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Research – including clinical, translational and innovation

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Characteristics of Presentation and Management of People with Hypoglycaemia whilst on Continuous Glucose Monitoring Devices Pilot Data from DEKODE Hypoglycaemia

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Background

Continuous glucose monitoring (CGM) is an important technology in diabetes management that has the potential to facilitate the avoidance of low glucose values and hypoglycaemic episodes.[1-2]

However, there is a lack of data on patients' characteristics, management, and outcomes of those admitted with hypoglycaemia despite being on CGM.

Aim

To explore the characteristics of the patient population, precipitating factors and outcomes of people admitted with hypoglycemia whilst on CGM.

Methods

Retrospective study across five UK Hospitals.

Inclusion Criteria: All adults ≥18 years with hypoglycaemia whilst on CGM from November 2022 to October 2023.

Outcomes Measured: sociodemographics, precipitating factors, management, outcomes and total time spent during hypoglycaemic episodes.

Analysis: Data was analysed on SPSS 29.0.

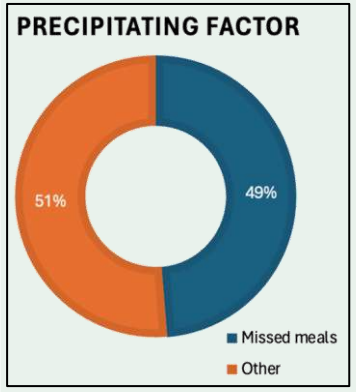
Key Results

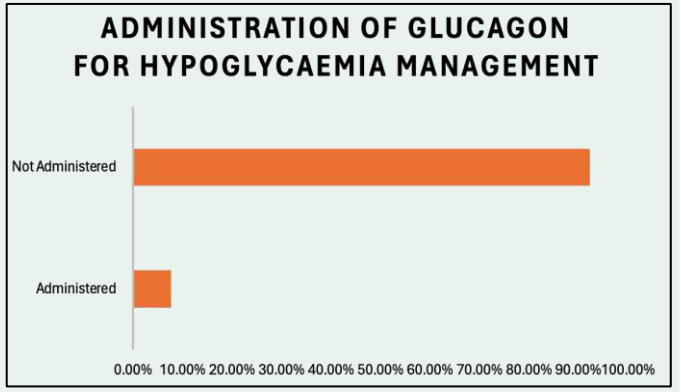
N=39

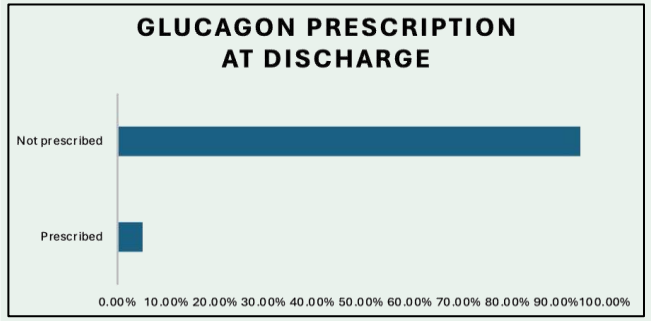
79.5% Male

94.9% T1DM

87% Inpatient







MEDIAN DURATION OF HYPOGLYCAEMIA

26 Minutes

Recommendations

1. Enhanced education for hospital staff and ambulance crew on management strategies for hypoglycaemia in patients with CGM.
2. Prescription of glucagon on discharge and patient education on management of at-home hypoglycaemic episodes.

References

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DIAGNOSTIC ACCURACY OF SERUM PROCALCITONIN LEVELS IN EARLY DETECTION OF BACTERIAL INFECTIONS

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Introduction

Infections and sepsis are a major cause of disease burden and have a vital role in determining the overall mortality in hospitals.[1] Antibiotics are frequently prescribed as empirical therapy until cultures are available for further guidance which remains the gold standard for diagnosing sepsis. Fear of not treating an infection results in over-prescription of antibiotics which is creating resistance.[1,2] Procalcitonin is a glycoprotein and a calcitonin precursor whose synthesis increases in the presence of bacterial endotoxins and pro-inflammatory cytokines.[2] Procalcitonin is not only used to dictate the time of antibiotics use once the diagnosis of sepsis is made but also to end the antibiotic therapy once septicemia is ruled out.In this way procalcitonin has developed significance in prevention of antibiotic resistance and inappropriate antibiotic prescription. [7]

Objective:

To determine the diagnostic accuracy of positive procalcitonin (PCT) level as an early biomarker in patients with bacterial infections taking positive blood culture as gold standard.

Materials and Methods

We conducted a cross-sectional validation study at Shifa International Hospital, Islamabad, Pakistan. 356 patients of either gender with age greater than 14 years but less than 80 years were enrolled in the study. The patients who presented with the primary complaint of documented fever (≥100 F) at home or in the hospital setting (OPD or ER) with initial workup showing TLC count >11000 were included. Samples were obtained for blood culture and serum PCT level before initiation of the antibiotic treatment. Data was analyzed through SPSS version 21. Mean and Standard Deviation were calculated for quantitative variables e.g. age of the patient and PCT levels. For qualitative variables, such as gender, diagnosis and blood culture, percentage and frequency were calculated. Sensitivity, specificity, NPV, PPV and ROC were determined

Results:

Out of 356 total patients, 51.4% were males and 48.6% were females. Mean age of males was 57.38 while that of females was 55.97 years.

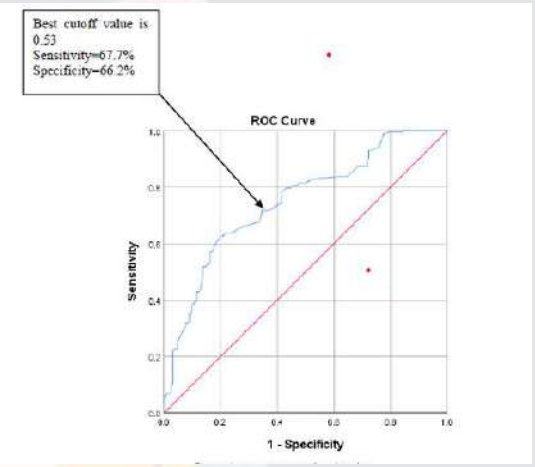
59.0% (n=210/356) of patients tested positive for PCT test while 63.5% (n=226/356) of patients had positive blood culture test. Among these patients 45.50% (n=162/356) had both a positive blood culture and a PCT test, 23.03% (n=82/356) tested negative for both blood culture and PCT, 13.48% (n=48/356) had a negative blood culture but a positive PCT test and 17.98% (n=64/356) had a positive blood culture but negative PCT test as shown in table 01.

Bacteremia /Sepsis on PCT test	Bacteremia/Sepsis on blood culture		
	Positive	Negative	Total
Positive	162	48	210
Negative	64	82	146
Total	226	130	356

Our study results showed sensitivity of 71.7% and specificity of 63.1%. The positive predictive value was calculated to be 77.1% and negative predictive value was 56.2%.

Accuracy and likelihood ratio were 68.5% and 41.37 respectively. ROC curve was generated

A cut-off value more than 0.5 ng/ml is sensitive for bacteremia.



Conclusions:

Serum PCT proved to be moderately sensitive and specific in predicting the presence of bacteremia. This may be a helpful auxiliary biomarker for early detection of bacterial infection and limiting the use and over-prescription of antibiotics.

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2. Ahmed S, Siddiqui I, Jafri L, Hashmi M, Khan AH, Ghani F. Prospective evaluation of serum procalcitonin in critically ill patients with suspected sepsis- experience from a tertiary care hospital in Pakistan. Ann Med Surg [Internet]. 2018;35:180–4.
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Characterising disease mechanisms in patients with angina and non-obstructive coronary arteries to guide management

A. Sinha, H. Rahman, H. Morgan, M. LiKamWa, O. Demir, M. Ryan, S. Ezad, K. De Silva, H. Ellis, A. Chiribiri, A. Shah, A. Webb, M. Marber, D. Perera

The problem:

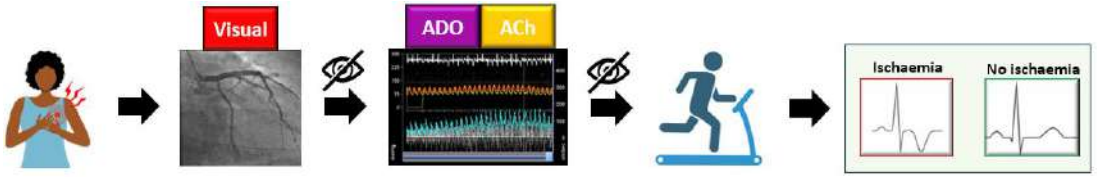
- Coronary microvascular disease (CMD) is the commonest endotype of ANOCA
- **Diagnosis** of CMD is hampered by lack of readily available tools
- **Management** is empirical, resulting in poor patient outcomes and satisfaction

Aims of my studies:

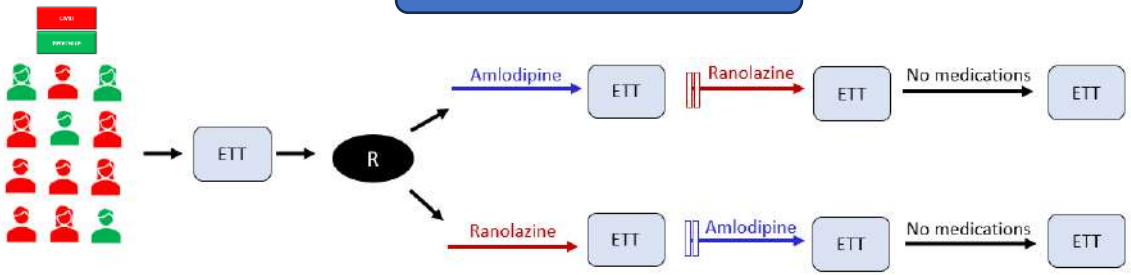
- Assess the utility of a widely available tool in diagnosing CMD
- Assess the utility of coronary physiology-stratified vs empirical management in patients with ANOCA

Method

Improve diagnostics

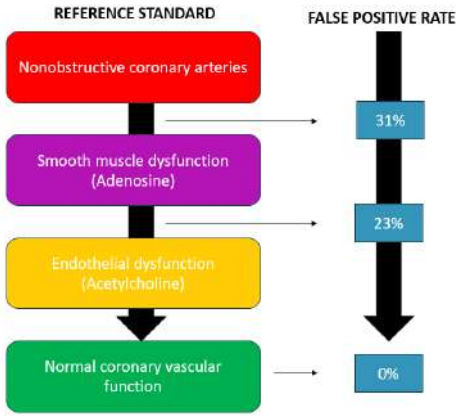


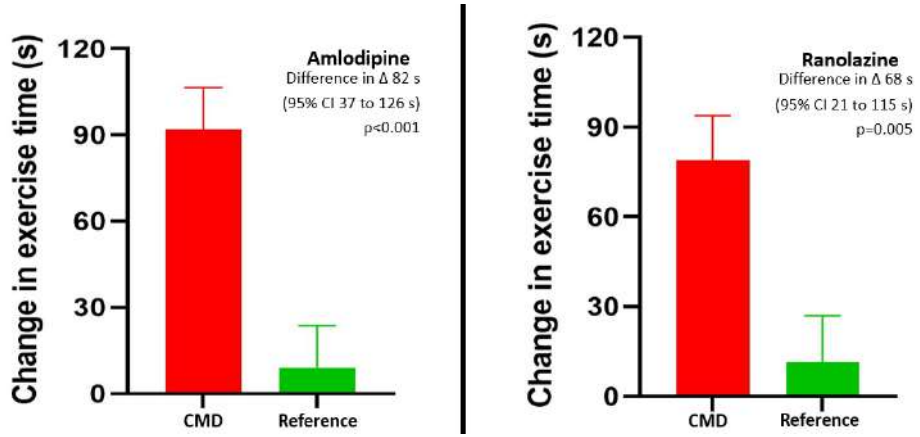
Refine therapeutics



Results

	Ischaemic group (n=32)	Non-ischaemic group (n=70)
Coronary physiology		
Smooth muscle dysfunction, n(%)	20 (63)	30 (43)
Endothelial dysfunction, n (%)	31 (97)*	39 (56)*
CMD, n (%)	32 (100)*	46 (66) *
Exercise stress testing		
Exercise time, seconds	348±164	342±164





Conclusion

- In patients with ANOCA, an ETT may be a good rule-in strategy to diagnose CMD
- This may obviate the need for invasive and expensive tests in many patients

- In patients with ANOCA, invasive CFR measurement predicts response to therapy
- Routine CFR measurement in patients with refractory symptoms may lead to better patient outcomes

Carotid Intima-Media Thickness in Fibromyalgia Patients: A Meta-Analysis

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Introduction

- Fibromyalgia is a chronic musculoskeletal pain syndrome characterized by prominent somatic symptoms, neurocognitive deficits, and psychiatric disturbances.
- Carotid intima-media thickness (cIMT) is a validated tool for cardiovascular risk stratification.
- It is speculated that fibromyalgia patients may have autonomic impairment predisposing to a higher cardiovascular event risk.[1,2]
- We perform a meta-analysis comparing cIMT in cases and controls to investigate subclinical atherosclerosis in fibromyalgia patients.

Materials and Methods

- Existing literature was screened using MeSH terms from PubMed, Embase, and Cochrane databases to identify relevant studies that compare cIMT between fibromyalgia patients and controls.
- A total of 4 recent studies were included in this meta-analysis[1-4]. For each study, mean age and baseline comorbidities were observed. These studies reported the mean of bilateral carotid arteries cIMT, right and/or left carotid artery cIMT.
- Statistical analysis was performed using the Hedges g equation, and standardized mean difference (SMD) of cIMT between both groups. Publication bias was assessed by the Egger test. Forest plot was utilized as demonstrated in **image 1.**

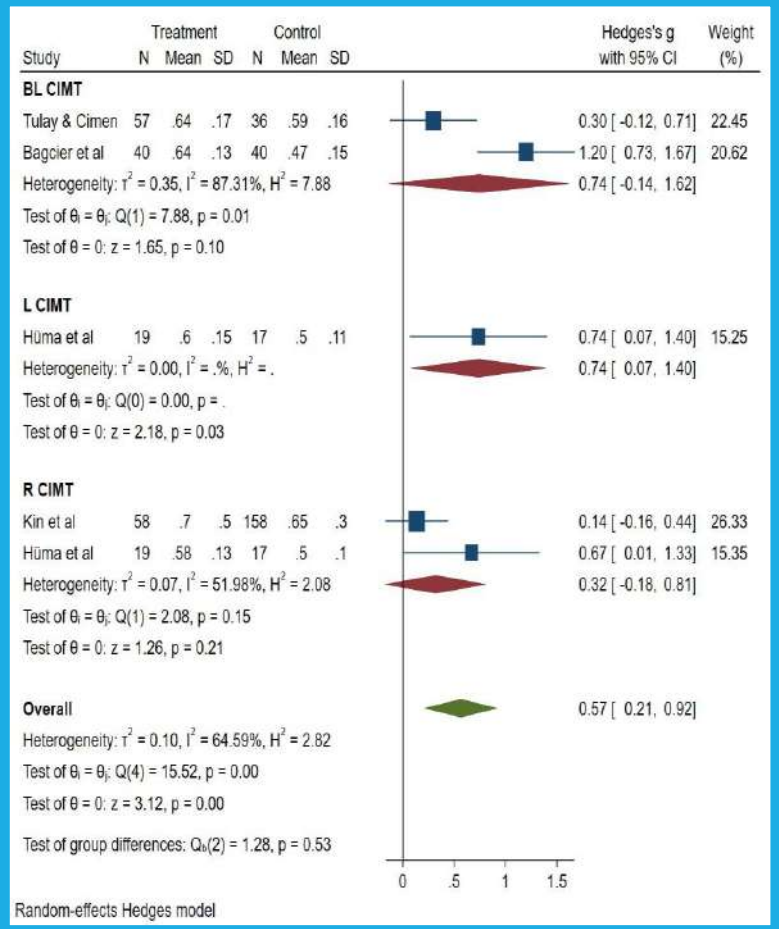

Image 1: Forest Plot representing the standard mean difference (SMD) of the carotid intima-media thickness between Fibromyalgia patients and healthy controls.

Results and Discussion

- From 4 studies, we included a total of 425 patients, of which 174 had fibromyalgia.
- Two studies reported the mean of bilateral cIMT, two reported only right cIMT and one reported left-sided cIMT. All the patients in the studies were females.
- Although all studies reported a higher cIMT value for fibromyalgia patients, two studies reported the difference to be statistically insignificant.
- The overall standardized mean difference (SMD) of bilateral, left, and right cIMT measurements was 0.57 mm [95%CI: 0.21-0.92], with a summary effect of z=3.12, p-value < 0.01.
- Overall SMD for the right carotid artery cIMT difference was not significant [0.32 mm, 95%CI: -0.18-0.81], but the left carotid artery cIMT difference was significant [0.74 mm, 95%CI: 0.07-1.40].

Conclusions

- Our analysis showed an increased risk of cardiovascular complications measured by cIMT in fibromyalgia patients. There is significantly higher cIMT in fibromyalgia patients compared to healthy controls.
- It would be reasonable to consider establishing screening guidelines or utilizing cIMT as a parameter to identify significant atherosclerosis in patients with fibromyalgia and especially in those with additional risk factors.

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2. Bağcıer F, Tufanoğlu F, Kadıçeşme Ö. Is There Any Relationship Between Serum Endocan Levels and Carotid Intima-media Thickness in Patients with Fibromyalgia? *Turk J Osteoporos* 2019;25:49-52
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4. Koca T and Çimen A. The association of carotid intima-media thickness with body mass index and cortisol level in fibromyalgia syndrome *The European Research Journal* 2019;5(1):83-87

Sleep Deprivation Management During Cardiac Rehabilitation

Ali Alzarka[1], Almurtada Razok[2]

Presenting author: **Ali Alzarka**

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2. John H. Stroger, Jr Hospital of cook County

Introduction

- Cardiac rehabilitation (CR) is an integrated process that covers cardiovascular, behavioural, and psychological aspects.
- Sleep disturbance is a common problem among cardiac rehabilitation patients and showed a positive correlation with poor quality of life and depression.
- Multiple factors including **advanced age, psychological distress, pain, and medications may affect the quality of sleep.**
- Poor sleep quality causes adverse effects on **HR and BP**.
- The heart rate slows, and the breathing process stabilizes during the non-rapid eye movement (NREM) phase.
- These changes **reduce stress on the heart and allow the heart to recover from the strain during waking hours and sympathetic activity**. [1]

Methods and Materials

- All relevant articles spanning between 2002 and 2024 in PubMed database.
- Included studies compared the efficacy of sleep interventions by using Insomnia Severity Index (ISI), Sleep Condition Indicator (SCI), or Pittsburgh Sleep Quality Index (PSQI) scoring systems.
- **Eight relevant articles consisted of 804 cardiac patients were included.**

Results and Discussion

- Three studies used different types of **exercise programmes** as interventions and showed **reduction in insomnia scores but without any clinical significance**. One programme **decreased total cholesterol and LDL levels** while a different one **reduced both systolic and diastolic blood pressure means**. [2]
- Two studies applied **behavioural interventions for insomnia** and one of them showed a **clinically significant** improvement in ISI score. Another study applied a **combination of stress management and cognitive behavioural therapy interventions for insomnia** for seven weeks and SCI score showed a **significant statistical and clinical improvements.** [3]
- A **combination of interventions** was applied in three studies. Eight weeks of Multidisciplinary Cardiac Rehabilitation Programme including physical training, health education, and psychological treatment showed **reduction in PSQI score and better functional capacity**. [4] Another 8-week programme of exercise and lifestyle training also reduced PSQI score. A 12-week programme of exercise and sleep improvement sessions reduced PSQI score by 4.8 and was **clinically effective**. [5]

Conclusions

- **Multiple sleep interventions were successful and beneficial in treating sleep deprivation in cardiac rehabilitation patients.**
- This significant problem requires **further studying and monitoring** of CVD risk factors to generalise the results and provide helpful recommendations.

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Pattern of Atherosclerotic Plaque and Type of MI in the Patients of Cardiovascular Disease with and without Standard Modifiable Cardiovascular Risk Factors (SMuRF)

Anfal Hamza, Dr. Muhammad Khalid Razaq, Dr. Ghulam Mustafa, Professor Dr. Muhammad Saleem, Umair Choudhary, Ali Ayan, Dr. Bismillah Sehar

Sheikh Zayed Medical College, Rahim Yar Khan

INTRODUCTION

Absence of Standard Modifiable Cardiovascular Risk Factors (SMuRF) like diabetes mellitus, hypertension, dyslipidemias and smoking show a concerning trend in literature[1].

OBJECTIVES

To determine the severity of Coronary Artery Disease among patients with and without Standard Modifiable Cardiovascular Risk Factors.

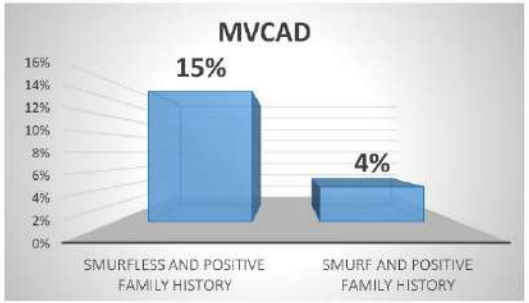
METHODOLOGY

Study Design : Retrospective study
Study Site : Cardiology ward, Sheikh Zayed Medical College/Hopital, Rahim Yar Khan, Pakistan
Study Duration : January to December 2023
The data of STEMI patients who underwent Primary PCI was retrieved from records of the Cardiology ward.

STEMI patients were classified as patients with Standard Modifiable Cardiovascular Risk Factors as SMuRFs and without Standard Modifiable Cardiovascular Risk Factors as SMuRFless. Detailed patient demographic data was collected and CAD severity was assessed on angiographic findings (single vessel vs multi vessel including double and triple vessel) using a predefined form. Statistical analysis, executed via SPSS version-23, involved descriptive and inferential methods, controlling for potential effect modifiers like age, gender, and family history through stratification. Chi-square test and correlation analysis were applied. P-value ≤ 0.05 was taken as significant.

RESULTS

The sample size was 486. Most patients were within the age range of 46 to 60 years 259 (53.3%), with males comprising 367 (75.5%). Hypertension emerged as the most prevalent risk factor 241 (66.4%). 123 (25.3%) patients presented without Standard Modifiable Cardiovascular Risk Factors (SMuRFless). Several studies illustrate this phenomenon[2,3]. STEMI without SMuRF was more common in younger patients with a statistical significance of p-value (0.005). Patients with a Family History of Coronary Artery Disease and without SMuRF exhibited a predominant Multi Vessel Coronary Artery Disease of 15% vs 4% in patients with SMuRF (p=0.05).



Notably, there was a weak correlation (r=0.10) between CAD and multiple risk factors, which slightly increased (r=0.12) in cases with a positive family history.

CONCLUSION

The study highlights the complexity of ST-elevation myocardial Infarction (STEMI) causation determining significantly more young STEMI cases among SMuRFless cases and more STEMI with multi vessel disease among SMuRFless patients having family history.

REFRENCES

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Night sweats and haematological malignancies: are "sweats" truly a "red flag" symptom? An insight into 2-week-wait haemato-oncology referrals at St Bartholomew's Hospital, London, UK

Dr Carola Maria Bigogno, Dr Rifca Le Dieu, Dr John Riches

Background

Haematological cancers, such as leukaemia, myeloma, Hodgkin's and non-Hodgkin's lymphomas, account for over 40,000 new diagnoses every year (1,2). Furthermore, prognosis can vary, especially amongst subtypes of leukaemia (2).

Signs and symptoms can also vary and include anaemia, leukopenia and thrombocytopenia (leukaemia), bone pain alongside kidney failure (myeloma), lymphadenopathy and B symptoms - fever, sweats, weight loss (lymphoma). However, many haematological cancers can be completely asymptomatic (2).

There are several criteria for primary care to consider when submitting a 2-week wait referral for suspected malignancy. These include blood film reports, abnormal blood results and lymphadenopathy on examination, as well as subjective measures such as the B symptoms (3). In particular, sweats can be challenging to define, standardise and apply to clinical practice, which is what we aim to address.

Methods

Patients referred to 2-week-wait haematology clinics at St Bartholomew's Hospital with "sweats" between May and December 2018 were identified (n=51)

and divided into three groups:

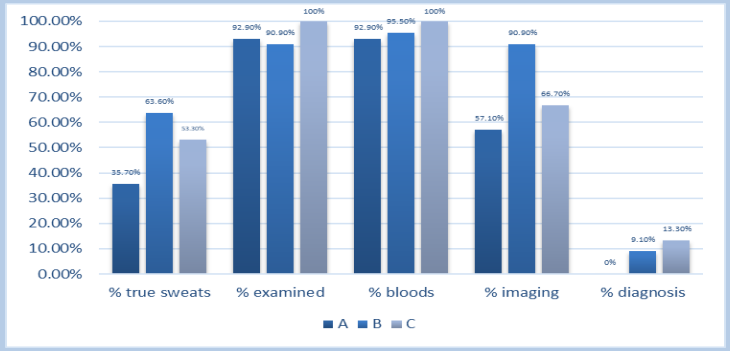
- *A, sweats only (n=14)*
- *B, sweats plus other B symptoms (n=22)*
- *C, sweats plus adenopathy and/or lymphocytosis (n=15).*

Aims and Results

The main aims of the study were firstly to explore the definition of "sweats", and also to understand whether "sweats" can be a predictor of hematological disease.

Overall, patients reported a low prevalence of true, classically defined "drenching night sweats" (A=35.7%, B=63.6%, C=53.3%).

As part of the clinic, most patients were examined (A=92.9%, B=90.9%, C=100%) and had follow-up blood tests (A=92.9%, B=95.5%, C=100%) or imaging (A=57.1%, B=90.9%, C=66.7%), and we explored the results of these in each group.



Nobody received a diagnosis of malignancy in group A (0%) versus two patients in group B (9.1%) and two in group C (13.3%). Interestingly, most patients were discharged or diagnosed with viral illness, tuberculosis, human immunodeficiency virus (HIV), rheumatological diseases or anaemia.

Conclusion and next steps

Sweats are, amongst other presentations, an established symptom of suspected cancer, especially haematological. However, it is also subjective and challenging to define - as our study demonstrates, only about half of the patients referred to the 2-week-wait haematology clinics at St Bartholomew's Hospital presented with the classically defined ("true") drenching night sweats.

Furthermore, we conclude from the study that "sweats" may not be an absolute predictor of hematological cancers, especially when not associated with other B symptoms, lymphadenopathy, or lymphocytosis. In fact, "sweats" can be common to several differential diagnoses, including viral and bacterial illnesses, rheumatological conditions and anaemia.

Lastly, it is essential to extend the study further, both the period analysed and the population size. It would also be useful to compare data from 2-week-wait clinics at other hospitals. These will allow to better define "sweats" and improve the guidelines for 2ww referrals to haemato-oncology services.

References

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Barts and The London School of Medicine and Dentistry

NHS Barts Health NHS Trust

Health-related Quality of Life Outcomes In Patients With Psoriatic Arthritis And Skin Disease: A Systematic Review

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[1]East Surrey Hospital, Surrey and Sussex NHS Trust, [2]British Medical Association Library, [3]King's College London, [4]University Hospital Lewisham, London

Introduction

- Psoriatic arthritis (PsA) is a chronic inflammatory condition affecting multiple organs including the musculoskeletal system and skin.
- PsA can be highly debilitating, affecting mental health and quality of life (QoL).

Aims

- To assess the **association between skin disease and QoL** in people with PsA
- To evaluate the **burden of disease** and identify areas for future research and management.

Methods

- Inclusion criteria: full articles related to adults with PsA, skin disease and QoL outcomes with a measure of psoriasis severity.
- Exclusion criteria: editorials, conference abstracts and reviews, non-English articles.
- Databases: Medline,Embase,Cochrane,PsychINFO
- Data extracted: demographics, treatment, type and severity of skin disease and QoL.
- Results were analysed by descriptive statistics

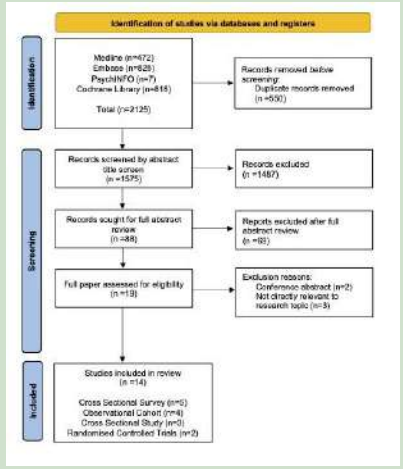

Figure 1: Flowchart of article selection

Results

- **14 studies included, comprising 16,652 patients** (Fig 1)**.** 52.5% male (fig 2) and a mean age of 48.5 years (SD 4.09).
- Study populations were from Europe (n=13), North America (n=8), South America (n=4), Australasia (n=4) and Asia (n=3); some were across multiple continents.
- Where specified treatment for PsA included: biologic disease-modifying anti-rheumatic drugs (DMARDs; n=7459); targeted synthetic DMARDs (n=1083); conventional synthetic DMARDs (n=1777); non-steroidal anti-inflammatory drugs (n=873); topical therapies (n=3584); no treatment (n=405). Five studies did not report the numbers of patients on each treatment.
- In assessment of psoriasis, seven studies used the Psoriasis Area and Severity Index tool (PASI), three used body surface area coverage (BSA) and four used others. PASI scores ranged from 2.6 (mild) to 9.88 (moderate) where reported, BSA was reported as ≥3% or ≥10%.
- QoL was assessed using Dermatology Life Quality Index (DLQI; n=6); EuroQol-5 Dimension (EQ-5D; n=3); 36-Item Short Form Survey (SF-36; n=3); four studies used other measures.
- **Nine of 14 studies reported an association between worse skin disease and poorer QoL** in people with PsA. Three studies reported no association between severity of skin disease and quality of life, while two were unclear.

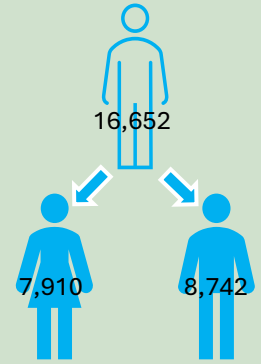

Figure 2: Gender Distribution

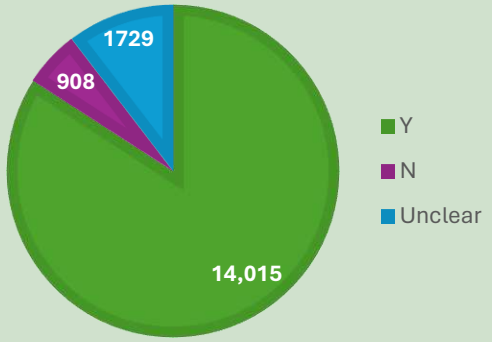

Figure 3: Number of patients categorised according to the association between skin disease and worse QoL

Figure 4: Map displaying the number of studies in each continent by colour intensity

Conclusion

- The majority of studies show patients with PsA contend with **poor QoL as a direct result of their condition**.
- In many patients, **skin involvement is associated with poor QoL**.
- There is a **direct and substantial association between dermatologic symptoms and QoL** in patients with PsA, indicating the importance of effectively managing dermatologic symptoms to lead to meaningful improvements in QoL.
- Clinicians managing PsA should be aware of the **impact of dermatologic manifestations in PsA.**
- **Improving skin** symptoms has potential to improve patients' lives, in conjunction with **multidisciplinary management and holistic care**.

Take Home Message

- **Studies included in this systematic review assessed multiple domains of healthcare-related QoL, including physical, emotional, and social aspects.**
- **Even in patients with milder disease, increased skin involvement had a stronger association with QoL than joint involvement.**

Determinants of Maternal Near Miss in Kenya: A Secondary Analysis of Data from a Nationally Representative Study

Chloe Lord, University of Leeds; Kenneth Juma, African Population and Health Research Center; Onikepe Owolabi, Guttmacher Institute

Introduction

Maternal mortality is a significant public health issue that disproportionately affects low- and middle-income countries, including Kenya. The maternal mortality ratio in Kenya remains high at 530 deaths per 100,000 live births[1]. The World Health Organization defines maternal near miss (MNM) as "a women who nearly died but survived a complication that occurred during pregnancy, childbirth or within 42 days of termination of pregnancy"[2]. Maternal deaths are considered as only the tip of the iceberg, with the true burden of maternal morbidity being much greater[3]. MNM events occur much more frequently than maternal deaths, and with similar causes and characteristics, can provide invaluable evidence about the factors related to maternal mortality[4]. The Three Delays Model defines three pivotal stages that impact obstetric outcomes: delays in seeking, reaching, and receiving care[5].

Aim: To investigate the determinants of MNM among women admitted to hospitals across Kenya, including the Three Delays Model, using a nationally representative sample.

Method

This study was a secondary data analysis of a study conducted in Kenya in 2018, that measured the incidence of MNM and the quality of clinical management[6]. Data analysis was conducted using Stata version 18. Variables with a p-value <0.2 in bivariate logistic regression were entered into the multivariate logistic regression model. Variables with p-value <0.05 in the multivariate analysis were considered statistically significant.

Results

A total of 2985 women were included in the study, which was weighted by region and level of health facility. The variables significantly associated with MNM in multivariate logistic regression included education level of women, women with a high-risk pregnancy, delay in reaching the health facility and delay in receiving treatment at health facility.

Variable	Category	aOR (95% CI)	P-value
Education	None	Ref	
	Primary	0.64 (0.31-1.34)	0.225
	Secondary	0.63 (0.24-1.64)	0.331
	College	0.51 (0.14-1.88)	0.296
	University	**0.23 (0.08-0.67)**	**0.009***
High Risk Pregnancy	No	Ref	
	Yes	**4.45 (2.82-7.02)**	**0.000***
Delay 2 – delay in reaching health facility	<1h	Ref	
	1-2h	**1.78 (0.89-3.59)**	**0.100***
	2-6h	1.45 (0.71-2.98)	0.293
	6-24h	0.68 (0.16-3.00)	0.601
	>1 day	3.10 (1.41-6.83)	0.007
	Unknown	1.89 (0.31-11.42)	0.473
Delay 3 – delay in receiving treatment	<1h	Ref	
	1-2h	**2.55 (1.17-5.55)**	**0.021***
	2-6h	1.27 (0.21-7.52)	0.785
	>6h	0.86 (0.39-1.90)	0.696
	Unknown	3.37 (0.61-18.53)	0.155

Table 1: Multivariate Logistic Regression Analysis of association between maternal near miss and significant risk factors (sample size = 2985)
aOR, adjusted odds ratio; CI, confidence interval

Discussion

This study highlights the importance of maternal education in reducing maternal mortality, which is consistent with other studies around the world. Mothers who received University level education were 77% less likely to develop MNM than mothers with no education. Maternal education reflects access to financial resources and health information, which in turn results in greater awareness about pregnancy and childbirth as well as engagement with maternal health services.

Women with a high-risk pregnancy (a history of stillbirth, miscarriage or ectopic pregnancy) were 4.45 times more likely to develop a MNM. Increased monitoring of these women has the potential to improve obstetric outcomes.

Furthermore, this study found that women who experienced a delay in reaching the health facility and a delay in receiving treatment were more likely to experience a MNM. This emphasises the importance of reducing barriers to accessing timely obstetric care in order to reduce the burden of maternal mortality in Kenya.

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1; The World Bank. Maternal mortality ratio (modelled estimate, per 100,000 live births) **2**; World Health Organization. The WHO near-miss approach for maternal health (2011). **3**; Filippi et al. A new conceptual framework for maternal morbidity (2018). **4**; Say et al. Maternal near miss--towards a standard tool for monitoring quality of maternal health care (2009). **5**; Thaddeus et al. Too far to walk: maternal mortality in context (1994). **6**; Owolabi et al. Incidence of maternal near-miss in Kenya in 2018 (2020)

ORAL Arsenic Trioxide To Combat Acute Promyelocytic Leukaemia

Cyrus, Kumana; Harinder, Gill; Yok-Lam Kwong *The University of Hong Kong*

Abstract

Introduction: For millennia, arsenicals were recognised poisons yet also touted as therapies. In Western Medicine, they were accepted as 'genuinely effective' haematological treatments starting about 200 years ago; Fowler's Solution (FS), a crude extract of arsenic trioxide(ATO) was one such product that became a primary leukaemia remedy. Chemotherapy, and radiotherapy evolving in the 20th century, led to FS being phased out (owing to 'perceived toxicity'). Nevertheless, Acute Promyelocytic Leukaemia (APL) patients prescribed the aforementioned newer treatments endured extremely poor outcomes; median survival after diagnosis being reported as <7 days. In the1990s, Chinese researchers reported far superior results when such patients received repeated 4-to-8 week daily courses of intravenous(IV) ATO, sometimes with all-trans-retinoic acid (ATRA). Since such results were confirmed worldwide, this strategy is universally adopted whenever feasible despite being very patient intrusive/cumbersome (hospital attendances, infusions required) and extremely costly in many respects. Typical IV ATO treatment for 1-month retails for about £8,000; substituting oral ATO halves such costs.

Materials and Methods: Based on 1950s Hong Kong (HK) leukaemia patient records exhibiting substantial benefits after imbibing FS, we prepared a 1 mg/ml oral ATO solution adopting Good Manufacturing Practice (GMP). After overcoming pharmaceutical, ethical, and research protocol related challenges - we showed its bioavailability in hospitalised haematology patients to be very similar to that of IV dosing. An electrocardiographic monitoring study and clinical reports suggested that oral ATO might also be less cardiotoxic than IV dosing, which enabled securing international patents for our formulation (Arsenol®). Having shown it was safe and well tolerated, we involved a local manufacturer to produce such oral ATO and established a protocol for its use in selected HK hospitals. We also chronic led the epidemiology of APL in HK patients given various treatment regimens during the years 1991-2020, and noted increasing numbers being treated with oral ATO, ATRA and Ascorbic acid (AAA regimen).

Results and Discussion: Figure 1 shows that in successive years, APL's annual incidence (recognised new cases/year per100,000inhabitants) increased somewhat, whilst prevalence (survivor numbers on a given date each year) increased dramatically (from muchbelow1 to 6 per 100,000 inhabitants). Figure 2 shows that among oral ATO recipients, deaths at presentation (1st month) were 5/282versus 39/469 among those taking regimes lacking ATO, whilst respective post 30 day survival rates after100 months of long-term treatment were 108/120 (90%) versus 198/263 (75%). Collaborative regional and international clinical trials and other studies of APL patients taking Arsenol® are underway or planned. Clinical and experimental studies also indicate that ATO might have a role in treating selected patients with several diseases/disorders other than APL (including some high prevalence/chronic conditions), for which oral dosing may also be preferable.

Conclusions: For treating APL, our GMP consistent oral ATO based regimen was well tolerated and safely conferred equivalent or greater efficacy compared to alternative regimens (avoiding early deaths and possible long-term treatment refractoriness), but with vastly greater patient convenience and affordability. Oral ATO may also have a role in treating diseases/disorders other than APL.

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Background to Arsenicals used by Humans

- Recognised as poisons for millennia yet also touted as therapies.
- In Western Medicine, accepted as 'genuinely effective' haematalogical treatments about 200 years ago.
- One such remedy was Fowler's Solution (FS), a crude extract of arsenic trioxide (ATO) that became a primary therapy for all Leukemias.
- The advent of chemotherapy, radiotherapy and BMT post world war 2, lead to the phasing out of FS owing to 'perceived toxicity'.

Rejuvenation of Arsenic Trioxide

- Nevertheless, patients presenting with Acute Promyelocytic Leukaemia (APL) an extremely lethal condition – endured extremely poor outcomes when offered such newer treatments; median survival after diagnosis was reported as <7 days.[3]
- However, 1990s reports from China claimed far better outcomes in patients with this type of acute leukemia given repeated 4-8 week daily courses of intravenous (IV) ATO† and such findings have been repeatedly confirmed worldwide.
- This led to the abandoning of most other therapies for APL.
- Yet repeated courses of IV ATO are also very disruptive to patient quality of life and health care services (hospitalisations; infusion paraphernalia; medical staff & patient time), apart from being prohibitively expensive.[∞]

† Similar reports emerged for All-Trans-Retinoic-Acid (ATRA), another Chinese innovation
∞ 30 days of typical IV ATO treatment currently retails for about £8,000; substituting oral dosing more than halves such costs

Rejuvenation of Oral Arsenic Trioxide

- A haematologist (my former student) meticulously trolled through 1950s case notes of Hong Kong (HK) leukemia patients enjoying consistent objective (yet limited) benefits safely, after taking FS.
- Thus, we opted to re-evaluate treating APL patients with oral ATO prepared according to Good Manufacturing Practice (GMP); since IV ATO ± ATRA were widely accepted as being more efficacious than all other prevailing therapies.
- Accordingly, we prepared such an oral formulation and showed that the extent of arsenic entering the bodies (bioavailability) of treated hospitalized patients after IV dosing and our oral preparation were virtually the same.
- Our oral ATO (Arsenol®) also appeared less cardiotoxic than IV dosing,† which enabled us to secure several international patents for our formulation.

† Significant cardiotoxicity is a suspected hazard of IV ATO dosing

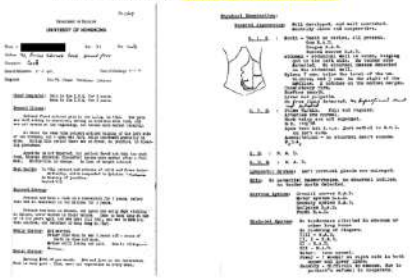
Challenges Overcome Introducing Oral ATO to Treat HK Patients

1. Sourcing pure pharmaceutical grade ATO to make a 1 mg/ml solution from a sparingly soluble powder, meeting GMP standards and with a suitable shelf-life.
2. Securing ethics committee approvals for a bioavailability study comparing identical single doses of commercially available IV ATO† to our Arsenol® in sick hospitalised leukemic patients, with their informed consent.
3. Conducting such a study safely, with an entirely novel/unconventional protocol, involving repeated blood sampling over 48 hours.
4. Establishing a suitable HK commercial manufacturing facility and securing Arsenol's use in selected HK public hospitals (but with certain caveats).

† Trisenox®

Case example

Transcribed Case notes of a 21 year old man admitted to hospital on 1/5/1950: Diagnosis - Chronic Myeloid Leukemia

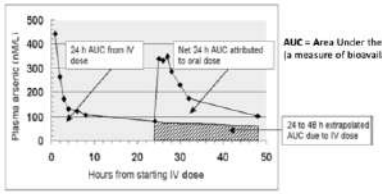


The huge Spleen and a blood WCC of nearly 300,000/μL on admission; both gradually resolve completely after repeated daily doses of FS.

(Transcript courtesy of Prof YL Kwong)

Oral versus IV Arsenic Trioxide Bioavailability

Study results from a single patient



AUC = Area Under the Curve (a measure of bioavailability)

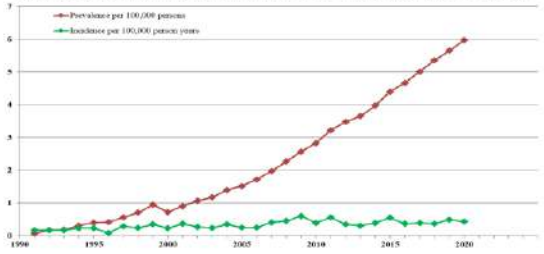
Average Area Under the Curve (AUC) of Plasma Arsenic Concentration/Time Plots (Nanomolar-hours) for all 9 Study Patients

	Day 1 (0-24 h) AUC attributed to IV Dose	Day 2 (24-48 h) AUC attributed to Oral Dose
Mean ± SEM	2673 ± 262	2640 ± 343
95% CI	1836-3507	1856-3410

Figure & table adapted from Kumana et al 2002, Eur J Clin Pharmacol 58:521–6

APL Incidence (new cases/year) & Prevalence (survivors on a given date/year) 1991-2020 Figure1

Based on available details in HK's Computerised Clinical Data Analysis and Reporting System (CDARS); assuming HK's population to be 7.5 million between 1991 and 2020.



Adapted from figure 1 (Kumana CR et al, Frontiers in Oncology 2022, 12:1026478)[8]

Key Findings on APL Patients Treated in Hong Kong (1-1-1991 to 31-3-2021) Figure 2

At 18 public hospitals with specialist haematology services

1 Deaths at Presentation (During Induction; 1st month)
Oral ATRA ± daunorubicin: 139/469 (30%)
p < 0.001
Oral AAA ± daunorubicin: 5/182 (2%)
2 Survivors among those offered long-term treatment (post-1st month) followed up for the next 100 months
Oral ATRA + 6-MP or MTX or no nil else: 198/264 (75%)
p < 0.001 for cumulative survival
Oral AAA maintenance: 108/120 (90%)

AAA = ATO + ATRA + Ascorbic acid; **6-MP** = 6 Mercaptopurine; **MTX** = Methotrexate

Details derived from HK's Computerised Clinical Data Analysis and Reporting System (CEDARS); Gill H, et al 2023, BMC Cancer 23:141.[9]

Inferences/Other Developments re Oral ATO Treatment

- To treat APL patients - entirely (or mainly) with oral regimes referred to as 'AAA' (ATO, ATRA, and Ascorbic acid) appeared to yield optimal overall outcomes
- For APL, collaborative international - outcome, quality of life, and affordability trials of IV versus oral ATO dosing are underway and/or planned (in SE Asia & UK)
- Experimental & clinical studies with IV ATO have yielded promising benefits for many non-APL maladies (e.g. Lupus and other high prevalence & chronic afflictions). If a role for such putative ATO responsive conditions is confirmed, oral rather than IV dosing is also likely to be preferrable.
- In collaboration with CIPLA (Indian Multinational Pharma company that pioneered affordable HIV meds), additional manufacturing facilities are being prepared to cope with a likely expanding worldwide demand for Arsenol®.

Conclusions

- Our GMP consistent oral ATO used (in an AAA regimen) - confers equivalent efficacy to IV ATO dosing and superior to those of regimes lacking ATO.
- It vastly enhances patient convenience (enabling IV infusion-free, home therapy with outpatient supervision) and is very likely less cardiotoxic.
- It saves on retail drug as well as other costs (hospitalisations; IV infusions; related medical staff & patient time commitments), making it more affordable and accessible worldwide.
- Clinical and other collaborative studies into treating APL (and other possible ATO responsive diseases) with Arsenol® are underway and/or planned.
- Reverting from IV to oral dosing may seem a small change but for individuals it was life-changing.
- Our research was a team effort; roles of my co-authors Prof YL Kwong and Dr H Gill were crucial and many others were involved.

Machine learning to identify community-dwelling individuals at higher risk of incident cardio-renal-metabolic diseases and death

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INTRODUCTION

- Cardiovascular disease (CVD) causes a quarter of all deaths in the UK,[1] and the NHS Long Term Plan emphasises that earlier detection and treatment of cardiovascular, renal and metabolic risk factors is a priority.[2]
- We trained, tested and implemented a machine learning algorithm in primary care electronic health record (EHR) to identify individuals at higher risk of incident cardio-renal-metabolic diseases and cardiovascular death.[3,4]

METHODS

- UK primary care EHR data from 2 081 139 individuals aged ≥30 years (Jan 2, 1998 - Nov 30, 2018) was randomly divided into training (80%) and testing (20%) datasets.
- We trained a random forest classifier using age, sex, ethnicity and comorbidities (OPTIMISE).
- We calculated the cumulative incidence rate for ten cardio-renal-metabolic diseases and death, and excluded individuals for the analysis of each disease who had a preceding diagnosis of that disease. Fine and Gray's models with competing risk of death were fit for each outcome between higher and lower predicted risk.
- We implemented OPTIMISE in a pilot interventional non-randomised single arm study across four primary care sites. Consenting individuals aged ≥30 years at higher predicted risk received community-based cardio-renal-metabolic phenotyping and assessment for guideline-adherence of current treatment.

RESULTS

Figure 1. Predicted risk and long-term risk of conditions in the testing dataset (n=416 228)

- In the pilot clinical implementation (n=82):
  - 78% had hypertension
  - 23.1% of those with type 2 diabetes and co-existent CKD were on SGLT2 inhibitor
  - 37% of those with previous CVD had LDL >2.0 mmol/L
  - 19.5% had undiagnosed moderate or high risk CKD
  - 49% were obese
  - 17% were eligible for GLP-1 RA therapy

CONCLUSION

- The machine learning OPTIMISE algorithm can identify people at higher risk of cardio-renal-metabolic diseases and death in UK primary care EHR data.
- On prospective evaluation higher risk individuals have unrecorded and undertreated cardio-renal-metabolic diseases, which are actionable targets for integrated multi-disciplinary preventative care.

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The Clinical Characteristics, Optimal Management, and Outcomes of Atrioventricular Blocks in Hyperthyroidism: A Systematic Review

Hassan Choudry[1], Bilal Ahmed[1], Fateen Ata[2], Tiago Lemos Cerqueira[3], Ben Illigens[3], Saddam Abbasi[4], Adeel Ahmed Khan[2]

Potential Mechanisms proposed to explain the AV blocks in Hyperthyroidism

- Reciprocal excitation and exacerbation of hypervagatonia by thyrotoxic state
- Thyroid myocarditis
- Autoimmunity leading to infiltration of conduction fibers

Introduction

Although uncommon, atrioventricular block (AVB) is associated with thyroid disorders, mainly hypothyroidism. Hyperthyroidism (HTH) is a hyperdynamic state in which cardiovascular manifestations mainly include increased cardiac contractility, tachyarrhythmias, and even high output cardiac failure in extreme cases. Although unexpected, AVBs have been reported in patients with HTH. Little is known about the true prevalence, clinical course, management, and outcomes of AVBs in Hhyperthyroid patients.

Objective

Atrioventricular block (AVB) is infrequently seen with hyperthyroidism (HTH). Little is known about its prevence, cinical course, management, and outcomes in such patients. This systematic review aims to pool available data on AVBs in HTH and summarize patients' clinical characteristics, management, and outcomes.

Methodology

A literature search was conducted using PubMedMedine, Google Scholar. Embase, and SCOPIJS up to June 14th, 2022. for English-
language articles reporting atrioventricular block (AVB) occurring in patients of any age having hyperthyroidism (HTH). Studies reporting Atrioventricular Blocks (AVB) in patients with Hyperthyroid (HTH) due to other established causes, studies reporting bundle branch or fascicular tiocks in HTH patients, and reporting secondary patient data were excluded.

Results

A total of 57 studies were extracted, including 43 case reports, 12 case series, one retrospective study. and one prospective observational study. The mean age was 38.3 ± 17.2 years, with 62% (n=49) females. Common features of hyperthyroidism (HTH) were goiter (42.6%), palpitations (35.3%), and ophthalmopathy (34.1%). Grave's disease (GD) was the most common cause of hyperthyroidism (n=25). Treatments for hyperthyroidism included thionamides (82.9%), radioactive iodine ablation (14.6%), and thyroidectomy (15.8%), with 67.1% achieving euthyroidism. Among the AV Blocks, complete heart block (CMB) was the most common (55%), followed by first-degree and second-degree AVBs (16% each).

The mean age was 33.8 ± 14.5 years in patients with first-degree AVB, 34.5± 17.2 years in patients with second-degree AVB, and 40.3 ± 17.3 years in patients with CMB. Shortness of breath and syncope were the most common signs and symptoms of atrioventricular blocks (AVBs). Pacing was required in three patients with first-degree AVB, one with second-degree AVB, and 16 with CMB. Permanent pacemaker (PPM) insertion was performed in one patient with second- degree AVB and six patients with CHB. Vasopressors and intubation were needed in 7 and 5 patients, respectively. One patient with CHB in the setting of Grave's Disease died.

	Variable	1 ° AV Block	2 ° AV Block	Complete Heart Block
	Number	13 (15.8%)	13 (15.8%)	45 (54.9%)
Clinical Features	Age	33.8 ± 14.5	34.5 ± 17.2	40.3 ± 17.3
	Goiter	6 (46.1%)	5 (38.4%)	22 (48.9%)
	Ophthalmopathy	5 (38.4%)	4 (30.8%)	19 (42.2%)
	Grave's Disease	4 (30.8%)	5 (38.5%)	15 (33.3%)
Tratment	Thionamides	3 (23%)	4 (30.8%)	11 (24.4%)
	Steroids	2 (15.3%)	1 (7.7%)	5 (11.1%)
	Lugol's Iodine	1 (7.7%)	2 (15.3%)	5 (11.1%)
	Beta Blockers	2 (15.3%)	3 (23%)	5 (11.1%)
	RAI ablation	3 (23%)	1 (7.7%)	8 (17.8%)
	Thyroidectomy	0	2 (15.3%)	10 (22.2%)
Prognosis	Euthyroidism achieved	10 (76.9%)	9 (69.25)	32 (71.1%)
	Resolution of AVB	8 (61.5%)	10 (76.9%)	40 (88.9%)
	Overall pacing	3 (23%)	1 (7.7%)	16 (35.6%)
	Permanent Pacemaker (PPM)	0	1 (7.7%)	6 (13.3%)

Conclusion

Existing data indicate CHB as the predominant AV Block type in Hyperthyroid patients. While many patients can be effectively managed with anti-thyroid treatment. a significant proportion may require PPM insertion. More research is needed to establish guidelines for the optimal management

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Ethnicity as a predictor of nonmotor symptoms impact on quality of life in patients with Parkinson's disease: A systematic review

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1- Introduction

- Parkinson's disease (PD) is a chronic progressive hypokinetic movement disorder characterised by both motor and non-motor symptoms (NMS)
- A substantial impact of NMS on quality of life (QoL) of patients with PD has been increasingly recognised, more than motor features. .[1] [2] [3]
- The prevalence and types of NMS might vary among PD patients from different ethnic backgrounds.[4]
- Ethnicity has been postulated as a determinant of PD symptoms and QoL. There is paucity of data on ethnicity impact on QoL of PD patients. [5]

2- Materials and methods

- This review was conducted according to recommendations in preferred reporting Items for Systematic Review and Meta-Analysis (PRISMA).
- We searched PubMed, Ovid Embase and Scopus between March & July 2023 for all studies reporting on PD NMS and QoL concomitantly.
- NMS were assessed by NMSS, NMQT, MDS-UDPRS I, and HADS. QoL was assessed by PDQ39. Ethnicity was defined based on country of study.
- We used a best-evidence synthesis to summarize demographics, study designs, NMS features in each ethnic group.
- NMS impact on QoL in each ethnic group using the power of correlations measures between NMS domains and QoL.

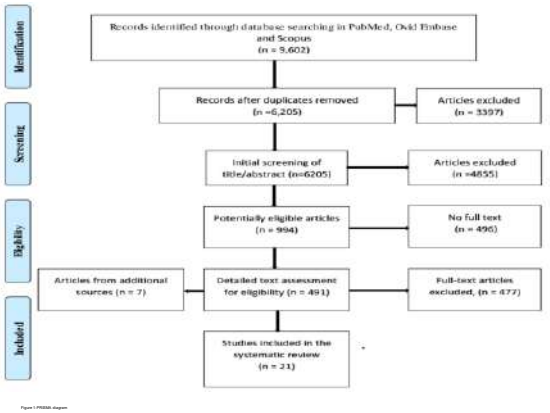
3- Objectives

This systematic review was conducted to:

- Identify the variability of NMS that affect QoL of people with PD from different ethnicities
- Examine if ethnicity could determine the impact of these NMS on the QoL of people with PD.

4- Results

- We identified 21 studies with 4246 patients.
- Patients represent 8 ethnic populations***: Caucasian, East Asian, Indian, North African, West African, Hispanic, Mediterranean, and Middle Eastern***
- Heterogeneous protocols and varied statistical methodologies were used in most studies to evaluate the relation between NMS and QoL.
- Depression, fatigue, sleep problems, and memory problems had the greatest impact on QoL across most ethnic populations.
- The impact of other NMS, such as CVS, GIT, and urinary symptoms, varied among different ethnic groups..
- QoL scores showed variability in different ethnicities with North African and Middle Eastern experiencing the worst QoL.



Author and Publication year	Country	Ethnicity	Sample size	Mean Age	Disease duration	PDQ39 Mean SD per study	PDQ39 Mean SD per ethnicity
(Song et al., 2014)	China	East Asian	693	61.5	4.8	21.5 ± 16.7	20.9 ± 16.5
(Wu et al., 2016)			301	58.4	2.1	16.8 ± 13.3	
(Li et al., 2018)			82	65	5.1	43.0 ± 14.7	
(Lee et al., 2015	Korea		159	68	1.4	20.9 ± 13.0	
(Liu et al., 2015)	Taiwan		210	66.1	6.1	16.1 ± 15.6	
(Duncan et al., 2014)	UK	Caucasian	158	66.5	0.5	38.1 ± 13.2	30.6 ± 18.2
(Kadastik-Eerme et al., 2016)	Estonia		298	74.2	7.6	31.4 ± 15.3	
(Kozyavek, 2015)	Slovakia		231	68	8.3	36.7 ± 19.7	
(Benganzo et al., 2016)	Spain	Mediterranean	103	66.5	6.9	21.4 ± 13.0	21.4 ± 13.0
(Rodriguez-Violante et al., 2013)	Mexico	Hispanic	177	62.4	6.4	33.5 ± 19.0	33.5 ± 19.0
(Gulunay et al., 2020)	Turkey	Middle eastern	25	NS	5.1	47.7 ± 15.5	38.2 ± 29.3
(Salari et al., 2017)	Iran		81	62	6.1	29.5 ± 18.5	
(Shalash et al., 2018)	Egypt	North African	92	55.3	5.3	37.5 ± 18.6	37.5 ± 18.6

5- Conclusion

- Our study demonstrates that ethnicity may have a significant impact on the correlation between NMS and QoL of patients with PD.
- There is deficiency in studies assessing the impact of PD NMS on QoL in Africans, Latin Americans, and Middle Eastern populations
- Ethnicity is poorly defined and frequently unaddressed in PD studies.

6- Recommendations

- Large multicentre, multinational multi-ethnic studies using rigorous unified protocols are required to properly evaluate the effect of ethnicity on PD NMS.
- Identification of these variabilities is crucial to aid efficient health policy planning based on each population needs and optimize the use of local resources.
- We need to focus on ethnicity in PD research and neurology in general. This might enhance our understanding of many yet poorly-understood neurological disorders.

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Intelligibility Testing Of The MedicCom Device

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Introduction

- Communication is vital for teamwork.
- Respirator reduces voice intelligibility.
- We tested a novel medical voice amplifier (the MedicCom).
- This study evaluated the effect on intelligibility.

Materials and methods

- The Matching Rhyme Test assessed intelligibility using a crossover design.
- Two groups of 3 subjects were tested.
- Group 1 heard test words from a researcher wearing a respirator (the researcher also wore the MedicCom microphone).
- Group 2 heard the same words in another room via a long electrical cable and the MedicCom device.
- Two groups then swapped rooms.
- Testing was repeated with 50dB and 60dB of background noise.

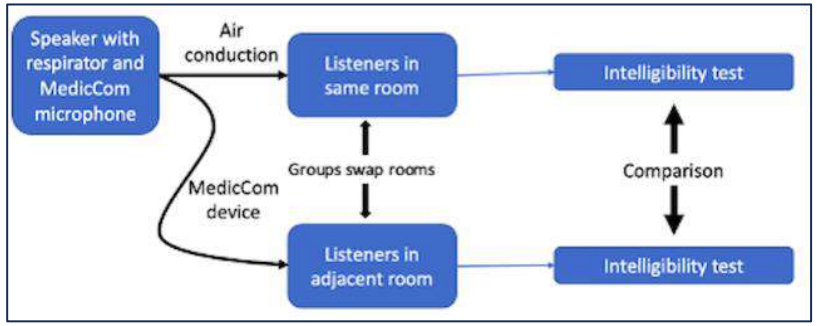

Figure 1: Structure of study

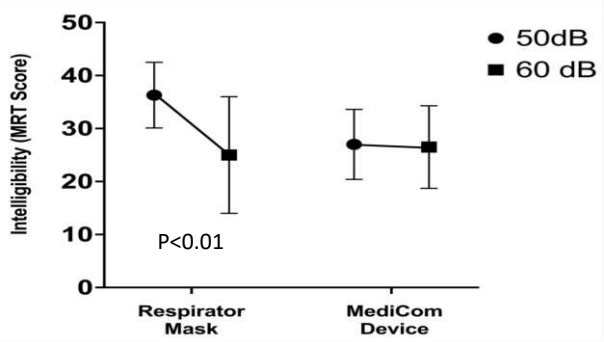

Figure 2: Results

Results

50dB background noise:
Respirator speech significantly more intelligible than MedicCom.

60dB background noise:
Significantly decreased respirator mask intelligibility.
No effect on MedicCom speech intelligibility.

Conclusion

No advantage to MedicCom.

Intelligibility using the MedicCom device unaffected by background noise.

Intelligibility using a respirator significantly worse with increased background noise.

The impaired intelligibility using MediCom is likely due to distortion from microphone – improvement here should be next development.

Reference

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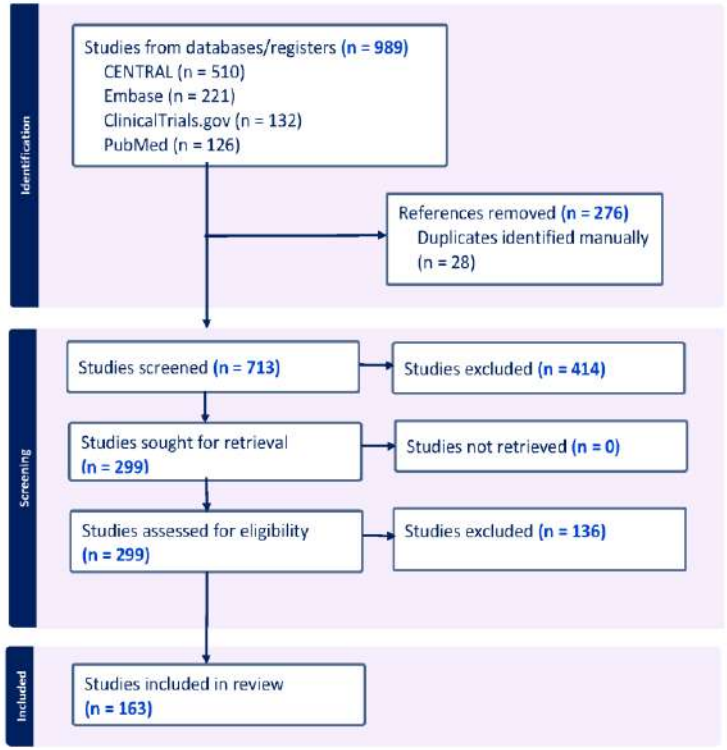
Efficacy of CGRP Inhibitors in Preventive Pharmacotherapy for Migraine
A Network Meta-Analysis and Systematic Review

Aman Bhonsale , Vinay Suresh , Muhammad Aaqib Shamim , Malavika Rudrakumar ,
Venkata Vamshi Krish Dondapati , Hariharan Seshadri , Bishal Dhakal , Poorvikha S , Dilip Suresh , Mainak Bardhan

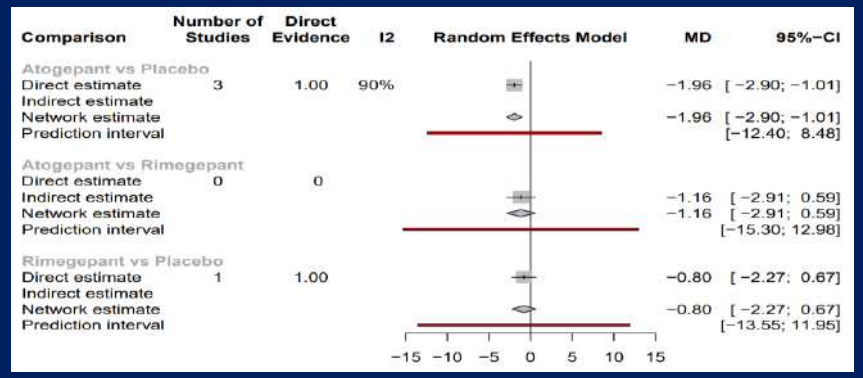
Introduction

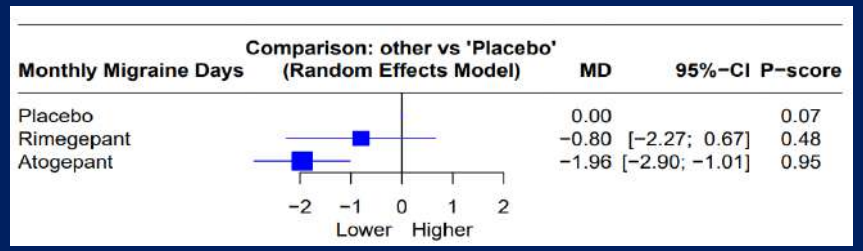
Calcitonin Gene-Related Peptide (CGRP) inhibitors have emerged as a promising approach in migraine prevention, reducing the frequency of migraine attacks while avoiding the typical side effects associated with other medications. But how effective are they really?

Methodology



*"Our study offers strong statistical evidence that Atogepant **is more effective** than Rimegepant in prevention of migraine."*





Scan the QR Code to read our abstract!

Results

- Atogepant (RR, 2.06) and Rimegepant (RR, 1.18) were more effective than placebo in 50% reduction of pain
- Atogepant being more effective than Rimegepant, network estimate (RR, 1.74)
- Mean difference in monthly migraine days (MMD) were -1.96 days with Atogepant and -0.80 days with Rimegepant with network estimate showing Atogepant (MD, -1.16) as more effective in reducing the number of monthly migraine days than Rimegepant.

Normal Distribution based on Relative Risk

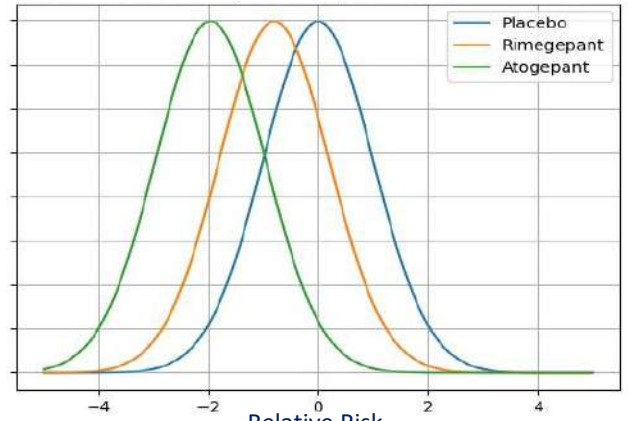


*Image not to be scaled.

Characteristics of presentation and management of people admitted with severe hypoglycaemia highlight the need for targeted educational interventions to mitigate occurrences – Pilot data from DEKODE Hypoglycaemia study.

Mariam Idrissi[1], Aashritha Buchipudi[1], Amanda Ling[1], Charles Page[1], Kalyaani Persad[1], Sam Sherratt-Mayhew[1], Dr Ahmed Iqbal[2], Dr Punith Kempegowda[3], DEKODE hypoglycaemia working group[3]

[1]University of Birmingham, [2]Department of Oncology & Metabolism, University of Sheffield & Sheffield Teaching Hospitals, [3]Institute of Applied Health Research University of Birmingham

Introduction

Severe hypoglycaemia, marked by blood glucose levels below 3 mmol/l (level 2) or needing third-party assistance (level 3), poses a significant risk leading to unplanned hospital admissions in individuals with diabetes[1].
However, there is an absence of information on admitted patients' characteristics, management, and outcomes.

Aims

To explore the characteristics of the population, precipitating factors and outcomes of people admitted with either level 2 or 3 hypoglycaemia.

Methodology

Retrospective study across five UK hospitals from October 2023 to January 2024

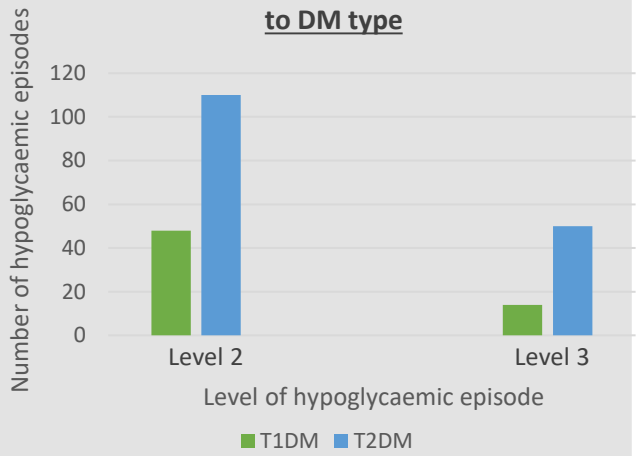
All adults aged >18 years admitted to hospitals with either level 2 or level 3 hypoglycaemia from November 2022 to October 2023 were included.

Data on **sociodemographic**, **precipitating factors**, **management**, and **outcomes** were collected.
Data was analysed on SPSS 29.0.

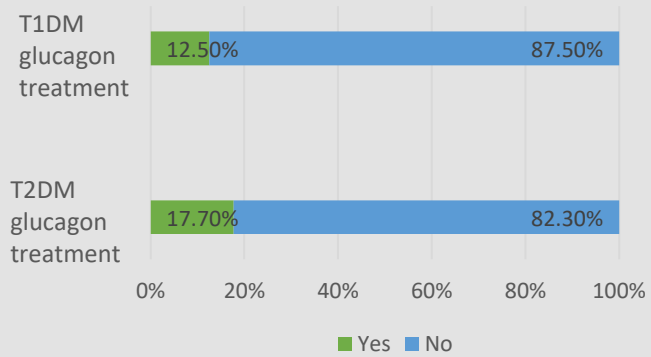
Results

- 222 episodes of hypoglycaemia: 160 in those with Type 2 Diabetes Mellitus (T2DM) and 62 in those with Type 1 Diabetes Mellitus (T1DM)
- The mean age was 44.5 in T1DM, and 80 in T2DM patients
- 22.5% of patients with T2DM received insulin treatment before admission
- Missed meals was a predominant cause in both T1DM (45.2%) and T2DM (58.8%)
- 11.3% of T1DM and 2.5% of T2DM patients were started on CGM after

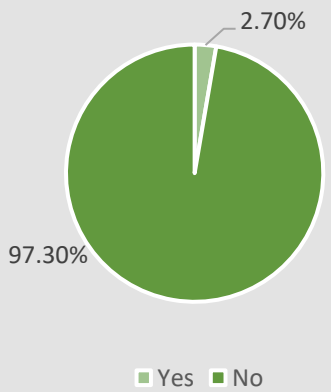
Level of hypoglycaemic episode according to DM type



Percentage of patients who received glucagon treatment



Number of patients who received glucagon on discharge



Discussion

Individuals requiring hospitalisation for severe hypoglycaemia were typically elderly and frail, and most had T2DM.
Major causes of episodes include missed meals and prior insulin treatment.
Majority of patients **did not** receive glucagon treatment for their severe hypoglycaemic episode.
Despite glucagon needs during episodes, prescriptions upon discharge were infrequent.

Recommendations

Targeted educational interventions to reduce occurrences of severe hypoglycaemia:

- Education of patients, carers and hospital staff of hypoglycaemia.
- An emphasis on protected mealtimes in hospitals, especially in frail, elderly diabetic patients
- Hospital staff awareness and education on the need for adequate prevention and management in severe episodes

References

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Post-operative cognitive dysfunction: Progressive multifocal leukoencephalopathy (PML), an unexpected finding in an elderly patient

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NHS Lewisham and Greenwich NHS Trust

Introduction

We present a case of rapidly progressive cognitive decline in an elderly patient under our care following a femoral neck screw fixation.

Initial Presentation

87-year-old woman presented to hospital following a fall and long lie. Identified to have a left sided neck of femur fracture.

She had a background of type 2 diabetes, stage 3 chronic kidney disease, multiple myeloma, endometrial cancer, hypertension, osteoporosis.

Her examination on admission identified an abbreviated mental test score of 2/10, slurred speech and weak left leg, attributed to her fracture

CT head - hypodensities suggestive of ischaemia

Initial working diagnoses:

Left sided neck of femur fracture with superimposed delirium

References:

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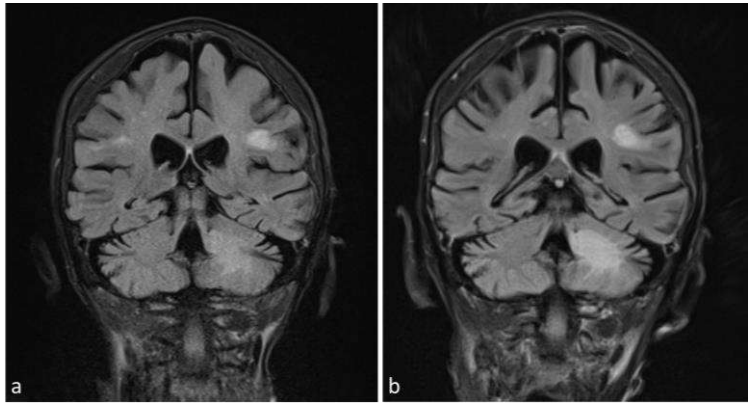


Figure 1. Interval MRIs showing progression of multifocal subcortical white matter abnormalities

Hospital Course

- She underwent a femoral neck screw fixation
- Post-operatively she had a sustained delirium and developed expressive and receptive dysphasia
- MRI head performed that corroborated admission CT findings, started treatment for stroke with anti-platelets
- Ongoing neurological impairment and drowsiness so repeat CT and MRI head performed, suggestive of PML
- Lumbar puncture performed which tested positive for JC virus, 372 copies/ml
- On MDT review it was thought this may be secondary to daratumumab[1] therapy used to treat her multiple myeloma previously
- Given the clinical features, typical imaging features and positive CSF JC virus, she was diagnosed with PML[2]

What is PML?

PML is a neurological condition where demyelination is caused by reactivation of JC polyomavirus due to reduced cell mediate immunity. It is commonly associated with HIV infection, but also other causes of immunosuppression. Clinical features vary according to distribution of lesions.

Discussion

Treatment of PML generally relies on reversal of underlying immunosuppression (e.g. giving antiretroviral therapy to patients with HIV). Treatment options are limited in patients without HIV. Pembrolizumab has been shown to have variable positive impact in a case series[3], it is considered a reasonable option if there is no other way to reverse immune suppression or restore cell mediated immunity[4].

Given this patient's frailty and the likely significant side-effects from pembrolizumab, an MDT decision was made to focus on comfort care and discharge facilitation for her.

Learning Points

- This case highlights the importance of thorough history taking and a detailed past medical history
- Ensure further investigations and alternative diagnoses are considered when the clinical picture does not fit the current working diagnosis
- PML is a plausible differential in older patients who are immunosuppressed even without a history of HIV

A Review On The Role Of Virtual Reality In The Rehabilitation Management Of Stroke And Parkinson's Disease

Reagan Lee [1], Pasin Chatchalermwit [1], Joseph Coong [1], Jingjing Wang [1]
(1) Edinburgh Medical School

1. Background

Stroke is a leading cause of long-term disability worldwide (1), necessitating effective rehabilitation strategies. Parkinson's disease is also a significant cause of disability, requiring similar rehabilitation strategies (2). **Virtual Reality (VR) has emerged as a promising technology for stroke (3) and Parkinson's disease rehabilitation**, offering a nascent platform for immersive interventions especially if coupled with next-generation feedback hardware and artificial intelligence input. However, the **evidence regarding the efficacy of VR interventions in stroke rehabilitation is diverse**, and a comprehensive review is needed to consolidate evidence of efficacy while identifying areas for focus and improvement.

This study aims to provide a **review of the existing literature on the use of VR in stroke and Parkinson's rehabilitation.** This will be performed with focus on the efficacy of VR applications while **highlighting current limitations of research.**

2. Methods

Medline/PubMed databases were searched systematically with PRISMA guidelines (7th October 2023)

Selection criteria: **English, full-text studies on adult patients (>18 years) with Stroke and Parkinson's disease managed with VR assisted therapy**

Three reviewers (RL, PC, JC) independently reviewed titles, abstracts and subsequently full texts, followed by data extraction

Outcome measures: **Fugl-Meyer Assessment (FMA) index** and/or the **Berg Balance Scale (BBS)**

3. Results

49 studies were included out of 1031 records. Studies were performed in 15 nations with most coming from South Korea (n=15), China (n=8), and Spain (n=5).

44 studies focused on stroke patients (n=1802) while 5 papers focused on Parkinson's patients (n=145). For stroke, records assessed either upper limb function (n=26), lower limb function (n=14) or both (n=4). For Parkinson's disease, all records assessed lower limb function (n=5).

All 49 studies were heterogeneous with variations in population selection, duration of therapy, software, hardware, and method of VR employment.

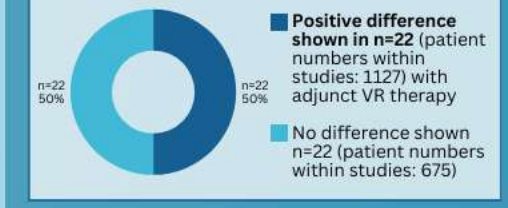
Population selection varied from patients with **Lacunar stroke** to **TACS**

Software varied from off the shelf **Oculus/Xbox gaming software** to **proprietary software designed for medical VR application**

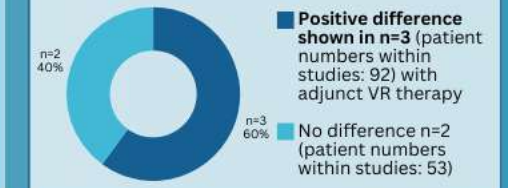
Hardware varied from **simple screens** to **VR suits with complex biomechanical movement feedback systems**

Duration of therapy ranged from **1.5 weeks - 1 year**

Stroke studies examining if the use of VR-assisted therapy made a difference in FMA/BBS scores



Parkinson's Disease studies examining if the use of VR-assisted therapy made a difference in BBS scores



4. Discussion

Results across all studies were highly variable with ~50% reporting **VR-assisted therapy, used as an adjunct to conventional therapy, had a significant positive difference** in FMA and/or BBS scores compared to conventional therapy. However, most studies supported the **potential utility of VR-assisted therapy in improving functional outcomes in patients with stroke and Parkinson's disease.**

This review was limited by study quality. Considering all studies used **large variations of copyrighted proprietary materials and assessment methods, study heterogeneity** has **limited the possibility of a meta-analysis** to draw a more definite conclusion regarding the utility of VR-assisted therapy.

5. Conclusion

Standardisation and collaboration across the MedTech VR industry is required for building a reliable evidence base rather than increased individual competition through creation of high-cost patented systems. **This can dilute conflict-of-interests pertaining to patented materials,** while contributing to patient benefit through **increased research corroboration.**

Heart failure caused by chronic obstructive pulmonary disease in the United Kingdom: A burden and trend analysis, 1990-2019.

Cortorreal Javier Rafael [1], Luis Sierra Michelle[1]

[1] Universidad Iberoamericana, UNIBE. Santo Domingo, Dominican Republic.

Introduction

- Chronic obstructive pulmonary disease generates a high pressure state for the right ventricle of the heart, over time this can lead to right heart failure[1].
- RHF is associated with an overall poor prognosis, especially when hospitalization is required and other factors are present[2].
- The aim of this study is to analyze the trends of heart failure caused by chronic obstructive pulmonary disease in the United Kingdom from 1990-2019 in adults older than 55 years.

Material and Methods

Data was extracted from Global Burden of Disease Study 2019[3]. Overall numbers of prevalence and Years Lived with Disability(YLDs) were analyzed by age(+55 years), sex, year and location from 1990-2019 in the United Kingdom. To analyze the burden trend, annual percentage change (APC) was used.

Results

Prevalence:

- Overall prevalence number showed a trend of 55,331(95%UI:35,179-86,205) in 1990 to 51,055(95%UI:35,114-74,281) in 2019.
- Overtime the APC in 1990-2010 showed a value of -0.16, but in the period 2010-2019 the APC showed an APC of 0.10 with a final APC from 1990-2019 of -0.08.
- Males went from an overall prevalence of 26,115(95%UI:16,708-40,263) in 1990 to 27,204(95%UI:18,759-39,096) in 2019 and an APC of 0.04,
- Women went from 29,215(95%UI:18,686-45,966) in 1990 to 23,851(95%UI:16,300-34,926) in 2019 accompanied by an APC of -0.18.

Figure. Sex-wise burden and trends of Heart failure caused by chronic obstructive pulmonary disease in the United Kingdom: 1990-2019.

Results

Years Lived with Disability (YLDs):

- Overall count went from 5,009(95%UI:2,796-8,413) in 1990 to 4,625(95%UI:2,710-7,369) in 2019 with the result of an APC of -0.08.
- England exhibited the highest prevalence number with a value of 44,921(95%UI:31,025-65,419) in 2019.
- Northern Ireland showed a prevalence burden of 1,159(95%UI:745-1,738) in 2019, meaning the lowest one.
- The location with the highest APC was England with -0.03.
- Scotland had the lowest APC with a value of -0.41.

Conclusions

- The data analyzed have shown a decrease in the overall prevalence of HF caused by COPD in the UK.
- Significant decrease of the burden within females but a concerning rise among men.
- Prevalence experienced a trend towards decrease between the years 1990-2010, and then experienced a trend towards increase between the years 2010-2019.
- The higher burden found in England is influenced by the fact of the highest number of population and territory in comparison with the other nations, conversely Northern Ireland with the lowest burden is also associated with the population magnitude.
- The negative APC prevalence shown by Scotland generates a curious direction for research and generates an opportunity for advantage.

References

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Sex related differences of chronic kidney disease due to diabetes mellitus type 1 in the United Kingdom: A comparative analysis of burden and trends, 1990-2019.

Cortorreal Javier Rafael [1], Luis Sierra Michelle[1]

[1] Universidad Iberoamericana, UNIBE. Santo Domingo, Dominican Republic.

Introduction

- In the United Kingdom, in 2019 there was a diabetes mellitus type 1 prevalence of 513,448 (95%UI:408,650-637,853) and a burden predominance among men, with a presence of chronic kidney disease due to DM1 of 35,732.90(95%UI:31,652.79-39,955.75) [1].
- Around the world the burden of chronic kidney disease has shown differences in the burden predominance related to sex [2].
- The objective of this study is to analyze the sex related differences of the burden trends of CKD due to DM1 in the United Kingdom.

Material and Methods

Data was extracted from Global Burden of Disease Study 2019. Overall numbers of prevalence, deaths and Disability-adjusted life years (DALYs) were analyzed by age, sex, year and location from 1990-2019 in the United Kingdom. To analyze the burden trend, annual percentage change (APC) was used.

Results

Prevalence:

- **Males** experienced an upward trend, from an overall numberof 14,618(85%UI:13,055-16,580) in 1990 to 16,893(95%UI:14,855-19,068) in 2019 and an APC of 0.16.
- **Women** went from 16,141 (95%UI:14,260-18,095) in 1990 to 18,839(95%UI:16,402-21,249) in 2019 with an APC of 0.17.

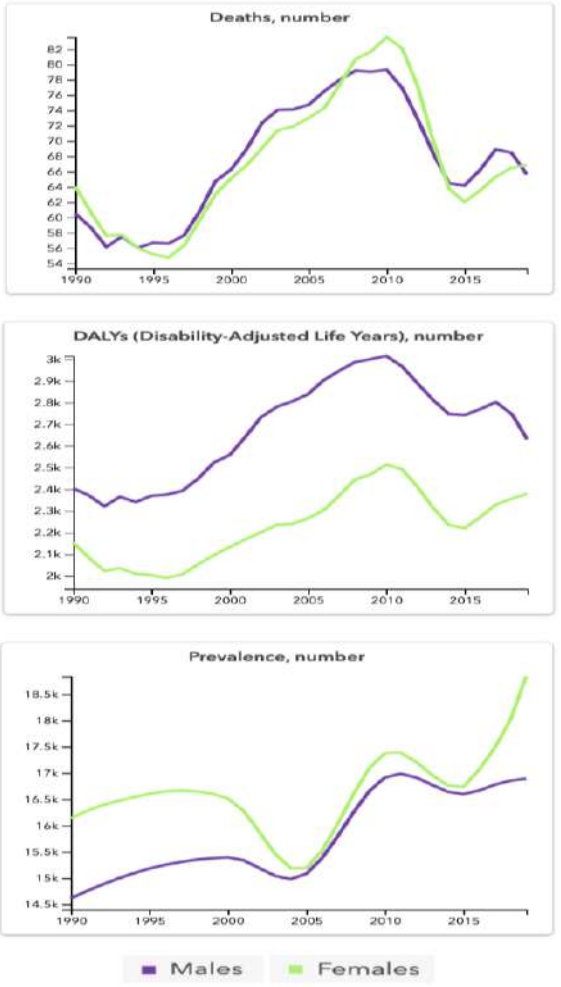

Figure. Sex related differences in the trends of Chronic Kidney Disease caused by Diabetes Mellitus type 1 in the United Kingdom, 1990-2019.

Results

Number of deaths:

- **Males** went from 60(95%UI:35-96) in 1990 to 65(95%UI:38-103) in 2019 with an APC of 0.08.
- **Women** went from 64(95%UI:36-106) in 1990 to 66(95%UI:38-108) in 2019 and an APC of 0.04.

DALYs:

- Males went from 2,403(95%UI:1,618-3,378) in 1990 to 2,629(95%UI:1,769-3,691) in 2019 and an APC of 0.09,
- Women went from 2,154(95%UI:1,476-3,121) in 1990 to 2,379(95%UI:1,631-3,353) in 2019 with an APC of 0.10.

Conclusions

- Data analyzed showed a burden predominance among women regarding prevalence and number of deaths, but in the last, the men showed a heavier APC.
- DALYs results demonstrate a greater burden in men but a heavier APC in women.
- Regardless of the predominance of DM1 in men, women appear to have a higher probability of higher burden of CKD due to DM1.

References

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A Genetic Paradigm Shift: Deciphering Stress-Induced Molecular Mechanisms Fuelling Cancer Genesis

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INTRODUCTION AND OBJECTIVES

Chronic psychological stress, a pervasive issue in contemporary society, has been intricately linked to the genesis and progression of various cancers. The complex biological underpinnings that connect stress to oncogenic processes, however, have remained largely uncharted[1,2].

This study aims to shed light on the sophisticated mechanisms by which sustained stress influences key molecular pathways critical for cancer initiation and progression.

We explore the profound genomic and epigenomic aberrations orchestrated under prolonged stressful conditions which create an internal milieu conducive to cellular transformation and the acquisition of hallmark cancer phenotypes.

METHODS

We carried out a detailed literature search across renowned scientific databases including PubMed, Scopus, and Web of Science.

Our search strategy encompassed key terms such as "chronic stress," "cancer," "genetic instability," "epigenetic modifications," and "carcinogenesis."

An exhaustive literature search across major scientific databases identified over 800 original articles associating emotional stress and cancer development. After systematic screening, 120 relevant studies were selected for in-depth review.

Table 1

Criteria Type	Description
Inclusion	- Original research articles. - Published in English. - Conducted within the last ten years. - Focused on molecular analyses of stress-induced genetic, epigenetic, and signaling disruptions in cancer.
Exclusion	- Review articles, commentaries, and editorials. - Studies not addressing chronic stress or its molecular implications in cancer. - Research older than ten years.

RESULTS

Statistical meta-analysis of epidemiological data reveals a 35% higher cancer incidence among individuals experiencing high psychological stress.

Genetic and Epigenetic Alterations:

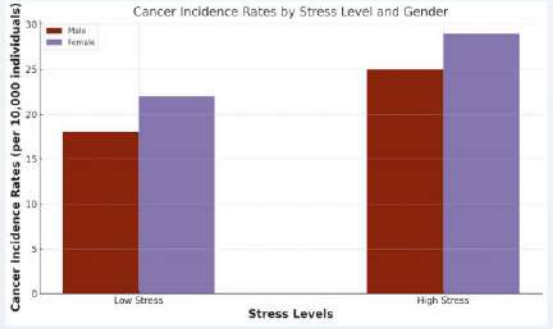
Chronic stress leads to genetic instability and reduced expression of DNA repair genes like BRCA1, compromising genomic integrity. It also causes epigenetic changes such as altered miRNA profiles and histone modifications that can activate oncogenes and suppress tumor suppressor genes.

Pathway Disruptions and Cancer Phenotype Acquisition:

Genetic and epigenetic changes due to chronic stress disrupt key cellular pathways, including those for cell cycle control and DNA repair, which can culminate in the development of cancerous traits in cells.

Disruption of Cellular Homeostasis and Cancer Progression

This multifaceted molecular dysregulation disrupts cellular homeostasis, conferring an environment permissive for the progressive acquisition of enabling characteristics fundamental to malignancy within susceptible cell populations.



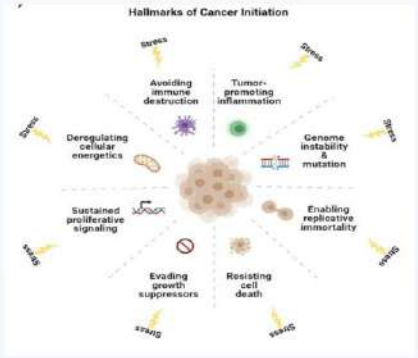


Fig 2: "Hallmarks of Cancer Initiation" in relation to stress.

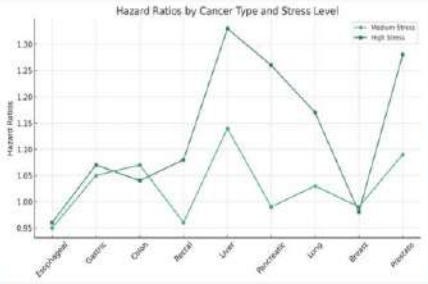


Fig 3: graph comparing the hazard ratios for various cancer types at medium and high stress levels.

DISCUSSION:

***Stress* as a Risk Factor in Carcinogenesis**:

Our study highlights the molecular basis of this risk, showing that stress is as potent as genetic or environmental factors in influencing cancer onset.

Molecular Impact of Stress on Genetic Integrity:

Stress's influence extends to DNA repair processes, with notable downregulation of genes like BRCA1. These stress-related molecular changes may serve as early indicators of cancer, offering targets for new treatments.

Psycho-Oncology in Cancer Management:

Our findings advocate for a holistic treatment approach, merging psycho-oncological care with medical treatments.

CONCLUSIONS

This systematic review project has demonstrated:

1.Molecular Impact of Chronic Stress: Our research has confirmed that chronic stress significantly disrupts genetic and epigenetic regulation, serving as a critical factor in the biological underpinnings of cancer.

2.Personalized Cancer Strategies: Identifying stress-induced molecular changes offers a blueprint for developing tailored cancer prevention and treatment strategies, emphasizing the importance of personal molecular profiles.

3.Integration of Psycho-Oncology: There is a pressing need to incorporate psycho-neuroimmunology and molecular psycho-oncology insights into traditional cancer care to better address the nuances of stress-related cancer risks.

4.Enhancing Carcinogenesis Understanding: A more profound understanding of how chronic stress contributes to carcinogenesis is essential for innovating cancer prevention and treatment approaches.

5.Future Research Directions: Future research should focus on the longitudinal effects of chronic stress on cancer development and the potential for interventions that target specific stress-responsive pathways to mitigate cancer risks.

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Targeting contributory factors in difficult-to-treat rheumatoid arthritis

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University of Birmingham, Rheumatology Research Group

TRAC TREATMENT REFRACTORY ARTHRITIS COHORT

NHS University Hospitals Birmingham NHS Foundation Trust

NHS Sandwell and West Birmingham NHS Trust

Introduction:

- There is a growing number of individuals with rheumatoid arthritis (RA) in whom stepwise treatment escalation remain ineffective[1].
- Improvement in disease activity can be impacted by non-inflammatory components
- EULAR defined this subset of RA patients as 'Difficult-to-treat' (D2T-RA), whereby there is failure of ≥2 b/tsDMARDs classes with signs/symptoms of disease activity/burden[2].
- D2T-RA represents an area of clinical unmet need in the NHS

Objectives:

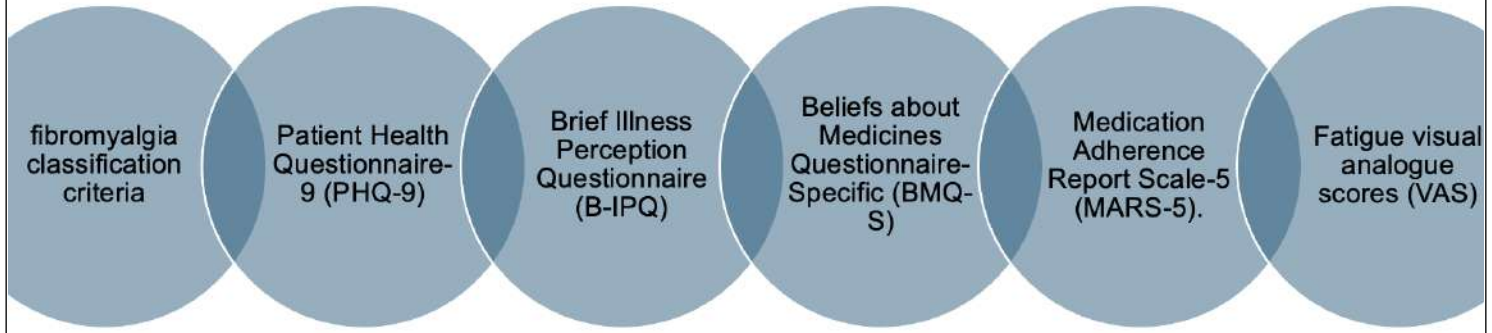
- To identify the presence of non-inflammatory aspects of D2T-RA
- Provide justification for the development of a novel multidisciplinary clinic through which we can approach and address the needs of patients with D2T-RA.

Inclusion Criteria:

- RA patients aged ≥18
- Failed two or more classes of b/tsDMARDs

Recruitment took place from two centres

Methods: Responses were collected to the following questionnaires:



Conclusions:

- Factors such as increased BMI, depression, fatigue, non-adherence, fibromyalgia, and a negative view of illness are present in a population of D2T-RA patients.
- These can impact on treatment response
- Creation of an MDT clinic identifying/managing these factors could be valuable in treating D2T-RA

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Results: Characteristics of a D2T-RA cohort

Patient characteristics		
Age		59 (52-63)
Female*		17, 90%
White British*		13, 68%
Ever Smoker*		9, 47%
BMI^		25.8 (25.3-30.3)
Disease characteristics		
Anti-CCP positive*		17, 90%
Tender 28 joint count		9(3-13)
Swollen 28 Joint count		2(2-4)
DAS28-ESR		4.25(3.8-4.8)
DAS28-CRP		4.18(3.61-5.2)
Prescence of erosions*		8, 42%
Outcomes		
Fibromyalgia*	Fulfill Fibromyalgia 2016 Revised classification	4, 21%
Ever non-adherence*	csDMARDs*	9, 47%
	b/tsDMARDs*	7, 37%
Fatigue	Visual analogue score (0-100)	74 (46-87)
Depression	PHQ-9	7(3.5-14)
BMQ-specific^^	NCD (-4 to +4)	1.4 (0.8-2)
B-IPQ^^	B-IPQ (0-80)	49 (42-54)

results presented as median (IQR); *n (%); ^n=15, ^^ n=18

Abdominal Pain with PR Bleeding : A Rare Case of STEC Causing Toxic Megacolon

Sajjal Almas, Awais Ali, Muhammad Faisal Awais, Javeria Mustafa, Tamar Saeed, Shoaib Muhammad
Acute Medicine, Russells Hall Hospital

Case Presentation

A 65-year-old Caucasian male presented with two days of severe abdominal pain, loose stools and progressively worsening blood in stools until he started to have PR bleeding. He recently travelled to France and was a smoker with 37.50 packs a year.

On examination, there was marked tenderness in the lower abdomen. Blood tests revealed CRP 93, WBC 20.2 and normal renal function. Given the above-mentioned findings, a provisional diagnosis of infective gastroenteritis was made, and blood cultures were sent.

Surgical team reviewed the patient, and the patient was started on IV fluids and antibiotics. CECT AP showed marked oedema of the whole large bowel sparing rectosigmoid region with paracolic fat stranding and no perforation consistent with diffuse colitis.

Surgical team advised a low threshold for flexible sigmoidoscopy if the PR bleeding continues. Patient developed worsening distension with exaggerated bowel sounds. He passed stools, but not flatus. CRP, Creatinine and WBC rose, and was started on fluconazole. Subsequently, he developed peripheral shutdown and was shifted to the operation theatre. Pancolectomy revealed a necrotic large bowel, consistent with toxic megacolon. Patient had increased vasopressor requirements, decreased urine output, developed renal shutdown and died despite provision of CVVH. Stool C/S confirmed the presence of Shiga Toxin producing E Coli.

H/P Specimen

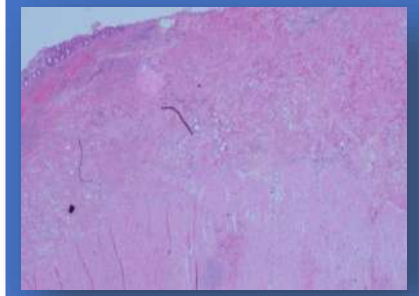

Figure 1

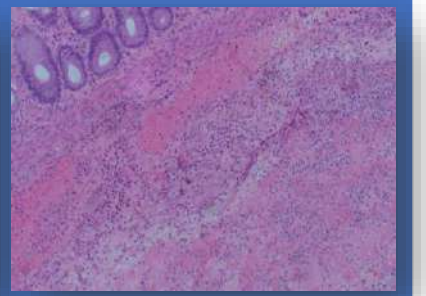

Figure 2

Figure 1 & 2: Colonic sections taken from pancolectomy specimen showing inflammatory infiltrates, consistent with infective etiology of toxic megacolon

	21-07	22-07	23-07	24-07	25-07	26-07	27-07
Egfr		77	78	70	64	59	25
Creat		90	89	97	105	112	225
Urea		6.8	7.4	7.8	7.6	9.1	12.3
WBC		21	24	26	25.5	38	61
CRP		120	235	251	243	172	144

Table 1

Table 1: Laboratory trends

References

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Discussion

STEC presents with diarrhoea, abdominal pain, fever and vomiting three days after ingestion. Our patient had bloody diarrhea, but later on developed PR bleeding. Cultures confirm the presence of STEC and diarrhoea improves in a week with spontaneous resolution in 85% of the cases, while the remaining 15% eventually develop HUS.

Almost all E. Coli O157:H7 contain a gene encoding Shiga toxin.

There are two types of shiga toxin, shiga toxin 1 usually does not cause bloody diarrhoea, while shiga 2 is typically associated with bloody diarrhoea.

Diagnosis of HUS is clinical with hemolytic anaemia, thrombocytopenia and renal damage which occurs suddenly in a patient with a history of diarrhoea in the last two weeks, as seen in our patient.

For definite diagnosis, STEC infection should be proven, similarly, stool culture showed Shiga toxin producing E Coli in our patient.

Fluid and electrolyte are the mainstay of management, we managed our patient with fluids and antibiotics. Symptomatic uremia and severe fluid overloading unresponsive to diuretics is treated with dialysis. Erythrocyte transfusion is recommended in patients with a haemoglobin level of <6.

Similarly, platelet transfusion is recommended only for the patient with life threatening bleeding or in the preparation of surgery.

Tackling Sexism In The Medical Profession

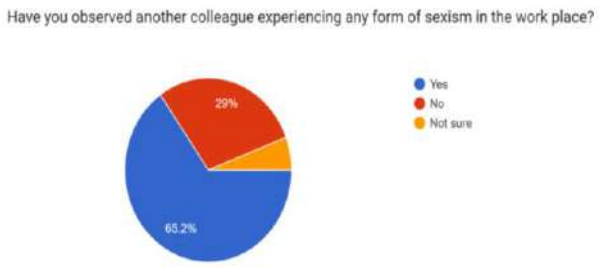
West Hertfordshire Teaching Hospitals NHS Trust

Dr Shamira Ghouse & Dr Rachel Hoey, Watford General Hospital

Introduction

In response to the BMA's sexism in medicine report which stated that a staggering 91% of female doctors in the UK had experienced sexism at work (1), our trust signed the BMA pledge to end sexism in the medical profession. We were committed to tackling underlying structural and cultural issues that were contributing to the issue.

A survey carried out in our trust across all grades and departments reported that almost two thirds of doctors surveyed had witnessed or encountered sexism in the workplace. An astounding 75% of female doctors who completed the survey had experienced sexism at work. Free text comments on individual experiences of sexism were shocking and eye opening. It displayed the immense amount of education, work and commitment needed by our trust to enact positive change



Contact: Shamira Ghouse
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Methods

An initiative we took was the introduction of grade specific lanyards in an attempt to reduce the unconscious bias female doctors may experience at work from patients and colleagues. The lanyards were brightly coloured and easily identifiable, with large white writing stating the word "doctor" and their grade.

A survey was disseminated across the trust 3 months after its introduction to understand its uptake and impact.

Results

The survey identified that there was excellent uptake with over 60% of doctors wearing their grade specific lanyard less than 3 months after introduction. Following the introduction of the lanyards, 65% of female doctors reported some improvement in their experience of sexism they encountered at work.

Comments with regards to the improvement following the introduction of the grade specific lanyards were positive and encouraging. Examples of comments included:

"Clear to all what grade a doctor is. Non doctor staff approaching the correct grade of doctor depending on the query they have, rather than making assumptions of grade e.g. based on gender."

"Reduces ageism/ sexism when attempting to identify registrars/ consultants."

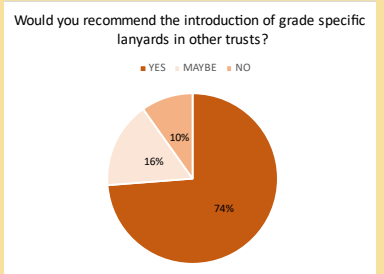
"More overt indication of your grade which has meant improved recognition from colleagues as to your seniority and so less unconscious bias from colleagues."

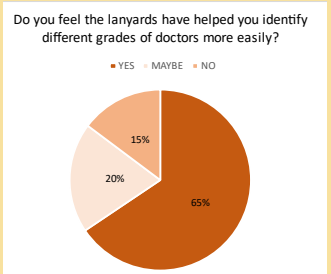
Conclusion

The lanyards are now widely used across all departments and grades and is an initiative that could easily be adapted by other trusts in their attempt to address and eliminate sexism in the medical profession.

Following the success of the lanyard intervention, our trust was interviewed and featured in the BMA's short film on ending sexism (2). Additionally, an article written by the BMA stated their endorsement for our colour coded lanyard scheme as an initiative to tackle sexism and unconscious bias. (3).

The trust remains committed to the signed BMA pledge and continues to explore other avenues to enact positive change.





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