hospital in Kuwait. These isolates were phenotypically tested for antimicrobial susceptibility using VITEK 2, Phoenix, and Microscan. The genomic DNA (gDNA) was isolated from the bacterial cultures using the Monarch Kit. The purified gDNA was used for library preparation and sequenced using the MinION Mk1C device (Oxford Nanopore technology). Genomes were assembled de novo using Flye, followed by polishing with Medaka, for genome quality evaluation with QUAST and quality and completeness check using BUSCO. Antimicrobial resistance (AMR) genes were identified using ABRicate. Comparative analysis was performed to investigate the relation between phenotypic and genotypic resistance profiles using AI-tool.

Results:
All K. pneumoniae isolates were multidrug resistant (MDR), with seven of them being extended-spectrum beta-lactamase (ESBL) producers. Phenotypic results showed high resistance rates against beta-lactams, followed by quinolones, aminoglycosides, nitrofurantoin, and trimethoprim-sulfamethoxazole. WGS data showed varied AMR gene profiles, often confirming the phenotypic resistance patterns. About 80-90% overlap was observed between the identified phenotypic resistance and resistance genes, particularly for beta-lactams (e.g., blaKPC-2, blaSHV-11), quinolones (qnrB1 and aac(6')-Ib-cr), aminoglycosides (aac^{3}-IIa), and trimethoprim-sulfamethoxazole (sul1 and dfrA14).

Conclusions:
This study highlights the role of WGS in conducting comprehensive AMR profiling of K. pneumoniae isolates. When WGS is integrated into routine hospital diagnostics, it may provide a thorough understanding of the mechanisms of resistance and improve the surveillance programs in Kuwait leading to effective antimicrobial stewardship.

• Acknowledgement: This work was supported by Kuwait University Research Sector grant no. MI04/22.

Key Words: Whole genome sequencing; Klebsiella pneumoniae; Oxford Nanopore Technologies;

Funding Agency: This work was supported by Kuwait University Research Sectorgrant no. MI04/22.

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Impact of DNA Extraction Methods on Nanopore-Based Whole Genome Sequencing of Staphylococcus aureus

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Introduction:
Whole genome sequencing (WGS) enables comprehensive genomic characterization, including structural variation analysis and antimicrobial resistance profiling, and is increasingly applied in public health surveillance. Interest has emerged in using artificial intelligence (AI)–assisted tools to support downstream genomic data interpretation. Staphylococcus aureus is a multidrug resistance and healthcare-associated infections. This study aimed to compare four genomic DNA (gDNA) extraction methods for S. aureus WGS using Oxford Nanopore Technology in terms of DNA genome completeness. And to explore the feasibility of AI-assisted tertiary data interpretation and workflow support as a complementary analytical aid.

Methods:
gDNA was extracted from S. aureus ATCC 29213 (n = 2 extractions/ method) using four approaches, all incorporating lysostaphin for cell wall lysis: [1] a modified CTAB protocol with extended enzymatic lysis; [2] a modified gel-based method involving agarose plug excision, enzymatic digestion, and DNA recovery using the QIAquick Gel Extraction Kit; [3] an in-house enzymatic protocol using lysostaphin, RNase, and proteinase K and heat inactivation; and [4] a commercial kit (Monarch® Spin gDNA Extraction Kit) selected for compatibility with long-read sequencing. Libraries were prepared using Oxford Nanopore protocols and sequenced on the MinION Mk1C platform. Genome assemblies were assessed using established bioinformatics tools, with ChatGPT-5 assisting in the generation of Python scripts to integrate analytical tools and produce data visualizations. Additionally, ChatGPT-5 applied post-analysis to support interpretation of the outputs; all interpretations were reviewed by the authors.

Results:
CTAB and kit extracted gDNA produced assemblies with higher genome completeness and lower fragmentation compared with gel-based and in-house methods. Detection of antimicrobial resistance genes, virulence factors, and plasmid sequences was comparable across all methods. AI-assisted interpretation supported structured summarization without altering primary analytical results.

Conclusions:
CTAB and commercial kit extraction methods generate higher quality S. aureus genomes suitable for long-read WGS. AI-assisted tools such as ChatGPT-5 can support bioinformatics workflow integration and tertiary data interpretation. However, their output remains dependent and requires expert validation.

Key Words: Whole genome sequencing; Staphylococcus aureus; Oxford Nanopore Technologies;

Funding Agency: None Funding

Microbiology and Immunology

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Distinct Microbiota–Metabolism Associations in Genetic and Diet-Induced Models of Obesity

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Introduction:
Obesity is a major risk factor for type 2 diabetes (T2D), whose global prevalence has risen sharply since 1990 and is expected to keep increasing. Beyond energy imbalance, genetic, metabolic, dietary, and environmental factors contribute to its development. Chronic obesity drives low-grade inflammation and insulin resistance, central mechanisms in T2D pathogenesis. Growing evidence highlights the gut microbiota as a key regulator of nutrient absorption, energy balance, and metabolic homeostasis, with its disruption causally linked to metabolic dysfunction. Here we hypothesize that genetic and dietary contributions to obesity can differently shape gut microbiota signatures and metabolic adaptation.

Methods:
Male C57BL/6J wild-type mice (7–9 weeks) were assigned to a control group fed normal chow for 12 weeks or a diet-induced obesity (DIO) group fed a high-fat diet (60% calories from fat) for 12 weeks. Male leptin deficient (ob/ob) mice were maintained on normal chow until 15-22 weeks of age. Body weight and blood glucose were monitored throughout. Systemic glucose homeostasis was assessed by insulin (ITT) and oral glucose tolerance testing (OGTT). Colon microbiota composition was analyzed by 16S rRNA sequencing to examine microbial composition and their associations with metabolic outcomes.

Results:
Ob/ob mice exhibited the greatest weight gain, followed by DIO mice. Ob/ob mice also maintained consistently elevated blood glucose levels. ITT demonstrated minimal glucose reduction in ob/ob mice compared with both groups, and OGTT revealed delayed glucose clearance. Microbiota analysis showed reduced alpha diversity in DIO mice, highest richness in ob/ob mice, and distinct beta diversity clustering among all groups. At the phylum level, DIO mice displayed the highest Firmicutes and lowest Bacteroidota, whereas ob/ob mice showed the opposite pattern; controls exhibited balanced proportions of both. At the species level, each group showed a unique taxonomic profile, with distinct dominant species and differential representation.

Conclusions:
DIO and ob/ob mice exhibit distinct metabolic and microbial profiles driven by different mechanisms. Integrating metabolic and microbiome data enhances understanding of how genetic and dietary factors jointly shape obesity-related pathophysiology.

Key Words: Obesity; Gut microbiota; metabolism;

Funding Agency: KFAS Funding #PN23-12MI-2021

Microbiology and Immunology

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Demographic Influences on Quality of Life and Patient Satisfaction in Primary Immunodeficiency: Predominant Emotional and Social Associations

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Introduction:
Primary Immunodeficiency (PID) is a chronic condition that can substantially affect patients' health-related quality of life (HRQoL) and their experience with healthcare services. While HRQoL and patient satisfaction have been previously studied in PID, limited data exist on how demographic factors interact with specific HRQoL domains to influence patient satisfaction. This study aimed to evaluate HRQoL and patient satisfaction in adults with PID, focusing on demographic influences and the relationship between HRQoL and satisfaction domains.

Methods:
This cross-sectional study included adult patients diagnosed with PID. HRQoL was assessed using the Medical Outcomes Study 36-Item Short Form Health Survey (RAND-36), and patient satisfaction was evaluated using the Patient Satisfaction Questionnaire Short Form (PSQ-18). Descriptive statistics summarized participant characteristics and outcome measures, while correlation analyses and general linear models examined associations between age, sex, HRQoL domains, and patient satisfaction domains.

Results:
A total of 34 adult patients were included, with a male-to-female ratio of 2.1:1, and a mean age of 34.9 ± 13.6 years. Participants reported moderate to high HRQoL across most domains, with preserved physical and social functioning. Energy/fatigue was the most impaired domain, indicating a persistent disease burden, while emotional well-being and bodily pain showed intermediate scores. Overall patient satisfaction was high across most PSQ-18 domains, with comparatively lower satisfaction related to accessibility and convenience of care. Increasing age was associated with poorer social functioning and general health. Female patients reported a greater emotional burden, higher satisfaction with physicians' interpersonal manner, and lower satisfaction with financial aspects of care. Significant associations between patient satisfaction and HRQoL were primarily observed in emotional well-being and social functioning, whereas physical HRQoL domains showed no significant correlations.

Conclusions:
Adults with PID generally report good physical and social functioning and high satisfaction with healthcare services. However, fatigue, emotional well-being, and social functioning remain key areas of impairment, particularly among female and older patients. The strong association between patient satisfaction and emotional and social HRQoL domains underscores the importance of integrating psychosocial support into routine PID management to enhance patient-centered outcomes.

Key Words:

Funding Agency: Nonen

Microbiology and Immunology

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IL-6 Drives inflammation And Metabolic Dysregulation

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Introduction:
Obesity is characterized by chronic low-grade inflammation that compromises intestinal barrier integrity, alters gut microbiota, and activates innate immune pathways that drive macrophage infiltration into adipose tissue. This inflammatory cascade disrupts insulin signaling, elevates circulating cytokines such as IL-6 and TNF-alpha, and promotes hepatic lipid accumulation and steatosis. Interleukin-6 (IL-6) is a major cytokine linking gut inflammation to systemic metabolic dysfunction, yet its direct role in coordinating gut–liver inflammatory interactions during obesity remains incompletely defined. This study aimed to determine whether IL-6 deficiency protects high-fat-diet (HFD)–fed mice from gut inflammation, hepatic steatosis, and insulin resistance.

Methods:
IL-6 knockout (IL-6$^{-/-}$) and wild-type (WT) C57BL/6 male mice (6–7/group), aged 8–10 weeks, were fed an HFD for 22 weeks with weekly monitoring of body weight and food intake. Colon RNA was analyzed by qRT-PCR for inflammatory gene expression. On week 21, an intraperitoneal glucose tolerance test (IPGTT) was conducted following a 12-hour fast, and an insulin tolerance test (ITT) was performed at week 22 after a 4-hour fast. Liver lipid accumulation was assessed using H&E and Oil Red O staining. All animal procedures were conducted in accordance with National Institutes of Health guidelines and were reviewed and approved by the Institutional Animal Care and Ethics Committee.

Results:
IL-6$^{-/-}$ mice demonstrated markedly reduced gut inflammation, showing substantially lower expression of key inflammatory genes compared with WT mice on the same HFD. These mice exhibited significantly improved glucose handling during IPGTT, greater insulin responsiveness during ITT, and lower fasting glucose levels. Histological analyses revealed striking attenuation of hepatic steatosis in IL-6$^{-/-}$ mice, with visibly fewer lipid droplets and reduced Oil Red O staining intensity compared with WT controls.

Conclusions:
Collectively, these findings indicate that IL-6 is a critical driver of HFD-induced gut inflammation, liver fat accumulation, and metabolic dysfunction, and that IL-6 deficiency confers strong protection across multiple metabolic tissues. Targeting IL-6–mediated inflammatory pathways may offer a promising therapeutic strategy for obesity-related metabolic disease.

Funding
This study was supported by the Kuwait Foundation for the Advancement of Sciences (KFAS) and the Dasman Diabetes Institute (DDI) under project number RA-AM-2020-007.

Acknowledgement
The authors gratefully acknowledge the Kuwait Foundation for the Advancement of Sciences (KFAS) for funding the project, and the Dasman Diabetes Institute (DDI) for the technical assistance and ani mal facility and laboratory facility and supporting provided by the staff.

Key Words: Interleukin-6 (IL-6); Metabolic Inflammation; High-Fat Diet (HFD);

Funding Agency: This study was supported by the Kuwait Foundation for the Advancement of Sciences (KFAS) and the Dasman Diabetes Institute (DDI) under project number RA-AM-2020-007.

Microbiology and Immunology

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Omega-3–Rich Fish Diet Improve Steatosis but Fails to Reverse Established Metabolic Inflammation

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Introduction:
High-fat diet (HFD) induces chronic inflammation in visceral adipose tissue (VAT) and liver, promoting steatosis, insulin resistance, and metabolic dysfunction. Although omega-3–rich anti-inflammatory diets are widely recommended, it remains unclear whether they can reverse established obesity-associated inflammation. This study aimed to determine whether switching from long-term HFD to either an omega-3–rich fish diet or back to standard CHOW can resolve liver/VAT inflammation and improve glucose regulation.

Methods:
Male C57BL/6J mice were divided into four experimental groups: CHOW, HFD, HFD followed by fish diet (IFD), and HFD followed by CHOW (ICD) (n = 6–7/group). Mice were maintained on CHOW or HFD for 18 weeks, or on HFD for 12 weeks followed by a 6-week dietary intervention. Liver and VAT inflammation were assessed by qRT-PCR for TNF-alpha and CCL2; metabolic function by IPGTT and ITT; and liver pathology by H&E, Oil Red O, and F4/80 staining. Quantitative data are presented as mean ± SEM, and statistical significance was determined using one-way ANOVA with appropriate post hoc testing ($p < 0.05$).

Results:
Long-term HFD induced strong hepatic and VAT inflammation, marked steatosis, elevated lipid droplets, and high macrophage infiltration. The interventions produced distinct outcomes. In the liver, IFD reduced steatosis and macrophage accumulation but elevated TNF-alpha and CCL2 compared to HFD, indicating persistent inflammation. Conversely, ICD nearly normalized TNF-alpha and markedly reduced CCL2, despite showing less improvement in steatosis. In VAT, IFD did not reduce TNF-alpha and only partially lowered CCL2, whereas ICD fully normalized both markers. Metabolic testing reflected similar differences, IFD worsened glucose excursions during IPGTT and did not improve ITT responses, while ICD consistently enhanced insulin sensitivity and lowered glucose levels compared to HFD.

Conclusions:
Changing from HFD to fish or CHOW diets yields divergent effects. The fish diet improves liver morphology but fails to resolve inflammation or restore glucose control. Whereas CHOW intervention effectively reverses inflammation in both liver and VAT and improves metabolic function. These findings indicate that omega-3–rich diets may not reverse established metabolic inflammation and highlight the tissue-specific nature of dietary intervention outcomes.

Acknowledgement
The authors gratefully acknowledge the Kuwait Foundation for the Advancement of Sciences (KFAS) for funding the project, and the Dasman Diabetes Institute (DDI) for the technical assistance and animal facility and laboratory facility and supporting provided by the staff.

Key Words: Metabolic Inflammation; Omega-3–Rich Fish Diet; High-Fat Diet (HFD);

Funding Agency: This study was supported by the Kuwait Foundation for the Advancement of Sciences (KFAS) and the Dasman Diabetes Institute (DDI) under project number RA-AM-2023-021.

Microbiology and Immunology

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Lymphadenitis as a complication of BCG vaccination in Kuwait: A case series

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Introduction:
Tuberculosis is a major infectious disease caused primarily by Mycobacterium tuberculosis (Mtb). Mycobacterium bovis bacillus Calmette-Guérin (BCG) is used as a vaccine against tuberculosis. Since BCG is a live attenuated vaccine with a potential pathogenic action, vaccination can cause several complications, both locally near the inoculation site and remotely through blood dissemination. This study, approved by HSC Ethical Committee (Approval no. VDR/EC/3762 dated June 30, 2021), reports four separate cases of BCG-related disease (lymphadenitis) which occurred during 2016 to 2024 in Kuwait.

Methods:
Clinical (swab) samples obtained from vaccine site wound of four patients (age 9-24 months) were tested for Mtb complex DNA by GeneXpert MTB/RIF qPCR assay and were cultured by using BACTEC MGIT 960 System. For specific BCG identification and its differentiation from Mtb and M. bovis, DNA was extracted from MGIT cultures and 4 separate uniplex PCR assays were performed by using four Mtb complex-specific primer pairs targeting esxA, mce3A, mce1A and rrs genes with appropriate positive and negative controls.

Results:
All four infants had wound with pus at the site of inoculation. Only 1 patient was immunocompromised (with severe combined immunodeficiency disease) while the other 3 were immunocompetent including 1 patient for whom extensive immunological screening was performed. GeneXpert MTB/RIF qPCR assay identified Mtb complex DNA in all 4 clinical samples. DNA from all 4 MGIT cultures was positive for BCG as PCR amplicons were obtained for mce1A and rrs genes but not for esxA and mce3A, as expected. All 4 patients responded to appropriate anti-TB therapy.

Conclusions:
Although BCG vaccine has a good safety record for most newborns, adverse reactions can still occur in some infants and should be promptly investigated. Our data also reinforce previous observations that BCG vaccination should be delayed in suspected immunocompromised infants.

Key Words: Mycobacterium bovis BCG; Vaccination; Lymphadenitis;

Funding Agency: None

Microbiology and Immunology

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Insights into the Prophage Islands of the Indigenous Gram-negative Bacterium Vibrio alginolyticus

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Introduction:
Prophages are integrated bacteriophage genomes within bacterial chromosomes that contribute to host evolution, pathogenicity, and environmental adaptation. Vibrio alginolyticus L1 is recognized as an opportunistic human pathogen, particularly in marine-associated infections, a clinical relevance underscored by its reservoir of genes associated with antibiotic resistance and virulence. These adaptive traits are often encoded within mobile genetic elements, such as prophages, which can introduce additional functions into strain L1. This study aimed to identify and characterize prophage regions within the indigenous Gram-negative Vibrio alginolyticus L1 genome using a multi-method scoring system.

Methods:
The whole genome of Vibrio alginolyticus L1, isolated from sea sediment, was sequenced. Subsequently, prophage regions within the genome were identified and characterized using an integrative approach combining bioinformatics tools and comparative genomics.

Results:
Three prophage regions were detected: Region 1 (45.3 Kb) and Region 3 (34.6 Kb) were classified as intact, while Region 2 (22.0 Kb) was incomplete. Intact regions exhibited high phage-hit protein content (80.5% in Region 1), elevated GC content compared to the host genome, and contained essential phage genes such as integrase, terminase, capsid, and tail proteins. Region 2 lacked structural genes and showed lower phage protein representation. A scoring methodology combining protein homology, GC deviation, and structural gene presence effectively categorized prophage integrity.

Conclusions:
These findings emphasize the role of intact prophages in genomic plasticity and suggest their potential influence on Vibrio physiology and ecology.

Key Words: Prophage; Bacteriophage; Gram-negative bacteria;

Funding Agency: None

Molecular Biology

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Box Behnken Design for Optimizing Ultra performance Liquid Chromatography in purification of chemically synthesized primers.

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Introduction:
Ultra-Performance Liquid Chromatography (UPLC) is widely used for the purification of synthetic primers. However, achieving optimal separation, resolution, and run efficiency requires careful tuning of multiple chromatographic parameters.
Objective:
In this pilot study, the Box–Behnken Design (BBD), a response surface methodology, was applied to systematically evaluate and optimize three critical UPLC factors

Methods:
Response Surface Methodology (RSM) was employed to optimize and evaluate chromatographic conditions and evaluate the effects of mobile phase composition (TEAA solvent concentration), flow rate, and column temperature on chromatographic performance. A 15-run Box–Behnken design (BBD) matrix was generated to assess both individual and interactive effects of the selected factors on key chromatographic responses, including peak resolution and retention behavior. A second-order polynomial model was fitted to the experimental data to investigate curvature and interaction among variables. The statistical significance of linear, quadratic, and interaction terms was evaluated using analysis of variance (ANOVA) and F-tests ($p < 0.05$). The results demonstrated significant curvature and interaction effects, with a TEAA concentration of 0.1 M, column temperature of 60 °C, and flow rate of 1.0 mL min^{-1} showing the strongest influence on chromatographic resolution.

Results:
Response surface plots and desirability functions were used to identify optimal conditions that balance sharp peak shape (at 260nm wavelength absorbance and 4.8nm resolution), improved separation, and reduced analysis time. Validation at the predicted operating point confirmed good agreement between experimental and model-predicted responses.

Conclusions:
This work demonstrates that Box–Behnken Design is an efficient and robust approach for optimizing UPLC primer purification, reducing trial-and-error experimentation, and enhancing method performance for nucleic acid purification protocols.

Key Words: UPLC; Purification; Box Behnken Design;

Funding Agency: SRUL02/13

Mycology

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Modulation of Vaginal Epithelial Cytotoxicity by Estrogen, Morphogenesis, and Lactobacilli in an in vitro VVC Model

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Introduction:
Up to 75% of females experience vulvovaginal candidiasis (VVC). Candida albicans and Lactobacillus species are components of the normal vaginal microbiota. Lactobacilli are the predominant vaginal flora of females at reproductive age and are responsible for the acidic vaginal environment, whereas C. albicans is sparsely present in the healthy vagina. Microbial, hormonal, and host response variables affect microbial balance and VVC pathogenesis. However, the key drivers of mucosal homeostasis and disease are still unknown. This study examined strain-level interactions between C. albicans and Lactobacillus spp. isolated from VVC patients, revealing novel contrasting behaviors of L. gasseri and L. jensenii. The objective was to establish an in vitro VVC model that closely mimics the vaginal milieu using clinical isolate pairs and to evaluate how estrogen and Lactobacillus species collectively influence epithelial cytotoxicity and pathology.

Methods:
The vaginal epithelial cell (VEC) monolayers were infected with standardised inocula of C. albicans, and the impact of Lactobacilli and estrogen (17β-estradiol (1 nM)) was assessed at 24 h post-incubation. Comparative analysis of host cytotoxicity was the main approach employed, using the lactate dehydrogenase (LDH) assay. Extracellular pH was measured using an InLab Nano pH microelectrode in both mono- and mixed-colonised VEC culture models. C. albicans morphology and hyphae formation were characterised by bright-field microscopy. Experiments were done in triplicate for three biological replicates. One-way ANOVA was used to analyse data for multiple comparisons.

Results:
C. albicans morphogenesis and hyphal formation, descriptively assessed, were found to be associated with VEC damage expressed by LDH release. Physiological concentrations of estrogen significantly increased VEC cytotoxicity in response to C. albicans, without affecting extracellular pH. L. gasseri suppressed LDH and acidified the extracellular environment (pH ≤ 4.3), while L. jensenii enhanced VEC monolayer toxicity, expressed by LDH fold changes relative to control.

Conclusions:
VVC is an estrogen-driven disease. L. gasseri but not L. jensenii significantly reduced cytotoxicity and the extracellular pH in the C. albicans-infected VECs model. Underscoring opportunities for precision microbiome-based diagnostics and therapies. This work has potential implications for vaginal health and for treating VVC.

Key Words: vulvovaginal candidiasis; Candida albicans; Lactobacillus, 17β-oestradiol,;

Funding Agency: PAAET, Kuwait

Nuclear Medicine and Radiology

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Evaluating of Normative Ranges and Predictors of Left Ventricular Function Using Rubidium-82 PET Myocardial Perfusion Imaging

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Introduction:
Quantitative Rubidium-82 (82Rb PET/CT) myocardial perfusion imaging (MPI) provides a powerful means of assessing coronary microvascular function and left ventricular performance. In fact, population-specific reference ranges remain limited, particularly across age groups, which can challenge interpretation in daily practice. Although this cohort does not represent a strictly normal population, most participants were confirmed to have normal perfusion scans with no prior cardiac history and were referred primarily for suspected cardiac disease.

Methods:
We retrospectively reviewed 330 82Rb PET/CT MPI studies (mean age = 63.5 ± 12.0 years; BMI = 31.5 ± 5.6 kg/m²). Each scan was analyzed for stress volume parameters (e.g., LVEF, EDV, ESV, SV) and perfusion parameters (e.g. myocardial blood flow for all arteries (MBF), flow reserve (MFR), and phase dyssynchrony indices (e.g., phase standard deviation (SD°)) using 4DM® (INVIA Medical Imaging Solutions, USA) . Participants were grouped by age: young (18–38 years), middle-aged (39–59 years), and senior (≥ 60 years) and corresponding reference ranges were established. Logistic regression and receiver operator characteristics (ROC) analysis were applied to identify predictors of abnormal perfusion and evaluate model performance.

Results:
Across the cohort, mean stress LVEF was 56.5 ± 14.7%, EDV 85.6 ± 38.5 mL, ESV 40.9 ± 32.4 mL, MBF 2.03 ± 1.01 mL/min/g, and MFR 2.07 ± 0.90. Stress MBF and MFR both declined steadily with age (young ≈ 3.1 and 3.7; middle-aged ≈ 2.2 and 2.5; senior ≈ 1.9 and 2.1). Although dyssynchrony parameters remained relatively stable overall, greater variability was seen in older adults. ESV and phase SD° emerged as significant positive predictors of abnormal perfusion, while higher resting LCX MBF and preserved phase synchrony were protective. The predictive model demonstrated strong discrimination (AUC = 0.86, $p < 0.001$) and good calibration.

Conclusions:
This study defines age-specific reference ranges for quantitative 82Rb PET/CT parameters within a Kuwaiti population. The results suggest that variations in left ventricular volume and phase synchrony can reliably distinguish normal from abnormal perfusion. Establishing such normative values supports more accurate clinical interpretation and provides a foundation for future multicenter and radiomics-based research. Ethics approval: This study was approved by MOH Research Ethics Committee (Approval No. 2465/2023).

Key Words: Rubidium-82 PET/CT; Myocardial Perfusion Imaging; Age-Specific Reference

Funding Agency: None

Nuclear Medicine and Radiology

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Correlation of Cytokine Production and MRI of femoral head in Avascular necrosis in Patients with Sickle Cell Diseas

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Introduction:
An imbalance between pro- and anti-inflammatory cytokines has been implicated in tissue damage in sickle cell disease (SCD), particularly following recurrent ischemia, which predisposes patients to complications such as avascular necrosis (AVN) of the femoral head. This study aimed to investigate cytokine profiles produced by mitogen-stimulated peripheral blood mononuclear cells (PBMCs) in SCD patients with or without AVN, as assessed by magnetic resonance imaging (MRI).

Methods:
SCD patients were recruited from outpatient hematology clinics at Mubarak Al-Kabeer Hospital, Kuwait. AVN was screened using MRI of both femoral heads. Cytokine levels secreted by mitogen-stimulated PBMCs were measured in 31 AVN-negative and 16 AVN-positive patients. Four pro-inflammatory cytokines (IL-1β, IL-6, IL-17A, TNF-α) and three anti-inflammatory cytokines (IL-4, IL-10, TGF-β) were quantified using multiplex ELISA.
Ethical Approval:
The study was approved by the Human Research Ethics Committees at the Faculty of Medicine, Kuwait University, and the Ministry of Health, Kuwait. Written informed consent was obtained from all participants prior to enrollment.

Results:
AVN-positive patients exhibited significantly higher levels of certain cytokines, including TGF-β and IL-4, compared to AVN-negative patients. Ratios of IL-17A/IL-4, TNF-α/IL-4, and IL-17A/TGF-β were significantly higher in AVN-negative patients, indicating a pro-inflammatory bias in this group. Multivariate pattern analysis revealed distinct clustering of AVN-positive patients, separating them from AVN-negative individuals.

Conclusions:
Cytokine profiling of mitogen-stimulated PBMCs, combined with multivariate analysis, can distinguish SCD patients with AVN from those without. This approach may serve as a predictive tool for identifying individuals at risk of AVN, enabling earlier intervention and improved clinical outcomes.

Key Words: Sickle cell disease; Avascular necrosis; Cytokine;

Funding Agency: KFAS Grant No, CR1713MM01

Nuclear Medicine and Radiology

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Glycyrrhizic Acid Suppresses Breast Cancer Metastasis: Insights from In Vitro and In Vivo Studies

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Introduction:
Breast cancer remains a leading cause of cancer mortality worldwide, highlighting the need for safer and more effective therapeutic agents. This study aimed to investigate the chemopreventive and therapeutic effects of glycyrrhizic acid (GA), a natural compound with known anti-inflammatory and anticancer properties, against breast cancer tumour cells in vitro and 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary cancer in vivo using female Sprague–Dawley (SD) rats.

Methods:
Both in vitro and in vivo experimental approaches were employed. In vitro analyses included cell viability assessment using the MTT assay, cell migration using a scratch (wound-healing) assay, and apoptosis evaluation by flow cytometry.For the in vivo study, a total of ten female Sprague–Dawley rats were used and randomly assigned into two groups: a control group (n = 5) receiving DMBA only and a GA post-treatment group (n = 5) receiving GA following DMBA-induced mammary tumour induction. Mammary tumours were induced using DMBA according to established protocols. Tumour response and progression were monitored longitudinally using radionuclide-based SPECT/CT imaging to assess tumour development and radiotracer biodistribution. All quantitative data are expressed as mean ± standard deviation (SD). Statistical analysis was performed using Student's t-test for comparisons between two groups, and one-way analysis of variance (ANOVA) was applied where appropriate. A P value < 0.05 was considered statistically significant. The study was approved by the Kuwait University Animal Resources Centre ethics committee (Approval No. MF-24-18).

Results:
GA demonstrated significant dose-dependent cytotoxicity in tumour cells, with reduced cell viability observed at concentrations of 0–5 mM and an IC_{50} of 4 mM ($P < 0.0001$). GA treatment induced apoptosis and significantly inhibited cell migration, confirmed by flow cytometry showing increased preapoptotic cell populations (n = 5).

In vivo, DMBA successfully induced mammary tumours in SD rats. GA-treated rats exhibited a marked reduction in tumour volume, progression, and metastatic spread compared to controls ($P < 0.0001$), indicating effective tumour suppression (n = 5 per group).

Conclusions:
Glycyrrhizic acid exhibits significant chemopreventive and therapeutic effects against DMBA-induced mammary tumorigenesis in vitro and in vivo, supporting its potential as a natural anticancer agent.

Key Words: Glycyrrhizic Acid ; Breast Cancer metastasis; Radionuclide imaging;

Funding Agency: Research Sector [MN02/19], [SRUL02/13], and [GM 01/18],Kuwait University, Kuwait

Nuclear Medicine and Radiology

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Assessing Injection Techniques for Optimized Radiopharmaceutical Delivery in Models

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Introduction:
This study evaluates the efficacy, consistency, and reproducibility of radiopharmaceutical administration via jugular vein catheterization (JVC) compared with tail-vein and intraperitoneal (IP) injections. Our goal is to identify the most suitable injection method for a longitudinal study requiring multiple weekly radiopharmaceutical administrations in mice over several weeks.

Methods:
30 Balb/c male mice were divided into 3 groups based on injection route: 5 mice for tail vein, 5 mice for IP, and 20 for JVC. Two catheter types were assessed for the JVC group: 10 mice for the commercially manufactured SoloPort™ and 10 mice for the in-house–manufactured PinPort™ system. All mice received weekly injections of [18F]NaF and [18F]FDG over 7 weeks, followed by PET/CT imaging. Residual radiopharmaceutical activity in the syringe was quantified for each method, and extravasation was assessed by drawing a ROI over the injection site.

Results:
For JVC injections, the mean residual activity after [18F]NaF administration was 11.61 ± 6.48%, and it was 10.88 ± 6.17% after [18F]FDG injection on the 1 mL syringe. For both tail vein and IP injections, the same insulin syringe type was used, and the mean residual activity was 3.86 ± 2.75% for [18F]NaF and 3.23 ± 1.69% for [18F]FDG. The tail-vein injection group had a mean leaked radioactivity from the tail of 7.43 ± 6.17% from [18F]NaF injections and 8.38 ± 8.70% from [18F]FDG. Tail-vein injections showed substantial extravasation at the injection site, with a mean of 14.02 ± 7.84% for [18F]NaF and 18.22 ± 18.35% for [18F]FDG. The IP group showed 0.37 ± 0.18% extravasation for [18F]FDG and no visible extravasation for [18F]NaF. Within the JVC group, significant differences in catheter residue between [18F]NaF and [18F]FDG were observed for both the PinPort™ ($p = 0.003$) and SoloPort™ ($p = 0.03$) systems. However, no significant differences were found between the two catheter systems for either tracer ([18F]NaF: $p = 0.39$; [18F]FDG: $p = 0.09$).

Conclusions:
All three routes had successfully delivered radiopharmaceuticals into mice. However, JVC requires specialized surgical expertise, and tail-vein injections exhibited notable dose loss through vein-puncturing and extravasation. IP administration demonstrated the best combination of consistency, reproducibility, and minimal radioactivity loss, making it the most suitable method for repeated radiopharmaceutical dosing in longitudinal studies.

Key Words: PET/CT; Radiopharmaceuticals; Nuclear Medicine;

Funding Agency: This work was supported and funded by Kuwait University Research Grant No. MN01/24.

Nutrition

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Vitamin D Deficiency and Obesity: A Systematic Review of Randomized Controlled Trials on Supplementation in Overweight and Adults with Obesity.

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Introduction:
Objectives: Explore the relationship between vitamin D deficiency and obesity through randomized controlled trials (RCTs).

Methods:
Eight studies were selected via the PICO-S approach (Population, Intervention, Comparison, Outcome, Study Design). The strategy adhered to PRISMA guidelines, which involve systematic identification, screening, and inclusion of studies. Studies must be peer-reviewed (RCTs) in English involving overweight or obese adults (18–70 years) that report serum vitamin D levels and obesity measures. Records were identified through database searching via Scopus, Web of Science, and PubMed. Ethical approval was waived as this study was a systematic review of published studies. Risk of bias was assessed using the Quality Criteria Checklist tool.

Results:
Vitamin D supplementation (VDS) consistently increased serum 25-hydroxyvitamin D concentrations across included studies, with a high prevalence of vitamin D deficiency observed among individuals with obesity. Six studies reported statistically significant reductions in at least one anthropometric or body composition outcome, including body weight, BMI, fat mass, or waist circumference, as indicated by confidence intervals (CIs) entirely below zero. In contrast, two studies reported non-significant effects. Overall, effect sizes and CI widths varied substantially across studies, reflecting heterogeneity in study design, sample size, and measurement precision, and indicating mixed and uncertain effects of (VDS) on body composition outcomes.

Conclusions:
This review indicates that vitamin D deficiency is commonly observed among individuals with obesity. Although some studies report modest improvements in body weight or fat mass with (VDS), the overall evidence is limited. Current findings do not support a definitive relationship or benefit of (VDS) for obesity outcomes. Further high-quality (RCTs) are needed to clarify the connection.

Key Words: Vitamin D deficiency; Vitamin D insufficiency; Obesity; Overweight

Funding Agency: None Funding

Oncology

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Integrative Multi-Omics Discovery of ANGPT2 and FLT4 as Vascular PI3K-Axis Prognostic Biomarkers in Human Glioblastoma

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Introduction:
Glioblastoma (GBM), the most common and aggressive primary brain tumor, accounts for 54% of gliomas and 16% of primary brain tumors globally. In Kuwait, CNS cancers are less frequent but disproportionately lethal, with 76 new cases in 2022 contributing to 3.3% of cancer deaths. Despite multimodal therapy, GBM remains highly treatment-resistant, with a median survival of ~15 months, underscoring the need for robust prognostic biomarkers. This study used integrative multi-omics and machine learning to identify biomarkers and pathways linked to progression-free outcomes.

Methods:
GBM datasets from the publicly available Clinical Proteomic Tumor Analysis Consortium were analyzed, with patients stratified into progressed and non-progressed groups based on progression-free survival (PFS). Integrated miRNA, RNA-Seq, proteomics, and phosphoproteomics data underwent MB-PLS-DA to assess inter-omics correlations and identify discriminative features. Complementary knowledge-driven analyses including joint gene–protein pathway enrichment, phosphoproteomic kinase activity inference, and miRNA over-representation were combined with data-driven findings to nominate biomarkers and pathways explaining differential PFS outcomes.

Results:
Multi-omics integration showed strong concordance across datasets ($r = 0.78–0.99$) and consistently highlighted PI3K signaling as a central pathway, supported by gene–protein, miRNA, and phosphoproteomic enrichment. ANGPT2 and FLT4 emerged as recurrent angiogenesis-linked features within this axis, along with additional pathways such as MAPK/ERK, JAK–STAT, AMPK, and ECM/focal adhesion signaling, indicating coordinated proliferative and microenvironmental reprogramming in progressive GBM. Data-driven analyses also revealed molecular chaperones (HSP90, HSP70, and DNAJ) that stabilize PI3K-related receptor kinases, supporting a chaperone–PI3K–ANGPT2/FLT4 network. Validation confirmed elevated ANGPT2 and FLT4 in progressed cases, each achieving AUC ≈ 0.70 for distinguishing progression status.

Conclusions:
PI3K signaling emerged as a key driver of GBM progression, with ANGPT2 and FLT4 consistently identified across omics layers as vascular prognostic biomarkers. Their elevated expression and moderate predictive performance support evaluating ANGPT2 and FLT4 expression for outcome stratification and informing PI3K-targeted therapies. Integrating these markers into clinical workflows could improve risk prediction, therapeutic selection, and personalized GBM management

Key Words: Glioblastoma; Machine learning; PI3K signaling;

Funding Agency: None

Ophthalmology

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Efficacy and Safety of Ranibizumab Biosimilars Relative to a Reference Ranibizumab Anti-VEGF Therapy for Neovascular Age-Related Macular Degeneration Treatment: A Systematic Review, Meta-Analysis, and Trial Sequential Analysis

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Introduction:
Background: Neovascular age-related macular degeneration (nAMD) is a leading cause of irreversible central vision loss in older adults. Intravitreal anti vascular endothelial growth factor (VEGF) therapy, particularly ranibizumab, has significantly improved outcomes but requires frequent injections, creating a substantial treatment and economic burden. Biosimilars of ranibizumab have been developed to reduce costs and expand accessibility without compromising clinical efficacy or safety. To systematically evaluate and compare the efficacy and safety of ranibizumab biosimilars versus reference ranibizumab in adults with nAMD.

Methods:
A systematic review and meta-analysis were conducted according to PRISMA 2020 and Cochrane guidelines. PubMed, Embase, Scopus, Web of Science, and the Cochrane Library were searched from inception to October 2025. Randomized controlled trials (RCTs) comparing ranibizumab biosimilars with the reference product were included. Data were pooled using random-effects meta-analyses, and trial sequential analysis (TSA) was performed for major outcomes. The certainty of evidence was assessed using GRADE.

Results:
Nine RCTs with 3,366 participants (1,773 in biosimilar groups and 1,593 in reference groups) were included. There were no significant differences between biosimilars and the reference in best-corrected visual acuity (MD = −0.40, 95% CI: −1.04 to 0.23), ocular or systemic adverse events, or treatment-emergent adverse events. Heterogeneity was minimal ($I^2 < 20\%$), and no publication bias was detected. TSA confirmed adequacy of evidence for safety but was inconclusive for some efficacy outcomes.

Conclusions:
Ranibizumab biosimilars demonstrate equivalent efficacy and safety to reference ranibizumab in nAMD management, supporting their use as effective and cost-efficient therapeutic alternatives.

Key Words: Ranibizumab; VEGF; Reference, Cost; nAMD;

Funding Agency: Nil

Orthopedic Surgery

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Association Between Lumbar Lordosis and Proximal Junctional Failure Following Adult Spinal Deformity Surgery: A Systematic Review and Meta-analysis

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Introduction:
Proximal junctional failure (PJF) remains a challenging complication following instrumented posterior fusion for adult spinal deformity (ASD). Although radiographic parameters such as lumbar lordosis (LL) and pelvic incidence–lumbar lordosis mismatch (PI–LL) are frequently cited, their specific association with PJF risk is not fully defined. This systematic review and meta-analysis aimed to clarify whether postoperative LL, changes in LL (ΔLL), postoperative PI–LL, or changes in PI–LL (ΔPI–LL) are predictive of PJF in ASD.

Methods:
Following PRISMA 2020 and Cochrane guidelines, a comprehensive search of PubMed, Embase, Scopus, and Web of Science was conducted through August 2025. Eligible studies included adult cohorts undergoing instrumented fusion for ASD with extractable data on alignment exposures and PJF outcomes. Two independent reviewers performed study selection, data extraction, and quality appraisal using the NIH assessment tool. Random effects meta-analysis was performed with mean differences (MD) and 95% confidence intervals, with heterogeneity evaluated via I^2.

Results:
From 3,449 records, seven retrospective cohorts comprising 710 patients met inclusion. PJF occurred in 123 patients (17.3%), while 587 remained event-free. Absolute postoperative LL did not differ significantly between groups (MD = 0.70, 95% CI -2.02 to 3.42, p = 0.61). However, patients with PJF demonstrated greater ΔLL (MD = 4.24, 95% CI 0.19 to 8.28, p = 0.04). Postoperative PI–LL was also higher in the PJF group (MD = 4.25, 95% CI 0.46 to 8.05, p = 0.02). ΔPI–LL was not significantly associated (MD = -0.44, 95% CI -7.23 to 6.34, p = 0.89).

Conclusions:
Greater ΔLL and residual postoperative PI–LL mismatch significantly correlate with PJF, while final LL alone does not. These findings highlight the importance of proportional, age-adjusted alignment strategies and cautious correction magnitude to reduce mechanical failure risk in ASD surgery.

Key Words: Adult spinal deformity, proximal junctional failur; lumbar lordosis; pelvic

Funding Agency: None

Orthopedic Surgery

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Virtual Reality as a Distraction Technique in Pediatric Patients Undergoing Orthopedic Procedures: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Introduction:
Pain and anxiety are common in pediatric orthopedic procedures such as cast or pin removal, often leading to distress and physiological stress responses. Virtual reality (VR) offers immersive distraction and has shown promise in pediatric procedural care; however, evidence in orthopedic procedures remains limited. This meta-analysis aimed to evaluate the effectiveness of VR compared with standard care in reducing pain, anxiety, and heart rate in children undergoing orthopedic procedures.

Methods:
A systematic search was conducted in PubMed, Scopus, and Cochrane Library from inception to 20 October 2025 for randomized controlled trials (RCTs) comparing VR distraction and standard care in pediatric patients undergoing orthopedic procedures. Outcomes of interest included pain, anxiety, and heart rate. Statistical analysis was performed with R 4.3.1. Standardized mean differences (SMD) using the Inverse Variance method and random-effects method.

Results:
A total of four RCTs were included in the final meta-analysis, compromising 624 patients, of whom 315 (50%) were distracted with VR during clinical orthopedic procedures (mean age 9.84 years, mean 40% females). In the pooled analysis, VR distraction significantly reduced anxiety (SMD -0.55; 95% CI [-0.76; -0.34]; $p < 0.01$; $I^2 = 0\%$), pain (SMD -0.43; 95% CI [-0.68; -0.19]; $p < 0.01$; $I^2 = 44\%$), and heart rate (SMD -0.34; 95% CI [-0.60; -0.07]; $p = 0.01$; $I^2 = 53\%$).

Conclusions:
VR distraction significantly reduces anxiety, pain, and heart rate compared to standard care in pediatric patients undergoing orthopedic procedures. The integration of this child-friendly, non-pharmacological approach provides enhanced procedural comfort and effective anxiety management.

Key Words: Virtual Reality; Pediatric Population; Orthopedic Procedure;

Funding Agency: None

Orthopedic Surgery

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Efficacy and Safety of Esketamine in Total Hip and Knee Arthroplasty: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Introduction:
Total hip and knee arthroplasty (THA/TKA) are common procedures, but post-operative recovery is often complicated by severe pain, opioid-related side effects, and psychological distress. Esketamine has been proposed as an adjunct to improve outcomes due to its analgesic and antidepressant properties, but the evidence for its use remains inconsistent.

Methods:
A systematic review and meta-analysis was conducted, synthesizing evidence from randomized controlled trials (RCTs) obtained from PubMed, Scopus, Web of Science, and CENTRAL up to July 2025. Using Stata MP v. 18, we pooled dichotomous and continuous outcomes using risk ratios (RR) and standardized mean differences (SMD) or mean differences (MD), respectively, along with 95% confidence intervals (CI).

Results:
Seven RCTs, including 1,145 patients, were analyzed. Esketamine did not significantly reduce post-operative pain at rest at 12 or 24 hours ($p > 0.05$). It did, however, significantly decrease pain during activity at 12 hours (SMD: -0.28; 95% CI [-0.45, -0.12]; $p < 0.001$), though this effect did not persist at 24 hours ($p = 0.06$). Esketamine significantly reduced anxiety on post-operative day 7 (SMD: -0.72; 95% CI [-1.40, -0.04]; $p = 0.04$), but not on day 1 ($p = 0.33$). There was no significant effect on depression at any time point ($p > 0.05$). Critically, esketamine use was associated with a significantly higher risk of hallucinations (RR: 4.36; 95% CI [1.48, 12.88]; $p = 0.01$). There was no significant difference in the incidence of delirium, nightmares, or post-operative nausea and vomiting.

Conclusions:
In patients undergoing THA or TKA, esketamine provides a transient reduction in pain during activity and a delayed decrease in anxiety. These limited benefits are offset by a significantly increased risk of post-operative hallucinations, while offering no advantage in reducing pain at rest, depression, or other adverse events, such as delirium or PONV.

Key Words: Pain; Orthopaedics; Depression;

Funding Agency: None

Orthopedic Surgery

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Mulligan Mobilization Combined with Conventional Therapy vs. Conventional Care Alone in Patients with Rotator Cuff Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Introduction:
Rotator cuff disease (RCD) commonly causes pain, reduced range of motion (ROM), and functional limitation. Mulligan Mobilization with Movement (MWM) may enhance outcomes when added to conventional therapy, but evidence in RCD remains inconsistent. This meta-analysis evaluated the effectiveness of Mulligan mobilization plus conventional therapy versus conventional therapy alone on pain, function, ROM, joint position sense, and quality of life (QoL).

Methods:
A systematic search of PubMed, Web of Science, Scopus, and Cochrane Library (inception–12 October 2025) identified randomized controlled trials (RCTs) comparing Mulligan mobilization with conventional therapy against conventional therapy alone in individuals with rotator cuff–related pain. Outcomes included pain, ROM, QoL, joint position sense, and functional performance. Analyses were performed using R 4.3.1 with random-effects models (REML). Heterogeneity was evaluated using the I^2 statistic and Cochrane Q test. PROSPERO registration: CRD420251166854.

Results:
Four RCTs (160 participants) met inclusion criteria; 80 received Mulligan mobilization with conventional therapy (mean age: 51 years; 45% female). Compared with conventional therapy alone, Mulligan mobilization significantly improved pain at rest (MD −1.19; 95% CI −1.64 to −0.74; $I^2 = 0\%$), pain during activity (MD −2.25; 95% CI −3.18 to −1.31; $I^2 = 67\%$), functionality (MD −14.71; 95% CI −20.10 to −9.33; $I^2 = 51\%$), ROM (MD 19.92; 95% CI 11.25 to 28.39; $I^2 = 58\%$), and joint position sense (MD −3.31; 95% CI −6.22 to −0.40; $I^2 = 80\%$). No significant improvement was found in QoL (MD 10.58; 95% CI −3.18 to 24.34; $I^2 = 76\%$).

Conclusions:
Mulligan mobilization combined with conventional therapy significantly improves pain, ROM, functionality, and joint position sense in RCD, though QoL benefits were not significant. Incorporating Mulligan techniques may enhance rehabilitation outcomes for patients with rotator cuff–related dysfunction.

Acknowledgment: Not applicable.
Ethical Statement: Ethical approval was not required for this study as it is a systematic review and meta-analysis of previously published, publicly accessible data. The protocol was prospectively registered in PROSPERO (CRD420251166854).

Key Words: Rotator cuff disease; Mulligan mobilization; Conventional therapy;

Funding Agency: None

Orthopedic Surgery

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Association between Exposure to Air Pollution and Hip Fracture: A Systematic Review and Meta-Analysis

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Introduction:
Hip fracture represents one of the most serious orthopedic injuries and is associated with major functional loss, high complication rates, and elevated short- and long-term mortality. Emerging data suggest that environmental exposures, particularly ambient air pollution, may further worsen post-fracture outcomes, yet the evidence remains fragmented. To systematically review and meta-analyze the available observational evidence linking exposure to ambient air pollutants with patients with hip fracture.

Methods:
PubMed, Embase, Scopus, Web of Science, and the Cochrane Library were searched from inception through October 2025, combining controlled vocabulary and free-text terms for hip fracture and air pollution. Observational studies enrolling adults with hip fracture and comparing higher versus lower pollutant exposure were included. Two reviewers independently screened records, extracted data, and assessed bias using the NIH tool for cohort studies. Certainty was rated by GRADE. Pooled odds ratios (ORs) with 95% CIs were estimated using random-effects models.

Results:
Of 1,861 records identified, five studies (n = 945,461) met the inclusion criteria. Studies were conducted in China, the UK, Spain, Italy, and South Korea, encompassing ecological, cohort, and case-crossover designs. Methodological quality was generally good. For PM2.5, the pooled OR was 1.23 (95% CI 0.91–1.67; p = 0.16; I^2 = 99.9%), indicating no significant association overall; sensitivity analysis excluding one large study yielded a modest but significant association (OR 1.07, 95% CI 1.02–1.13). For PM10, the pooled OR was 1.05 (95% CI 1.01–1.09; p = 0.007; I^2 = 96.5%), suggesting higher pollution exposure modestly increased adverse outcomes. Publication bias was not detected. Certainty of evidence for both pollutants was rated very low due to observational design, heterogeneity, and imprecision.

Conclusions:
Higher ambient particulate exposure may be linked with hip fracture, though current evidence is limited and heterogeneous. Larger, well-adjusted longitudinal studies are needed to clarify causality and mechanisms.

Key Words: Hip fracture ; Orthopedic ; Air pollution ;

Funding Agency: None

Pathology

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Skeletal and Extraskeletal Presentations of Ewing (FET::ETS-Rearranged) Sarcomas and Their "Ewing-like" Mimics: Clinicopathologic Correlates and Survival Outcomes in a 90-Patient Cohort

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Introduction:
Ewing sarcoma (ES) is an aggressive but rare malignancy of bone and soft tissue, affecting only 1–3 individuals per million each year. ES (FET::ETS-rearranged) and the unrelated Ewing-like small round-cell sarcomas (SRCSs) form a morphologically overlapping yet molecularly diverse group of neoplasms that differ in genotype, anatomic distribution, age profile, and clinical behavior. Clarifying genotype–anatomic correlations—particularly distinctions between ES vs. non-Ewing tumors and skeletal vs. extraskeletal presentations within the Ewing group—is essential for accurate diagnosis and treatment planning, especially in morphologically ambiguous cases.

Methods:
We retrospectively reviewed 90 SRCSs diagnosed at a tertiary cancer center (2016–2025). All undifferentiated SRCSs with successful molecular testing during the study period were included, while cases with failed, insufficient, or absent results were excluded. Clinical, radiologic, and pathologic data were integrated with genomic findings. Molecular characterization was performed using targeted RNA sequencing (Archer FusionPlex Sarcoma Panel) and break-apart FISH for EWSR1 and FUS rearrangements on FFPE tissue. Ewing and Ewing-like subsets were compared across skeletal and extraskeletal sites using univariate analysis, and therapeutic and survival outcomes were assessed. This study was approved by the Ethics Committee for Medical Research at the Ministry of Health, Kuwait (Ref# 278, Study# 2025/2816, dated May 15, 2025).

Results:
Among 90 cases (47 males, 43 females; median age 18.5 years), 76 (84%) harbored FET::ETS fusions and/or EWSR1/FUS rearrangements consistent with the Ewing family. Of 44 fusion-confirmed tumors, EWSR1::FLI1 predominated (89%), followed by EWSR1::ERG (9%) and FUS::ERG (2%). Fourteen tumors (16%) were Ewing-like sarcomas, including CIC::DUX4 (n=5), BCOR-altered (n=1), EWSR1::ATF1 (n=1), EWSR1::CREB1 (n=1), YWHAE::NUTM2B (n=1), and five fusion-negative SRCSs. ESs showed a strong osseous predilection (48/76; 63%), particularly axial ($p<0.001$), and peaked during adolescence, while Ewing-like SRCSs were significantly more often extraskeletal ($p<0.001$) and spanned a broader age range, including infantile cases. Skeletal vs. extraskeletal presentation had no significant impact on stage, progression, or overall survival. In contrast, metastatic disease at diagnosis was the strongest adverse prognostic factor ($p=0.007$).

Conclusions:
ESs and Ewing-like SRCSs exhibit marked molecular diversity despite shared morphology. Within ES, skeletal vs. extraskeletal origin did not influence outcome, whereas metastatic presentation remained the dominant prognostic factor. Integrating molecular diagnostics with anatomic and histopathologic assessment is essential for accurate classification and optimal management of these rare tumors.

Key Words: Ewing sarcoma; Extraskeletal; RNA sequencing;

Funding Agency: None

Pathology

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Golgi-pattern PDGFRA immunoreactivity aids identification of PDGFRA mutations in gastric epithelioid and mixed-type gastrointestinal stromal tumors

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Introduction:
Background: Gastrointestinal stromal tumors (GISTs)—the most common mesenchymal neoplasms of the gastrointestinal tract—demonstrate a mutational profile that shapes their biological behavior and predicts response to tyrosine kinase inhibitors (TKIs). Approximately 75–80% harbor KIT mutations sensitive to imatinib, whereas 5–10% carry PDGFRA mutations associated with primary imatinib resistance but responsiveness to avapritinib. The diagnostic performance of PDGFRA immunohistochemistry (IHC) as a surrogate marker for mutation status warrants further evaluation. This study assessed the diagnostic accuracy, specificity, and reproducibility of PDGFRA IHC for predicting underlying PDGFRA mutations to refine triaging strategies for molecular testing.

Methods:
A total of 117 tumors were evaluated (19 PDGFRA-mutant GISTs, 40 GISTs without PDGFRA mutations, 49 GISTs of undetermined genotype, and 9 non-GIST mimics). IHC for KIT, DOG1, CD34, and PDGFRA was performed on whole paraffin sections and tissue microarrays. Three pathologists independently scored PDGFRA staining for intensity, extent, and the presence of a characteristic perinuclear Golgi-pattern accentuation.

Results:
PDGFRA-mutant GISTs were predominantly gastric (94.7%) and showed epithelioid or mixed morphology. Sixteen cases harbored the D842V variant, and three carried other PDGFRA mutations. KIT expression was reduced (47.4%) compared with non-PDGFRA-mutant GISTs (85%), whereas DOG1 remained consistently positive. PDGFRA IHC demonstrated 94.7% sensitivity and 77.5% specificity for predicting PDGFRA mutations, though it did not distinguish D842V from non-D842V variants. High-level PDGFRA expression was observed in 84.2% of PDGFRA-mutant tumors versus 25% of non-PDGFRA GISTs ($p<0.001$). Golgi-pattern staining was present in 89.5% of PDGFRA-mutant GISTs but was uncommon in other groups. Among 49 GISTs with undetermined genotype, 7 (14%) demonstrated PDGFRA immunoreactivity. Targeted molecular testing was subsequently performed in 6 cases with available tissue, identifying PDGFRA mutations in 4—all gastric tumors with epithelioid or mixed morphology and Golgi-pattern staining. Among non-GISTs, only one case (monophasic synovial sarcoma) showed diffuse PDGFRA positivity. Interobserver agreement was substantial ($\kappa = 0.691$).

Conclusions:
PDGFRA IHC is a robust adjunct for identifying PDGFRA-mutant GISTs, particularly when diffuse Golgi-pattern staining is present in gastric epithelioid or mixed-type tumors with reduced KIT expression. However, in advanced disease, therapeutic decisions rely on precise identification of D842V mutations—highlighting the continued necessity of targeted molecular sequencing.

This study was approved by the Ethics Committee for Medical Research, Ministry of Health, Kuwait (Ref # 1088, Study # 2024/2586, dated July 10, 2024) and the Health Sciences Center Ethical Committee, Kuwait University (Ref # 755, dated July 14, 2024) -- attached.

Key Words: Gastrointestinal stromal tumor; PDGFRA; p.D842V;
Funding Agency: This work was supported and funded by the Research Sector, Kuwait University (Research Grant No. MG01/24).

Pathology

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An Audit On The Compliance of Oestrogen And Her2 Receptors Reporting In Breast Cancers

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Introduction:
Background: Major laboratories are required to maintain standards of receptor positivity testing in order to uphold the standard of care for patient's with breast cancer. Oestrogen receptors (ER) and human epidermal growth factor (HER2) receptors are essential targets for breast cancer treatment. It can help guide more personalised treatments and improve disease outcomes.
Aim: Evaluate whether Salford Royal Pathology Laboratories matched recommended British national standards for analysing ER and HER2 receptor positivity by comparison to the British National Breast Screening Audit.

Methods:
This is a retrospective study investigating samples of invasive breast cancer biopsies sent to Salford Royal Pathology Laboratories for reporting and analysis of ER and HER2 status from January 1, 2019, to August 31, 2024 (n=2738). No ethical approval was required.

Results:
The areas covered by this department concerning breast cancer pathology is the South Lancashire Breast screening centre which is based at Wrightington, Wigan and Leigh (WWL) NHS foundation trust, and comprises 710,000 people. On average, from 2019 to 2024, the ER positivity was 80.45% and HER2 positivity was 14.02%. The National Breast Screening Audit positivity rate is 91% for ER and 9% for HER2. In 2019, the ER positivity percentage was 77.33% and HER2 was 13.97%. In 2020, 76.67% were ER positive, and 18.43% were HER2 positive. As for 2021, 85.12% were ER positive, and 8.98% was HER2 positive. In 2023, the ER positivity was 81.5% and HER2 was 15.69%. In 2024, 82.5% were ER positive and 12.93% were HER2 positive.

Conclusions:
Salford Royal Pathology Laboratories have maintained the quality of the service provided in comparison to the British National Breast Screening Audit.

Key Words: Breast Cancer; Oestrogen Receptors; HER2 Receptors ;

Funding Agency: None

Pediatrics

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An Accurate Model Based on Readily-Available Information for Accurate Assessment of Fatmass in Arab Children from the Mena Region

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Introduction:
Childhood obesity and diabetes prevalences are very high across The Middle East and North Africa (MENA). Accurate and practical methods for childhood adiposity assessment are needed to aid diabetes prevention efforts. A prediction model, which uses weight, height, age, sex and ethnicity to estimate childhood fat mass (FM), has been validated in many childhood settings, but MENA region validations are lacking. We evaluated the model in three MENA region settings– Kuwait, Lebanon and Morocco.

Methods:
This study contained 471 children (6-15years) with deuterium dilution assessed FM, weight, height, age, sex and ethnicity data. Data from Lebanon also included bioimpedance-assessed FM. We quantified country-specific predictive performance using R2, calibration (i.e. agreement of observed and predicted FM) and root mean square error (RMSE) statistics. For Lebanese children, bioimpedance-assessed FM was also compared with FM from the reference standard, deuterium dilution.

Results:
The model showed good predictive ability in all settings, with R-squared>90% in all countries, good overall calibration,and low RMSE values. The model intercept was re-calibrated in each country to improve the accuracy ofpredictions. After re-calibration, RMSE was 1.3kg, 1.6kg and 2.8kg in Kuwait, Lebanon and Moroccorespectively. Amongst Lebanese children, bioimpedance was less accurate (RMSE=2.4kg) on average than the model

Conclusions:
The model, using only weight, height, sex, age and ethnicity, produced accurate childhood FM predictions in the MENA region. Crucially, the model produced more accurate FM estimates than bioimpedance with fewer time and monetary costs, indicating it's potential for implementation at the individual- and population-level to aid diabetes prevention strategies.

Key Words: Obesity; Body Composition; Pediatrics;

Funding Agency: Pfizer Inc. Global Obesity ASPIRE Research Grant (Grant/Award Numbers: Ref, 91629725)

Pediatrics

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A Novel Founder Homozygous Intronic LZTR1 Variant in Three Kuwaiti Families from the Same Tribe: Clinical Expansion of Autosomal Recessive Noonan Syndrome

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Introduction:
Noonan Syndrome (NS; OMIM #163950) is a clinically and genetically heterogeneous condition characterized by distinct facial features, congenital heart defects, short stature, and developmental delays. While most NS cases follow an autosomal dominant inheritance pattern, recent studies have identified biallelic variants in the LZTR1 gene (OMIM #600574) as a cause of autosomal recessive NS, particularly in consanguineous populations. Here, we present the first cohort from Kuwait with a homozygous LZTR1 deep intronic variant and compare their phenotypes to published recessive and dominant LZTR1 NS cases.

Methods:
We describe five pediatric cases from three Kuwaiti families belonging to the same tribe, all presenting with a consistent NS phenotype: global developmental delay, facial dysmorphism (e.g., hypertelorism, broad nasal bridge, long philtrum), hypotonia, and hypertrophic cardiomyopathy. Their age group ranged from infancy to early childhood, with initial presentations during early infancy.

Results:
Previous quadro whole exome sequencing in two of the families failed to identify a definitive diagnosis. Subsequently, quadro whole genome sequencing for these two families revealed a novel homozygous intronic variant in LZTR1 gene (NM_006767.4:c.1943-351G>C), shared among affected individuals and segregating with disease status in a recessive pattern. Targeted molecular testing in the fifth affected case, confirmed the presence of the same variant in a homozygous state. Based on its absence from the public variant databses, clear seggregation across multiple affected family members and the high specificity of the observed phenotype for LZTR1-related NS, we consider this variant as likely pathogenic.

Conclusions:
This report expands the mutational and geographic spectrum of autosomal recessive LZTR1-associated NS, representing the first documented familial cluster from Kuwait and the broader Arabian Penninsula. Our findings emphasize the diagnostic value of genome-wide sequencnig in complex syndromic cases with negative exome or microarray analyses. We further highlight the importance of including LZTR1 in diagnostic evaluation of children presenting with developmental delay, hypotonia, and early hypertrophic cardiomyopathy, particularly in populations with high consanguinity rates. Early recognition facilitates tailored counseling and multidisciplinary care.

Key Words: Noonan Syndrome; Autosomal Recessive Inheritance ; Genetics ;

Funding Agency: None

Pediatrics

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A Silent Threat: Understanding ESBL-KP Risk Factors in the Neonatal ICU

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Introduction:
The Neonatal Intensive Care Unit (NICU) provides essential care for vulnerable neonates, yet the spread of hospital-acquired infections (HAIs), specifically extended-spectrum beta-lactamase (ESBL)–producing bacteria, is a major threat. Klebsiella pneumoniae (KP) is one of the primary gram-negative pathogens responsible for ESBL infections in NICUs. The objectives of this study were to: [1] identify risk factors for ESBL-KP acquisition among neonates and [2] evaluate the clinical impact of ESBL-KP acquisition on neonatal outcomes (survival, mortality due to sepsis or mortality due to other causes) at NICU discharge.

Methods:
Method and Ethical Approval: This retrospective case-control study analyzed 600 neonates admitted to a Kuwaiti NICU (August 2022–December 2023). Data included clinical, demographic, antibiotic and laboratory records. The primary outcome was ESBL-KP acquisition (positive vs. negative culture). The secondary outcome was status at NICU discharge: survival, mortality due to sepsis, or mortality due to other causes. Univariable and multivariable logistic regression evaluated associations with the primary outcome while multinomial regression was used to analyze the secondary outcome. The Joint Ethical Committee at the Ministry of Health approved the protocol (2024/2695).

Results:
Of 600 neonates, 177 (30%) acquired ESBL-KP. Of these, 12% had bloodstream infections (BSI), with a 50% mortality rate among BSI cases; the remainder were rectal colonizations. With regards to the primary outcome, the multivariable logistic regression model identified significant risk factors for ESBL-KP acquisition: length of NICU stay (OR:1.02, 95% CI:1.01–1.03), intrauterine growth restriction (IUGR) (OR:2.08, 95% CI:1.01–4.38), extreme prematurity (OR:2.17, 95% CI:1.20–3.94), previous hospital admission (OR:3.99, 95% CI:1.59–7.71) and prior ampicillin use (OR:3.84, 95% CI:2.35–6.28). With regards to the secondary outcome, after adjusting for confounders, ESBL-KP positive neonates had 9.82 times higher odds of death due to sepsis (p=0.01) compared to ESBL-KP negative neonates.

Conclusions:
ESBL-KP acquisition in the NICU was significantly associated with length of stay in NICU, IUGR, extreme prematurity, previous hospital admission and ampicillin use. Crucially, acquisition dramatically increased the risk of sepsis-related mortality. Interventions targeting neonates at risk and judicious antibiotic stewardship are vital to improve neonatal outcomes.

Key Words: ESBL-KP; risk factors; case control;

Funding Agency: None

Pediatrics

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Gene Therapy with Onasemnogene Abeparvovec for Spinal Muscular Atrophy: Clinical Experience from Kuwait

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Introduction:
Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disorder and a leading genetic cause of infant mortality. It is caused by SMN1 gene mutations resulting in progressive motor neuron degeneration.In May 2019, the U.S. Food and Drug Administration (FDA) approved onasemnogene abeparvovec (Zolgensma), the first gene replacement therapy for children under the age of two with SMA, leading to significant reduction in morbidity and mortality. Despite its global impact, data from the Middle East remains limited.

Aim:
To evaluate the clinical outcomes of children with genetically confirmed SMA treated with Zolgensma in Kuwait.

Methods:
A retrospective analysis of children who received Zolgesma from 2019-2025 was conducted using Kuwait Medical Genetics Center registry.

Results:
Fifteen children (8 females and 7 males) diagnosed with genetically confirmed SMA (13 with type 1 and 2 with type 3) were included. Age at presentation ranged from 1 month to 22 months and age at gene therapy infusion ranged from 2 months to 2 years and 5 months. Ten individuals had previously received nusinersen therapy. At the latest follow-up, all 15 individuals were alive. Motor assessment was available for 10 cases: 5 achieved independent walking, while the remaining 5 attained sitting or standing milestones. Respiratory status remained stable; two children continued with tracheostomy support, one remained on nocturnal BiPAP, and the rest remained on room air and did not require assisted ventilation. The most common adverse event was transient transaminitis in 6 cases. No cases of liver failure or thrombocytopenia were reported.

Conclusions:
This is the first report on SMA gene therapy outcomes from Kuwait. Gene replacement therapy with Zolgensma demonstrated favorable clinical outcomes, including motor function improvement, respiratory stability, no mortality and only mild, manageable adverse events. These findings emphasize the value of early gene therapy and the importance of regional data to guide future practice.

Key Words: SMA, gene therapy, zolgensma, clinical experience ; Motor outcomes ; Adverse

Funding Agency: None

Pediatrics

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Liver Transplantation Management for Children with Metabolic Liver Disease in Kuwait

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Introduction:
The liver is a highly active organ since many pathways of intermediary metabolism are located. Dysfunction in any of those pathways lead to various metabolic liver disease (MLD). Liver transplantation (LT) is an effective therapy for several types of MLD. Our objective is to study MLD children who underwent LT in Kuwait.

Methods:
The hospital records of MLD cohort managed with LT during 1998-2023 were retrospectively reviewed. Ethical approval was obtained from the Standing Committee for Coordination of Health and Medical Research, Ministry of Health (2024/ 2737).

Results:
Ninety-six children received LT; 57 (59%) had MLD. Transplant age range for MLD patients: 4 months-13 years; MLD patients were older than non-MLD (median: 3.8 vs. 1.8 years; p = 0.025). Among MLD patients, males were 56% and 88% were Kuwaitis. Crigler Najjar syndrome (30%) and progressive familial intrahepatic cholestasis (24%) were the main categories among MLD cases. Cadaveric grafts were transplanted in 60% and 58% received split grafts. Combined liver and kidney transplants were performed in 7%. All MLD patients were maintained on tacrolimus, but a combination with prednisolone and mycophenolate mofetil were required in 54% and 49%, respectively. Post-LT complications included biliary (15.8%), vascular (14%), chronic rejection (12.3%), and lymphoproliferative disease (7%). Re-transplantation was required in 5 (7%) patients. Patient survival at 1 year: 98%; at 5 and 10 years: 96%. Graft survival at 1 year: 98%; at 5 and 10 years: 94%. No statistical significance between MLD and non-MLD regarding post-LT complications, patient and graft survival rates. LT was performed in several centers abroad due to the lack of a local program in Kuwait, hence different management protocols were used.

Conclusions:
MLD is the major indication of pediatric LT in Kuwait with high survival rates. Most MLD families prefer post-LT quality of life, but it is difficult to transfer several cases abroad especially those with no hepatic disease. A local LT center is highly recommended to tackle such a problem.

Acknowledgment: we acknowledge the patients' families for their support in the care of LT children during their difficult journey.

Key Words: Liver Transplant; Metabolic Liver Disease; Children;

Funding Agency: None

Pediatrics

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Early Diagnosis of Phenylketonuria (PKU) in Kuwait Through Newborn Screening: A 10-Year Experience

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Introduction:
Phenylketonuria (PKU) is a treatable autosomal recessive inborn error of metabolism caused by phenylalanine hydroxylase deficiency. Early detection and intervention are essential to prevent neurocognitive impairment. Kuwait's National Newborn Screening (NBS) Program has included PKU since its expansion in October 2014 as part of its core panel.

Methods:
A retrospective analysis of the data registry for the NBS was conducted over a 10-year period in Kuwait. Only dried blood spots (DBS) samples that showed elevated phenylalanine levels detected via tandem mass spectrometry were included. Amino acid analysis was performed using a triple quadrupole tandem mass spectrometer coupled with liquid chromatography-tandem mass spectrometry. Diagnosis was confirmed based on persistent plasma phenylalanine ≥150 µmol/L and a Phe/Tyr ratio >2.0.

Results:
A total of 504,531 newborns were screened during the 10-year period. Of 740 screen-positive cases, 31 were confirmed as true positive PKU, resulting in an overall incidence of 6.15 per 100,000 live births. Among these, 7 were Kuwaiti nationals, with a specific incidence of 2.30 per 100,000 Kuwaiti newborns. All Kuwaiti cases presented with mild hyperphenylalaninemia, either not requiring dietary intervention or shown to be responsive to sapropterin (BH4).The median age at NBS sampling was 3 to 5 days, with confirmatory diagnosis typically completed within two weeks. Initial phenylalanine concentrations ranged from 125 to 930 µmol/L, and Phe/Tyr ratios reached up to 4.8. Confirmatory plasma amino acid analysis supported all diagnoses. All affected infants born at ≥36 weeks gestation, supporting the reliability of early screening and biochemical markers in this cohort. Kuwaiti newborns had comparatively lower levels, and all presented with milder biochemical profiles.The positive predictive value (PPV) of the PKU screening algorithm was 4.2%.

Conclusions:
This 10-year national experience highlights the effectiveness of Kuwait's NBS program in early detection and management of PKU. All Kuwaiti cases presented with mild hyperphenylalaninemia.The observed low PPV emphasizes the need for optimizing recall criteria. Future improvements should focus on refining cutoff thresholds, implementing second-tier testing, and integrating molecular diagnostics to further enhance specificity and reduce false positives.

Funding Agency: None
Key Words: Phenylketonuria; Newborn Screening; Tandem Mass Spectrometry;

Pediatrics

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Types, Genotypic Spectrum, and Prevalence of Osteogenesis Imperfecta in the Kuwaiti Population: A National Registry-Based Study

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Introduction:
Osteogenesis Imperfecta (OI) is a rare connective tissue disorder characterized by increased bone fragility, recurrent fractures, skeletal deformities, and variable extraskeletal features such as dentinogenesis imperfecta and hearing loss. While the global prevalence is estimated at 1 in 15,000–20,000 live births, no prevalence data exist for Kuwait, where high consanguinity rates may increase the burden of recessive forms and founder mutations. Local molecular and epidemiological data are essential to improve diagnosis, management, and genetic counseling, and to prepare for emerging gene-targeted therapies.

Methods:
A retrospective chart review was conducted to identify all patients diagnosed with OI)in Kuwait using data from the Kuwait Medical Genetic Center (KMGC) between 2000 and 2025. All Kuwaiti and non-Kuwaiti patients with a clinically and molecularly confirmed diagnosis of OI were included, while cases lacking molecular confirmation or complete clinical documentation were excluded. Clinical and molecular data were extracted from medical records, including demographics, clinical features, OI classification, genetic variants, inheritance patterns, family history, and consanguinity. The clinical characteristics of OI subtypes in the Kuwaiti cohort were analyzed and compared with published regional data. No formal statistical testing was performed.

Results:
A total of 83 patients with OI were identified. The most frequently implicated genes were COL1A2 (51%) and COL1A1 (26%). Additional pathogenic variants were detected in WNT1 (8%), TMEM38B (4%), and several rare genes including SERPINF1, LEPRE1, CREB3L1, KIF5B, IFITM5, EFNB1, and IDS, demonstrating marked genetic heterogeneity.OI type IV was the most prevalent subtype (42%), followed by type I (23%), with multiple recessive and non-classical forms observed. Autosomal dominant inheritance was identified in 60 patients (74.1%), autosomal recessive inheritance in 12 patients (14.8%), X-linked inheritance in 1 patient (1.2%), while inheritance could not be clearly determined in 1 patient (1.2%). Positive family consanguinity was reported in 57% of cases.

Conclusions:
This is the first national study of OI in Kuwait, establishing a comprehensive registry to describe its clinical and molecular spectrum. The findings highlight the contribution of consanguinity and recessive inheritance to disease burden and provide a foundation for improved clinical care, genetic counseling, and readiness for future gene-based therapies.

Key Words: OI, Kuwait; Consanguinity; Genotype-phenotype correlation;

Funding Agency: None

Pediatrics

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Acute Soft Head Syndrome: A Paediatric Case Report and Clinical Framework for Management

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Introduction:
Background: Sickle Cell Disease (SCD) is a chronic, inherited blood disorder that affects millions worldwide, particularly in sub-Saharan Africa, the Middle East, and parts of India. It can lead to numerous complications due to the presence of haemoglobin S, affecting multiple organs. Common complications include vaso-occlusive pain crises and stroke. Rarer complications, such as Acute Soft Head Syndrome (ASHS) are often overlooked. ASHS is characterised by acute painful scalp swellings due to underlying subgaleal haemorrhage.

Methods:
Inpatient data was collected on a single patient. Written informed consent was obtained from our patient and his guardian prior to the inclusion of their data in this case report.

Results:
We describe a case of a 15 year old Kuwaiti male who presented with a two day history of headache associated with multiple scalp swellings and low grade fever. The patient had a background of sickle cell disease with a significant history of complications, including acute chest syndrome, stroke, splenectomy and osteomyelitis. The patient was found to have raised acute inflammatory markers and leucocytosis, as well as multiple subgaleal haemorrhages on neuroimaging, consistent with a diagnosis of ASHS. The patient was managed conservatively with empirical antibiotics as well as supportive hydration and pain management. Based on our case and similar cases of the literature, we present a proposed framework for the recognition and management of ASHS, as described in Figure 1 of the study.

Conclusions:
This case further draws the attention to ASHS as a potential differential diagnosis of painful scalp swellings in patients with SCD. Early recognition is crucial as most cases resolve with supportive treatment, thus preventing unnecessary medical intervention.

Key Words: Acute Soft Head Syndrome; subgaleal haematoma; sickle cell disease ;

Funding Agency: None funding

Pediatrics

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Phenylketonuria (PKU) in Kuwait: Insights from a 95-Patient Registry

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Introduction:
Phenylketonuria (PKU) is an autosomal recessive metabolic disorder caused by a deficiency of phenylalanine hydroxylase (PAH). If left untreated, elevated phenylalanine levels can lead to irreversible neurocognitive impairment. While Kuwait's National Newborn Screening (NBS) program has played a critical role in early detection, limited data exist on the long-term outcomes, treatment responses, and population-specific characteristics of patients with PKU. This study examines the clinical and demographic profiles of patients enrolled in the national PKU registry.

Methods:
A retrospective analysis was conducted using a de-identified registry of 95 patients with confirmed PKU who were followed at the Kuwait Medical Genetics Center. Collected data included age and mode of diagnosis, gender, nationality, treatment modalities (dietary management, sapropterin), and available neurodevelopmental outcomes.

Results:
The cohort consisted of 50 males and 45 females. Of the total, 24 patients (25.3%) were Kuwaiti nationals, while 71 (74.7%) were non-Kuwaitis, primarily from Syria, Egypt, Saudi Arabia, India, and Lebanon.A total of 31 patients (32.6%) were diagnosed via newborn screening (NBS), whereas the remaining 64 (67.4%) were diagnosed later through clinical presentation. Age at diagnosis ranged from 7 to 12 days in NBS-detected cases to 6 months and up to over 20 years in those diagnosed late, including adolescents and adults. Most patients were managed with dietary phenylalanine restriction. A small subset underwent trial therapy with sapropterin (BH4), although responsiveness data were incomplete. Preliminary developmental outcomes suggested better cognitive and academic performance among early-diagnosed and treatment-compliant individuals. However, neurodevelopmental documentation was inconsistently reported across the registry.

Conclusions:
This registry-based analysis underscores the vital impact of newborn screening (NBS) in enabling early diagnosis and better outcomes for individuals with PKU in Kuwait. The high proportion of late diagnoses, especially among non-Kuwaiti patients, highlights gaps in screening coverage for those born outside the country. Strengthening NBS programs across the MENA region and improving follow-up and developmental monitoring are essential steps toward ensuring timely care and improving long-term outcomes.

Key Words: PKU; genetics; Newborn Screening ;

Funding Agency: None

Pharmacology and Toxicology

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Unleashing the cardioprotective potential of berberine against doxorubicin cardiotoxicity: Innovative exploitation of the peculiar antipyroptotic/antioxidant/anti-inflammatory capacity via modulation of inflammasome/caspase-1/interleukin pathway in rats

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Introduction:
Doxorubicin (DXR) anthracycline has proven well-established chemotherapeutic efficacy against numerous malignancies. Nevertheless, its use is limited by the drug-induced irreversible cardiotoxicity. Berberine (BER) isoquinoline alkaloid is endowed with multispectral promising biological activities, namely, cardioprotective and anticancer effects. Pyroptosis, the lytic/inflammatory form of programmed cell death, has been implicated in DXR-provoked cardiomyopathy.

Methods:
This study inspected the protective role of BER in DXR-induced cardiotoxicity and its probable underlying molecular mechanism. Rats were treated with BER (50 and 100 mg/kg, p.o.) for 10 days. Cardiotoxicity was generated in rats by injecting DXR (22.5 mg/kg, i.p.) on the tenth day.

Results:
Elevated serum troponin I, creatine kinase and total lactate dehydrogenase were observed in DXR-challenged rats and was accompanied by detrimental hemodynamic and histopathological alterations. Moreover, DXR administration incited oxidative stress manifested by elevated MDA level and decreased GSH and SOD cardiac content. Parallelly, elevated inflammatory markers TLR4, NF-ƙBp65, caspase1, IL-18 and IL-1β cardiac protein contents was documented. Importantly, DXR administration significantly upregulated the pyroptotic markers, NADPH oxidase 4 (NOX4), dynamin-related protein 1 (DRP1), NOD-like receptor pyrin like protein 3 (NLRP3) and gasdermin-D (GASDMD) concurrently with the downregulation of nuclear factor erythroid 2-related factor 2 (NRF2). Of interest, berberine administration ameliorated the DXR-induced biochemical, hemodynamic and histopathological deleterious changes. Furthermore, berberine effectively hampered DXR-provoked oxidative stress, inflammation and pyroptotic cell death.

Conclusions:
The cardioprotective effect of berberine was partly attributed to its suppressive action on the DXR-triggered Nrf2/NLRP3/Caspase-1/GSDMD pyroptotic pathway, as well as its antioxidant and anti-inflammatory capacities.

Key Words: Doxorubicin Berberine Pyroptosis GASDMD NOX4 DRP1; pyroptosis; NOX4;

Funding Agency: None

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1,2,4-Triazole Derivatives: Synthesis, Characterization, In-Silico Investigation, Anti-Cancer, and Anti-Microbial Activities

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Introduction:
The triazole nucleus is an important heterocyclic compound known for its diverse pharmaceutical properties, including antimicrobial, anti-inflammatory, antiepileptic, antiviral, antineoplastic, antihypertensive, and anticancer activities. Continuous research seeks to design new triazole derivatives with enhanced biological potential. This study aimed to synthesize novel 1,2,4-triazole derivatives, characterize them using advanced analytical techniques, and evaluate their anticancer and antimicrobial activities both experimentally and computationally.

Methods:
New 1,2,4-triazole derivatives were synthesized and characterized using mass spectrometry, ^1H NMR, ^13C NMR, FTIR, and X-ray single-crystal analysis (for agent 4f). Particle size and morphology were measured, and agents were encapsulated into nano-LDL particles to enhance intracellular delivery via lipid metabolic pathways. Biological evaluation was conducted against breast (MDA468) and prostate (DU145) cancer cell lines. In-silico molecular docking was performed to predict binding affinities toward β-tubulin and HER2 receptors. Antimicrobial screening was carried out using gram-positive, gram-negative, and fungal strains at 1 µg/mL.

Results:
All synthesized triazole derivatives exhibited nanoscale size, which increased after LDL encapsulation. Agent 4f demonstrated the highest cytotoxic activity toward MDA468 and DU145 cell lines (IC_{50} = 1.23±0.18 µM and 1.20±0.78 µM, respectively). Western blot analysis revealed that cancer cell death occurred through inhibition of β-tubulin in MDA468 and both β-tubulin and HER2 receptors in DU145. Docking studies supported these findings, showing that compound 4f achieved a binding score of –5.9 kcal/mol compared to doxorubicin (–6.8 kcal/mol). Additionally, compounds 4g and 4h showed potent antifungal activity against Candida albicans, confirmed by docking scores comparable to the co-crystallized ligand 4C7 (–5.5 vs. –5.3 kcal/mol).

Conclusions:
The synthesized 1,2,4-triazole derivatives demonstrated strong anticancer and antimicrobial activities, with agent 4f exhibiting the most promising therapeutic potential. The combination of chemical synthesis, LDL-based drug delivery, biological testing, and in-silico modeling provides an integrated strategy for designing future triazole-based drugs.

Key Words: Triazole derivatives; Candida albicans; Invitro ; In-silico study and Molecular

Funding Agency: This work was supported and funded by Kuwait University, Research Grant No. (SC03/23).

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Proteomic Network Analysis Reveals PPARγ Antagonism Restores Mitochondrial and DNA Repair Pathways in Pioglitazone-Treated Cardiomyocytes

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Introduction:
Pioglitazone (PGZ) is an insulin sensitiser used in type II diabetes but has been associated with an increased risk of heart failure. Previous studies demonstrated that PGZ disrupts cardiomyocyte bioenergetics, with partial restoration of ATP levels observed following co-treatment with the PPARγ antagonist GW9662. However, the molecular mechanisms underlying this rescue remain unclear. Accordingly, this study aimed to elucidate the proteomic pathways involved in antagonist-mediated rescue in cardiomyocytes.

Methods:
LC-MS-based proteomic profiling was performed in human AC16 cardiomyocytes using a three-arm design: untreated control cells, cells treated with PGZ (2 μM; IC_{50}), and cells treated with PGZ (2 μM) plus GW9662 (5 μM). Cells were treated for 24 hours, with nine biological replicates per condition (n = 9). Raw data were processed using Proteome Discoverer, and proteins were classified according to their fractional rescue behaviour, defined by the relative change from PGZ treatment to the combination treatment compared with the change from control to PGZ. This enabled assignment into rescue categories including true rescue, over-rescue, independent antagonist, and no rescue. WGCNA was then applied to identify protein modules associated with antagonist-mediated rescue, followed by pathway enrichment analysis to elucidate the underlying mechanisms.

Results:
Module-trait profiling revealed a yellow module with a significant positive correlation to the rescue condition ($r \approx 0.6$), which was selected for pathway interrogation. Enrichment analysis of this module revealed a pronounced restoration of mitochondrial bioenergetics, driven by coordinated upregulation of ATP synthase and respiratory chain proteins, exemplified by increased expression of catalytic ATP synthase subunits, including ATP5F1A. In parallel, significant enrichment of DNA repair-related processes was observed, including proteins involved in DNA replication fidelity and genome maintenance, with RFC4 detected as a representative component of replication-coupled DNA repair and mismatch repair pathways.

Conclusions:
These findings indicate that PPARγ antagonism effectively reverses key PGZ-induced disturbances in cardiomyocytes, not only restoring cellular ATP production but also reactivating DNA repair and mismatch repair pathways to recover genomic stability impaired by PGZ exposure. This coordinated rescue provides a mechanistic basis for mitigating the adverse cardiac effects associated with PGZ treatment.

Key Words: Cardiotoxicity ; PPARγ antagonism; Proteomics;

Funding Agency: None

Pharmacology and Toxicology

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Investigating the Impact of Binding Kinetics on Biased Signalling at GLP-1R

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Introduction:
Tirzepatide is a dual-GIP/GLP-1 receptor agonist that has demonstrated superior efficacy for weight loss and glycemic control compared to mono-GLP-1R agonists. The contribution of GIPR activation, if any, to this superior efficacy is currently unknown. Tirzepatide also acts as a partial agonist at GLP-1R compared with GLP-1 in terms of G protein signalling and is reported to cause less receptor desensitization and internalization than GLP-1, which may, at least in part, explain this superior efficacy. This project aimed to investigate the binding kinetics and signalling properties of the non-lipidated precursor of tirzepatide (NLT) compared to native GLP-1 at GLP-1R.

Methods:
G protein and arrestin recruitment to GLP-1R, as well as agonist-mediated receptor endocytosis, were assessed using BRET-based methods. Binding assays were performed using HEK-293 cells stably expressing Nluc-GLP 1R and fluorescently labelled LUXendin645. The affinities of GLP-1 and NLT were calculated using the Cheng-Prusoff method, and association and dissociation rates were calculated using the Motulsky-Mahan method.

Results:
NLT recruited mini-Gs to GLP-1R with a lower Emax (P=0.037) than GLP-1. Unlike GLP-1, NLT-mediated arrestin recruitment to GLP-1R was undetectable, and NLT-stimulated receptor endocytosis occurred at a slower rate (P=0.026) and to a lesser extent (P=0.0049) than GLP-1. In contrast, NLT had a higher affinity (P=0.0005) for Nluc-GLP-1R than for GLP-1. There was no difference in their dissociation rates; however, NLT's association rate was faster (P=0.0008) than that of GLP-1. All experiments were performed in duplicate and repeated at least three times independently.

Conclusions:
NLT is a G protein-biased agonist at GLP-1R and a partial agonist in terms of G protein recruitment relative to native GLP-1. A faster rate of association drives NLT's higher affinity for Nluc-GLP-1R relative to GLP-1.

Key Words: GPCR; GLP-1; Cell Signalling;

Funding Agency: General Facility KU Projects GM 01/15 and SRUL02/13

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Metabolomic Profiling Reveals PPARγ Antagonism Restores Carnitine Shuttle and Redox Balance in Pioglitazone-Treated Cardiomyocytes

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Introduction:
Pioglitazone (PGZ), an insulin-sensitising agent used in type II diabetes, has been linked to adverse cardiac effects. Previous metabolic studies showed that PGZ disrupts cardiomyocyte bioenergetics by impairing the carnitine shuttle and inducing oxidative stress, with partial ATP restoration observed following co-treatment with the PPARγ antagonist GW9662. However, the mechanisms underlying this rescue remain unclear. Therefore, this study aimed to elucidate the metabolic basis of this antagonist-mediated rescue.

Methods:
LC-MS-based metabolomic profiling was performed in human AC16 cardiomyocytes using a three-arm design: untreated control cells, PGZ-treated cells (2 μM; IC_{50}), and cells treated with PGZ (2 μM) plus GW9662 (5 μM). Cells were treated for 24 hours, with six biological replicates per condition (n = 6). Raw data were processed using Compound Discoverer, and metabolites were classified according to their fractional rescue behaviour, defined by the relative shift from PGZ treatment to the combination treatment compared with the shift from control to PGZ. Metabolites were assigned to rescue categories including true rescue, over-rescue, independent antagonist, and no rescue. WGCNA was then applied to identify co-regulated metabolite modules associated with antagonist-mediated rescue, and pathway enrichment of these modules was performed to delineate the metabolic mechanisms underlying the rescue effect.

Results:
WGCNA module-trait profiling identified a brown module with a significant positive correlation to the PGZ+GW9662 rescue condition and an inverse correlation to PGZ alone ($r \approx 0.98$). Metabolites in this module were unchanged or reduced by PGZ but markedly increased with antagonist treatment. Key rescuing metabolites included several acylcarnitines, indicating restoration of the carnitine shuttle and β-oxidation, as well as amino acids such as valine, histidine, and dipeptides including Asp-Leu and Gly-Phe, suggesting improved amino-acid metabolism and anaplerotic support. Elevated ascorbic acid and related molecules further pointed to enhanced antioxidant capacity and attenuation of PGZ-induced oxidative stress.

Conclusions:
Collectively, these findings demonstrate that PPARγ antagonism mitigates PGZ-induced metabolic disturbances in cardiomyocytes by restoring mitochondrial fatty-acid oxidation, supporting amino-acid metabolism, and reinforcing antioxidant defences, providing a mechanistic basis for the observed bioenergetic rescue.

Key Words: Cardiotoxicity ; PPARγ antagonism; Metabolomics;

Funding Agency: None

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Investigation of the Vasoprotective Effects of the H2S Donor GYY4137 and the Possible Dependency on ACE2/Ang-(1-7)/Mas Receptor Pathway of the Renin Angiotensin System in a Murine Model of Streptozotocin-Induced Diabetes Mellitus.

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Introduction:
It is well known that the gasotransmitter hydrogen sulfide (H2S) prevents the vascular dysfunction observed in several pathologies. The main mechanism for this beneficial effect has not been fully characterized, especially in the context of diabetes. The possible interaction of H2S with the renin angiotensin system (RAS) and the modulation of its various effector enzymes and receptors have been poorly understood. Therefore, the aim of this study is to investigate the vasoprotective effects of GYY4137, a slow-releasing H2S donor, and the possible dependency on the angiotensin converting enzyme (ACE) type 2 (ACE2)/angiotensin-(1-7) (Ang-(1-7))/Mas receptor pathway of the RAS (using the Mas receptor antagonist A779) in a murine model of streptozotocin-induced diabetes mellitus.

Methods:
Measurements of: 1) blood glucose, angiotensin II (Ang II) and Ang-(1-7) levels; 2) ACE and ACE2 protein expression and enzyme activity; 3) vascular response to pharmacological stimulation; and 4) fibromuscular tissue structural changes in isolated mesenteric vascular beds from diabetic Wistar rats.

Results:
Significant improvement in vascular response was observed in GYY4137-treated diabetic animals (n=18-20 animals per group). This protection was reduced when Mas receptors were blocked with A779.

Conclusions:
GYY4137 protective effects are dependent, at least in part, on Mas receptors pathway of RAS. Findings from this study may help identify potential novel strategies for treatment or prevention of diabetic complications and reduction of cardiovascular risk. This study is granted the ethics committee approval # PF-24-19.

Key Words: Hydrogen sulfide ; Diabetes ; cardiovascular ;

Funding Agency: Research Sector, Kuwait University. Project Number PT01/24

Pharmacy

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Multiple low doses of streptozotocin induce glucose intolerance in female BALB/c mice

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Introduction:
Streptozotocin (STZ) is used to induce diabetes in research. BALB/c mouse strain shows low sensitivity to STZ, with female mice showing greater resistance. Thus, we assessed the effect of different multiple low doses (MLD) protocols of STZ on inducing diabetes in female BALB/c mice.

Methods:
MLD (50 mg/kg) of STZ were administered once daily to female BALB/c mice for 2, 3, 4 or 5 consecutive days. Mice were distributed into 5 groups (n=67). Group 1 (vehicle n=13), group 2 (2 days n=13), group 3 (3 days n=12), group 4 (4 days n=16), and group 5 (5 days n=13). The experimental animals were handled in accordance with the regulations of the Ethical Committee in the Health Sciences Centre, Kuwait University (Ethical approval no. PF-25-23). Random (RBG), fasting (FBG) blood glucose, food intake, and body weight were measured to assess the effect of STZ. Oral and intraperitoneal (IP) glucose tolerance tests (GTT) were done. Plasma insulin and total pancreatic insulin content were assessed by enzyme-linked immunosorbent assay. All data except pancreatic insulin content and plasma insulin levels were normally distributed so one- or two-way analysis of variance followed by Tukey's or Dunnett's multiple comparisons tests were used for statistical analysis. Kruskal-Wallis test followed by Dunnett's test for multiple comparisons were used for pancreatic insulin content and plasma insulin levels. $p < 0.05$ indicated a significant difference between the groups.

Results:
4 or 5 doses of STZ showed an increase in RBG on day 9 post first injection (pfi) of STZ. FBG significantly increased on day 10 pfi with 4 and 5 doses, and on day 45 pfi with 3 doses. The response to GTT was dose-dependent, where glucose intolerance was observed on day 10 pfi in IPGTT with 4 and 5 doses, and only with 5 doses in oral GTT. The effect of STZ on total pancreatic insulin content was dose-dependent, where longer treatments lowered insulin concentrations. Food intake increased significantly only in week 2 with 4 and 5 doses of STZ. However, body weight and plasma insulin levels showed no significant difference.

Conclusions:
Longer durations of MLD of STZ can induce glucose intolerance in female BALB/c mice. RBG, FBG, and GTT can be used for early glucose intolerance screening, whereas total pancreatic insulin content can be used to detect changes in insulin levels.
Acknowledgment: This project was funded by Kuwait University College of Graduate Studies and Research Sector grant #YP03/24.

Key Words: streptozotocin; BALB/c; diabetes mellitus;

Funding Agency: College of Graduate Studies, Kuwait University, and Research Sector, grant number #YP03/24.

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The Metabolic Response of Triple Negative Breast Cancer Cells to Capecitabine.

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Introduction:
Triple-negative breast cancer (TNBC) is a biochemically heterogeneous and highly aggressive subtype lacking oestrogen, progesterone, and HER-2 receptors. Absence of targeted therapies, high recurrence rate, and poor survival classifies TNBC as a challenging disease, mainly affecting women under the age of 40 years, presenting with invasive tumours and early metastasis. To explore potential treatment targets, we performed an untargeted metabolomics analysis of the metabolic response of TNBC cells in comparison to non-TNBC cells after treatment with capecitabine, a cytotoxic agent that inhibits thymidylate synthase and disrupts DNA synthesis.

Methods:
MCF-7, MDA-MB-231, BT-20, and BT-549 cells were exposed to increasing concentrations of capecitabine, and cell viability was assessed using an MTS assay to determine IC_{50} values. Cells were then treated at their respective IC_{50} doses for 4 days and analysed by untargeted metabolomics using a UHPLC-MS. Principal component analysis assessed global clustering patterns between treated and control groups. Volcano plots identified significantly altered metabolites (fold change > 1.5 and p-value < 0.05). Finally, MetaboAnalyst 5.0 was used for pathway enrichment analysis (FDR-adjusted p-value < 0.05 and/or pathway impact > 0.1).

Results:
Capecitabine reduced cell viability in a dose-dependent manner, with IC_{50} values of 15 µM (MCF-7), 1.96 µM (MDA-MB-231), 18.3 µM (BT-20), and 30 µM (BT-549). Significantly altered amino acid across all cell lines included arginine, aspartate, and glutamate metabolism. Citrate cycle was a main alteration in BT-549 cells, whereas BT-20 cells showed changes specifically in phenylalanine, tyrosine, glyoxylate and dicarboxylate metabolism. Butanoate and nitrogen metabolism were altered in MDA-MB-231 and MCF-7 cells, respectively. Histidine metabolism was altered in all cell lines except MCF-7, while altered vitamin B6 metabolism was specific to MCF-7 cells.

Conclusions:
Capecitabine induced broad amino acid perturbations, suggesting increased metabolic demand to compensate for impaired DNA synthesis. Citrate cycle alterations supported the shift of glucose metabolism of TNBC cells toward aerobic glycolysis. Metabolic profiling revealed distinct signatures across breast cancer subtypes, highlighting potential biomarkers and therapeutic targets for future validation.
Acknowledgments: Lab of Complex Bioanalysis, University of Strathclyde and College of Pharmacy, Kuwait University.

Key Words: Breast cancer; Metabolomics; TNBC;

Funding Agency: None

Pharmacy

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Development of the Kuwait National Prescribing Competency Framework - A Pilot study

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Introduction:
The practice of prescribing safely and effectively is a challenge to prescribers, especially when prescribing for people with numerous chronic co-morbidities and a complicated dosage regimen of multiple medications. Prescribers are expected to master prescribing competencies that extend beyond the identification of an appropriate medicine for an individual patient. The need to standardize care by healthcare professionals to offer reliable quality care has been repeatedly expressed, particularly with the shift in the models of care delivery in many countries to include other healthcare professionals in prescribing. Development of a prescribing competency framework, with a generic patient-centered set of competencies, will support prescribers at all levels and will standardize prescribing in the wider context. Objective: This study used an adopt and adapt methodology to develop a country specific prescribing competency framework for Kuwait, to ensure safe and effective prescribing for all patients in Kuwait.

Methods:
This study outlines the first 2 phases of this approach, the translation and the validation of standards using a 2 round e-Delphi method followed by two focus group discussions, and a pilot survey. Qualitative data were thematically analyzed, while quantitative data were analyzed descriptively using Microsoft Excel.

Results:
The translation phase yielded a bilingual framework, with two domains and 7 Competency areas. The 2 rounds of e-Delphi resulted in total consensus for Competency Areas 1, 4, 5, and 6, and the removal of one statement from Competency areas 3 and 7. The focus group interviews confirmed clarity on the translation of the standards and their relevance to Kuwait. A pilot study was conducted on 31 healthcare professionals to assess content validity. Two methods (I-CVI and the modified Kappa) were used to quantify content validity. This resulted in 1 standard being removed and 2 standards being merged.

Conclusions:
This study presents the first draft of a country-specific bilingual (Arabic/English) prescribing competency framework. The competency framework developed will be administered as a national survey to assess the relevance of standards to the Kuwaiti setting. The final prescribing competency framework can be used by medical educators in under and post graduate training to harmonize education for prescribers at any stage in their career, and by professional regulators to ensure prescribers adhere to standardized competencies when prescribing.

Key Words: Prescribing; Rational use of medicines; Competency;

Funding Agency: Kuwait Foundation for the Advancement of Sciences - PO23-13NH-1834

Pharmacy

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Isolation and Evaluation of the Sesquiterpene Carotol as a Potential CYP450 Enzymes Inhibitor and Antioxidant Agent.

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Introduction:
Natural products have long been used as medicines and remain an important source of modern drugs. Recently, interest in natural products has increased because of their safety and environmental compatibility. Essential oils from plant roots contain many bioactive compounds, especially terpenoids, which are known for their antioxidant, anti-inflammatory, antimicrobial, and anticancer activities. Carrot seed essential oil is a rich source of carotol, a sesquiterpene alcohol with potential biological activity. In addition, some terpenoids are known to inhibit CYP450 metabolic enzymes, suggesting that carotol may have similar effects.

Objectives: The objectives of this study is to extract, isolate, purify carotol from carrot seed oil, and to evaluate its potential antioxidant activity and CYP450 metabolic enzyme inhibition effects.

Methods:
Carotol was extracted from carrot seed essential oil and purified using preparative high-performance liquid chromatography. Furthermore, three microbial metabolites of carotol were obtained using *Absidia coerulea* ATCC 6647 culture. The identities of carotol and its metabolites were confirmed using different spectral techniques including IR, MS and 1D and 2D NMR. The purified carotol and its metabolites were evaluated in vitro using commercial assay kits for its antioxidant activity and its inhibitory effects on CYP450 metabolic enzymes.

Results:
Carotol was successfully isolated and its metabolites were prepared and isolated. Carotol and its metabolites have shown mild antioxidant activity at micromolar range, and it is anticiapted to have potential inhibitory effects on CYP450 enzymes.

Conclusions:
Carotol emerges as a promising natural compound exhibiting notable antioxidant and enzyme inhibitory activities. These findings highlight its potential relevance in natural medicine and contribute to a deeper understanding of terpenoid-based bioactive compounds.

Key Words: Natural products ; Carotol; Antioxidants;

Funding Agency: This work was funded by the College of Graduate Studies and Research Sector (YP01/25). Spectral analyses were done at RSPU, Research Administration, Kuwait University, supported by Grant numbers GS01/01 and GS01/03.

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Micro-costing of Dialysis in Kuwait

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Introduction:
Background End-stage renal disease (ESRD) imposes substantial economic burden on healthcare systems globally. Understanding dialysis costs in Kuwait is essential for healthcare policy and resource allocation given increasing chronic kidney disease prevalence.
Objectives: To estimate the economic burden of hemodialysis (HD) and peritoneal dialysis (PD) from the healthcare provider perspective in Kuwait by calculating average cost per dialysis session.

Methods:
A comprehensive micro-costing analysis assessed average cost per dialysis session across direct medical costs (consumables, medications, laboratory tests, staff time), capital costs (machines, water treatment systems, building infrastructure), and utilities/overheads (electricity, water, maintenance, administration). The analysis included 500 HD and 180 PD patients at a major dialysis center. HD utilization was modeled at 156 sessions/year (3 sessions/week); PD at 365 sessions/year (daily). Data sources included Ministry of Health procurement records, healthcare professional interviews, and technical specifications. Capital costs were annuitized using 3% discount rate per international pharmacoeconomic guidelines.

Results:
HD cost 162–225 KWD per session versus 56.5 KWD for PD. Direct medical costs dominated both modalities: 57–69% of HD costs and 82% of PD costs. HD consumables and medications alone reached 92–155 KWD per session, with labor at 46 KWD. Machine depreciation and maintenance were comparable (≈3 KWD per session). Annual per-patient costs were projected at 25,000–35,000 KWD for HD and 20,600 KWD for PD. Infrastructure costs included water treatment (12,200 KWD initial setup, 1,220 KWD annually) and 4.6-5.0 million KWD for a 20,000 m² facility. Kuwait's HD costs (216 KWD/$720 per session) exceeded global averages (US$368), while PD costs (54 KWD/$180) were lower than global averages (US$318). HD annual expenses exceeded PD by 11-33%, consistent with international patterns.

Conclusions:
This first comprehensive micro-costing of dialysis in Kuwait identifies the main cost drivers. HD's higher per-session costs are mostly due to consumables, medications, and staffing. Although PD has a lower cost per-session, it has a higher treatment frequency, resulting in comparable annual costs. These findings offer crucial insights for healthcare policy and resource allocation, providing a framework for economic studies in other Gulf Cooperation Council countries.

Key Words: End Stage Kidney Disease; Hemodialysis - Peritoneal dialysis ; Micro-costing;

Funding Agency: None

Pharmacy

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Discovery of betulin diacetate as a potent monoacylglycerol lipase inhibitor: Using in silico, in vitro and in vivo techniques

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Introduction:
Triterpenes are secondary plant metabolites with pharmacological activity. Pristimerin was the first triterpene identified as a monoacylglycerol lipase (MAGL) inhibitor. MAGL inhibitors alleviate neuropathic pain induced by chemotherapeutic drugs such as paclitaxel. Aims: To find new triterpenes as MAGL inhibitors effective in preventing development of paclitaxel-induced mechanical allodynia (PIMA).

Methods:
300 triterpenes found in various databases and literature, with 3D structure on PubChem database, were docked to MAGL using CB-Dock 2. Triterpenes which had docking Vina scores lower than pristimerin were tested in vitro against recombinant human MAGL,using MAGL inhibitor screening assay kit. The most potent compound was tested on mouse paw skin ex vivo, using MAGL activity assay kit, and administered to female BALB/c mice before paclitaxel for five days. The development of PIMA was assessed using the dynamic plantar aesthesiometer. The animal experiments was approved by the Ethical Committee for the use of Laboratory Animals in Research, Health Science Centre,Kuwait University. Study ethical approval # PF -25-24. Statistical analyses were performed using one-way or two-way ANOVA using GraphPad Prism software.

Results:
The order in terms of affinity (lower Vina scores in kcal/mol) in molecular docking were betulin diacetate (-14.1) > acetoxyganoderic acid (-11.8) > celastrol (-11.6) > oxopristimerol (-11.5) > pristimerin (-11). In vitro betulin diacetate was the most potent in inhibiting recombinant human MAGL with an IC50 of 48.87 pM (n=5; $p < 0.05$) as compared to 54.37 nM for pristimerin (n=7), 88.6 nM for celastrol (n=7). 12β-acetoxyganoderic acid (n=3) and oxopristimerol (n=5) inhibited MAGL but not in a concentration-dependent manner. Betulin diacetate test (n=5) inhibited MAGL activity in the mice paw skin significantly ($p < 0.05$) and in a concentration-dependent manner. Betulin diacetate prevented the development of PIMA in a dose-dependent manner ($p < 0.05$, n = 6-9 mice per group).

Conclusions:
Betulin diacetate is a potent MAGL inhibitor, about 1000 times much more potent than pristimerin ($p<0.05$; IC50 of 48.87 pM vs 54.37 nM) in vitro, and it prevented the development of PIMA ($p < 0.05$, compared to vehicle and baseline) in a dose-dependent manner.
Acknowledgments: This work was supported by the CGS and KURS, project YP04/24. We thank Simran,Rania and the staff from the Animal Resources Centre, Kuwait University for their support.

Key Words: Triterpenes; betulin diacetate; pristimerin; monoa; molecular docking; paclitaxel-

Funding Agency: This work was supported by the CGS and KURS grant number is YP04/24.

Pharmacy

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Use of Voriconazole in Treatment of Invasive Fungal Infections in Tertiary Care Centers in Kuwait

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Introduction:
Immunocompromised patients are highly susceptible to invasive fungal infections (IFIs), which significantly contribute to mortality and morbidity. Voriconazole (VCZ), a triazole antifungal agent, is widely used for the treatment of fungal infections including Candida and Aspergilus species. However, data on its clinical outcome in immunocompromised patients remain limited globally and nationally. The aim of this study was to assess the effectiveness and safety of VCZ in the management of proven, probable, and possible fungal infections in immunocompromised patients.

Methods:
An observational retrospective study was conducted in three tertiary hospitals in Kuwait: two specialized hematology/oncology centers and one specialized solid-organ transplantation center. Ethical approval was obtained from the health science center of Kuwait university and the Ministry of Health Students' committee (No: 1625/2024). Patients who received VCZ for treatment (not prophylaxis) of IFIs from September 2023 to September 2024 were included. Primary outcomes were clinical cure at weeks 6 and 12 of therapy, and the incidence of hepatotoxicity during treatment. Secondary outcomes were achievement of VCZ therapeutic target concentration (≥1-5.5 mg/L). Descriptive statistical analysis was conducted using Microsoft Excel.

Results:
A total of 91 patients were reviewed, and 31 patients (16 pediatrics and 15 adults) were included for analysis. The IFIs were classified as proven in 15 patients (48.4%), probable in 11 patients (35.4%), and possible in 5 patients (16.1%). Candida albicans was the most frequently isolated fungus (32.2%), followed by Aspergillus fumigatus (9.7%) and Trichosporon asahii (6.5%). The overall clinical improvement was documented in 71% (n= 22 out of 31) of patients by week 6, and 75% (n=3 out of 4) by week 12. Hepatotoxicity occurred in 10 patients (32%). Measurement of VCZ levels was done in four patients, with three levels were within the therapeutic range.

Conclusions:
VCZ demonstrated moderate effectiveness in the treatment of IFIs among immunocompromised patients. However, the incidence of hepatotoxicity is of concern and requires attention and monitoring. VCZ monitoring was underutilized during the study period. This calls to raise awareness about importance of voriconazole routine VCZ monitoring to optimize therapeutic response and minimize toxicity.

Key Words: Voriconazole ; Invasive fungal infections; Immunocompromised patients;

Funding Agency: None

Pharmacy

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Knowledge, Attitude and Practices (KAP) about Vaccines among students in the Health Sciences Faculties in Kuwait

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Introduction:
Background: Vaccination remains one of the most effective public health interventions, yet hesitancy persists even among healthcare students who aid in promoting immunization. Understanding students' perspective plays a crucial role in designing targeted educational interventions. The purpose of this study was to evaluate knowledge, attitude, and practices of healthcare students (HSCs) in Kuwait about vaccines.

Methods:
A quantitative, cross-sectional study was conducted between August and October 2024. A validated 21-item questionnaire was used to assess vaccine-related knowledge, attitude, and practices, along with demographic data. Descriptive statistics and binary logistic regression were used to identify predictors of higher knowledge and positive attitude.

Results:
A total of 351 students participated (mean age 23.0 ± 2.4 years; 90.6% female). The mean knowledge score was 3.9/7 (55.7%), indicating moderate knowledge, with misconceptions noted regarding benefits of post-infection vaccination and extra vaccine doses. The mean attitude score was 3.6/6 (60%), indicating moderately positive attitude, yet safety concerns, particularly about long-term effect, were common (59.3%). Nearly half (45.9%) delayed vaccination until mandatory. Vaccine uptake was highest for COVID-19 (92.3%), followed by hepatitis B (73.8%). Older age, male gender, and being a medical student predicted higher knowledge ($p = 0.011$), while older age and being in later study years predicted more positive attitude ($p = 0.032$).

Conclusions:
HSCs demonstrated moderate knowledge and attitude toward vaccines, with significant hesitancy driven by safety concerns despite high eventual uptake. Early targeted curricular interventions addressing vaccine safety evidence, benefits of timely immunization, and professional responsibility are warranted to improve confidence and proactive vaccine acceptance among future healthcare professionals (HCPs).

Key Words: Kuwait; health sciences students; vaccines; hesitancy; knowledge; attitude; practice;

Funding Agency: N/A

Pharmacy

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Increased Monoacylglycerol Lipase Activity in the Periphery, But Not in the Central Nervous System, is a Druggable Target for Chemotherapy-induced Neuropathic Pain

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Introduction:
Monoacylglycerol lipase (MAGL) inactivates the endocannabinoid 2-arichodonoylglycerol (2-AG). Previously, we observed that 2-AG levels were reduced and MAGL activity was increased in paw skins of mice with paclitaxel-induced mechanical allodynia (PIMA). However, whether other chemotherapeutic drugs affect MAGL activity and in the central nervous system during chemotherapy-induced neuropathic pain (CINP) is not known.
Objectives: To evaluate whether another chemotherapeutic drug, bortezomib, affect MAGLactivity in the paw skin and whether both paclitaxel and bortezomib affect MAGL activity in the spinal cord and brain.

Methods:
Female BALB/c mice, ethical approvals (Ref: 5025, Date 11/5/2023 and #PF -25-29), were treated intraperitoneally with chemotherapeutic drugs, paclitaxel and bortezomib, and development of mechanical allodynia was assessed using an aesthesiometer. Control animals were administered drug vehicles. MAGL protein expression was measured using Wes™, in the brain, spinal cord and paw skin, of mice with PIMA or bortezomib-induced mechanical allodynia (BIMA). MAGL enzyme activity in mouse tissues was measured using the MAGL Activity Fluorometric assay. Statistical analyses were performed using Kruskal-Wallis test, one-way or two-way ANOVA using GraphPad Prism software.

Results:
MAGL protein expression was increased in brains ($p < 0.05$; $n = 16$), but not in spinal cords ($n = 5$) or paw skins ($n = 6$-7), of mice with PIMA ($n = 5$-8). There was no change in MAGL protein expression in the three tissues of mice with BIMA ($p > 0.05$, $n = 4$-7). MAGL enzyme activity was increased only in paw skins ($p < 0.05$), but not in spinal cords or brains, of mice with PIMA ($n = 7$-8) or BIMA ($n = 3$-5). Pristimerin, a MAGL inhibitor, prevented development of PIMA and MAGL activity ($p < 0.05$; $n = 7$-8). JZL184, another MAGL inhibitor, prevented development of BIMA ($p < 0.05$, $n = 7$).

Conclusions:
Chemotherapy drugs like paclitaxel and bortezomib cause mechanical allodynia and increase MAGL activity specifically in the paw skin, possibly leading to reduced 2-AG levels in peripheral tissues but not in the spinal cord or brain. Thus, increased MAGL enzyme activity in the periphery, paw skin, but not in the CNS, is a pathophysiological feature of CINP, which can be targeted by drug treatment to alleviate CINP.
Acknowledgements: This work was supported by grant PT02/23. We thank Aisha Albaloushi, Amal Thomas, Esraa Aly, and Liny Jose for technical assistance with the experiments, the staff from the Animal Resources Centre, HSC, Kuwait University for their support.

Key Words: Monoacylglycerol lipase (MAGL); 2-arachidonoyl glycerol (2-AG); Chemotherapy-

Funding Agency: KUWAIT UNIVERSITY PT02/23

Physiology

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Effects of IL-6 on the Microglia Density and Morphology in the Prefrontal Cortex and the Hippocampus of Maternally Immune Challenged Rats: A Sex Dependent Effect.

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Introduction:
Exposure to pathogens such as bacterial lipopolysaccharide (LPS) during pregnancy has detrimental impacts on the developing fetal brain, likely through long-lasting alterations on fetal microglial activity. We sought to investigate the effects of maternal exposure to LPS on the microglia density and morphology in the prefrontal cortex and hippocampus of juvenile rats, and to assess whether interleukin-6 (IL-6) contributes to such effects.

Methods:
All experiments were approved by Kuwait University Health Science Center animal ethics committee. Pregnant rats were given intraperitoneal injections (on gestation days 15, 17, and 19) of either pyrogen-free saline or LPS (100 µg/Kg) in the presence or the absence of an IL-6 neutralizing antibody (IL-6Ab, 10 µg/Kg). Each group consists of 5-6 rats. Immunofluorescent staining of microglia marker (Iba1) was performed on the brains of male and female rat offspring at postnatal day 30. A series of z-stack confocal microscopy images were collected from the prefrontal cortex and hippocampal subregions and analyzed using Sholl analysis software in MATLAB. All data were compared using two-way ANOVA followed by Bonferroni post-hoc test. Statistical significance is declared when p-value was less than 0.05.

Results:
Maternal exposure to LPS induced a significant increase in microglial cell density in the CA3 region of the hippocampus in male rat offspring and a significant decrease in microglial cell density in the CA1 region in female rat offspring ($p<0.05$). However, LPS did not significantly alter microglial density in the prefrontal cortex of either male or female rat offspring. Maternal exposure to LPS induced a significant increase in branching complexity indicated by Sholl analysis in all hippocampal regions of female rats and selective regions (CA1 and CA3) in male rat offspring ($p<0.05$). These changes in microglial cell density and morphology were reversed when the IL-6Ab was prenatally co-administered with LPS.

Conclusions:
Maternal exposure to LPS reduced microglial cell density in the CA1 region in female and increased it in the CA3 region in male rat offspring hippocampi. Maternal LPS altered microglia branching complexity in female rat hippocampi. These effects were not observed when IL-6Ab was co-administered with LPS. Future explorations are needed to address the functional significance of these findings.
Acknowledgements: Animal Resources Centre and Research Core facility.

Key Words: Maternal Immune Activation; Microglia; Sholl Analysis;

Funding Agency: None

Physiology

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Multiparity Enhances Remyelination and Preserves White Matter Integrity in the Aging Female Rat Brain

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Introduction:
Aging is associated with a decline in myelin integrity and a reduced capacity for remyelination. The effect of reproductive experience on white matter repair processes remains unclear. In this study, we investigate the effect of multiparity on age-related decline in white matter integrity and remyelination capacity.

Methods:
Sprague Dawley rats were obtained from the Animal Resources Centre, Faculty of Medicine, Kuwait University. Rats were divided into 3 groups: Multiparous female rats that delivered 9-10 litters (MP-O), age-matched females (18 months-old) with no reproductive experience (Vir-O) and 3 months-old virgin females (Vir-Y). Rats underwent stereotaxic surgery to induce demyelination in their corpora callosa in the left side of the brain by injecting the demyelinating agent lysolecithin. The corpora callosa in the right side of the brain were collected to serve as control. On the 8th day post-surgery, rat brains were collected and subjected to a series of histological and transmission electron microscopy studies to explore remyelination. All rats' experimental procedures were approved by the Animal Research Ethics committee at the Faculty of Medicine/Kuwait University.

Results:
The Vir-O rat group exhibited a significantly higher myelin g-ratio compared to both Vir-Y ($p<0.001$) and MP-O rats ($p<0.05$) in the corpus callosum. Following demyelination lesion, Both Vir-O and MP-O rat gropus showed a significantly lower myelination (high g-ratio) compared to Vir-Y ($p<0.001$). There was a significantly lower percentage of unmyelinated axons and a higher percentage of myelinated axons in MP-O rats compared to Vir-O ($p<0.05$).

Conclusions:
The reproductive experience alleviates the aging-induced myelin damage under basal condition and aging-induced altered myelin recovery after demyelination injury.Further studies are needed to explore the cellular and molecular mechanisms underlying the beneficial impact of reproductive experience on myelin integrity in health and disease.

Acknowledgment: The authors would like to thank the personnel of the Animal Resource Centre and the personnel of the Electron Microscopic Unit at the Faculty of Medicine, Kuwait University, for their help.

Key Words: Electron Microscopy; Remyelination; Aging;

Funding Agency: None

Physiology

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Investigating Cisplatin Induced Cell Death Mechanisms in Vitro

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Introduction:
Cisplatin is a widely used chemotherapeutic agent whose clinical utility is limited by ototoxicity, resulting in irreversible sensorineural hearing loss. Mechanistic studies implicate oxidative stress, inflammation, and disrupted RNA metabolism, including altered stress granule (SG) dynamics, in cochlear cell death. SGs are transient ribonucleoprotein assemblies that regulate mRNA translation during cellular stress and are increasingly recognised as determinants of cochlear cell fate. RBM24, an RNA-binding protein essential for auditory hair cell development, has been proposed to modulate cellular stress responses. This study investigates SG dynamics following cisplatin exposure in an auditory cell model, examines potential associations between RBM24 and SGs, and evaluates candidate otoprotective compounds for mitigating cisplatin-induced ototoxicity (CIO) in vitro.

Methods:
OC2 cells derived from the Immortomouse organ of Corti were used as an auditory hair cell model. SGs were induced using sodium arsenite (0.5 mM, 1 h) or cisplatin (100 µM, 24 h), thereby inducing cytotoxicity. Candidate protective compounds (A–C) were co-administered with cisplatin. SG markers (Caprin1, HuR, eIF4G, G3BP1) and RBM24 were visualised by immunofluorescence and quantified using ImageJ. Cell viability was assessed by DAPI-based nuclear counts, and SG burden was quantified using SG counter plug-ins. Statistical analyses were performed in Jamovi.

Results:
Caprin1+HuR and eIF4G+G3BP1 co-localised in arsenite-induced SGs (~0.44 µm2), with Caprin1+HuR providing clearer and more reproducible detection (2.83 vs. 2.08 SGs/cell)(n=3). Cisplatin significantly increased SG number (1.91 vs. 0.37 baseline) while reducing mean SG size (0.50 µm2 vs. 0.61 µm2;$p<0.05$) (n=3), consistent with formation of smaller, more numerous SGs. Compound B modestly reduced SG burden and improved cell survival, whereas Compound C reduced SG number but was cytotoxic. RBM24 immunostaining remained diffuse and did not co-localise with SG markers under any condition(n=2) Each repeat (n) consists of 9 coverslips per condition.

Conclusions:
Cisplatin induces robust SG formation in auditory cells, reflecting translational stress responses central to ototoxicity. Caprin1+HuR are reliable SG markers in this model. RBM24 does not associate with SGs, suggesting its protective role may involve alternative pathways. Candidate compounds showed variable efficacy, warranting further investigation.

Key Words: cisplatin-induced ototoxicity (CIO); Stress Granules (SG); RBM24;

Funding Agency: UCL Ear Institute – MSc Audiovestibular Medicine: Advanced Audiology Research Project

Physiology

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Hypoxemia exerts detrimental effects on the cerebral cortex and ventricular system, but not on the hippocampus in the rat brain: the role of TNFα signaling.

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Introduction:
Hypoxemia can cause secondary brain injury and cognitive impairment. The mechanisms may involve direct neuronal injury, lung injury-related systemic inflammation, hypoxia-triggered local brain inflammation, or disrupted extracellular fluid homeostasis. Objectives: This study investigated the effects of hypoxemia on the brain regions most vulnerable to hypoxia, which are cerebral cortex (CC), hippocampus (HC), and ventricular system, including choroid plexus (CP), which produces cerebrospinal fluid, and the ependymal lining (EL) of the ventricles. Another aim was to assess the role of tumor necrosis factor-α (TNFα) signaling, as a key pro-inflammatory cytokine, in regulating cell survival and immune responses in these regions. M

Methods:
All procedures were approved by the Institutional Animal Ethics Committee of Kuwait University (No. 3643). Adult Sprague–Dawley rats were exposed to 8% O_2 (hypoxemia) or 21% O_2 (normoxia) for 48 h. Cell death was assessed using TUNEL assay, while the density and morphology of Iba1-positive cells (microglia and macrophages) were analyzed with immunostaining. Both analyses were conducted with or without pharmacological inhibition of TNFα signaling using Etanercept. Brain ultrastructure and glucose metabolism were evaluated by transmission electron microscopy and positron emission tomography, respectively. Data were analyzed using Student's t-test or one-way ANOVA followed by Bonferroni post-hoc test, $p<0.05$ was considered statistically significant.

Results:
Hypoxemia caused marked cell death (~30%) with necrotic/apoptotic morphology in the CC, CP, and EL, but not in the HC. This was accompanied by a pronounced reduction in 8F-fluorodeoxyglucose in all brain regions. Hypoxemia reduced macrophage density in the CP, did not affect microglial density in the CC, but induced a five-fold increase in activated microglia. TNFα inhibition increased cell death in the CC, CP, and EL, while restoring macrophage density and reverting microglia to their resting branched phenotype, suggesting a protective role for TNFα signaling under hypoxemic conditions.

Conclusions:
Hypoxemia exerts detrimental effects in the cerebral cortex and ventricular system, but not in the hippocampus. TNFα signaling appears to mediate neuroimmune protection by limiting cell death and modulating microglial activation during hypoxemia. Acknowledgement: This work was Funded by the Kuwait University Research Sector Grant no MY 03-22 and MY 02-18.

Key Words: Hypoxemia; Brain; Tumor necrosis factor-α (TNFα) signaling;

Funding Agency: Kuwait University Research Sector Grant no MY 03-22 and MY 02-18.

Psycology

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Psychometric Properties of the Arabic version of PID-5-BF among Community Sample

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Introduction:
The Personality Inventory for DSM-5—Brief Form PID-5- BF, is a brief measure of Personality Inventory for DSM-5, including Negative Affectivity, Detachment, Antagonism, Disinhibition, and Psychoticism.
Objectives: To examine the psychometric properties of Arabic (PID-5- BF).

Methods:
The Arabic version of the PID-5-BF (25-item with 0–3 Likert-type scale) and the Big Five Inventory-2-Short Form BFI-2-S (30-item with 1-5 Likert-type scale) scales were administered to 3900 Kuwait university undergraduates (1440 males mean age = 21.79±1.06 and 2460 females; mean age = 20.95±1.31). The internal consistency reliability, factor structure, and convergent validity of the BFI-2-S (30-item with 1-5 Likert-type scale) were assessed.

Results:
Cronbach's alpha was satisfactory for the Disinhibition, Negative Affectivity, Detachment, Psychoticism, and Antagonism subscales respectively were ranged (.74, .71, .67, .66, .62). The results revealed significant gender differences in Negative Affectivity, Detachment with a favor for females. PCA showed that PID-5-BF five factors explain 50.68% of the total variance. In order to determine the relationship between normative and pathological personality,, correlation analysis, the PID-5-BF Negative Affectivity domain and the BFI-2-S Neuroticism (0.78), while the PID-5-BF Detachment, Antagonism, Disinhibition, and Psychoticism domains had negative relationships with the BFI-2-S Extraversion (–0.49), Agreeableness (–0.70), Conscientiousness (–0.76) and Openness (–0.85).

Conclusions:
This study provided evidence for the reliability and validity of the Arabic PID-5-BF for Community Sample.

Key Words: Psychometric Properties ; PID-5-BF ; Arabic version ;

Funding Agency: None

Psycology

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Delivering Trauma-Focused Cognitive Behavioral Therapy in Kenya: Linking Implementation Constructs to Clinical Outcomes

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Introduction:
Background: Treatment fidelity – the degree to which a treatment is delivered as intended – is an indicator of successful treatment implementation and can lead to positive clinical outcomes. Little is known about how organizational readiness for change may affect treatment fidelity. This study explored relationships between organizational readiness for change, treatment fidelity, and clinical outcomes in the context of delivering trauma-focused cognitive behavior therapy (TF-CBT) to youth in Kenya.

Methods:
Data for this secondary data analysis came from a randomized controlled trial (RCT) evaluating the lay-counselor delivery of a culturally adapted group-based TF-CBT to orphaned youth in schools in Kenya. Lay counselors included clusters of teachers and community health volunteers from 40 schools and 39 community health facilities, respectively. They completed self-report measures on organizational readiness for change, whereas their supervisors completed live fidelity ratings for child- and guardian treatment groups. 848 Kenyan children (Mage = 12.7) reported pre- and post-treatment post-traumatic stress symptoms (PTSS). Relationships between organizational readiness for change, TF-CBT fidelity, and clinical outcomes were explored using multilevel path analyses, adjusting for Baseline PTSS, child sex, and child age. Ethical approval was obtained from the Institutional Review Boards of Duke Health and the Kenya Medical Research Institute.

Results:
Treatment fidelity scores and organizational readiness for change were relatively high and comparable for teacher- and CHV-delivered treatment groups. In the teacher-delivered treatment groups, higher levels of organizational readiness for change predicted higher levels of child-group treatment fidelity (b = 0.41, SE = 0.18, p = 0.02). Further, higher levels of guardian-group treatment fidelity predicted statistically significantly lower post-treatment PTSS. In the CHV-delivered treatment groups, higher levels of guardian-group treatment fidelity predicted lower levels of post-treatment PTSS. No mediation effects were found.

Conclusions:
Guardian-group treatment fidelity improved clinical outcomes, highlighting the importance of caregiver involvement in treatment. Moreover, organizational readiness for change only predicted higher fidelity in the child-group in the teacher-delivered treatment group, likely due to teacher-counselors' embeddedness and daily interactions in their schools compared to CHV-counselors.

Key Words: Youth Mental Health; Treatment Fidelity ; Cognitive Behavioral Therapy ;

Funding Agency: National Institute of Mental Health (R01 MH112633; Dorsey & Whetten, MPIs)

Public Health

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Factors influencing medium-term weight loss in adults living with overweight or obesity in the general population – A UK Biobank study

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Introduction:
Obesity affects a substantial proportion of adults, and the proportion attempting weight loss has increased over time, influenced by sociodemographic, behavioural, and clinical factors. However, the incidence and determinants of weight loss occurring naturally in the general population, prior to widespread use of pharmacological therapies, remain poorly understood. To address this gap, this study aimed to determine the incidence of 'healthy weight loss' in individuals in the general population and to identify sociodemographic, clinical, and behavioural factors associated with medium-term weight loss in healthy individuals in the general United Kingdom population, before widespread GLP-1RA use.

Methods:
We used data from the UK biobank (n=502484), a large population-based prospective study including middle-aged men and women in the UK. Baseline assessments were conducted between 2006 and 2010, with repeat assessments at follow-up between 2012 and 2013. To explore the relationship between sociodemographic, clinical, and behavioural variables and successful medium-term weight loss over ~4 years (defined as ≥5% of baseline body weight), associations with weight loss were assessed using independent t-tests (normal data), rank-sum tests (skewed data), or Chi-square tests (categorical variables).

Results:
A large proportion (19.7%) of healthy individuals with overweight or obesity lost a significant amount of weight (≥ 5%) over ~4 years. The mean age was 56.6 years (SD= 7.35), 41.9% were female, and 98.0% were White. The median body mass index was 28.1 kg/m² (IQI= 26.5–30.6), median HbA1c was 35.1 mmol/mol (IQI= 32.7–37.6), and the median Townsend deprivation index was −2.71 (IQI= −3.95 to −0.77). Greater weight loss was associated with younger age (56.2 vs. 56.7 years; p= 0.01), female sex (51.5% vs. 39.6%; $p < 0.001$), and higher baseline BMI (28.9 vs. 27.9 kg/m²; $p < 0.001$).

Conclusions:
A substantial proportion of healthy individuals with overweight or obesity experience weight loss. However, the underlying reasons remain unclear due to limited information on participants' engagement in weight-loss interventions. Younger age, female sex, and higher baseline BMI were associated with greater weight loss. Future work will extend these analyses by developing prediction models using the same variables.

Key Words: Weight loss success; Overweight and obesity; Weight change determinants;

Funding Agency: None

Public Health

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Assessing the Risk of Developing Type 2 Diabetes Among University Employees in Kuwait: A Cross-Sectional Study

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Introduction:
Type 2 diabetes mellitus (T2DM) is a major global public health concern, with Kuwait reporting one of the highest prevalence rates in the region. The Finnish Diabetes Risk Score (FINDRISC) is a simple, cost-effective screening tool that helps identify individuals at high risk of developing T2DM. To date, no studies have assessed diabetes risk among university employees in Kuwait. This study aimed to assess the risk for T2DM among employees at Kuwait University (KU) using the FINDRISC tool.

Methods:
A cross-sectional study was conducted from February to April 2025 using a structured questionnaire adapted from the FINDRISC tool. A total of 407 KU employees were included in the study. Data were collected in person across all KU campuses with anthropometric measures obtained for participants who did not know their own. Categorical variables were reported as frequencies and percentages, while continuous variables were reported as means and standard deviations (SD). Participants with a FINDRISC score > 11 were categorized as being at increased risk of T2DM. Multivariable logistic regression was used to identify predictors of increased risk. All analyses were performed using STATA version 14. Ethical approval for the study was obtained from the Health Sciences Center (HSC) Ethical Committee on December 18, 2024 (Ref: 831)

Results:
Of the 407 participating KU employees, 58% were female, 65% were aged 18-44 years, and 67% were Kuwaiti. The mean FINDRISC score was 9.4, with female employees having a statistically significant higher average risk score (10.3) compared to male employees (8.3). Among the participants, 137 (34%) were classified as being at increased risk of T2DM, whereas 270 (66%) were not. Being at increased risk of T2DM was significantly associated with being female (OR: 3.3, 95% CI: 1.7-6.3), married (OR: 2.27, 95% CI: 1.2-4.3), and those with a perception of having future diabetes. Compared to those perceiving themselves as “not at all likely” to develop diabetes, participants who believed they were “very likely” had nearly eight times greater odds (OR: 7.79, 95% CI: 3.2-18.5) and those “somewhat likely” had about twice higher odds (OR: 2.44, 95% CI: 1.3-4.5).

Conclusions:
A substantial proportion of KU employees are at increased risk of T2DM. The findings of the study highlight the need for targeted diabetes preventive initiatives and awareness programs in university settings to promote early identification and intervention.

Key Words: Diabetes mellitus; FINDRISC; Risk assessment;

Funding Agency: None

Public Health

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Exploring Consumer Purchasing Behaviour: Trends and Artificial Intelligence Applications

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Introduction:
Background: The global rise in ultra-processed foods consumption is associated with obesity, cardiovascular disease, and mortality. This trend's impact is evident in Kuwait where consumption of processed and ready-to-eat food is high. Classification of foods by processing level is crucial to monitor dietary trends but remains challenging at scale. This study aimed to characterize consumer purchasing patterns and assess the reliability of Large Language Models (LLMs) in classifying foods by processing level using the NOVA system.

Methods:
A secondary data analysis was conducted on 61,831 products from Mishref Co-Op (2019-2023). Purchasing patterns were assessed based on sales volume, revenue, and affordability using Chi-square, Wilcoxon rank-sum, and Kruskal-Wallis tests. Affordability was determined based on Consumer Price Index adjusted prices using quartile-based thresholds (≤25th percentile: cheap; 25th–75th percentile: affordable; ≥75th percentile: expensive), ensuring a balanced distribution of products. A random subset of 500 Food products was independently classified by two human raters and six LLMs (ChatGPT 3.5, ChatGPT 5, Perplexity, Copilot, Gemini, DeepSeek). Inter-rater reliability was assessed using Cohen's and Fleiss' Kappa coefficients. Ethical approval was not required.

Results:
Food products made up 79% of all products, with higher sales volumes but lower revenue and prices than Non-Food products, and were mostly affordable. Affordability was the main purchasing driver. While prices remained stable, revenue and sales volume peaked in March and October, reflecting crisis and seasonal demand. LLMs showed moderate to substantial agreement with human raters, with Perplexity aligning most closely with experts, but lowest agreement for the "Processed Foods" category.

Conclusions:
Automated classification using LLMs shows potential for larger-scale dietary surveillance, though refining category definitions is needed to improve reliability. These findings support integrating AI-based tools to advance nutritional research and inform public health policy in Kuwait.

Key Words: Food Classification; Artificial Intelligence; Consumer Behavior;

Funding Agency: None

Public Health

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Attitudes, And Perceptions of Pregnant Women Towards Respiratory Syncytial Virus (RSV) Immunization in Kuwait.

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Introduction:
Respiratory syncytial virus (RSV) is a leading cause of acute lower respiratory tract infections in young children, with up to 90% infected within the first two years of life. With the introduction of maternal immunization and infant immunoprophylaxis, new preventive strategies are now available. Previous studies from Saudi Arabia and the United Arab Emirates report parental vaccine hesitancy rates ranging from 11% to 36%. This study aimed to identify predictors of maternal RSV vaccine acceptance in Kuwait.

Methods:
A cross-sectional survey was conducted between April and November 2025 among pregnant women aged ≥18 years attending antenatal clinics at three primary care centers and two public hospitals in Kuwait. Participants completed a self-administered, electronic, anonymous questionnaire assessing knowledge of bronchiolitis, attitudes toward RSV vaccination, and sources of medical information. Descriptive statistics were performed, and predictors of RSV vaccine acceptance were analyzed using logistic regression.

Results:
A total of 413 respondents were included, of whom 267 (64.6%) were Kuwaiti nationals. Most participants held a bachelor's degree (279, 67.6%), and 125 (30.3%) were primigravida. Overall, 217 respondents (52.5%) reported acceptance of the maternal RSV vaccine. Median age did not differ between acceptors and non-acceptors (30 years). No significant differences were observed in household income, gravidity, or receipt of a non-COVID-19 vaccine within the preceding five years. In multivariable logistic regression, Kuwaiti nationality (adjusted odds ratio [aOR] 1.8, 95% CI 1.03–3.22) and higher educational attainment—particularly bachelor's (aOR 2.88, 95% CI 1.24–6.72) and master's degrees (aOR 10.87, 95% CI 2.41–49.07)—were independently associated with increased odds of RSV vaccine acceptance. Age, income, and gravidity were not significant predictors.

Conclusions:
Approximately half of pregnant women accepted the maternal RSV vaccine. Higher educational attainment and Kuwaiti nationality were the strongest predictors of acceptance, whereas age, income, and gravidity were not associated. Enhanced awareness of RSV infection and available preventive strategies is needed to improve maternal RSV vaccine acceptance and strengthen public understanding of its importance.

Key Words: Respiratory syncytial virus, ; vaccine,; pregnant, acceptance;

Funding Agency: None

Public Health

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The prevalence of physical activity among Kuwait University students, and factors that promote or impede it: a cross-sectional study

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Introduction:
Background and Aims: Physical activity (PA) is any activity involving muscular movement that requires energy, and it is crucial for health and preventing chronic diseases. Low levels of PA are a growing global problem, as it is the fourth leading risk factor for global mortality. Studies indicate that PA is low among university students due to their sedentary lifestyle. This study aims to assess the prevalence of PA among Kuwait University (KU) students in Al-Shadadiya and Health Sciences Center (HSC), and the factors that promote or impede it using the Social Ecological Model (SEM).

Methods:
A cross-sectional study design was conducted using the International Physical Activity Questionnaire (IPAQ) and the Capabilities Assessment for Diet and Activity (CADA) to collect data from students. Based on the World Health Organization (WHO) guidelines, IPAQ scores were categorized as low, moderate, or high; students with moderate or high PA were considered physically active. Data were analysed using IBM SPSS Statistics version 29 to perform regression models and chi-square tests. Ethical approval was obtained from the HSC Undergraduate Ethics Committee.

Results:
The sample included a total of 487 KU students. The results showed that 45.8% of students met WHO PA guidelines. Chi-square testing revealed significant associations with PA, and motivators for PA included spending time outside university during break time and improving mood and enjoyment. Lack of awareness of the importance of PA, gym affordability, anxiety about exercising in public, frustration, academic obligations, and use of elevators and escalators were negative predictors. Logistic regression revealed that gender was significantly associated with PA, as males had higher odds (OR = 2.09, 95% CI:1.27–3.45, p = 0.004). Factors that promoted PA were access to nearby places for outdoor PA (OR= 1.871, 95% CI:1.13–3.10, p= 0.015), aiming to build muscle (OR= 1.914, 95% CI:1.24–2.95, p= 0.003), and self-challenge (OR= 1.867, 95% CI:1.14–3.05, p= 0.012), while eating during break (OR= 0.562, 95% CI: 0.37–0.86, p= 0.007) impeded it.

Conclusions:
PA is low among KU students. SEM confirms that multiple levels influence PA. Therefore, tailored multilevel interventions are needed to promote PA among students and reduce the health and economic burden in Kuwait.

Acknowledgment: The authors would like to thank Dr. Manar Alawadhi, Dr. Ahmad Salman & Dr. Fatima Alghadhban for their academic guidance and support.

Key Words: Physical Activity ; University students ; Social Ecological Model;

Funding Agency: None

Public Health

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Do Consumers in Kuwait really understand GMOs? Unpacking Mistrust and Misconceptions: Insight from a Public Questionnaire

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Introduction:
Recent progress in biotechnology enables precise genetic editing of organisms, resulting in the commercial cultivation of transgenic crops that possess beneficial traits. In 2024, Al Mazrooei et. al. confirmed the presence of GMO sequences in several products sold in Kuwait without being labelled as GMO product. Public understanding of GMOs in Kuwait is limited, and, to the best of our knowledge, there are no existing public surveys or peer-reviewed research that assess public awareness of GMOs in Kuwait. Consequently, this study aims to explore the awareness, perceptions, and attitudes of consumers in Kuwait, towards GMOs Food.

Methods:
The study utilized a comprehensive questionnaire designed through Microsoft 365 Forms, and distributed electronically from July 2025, until present date. The questionnaire included questions about participants' knowledge and attitudes towards GMOs. Data was analyzed using SPSS and Microsoft Excel. Descriptive analyses were expressed in terms of percentages. Pearson's Chi-square homogeneity test was conducted. The level of significance for these tests was set at $P < 0.05$.

Results:
The study assessed the sample of 1121 participants of various ages, genders, and educational backgrounds (80% females and 20% males). Only 718 reported hearing of GMO foods. 81% of participants reported reading food labels before buying them, however, food label reading is not correlated with high levels of awarenes. 70.75% of participants believed GMO foods are sold in Kuwaiti market, indicating high awarness. Also, 74.66% of participants believed that the genetic modification would affect the nutritional value of products, proving a widly spread misconception. Consequently 84.40% of participants would not choose GMO food product, and only 20.47% of participants believed GMOs to be safe for human consumption, showing clear mistrust.

Conclusions:
While most participants in Kuwait are aware of GMOs, their understanding remains limited and often shaped by misconceptions. Findings revealed that a significant portion of the Kuwaiti public exhibited a lack of basic understanding and a great mistrust towards GMO foods. Most participants preferred non-GMO foods, and were primarily informed about GMOs through the internet rather than other sources. Additionally, the results underscore the need for greater public education and awareness campaigns to address GMOs misconceptions. This study also highlights the need for better food labeling.

Key Words: GMOs Food; Public Questionnaire; Consumers in Kuwait ;

Funding Agency: None

Public Health

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Trends in Hospital Utilization Among Kuwaiti Citizens (2013-2019): A Comparative Analysis of Public and Private Healthcare Services.

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Introduction:
Hospital utilization patterns are key indicators of health system performance and reflect the balance between public and private healthcare sectors. In Kuwait, major health financing reforms and increased private sector participation have occurred over the past decade, most notably the introduction of the Afya health insurance scheme in 2016. However, evidence on how these reforms influenced hospital utilization among Kuwaiti citizens remains limited. This study examines trends in hospital discharges, outpatient visits, and bed availability in public and private hospitals from 2013 to 2019 and evaluates changes associated with the Afya policy intervention.

Methods:
Secondary data were obtained from Kuwait's Annual Health Statistics Reports (2013–2019). Outcomes included annual hospital discharges, outpatient visits, and bed capacity by sector (public versus private). Descriptive statistics and bivariate analyses were conducted to compare utilization patterns across sectors and over time. Interrupted Time Series analysis was applied to assess policy impact, with 2016 defined as the intervention year corresponding to Afya scheme implementation. Pre-intervention (2013–2015) and post-intervention (2016–2019) periods were analyzed. Analyses were conducted using SPSS version 25, with significance set at $p < 0.05$.

Results:
Following 2016, public hospital discharges and outpatient visits showed a downward trend, while private sector utilization increased. Private hospital discharges and outpatient visits rose steadily in the post-intervention period, with a clear positive trend compared to the pre-intervention phase. Bed capacity remained relatively stable in public hospitals across the study period but increased consistently in private hospitals. Interrupted Time Series estimates indicated a change in level and trend direction favoring private sector utilization after the Afya policy introduction.

Conclusions:
Hospital utilization patterns among Kuwaiti citizens shifted toward greater private sector use following the implementation of the Afya health insurance scheme. These findings highlight the growing role of private healthcare within Kuwait's health system and underscore the need for policies that promote equity, system integration, and improved access to sector-specific utilization data to support evidence-based health planning.
Funding/Acknowledgements:
This study used publicly available secondary data, with ethical approval obtained from the MOH in accordance with Kuwait University guidelines.

Key Words: Hospital Utilization; Public–Private Healthcare; Comparative Analysis;

Funding Agency: Nonen

Public Health, Adolescent, Epidemiology

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Electronic Nicotine Delivery System Use and its Relation to Waterpipe Smoking among Youth in Seven Arab Countries

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Introduction:
The increasing use of Electronic Nicotine Delivery Systems (ENDS) and Waterpipe Tobacco Smoking (WTS) highlights a growing tobacco epidemic among youth in the Arab world. This study aimed to estimate the prevalence of ENDS use among adolescents in seven Arab countries and to explore the bidirectional relationship between ENDS use and WTS.

Methods:
Data from the World Health Organization's Global Youth Tobacco Survey (GYTS 2014–2018) were analyzed, involving 18,536 schoolchildren aged 12-16 from Mauritania, Morocco, Oman, Qatar, Tunisia, Yemen, and Iraq. Weighted prevalence estimates were calculated for nationally representative data and adjusted multilevel logistic regression models were employed to examine associations between ENDS use and WTS.

Results:
The analysis included 18,536 participants from 216 schools, representing approximately 4,171,719 schoolchildren across the seven Arab countries. The pooled weighted prevalence rates were 9.5% for ENDS use and 10.0% for WTS. Significant associations were found between ENDS use and WTS (AOR: 5.26, 95% CI: 4.28–6.46), conventional cigarette smoking (AOR: 1.54, 95% CI: 1.23–1.94), and early tobacco initiation before age 12 (AOR: 1.40, 95% CI: 1.14–1.72). Lower odds of ENDS use were noted among females and adolescents who received education on tobacco dangers in school.

Conclusions:
WTS was linked to a more than fivefold increase in the likelihood of ENDS use, and conventional cigarette smoking was identified as a common risk factor for both behaviors. Early tobacco consumption before age 12 correlated with higher odds of ENDS use but lower odds of WTS. Furthermore, females and those educated about tobacco risks were less likely to report ENDS use.

Acknowledgment: The initial concept for this research was developed during the KFAS-Harvard collaboration workshop in 2023, which provided valuable scientific discussion and idea refinement. No funding was received for this work.

Key Words: Adolescent; Smoking; Public Health;

Funding Agency: Nill

Public health, Health policy and management

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Management Costs of Type 2 Diabetes Mellitus in the Primary Healthcare Center: A Study in Kuwait

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Introduction:
Type 2 Diabetes Mellitus (T2DM) creates a substantial economic burden worldwide and in Kuwait, where prevalence remains among the highest globally. Primary Healthcare Centers (PHCs) form the cornerstone of diabetes management, yet limited evidence exists on the true cost of care within this setting. Understanding these costs is vital for effective planning, equitable resource allocation, and sustainable policy development. This study estimated the annual direct costs of managing T2DM in Kuwaiti PHCs and identified demographic and clinical factors influencing these costs.

Methods:
A cross-sectional cost-of-illness study was carried out in 2024 across six randomly selected PHCs (one per governorate). A sample of 480 adult T2DM patients, who had diabetic clinic visits in 2023, was randomly selected (80 per center). Patient-level demographic and clinical data were extracted from electronic medical records, while financial and administrative data were collected from the Ministry of Health and PHC management. Costs were calculated from the provider perspective using a combined activity-based costing and top-down approach. The Study was approved by Health Sciences Center Ethical Committee, Kuwait university (HSCEC Approval number VDR / EC - 105). The study and use of secondary data was also approved By MOH ethical review committee (approval letter Number 207 / 16-3-2025). A generalized linear model (Gamma distribution, log link) identified predictors of annual cost. Model robustness was evaluated through AIC, BIC, VIF, residual analysis, and bootstrapping.

Results:
The mean annual cost per patient was 334.5 KWD. Medications represented the largest share (73.7%), followed by overheads (10.8%) and physician salaries (4.9%). Injectable therapy increased cost by 33%. Additional cost drivers included longer disease duration, hypertension, dyslipidaemia, higher clinic visits, and residence in Hawalli.

Conclusions:
T2DM management in Kuwait's PHCs imposes a considerable financial burden. Optimizing medication use, reducing unnecessary visits, and strengthening PHC through unified family medicine models and automated refill systems may enhance efficiency.

Key Words: Type 2 Diabetes Mellitus; Managment Cost analysis; Primary healthcare;

Funding Agency: None

Pulmonology

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Endobronchial Ultrasound (EBUS) with Endoscopic Ultrasound (EUS) Utility and Diagnostic Yield for Malignant and Benign Disease.

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Introduction:
Endobronchial ultrasound–guided transbronchial needle aspiration (EBUS) is an established first-line diagnostic tool for mediastinal and lung lesions, especially in lung cancer diagnosis and staging. Studies show that combining EBUS with endoscopic ultrasound (EUS) improves accuracy for malignancy. However, evidence on combined EBUS/EUS in benign mediastinal disease remains limited, with reported diagnostic yields of 60–70% for EBUS alone.
Objectives:
To evaluate the diagnostic performance of EBUS, EUS, and combined EBUS/EUS for benign and malignant mediastinal and lung lymphadenopathy in a tertiary interventional pulmonology center.

Methods:
A retrospective descriptive review was conducted on all EBUS/EUS procedures performed at the Chest Diseases Hospital (Kuwait) from 2024–2025. Included patients presented with mediastinal lymphadenopathy, lung nodules, or masses requiring biopsy for suspected malignancy or benign conditions such as sarcoidosis or tuberculosis. Patients with bleeding diathesis or who opted for alternative diagnostic methods were excluded.

Results:
A total of 175 patients underwent EBUS and/or EUS. The overall diagnostic yield for both benign and malignant disease was 91% (n=159). Of these, 60% (n=105) were evaluated for suspected lung cancer and 40% (n=70) for benign disease. Diagnostic yield was 92% (n=97) for malignant cases and 88.6% (n=62) for benign cases. Yields by modality were: EBUS 89.7% (113/126), EUS-B 88.9% (8/9), EUS 100% (22/22), and combined EBUS/EUS 88.9% (16/18).

Conclusions:
EUS demonstrated higher diagnostic yield than EBUS, likely due to its ability to obtain larger tissue samples. EUS was associated with a higher diagnostic yield compared to EBUS, with results comparable to cryo-EBUS, suggesting a potential role as an initial diagnostic approach for mediastinal biopsy. Wider incorporation of EUS and EUS-B may improve diagnostic accuracy and reduce nondiagnostic procedures.

Key Words: Pulmonology ; EBUS; EUS;

Funding Agency: None

Surgery

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Interrupted versus Continuous Fascial Closure after Emergency Midline Laparotomy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Introduction:
Wound dehiscence after emergency midline laparotomy is a severe complication linked to high morbidity and mortality. While continuous closure is standard in elective surgery, its superiority is not established in high-risk emergency settings, where patient factors like infection and malnutrition can compromise healing. This systematic review and meta-analysis of randomized controlled trials (RCTs) aimed to compare the efficacy and safety of interrupted versus continuous fascial closure techniques after emergency midline laparotomy.

Methods:
A comprehensive search of PubMed, Scopus, CENTRAL, Google Scholar, and Web of Science was conducted for RCTs up to October 2025. The primary outcome was wound dehiscence. Secondary outcomes included wound infection, incisional hernia, and length of hospital stay (LoS). Risk ratios (RR) and mean differences (MD) were pooled using STATA 19.5, with 95% confidence intervals (CI).

Results:
Twenty-five RCTs involving 3,548 patients were included. Interrupted closure significantly reduced the risk of wound dehiscence compared to continuous closure (RR: 0.47, 95% CI [0.38, 0.87]; $p < 0.001$). There was no significant difference in wound infection (RR: 0.91, 95% CI [0.76, 1.09]; $p = 0.31$) or incisional hernia (RR: 0.83, 95% CI [0.57, 1.22]; $p = 0.34$). However, interrupted closure was also associated with a significantly shorter LoS (MD: -3.52 days, 95% CI [-4.75, -2.29]; $p < 0.001$).

Conclusions:
In the high-risk emergency midline laparotomy setting, current evidence suggests that interrupted fascial closure may be associated with a reduction in wound dehiscence and a shorter LoS compared to continuous closure. However, given the risk of bias and clinical heterogeneity among the included studies, these findings should be interpreted with caution, and further high-quality, standardized trials are warranted.

Key Words: Midline incision; burst abdomen; incisional hernia;

Funding Agency: None

Surgery

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Granulomatous Mastitis in Kuwait: Case Series of Clinical Presentation, Diagnosis and Management

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Introduction:
Granulomatous mastitis (GM) is an uncommon chronic inflammatory breast disease with unclear etiology that often mimics malignancy, posing diagnostic and therapeutic challenges. This study aimed to describe the detailed clinical characteristics of patients with GM and demonstrate its diagnosis and management.

Methods:
A retrospective review of prospectively maintained records from January 2019 to October 2024 in a private clinic in Kuwait. The study protocol was approved by the ethical review committee of Ministry of Health, Kuwait and was performed in full accordance with the principles of the Declaration of Helsinki, the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and Case Report (CARE) guidelines.

Results:
The mean age of the patients was 38.2 years. Nine of the 10 patients were of reproductive age, with prolonged breastfeeding histories and high parity. Common presentations included breast masses (n=8, 80%), mastalgia (n=8, 80%), skin changes (n=5, 50%), axillary lymphadenopathy (n=4, 40%), nipple retraction (n=3, 30%), and discharge (n=2, 20%). Bilateral involvement occurred in 40% of cases. Ultrasound typically showed hypoechoic masses, edema, distortion, and sometimes abscess or sinus tracts. Mammography was performed in four cases, revealing asymmetric densities, masses, calcifications, and lymphadenopathy. Histopathology demonstrated lobulocentric granulomas, special stains were negative for tuberculosis and fungal elements, with one case positive for Gram-positive bacilli. Initial management was medical therapy in all cases, corticosteroids (n=9, 90%), antibiotics (n=8, 80%), and methotrexate (n=1, 10%). Two patients underwent surgical intervention. Symptom resolution occurred within one year for 90% of cases.

Conclusions:
This series of cases underscores GM as a rare yet increasingly acknowledged condition in Kuwait. There is no definite treatment for GM. The diagnosis relies on strong clinical suspicion and biopsy, while imaging aids in differential diagnosis. Management is generally decided on patient's presentation, severity on symptoms, size of the lesion and overall health of the patients. Surgical intervention is reserved for cases that are refractory or complicated; otherwise, conservative treatments like corticosteroids and antibiotics prove to be very effective. However, the findings of this study should be interpreted with caution due to the small sample size, which limits the generalizability of the results. Larger, multicenter studies are needed to better define optimal diagnostic and therapeutic strategies for GM

Key Words: Granulomatous mastitis; Women's health; Management;

Funding Agency: None

Surgery

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Clinical Outcomes of Upper Thoracic versus Lower Thoracic Upper Instrumented Vertebrae for Adult Deformity: A Systematic Review, Meta-Analysis and Meta-Regression

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Introduction:
Adult spinal deformity represents a heterogeneous set of spinal malalignments in skeletally mature patients, often leading to chronic pain, disability, and reduced quality of life. Long posterior fusion with deformity correction remains the mainstay for severe cases; however, the optimal upper instrumented vertebra (UIV), whether upper thoracic or lower thoracic, remains controversial. The decision affects mechanical stability, perioperative morbidity, and long-term complications such as proximal junctional kyphosis or failure.

Methods:
Following PRISMA 2020 and Cochrane guidance (PROSPERO ID CRD420251168384), PubMed, Embase, Scopus, Web of Science, and Cochrane Library were searched to October 2025. Comparative cohort studies evaluating UT versus LT UIVs in adult deformity surgery were included. Primary outcomes were Oswestry Disability Index (ODI) and Scoliosis Research Society (SRS) scores; secondary endpoints included blood loss, operative time, hospital stay, radiographic alignment, and revision rates. Random-effects meta-analyses and meta-regressions were performed using the most adjusted data.

Results:
Nineteen studies (n = 3,306; UT = 1,382, LT = 1,844) met inclusion criteria, with a mean patient age exceeding 60 years. No significant differences were detected for ODI (SMD = −0.53; 95% CI −1.23 to 0.17; p = 0.13) or SRS scores (SMD = −0.41; 95% CI −1.39 to 0.57; p = 0.40). UT fixation resulted in greater blood loss (SMD = 0.63; 95% CI 0.22–1.04; p = 0.0025), longer operative time (SMD = 0.55; 95% CI 0.38–0.72; p < 0.001), and prolonged hospital stay (SMD = 0.50; 95% CI 0.01–0.98; p = 0.04). No significant differences were found in sagittal vertical axis (SMD = −0.06; p = 0.78), lumbar lordosis (SMD = −0.12; p = 0.45), thoracic kyphosis (SMD = −1.16; p = 0.24), or revision rate (OR = 0.78; 95% CI 0.44–1.38; p = 0.38). Meta-regression identified follow-up duration (p < 0.001) and age (p = 0.003) as moderators for select outcomes.

Conclusions:
Both UT and LT UIV strategies yield comparable long-term functional and radiographic outcomes in adult spinal deformity correction. However, LT constructs demonstrate shorter operative time, reduced blood loss, and shorter hospitalization. These findings support individualized UIV selection guided by patient age, alignment goals, and risk for junctional complications.

Key Words: Spine; Deformity; Thoracic;

Funding Agency: None

Surgery

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Vagus Nerve Stimulation in patients with drug-resistant epilepsy: a retrospective study of clinical outcomes, quality of life and healthcare utilization, and safety.

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Introduction:
Drug-resistant epilepsy (DRE) remains a major challenge, with many patients continuing to experience disabling seizures despite multiple anti-seizure medications. Although vagus nerve stimulation (VNS) is an established adjunctive therapy, data from the middle east regarding its efficacy and related outcomes are very limited, with no previously published reports from Kuwait.
Objective:
To asses seizure-related outcomes, quality of life (Qol) and healthcare utilization, and safety following VNS implantation in patients with DRE.

Methods:
Approval by the ethical committee of MOH was obtained. A sample of 12 patients who recently underwent VNS implantation or generator replacement in Jaber Al-Ahmad Hospital was selected. During the period from November to December 2024, data were collected using an online survey after having the patient's or the caregiver's consent, if applicable. The survey consisted of four part, which are baseline characters, seizure-related outcomes, Qol and healthcare utilization, and safety. Then we compared it with the literature through searching databases like Google Scholar and PubMed. Studies published up to 2025 were included

Results:
DRE frequency was reported to be reduced >50% among 41% of the cohort at 3 months and among 58.8% after 6 months. Also, status epilepticus (SE) frequency reduction by >50% was reported by 83.8%. In addition, different aspects of SE, such as recovery duration, motor recovery, physical symptoms, and cognitive recovery, were reported to be improved among 83.8%, 50%, 33%, and 25% of the patients, respectively. Regarding Qol, 66.6% reported an improvement in at least one domain, with 50% reporting an improvement in mood and/or alertness, while memory and/or social function improved in 16.6%. Also, depression improved in 1 out of 2 patients. However, no worsening of any Qol domain was reported. In parallel, healthcare utilization decreased, with a >50% rate decline in emergency visits / hospitalization among all the patients. In addition, 41.6% reported having device-related site pain and/or cough. In comparison, hoarseness and dyspnea were reported among 25% and 16.6% respectively.

Conclusions:
Although it's not a first-line therapy, such significant results, which align with the literature, in different subjective and objective outcomes might shift the practice by considering VNS earlier than the average 15-20 years it takes after DRE diagnosis.
Acknowledgments:Nil

Key Words: Vagus nerve stimulation; Seizure reduction; Quality of life ;

Funding Agency: None

Surgery

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Does Timing of Cholecystectomy for Acute Cholecystitis Affect Perioperative Outcomes? A Retrospective Study of 502 Patients

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Introduction:
Acute cholecystitis is a common cause of surgical admissions, and laparoscopic cholecystectomy remains the standard treatment. However, the optimal timing of surgery continues to be debated. Some studies suggest increased morbidity with delayed intervention. In this study, we aimed to evaluate the impact of timing of laparoscopic cholecystectomy on perioperative outcomes in patients with acute cholecystitis.

Methods:
In this retrospective multicentric study, all patients who underwent laparoscopic cholecystectomy for acute cholecystitis between January 2021 and July 2025 were included. Demographic and clinical data were collected. Outcomes of interest included conversion to open surgery, hospital length of stay (LOS), postoperative complications, and 30-day readmission.

Results:
A total of 3500 laparoscopic cholecystectomies were performed during the study period across the two participating hospital, 502 (14%) of which were for acute cholecystitis. Mean age of the study cohort was 43 years, and 51% were females. The majority of cholecystectomies (74%) were performed between 3-10 days from the onset of symptoms of cholecystitis, while 16% and 10% were performed within less than 3 days and beyond 10 days, respectively. The rate of conversion to open surgery was 2% in the delayed cholecystectomy group (>10 days) and in none of earliest groups (p=0.10). The rate of performing an intraoperative cholangiography (IOC) was around 2% in each cohort (p=0.62); however, common bile duct (CBD) injury occurred in 2% of patients in the delayed cholecystectomy 1% of 3–10-day cases, and none of the early group (p=0.54). Mean LOS was significantly longer in the delayed group (p<0.05), while ICU admission rates were similar across groups. Thirty-day readmission was 8% in the delayed group versus 3% in others (p=0.06).

Conclusions:
Timing of laparoscopic cholecystectomy for acute cholecystitis appears to influence perioperative outcomes. In this cohort, delayed cholecystectomy was associated with significant longer LOS and showed higher though not statistically significant rates of CBD injury, conversion to open and 30-day readmission.

Key Words: Acute Cholecystitis; Cholecystectomy; Timing of surgery ;

Funding Agency: None

Surgery

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Efficacy of Prophylactic Ursodeoxycholic Acid in Preventing Gallstone Formation after Sleeve Gastrectomy Versus Gastric Bypass: A Systematic Review and Meta-Analysis of Randomized Control Trials

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Introduction:
Obesity remains a significant global health challenge and is particularly prevalent in Kuwait, where bariatric surgery has emerged as a leading therapeutic intervention. Rapid weight loss following sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) is strongly associated with an increased risk of de novo gallstone formation. To mitigate this complication, prophylactic ursodeoxycholic acid (UCDA) is commonly prescribed. UCDA reduces cholesterol supersaturation and improves bile flow, thereby preventing crystal formation and gallstone development.

Objectives:This study aims to evaluate the efficacy of prophylactic UDCA in preventing gallstone formation after bariatric surgery, explore dose-response relationships, and generate evidence-based recommendations for routine postoperative care.

Methods:
We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) using PubMed, Cochrane, and Embase databases covering the years 2010 to 2025. A total of eight RCTs (n=1,452 patients) comparing UDCA to placebo or no treatment met the inclusion criteria. Primary outcomes were radiologically confirmed gallstones or biliary sludge. Secondary outcomes were symptomatic gallstones and cholecystectomy rates. Pooled risk ratios (RR) with 95% confidence intervals (CI) were generated using random-effects models. This review adhered to the PRISMA 2020 statement and has been registered on PROSPERO. Ethical approval was not required.

Results:
Prophylactic UDCA was associated with a reduction in the incidence of radiologically detected gallstones (pooled RR 0.33, 95% CI 0.15–0.76; I^2=72.5%), symptomatic gallstones (RR 0.61, 95% CI 0.43–0.86; I^2=48.7%) and cholecystectomy rates (RR 0.49, 95% CI 0.34–0.70;I^2=56.3%). Subgroup analyses showed greater effectiveness after SG (RR 0.29) compared with RYGB (RR 0.46). Meta-regression demonstrated a significant dose-response effect (p=0.021), with higher doses (>600 mg/day) providing greater protection.

Conclusions:
UDCA prophylaxis markedly reduces the risk of gallstone formation following bariatric surgery and may warrant incorporation into standard postoperative management during the rapid weight-loss phase. Regimens of ≥600 mg/day for six months appear to provide the greatest protection. However, future research is needed to establish optimal dosing, treatment duration, and patient selection criteria.

Acknowledgements:We would like to thank Dr.Sarah AlYouha and Dr.Ghadah AlAinati for their support.

Key Words: ursodeoxycholic acid; Bariatric surgery.; De novo gallstone.;

Funding Agency: N/A

Surgery

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Does Fibrin Sealant Glue Improve Outcomes in Open Rhinoplasty: A Systematic Review and Meta-analysis

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Introduction:
Fibrin sealant is increasingly being used in rhinoplasty to mitigate post-operative soft tissue sequelae. This systematic review and meta-analysis evaluated its efficacy in reducing postoperative edema, ecchymosis, and pain.

Methods:
We searched PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials databases. Randomized controlled trials (RCTs) and cohort studies comparing fibrin sealants with control rhinoplasty were included. The Cochrane Risk of Bias 2.0 tool was used to assess the study quality. The pooled effect sizes were calculated using standardized mean differences (SMDs) in RevMan. Heterogeneity was assessed using the I2 analysis.

Results:
Six studies (five RCTs, one cohort) comprising 428 patients met the inclusion criteria and 248 (57.9%) in the fibrin sealant group. Only two studies demonstrated a high risk of bias. The fibrin sealant significantly reduced postoperative day 1 edema (SMD = -0.84, 95% CI: -1.44 to -0.24, p = 0.006) and ecchymosis (SMD = -1.17, 95% CI: -1.78 -0.56, p = 0.0002). However, no statistically significant differences were observed on day 7 for edema (SMD = -0.30, 95% CI: -0.78 to 0.17, p = 0.21), ecchymosis (SMD = -0.16, 95% CI: -1.28 to 0.96, p = 0.78), or day 1 pain (SMD = -0.27, 95% CI: -0.77, 0.23, p = 0.29).

Conclusions:
In patients undergoing open rhinoplasty, fibrin sealant provides significant early reduction in periorbital edema and ecchymosis, particularly within the first 24 h postoperatively. However, its benefits do not extend beyond the first postoperative week and its effect on pain is minimal. These findings support its selective use for enhancing immediate postoperative recovery.

Key Words: Septorhinoplasty; Edema; Ecchymosis; Fibrin Sealan; Fibrin glue; Rhinoplasty;

Funding Agency: None

Surgery

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Sleeve Gastrectomy Reverses Hepatic and Circulating Transcriptomic Dysregulation by Restoring Lipid and Energy Metabolism in a Rat Model of Diet-Induced MAFLD

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Introduction:
Metabolic-associated fatty liver disease (MAFLD) is one of the most prevalent causes of chronic liver disease globally, strongly linked to obesity and metabolic syndrome. Bariatric surgery, particularly sleeve gastrectomy (SG), has emerged as an effective intervention to reverse metabolic dysfunction, though the underlying molecular mechanisms remain incompletely understood. This study aimed to identify key hepatic genes involved in MAFLD pathogenesis and determine whether SG attenuates high-fat diet (HFD)-induced hepatic steatosis in a rat model.

Methods:
Thirty-two male Sprague–Dawley rats were divided into four groups: Control (lean), Obese control, Sham, and SG. Four weeks post-surgery, liver tissues, whole blood and plasma samples were collected. Expression profiling of MAFLD-related genes was performed using RT² Profiler PCR arrays. Circulating metabolic and liver function markers, including leptin, amylin, adiponectin, and hepatic triglycerides, were also quantified. The study was performed as per the guidelines of the Ethics Committee of the Research, Health Sciences Center for the care and use of animals.

Results:
SG significantly reversed obesity-induced upregulation of lipogenic (Fasn, Acly, Srebf1, Dgat2), gluconeogenic (G6pc, Gck), and inflammatory (Nfkb1, Il1b) genes, while enhancing fatty acid oxidation and mitochondrial genes (Cpt1a, Ppargc1a, Acadl). Pathway enrichment analysis revealed modulation of PPAR and AMPK signaling, fatty acid oxidation, and insulin sensitivity pathways. Leptin, amylin and hepatic triglyceride levels were significantly reduced following surgery, supporting systemic metabolic improvement. The normalization of Srebf1 and Dgat2 expression highlighted a shift toward restored hepatic lipid homeostasis and improved insulin sensitivity. Notably, the identification of overlapping hepatic–whole blood cellular gene networks represent a novel finding of this study, demonstrating strong concordance between tissue and circulating gene expression.

Conclusions:
Altogether, our results suggest that SG can reduce liver fat accumulation and mitigate MAFLD. SG induces broad transcriptional and metabolic reprogramming of hepatic lipid, oxidative, and inflammatory pathways, with benefits extending beyond weight loss alone. The identification of shared hepatic–cellular whole blood signatures and improved circulating biomarkers underscores the systemic impact of SG and highlights potential translational targets for non-invasive metabolic disease monitoring and therapy.

Key Words: Sleeve Gastrectomy; MAFLD; Transciptomics;

Funding Agency: KFAS and CN19-13MM-01

Surgery

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Efficacy of Corticosteroids in Patients with Otosclerosis Undergoing Stapedotomy: A Systematic Review and Meta-Analysis with Trial Sequential Analysis

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Introduction:
Stapedotomy is the primary treatment for otosclerosis, but the procedure carries a risk of surgical trauma leading to inner ear inflammation and potential sensorineural hearing loss. Corticosteroids are widely used perioperatively to lower this risk, but evidence regarding their overall efficacy on outcomes remains inconsistent. This systematic review and meta-analysis aimed to evaluate the effect of corticosteroid administration compared with no treatment on hearing, air-bone gap, and length of hospital stay in patients with otosclerosis following stapedotomy.

Methods:
A systematic search was conducted in PubMed, Scopus, Web of Science and Cochrane Library from inception to 1 November 2025 for studies comparing perioperative corticosteroids to controls in patients undergoing stapedetomy. Outcomes of interest included hearing, air-bone gap, and length of hospital stay. Statistical analysis was performed with R 4.3.1. Heterogeneity was assessed using the I2 statistics and the Cochrane Q test. Mean differences (MD) using the Inverse Variance method with the restricted maximum-likelihood estimator random-effects method were computed for all outcomes.

Results:
A total of five studies (3 RCTs and 2 observational) were included in the final meta-analysis, compromising 384 patients (mean age 42.4 years, mean 65% females), of whom 175 (45%) received corticosteroids. In the pooled analysis, the administration of corticosteroids significantly improved hearing compared to no corticosteroid treatment (MD 2.65; 95% CI [0.46; 4.84]; p= 0.02; I2= 43.5%), futher confirmed by trial sequential analysis. However, the treatment showed no significant effect on the postoperative air-bone gap (MD 0.14; 95% CI [-2.31; 2.58]; p= 0.91; I2= 95%) or the length of hospital stay (MD 0.27; 95% CI [-1.05; 1.59]; p = 0.69; I2= 91%).

Conclusions:
Perioperative corticosteroid administration significantly improves postoperative hearing following stapedectomy. However, there were no significant differences on the postoperative air-bone gap or the length of hospital stay.

Key Words: otosclerosis; stapedotomy; corticosteroids; hearing; air-bone gap;

Funding Agency: NA

Surgery

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Efficacy and Safety of 6.3 Fr Versus 7.5 Fr Single-Use Flexible Ureteroscopes for Upper Urinary Tract Stones: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Introduction:
Retrograde intrarenal surgery (RIRS) is a cornerstone in managing upper urinary tract stones, with a growing trend towards instrument miniaturization. The introduction of the ultra-slim 6.3 Fr single-use flexible ureteroscope presents a potential advancement over the standard 7.5 Fr device, but clinical evidence remains scarce. This systematic review and meta-analysis aims to synthesize data from randomized controlled trials (RCTs) to compare the efficacy and safety of the 6.3 Fr versus the 7.5 Fr ureteroscope.

Methods:
A systematic search of PubMed, Scopus, CENTRAL, and Web of Science was conducted for RCTs published up to September 2025. Eligible studies included adult patients aged 18–75 years diagnosed with upper urinary tract stones and undergoing RIRS, who were randomized to treatment with either a 6.3 Fr or a 7.5 Fr flexible ureteroscope. The primary outcomes were the stone-free rate and procedural success rate. Secondary outcomes included operation duration and postoperative complications. Risk ratios (RRs) for dichotomous data and mean differences (MDs) for continuous data, with 95% confidence intervals (CIs), were pooled for analysis.

Results:
Three RCTs involving 140 patients were included. There was no significant difference between both groups in stone-free rates (RR: 1.06, 95% CI [0.96, 1.18], p = 0.22) or success rates (RR: 1.06, 95% CI [0.97, 1.16], p = 0.17). However, the 6.3 Fr ureteroscope was associated with a significantly shorter operation duration (MD: □6.66 min, 95% CI [□11.29, □2.03], p < 0.001). No significant differences were found in laser operating time (MD: □1.46 min, 95% CI [□3.93, 1.01], p = 0.25), length of hospital stay (MD: □0.09 days, 95% CI [□0.23, 0.05], p = 0.19), or postoperative complications (Clavien I: RR 0.86, 95% CI [0.30, 2.43], p = 0.77; Clavien II–III: RR 0.67, 95% CI [0.12, 3.84], p = 0.65).

Conclusions:
Based on low-certainty evidence, the 6.3 Fr ureteroscope does not significantly improve stone-free rates but may reduce overall operation duration compared to the 7.5 Fr scope, with a comparable safety profile. These findings are limited by the small number of available studies, highlighting a clear need for larger, high-quality RCTs to confirm these preliminary results.
Ethical Considerations:
This study did not require Institutional Review Board approval or informed consent, as it involved no new data. The authors declare no conflicts of interest.

Key Words: kidney stone; urology; urolithiasis; ureteroscopy

Funding Agency: None

Transfusion Medicine/Blood Banking

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Study of Blood Unit Withdrawal Processes in Kuwait Central Blood Bank.

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Introduction:
A safe and sufficient blood supply relies on healthy, voluntary, and well-screened donors. This study focuses on unit withdrawal, defined as the removal of blood components from inventory when post-donation information reveals donor-related risks to transfusion safety. Understanding these withdrawals is essential for improving both safety and operational efficiency. Accordingly, this study evaluates the frequency and causes of unit withdrawal at the Kuwait Central Blood Bank (KCBB) to help minimize unnecessary donations and enhance overall blood quality and safety.

Methods:
The study analyzed discarded blood bags and components classified as withdrawals. Data were collected from official KCBB records over a five-year period, including total donations and withdrawn units. The percentage of discarded bags was calculated to assess trends and reasons for discard were included. Additionally, the most common reasons for unit withdrawal were documented. The study protocol was reviewed and internally approved by the Kuwait Central Blood Bank (KCBB) using the institution's designated ethical approval form.

Results:
During the five-year study period (2020–2024), a total of 452,979 donations were recorded, of which 738 were classified as unit withdrawals. Although yearly variations were observed, the rate of withdrawn units showed an overall increasing pattern. For example, the withdrawal rate increased from 0.12% in 2020 to 0.17% in 2024 (P=0.007). In 2024, units classified as withdrawals ranked ninth among all discarded blood components. The most common reasons for withdrawal were post-donation information, including undisclosed medication use, travel to malaria-endemic regions, severe infections, unsterilized hormonal injections.

Conclusions:
Blood unit withdrawals showed a gradual upward trend during the study period, indicating the need for continued evaluation of donor selection and post-donation reporting practices. Strengthening donor education, particularly regarding common deferral reasons, and improving the clarity of pre-donation communication may help reduce preventable withdrawals. Further research is needed to clarify contributing factors and assess donor awareness and behaviors influencing post-donation eligibility.

Key Words: Blood Unit Withdrawal; Blood Bank; Donor Eligibility;

Funding Agency: None

Transfusion Medicine/Blood Banking

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From Experience to Error Prevention: How Blood Bank Staff Use Their Senses to Detect Mistakes.

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Introduction:
Human factors remain central to transfusion safety, even in technology-rich environments. Blood bank staff use sensory perception, experience, and intuition to identify abnormalities such as sample contamination, donor reactions, equipment malfunction, and cross match inconsistencies. However, the balance between human judgment and technological systems has not been fully evaluated in Middle East transfusion settings.

Methods:
A cross-sectional questionnaire study was conducted among 211 staff at Kuwait Central Blood Bank (KCBB), including laboratory technologists, nurses, physicians, and quality personnel. An online questionnaire collected demographic data and 11 Likert-scale items assessing sensory reliance (sight, touch, hearing, smell), experience and intuition, and technology in error detection. Descriptive statistics summarized the data, age was calculated from date of birth, composite scores were created for Sensory Reliance, Experience and Intuition, and Technology Reliance, and correlations among these variables were examined. The composite scales showed acceptable reliability (Cronbach's α = 0.79–0.82). The study protocol was reviewed and internally approved by the Kuwait Central Blood Bank (KCBB) using the institution's designated ethical approval form.

Results:
Among 211 participants, most were laboratory professionals (67.8%) and female (79.1%), with a mean age of 35.6 years. Sensory reliance was highest for sight (M = 4.12) and hearing (M = 4.05), while touch (M = 3.28) and smell (M = 3.16) were less relied upon. Experience and intuition showed a high composite score (M = 4.13, α = 0.82), with 80% reporting it helps prevent errors and is prioritized over technology. Technology reliance was moderate (M = 3.66) and correlated positively with experience (r = 0.39). Sensory reliance and experience were strongly correlated (r = 0.67), highlighting that human senses and technology function complementarily in error prevention.

Conclusions:
Blood bank professionals depend heavily on human senses and experience for detecting potential errors. Technology plays a supportive role but does not replace human judgment. Policies, training, and QC systems should emphasize balanced decision-making that respects staff intuition while ensuring appropriate technological verification.

Key Words: Error Detection; Sensory Reliance; Experience and Intuition;

Funding Agency: None

Transplant

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Outcomes of Pediatric Intestinal Transplant Patients in Kuwait

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Introduction:
Intestinal transplantation (ITx) remains the primary treatment for permanent intestinal failure. Advancements in surgical techniques and immunosuppressive medications have improved the success rate of pediatric ITx. The goal of ITx is to reverse bowel malabsorption, eliminate parenteral nutrition (PN) dependence, early transition to enteral nutrition (EN), and ultimately achieve exclusive oral intake. This study aims to examine post-ITx outcomes of pediatric patients in Kuwait.

Methods:
Medical records of pediatric ITx patients (n=13) during 2000-2024 were retrospectively reviewed. Data collection included indications, transplant types, complications, nutrition intake, patient and graft survival. Ethical approval was obtained from the Standing Committee for Coordination of Health and Medical Research is pending (2025/2944).

Results:
Approximately 54% of the patients were female, and all except one were Kuwaiti. Age at transplant: 9 months to 8 years [median 2.3 (IQR: 4.2)]. Functional intestinal failure was the main indication (62%), mostly due to congenital disorders. The transplant graft consisted of isolated intestine in 69%; liver-intestine: 15.4% and multi-visceral: 15.4%. All patients discontinued PN [median 5 weeks (IQR: 9.0)] and achieved EN autonomy post-ITx [median 1.5 years (IQR: 3.5)]. Exclusive oral intake was achieved in approximately 54% of patients within 1-2 years post-ITx. Major post-ITx complications: surgical intra-abdominal (77%); kidney disease (62%); severe rejection (31%); others (23%). Only two patients had re-transplantation. Patient survival at 1-year: 100%; 5-year: 83%; and 10-year: 67%. Graft survival at 1-year: 100%; 5-year: 91%; and 10-year: 51%. Patients who achieved exclusive oral intake had a significantly higher graft survival rate ($p = 0.016$). Limitations: The sample size is small due to the rarity of this population.

Conclusions:
ITx remains a life-saving treatment, but it should be considered only with absolute indications. Strong efforts should focus on establishing a local intestinal rehabilitation program using a multidisciplinary approach.

Key Words: pediatrics; intestinal transplantation; intestinal failure;

Funding Agency: None

Transplant

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Early vs. late acute antibody mediated rejection among renal transplant recipients: risk factors that affect the outcome

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Introduction:
Antibody-mediated rejection (ABMR) is one of the major determinants of graft survival. Although diagnostic precision and treatment options have improved, response to therapy and graft survival has not improved very significantly. The phenotypes of early and late acute ABMR differ in many ways.
Aim of the study:
We aimed to compare the outcome of early and late acute AAMR phenotypes among renal transplant recipients.

Methods:
Out of 4100 kidney transplant recipients who were followed up in Hamed Al-Essa Organ Transplant Center of Kuwait over the last 10 years, 85 developed acute AAMR and were subcategorized into 2 groups according to the onset of rejection. Early rejectors represented group 1(n=35) while late rejectors represented group2(n=51). All patients received the standard management of AAMR according to our protocol (pulse steroid, IVIG and Rituximab but plasma exchange was added only to early ABMR). We compared the 2 groups with different phenotypes regarding graft and patient outcome.

Results:
Patients in the two groups were comparable regarding pretransplant comorbidities (original kidney disease, pre-transplant mode of dialysis, viral profile, blood group, hypertension, diabetes, ischemic heart disease, urological problems, hyperlipidemia, and HLA mismatch) ($p>0.05$). Moreover, the two groups were matched regarding gender, type of donors, and maintenance immunosuppressive regimen($p>0.05$) but group 1 received significantly more potent induction($p=0.03$). Patients in both groups were comparable regarding the graft function immediately after transplant ($p=0.038$). We found no significant difference in the 2 groups regarding BK viremia and BKN ($p>0.05$) but post-transplant diabetes was significantly higher in group 1 while CMV viremia was more prevalent in group 2($p<0.05$). Graft outcome was significantly better in group 1 compared to group 2 ($p=0.001$). However, patient outcome was comparable in the 2 groups ($p=0.71$).

Conclusions:
We observed better graft outcome among patients with early ABMR despite higher prevalence of PTDM, DGF /SGF possibly because of early and more potent antirejection therapy.

Key Words: Kidney transplant ; ABMR; outcome ;

Funding Agency: None

Transplant

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TGF-β1 C (+869) T Codon 10 Polymorphism Predicts COVID-19 Susceptibility among Kidney Transplant Recipients in Kuwait

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Introduction:
The COVID-19 pandemic has disproportionately affected immunocompromised populations, particularly kidney transplant recipients. Cytokine storm syndrome (CSS), mediated by dysregulated Th1/Th2/Th3 responses, drives disease progression. We investigated the association between cytokine gene polymorphisms and COVID-19 outcomes in transplant recipients.
Aim :In this cohort study, we genotyped 309 kidney transplant recipients (64 COVID-19-positive, 245 controls) for key cytokine polymorphisms (TGF-β1, IFN-γ, IL-6, IL-4) using PCR-RFLP between February 2020-2022. Clinical outcomes were correlated with genetic variants.

Methods:
In this cohort study, we genotyped 309 kidney transplant recipients (64 COVID-19-positive, 245 controls) for key cytokine polymorphisms (TGF-β1, IFN-γ, IL-6, IL-4) using PCR-RFLP between February 2020-2022. Clinical outcomes were correlated with genetic variants.

Results:
We found that COVID-19 incidence was 20.7% (64/309). Our results showed that except TGF-β C (+869) T, codon 10 but neither of interferon -μ T (+874) A, IL-6 G (-174) C, IL-4C (-490) T showed to be significantly associated with progression of COVID-19 and CSS mechanism, p=0.0004).

Conclusions:
The TGF-β1 codon 10 polymorphism emerges as a critical genetic determinant of COVID-19 susceptibility and CSS development in transplant recipients, suggesting potential for risk stratification and targeted therapies.

Key Words: Gene polymorphism; Kidney transplant; COVID-19, prediction;

Funding Agency: None

Transplant

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T-Cells Orchestrate the Pathogenesis of Post-Transplant Diabetes among kidney transplant recipients: A Cytokine Polymorphism Study

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Introduction:
Post-transplantation diabetes mellitus (PTDM) represents a significant metabolic complication following renal transplantation. While cytokines are known to mediate β-cell inflammation in diabetes, their role in PTDM remains understudied.
Aim: To investigate the association between T-cell and macrophage-derived cytokine gene polymorphisms and PTDM development in renal transplant recipients (RTRs).

Methods:
We analyzed 309 RTRs, comparing PTDM (n=103) and non-PTDM (n=206) cohorts. Using established laboratory techniques, we genotyped key functional polymorphisms as TH1: IFNG (+874)T>A, TH2: IL-4 (-590)C>T, TH3: TGF-β1 (29)T>C, Macrophage-derived: IL-6 (-174)G>C .

Results:
We observed that TT genotype (high IFN-γ producer) was significantly associated with PTDM (p=0.005), while AA (low producer) predominated in controls (p=0.004). IL-4: CC genotype (low IL-4 producer) was more frequent in PTDM (p=0.02), whereas TT (high producer) was protective (p=0.003). Moreover, IL-6/TGF-β1: high-producer genotypes (GG and TT respectively) showed strong PTDM association (p=0.002 and p=0.03)

Conclusions:
Our findings demonstrate that TH1/TH2 cytokine imbalance, particularly high IFN-γ/IL-6 and low IL-4 production, may drive β-cell inflammation in PTDM. These results highlight the crucial orchestrating role of T-cell immunity in PTDM pathogenesis and warrant validation in larger
cohorts.

Key Words: Cytokine polymorphism; Post-transplant DM; kidney transplant ;

Funding Agency: None

Transplant

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Recurrent urinary tract infections among renal transplant recipients: risk factors and outcome with developing resistance

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Introduction:
Urinary tract infection(UTI) is the most common type of bacterial infection among kidney transplant recipients, with adverse effects on graft and patient survival.
Aim of the study:
To assess risk factors and outcome of renal transplant recipients with recurrent episodes of urinary tract infection.

Methods:
Out of 2950 kidney transplant recipients who are followed up in Hamed Al-Essa organ transplant center of Kuwait, 576 (19.5%) were suffering at least one episode of UTI. Moreover, 120 cases(4%) suffered recurrent UTI comprised group 1, while the remaining cases comprised group 2 (n=2830).Cases with clinically evident pyelonephritis (PN represented, n=32) were assessed against those cases without PN (n=88). In this retrospective study, we assessed those patients regarding risk factors of recurrent UTI and their outcome. The study was approved by the ethical committee of MOH.

Results:
The two groups were comparable regarding their demographics. Recurrent UTI was significantly higher in Kuwaiti, females, anemic with more potent induction IS(P,0.05). Moreover, pretransplant urological problems (vesico-ureteric reflux was noted in 63.6% of cases in group 1 vs. 21.3% in group 2) and deceased donor were another risk factors for recurrence($p<0.05$). Positive gallium scan was confirmed in 59.4% of clinically suspected cases (vs. 25.8% of non-pyelonephritis group, $p=0.03$). The two groups were comparable regarding diabetes and immunoglobulin levels. E coli and Klebsiella Pn. were isolated in the majority of patients in the 1st and 2nd episodes of UTI with increasing risk of resistance after the 3rd episode onwards (up to > 60% in the 4th episode).

Conclusions:
Recurrent UTI is not uncommon among kidney transplants. The most prevalent risk factors for recurrent UTI in our cohort were anemia, female gender, preemptive transplantation, urological problems, cadaveric donor, lymphocytic depleting agents, and prolonged lymphopenia. Clinically suspected pyelonephritis can be confirmed by gallium scan in most cases. Increasing incidence of resistant bacteria with the 3rd episode onwards.

Key Words: urinary tract infection, recurrent ; Kidney transplant; Outcome;

Funding Agency: None

Transplant

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Kidney Re-Transplantation: A Single-Center Experience from the MENA Region

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Introduction:
Kidney re-transplantation is a common procedure in the field of solid organ transplantation. With advances in immunosuppressive therapy and surgical techniques leading to improved initial graft survival, a growing number of patients are facing the eventual failure of their first allograft, creating a significant population requiring repeat transplantation. The decision to pursue a second or subsequent kidney transplant is often preferred over long-term dialysis because of significant patient survival and better quality of life. Comprehensive data from the Middle East and North Africa (MENA) region remains scarce regarding kidney re-transplants.

Aim: This study presents our center's four-decade experience with kidney re-transplantation, specifically evaluating the impact of donor source on clinical outcomes.

Methods:
After getteing approval from the ethical committee of MOH, we conducted a retrospective analysis of all renal re-transplants performed at our institution between 1980-2019. From a total of 3,038 kidney transplants, we identified 198 re-transplant cases (6.51%), including 150 living-donor recipients (Group 1), 48 deceased-donor recipients (Group 2), and 15 third transplants. The study compared demographic characteristics, rejection episodes (both antibody-mediated [ABMR] and T-cell-mediated [TCMR]), and long-term graft/patient outcomes between living and deceased donor cohorts. All patients received standardized immunosuppressive protocols and were followed through our transplant clinic with regular monitoring.

Results:
Our analysis revealed comparable rejection rates between groups, with AMR occurring in 18.7% of deceased-donor versus 16.6% of living-donor recipients, and ACR in 10% versus 9.33% respectively (all $p>0.05$). While deceased-donor recipients showed numerically higher graft failure rates, this difference did not reach statistical significance. Importantly, patient survival outcomes were equivalent between groups. The living-donor cohort had a higher proportion of pre-emptive transplants (32% vs 18%), but this did not significantly impact the primary outcomes. Both groups maintained similar renal function parameters at last follow-up.

Conclusions:
This is the largest reported MENA-region series that demonstrates that kidney re-transplantation yields equivalent outcomes regardless of donor source, with no significant differences in rejection patterns or long-term survival. It is providing critical opportunities for those who have lost primary grafts. These findings should encourage broader utilization of available donor organs in our region while maintaining excellent outcomes.

Key Words: Kidney retransplant; Outcome; Risk factors ;

Funding Agency: None

Transplant

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Cystinosis in pediatric renal transplant recipients: case control study from Kuwait

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Introduction:
Cystinosis is an autosomal recessive liposomal storage multisystem disease characterized by deficient cystinosis that results in cystine accumulation in the lysosomes. It can lead to end-stage kidney disease in most cases before 20 years' age.
Aim:
We aimed to evaluate the outcome of renal transplantation in pediatric renal transplants with cystinosis.

Methods:
Data of renal transplant recipients with Cystinosis (n=20) in Hamed Al-Essa organ transplant center were retrospectively evaluated against matched control cohort without cystinosis (n=126). Demographic data in both groups were compared and post-transplant complications and both graft and patients' outcomes were assessed. This study was approved by the ethical committee of the MOH.

Results:
Most of cystinosis patients were, Females in their second decade of life with their mean age 12.4 ± 3.9 vs. 14 ± 3.1 years in the control group. The two groups were comparable regarding type of donor, pre-transplant comorbidities (p>0.05). The percentage of cystinosis cases with immediate graft function was significantly higher than the control (p=0.024), and this was reflected by relatively lower basal creatinine but did not rank to significance (>0.05), and they received significantly less induction therapy (p=0.002). The two groups were maintained on a comparable immunosuppressive regimen and we did not find any significant difference between the two groups regarding post-transplant complications like PTDM, viral infections. Graft function at 1,3,5,10 years, and both graft and patient outcomes were comparable (p>0.05).

Conclusions:
Under standard immunosuppression therapy with steroid calcineurin inhibitors, mycophenolate mofetil, renal transplant is safe with good long term outcome in patient with cystinosis.

Key Words: Cystinosis; Rare disease in kidney transplant ; Outcome;

Funding Agency: None

Urology

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The Efficacy of Metastasis-Directed Therapy in Patients with Oligometastatic Prostate Cancer: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Introduction:
Oligometastatic prostate cancer (OMPC; one to five metastatic lesions) represents an intermediate disease state in which metastasis-directed therapy (MDT), most commonly stereotactic body radiotherapy, may improve outcomes. However, randomized evidence remains limited and heterogeneous. We performed a systematic review and meta-analysis of randomized controlled trials to quantify the effect of MDT on overall survival (OS; primary outcome) and progression-free survival (PFS) in patients with OMPC.

Methods:
PubMed, Scopus, and the Cochrane Library were searched from inception to 15 November 2025 for randomized controlled trials comparing MDT plus usual care versus usual care alone in adults with OMPC. Outcomes were OS, biochemical PFS (bPFS), and radiographic PFS (rPFS). Hazard ratios (HRs) with 95% confidence intervals (CIs) were pooled using random-effects models with the restricted maximum-likelihood estimator, and heterogeneity was assessed with the I^2 statistic and Cochran's Q test.

Results:
Five randomized trials including 590 patients (mean age 66.9 years; mean follow-up 31.4 months) met the eligibility criteria; 306 patients (51%) received MDT plus usual care. Compared with usual care alone, MDT significantly improved rPFS (HR 0.44; 95% CI 0.32–0.60; $p < 0.01$; $I^2 = 0\%$), bPFS (HR 0.48; 95% CI 0.38–0.62; $p < 0.01$; $I^2 = 0\%$), and OS (HR 0.53; 95% CI 0.34–0.82; $p < 0.01$; $I^2 = 0\%$).

Conclusions:
In patients with OMPC, the addition of MDT to usual care is associated with clinically and statistically significant improvements in PFS and a substantial reduction in the hazard of death. These findings support MDT as a survival-enhancing treatment strategy in appropriately selected patients, while larger phase III trials with longer follow-up are needed to confirm and refine these results.

Key Words: oligometastatic, prostate cancer; metastatic-directed therapy (MDT), stereotactic

Funding Agency: None

Vascular Surgery

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Outcomes of Staged Carotid Endarterectomy Prior to Coronary Artery Bypass Grafting

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Introduction:
Patients with severe carotid artery disease face a perioperative stroke risk of up to 10% following CABG, compared with less than 2% in the absence of carotid artery occlusion. This disparity highlights the importance of carotid endarterectomy in selected patients undergoing CABG, though the timing of intervention remains debated. This study examines perioperative outcomes after staged CEA followed by CABG

Methods:
Retrospective study of all patients who underwent CEA before CABG at a single tertiary center from 2017 to 2024. Demographics, vascular risk factors, operative details, and perioperative outcomes were analyzed. The primary endpoint was postoperative stroke after CABG, with secondary outcomes including postoperative complications and mortality. Carotid artery disease severity was evaluated using duplex ultrasonography and classified according to NASCET criteria as per severity of stenosis. Staged CEA prior to CABG was performed on selected patients In line with the SVS and ESVS guidelines.

Results:
A total of 35 patients underwent CEA at the main vascular tertiary care center during periods from 2017 to 2024. The mean age of the patients was 70.5 years and 72.2% were male. Vascular risk factors were highly prevalent: hypertension (94.3%) (33/35), diabetes (88.6%) (31/35), hyperlipidemia (74.3%) (26/35), smoking (51.4%) (18/35), peripheral arterial disease (37.1%) (13/35), and chronic kidney disease (17.1%) (6/35). A prior history of CVA/TIA was present in (40.0%) (14/35), of patients, and previous myocardial infarction in (57.1%) (20/35). No patient developed CVA following CEA or CABG, and there was no nerve injuries or mortality after CEA. The predominant postoperative complications after CABG included atrial fibrillation in (34.3%) (12/35) in patient, hypotension in (40.0%) (14/35). The post-CABG mortality rate was (5.7%) (2/35), with myocardial infarction identified as the main cause

Conclusions:
Staged CEA prior to CABG was associated with a low postoperative stroke and mortality rate, reinforcing the procedure's safety and efficacy in selected candidates. Standardization of protocols and multi-institutional registries are required for outcome reproduction and validation

Acknowledgements
Ethical approval has already been submitted to MOH. The study meets exempt status as it is a retrospective review

Key Words: Vascular Surgery; Carotid Endarterectomy ; Stroke ;

Funding Agency: None

Artificial Intelligence and Ophthalmology

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Early validation of automated detection of diabetic retinopathy: A Kuwaiti contribution to AI in Ophthalmology

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CASE REPORT

Background:
In the early 2000s a collaborative project with the Bro Taf diabetic retinopathy screening program in Wales, UK was led by a Kuwaiti ophthalmology fellow aimed at the evaluation of the operating characteristics of a reading software (Retinalyze System, Retinalyze A/S, Hørsholm, Denmark) for automated prescreening of digital fundus images for diabetic retinopathy.

Case Summery:
The automated lesion detection reading software was based on advanced mathematical analysis of the gray-level intensity of the retinal images. This form of early artificial intelligence (AI), from the pre–deep-learning era, often referred to as classical machine learning or rule-based AI in medical imaging is an automated pattern recognition system that analyzed grey-level intensities, searched for lesion candidates, excluded vessels and optic disc automatically, applied thresholds to classify structures as lesions.Although this algorithmic pattern analysis may not have been trained with large datasets like modern convolutional neural networks (CNNs), the system still at the time adjusted sensitivity, and used thresholds detection rules.Reflective analysis of this early work revealed the following: 1) This work from 2008 anticipated today's explosion of AI in ophthalmology, 2) The bibliometric evidence showed near-zero citations in the first years after publication with a rise over the last decade spiking in recent years confirming that this early contributions gained influence over time.3) Weaknesses at the time in the form of limited datasets, rudimentary image-processing tools, and scarce computational resources are a matter of the past now with availability of standardized datasets, improved imaging and annotation baselines. 4) Finally, many challenges remain with the limited regulatory and ethical oversight, inadequate translation of algorithmic outputs into actionable and affordable clinical workflows that improves outcomes for patients and care providers alike.

Conclusion:
The citation map demonstrates that this early, clinician-led effort seeded subsequent methodological and clinical studies. The steady growth in citations mirrors parallel advances in machine learning infrastructure and in ophthalmology's acceptance of AI tools. For healthcare professionals in training today, the lesson is clear: pioneering clinically-grounded AI requires curiosity, teamwork, patience, and a focus on clinical utility.

Key Words: Artificial Intelligence; Machine Learning; Diabetic Retinopathy;

Cinical Neurophysiology, Epilepsy

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When Touch Becomes a Seizure Trigger: Severe Stimulus-Induced Rhythmic Discharges in a Child With Dual Chromosomal Micro-abnormalities

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CASE REPORT

Background: Stimulus-induced rhythmic, periodic, or ictal discharges (SIRPIDs) are rare in children and typically associated with acute structural or metabolic encephalopathy. Their occurrence in chronic genetic epileptic encephalopathies is poorly documented. Tactile-triggered seizures represent a severe form of cortical hyperexcitability and may signal ongoing status epilepticus.

Case Summary: A 13-year-old developmentally delayed boy, born to consanguineous parents, carried XP11.23 submicroscopic microduplication and chromosome 8 microdeletion. His epilepsy began with infantile spasms treated with ACTH and vigabatrin, later evolving into Lennox–Gastaut syndrome managed with levetiracetam, valproate, lamotrigine, and clobazam. After an aspiration pneumonia a year earlier, he developed progressive seizure worsening, daily myoclonic jerks, dystonia, and prominent seizures triggered by even minimal tactile stimulation. A 2-hour EEG showed diffuse slowing, poor reactivity, and frequent focal electrographic seizures over bilateral occipital and parietal regions. Crucially, every tactile or painful stimulus induced 10–12 seconds of rhythmic 6–7 Hz theta followed by 2–3 Hz delta discharges, consistent with SIRPIDs, with some events evolving into electroclinical seizures. These findings established a diagnosis of focal status epilepticus with stimulus sensitivity.

Conclusion: This case represents a rare pediatric presentation of severe stimulus-induced epileptic activity in a genetically complex epilepsy syndrome. Recognition of SIRPIDs is essential in refractory childhood epilepsies, as stimulation may inadvertently precipitate seizures and exacerbate status epilepticus risk. This report expands the phenotypic spectrum associated with XP11.23 microduplication and chromosome 8 microdeletion.

Key Words: SIRPIDs; Lennox–Gastaut syndrome; tactile-triggere; chromosomal microdeletion; microduplication; ; pediatric EEG; status epilepticus.;

Cinical Neurophysiology, Epilepsy

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Anti–N-Methyl-D-Aspartate Receptor Encephalitis in a Previously Healthy 5-Year-Old Girl: A Case of Rapid Neuropsychiatric Decline with Excellent Response to Early Immunotherapy

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CASE REPORT

Background: Anti–NMDA receptor (NMDAR) encephalitis is a leading cause of autoimmune encephalitis in children, presenting with acute psychiatric changes, seizures, language dysfunction, and autonomic instability. Early recognition is crucial, particularly as neuroimaging may be normal. We describe a pediatric case with rapid deterioration and delayed presentation due to cultural beliefs.

Case Summary: A previously healthy 5-year-old girl developed sudden behavioral changes including hair pulling, agitation, excessive crying, facial grimacing, and insomnia. Within 48 hours, she developed urinary incontinence, aphasia, and difficulty swallowing. By day three, she experienced recurrent brief generalized tonic–clonic seizures with upward gaze deviation. Medical evaluation was delayed due to parental belief in supernatural possession. On admission, vital signs were stable and systemic examination was unremarkable except for altered behavior and decreased verbal output. Laboratory studies were normal. CT brain and MRI brain/MRA showed no acute abnormalities. CSF chemistry was normal; PCR for HSV and enterovirus was negative. Initial EEG was normal; repeat EEG demonstrated diffuse slowing and rare right fronto-central epileptiform discharges. CSF anti-NMDAR antibodies were positive; serum antibodies were negative. Pelvic MRI excluded ovarian teratoma. Autoimmune panel revealed ANA with Anti-DFS70 positivity. The patient received pulse methylprednisolone for 5 days, two courses of IVIG (initial course in PICU, second on 05/09/2025), and rituximab (first dose 27/08/2025, second dose planned). She was also treated with levetiracetam, supportive care, and multidisciplinary rehabilitation. Behavioral agitation improved with sleep regulation and psychiatric input.

Conclusion: This case demonstrates the classical evolution of anti-NMDAR encephalitis despite normal neuroimaging. It emphasizes the importance of considering autoimmune encephalitis in acute pediatric behavioral regression with seizures, even without fever or focal signs. Early immunotherapy led to progressive improvement. Sociocultural factors delayed presentation, highlighting the need for community education regarding early symptoms of encephalitis.

Key Words: Anti–N-Methyl-D-Aspartate Receptor Encephalitis ; Epilepsy; Autoimmune;

Cinical Neurophysiology, Epilepsy

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Beyond Sepsis: A Metabolic Masquerade in a Toddler with Bloody Diarrhea and Acute Encephalopathy

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CASE REPORT

Background: Glutaric acidemia type I (GA-I) is an autosomal recessive metabolic disorder that may present atypically, particularly in populations with high consanguinity. Fever, diarrhea, seizures, and encephalopathy frequently mimic infectious or autoimmune conditions, delaying diagnosis.

Case Summary: A previously healthy 23-month-old Sudanese boy, born to first-cousin parents, presented with fever, vomiting, and profound bloody diarrhea. On day five of illness he developed three generalized tonic seizures and altered consciousness. Examination showed lethargy, generalized hypotonia, hyporeflexia, and bilateral extensor plantar responses. Initial laboratory studies revealed elevated CRP, prolonged APTT, and normal CSF with negative viral/bacterial PCRs. Broad antimicrobials, IVIG, and high-dose steroids were initiated for presumed infectious or autoimmune encephalitis.MRI demonstrated ventricular dilatation, bilateral basal ganglia and tectal hyperintensities, and delayed myelination, raising suspicion for a metabolic disorder. Urine organic acids confirmed markedly elevated glutaric acid and dicarboxylic acids, establishing a diagnosis of GA-I despite normal acylcarnitine and plasma amino acids. During hospitalization the child developed progressive generalized dystonia, which responded partially to gabapentin and improved significantly with trihexyphenidyl. Consciousness gradually improved by day five of admission, and dystonia stabilized with therapy.

Conclusion: This case underscores a rare pseudosepsis presentation of GA-I, characterized by bloody diarrhea and acute encephalopathy that initially mimicked infectious and autoimmune etiologies. Recognition of characteristic MRI findings and early metabolic testing are essential for timely diagnosis. Clinicians should consider GA-I in any child with acute striatal injury, especially in consanguineous families.

Key Words: Glutaric acidemia type I; dystonia; ; acute encephalopathy; basal ganglia; consanguinity; metabolic disorder.;

Cinical Neurophysiology, Epilepsy

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Fulminant Fatal Influenza A Encephalopathy Following MMR Vaccination in a Previously Healthy Toddler: A Tragic Contrast Between Identical Twins

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CASE REPORT

Background:
Acute necrotizing or fulminant influenza-associated encephalopathy (IAE) is a rare but devastating complication of influenza infection in young children. It remains incompletely understood. This case highlights a unique and tragic presentation of rapidly progressive influenza A–related encephalopathy in a previously healthy 2-year-old girl, occurring shortly after measles–mumps–rubella (MMR) vaccination and in striking contrast to her genetically identical twin and family members, all of whom had concurrent but self-limited influenza A infections.

Case Summary:
A previously healthy 2-year-old female, one of non-identical twins, presented with a 2-day history of fever (up to 42°C), vomiting, and progressive altered consciousness following MMR vaccination five days earlier. On arrival, she was febrile, tachycardic, and developed a generalized tonic–clonic seizure followed by hypotension and respiratory failure, requiring intubation. Laboratory workup revealed profound metabolic acidosis, hepatic dysfunction (AST 4115 IU/L, ALT 989 IU/L), coagulopathy (PT > 240 s, INR uncalculable), thrombocytopenia (31×10^9/L), hyperferritinemia (26,805 µg/L), and markedly elevated LDH (8964 IU/L). PCR confirmed influenza A, with negative results for influenza B and RSV. CT brain demonstrated diffuse loss of gray–white matter differentiation, basal ganglia and thalamic blurring, and features of hypoxic–ischemic injury. EEG showed a low-voltage, non-reactive background. Despite aggressive supportive management, the patient succumbed within 23 hours of admission. Her twin, vaccinated simultaneously and infected with the same influenza strain, recovered fully.

Discussion:
This case underscores the unpredictable severity of influenza A encephalopathy, even among genetically and environmentally matched individuals. The temporal association with MMR vaccination raises complex questions regarding immune modulation and viral neurotropism but does not imply causation. The disproportionate response—culminating in fatal cytokine storm and multiorgan failure—emphasizes the need for vigilance, early recognition, and prompt antiviral and supportive therapy in suspected cases of IAE.

Conclusion:
Fulminant influenza A encephalopathy may develop rapidly and fatally in otherwise healthy children. This case uniquely demonstrates the interplay between host immune response and viral factors, challenging our understanding of susceptibility even in identical twins.

Key Words: Influenza A, encephalopathy, MMR vaccine, ; cytokine storm, pediatric neurology, ; immune modulation, twin case;

Cinical Neurophysiology, Epilepsy

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Early Multimodal Immunotherapy in Post-Viral Opsoclonus-Myoclonus-Ataxia Syndrome: A Toddler Case Study

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CASE REPORT

Background: Opsoclonus-myoclonus-ataxia syndrome (OMAS) is a rare pediatric neuroimmunological disorder characterized by abrupt neurodevelopmental regression, chaotic eye movements, myoclonus, ataxia, and behavioral disturbances. Prompt recognition and early immunotherapy are critical for optimizing outcomes.

Case Description: We report a previously healthy 1-year-8-month-old child presenting with sudden loss of speech, truncal ataxia, jerky movements of the head, shoulders, and trunk, and episodic multidirectional eye movements, following a viral prodrome with no pathogen identified. Behavioral changes included irritability, inconsolable crying, and poor concentration. Extensive neuroimaging, EEG, CSF, and autoimmune/paraneoplastic panels were unremarkable, effectively ruling out tumor-associated OMAS. Intervention and Outcome: The patient received intravenous immunoglobulin (IVIG), pulse and maintenance corticosteroids, and two cycles of Rituximab, along with multidisciplinary rehabilitation. Significant improvement was observed in motor function and behavioral regulation, while speech recovery remained limited. Transient recurrence of opsoclonus and gait instability occurred when monthly IVIG was delayed, resolving promptly after therapy resumption.

Conclusion: This case underscores the importance of early recognition of post-viral OMAS and the efficacy of multimodal immunotherapy, including IVIG, corticosteroids, and Rituximab, for achieving functional recovery. Strict adherence to treatment schedules is critical to prevent transient relapses. Persistent speech deficits highlight the ongoing need for targeted rehabilitation and long-term follow-up.

Key Words: Opsoclonus-myoclonus-ataxia syndrome, OMAS, pediat; VIG, Rituximab; neurodevelopmental regression;

Cinical Neurophysiology, Epilepsy

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Early-Onset Neurofibromatosis Type 1 in Consanguineous Families: Novel Variants, Epilepsy, and Multisystem Phenotypes in Twelve Children

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CASE REPORT

Background: Neurofibromatosis type 1 (NF1) is a multisystem autosomal dominant disorder with highly variable pediatric expression. Consanguinity may amplify disease severity, yet detailed clinical, neuroimaging, EEG, and genetic data from early-onset cases are limited. Understanding genotype–phenotype correlations in such populations is critical for risk stratification and management.

Case Summaries: We retrospectively evaluated twelve children (<16 years; 8 males, 4 females) from four consanguineous Middle Eastern families. All exhibited café-au-lait macules and axillary/inguinal freckling. Plexiform neurofibromas were present in 5/12 (42%), optic pathway gliomas in 4/12 (33%), cutaneous neurofibromas in 3/12 (25%), and developmental delay in 6/12 (50%). Three children (25%) experienced seizures, including generalized-onset tonic-clonic, focal-onset impaired awareness, and combined generalized/focal, with EEG correlates confirming semiology per ILAE 2022/2023 classification. Genetic testing identified seven NF1 variants, including two novel truncating variants (c.2045delG and c.3379_3380insT). Severe multisystem phenotypes clustered with truncating variants, though intra-familial variability
suggested additional genetic modifiers. Two children underwent surgical excision of progressive plexiform neurofibromas.

Conclusion: Early-onset NF1 in consanguineous families exhibits mixed severity, with significant risk for plexiform neurofibromas, optic pathway gliomas, developmental delay, and epilepsy. Novel truncating variants expand the NF1 mutation spectrum and highlight the importance of early family-wide genetic screening, EEG and MRI surveillance, and longitudinal multidisciplinary care. These findings provide actionable insights for clinicians managing high-risk pediatric NF1 populations.

Key Words: Neurofibromatosis type 1, NF1, pediatric, consangu; plexiform neurofibroma, ; optic pathway glioma, epilepsy;

Cinical Neurophysiology, Epilepsy

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The Silent Ring of Childhood Epilepsy: Mosaic Ring Chromosome 20 Revealed Through Prolonged Nocturnal Seizures

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CASE REPORT

Background: Ring chromosome 20 syndrome (r(20)) is a rare chromosomal epileptic encephalopathy characterized by drug-resistant focal seizures, prolonged nonconvulsive episodes, behavioral dysregulation, and normal neuroimaging. Diagnosis is frequently delayed because routine epilepsy gene panels are negative and EEG features evolve over time. Mosaicism levels correlate with clinical severity, and sleep-activated bifrontal epileptiform activity is a hallmark. Early identification is essential for prognostication, family counseling, and seizure management.

Case Summary: We report a 10-year-old boy, born to consanguineous parents, who developed refractory epilepsy at age five, beginning with nocturnal clusters of prolonged behavioral arrest, vocalization, eye staring, and tonic stiffening of the upper limbs. Episodes lasted from seconds to 20 minutes, occurred every 2–3 days during sleep, and were followed by brief convulsions or repeated brief staring spells. Multiple antiseizure medications—including levetiracetam, valproate, lamotrigine, clobazam, phenytoin, and others—failed to control the seizures; partial reduction occurred only on carbamazepine and lacosamide. The child demonstrated progressive learning difficulties, behavioral dysregulation, and mild intellectual disability (IQ 59).

Serial EEGs showed persistent bifrontal epileptiform discharges and generalized slow spike-wave activity during sleep. A 24-hour long-term EEG captured a 13-minute atypical absence seizure with unresponsiveness, fear, and automatisms, accompanied by continuous slow spike-wave discharges—strongly suggestive of r(20). MRI brain, abdominal ultrasound, ECG, and metabolic testing were normal, and an epilepsy gene panel was negative. Cytogenetic analysis revealed mosaic ring chromosome 20: mos 46,X,r(20)[32]/45,X,-20^{5}/46,XY[72], confirming the diagnosis.

Conclusion: This case illustrates the characteristic electroclinical profile of r(20): refractory nocturnal seizures, long absence-like episodes, continuous bifrontal epileptiform activity, normal MRI, and negative gene panel. The diagnosis was established only through karyotyping, underscoring the importance of cytogenetic testing when evaluating unexplained, sleep-activated childhood epilepsies. Early recognition of r(20) syndrome is crucial to guide counseling, anticipate cognitive and behavioral decline, and optimize safety planning for prolonged nocturnal seizures.

Key Words: Ring chromosome 20; ; genetically determined epilepsy; ; atypical absence.;

Cytopathology

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Epithelioid sarcoma of the mons pubis in a young female – A rare case

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CASE REPORT

Introduction
Epithelioid sarcoma is a rare (< 1% of all adult soft tissue sarcoma) malignant neoplasm of connective tissue/soft tissue with an unpredictable clinical course. Although it can occur anywhere it is mostly seen in the upper extremity. Here we are presenting a case with rare location for a rare sarcoma.

Case History
A 24-year-old female presented with a painful swelling in the pubic region of five weeks' duration, which had increased in size over the preceding days and was associated with mild pain.

Gross and Microscopic Findings
Clinical examination revealed a subcutaneous mass measuring 3.7 cm located lateral to the right of the mons pubis. Ultrasound-guided fine needle aspiration cytology identified a malignant biphasic tumor comprising both epithelioid and spindle cell components within a myxoid stroma, accompanied by areas of tumor necrosis. Immunocytochemical analysis demonstrated that the tumor cells were positive for Vimentin, CK (AE1/AE3), EMA, and CD34. INI-1 staining showed loss of expression. The Ki67 proliferation index was approximately 80%.

Conclusion: Early diagnosis—especially using fine-needle aspiration cytology (FNAC)—and wide surgical excision are crucial for effective management due to its rapid progression and poor prognosis. Immunohistochemical analysis commonly shows cytokeratin, EMA, and CD34 positivity, with loss of SMARCB1/INI1 expression detected in most cases.

Key Words: Epithelioid sarcoma; Mons pubis; INI1;

Cytopathology

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Prostatic Adenocarcinoma Presenting As Malignant Ascites

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CASE REPORT

Background: Prostate cancer is a common cancer affecting elderly men worldwide and the second leading cause of death in the United States. It usually metastasizes to the bones, lungs, and lymph nodes. However, involvement of the peritoneum and presentation as malignant ascites is extremely rare and may occur via hematogenous or lymphatic spread. Recognition of this unusual manifestation is important for accurate diagnosis and management.

Case summary: A 72-year-old male, presented with progressive abdominal distension, mild dyspnea and chronic kidney disease. His blood parameters were deranged, platelet count reduced, CRP elevated and D-dimer markedly raised. He had past history of polyps in ascending, descending and sigmoid colon diagnosed as tubular adenoma with low grade dysplasia. Ultrasound-guided paracentesis of ascitic fluid yielded hemorrhagic fluid which on cytological examination showed clusters of cells exhibiting high nuclear-cytoplasmic ratio, vesicular chromatin, prominent nucleoli and cytoplasmic vacuolation. Immunocytochemistry done on cell block sections showed the tumor cells to stain positive for prostate-specific antigen (PSA) and Alpha methyacyl CoA Racemase (AMACR) and negative for Calretinin, CK7 and CK20. The diagnosis of metastatic prostatic adenocarcinoma was rendered. Serum PSA levels done were markedly elevated (636.38 ng/ml). Computed tomography of the abdomen did not reveal any liver, bone or other primary intra-abdominal malignancy. The patient was started on androgen deprivation therapy (ADT) and supportive care. The patient is doing well on follow-up.

Conclusion: Only 32 cases of prostate cancer with peritoneal carcinomatosis and ascites have been reported in the literature of which nine cases presented initially with malignant ascites. Commonly prostatic adenocarcinoma spreads via the hematogenous route (35%) and frequently involved sites being bone (90%), lung (46%), liver (25%), pleura (21%), and adrenals (13%). Prostatic adenocarcinoma, presenting as malignant ascites is rare and should be considered in elderly males presenting with unexplained ascites. Its presentation as ascites indicates a very poor prognosis as it can also show resistance to ADT. Measurement of serum PSA may be a valuable adjunctive study for the diagnosis of malignant effusions in cases of prostate carcinoma. Early recognition through cytology and immunostaining allows appropriate treatment and prevents diagnostic delay.

Key Words: Ascitic fluid ; prostatic adenocarcinoma; Immunocytochemistry;

Cytopathology

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Pulmonary Alveolar Proteinosis (PAP)- A case report

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CASE REPORT

Background: Pulmonary alveolar proteinosis [PAP] is an ultra-rare disease in which surfactant components, that impair gas exchange, accumulate in the alveoli. There are three types of PAP. The most frequent form, primary PAP, includes autoimmune PAP which accounts for over 90% of all PAP, defined by the presence of circulating anti-granulocyte macrophage colony-stimulating factor [GM-CSF] antibodies. Secondary PAP is mainly due to haematological diseases, infections or inhaling toxic substances, while genetic PAP affects almost exclusively children.

Case summary: A 43-year-old, male, smoker one pack per day for more than 20 years, during routine medical check-up was found to have bilateral lung infiltrates [mainly left side] on chest x-ray. High resolution computed tomography [HRTC] done showed a crazy paving pattern, ground glass opacity, septal thickening more dominant in upper lobes. Bronchoalveolar lavage [BAL] was sent for cytology, BAL sample was milky and showed alveolar macrophages, bronchial cells and extracellular proteinaceous material which stained positive for PAS. BAL was negative for acid fast bacilli, legionella, and pneumocystis jirovecii. Transbronchial biopsy revealed occasional collections of amorphous eosinophilic material within some alveoli, which stained positive for PAS, suggestive of pulmonary alveolar proteinosis.

Conclusion: We present the clinical, imaging, histological and cytological findings in a rare case of pulmonary alveolar proteinosis. Till date 363 cases have been reported in the literature. The prevalence varies among countries, from four to 40 cases per million, and the incidence is estimated at almost 0.2 cases per million. Pulmonary alveolar proteinosis [PAP] has rarely been reported in Kuwait

Key Words: BAL; alveolar proteinosis.; PAS;

Dentistry

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Can A Small Rock Stop A Truck? Case Report of Enamel Pearl Blocking Eruption

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CASE REPORT

Background
A fairly common observation in the mixed dentition is the delayed eruption of a maxillary central incisor, which is typically linked to factors such as previous trauma, supernumerary teeth, or local obstruction. Enamel pearls, however, are uncommon developmental anomalies that are rarely observed in the anterior region and usually occur on molar roots. Presentations of this nature are particularly notable because their involvement as a cause of delayed eruption is exceptionally uncommon.

Case Summary
A 9.1-year-old Kuwaiti male presented with an unerupted #11. The patient was medically fit, with no history of trauma or infection in the maxillary anterior region, and had been monitored for spontaneous eruption without progress. Clinical examination revealed a palpable labial bulge at the expected site of eruption, with adequate space available in the dental arch and the contralateral incisor already erupted. Radiographic assessment using periapical and panoramic imaging identified a well-defined radiopaque mass on the labial aspect of the unerupted incisor, consistent with an enamel pearl. No other anomalies or supernumerary teeth were detected. The enamel pearl appeared to act as a mechanical obstruction preventing normal eruption. Management involved planning surgical exposure of the tooth with removal of the enamel pearl, followed by orthodontic guidance to facilitate eruption.

Conclusions
An enamel pearl acting as a mechanical barrier to eruption of a maxillary central incisor represents an uncommon presentation and should be considered when investigating the causes of delayed eruption. Radiographic assessment and appropriate investigations are crucial for guiding diagnosis and timely interceptive treatment in order to minimise the need for more complex intervention.

Acknowledgments
Clinical assessment, radiographic investigation and orthodontic management was provided by Dr. Saud Al-Enzi, an Orthodontic Consultant. Surgical flap was made by the Periodontal Team at Bneid Al-Gar Dental Centre.

Consent Statement
Written informed consent was obtained from the patient's mother.

Key Words: Delayed Eruption ; Enamel Pearl; Interceptive Orthodontics ;

Ethics

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Don't let laws be written by blood: A student reflection on aviation and patient safety.

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CASE REPORT

Background
We are a group of five fifth-year medical students enrolled in the ethics and professionalism course titled "Patient Safety – Better Knowledge for Safer Care." Throughout this elective, we learned the basics of root cause analysis and were introduced to several case scenarios, including the tragic case of J.H, a cancer patient in the UK who accidentally received an intravenous medication (Vincristine) intrathecally, which led to paralysis and eventual death. The analysis was done through a series of videos, one of which highlighted the use of simulation training in aviation and its potential application in medicine. A key point emphasized was the importance of valid, standardized, regularly repeated training. This was reinforced by the observation that pilots undergo mandatory simulator-based training every six months, prompting us to explore this concept further within the healthcare context.

Case Summary
We conducted an expert-informed reflection and invited Captain M.A.J., a senior co-pilot with 10 years of experience, for an expert discussion. Through this combined approach, we identified parallels between aviation and healthcare, particularly in training, safety systems, and error prevention. However, aviation applies these measures in a more standardized and structured manner and pairs them with effective communication and teamwork, resulting in safer and more reliable performance. In addition, aviation has stricter fatigue management policies and a more comprehensive investigation process, where every incident is thoroughly examined and documented, further enhancing safety.

Conclusion
Healthcare must embrace established aviation safety principles, but their implementation must be tailored to the unique clinical complexity of medicine. By incorporating these proven approaches in a way that aligns with medical practice, the healthcare sector can strengthen reliability, reduce errors, and ultimately improve patient outcomes.

Acknowledgement
We gratefully acknowledge Captain Mohammed Abdullah Jarragh for generously sharing his experience in aviation and providing valuable insights on how aviation safety practices can enhance systems within healthcare. His contributions greatly supported the development of this work.

Key Words: Aviation ; Simulation ; Patient's safety;

Ethics

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A Stroke Before Its Time: Reflecting on the Interplay of Dyslipidemia, Past Trauma, and Occupational Neck Extension in a Young Worker.

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CASE REPORT

Background
An ischemic stroke is defined as blockage or reduced blood supply to part of the brain, resulting in tissue injury. Risk factors (RF) include lifestyle, hypercoagulable states, metabolic conditions, and cardiovascular diseases, pervious cervical truama. Moreover, occupational RF's have been identified to increase the likelihood of developing a stroke, and examples include, but are not limited to, jobs that involve chemical and dust exposure and ergonomically related RF.

Case Summary
A 42-year-old Indian lift maintenance worker presented to the ER with dizziness, gait imbalance, left-sided weakness, and dysarthria. On examination, his blood pressure was 194/118, he was disoriented, showed lower facial asymmetry, and his left UL and LL power scores were reduced while the right UL and LL were normal. His National Institutes of Health Stroke Scale score was 10, indicating a moderate stroke. He had a 1-year history of a cardiovascular accident that was managed in India with full recovery. He also suffered spinal trauma due to a road traffic accident (RTA) 6 years ago, for which he underwent cervical spinal fixation surgery. The patient's blood workup showed dyslipidemia, but diabetes was ruled out. An echo with bubble study was negative, ruling out a structural heart defect. The CT scan showed a hyperdense middle cerebral artery (MCA) representing a recent brain infarct, and the left basal ganglia showed an old brain infarct. A CT angiography revealed total occlusion of the right internal carotid artery (ICA) after bifurcation of the right common carotid, and partial thrombosis of the right ICA before its bifurcation into the right anterior cerebral artery (ACA) and MCA. The patient underwent a mechanical thrombectomy with a stent placed in the right ICA.Based on the mechanism of rapid deceleration with neck hyperextension and rotation that may lead to an intimal tear of the carotid artery as seen in RTA, blunt trauma to the head with neck hyperextension, and the abrupt extension of the neck during weightlifting, we can hypothesize that this mechanism may have occurred similarly in our case and led to dissection of the ICA, along with his underlying dyslipidemia and history of RTA.

Conclusion
In conclusion, this patient has dyslipidemia, a history of cervical trauma, and an occupational RF. A stroke at his young age may indicate that the physical strain of working as a lift maintenance worker may have contributed to his stroke along with the RFs mentioned above.

Key Words: Stroke; Occupational risk factor; Dyslipidemia ;

Ethics

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A Local Lens on Parkinson's: Quality of Life Insights From Medical Students' Ethical Reflection

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CASE REPORT

Background:
Quality of life (QoL) in Parkinson's disease (PD) extends far beyond motor symptoms, encompassing physical, emotional, cognitive, and social aspects that reduce independence and lead to significant decline in QoL. Reflecting on this case by utilizing the WHOQOL-BREF neurotoolkit allowed us to truly see the person behind the diagnosis, including frustration, stigma, and the resilience of the patient. Such insight deepens our compassion as future healthcare providers in our journey of education and training and guides us to deliver care that honors dignity and meets patients' true needs.

Case Summary:
We present in this case report a 69-year-old Lebanese woman living with progressive motor and non-motor symptoms and a 45-year chronic history of PD. Her main symptom is tremors, primarily in her lower limbs and hands that last for a short period of time. Regarding her drug history, she is compliant and reports being dependent on her medications. She has undergone multiple battery replacement surgeries in multiple countries around the world every 3 to 5 years for her device-assisted therapy. During periods when the battery expired and was no longer effective, it resulted in persistent tremors, severe insomnia, decreased motor ability, and slurred or unclear speech. Within the last 3 years, the patient has suffered from significant weight loss and urinary incontinence. The patient also reports that PD has had a large impact on her social life. As a result, she is fearful of not being understood due to her difficulty in speech and she no longer drives or leaves the house to avoid any accidents, like falls, in public. The WHOQOL-BREF neurotoolkit is a patient reported outcome tool that utilizes 4 main health domains to assess the global health status of patients independent of current disease. The outcome of these 4 domains is physical health (75%), psychological (56%), social relationships (75%), and environment (88%).

Conclusion:
This case highlights the profound impact of PD on a patient's QoL and how it affects emotional wellbeing, social life, and independence. The patient's history of early-onset PD, complex treatment regimen, and ongoing reliance on medications and device-assisted therapy highlights significant challenges. The patient's coping is shaped by factors such as cultural expectations, social support, education, and spirituality. This reflection reinforces the importance of empathy, cultural sensitivity, and ethical awareness in supporting patients' autonomy and QoL.

Key Words: Ethical Reflection; Quality of Life; Parkinson's Disease;

Genetics

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PLCG1 gene mutation in a child with autoimmune hemolytic anemia: A case report

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CASE REPORT

Background:
Phospholipase C gamma (PLCG) gene is a protein coding gene which catalyzes the formation of secondary messengers essential for immune signaling. PLCG1 is ubiquitous and it is responsible for a transmembrane signaling enzyme that catalyzes the conversion of phosphatidylinositol 4,5- bisphosphate (PIP2) into inositol 1,4,5-triphosphate (IP3) and diacylglycerol (DAG). IP3 and DAG are second messenger molecules that transmit signals from growth factor receptors and immune system receptors across the cell membrane. It regulates processes such as growth, maturation, motility, and apoptosis. In this report, we report a patient with PLCG1gene mutation, who developed, among other manifestations, immune dysregulation and autoimmunity. Our aim is to elaborate on PLCG1 gene mutation in human diseases since the number of reported cases with this gene mutation are scarce.

Case summary:
We describe a 13-year-old Egyptian boy, product of non-consanguineous parents, with a history of autoimmune hemolytic anemia (AIHA) diagnosed at 11 months of age, who was found to have PLCG1 gene mutation. He experienced multiple episodes of severe AIHA following febrile illnesses, necessitating hospitalization, multiple blood transfusions, and courses of corticosteroids, and eventually, immunosuppressants. Laboratory workup confirmed autoimmune hemolytic anemia. His immune status was followed over the years; the only derangement was decreased memory B cells with no significant infections. The patient's condition was stabilized, with his hemoglobin and reticulocyte count returning to normal levels. At the age of 13 years, he was transferred to adult care and is doing well. Next-Generation Sequencing was done in 2023, which detected a missense variant c.2617C>T p.(ARG873Trp) in PLCG1 substituting the positively charged hydrophilic arginine with the aromatic tryptophan.

Conclusions:
This report highlights a rare case linking PLCG1 mutation to immune dysregulation, autoimmunity and immunodeficiency. The role of PLCG1 gene in human health and disease is to be elucidated.

Acknowledgments: We like to thank the patient and his family for their consent and help to report this case study.

Key Words: PLCG ; Autoimmune hemolytic anemia; next-generation sequencing;

Genetics

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Unmasking a New LARS1 Mutation: Expanding the Genotype–Phenotype Landscape of Infantile Liver Failure Syndrome Type 1

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CASE REPORT

Background
Infantile liver failure syndrome type 1 (ILFS-1) (OMIM: 615438) is a rare autosomal recessive cytoplasmic transcription and translation disorder caused by biallelic variants in LARS1 gene. Fewer than 40 cases have been documented worldwide, and the phenotype continues to evolve as new mutations and presentations are recognised.

Case Summary:
We report a preterm girl with a history of intrauterine growth restriction who presented with rapidly progressive jaundice, acute liver failure, hepatomegaly, coagulopathy, and acute liver failure in early infancy. Her clinical course was notable for multisystem involvement and dysmorphic features not previously linked to ILFS-1, including hemolytic anaemia and metabolic bone disease of the newborn. Comprehensive metabolic evaluation was inconclusive, prompting genomic testing, which revealed a novel biallelic LARS1 variant not previously associated with the disease. The variant's predicted pathogenicity, combined with the patient's compelling clinical phenotype, supports its classification as likely pathogenic and broadens the known mutational spectrum of ILFS-1.

Conclusion:
This report highlights a newly identified LARS1 mutation and expands both the genotypic and phenotypic boundaries of ILFS-1. The case emphasizes the importance of considering ILFS-1 in infants presenting with unexplained liver failure, particularly in regions with high consanguinity. Early recognition and molecular diagnosis are critical for prognostication, family counseling, and expanding our understanding of this under-recognized cytoplasmic cytopathy.

Key Words: Infantile liver failure syndrome type 1; ILFS-1; LARS1;

Genetics

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Expanding the Neurometabolic Phenotypic Spectrum of SLC25A42 Related Disease: Report of Four Kuwaiti Cases

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CASE REPORT

Biallelic pathogenic variants in SLC25A42, encoding the mitochondrial CoA transporter, cause a rare neurometabolic disorder with variable clinical manifestations. Although developmental regression, lactic acidosis, and basal ganglia involvement have been described, phenotypic variability among individuals carrying the same founder mutation remains underrecognized. This study characterizes the clinical, biochemical, neuroimaging, and genetic features of Kuwaiti individuals with SLC25A42-related disease and highlights novel phenotypic associations.

A retrospective chart review was conducted on four affected individuals, all harboring the same Saudi founder variant, SLC25A42 c.871A>G (p.Asn291Asp). Ages at presentation ranged from infancy to early childhood. Clinical presentation, biochemical profiles, imaging findings, and molecular results were analyzed. Most individuals presented following febrile illnesses, leading to metabolic decompensation with lactic acidosis and encephalopathy. Developmental regression and speech delay occurred in three cases. One child presented with ketotic hypoglycemia and metabolic acidosis without neurological symptoms, aside from mild academic decline at age seven, and was also diagnosed with stage I hypertension, while blood pressure remained normal in others. Despite sharing an identical mutation, phenotypic expression varied widely, ranging from severe cognitive impairment to mild gait abnormalities, with one individual remaining neurologically intact and ambulatory. Dysmorphic features were observed in three individuals without a consistent pattern. Notably, three individuals exhibited evidence of immunodeficiency, representing a novel association not previously reported in this disorder, while one was not evaluated. One case had congenital heart disease, whereas no cardiac abnormalities were identified in the others. Brain MRI findings (available for three individuals) revealed bilateral basal ganglia and putaminal hyperintensities consistent with mitochondrial encephalopathy.

This case series broadens the phenotypic spectrum of SLC25A42-related neurometabolic disease. The observation of immunodeficiency and highly variable neurodevelopmental outcomes, despite a shared mutation, suggests the influence of additional genetic or environmental modifiers. Comprehensive metabolic, immunological, and systemic evaluation is essential for accurate characterization and optimized clinical management.

Key Words: SLC25A42; Neurometabolic disease; Mitochondrial disorder;

Histopathology

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Chronic sinusitis? Be on the lookout for limited Rosai-Dorfman disease: Report of two cases

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CASE REPORT

Background
Rosai-Dorfman disease is an uncommon non-Langerhans cell histiocytosis characterized by heterogeneous clinical manifestations primarily affecting lymph nodes. Extranodal involvement occurs in approximately 40% of cases, which may present as either localized or disseminated disease. The sinonasal tract represents a frequent extranodal site for Rosai–Dorfman disease (RDD). Recently, histiocytes displaying RDD features have been identified in patients presenting with chronic sinusitis. This report describes two cases of chronic sinusitis and sinonasal polyposis exhibiting features consistent with limited RDD.

Case Summary:
Case 1 concerns a 17-year-old female presenting with nasal obstruction attributable to a left antro-choanal polyp, while Case 2 involves a 26-year-old male diagnosed with allergic sinusitis and bilateral sinonasal polyposis. Both individuals underwent functional endoscopic sinus surgery (FESS), with the resected specimens comprising polypoidal mucosa fragments. Microscopic examination revealed edematous sinonasal mucosa exhibiting varying degrees of polyp formation and subepithelial stroma characterized by nodular granuloma-like aggregates of histiocytes and lymphocytes. The histiocytes appeared to be large and epithelioid, possessing abundant eosinophilic cytoplasm and demonstrating prominent emperipolesis. Immunohistochemical analysis highlighted these cells via S100, CD68, and Cyclin D1 markers. The final diagnosis was chronic sinusitis with inflammatory polyps and associated limited sinonasal Rosai–Dorfman disease.

Conclusion
The presence of diagnostic histological features, MAPK/ERK pathway activation through cyclin D1 positivity, and occasional oncogenic mutations indicate that this phenomenon constitutes a distinct, limited presentation of RDD. This histologic pattern is frequently underrecognized by pathologists, yet its identification is essential due to an increased risk of recurrent chronic sinusitis and implications for managing sinus disease. Importantly, these findings are not associated with systemic involvement.

Key Words: Rosai Dorfman disease; histiocyte aggregates; emperipolesis;

Medicine

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Neurosyphilis Reactivation in Patient with Multiple Sclerosis on

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CASE REPORT

Background: Neurosyphilis remains a diagnostic challenge due to its diverse neurological manifestations and ability to mimic demyelinating diseases such as multiple sclerosis (MS). Diagnostic complexity increases in patients receiving immunosuppressive therapies, where atypical infections or latent reactivation may occur. This case highlights neurosyphilis in a patient with multiple sclerosis receiving B-cell–depleting therapy, illustrating the diagnostic challenges and clinical implications of latent infection reactivation. As no identifiable data or images were included, written consent was waived.

Case Summary: A 43-year-old man with established MS on ocrelizumab presented with urinary incontinence, gait imbalance, and intermittent limb weakness. Initial evaluation suggested MS relapse, and he received high-dose corticosteroids without clinical improvement. His condition deteriorated into encephalopathy, prompting CSF analysis, which revealed marked pleocytosis, low glucose, and elevated protein. Broad-spectrum antimicrobial therapy failed to produce improvement. Subsequent infectious workup demonstrated positive treponemal and non-treponemal serology, confirming neurosyphilis. Intravenous Penicillin G was initiated, resulting in rapid neurological recovery within 48 hours and sustained improvement over the treatment course.

Conclusion: This case illustrates the significant clinical overlap between neurosyphilis and MS, which can delay the diagnosis. Neurosyphilis should remain an important differential diagnosis in MS patients with unexpected neurological decline, especially those receiving immunosuppressive therapies. Incorporating routine syphilis screening prior to initiating B-cell–depleting agents may facilitate earlier detection and prevent morbidity associated with delayed recognition.

Key Words: Neurosyphilis, Syphilis reactivation; Multiple Sclerosis, Demyelination; Ocrelizumab;

Medicine

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Multimodal Approach for Recalcitrant Melasma Using Picosecond Laser and Topical JAK Inhibition

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CASE REPORT

Background:
Melasma is a chronic hyperpigmentary disorder with high relapse rates, especially in darker phototypes, where conventional therapies often fail. Emerging evidence implicates not only ultraviolet radiation but also visible light and inflammatory cytokine signaling in melasma pathogenesis. This highlights the need for innovative, mechanism-based treatment strategies.

Case Summary:
A woman in her early 30s (phototype IV) presented with a five-year history of centrofacial melasma refractory to hydroquinone, oral tranexamic acid, and superficial chemical peels. Baseline modified Melasma Area and Severity Index (mMASI) was 8.4. She underwent a multimodal regimen consisting of picosecond 755 nm alexandrite laser (flat and focus lenses, conservative fluence protocol), short-term topical corticosteroid post-laser, long-term compounded topical tofacitinib 2% cream (twice daily for 11 months), and daily iron oxide–based visible light-blocking sunscreen. Laboratory monitoring during treatment was normal, and no adverse events occurred. At 11 months, near-complete clearance was achieved with an 86% reduction in mMASI (from 8.4 to 1.2). Skin texture and tone improved significantly, and remission persisted for three months after discontinuation of therapy.

Conclusions:
This case demonstrates the potential of a rational multimodal regimen addressing the three key drivers of melasma: melanin overproduction, cytokine-mediated inflammation, and visible light–induced photoreactivation. The combination of low-fluence picosecond laser, topical JAK inhibition, and tailored photoprotection achieved durable remission without complications. While promising, this approach remains off-label and warrants validation in controlled clinical studies.

Acknowledgments: We thank the Ministry of Health, Kuwait, and Newcastle University for institutional support.

Consent Statement: Written informed consent was obtained from the patient for publication of clinical details and images.

Key Words: Melasma; Picosecond laser; JAK inhibitor;

Medicine

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A Novel Homozygous SETX Variant Causing AOA2: A Case Report

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CASE REPORT

Background:
Ataxia with oculomotor apraxia type 2 (AOA2) is an autosomal recessive neurodegenerative disorder caused by pathogenic variant in SETX, presenting with cerebellar ataxia, sensorimotor peripheral neuropathy, cerebellar atrophy and elevated alpha-fetoprotein. We report a young patient with a novel SETX variant presenting with a classic AOA2 phenotype, a finding of particular relevance in Middle Eastern population where such disorders remain under-recognized.

Case summary:
A previously healthy 19-year-old female presented with a two-year history of progressive gait unsteadiness, recurrent falls, bilateral distal paresthesia, and mild congenital dystonia. She was born to a second-degree consanguineous parents. Neurological examination revealed bilateral dysmetria and absent deep tendon reflexes. Ophthalmic examination showed bilateral horizontal gaze-evoked nystagmus. Electrophysiological studies demonstrated a purely sensory axonal peripheral neuropathy, more pronounced in the legs. Visual evoked potentials (VEP) and somatosensory evoked potentials (SSEP) were abnormal, while brainstem auditory evoked potential (BAEP) was normal. Brain MRI showed a mild diffuse prominence of the cerebellar folia, consistent with generalized cerebellar atrophy. Laboratory investigations revealed elevated alpha-fetoprotein (AFP) level of 16.1 ng/mL. The patient underwent genetic testing for three most common autosomal dominant spinocerebellar ataxias (SCA1, SCA2, SCA3) and all genes demonstrated normal repeat range. A comprehensive 153-gene ataxia panel identified a homozygous pathogenic variant, c.4823G>T (p.Gly1608*), consistent with a molecular diagnosis of AOA2 along with additional variants of potential clinical relevance.

Conclusions:
This case provides valuable clinical and genetic insight into the expanding spectrum of SETX-related ataxia and highlights the importance of broader gene-sequencing panels for accurate diagnosis, in regions with high consanguinity. Expansion of molecular-genetic research in hereditary cerebellar ataxia will promote further understanding of pathogenic mechanisms and support the development of targeted disease-modifying therapies.

Acknowledgment: We acknowledge the patient and her family for their cooperation and for providing their informed consent for this case to be reported.

Consent statement: Written informed consent was obtained from the patient for publication of clinical details, genetic findings, and accompanying images in this case report.

Key Words: Ataxia with Oculomotor Apraxia type 2; Cerebellar Ataxia ; SETX gene ;

Medicine

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Beyond the Obvious: Maturity-Onset Diabetes of the Young in the Shadow of Familial Type 1 Diabetes in Kuwait: A Case report of two generations misdiagnosed with Type 1 Diabetes

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CASE REPORT

Background:
Kuwait has one of the highest reported incidence rates of type 1 diabetes (T1D) in children globally, coupled with a striking prevalence of familial diabetes. In such high-risk populations, monogenic forms of diabetes, particularly Maturity-Onset Diabetes of the Young (MODY), are often overlooked or misdiagnosed.
Aim:
To present a case highlighting the diagnosis of MODY3 across two generations in a family initially misdiagnosed with T1D.

Case summary:
A 12-year-old girl presented with hyperglycemia with no features of ketoacidosis at presentation or clinical signs of insulin resistance with family history of T1D in her mother and two sisters diagnosed at adolescence. The child was initially presumed to have T1D and was initially started on Tresiba (insulin degludec) along with rapid-acting insulin as needed. Laboratory workup showed HbA1c diagnostic of diabetes, negative pancreatic autoantibodies (GAD65, IA-2, ICA, ZnT8), preserved C-peptide, and no evidence of thyroid or celiac autoimmunity.

Given negative pancreatic autoimmunity and the strong family history of diabetes in her mother and two sisters, a monogenic form was suspected. Genetic testing revealed a pathogenic HNF1A mutation (heterozygous for the c.394G>A;p.(Glu132Lys) variant in the HNF1A gene) consistent with MODY3 in the index case, mother, and three of her siblings (2 sisters aged 18 and 20 years, already diagnosed with diabetes and one asymptomatic brother at the age of 7 years). The index case was gradually transitioned from insulin to oral sulfonylurea therapy (Gliclazide Modified Release (MR) 30 mg daily). Subsequent monitoring showed excellent glycemic control with her glucose readings to be in range in 85% of the time with no hypoglycemia. HbA1C had improved from 8.6% when she was on insulin to 6.9% after transitioning to oral therapy. Her mother and two sisters were all successfully switched to oral sulfonylurea. Her brother is currently asymptomatic with no clinical or biochemical evidence of diabetes. The family received structured education on inheritance, monitoring and treatment.

Conclusion:
This case emphasizes the importance of considering monogenic diabetes in young patients with a strong family history of non-autoimmune diabetes. Genetic diagnosis can prevent unnecessary insulin use and guide more effective and less invasive therapy.

Key Words: Pediatrics ; Diabetes ; Maturity Onset Diabetes of the Young ;

Medicine

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A Double-Edged Cure: Severe Drug-Induced Liver Injury After Chemotherapy and High-Dose Intravenous Curcumin

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CASE REPORT

Background:
Drug-induced liver injury (DILI) is a challenging diagnostic entity, especially when patients receive both chemotherapeutic and unregulated complementary therapies. Temozolomide, an alkylating agent used in glioblastoma, is rarely hepatotoxic, whereas high-dose intravenous curcumin—promoted as a natural, harmless intervention—has recently been implicated in acute liver injury. We report a striking case of severe cholestatic hepatitis following sequential exposure to temozolomide and high-dose intravenous curcumin.

Case summary:
A 68-year-old man with newly diagnosed high-grade glioblastoma completed chemoradiation, receiving his final dose of temozolomide on 9 August 2024. Seeking supportive treatment abroad, he then underwent a 10-day course of high-dose intravenous curcumin. Within days, he developed deep jaundice, pruritus, dark urine, and profound fatigue, presenting to Amiri Hospital on 25 August 2024. Laboratory evaluation revealed total bilirubin 225 mmol/L (direct 136), ALT 236 U/L, AST 217 U/L, GGT 717 U/L, ALP 510 U/L, albumin 30 g/L, and INR 0.90. Viral hepatitis serologies (HAV, HBV, HCV, HEV), CMV, and EBV were negative. Autoantibodies showed mild positivity (ASMA 1:80, ANA 1:160). Ultrasound excluded obstruction, and MRI showed multiple benign hepatic cysts. Liver biopsy demonstrated marked cholestatic DILI with canalicular stasis and portal inflammation. Prednisolone 30 mg daily led to gradual symptomatic and biochemical improvement.

Discussion:
The temporal pattern strongly implicates intravenous curcumin as the primary hepatotoxic trigger. Although temozolomide can cause DILI, the patient remained stable throughout chemotherapy and declined rapidly only after curcumin infusions. Recent reports highlight severe liver injury linked to intravenous curcumin products, potentially due to contaminants, high excipient load, or unregulated preparation methods. Oncology patients may be especially susceptible due to metabolic stress and treatment-related vulnerability.

Conclusion:
This case underscores the potential severity of DILI associated with high-dose intravenous curcumin, particularly when used alongside chemotherapy. Clinicians should actively inquire about alternative therapies and counsel patients on the risks of unregulated infusion-based treatments.

No identifiable patient data were collected; ethical approval was waived.

Key Words: Drug induced liver injury ; High dose chemotherapy ; intravenous curcumin;

Microbiology and Immunology

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Candida intermedia: an emerging yeast pathogen causing candidemia in a tertiary cardiac center in Kuwait

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CASE REPORT

Background: The incidence of invasive fungal infections is increasing worldwide due to increasing population of immunocompromised/immunosuppressed patients and fungemia is the most common invasive form. Fungemia cases due to rare yeast species have also increased in recent years and usually have poor prognosis due to resistance of rare yeasts to one or more antifungal drugs. Here we describe a rare case of fungemia due to Candida intermedia (now known as Sangouiella intermedia) in a cardiac patient in Kuwait, which was successfully treated with caspofungin.

Case Summary: A 37-year-old male, who is diabetic and hypertensive, was admitted because of myocardial infarction. On Day 48, he developed fever and leukocytosis (WBC 15 x10⁹/L) with elevated sepsis markers (CRP 124 mg/L). A catheter drawn blood culture grew a yeast after nearly 2 days of incubation. VITEK 2 (BioMérieux) failed to identify the yeast species. Using MALDI TOF MS (VITEK MS/ BioMérieux), the yeast was identified as Candida intermedia, which was confirmed by PCR-sequencing of ribosomal DNA (rDNA). The patient was treated with caspofungin (70 mg loading dose, followed by 50 mg daily). No other bacterial or viral co-infections were documented. Repeat blood cultures remained positive till central line was removed. Subsequently, the patient made successful recovery. Echocardiogram did not show valve vegetations. In vitro antifungal susceptibility testing was performed using Etest (BioMérieux) and showed the following minimum inhibitory concentration (MIC) values (in mg/L): amphotericin B, 0.023; micafungin 0.023; fluconazole, 1.5 and voriconazole, 0.016.

Conclusions: C. intermedia fungemia in an immunocompromised patient in Kuwait is described which was successfully treated with caspofungin. The case reveals the growing role of MALDI TOF MS as a routine laboratory diagnostic tool in the identification of clinical fungi. This is the third report from the Middle East and seventh globally on C. intermedia fungemia in the PubMed and highlights the increasing role of rare and emerging yeast pathogens in invasive fungal infections in at-risk patients.

Key Words: Candida intermedia; Fungemia in Kuwait; Successful caspofungin treatment

Microbiology and Immunology

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Solving a clinical enigma: Nigrocephalum cycadicola as a new cause of chromoblastomycosis

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CASE REPORT

Background: Chromoblastomycosis (CBM) is a chronic, progressive subcutaneous mycosis recognized by the World Health Organization as a Neglected Tropical Disease (NTD). It typically presents as verrucous or nodular lesions on the extremities and is characterized by sclerotic (muriform) cells in tissue. The most common etiological agents are melanized fungi belonging to the order Chaetothyriales.

Case Summary: A 72-year-old female from Mexico presented with a progressive lesion on the right lower limb after a fall onto her knees. The large nodular and verrucous lesion developed over 35 years from an initial small papule. Direct examination of skin biopsy consistently revealed muriform cells while histology showed a suppurative granuloma with multiple muriform cells, leading to initiation of itraconazole therapy (100 mg/day, later increased to 400 mg/day). Despite partial improvement, muriform cells persisted in repeated skin samples. Culture of biopsy tissue yielded a dark, yeast-like fungus. Micromorphology revealed simple branched conidiophores bearing phialides with conspicuous funnel-shaped collarettes. Conidia were single-celled, ellipsoidal, pale brown, and aggregated into slimy black heads. The ITS and partial 28S of rDNA were sequenced at the College of Medicine, Kuwait University, and the data showed no match to any known CBM agent. Instead, 100% similarity of ITS region to Nigrocephalum cycadicola and 100% similarity of D1/D2 domains to Acremoniisimulans thailandensis and N. cycadicola was obtained. Multilocus phylogenetic analysis confirmed its placement within N. cycadicola. Given the refractory nature of the infection, antifungal susceptibility testing was performed against 13 agents using EUCAST broth microdilution. High MICs (>4 mg/L) were observed for amphotericin B, itraconazole, isavuconazole, fluconazole, 5-flucytosine, anidulafungin, micafungin, and ibrexafungerp. Lower MICs (<1 mg/L) were recorded for voriconazole, posaconazole, and miconazole. The lowest MICs (≤0.016 mg/L) were obtained for fosmanogepix and olorofim, indicating promising therapeutic potential for refractory CBM.

Conclusions: This report identified N. cycadicola as a newly recognized etiological agent of the NTD chromoblastomycosis. Integration of morphology and multilocus phylogeny supports its taxonomy and highlights the importance of advanced molecular diagnostics in detecting rare and emerging melanized fungi with distinct antifungal susceptibility profiles as new agents of CBM.

Key Words: Chromoblastomycosis; Nigrocephalum cycadicola; Neglected Tropical Disease;

Neurology

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Fulminant Guillain-Barré Syndrome: Clinical Uniquities in a Young Patient

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CASE REPORT

Background:
Guillain-Barre syndrome (GBS) is an autoimmune polyradiculopathy that causes weakness of muscles. GBS is divided into many subtypes, of which there is acute motor axonal neuropathy (AMAN). A majority of all GBS patients who have high levels of anti ganglioside antibodies (Anti-GM1) were previously infected with C. Jejuni, which is likely to cause the AMAN subtype of GBS. In this case report, we will present the clinical uniquities of this patients presentation, progression, treatment, and complications.

Case summary:
A previously healthy 17-year-old non-kuwaiti male presented with rapidly progressive symmetrical limb weakness after experiencing gastroenteritis two weeks prior. Symptoms began with bilateral distal paresthesias, after which a nerve conduction study (NCS) was done, which did not show any abnormalities. Within a few hours, the patient experienced ascending weakness involving the lower and upper limbs. In less than 24 hours the patient became almost completely quadriplegic. On examination, he was fully conscious yet muscle tone was globally reduced. Deep tendon reflexes were absent except for his knee reflexes. Cranial nerves were initially normal except for intermittent choking with liquids. Serum ganglioside panel showed GM1 IgG positive. A second nerve conduction study, taken later in the progression of the condition demonstrated a pure motor axonal pattern, which is consistent with AMAN. The patient was diagnosed with AMAN and was given IVIG. After the first dose of IVIG, he developed new bilateral lower motor neuron facial palsy consistent with treatment-related fluctuation (TRF). A second course of IVIG was administered, after which, gradual improvement was noted. The patient then had a second relapse which involved his respiratory muscles causing CO2 retention, and this was managed with IVIG and the use of a negative pressure ventilator which was previously unused for GBS patients in Kuwait.

Conclusions
It's important to bear in mind that GBS can have normal NCS and may progress rapidly. Furthermore, early symptoms of GBS can easily be misinterpreted as stress related particularly in adolescents. Early detection of GBS can drastically improve prognosis and reduce the likelihood of complications.

Acknowledgements
We would like to thank the staff of Mubarak hospital for their professionalism and facilitation of a smooth data collection process.

Key Words: Guillain–Barré Syndrome; Acute Motor Axonal Neuropathy; Negative Pressure Ventilator;

Obstetrics and Gynecology

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Concurrent Torsion of Pedunculated Subserous Uterine Fibroid and Acute Appendicitis in a 41-Year-Old Woman: A Case Report

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CASE REPORT

Background:
Concurrent presentation of gynecologic and gastrointestinal surgical emergencies is rare making diagnosis and management challenging.

Case Summary:
A 41-year-old woman presented with right iliac fossa pain. Clinical examination and investigations were consistent with acute appendicitis. Diagnostic laparoscopy revealed both an inflamed appendix and torsion of a subserous uterine fibroid, which were managed simultaneously via laparoscopic appendectomy and myomectomy. The patient recovered uneventfully and was discharged on postoperative day 4.

Conclusion:
Concomitant gynecologic pathology such as uterine fibroid torsion may coexist with another acute abdominal emergency like appendicitis. Comprehensive intra-operative assessment allows for simultaneous management, avoiding delayed treatment and repeated surgical interventions.

Key Words: Laparoscopic myomectomy, subserous uterine fibroid; acute appendicitis, peri-appendicitis; combined surgical management;

Ophthalmology

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From Agony to Advocacy: A Patient Journey With Extremely High Myopia

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CASE REPORT

Background:
Pathologic myopia is high myopia that results in the loss of best-corrected visual acuity due to degenerative complications. This case highlights the complex and lifelong challenges associated with extremely high and pathologic myopia, emphasizing how early-onset disease can progress through multiple stages. Following her prolonged journey, the patient has shifted from vulnerability to advocacy, including involvement in raising awareness of preventable causes of blindness and supportive voluntary services to patients with visual impairment or blindness. The patient recently introduced Be My Eyes application, which supports individuals with visual impairment to her workplace recruiting many voluntaries with different cultural and linguistic backgrounds

Case Summary:
A 42-year-old Kuwaiti woman with high myopia since early childhood was first diagnosed at the age of five and began wearing glasses, but her myopia continued to progress, and by the age of 18 she relied primarily on contact lenses due to the extreme thickness and limited compressibility of her high-prescription glasses. She later developed intolerance to contact lenses, reporting increasing sensitivity, irritation, and recurrent infections. At the age of 22, she elected to undergo bilateral phakic intraocular lens implantation under general anaesthesia. A few years later, she developed a squint attributed to abducent nerve involvement and was correct with incorporating prism into her prescription glasses. In 2024, she developed a new type of blurring and was diagnosed with a cataract. The surgery was considered high risk because her phakic intraocular lens had to be removed, and accurate IOL power calculation was difficult due to the absence of her original refractive measurements. As the cataract progressed rapidly, she was counselled that although the procedure carried a high risk and could fail, leaving it untreated carried the same poor visual outcome. She proceeded with cataract extraction on two separate dates and currently uses bifocal glasses for daily vision. OCT imaging later revealed posterior capsular opacification.

Conclusion:
This case highlights the complexity and lifelong impact of ocular pathology. Some patients not only endure significant challenges but also become advocates who raise community awareness and help recruit volunteers. In our journey as students and future health care professionals its paramount to consider our patients not only as stake holder but partners in advocacy in our community

Key Words: Pathological myopia; Patient lead advocacy ; Ophthalmology ;

Orthopedics and connective tissue disorders

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Invisible Risk in Orthopedics: Case Report and Interview on Surgical Failure in Undiagnosed Hypermobility Spectrum Disorder

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CASE REPORT

Case Summary:
We present the case of a 40-year-old woman, who underwent multiple failed orthopedic surgeries undiagnosed with Hyper-mobility Spectrum Disorder (HSD). She underwent four left ACL reconstructions followed with total knee arthroplasty, and two right quadriceps tendon repairs with persistent instability.

Accurate diagnosis and individualized hyper-mobility-specific multidisciplinary care resulted in a surgery-free period of approximately three years, with objective follow-up measures demonstrating improvements and a significant enhancement in quality of life. To better understand the lived experience of the patient, a qualitative interview was conducted. The patient described the emotional and physical burden of repeated surgical failures, diagnostic delays, and systemic shortcomings in supporting hyper-mobile individuals. Themes from this interview highlighted the gap between clinician expectations and patient realities, emphasizing the need for early diagnosis, individualized planning, and informed preoperative counseling in managing patients with connective tissue disorders.

Conclusion: This case raises an urgent call for the necessity of early recognition and hyper-mobility-specific multidisciplinary care strategies.

Key Words: Hyper-mobility, Connective Tissue Disorders, Ortho; ACL ; Arthroplasty;

Pathology

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Incidental Finding of Invasive Lobular Carcinoma Within a Benign Phyllodes Tumor of the Breast: A Case Report

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CASE REPORT

Background:
Phyllodes tumors account for approximately 1% of all breast neoplasms and are characterized by their biphasic fibroepithelial composition. The occurrence of invasive lobular carcinoma (ILC) within a phyllodes tumor is exceptionally rare, with less than six cases reported in the literature to date. We hereby present the first documented case in Kuwait.

Case summary:
A 42-year-old woman presented with a well-defined, heterogeneous, macro-lobulated left breast mass, radiologically scored as BI-RADS 4, with an initial core biopsy diagnosis of a fibroepithelial lesion favoring fibroadenoma. A lumpectomy was subsequently performed, and gross examination revealed an unoriented 53 mm lobulated mass.

Microscopic examination demonstrated a benign phyllodes tumor containing an incidental focus of invasive lobular carcinoma infiltrating the stromal component. By immunohistochemistry (IHC), the invasive component showed positivity for pan-cytokeratin (Pan-CK), estrogen receptor (ER), and progesterone receptor (PR), with HER2 score 1+, and was negative for E-cadherin and p63, supporting the diagnosis of ILC.

Given the unexpected carcinoma findings, the absence of a clear orientation of the specimen, and the nature of the excision, the invasive tumor was staged as at least pT2, with 2-mm distance from the nearest margin.
Conclusions:
The incidental identification of invasive lobular carcinoma arising within a benign phyllodes tumor underscores the importance of thorough histopathological sampling and assessment to avoid a missed diagnosis. It also highlights the critical role of the multidisciplinary team's collaborative expertise, particularly when discrepancies in the breast triple assessment are identified.

Acknowledgements:
I would like to thank the Department of Pathology in Mubarak Hospital for giving me the opportunity to present this rare case in the HSC Annual Poster Conference.

Key Words: ILC; Incidental ; Phyllodes;

Pathology

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Tongue Metastasis of Malignant Mesothelioma: A Case Report

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CASE REPORT

Background
Malignant mesothelioma is characterized by its aggressive nature and propensity for widespread metastatic spread. Nonetheless, metastasis to the oral cavity, and specifically to the tongue, is an uncommon event. This rarity introduces notable diagnostic complexities, as the tumor's histopathological features may closely resemble those of primary oral cancers, thereby complicating accurate diagnosis and optimal management.

Case Presentation
A 65-year-old male, previously diagnosed with sarcomatoid type malignant mesothelioma in 2019, had been treated with cisplatin, pemetrexed, immunotherapy, and radiation therapy to the chest, which showed clinical benefit. The patient remained on immunotherapy and underwent scheduled PET/CT evaluations through 2024. In August 2024, he presented with a mass in the left lateral posterior tongue. Radiologic imaging of the oropharynx revealed a hypermetabolic lesion in the posterior tongue extending to the base, abutting the right genioglossus and lingual arteries, without evidence of bone invasion.

The patient underwent wide local excision of the tongue lesion, which grossly appeared as a firm yellow-white nodule. Histopathological examination showed stratified squamous epithelium with subepithelial multinodular infiltrative tumor with desmoplastic reaction. The tumor consisted of pleomorphic cells with vesicular chromatin, irregular nuclear contours, visible nucleoli, and pale eosinophilic to clear cytoplasm. Mitotic figures were easily identified. Immunohistochemical analysis revealed diffuse positivity for calretinin, D2-40, and CK5/6, with focal weak expression of WT1, patchy p63 positivity, and CK7 negativity. A diagnosis of metastatic mesothelioma was made.The patient subsequently received palliative radiotherapy to the oral cavity (21 Gy/3 fractions) and continued pembrolizumab, which was well tolerated.

Conclusion
This case highlights a rare occurrence of mesothelioma metastasising to the tongue. It emphasises the importance of integrating clinical history, imaging findings, and immunohistochemical studies to avoid misdiagnosis. Recognizing such atypical metastatic sites extends the known patterns of mesothelioma dissemination and underscores the need for multidisciplinary collaboration in advanced disease management.

Key Words: Tongue; Metastasis ; Malignant mesothelioma;

Pathology

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A Case of Enteropathy Associated T-Cell Lymphoma (EATL) Without Prior Diagnosis of Celiac Disease: A Case Report

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CASE REPORT

Background:
EATL type 1 is a rare intestinal lymphoma arising from intraepithelial T cells, occurring in approximately 0.1 per 100,000 people per year, most often involving the jejunum in the 6th to 7th decades of life. Although commonly associated with celiac disease, a significant proportion of EATL cases occur in patients without a previously known diagnosis of celiac disease, making the lymphoma the first clinical manifestation. This subtype is characterised by pleomorphic infiltrates of medium to large cells that are positive for CD30 by immunohistochemistry. In contrast, monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL), which was formerly known as EATL type 2, lacks association with celiac disease and features monomorphic small to medium sized CD8 and CD56 positive T cells.

Case summary:
A 62-year-old Kuwaiti female, known case of iron deficiency anemia with no history of celiac disease or related serologic testing, presented to the emergency department with a 2-day history of acute abdomen associated with nausea, vomiting and constipation. Chest radiography showed air under the diaphragm. CT abdomen revealed thickened hyper-enhancing small bowel loops, abdominopelvic free fluid with large hemoperitoneum, large amount of intrabdominal free gas, and small gas pockets. Laparotomy revealed a perforated jejunal segment with markedly thickened wall and enlarged mesenteric lymph nodes. Histopathological examination showed transmural infiltration by medium to large atypical lymphoid cells with marked flattening of surface villi and intraepithelial lymphocytosis (>60 intraepithelial lymphocytes per 100 enterocytes). On immunohistochemistry, the medium to large sized atypical cells were positive for CD3, CD7, CD30 and Granzyme B, and negative for CD20, CD79a, CD2, CD4, CD5, CD8, CD56, CD10, BCL2 and ALK1 with high proliferation index of Ki67. Mesenteric lymph nodes showed sinusoidal involvement by neoplastic cells.

Conclusion:
EATL may present as the initial manifestation of previously unrecognized celiac disease. Recognition of enteropathy associated features, integration of morphology and immunophenotype and appropriate serologic testing are essential for diagnosis and management.

Acknowledgments:
I would like to thank the pathology department in Mubarak Al-Kabeer hospital for allowing me to present this case.

Key Words: EATL; No History of Celiac; lymphoma;

Pathology

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Unveiling a Rare Case of Testicular Follicular Lymphoma in a Young Adult

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CASE REPORT

Background:
Testicular Follicular Lymphoma (TFL) is a recognized, rare indolent form of extra-nodal follicular lymphoma that affects children and young adults. Up to our knowledge, 23 cases have been reported in literature. Unlike conventional follicular lymphoma, TFL usually presents as a localized disease and exhibits distinct morphologic, immunophenotypic, and genetic features. It displays either a purely follicular or mixed follicular and diffuse architecture and characteristically lacks the BCL2 protein expression and t(14;18)/IGH-BCL2 translocation. It carries an excellent prognosis and requires distinction from other entities.

Case Summary:
A 20-year-old male, presented with right testicular pain and swelling for 6 months. Serum tumor markers (AFP, β-hCG, LDH) were within normal limits. Pelvic MRI revealed a right testicular ill-defined heterogenous mass. The patient underwent right radical orchiectomy. Gross examination showed a distended tunica vaginalis containing yellowish serous fluid. Serial sections revealed a tan, rubbery lesion involving the testis with extension into the epididymis. Histologic sections showed a dense lymphocytic infiltration of the testis and epididymis arranged in neoplastic follicles permeating among hyalinized seminiferous tubules. The follicles were composed of predominantly medium to large-sized lymphoid cells with centroblast-like morphology and few centrocytes. Mantle zones around the follicles were not well-defined. The neoplastic cells were immunophenotypically positive for CD45, CD20, CD79a, CD10 and BCL6 while negative for BCL2 and CD3. Stains for CD21 and CD23 highlight expanded and focally disintegrated follicular dendritic cell meshwork. Ki67 proliferative index was high (about 70-80%). Screening with germ cell origin immunohistochemical stains was negative. Cytogenetic testing for t(14,18)/IGH-BCL2 fusion was negative. A postoperative bone marrow biopsy revealed no involvement by lymphoma and a follow up FDG-PET/CT showed no abnormal uptake.

Conclusion:
This case highlights a classic presentation of TFL in a young adult with typical histologic and immunophenotypic findings and an indolent clinical course. TFL should be considered in the differential diagnosis of a testicular mass, especially in children and young adults. Awareness of its unique morphology and absence of BCL2 expression and cytogenetic testing aids in accurate diagnosis and appropriate management.

Key Words: Testicular ; Follicular; Lymphoma;

Pathology

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Challenges in the diagnosis of Gastrointestinal Sarcoidosis: Report of a Case

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CASE REPORT

Background:
Sarcoidosis is a multisystem inflammatory disease characterized by the formation of non-caseating granulomas of unknown origin. These granulomas are the hallmark histological finding and can affect almost any organ in the body, although the lungs and hilar lymph nodes are most frequently involved. The gastrointestinal (GI) tract is another possible site of disease, with involvement ranging from the oral cavity to the colon. However, GI sarcoidosis is rare and poses significant challenges for diagnosis and treatment, as its symptoms are often nonspecific and resemble other gastrointestinal disorders.

Case Summary:
A 20-year-old chronic smoker had been experiencing ongoing epigastric pain, reduced appetite, and significant weight loss for three years. Despite multiple hospitalizations for persistent symptoms resembling gastritis, standard treatments offered no relief. A CT scan revealed several enlarged mesenteric lymph nodes and thickening in the distal stomach, leading to luminal obstruction. Upper endoscopy found multiple gastric ulcers; biopsies from these ulcers indicated granulomatous gastritis. During an appendectomy performed for appendicitis, a mesenteric lymph node was also excised. Histological examination of the excised lymph nodes showed well-formed, non-necrotizing epithelioid granulomas, with no signs of infection or foreign material. Based on the correlation of both biopsy findings, a diagnosis of sarcoidosis was established, further supported by elevated angiotensin-converting enzyme levels. The patient exhibited a positive response to treatment with corticosteroids and methotrexate.

Conclusion:
Patients with established systemic sarcoidosis, especially those with extrapulmonary involvement, are at increased risk of developing gastrointestinal manifestations. Despite this association, GI sarcoidosis remains under-recognized and may significantly contribute to patient morbidity and mortality. Gastric involvement typically arises from granulomatous inflammation and subsequent scarring, which can lead to mucosal ulceration and related symptoms.

Diagnosing GI sarcoidosis on biopsy is challenging, as granulomas in the GI tract are not specific for this disease. Diagnosis requires non-caseating granulomas in the GI tract, evidence of another organ's involvement, and exclusion of other causes. A thorough clinical evaluation is necessary to confirm sarcoidosis.

Key Words: Sarcoidosis; Non caseating granuloma; Gastro intestinal tract;

Pathology

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CIC::DUX4 Positive Sarcoma; An Intriguing, Ultra-Rare Soft Tissue Tumor In A Young Female With Potentially Aggressive Outcome, Presenting As Right Flank Mass With Inguinal Lymphadenopathy

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CASE REPORT

Background:
CIC::DUX4 positive sarcoma(CDS) represents an aggressive subtype of undifferentiated round cell sarcoma, accounting for less than 1% of all sarcomas. CDS occurs mostly in children and young male adults (15–35 years), with median age in the second decade. Most tumors have a predilection to occur in the soft tissue (87%), with the most frequent primary tumor location in the limb, followed by trunk. We present the case of young female who was diagnosed as having high-grade undifferentiated round cell sarcoma confirmed to be a CDS by next-generation sequencing.

Case summary:
20-year-old young female patient presented with history of right flank pain with palpable, tender, mobile mass with right inguinal lymph node, revealed metastatic malignant high grade round cell neoplasm. CT shows a large multilocular, heterogeneously enhancing solid lesion (12.0 x 8.5 x 5.5 cm). Post neo-adjuvant, wide local excision specimen (19.0 x 9.0 x 6.5 cm), variegated solid cystic mass with areas of necrosis and calcification. Microscopy reveals sheets and lobules of round to epithelioid tumor cells arranged in pattern less pattern, separated by thick fibrous septa, clear to eosinophilic cytoplasm, few rhabdoid like cells, highly pleomorphic tumor giant cells, atypical mitosis and focal coagulative necrosis. IHC shows diffuse positivity for CD 99 and WT1. However, FISH probes for EWSR1, SS18 and CIC rearrangement revealed negative results. Targeted RNA sequencing revealed no detectable gene fusion. Accordingly, Ewing sarcoma and other EWSR1- altered related entities are excluded except for the possibility of CDS. The panel used is not able to detect CDS, an internal validated and published algorithm based on the expression data of 20 vs. 100 top expressed genes. Results of the assay revealed a probability of the CDS of 0.87, which is clearly above the cut-off of 0.75. Accordingly, CDS-rearranged undifferentiated small round cell sarcoma was diagnosed. This case has been reported with expert opinion from Prof Abbas Agaimy (Soft tissue pathology expert)

Conclusion:
CIC-rearranged sarcoma; CIC::DUX4; is highly aggressive and rapidly develops a lethal metastatic disease and chemoresistance which necessitates a high index of suspicion. They pose a diagnostic challenge, owing to its histological similarity with Ewing sarcoma and other small round cell tumor. Definitive tumor diagnosis relies on genetic(IHC, FISH) and molecular techniques(NGS).

Key Words: CIC-rearranged sarcoma ;CIC::DUX4; Ewing-like sarcoma; small round cell tumor;

Pathology

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Extramedullary Hematopoiesis as An Intriguing Finding in Pericardial Fluid Cytology, In a Newborn with Non-Immune Fetal Hydrops

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CASE REPORT

Background: Non-immune fetal hydrops (NIFH) is characterized by excessive accumulation of fluid in two or more fetal body cavities. The common causes broadly include cardiovascular, chromosomal, hematologic, genetic disorders, and infections, among others.

Case Summary:
We present a case of a newborn male, diagnosed clinically with atrioventricular septal defect and NIFH. Pigtail drainage of pericardial fluid was done and 20 ml of fluid was sent for cytological evaluation. One cytospin slide stained with Giemsa, one ThinPrep, and one cell block was prepared. Smears and cell block sections, in addition to the expected reactive mesothelial cells and macrophages, also revealed megakaryocytes, nucleated RBCs, and rare myelocytes. No atypical cells were seen. A diagnosis of extramedullary hematopoiesis (EMH) was offered.

Conclusions:
EMH occurs when the bone marrow is under stress, resulting in production of hematopoietic cells outside the marrow elsewhere, most commonly in the liver and spleen. It occurs rarely in body fluids, and even rarer in pericardial fluid. Common causes of EMH include chronic hemolytic anemias, myeloproliferative neoplasms, hematological malignancies, metabolic stress, and infections, among others. EMH in this neonate may be due to infection or metabolic stress; however hemolytic anemias need exclusion. The neonate is also under investigation for Down's syndrome, as a part of the work up for NIFH.

Acknowledgements: Dr. Shyhab, NICU Consultant, Maternity Hospital, Kuwait; Chest Disease Hospital, Kuwait.

Consent statement: Not applicable.

Key Words: Extramedullary Hematopoiesis; Pericardial fluid; Non immune fetal hydrops;

Pathology

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A Challenging Case of BRAF Mutated and Morphologically Spitzoid Tumor

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CASE REPORT

Background:
BRAF-mutated and morphologically spitzoid (BAMS) neoplasm is a melanocytic tumor with spitzoid morphology that harbors activating BRAF or NRAS mutations, placing it outside the true Spitz category. BAMS is a recently described entity requiring correlation of clinical, morphological, and molecular findings.

Case Summary:
12-year-old female presented with an irregular, pigmented, papular plaque above the left elbow. The lesion appeared shortly after birth and was initially identified as a birthmark (melanocytic nevus). One year ago, a second lesion developed as a small bleb in the center of the pre-existing one, bled on touch and progressively increased in size. Histopathology: Asymmetrical melanocytic lesion composed of two populations. The first population involves the dermo-epidermal junction with a predominantly lentiginous component and a bland intradermal nested component, with overlying epidermal papillomatosis. A second intradermal population is noted subjacent to the first, showing a vaguely nested/expansile dermal component with sheeting and a thickness of 1.9 mm (measured from the granular layer). The anatomic (Clark) Level is IV. The neoplastic cells are epithelioid with mild to moderate atypia, featuring vesicular nuclei, limited hyperchromasia, and prominent nucleoli. Few dermal mitotic figures are noted, with a mitotic rate of up to 4 per mm² (a total of 8 in the examined tissue). A limited lentiginous component is present over one edge of the second lesion. Tumor-infiltrating lymphocytes are identified and appear non-brisk; no tumor regression is seen. The lesion measures 0.4 cm in its largest dimension. It is 1 mm from the peripheral margin and 0.5 cm from the deep margin. IHC: The lesional cells are positive for S100 and Melan-A but negative for HMB-45. P16 immunostain shows patchy positivity. Ki-67 shows a low proliferation index of at least 5-7%. BAP-1 shows cytoplasmic staining with equivocal loss of nuclear stain. PRAME is non-contributory. Molecular testing: The mutation identified by the Oncomine Comprehensive Assay (DNA) is BRAF:c.1799T>A, p.(V600E). This class I activating exon 15 BRAF V600E mutation is located in the kinase domain of the BRAF protein and is highly recurrent in melanoma, as well as lung and thyroid cancers, among others.

Conclusion: Based on the morphology and molecular results, the favored diagnosis is a BRAF-mutated and morphologically spitzoid tumor (BAMS) with features of an atypical spitzoid tumor.

Key Words: melanocytic ; Spitz ; BRAF;

Pathology

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Ewing Sarcoma Beyond Bone: A Rare Extra-skeletal Presentation in the Lip with Prognostic Insight

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CASE REPORT

Background:
Ewing sarcoma (ES) is a highly aggressive, undifferentiated small round cell sarcoma that predominantly arises in bone. Its extra-skeletal counterpart (EES) is uncommon, and primary occurrence in the soft tissue of the oral cavity is exceptionally rare. The overlapping morphology of EES with other small round cell tumors often presents a diagnostic challenge.

Case Summary:
A 22-year-old male presented with a painless, progressively enlarging submucosal nodule on the inner aspect of the lower lip. Overlying mucosa appeared intact. PET-CT revealed no other metabolically active lesions. The lesion was completely enucleated under local anesthesia. Grossly, tumor was well circumscribed, firm, and measured 1.4 × 1.4 × 0.8 cm. Microscopy revealed a malignant small round cell tumor arranged in diffuse sheets separated by delicate fibrovascular septa and surrounded by a thin fibrous capsule. Tumor cells were uniform, with scant vacuolated cytoplasm, vesicular nuclei, and inconspicuous nucleoli. Immunohistochemistry demonstrated diffuse membranous positivity for CD99, NKX2.2, FLI-1 and Vimentin with negativity for epithelial, lymphoid, myogenic, vascular, melanocytic, and BCOR markers. Fluorescence in situ hybridization using a dual-color break-apart probe for EWSR1 revealed a breakpoint at chromosome 22q12. Next-generation sequencing detected no additional pathogenic variants. Based on the integrated histologic, immunophenotypic, and cytogenetic findings, a final diagnosis of EES was established. At 30 months of follow-up, the patient remains asymptomatic with no recurrence or metastasis.

Conclusion:
This case highlights the importance of considering EES in the differential diagnosis of small round cell neoplasms at unusual soft-tissue sites such as the oral cavity. Consistent with literature and our observation, oral cavity EES tends to be encapsulated, smaller in size, and demonstrates excellent outcomes following complete excision. These features suggest that tumor site may hold prognostic value. A meticulous, multimodal diagnostic approach is essential for accurate identification and optimal patient management.

Key Words: Extra-skeletal Ewing sarcoma; oral cavity; EWSR1 rearrangement; Favourable prognosis;

Pathology

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Clinicopathologic Spectrum of Syphilis—Diagnosis Not to Be Missed: A Case Series from Kuwait

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CASE REPORT

Background
Syphilis is renowned for its highly variable clinical and pathological manifestations, which can complicate timely and accurate diagnosis. This case series presents the extensive anatomical diversity of syphilitic lesions encountered at a single tertiary care center in Kuwait. By focusing on the broad spectrum of presentations, this report underscores the diagnostic difficulties clinicians and pathologists may face and highlights the importance of correlating clinical impressions with pathological evidence.

Case Summary
In this series, six cases of biopsy-confirmed syphilis were analyzed, each affecting different anatomical regions. The sites involved included the lower labial mucosa and tongue within the oral cavity, the larynx, rectum, perianal skin, and the inguinal lymph node. Patients presented with a wide range of symptoms, such as mucosal lesions, persistent hoarseness, lymphadenopathy, and the presence of a rectal mass, reflecting the disease's diverse clinical manifestations. Histopathological evaluation of all cases revealed several consistent features: epithelial hyperplasia, infiltration of intraepithelial neutrophils, microabscess formation, and a dense inflammatory infiltrate that was notably rich in plasma cells. Additionally, some cases displayed endothelial swelling and ill-defined granulomas. Diagnostic confirmation was achieved in four cases with positive Treponema pallidum immunohistochemistry, while serological testing established the diagnosis in the remaining two cases. This series demonstrates the diverse morphological patterns of secondary syphilis and its ability to mimic various reactive, infectious, and neoplastic conditions.

Conclusions
Syphilis may present with a broad range of clinicopathologic features, affecting multiple anatomical sites. Accurate recognition of its wide-ranging presentations and identification of key histological hallmarks are crucial for correct diagnosis and treatment. In circumstances where morphological findings are inconclusive, Treponema pallidum immunohistochemistry remains an essential diagnostic tool.

Acknowledgments
The authors express their appreciation to the Department of Pathology for their invaluable assistance in the review of these cases.

Consent Statement
All cases included in this report were anonymized, and no patient-identifiable information has been disclosed.

Key Words: syphilis; treponema pallidum; plasma cell-rich inflammation;

Pediatric Endocrinology

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Central Hypothyroidism and Dyslipidemia Induced by Oxcarbazepine: A Case Highlighting Early Lipid Response to Low-Dose Thyroxine Without Biochemical Normalization

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CASE REPORT

Background
Antiepileptic drugs (AEDs) such as oxcarbazepin (OXC) are widely used in pedeatric nuerology but can disrupt the hypothalamic-pituitary-thyroid axis, leading to central hypothyroidism characterized by low FT4 and inappropriately normal or low TSH. Although often clinically silent, this alteration may contribute to metabolic complications like dyslipidemia. We report a pediatric case of oxcarbazepine-induced central hypothyroidism with dyslipidemia, where lipid levels significantly improved following low-dose levothyroxine therapy despite persistent biochemical hypothyroxinemia, highlighting the complexity of managing thyroid function in patients on long-term AEDs.

Case Summary
A 12-year-old boy with a history of seizure disorder, maintained on oxcarbazepine 600 mg twice daily, was referred to the pediatric endocrine clinic for evaluation of dyslipidemia. Laboratory investigations showed elevated LDL-cholesterol 3.66 mmol/L, total cholesterol 6.18 mmol/L, and low free T4 7.7 pmol/L with normal TSH 1.9 µIU/mL, indicating central hypothyroidism. There was no family history of thyroid or lipid disorders. The patient was started on levothyroxine 25 µg daily. On follow-up, LDL-cholesterol improved to 3.13 mmol/L, free T4 was 7.6 pmol/L, and TSH was 1.559 µIU/mL.

Conclusions
This case emphasizes the importance of routine endocrine surveillance in children receiving antiepileptic medications, even in the absence of overt clinical symptoms. Central hypothyroidism secondary to oxcarbazepine may present with dyslipidemia that responds to small doses of thyroid hormone, without the need to fully normalize thyroid function tests. Such cases highlight a management challenge for clinicians, distinguishing between clinically relevant endocrine dysfunction and isolated biochemical alterations. Early recognition and individualized treatment can mitigate metabolic complications while avoiding excessive intervention.

Acknowledgments
We acknowledge the Pediatric Department at Mubarak Hospital for case management.

Consent Statement
Informed consent was obtained from the patient’s guardian for publication

Key Words: Oxcarbazepine; Central Hypothyroidism ; Dyslipidemia;

Pediatrics

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A Novel ETHE1 Mutation in Ethylmalonic Encephalopathy: Diagnostic Challenges in a Kuwaiti Infant

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CASE REPORT

Background

Ethylmalonic encephalopathy (EE) is a rare autosomal recessive metabolic disorder caused by biallelic pathogenic variants in the ETHE1 gene. It presents with progressive neurological, gastrointestinal, and vascular involvement. Diagnosis can be challenging, particularly when the condition is not included in the standard newborn screening program.

Case Summary

We report a Kuwaiti male infant who had chronic watery diarrhoea since birth, followed by progressive neurological decline. At the age of three months, he developed cough and acute respiratory distress (rhinovirus acute bronchiolitis) followed by poor oral intake and vomiting and was admitted to PICU with encephalopathy, bradycardia, apnea, cyanosis, and received ventilatory support for two weeks. Clinical examination was notable for hypotonia, absent gag reflex, seizures, global developmental delay, transient acrocyanosis, and mottled skin changes. Brain MRI showed bilateral basal ganglia necrosis with white matter abnormalities, consistent with metabolic encephalopathy. Biochemical testing revealed elevated plasma lactate, mild hyperammonemia, filter paper acylcarnitine profile was within normal limits, but urine organic acids showed persistent very significant ethylmalonic aciduria. Notably, newborn screening failed to detect the disorder, likely due to the absence of C4 acylcarnitine measurement, with a normal C5 acylcarnitine level of 0.35 µmol/L (cutoff <0.73). Genetic testing confirmed a novel homozygous exon 4 deletion in the ETHE1 gene (NM_014297.5), predicted to be pathogenic. Treatment with metronidazole, N-acetylcysteine and mitochondrial supportive therapy led to clinical improvement, including significant reduction in diarrhoea and successful extubation after two weeks in PICU. Later a methionine-restricted diet was added. He continued to show slow but progressive improvement in the ward. Despite this progress, the patient subsequently developed severe deterioration after aquiring influenza during hospital admission and unfortunately passed away at 9 months of age.

Conclusion

This case highlights the limitations of newborn screening in detecting EE and underscores the importance of clinical vigilance in infants with unexplained diarrhea and encephalopathy. As the third reported case in Kuwait, it adds to the sparse regional data and introduces a novel ETHE1 variant, expanding the known mutational spectrum. Comprehensive molecular testing remains essential for accurate diagnosis and early therapeutic intervention.

Key Words: Ethylmalonic encephalopathy; ETHE1; Newborn screening ;

Pediatrics

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Primary hyperoxaluria type 1: A case report of a child from Kuwait:

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CASE REPORT

Back ground:
Primary hyperoxaluria type 1 (PH1) is a rare autosomal recessive disorder caused by AGXT gene mutation that leads to an inborn error of metabolism characterized by marked hepatic overproduction of oxalate due to deficiency of hepatic peroxisomal alanine-glyoxylate aminotransferase. Oxalate cannot be metabolized and is excreted through the kidney. Therefore, patients of PH1 will have hyperoxaluria which will present mainly with recurrent calcium oxalate renal stones and eventually end stage renal failure ESRF. Although PH1 is globally rare, in Kuwait the overall prevalence rate of PH1 was estimated to be 7-10 / million child /year which are higher than rates reported in other parts of the world most probably due to the high rate of consanguinity and first degree-cousin marriages which is traditionally popular in the gulf area. We hereby reporting a Kuwaiti boy genetically documented to have PH1 to highlight the clinical presentation, disease progression, and recommended management of this disease among general paediatrician.

Case report:
A ten year Kuwaiti boy, product of full term normal delivery to consanguineous parents, presented at age of seven months with recurrent attacks of abdominal pain, vomiting and haematuria. He was found to have bilateral renal stones. In spite of several extracorporeal shock wave lithotripsy ESWL and urethral tube insertion, the disease rapidly progressed to end stage renal failure ESRF. Due to a strong family history of hyperoxaluria (three elder brothers, one cusion, and one uncle), the patient was proved to have AGXT mutation by gene testing. He underwent liver and renal transplant at age of 6 year. Currently, he is doing well with normal renal function blood tests and mildly elevated liver enzymes.

Conclusion and recommendation:
Primary hyperoxaluria type 1 (PH1) has a relatively higher incidence in Kuwait. Al Eisa etal (2015) reported that PH1 accounts for 3.5% of CKD cases and 10.4% of ESRD cases in pediatric population in Kuwait. Awareness of the disease severity, its rapid progression to ESRF, and eventually its need for renal and liver transplant will empower general paediatrician for early diagnosis and early referral to proper management.

Key Words: primary hyperoxaluria type 1; end stage renal failure; AGXT gene mutation;

Pediatrics

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Infantile myofibromatosis: A case report and literature review

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CASE REPORT

Background

Infantile myofibroma (IM) is a rare benign soft tissue tumour characterized by the proliferation of myofibroblasts. These tumours typically present before the age of two years, manifest as solitary or multiple superficial painless coetaneous and subcutaneous nodules mainly affecting the head, neck, and perioral structures.1We are reporting a three year old Kuwaiti girl who presented with multiple painless ganglion cyst like swellings mainly on the forehead and mandible but then rapidly increased all over the body. An excision biopsy documented the diagnosis myofibroma associated with NOTCH3 gene mutation. This case report raises the awareness of this tumour and demonstrates that although this tumour might be multicentric, recurrent, and sometimes with visceral or bony involvement, usually it carries good prognosis with no definitive treatment.

Case report:

A three year old Kuwaiti girl, product of full term normal delivery to a consanguinant parents who have another 6 normal children. She is known to be well with normal development. She presented initially with subcutaneous nodules on the forehead. Subsequently, further nodules appear on her shin, arms, trunk, and submandibular area. The nodules were painless, of different sizes and shapes feels cystic and movable with no skin changes over them. All premillinary investigations were normal. MRI was normal. Diagnosis was confirmed by an excisional biopsy and genetic study reveiling infantile myofibromatosis with NOTCH3 gene mutation. The patient was send to Newcastle for further openion. This was only because there was arapid progression of the disease mainly in developing multiple lesions of different sizes all over the body over a short period of time. No additional treatment was recommended since it is symptomless and has no visceral manifestations.

Conclusion and recommendations

Infantile myofibroma (IM) should be considered in the differential diagnosis of solitary/ multiple painless swellings in infants. Excision biopsy and genetic study is the corner stone of diagnosis. Continuous follow up with closed observation and parents' reassurance might be the only needed management in children with documented diagnosis of IM.

Key Words: infantile myofibroma; NOTCH3 gene mutation; ganglion cyst;

Pediatrics

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Six years old boy with post covid-19 isolated palatal paralysis

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CASE REPORT

Background:
Unilateral acquired isolated palatal paralysis is rarely seen in COVID 19 children with unclear pathogenesis. Post-infectious immune-associated cranial mono-neuropathy is a suggestive theory. Cases due to trauma, tumor, and brainstem lesions have been also reported. The presentation is usually nasal regurgitation and uvular deviation. A case report of acquired isolated palatal palsy in a 6 years old boy is presented below with a good response to treatment.

Case summary:
6 years old boy presented with sudden onset of difficulty in swallowing, nasal sounding speech and nasal regurgitation especially for fluids for 2 days prior to admission associated with low grade fever. There was no history of trauma, travelling abroad or recent vaccination but there was a history of coryzal symptoms one week ago. No history of seizures, altered sensorium, squint, facial asymmetry or neck stiffness.On examination: the boy was fully conscious, alert and had normal vitals. He has normal respiratory system examination with no drooling. Neurological examination revealed deviation of the uvula to the right side and the sensation over the posterior pharyngeal wall was intact going with lower motor neuron weakness of the pharyngeal branch of vagus nerve. Gag reflex was preserved but weak. Other cranial nerves were intact and there was no other neurological deficits. other systemic examination was unremarkable. His gait was normal. CBC, RFT, LFT and electrolytes were normal. Lumbar puncture was done showing normal cytology, chemistry and cultures. Nasopharyngeal swab was COVID 19 positive. MRI brain also was normal. The child was treated with IV pulse steroid for 5 days followed by a tapering course with gradual improvement.

Conclusion: Isolated palatal palsy can occur as a post COVID 19 infection. Pediatrician should be aware of this rare manifestation for early diagnosis and management

Key Words: Palatal; COVID 19; Paralysis;

Pediatrics

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PLCG2 gene mutation in a child with Hypogammaglobinemia, autoinflammation, and immune dysregulation: A Case Report

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CASE REPORT

Phospholipase C γ2, or PLCγ2, is q protein coding gene, that catalyzes the conversion of secondary messengers 1D-myo-inositol 1,4,5-trisphosphate (IP3) and diacylglycerol (DAG). It transmit signals from growth factor receptors and immune system receptors across the cell membrane. It regulates multiple cellular processes, including growth, maturation and apoptosis. It is expressed primarily in hematopoietic and immune cells. Mutations have been found in autoinflammation, antibody deficiency, and immune dysregulation syndrome and familial cold autoinflammatory syndrome 3.

Case Summary:
We present to you a case of a 9-year-old girl, product of non-consanguineous healthy parents, with a history of Autoimmune hemolytic anemia (AIHA), giant cell hepatitis, chronic sinusitis and Autoinflammation with PLCG2-associated antibody deficiency and immune dysregulation (APLAID). First diagnosed with AIHA at 7 months, when she presented with hemolysis following febrile illness, and since then she has had multiple admission for her condition, requiring multiple pRBCs transfusions and prednisolone. Few months after, she was diagnosed with Giant cell hepatitis was confirmed by US-guided biopsy. The patient showed partial response to multiple immunosuppressant agents, including Rituximab and Azathioprine. Her condition was controlled with Mycophenolate mofetil and corticosteroids. She remained on this regimen with weaning doses until the age of 3, when was admitted with pyrexia of unknown origin, and found to have critically low Immunoglobulin G (IgG), for which she was started on immune-reconstitution dose of IVIG. Further immune work-up showed poor response to vaccines, variable degrees of lymphopenia, fluctuating T cell function and low memory B cell. She was given the diagnosis of CVID. The differential diagnosis included secondary hypogammaglobulinemia due to Rituximab. Genetic testing shows c.547C>T ; p.(Leu183Phe) PLCG2 mutation. Segregation study was negative. After which, she was diagnosed with Hypogammaglobinemia, autoinflammation, and immune dysregulation. She was started on daily prophylaxis antibiotics and monthly IVIG infusions. She did not have any other significant infections and is doing well.

Conclusion: The case report highlights a rare case of PLCG2 mutation in a patient with immune dysfunction leading to both autoimmunity and immunodeficiency, in a poorly understood mechanism. The role of PLCG2 gene in human health is yet to be understood.

Key Words: PLCG2 mutation; Autoimmune hemolytic anemia; Autoinflammation with PLCG2-associated antibody deficiency and immune dysregulation (APLAID);

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Infantile Spasms in a Baby Girl with Mosiac Turner Syndrome

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CASE REPORT

Turner syndrome (TS) is a genetic disorder affecting females, most commonly characterized by short stature, gonadal dysgenesis, and cardiovascular anomalies. Neurological involvement, particularly epilepsy, is rare. We report a 3½-month-old girl with mosaic Turner syndrome who presented with infantile spasms. EEG revealed hypsarrhythmia, and treatment with vigabatrin achieved clinical improvement. This case highlights the importance of early recognition of neurological manifestations in TS and the need for multidisciplinary management.

Case Presentation
A 3½-month-old girl, prenatally diagnosed with mosaic Turner syndrome by amniotic fluid genetic testing, presented with a 3-day history of recurrent abnormal movements. These episodes consisted of sudden flexion of the upper and lower limbs, followed by crying, raising concern for infantile spasms.On examination, she exhibited dysmorphic features, including low-set ears, micrognathia, a high-arched palate, webbed neck, and widely spaced nipples. Neurological assessment revealed generalized hypotonia, poor head control, poor eye fixation, and a weak sucking reflex, though the Moro reflex was preserved and the anterior fontanelle was at level. Systemic examination showed bilateral fair air entry with inspiratory stridor on chest auscultation. Cardiac examination revealed normal S1 and S2 with a grade 2/6 pansystolic murmur at the left lower sternal border. The abdomen was soft and lax, with no hepatosplenomegaly.The patient's growth was suboptimal. She was born with a weight of 2.5 kg, and her current weight was 3.0 kg, consistent with failure to thrive. As oral feeding was inadequate, nasogastric tube feeding with high-calorie formula was initiated. Investigations showed normal CBC, CRP, liver, renal, thyroid, and metabolic panels. A chest X-ray was unremarkable. Echocardiography revealed a small muscular ventricular septal defect (VSD) and a closing patent ductus arteriosus (PDA). ENT evaluation with fiberoptic laryngoscopy confirmed the presence of laryngomalacia. EEG demonstrated hypsarrhythmia with multifocal epileptiform discharges and frequent spasms, consistent with infantile spasms. The patient was started on vigabatrin, with cessation of spasms and good clinical response. Brain MRI was planned but postponed due to respiratory compromise and excessive secretions. She was eventually discharged in stable condition, maintained on nasogastric feeding, and scheduled for multidisciplinary outpatient follow-up including hearing and vision assessments, physiotherapy, endocrinology, and speech and swallow services.

Conclusion
Infantile spasms are a rare but serious neurological manifestation of mosaic Turner syndrome. Early recognition and treatment are essential to optimize outcomes. This case underscores the importance of comprehensive, multidisciplinary follow-up in patients with TS.

Key Words: Turner; Spasm; Mosaic;

Surgery

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Bilateral External Auditory Canal Papillomas in an Adolescent: A Rare Case Report

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CASE REPORT

Background
Papillomas are benign epithelial proliferations associated with human papillomavirus (HPV). Involvement of the external auditory canal (EAC) is uncommon; bilateral disease, particularly in adolescents, is exceptionally rare. Clinical recognition is important to prevent canal morbidity and hearing sequelae.

Objective: To describe the presentation, histopathology, management, and short-term outcome of bilateral EAC papillomas in an adolescent and to outline practical diagnostic and surgical considerations.

Single-patient case report with endoscopic examination, audiologic assessment, histopathologic confirmation, and operative excision using carbon dioxide laser under general anesthesia.

Case Presentation
A 16-year-old female presented with gradually enlarging bilateral EAC masses since childhood, causing aural fullness and subjective hearing loss. Otoscopy revealed papillomatous lesions (right 1.0 × 0.5 cm; left 0.5 × 0.5 cm). Tympanic membranes were intact; tuning forks and audiometry were normal. Biopsy confirmed benign squamous papilloma.

Intervention:
Bilateral canal lesions were excised with a continuous-mode carbon dioxide laser (3–5 W), enabling precise resection with minimal bleeding and limited thermal injury. Standard postoperative analgesia and prophylactic antibiotics were provided.
Histopathology: Excised specimens showed papillary fronds with fibrovascular cores lined by stratified squamous epithelium, consistent with papilloma.

Results:
Recovery was uneventful. At two-week follow-up, canals demonstrated excellent healing without stenosis or recurrence; hearing remained normal.

Conclusion
Bilateral EAC papillomas are rare but should be considered in the differential diagnosis of external auditory masses in young patients. Histopathologic confirmation is essential. Complete excision—facilitated by laser micromanipulation—can achieve disease clearance with low morbidity. Given reported risks of recurrence and rare malignant transformation, structured surveillance is recommended.

Key Words: External Auditory Canal; Papilloma; Human Papillomavirus;

Surgery

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Surgical management of Duodenal Gangliocytic Paraganglioma causing upper gastrointestinal bleeding: A case report

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CASE REPORT

Background: Gangliocytic paraganglioma is rare duodenal tumor characterized by distinctive histological features including neuroendocrine, ganglion and Schwann-like cells. It is typically benign, though occasional regional lymph node metastasis have been reported, and most patients present with gastrointestinal bleeding or obstruction. Recurrence after resection is rare.

Case Summary: We present a 46-year-old male presented with a 15-day history of melena, fatigue and dizziness. Initial hemoglobin was 10.7 g/dL, which dropped to 8.2 g/dL during admission. Upper GI endoscopy revealed a large pedunculated lesion in the second part of duodenum. Endoscopic ultrasound (EUS) demonstrated a 3–4 cm submucosal mass without lymphadenopathy and EUS-guided biopsy confirmed gangliocytic paraganglioma. CT scan showed a 2.7 × 3.5 × 2.7 cm exophytic duodenal lesion. The patient subsequently underwent duodenal mass resection with sphincteroplasty and cholecystectomy. Final histopathology was consistent with gangliocytic paraganglioma. postoperative recovery was uneventful and he remained asymptomatic at 6 weeks follow-up.

Conclusion: Duodenal gangliocytic paraganglioma should be distinguished from other neuroendocrine tumors. The possibility of malignant behaviour with nodal or distant spread should be excluded prior to surgery. Careful treatment planning and long-term follow-up are essential.

Acknowledgment: Special thanks to the nurses, staff, and doctors who were directly or indirectly involved in the care of the patient.

Consent Statement: Written informed consent was obtained from the patient for this case report and the accompanying images

Key Words: Gangliocytic paraganglioma; Neuroendocrine tumor; Sphincteroplasty;

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KEYWORD INDEX

Sponsor: Kuwait University

The Organising Committee would like to thank the following for their support:

- Centre for Research Support and Conferences, Office of Vice Dean for Research & Postgraduate Studies, College of Medicine
- Administration, College of Medicine

Special thanks to the following staff for their contribution from Health Sciences Centre, Kuwait University:

- Mrs. Teena Sadan
- Mrs. Kawther Fakhra
- Mr. Waleed A Kamil

ACCREDITATIONS

Title of Activity:

30th Health Sciences Centre Poster Conference

Scheduling: 10-11 February 2026

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