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FOREWORD

As we launch the fifth edition of the SMJ, and our third issue as Co-Editors in Chief, we continue to be amazed by the dedication, ingenuity and teamwork demonstrated by UCC's medical students. It is this spirit of innovation and collaboration that we hope to display in the collection of work in this edition.

Now, more than ever, it is essential that the incoming generation of medical professionals build a strong foundation of inclusion, cultural literacy and advocacy to carry forward into their professional practice and academic pursuits. Learning to interpret research through the lens of each patient's unique backgrounds and lived experience is an invaluable skill that will make physicians a trusted and effective partner in healthcare. We hope that an early emphasis on this principle will continue to shape the careers of young researchers and how they apply evidence-based care to their practice.

The fifth edition once again boasts submissions from a variety of UCC medical societies, providing their unique perspective on diversity and inclusion in their particular fields of medicine. We are also thrilled to feature two collections of abstracts from research conferences held in the past year: the Neurovision conference at RCSI, hosted by the Dandy Ireland Student Neurosurgical Society, and our own annual Student Research Conference.

As always, this edition would not have been possible without the incredible team of students and faculty members who have volunteered their time and expertise to ensure the SMJ is kept to the highest possible standard. A heartfelt thank you to our editorial team, the many UCC students and faculty members who performed our peer review and, of course, the authors who submitted their work. Finally, we thank the UCC Medical School for their continued support of our publication. Thank you and happy reading!

KIND REGARDS,

Shobha Mehta & Pádraig Cronin

SHOBHA MEHTA & PÁDRAIG CRONIN

CO-EDITORS-IN-CHIEF

Address

I would like to begin by thanking the UCC Medical Research and Technology Society for inviting me to contriute to this issue. It is a privilege to address this edition of the UCC Student Medical Journal at such an exciting and transformative time.

When considering a topic for this foreword, I reflected on the forces reshaping medicine today: global health challenges, planetary crises, and rapid technological advances—particularly the rise of artificial intelligence (AI). These dynamics are redefining how we learn, research, assess, and deliver care. But rather than focusing solely on AI, I chose to explore a broader and equally urgent theme: the importance of understanding and integrating cultural diversity in medical research and practice.

This theme closely aligns with the UCC Strategic Plan, Securing Our Future 2023–2028, and the university's mission "to create and sustain an inclusive environment and culture to enable transformative research and learning for the enrichment of society and stewardship of our planet." This foreword builds on that vision by exploring how medical research must embrace cultural diversity and inclusion in order to address future challenges meaningfully.

Delivering high-quality healthcare to an increasingly diverse population remains a major challenge. There is growing recognition that culturally competent care is essential to improving health equity and outcomes. Research consistently shows that high-quality care must account for cultural differences. Yet, meaningful engagement with multicultural populations remains difficult in many settings. Language barriers, differing cultural norms, and underrepresentation in research continue to pose serious obstacles, particularly for marginalized communities. These challenges highlight the need for a more inclusive, person-centred approach—one that considers patients' cultures, values, and lived experiences.

Another critical issue is the lack of diversity in research populations. The underrepresentation of racial and ethnic minority groups undermines the generalizability and applicability of clinical findings. Including self-identified race and ethnicity in studies is vital for scientific accuracy and effective care delivery.

Moreover, language barriers and cultural disconnects persist as obstacles to equitable healthcare. Here, technology—including AI—has the potential to bridge some of these gaps, whether through translation support, tailored patient education, or improved cross-cultural communication. However, technology must be applied thoughtfully and inclusively, with careful consideration of its ethical and cultural implications.

Looking ahead, a multidisciplinary, culturally informed approach must become the standard in both research and clinical care. This includes designing systematic reviews that incorporate diverse perspectives and developing educational innovations that prioritize inclusion. I have been inspired by undergraduate students leading forward-thinking projects—leveraging AI to enhance patient understanding, reduce language barriers, and advocate for more representative research. Their work demonstrates not just the use of new tools, but critical engagement with their broader impact on research and healthcare.

The theme of this issue reflects an emerging spirit—one of interdisciplinary inquiry and cultural responsiveness aimed at bridging healthcare gaps. I encourage you to embrace diversity not as an obstacle, but as a strength. By working across disciplines and understanding the rich cultural mosaic of patient populations, you can help shape a more inclusive and diverse future for medical research.

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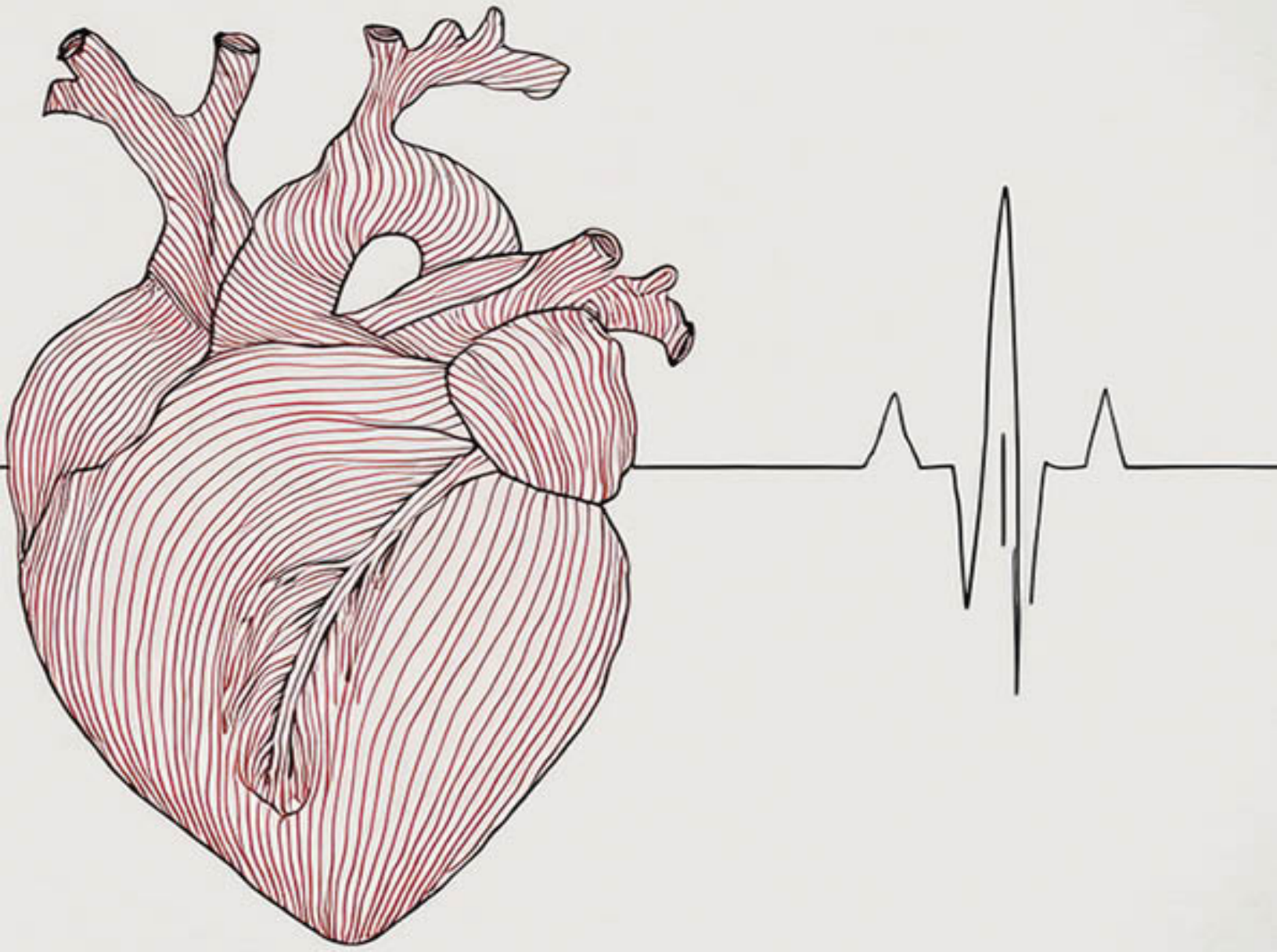
Table of Contents

Poems

Special Edition - Diversity & Cultural Differences in Medicine

Conference Abstracts: Neurovision 2024 Abstracts

Conference Abstracts: Student Research Conference UCC Abstracts



Aortic Valve Replacement via Mini-Sternotomy versus Full Sternotomy: A Single Centre Retrospective Cohort Study

JOEY HARRINGTON
https://doi.org/10.33178/SMJ.2025.1.1

Abstract

BACKGROUND: The traditional method of aortic valve replacement (AVR) is via full sternotomy. However, this incision may not heal properly and cause significant pain. Minimally-invasive methods have been adopted, including mini-sternotomy, gaining popularity due to a smaller incision, reducing surgical trauma. The hypothesis is that AVR via mini-sternotomy is a safe alternative to full sternotomy.

METHODS: This retrospective study compares 2 groups; AVR via mini- and via full sternotomy. Inclusion criteria were all patients 18 and over who underwent AVR between September 2016 and December 2022 in Cork University Hospital. Patients who underwent concomitant cardiac procedures were excluded. Statistical analysis was performed using STATA software. Continuous data was analysed using the student t-test. Categorical data was analysed using the Pearson chi-squared test. A p value of <0.05 was deemed statistically significant.

RESULTS: 169 patients were included; 96 and 73 in the mini- and full sternotomy groups, respectively. Groups were well matched in terms of baseline characteristics including age, BMI, and co-morbidities. The mini-sternotomy group showed a statistically significantly shorter hospital length of stay ($t(166)=4.24$, $p=0.000$). There were no statistically significant differences in intra- ($t(167)=1.8$, $p=0.067$) and post-operative blood transfusion requirements ($t(167)=0.53$, $p=0.592$). The mini-sternotomy group had significantly longer cross-clamp ($t(167)=-2.1$, $p=0.039$) and cardio-pulmonary bypass times ($t(167)=-2.45$, $p=0.015$).

CONCLUSION:AVR via mini-sternotomy has been associated with shorter hospital stay, with the drawback of increased cross-clamp and cardio-pulmonary bypass times. This retrospective study demonstrates mini-sternotomy as a safe alternative to full sternotomy, in the cohort studied.

Introduction

The aortic valve is one of two semilunar valves, the other being the pulmonary valve, which lies between the left ventricle and aorta. It is composed of three leaflets and, by definition, allows blood flow in one direction only, from the left ventricle to the aorta [1]. The structure of the valve allows it to withstand various mechanical and haemodynamic forces throughout the cardiac cycle [1]. Although the aortic valve is quite robust, there are various factors which can contribute to its demise. These include age-related calcification, congenital heart defects and connective tissue disorders [1]. The valve can either become stenosed or insufficient. Aortic stenosis is a narrowing of the valve opening, reducing the valve area [1]. Aortic regurgitation (insufficiency) is the backflow of blood from the aorta to the left ventricle when the valve leaflets fail to close normally [1]. Both pathologies can be asymptomatic or can cause symptoms of syncope, dyspnoea or heart failure [1]. Pathologies of the aortic valve can have detrimental effects on bodily functions due to perfusion deficits [2]. These pathologies are managed by either aortic valve replacement or repair [2].

Aortic valve replacement (AVR) is the gold standard treatment for those patients suffering from severe or symptomatic aortic stenosis or aortic regurgitation [3]. The traditional method of AVR is via a median sternotomy incision, where a cut is made from the manubrium of the sternum to the xiphoid process and sometimes, as far as the umbilicus. While this remains the 'gold standard' approach, it may lead to poor sternal wound healing, severe pain and prolonged recovery, especially in patients suffering from conditions such as osteoporosis, osteopenia or diabetes mellitus [3]. Various minimally-invasive techniques with many different access routes have evolved, with the aim of reducing surgical trauma and ultimately improving patient outcomes [3].

The use of minimally-invasive surgical techniques in patient care is well documented in ancient history, however, it is only since 1990 that technological advancements have allowed surgeons to utilize the approach to its fullest extent [4]. The approach has transformed the surgical landscape, significantly reducing post-operative pain, recovery time, length of hospital stay and overall surgical costs [4]. Examples of such methods include laparoscopic abdominal surgery and endovascular aneurysmal repairs, but to name a few.

'Minimally-invasive cardiac surgery' is defined as any procedure that is performed without a full sternotomy incision or cardiopulmonary bypass support [5]. Minimally-invasive AVR was first described by Cosgrove and Sabik in 1996, but the surgical uptake since then has been patchy at best [6]. This has been possibly due to inertia and perhaps, the need for additional training to perform a more technically challenging procedure [6]. Examples of minimally-invasive AVR techniques include a right parasternal approach, a right anterior mini-thoracotomy, a trans-sternal approach and a mini-sternotomy approach [5]. This paper focuses on the mini-sternotomy approach. In previous studies, the mini-sternotomy approach has been shown to lead to better cosmetic outcomes, shorter length of both ICU and hospital stay as well as lower amounts of blood loss [7].

However, research in the area has been limited and studies have had conflicting results. This paper is the first such study in an Irish hospital context. It will add to the existing body of knowledge and will further establish AVR mini-sternotomy as a safe alternative to the traditional approach. Mr. Kishore Doddakula and his colleagues have been performing this minimally-invasive procedure in Cork University Hospital (CUH) since 2011 [8].

The hypothesis of the study is that AVR via mini-sternotomy is a safe alternative to the full sternotomy approach. The objectives are to characterise the profile of the population who have undergone both procedures, to examine peri-operative outcomes for patients and to then compare results between the two cohorts.

Materials & Methods

This study is a retrospective database review conducted in the Department of Cardiothoracic Surgery, Cork University Hospital (CUH). The population studied was those who underwent aortic valve replacement (AVR) either via mini- or full sternotomy in CUH between September 2016 and December 2022. Data was obtained from the PATS (Patient Advocate Tracking System) and was input into a Excel file, which was encrypted on a password-protected computer in the Department of Cardiothoracic Surgery, CUH. This Excel file was the data collection sheet, which included parameters

such as operation time, cross-clamp time and length of hospital stay.

Inclusion criteria was all patients aged 18 years and older who underwent AVR either via mini- or full sternotomy in CUH between September 2016 and December 2022. Patients excluded were those aged less than 18 years and those who underwent concomitant cardiac procedures, such as a coronary artery bypass graft or an ascending aorta replacement.

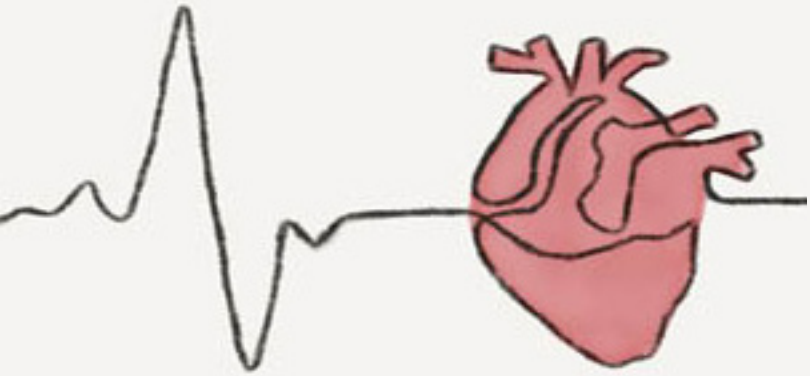
Statistical analysis was carried out using STATA software. Basic descriptive analysis was used to characterise the data, with results expressed as a mean and the absolute number (%). Continuous data was analysed using the student t-test and results were expressed as a mean and standard deviation. Categorical data was analysed using the Pearson chi-squared test, with results expressed as a number and percentage. A p-value of less than 0.05 was deemed as statistically significant. Ethical approval was obtained from the Clinical Research Ethics Committee of the Cork Teaching Hospitals (CREC).

Results

A total of 169 patients were included in the study, after inclusion and exclusion criteria were applied. Among them, 96 patients underwent AVR via mini-sternotomy and 73 patients underwent AVR via full sternotomy. Table 1 presents the demographics of the cohorts studied, Table 2 summarises the peri-operative outcomes for patients with results expressed as a mean, Table 3 presents the post-operative outcomes and complications and Table 4 presents the peri- and post-operative mortality of patients at various times following surgery.

Table 1: Demographic Data

Demographic Parameter	Mini-Sternotomy (n=96)	Full Sternotomy (n=73)	P-value
Age (years)	68 (+/- 1.3)	69 (+/- 1.2)	0.800
Male	54 (56%)	54 (74%)	0.170
Body Mass Index (kg/m^2)	29 (+/- 0.5)	31 (+/- 0.8)	0.003
Diabetes	12 (13%)	18 (25%)	0.040
Hypertension	64 (66%)	53 (73%)	0.408
Hyperlipidaemia	68 (71%)	55 (75%)	0.514
Coronary Artery Disease	18 (19%)	18 (25%)	0.353
Smoking History	43 (45%)	55 (75%)	0.000
COPD	18 (19%)	14 (19%)	0.944
Creatinine Clearance (ml/min)	84 (+/- 2.9)	86 (+/- 4.9)	0.660



The demographic data (Table 1) shows that both groups (AVR via mini-sternotomy and AVR via full sternotomy) were generally well-matched in terms of baseline characteristics, including age, sex, creatinine clearance and prevalence of co-morbidities, such as hypertension, hyperlipidaemia and coronary artery disease. However, the full sternotomy group showed a significantly lower mean BMI [p=0.003] and a higher prevalence of diabetes mellitus [p=0.04] and patients with a smoking history [p=0.000] (either past or current).

Table 2: Peri-Operative Outcomes

Peri-Operative Outcome Parameter	Mini-Sternotomy (n=96)	Full Sternotomy (n=73)	P-value
Operative time (mins.)	242 (+/- 48)	257.93 (+/- 58.94)	0.063
Cardio-pulmonary bypass time (mins.)	92.1 (+/- 16)	85.2 (+/- 19.66)	0.015
Cross-clamp time (mins.)	72.8 (+/- 14)	68.4 (+/- 13.35)	0.039
Ventilation time (hours)	15.29 (+/- 15)	19.29 (+/- 10.9)	0.002
Length of hospital stay (days)	11 (+/- 10.67)	19 (+/- 15.61)	0.000
Length of ICU stay (days)	3.09 (+/- 7.02)	2.93 (+/- 4.32)	0.995
Intra-operative blood transfusions (units)	0.26 (+/- 1)	0.57 (+/- 1.43)	0.067
Post-operative blood transfusions (units)	0.7 (+/- 1)	0.8 (+/- 1.29)	0.592

The mini-sternotomy group showed a statistically significantly reduced overall length of hospital stay and ventilation time. Although both intra- and post- operative transfusion requirements were lower in the mini-sternotomy group, this was not statistically significant. However, cross-clamp and cardio-pulmonary bypass time were significantly longer in the mini-sternotomy group versus the full sternotomy cohort. This is likely due to the initial technical challenges with the introduction of a new, more intricate procedure and has been demonstrated in the literature [9]. AVR via mini-sternotomy is associated with a steep learning curve due to the initial technical challenges of the procedure [10]. Although these prolonged times have been associated with increased numbers of complications in previous studies [11], they did not appear to increase the incidence of major post-operative adverse events in the cohort studied. Interestingly, overall operative time was longer in the full sternotomy group compared to the mini-sternotomy group, even with longer cross-clamp and cardio-pulmonary bypass times in the latter.

Table 3: Post-Operative Outcomes

Post-Operative Outcome Parameter	Mini-Sternotomy (n=96)	Full Sternotomy (n=73)	P-value
Stroke	1	1	0.845
Myocardial Infarction	0	1	0.432
Re-do Sternotomy	5	4	0.938
Sternal Wound Infection	2	0	0.506
Paravalvular leak	1	2	0.408
Acute Kidney Injury	0	2	0.185
Arrhythmias	25	23	0.435
Pulmonary Embolism	0	0	1
Deep Vein Thrombosis	0	1	0.432
Prolonged Use of Inotropes	18	15	0.77

Similar numbers of post-operative complications were observed between the two groups (Table 3). There was a higher number of patients suffering from arrythmias, prolonged use of inotropes and sternal wound infection in the mini-sternotomy group. However, none of these differences were determined to be statistically significant. There was a small number of patients in the full sternotomy group who experienced acute kidney injuries and deep vein thromboses, while there was no such complications in the mini-sternotomy group, but this again was not statistically significant.

Table 4: Post-Operative Outcomes

Mortality Parameter	Mini-Sternotomy (n=96)	Full Sternotomy (n=73)	P-value
Peri-operative mortality	0	0	1
30-day mortality	0	3	0.787
90-day mortality	0	0	1
1-year mortality	2	0	0.554
3-year mortality	3	2	0.811

No statistically significant differences were found when examining peri-operative, 30-day and 90-day mortality between the two groups (Table 4). The difference between 1-year and 3-year mortality between the two cohorts was also not determined to be statistically significant.

Discussion

SUMMARY OF MAIN FINDINGS

- Patients were very well matched in terms of baseline characteristics. These include age and sex, along with the prevalence of co-morbidities, such as hypertension, hyperlipidaemia and coronary artery disease. However, the mini-sternotomy group showed a significantly higher mean BMI [p=0.003] compared to the full sternotomy cohort and there was a much higher prevalence of diabetes mellitus [p=0.04] and a smoking history [p=0.00] in the mini-sternotomy group.
- There were some interesting findings noted on comparison of peri-operative outcomes. The mini-sternotomy group showed a significantly shorter ventilation time [p=0.022] and length of overall hospital stay [p=0.000]. This group also demonstrated a shorter operative time, but this was not statistically significant [p=0.063]. Although these are some positive results, the mini-sternotomy cohort did show statistically significantly longer cross-clamp [p=0.039] and cardio-pulmonary bypass times [p=0.015]. However, these prolonged times have been shown in the literature [7], and also did not appear to increase the incidence of post-operative complications.
- There were similar numbers of post-operative outcomes and complications between the two groups, such as stroke, myocardial infarctions and arrhythmias. None of these differences were determined to be statistically significant.
- There were no in-hospital mortalities in either group and there were similar numbers of deaths between both cohorts at 30 days, 90 days, 1 year and 3 years.

STRENGTHS AND LIMITATIONS OF THE STUDY

- Strengths:
- All data collected was readily accessible in the PATS centralised database. This allowed quick and efficient data collection without the need to review old patient charts individually.
- This study, and retrospective reviews generally are often much more cost- and time- effective compared to other study designs as the data already exists. Patients did not need to be recruited for participation and questionnaires did not need to be distributed. No follow-up was required in this study either.
- This study allowed for the analysis of a multitude of different variables. This meant that the relationship between a wide range of exposures and outcomes could be measured.
- There were no ethical concerns with this study. Consent was not required as this was a retrospective review that did not necessitate communication with patients. The study did not require an intervention either, again avoiding ethical concerns.
- Weaknesses:
- This study was performed in a single centre only (Cork University Hospital), which means that there is limited generalizability as it is difficult to determine if the population studied is representative of all patients both nationally and internationally undergoing AVR via mini- or full sternotomy.
- Selection bias is a weakness of a retrospective review like this. Since the data collected was from pre-existing records, the study population may not be representative of the general population.
- Inability to perform propensity-matching is a potential weakness. It was not performed as there was an insufficient sample size. However, both cohorts were already well matched in terms of baseline characteristics, decreasing the possibility of confounding.
- Missing data may be an issue with retrospective reviews. Existing databases, like the PATS database, occasionally have missing or incomplete data within individual patient records, which can lead to inaccurate results or false conclusions. Only a small number of patients in our study were missing some data.

EXISTING LITERATURE

Previous retrospective studies published support the findings of this study. A 2022 study entitled "Comparison Between Mini-Sternotomy and Full Sternotomy for Aortic Valve Replacement: A 10-Year Retrospective Study" found that AVR via mini-sternotomy was a safe alternative to full sternotomy, in the cohort studied, with a reduction in length of both hospital and ICU stay observed

[12]. Although, a prolonged ICU stay was not found in our study, prolonged cardio-pulmonary bypass and cross-clamp times were seen in both studies and were an expected result. A randomized controlled trial published in 2021 compared the two approaches and used the proportion of patients who received post-operative red blood cell transfusions as the primary outcome [13]. While it was found that mini-sternotomy reduced chest drain losses, it did not reduce red-cell transfusions [13]. This is in line with our study as although post-operative transfusion requirements were lower in the mini-sternotomy group, this was not statistically significant. This paper also demonstrated longer cardio-pulmonary bypass and cross-clamp times [13]. "Efficacy of Aortic Valve Replacement through Full Sternotomy and Minimal Invasion (Ministernotomy)" displayed some interesting results [14]. It found significantly longer bypass and cross-clamp times in the mini-sternotomy group, however it demonstrated shorter ventilation, shorter length of hospital stay and also better cosmetic results [14]. The conclusion then proposed AVR via mini-sternotomy as perhaps a better approach than full sternotomy [14]. Further investigation would be required to make this claim in our study. A comparative study published in 2015 further supported the results of our study. It found a shorter ventilation time, shorter length of hospital stay and reduced blood transfusions in the mini-sternotomy group [15]. Although, interestingly, it found shorter bypass and cross-clamp times in the mini-sternotomy group [15]. Perhaps, this was due to a high level of surgical skill and a substantial amount of time spent performing the procedure. Again, this study confirmed clinical benefits of the technique, similar to our study, without an increased incidence of post-operative complications [15].

IMPLICATIONS FOR FUTURE RESEARCH OR CLINICAL PRACTICE

This study is a follow-on from the paper entitled titled "Aortic Valve Replacement via Mini-Sternotomy: Results of a Single Centre Analysis", which was published in the 4th Edition of the UCC Student Medical Journal [8]. Like this paper, this is the first such study in an Irish hospital context and increases both the national and also international knowledge database surrounding this under-utilized minimally-invasive surgical technique. It is hoped that publication of this paper will further highlight and strengthen AVR via mini-sternotomy as a safe alternative to the 'gold standard' approach and prompt surgeons to learn the procedure and ultimately, perform on their own patients. It is also hoped that this study will act as a catalyst for others to research not just mini-sternotomy, but other minimally-invasive approaches to AVR both nationally and internationally.

Conclusions

The aim of the study was to demonstrate AVR via mini-sternotomy as a safe alternative to the full sternotomy approach, in the cohort studied. This was achieved through a retrospective database review of patients who underwent both procedures, in Cork University Hospital, between September 2016 and December 2022. Data for the 169 patients included in the study was analysed using STATA software. The results are presented in this paper and provide information surrounding patient demographics, such as the prevalence of co-morbidities, along with peri- and post-operative outcomes for patients, such as length of hospital stay and incidence of major adverse events. We demonstrated similar numbers of complications between the two groups. The mini-sternotomy group showed a significantly shorter length of hospital stay and also significantly shorter ventilation times. However, the mini-sternotomy technique requires greater surgical expertise as demonstrated by prolonged cross-clamp and cardio-pulmonary bypass times. The findings provide additional information surrounding this poorly-researched minimally-invasive surgical technique and increase both the national and international knowledge database. This is the first study of its kind in an Irish hospital context.

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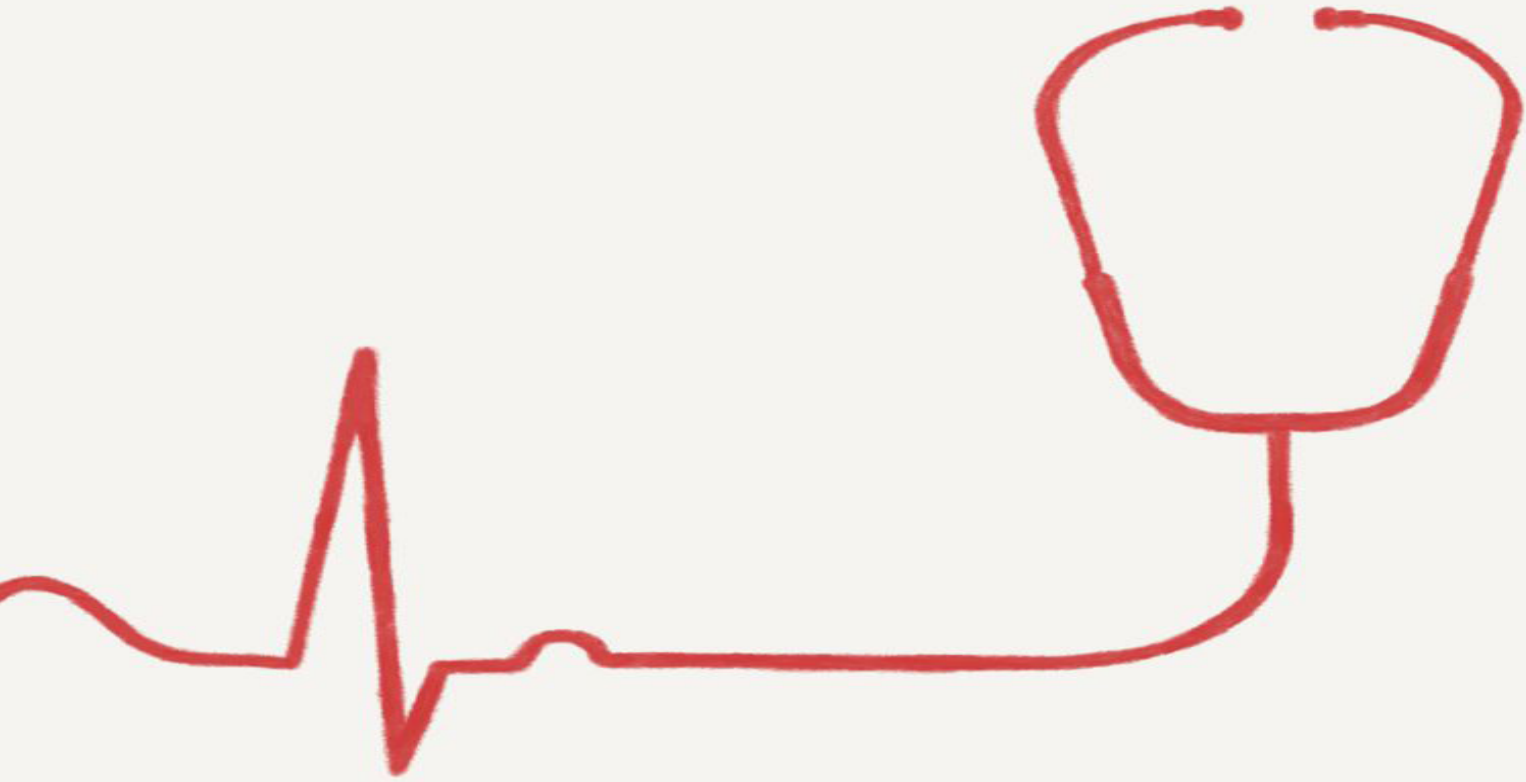

Indications and Quality of Care of Warfarin at King Abdulaziz Hospital, Al Ahsa

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Abstract

INTRODUCTION: The anticoagulation effect of warfarin is monitored through two laboratory tests: PT and INR. The quality of warfarin control in patients is assessed by calculating the TTR using INR values. However, there are only a few studies in Saudi Arabia that have investigated INR control in patients receiving warfarin.

METHODS: Demographical data, indications for anticoagulation, and INR values were extracted from electronic medical records of patients on warfarin therapy between November 1, 2020, and October 31, 2021. The TTR for each patient was calculated using the Rosendaal method.

RESULTS: A total of 88 patients were included in this study, comprising 29 males and 59 females. The indications for anticoagulation were categorised into four groups: 'Mechanical Valve' (28 patients), 'Atrial Fibrillation' (14 patients), 'Mechanical Valve + Atrial Fibrillation' (12 patients), and 'Other Indications' including haematological disorders (34 patients). The overall median TTR for the cohort was 58.73%. Patients with 'Mechanical Valves' had a median TTR of 62.50%, those with 'Atrial Fibrillation' had a median TTR of 50.18%, patients with 'Mechanical Valve + Atrial Fibrillation' had a median TTR of 54.61%, and patients with 'Other Indications' had a median TTR of 55.11%. The differences in TTR between these groups were not statistically significant ($p = 0.101$).

CONCLUSION: The INR control for patients taking warfarin was suboptimal, with a median TTR below the recommended threshold of 60%. This underscores the need for further studies to explore and improve the management of warfarin in patients.

LIST OF ABBREVIATIONS: PT: Prothrombin Time, INT: International Normalised Ratio, TTR: Time in Therapeutic Range, WHO: World Health Organisation, & DOAC: Direct Oral Anticoagulant

Introduction

Warfarin is an anticoagulant widely employed in the prevention and management of venous thromboembolism, myocardial infarction, and atrial fibrillation 1. It achieves its effect by inhibiting the synthesis of vitamin K-dependent clotting factors, thereby diminishing the blood's ability to form clots 1.

The anticoagulant effect of warfarin is monitored using two laboratory tests: PT and the INR 2. PT quantifies the time, measured in seconds, required for plasma to clot after the addition of thromboplastin to the patient's plasma sample 3. The INR, standardised by the WHO, represents the ratio of the patient's prothrombin time to a control prothrombin time, adjusted using an international reference thromboplastin reagent 3. In most clinical scenarios, the target INR range is set between 2 and 3, although specific circumstances may necessitate alternative target ranges 2.

The quality of anticoagulation control in patients on warfarin therapy is assessed using the INR values to calculate the TTR 4. TTR refers to the proportion of time during which a patient's INR remains within the target range, typically between 2 and 3, as previously noted 2. According to the 2017 Thrombosis Canada Guidelines, adequate INR control is generally defined as a TTR exceeding 60% 5. Suboptimal TTR has been associated with an increased risk of both thromboembolic events and major bleeding, highlighting the critical importance of maintaining effective anticoagulation control 5.

Limited studies in Saudi Arabia have evaluated the quality of warfarin therapy among patients receiving the medication for various indications 6, 7, 8, 9, 10. One such study reported that

patients spent less than half of their TTR within the target INR range. This suboptimal TTR underscores the necessity to enhance service quality and address factors influencing TTR outcomes 6.

This study aimed to optimise the management of warfarin therapy in patients treated for various indications at King Abdul-Aziz Hospital in Al Ahsa, Saudi Arabia. The primary objective was to identify the indications for warfarin use among adult patients aged 18 years and older over the past 12 months. The secondary objective was to evaluate the quality of warfarin control in this population by calculating the TTR for each patient.

King Abdul-Aziz Hospital, located in Al Ahsa, Saudi Arabia, is a tertiary care centre. This study aims to contribute valuable data on the quality of anticoagulation control in patients prescribed warfarin for various indications, providing insights that could benefit Saudi Arabia, the Middle East, and the global medical community.

Materials and Methods

STUDY DESIGN, PARTICIPANTS & STUDY ETHICS

This study was a retrospective review of all adult patients receiving warfarin therapy at King Abdul-Aziz Hospital from November 1, 2020, to October 31, 2021. It specifically focused on adult patients aged 18 years and older at the time of treatment, who were treated with warfarin at the hospital in Al Ahsa, Saudi Arabia.

The medical record numbers of eligible patients were retrieved from the anticoagulation clinic's electronically maintained database at the hospital.

Ethical approval for the study was obtained from the Institutional Review Board at King Abdul-Aziz Hospital on October 25, 2021, under registration number H-01-R-005.

STUDY MEASURES, PROCEDURES & DATA ANALYSIS

The electronic medical records of all eligible patients were reviewed to extract data on patient characteristics, including age, age at the start of warfarin therapy, and sex, as well as the indications for warfarin use and the quality of warfarin control, as measured by INR. The indications for warfarin use were classified into four groups: (1) patients receiving warfarin due to mechanical valve replacement, (2) patients receiving warfarin due to atrial fibrillation, (3) patients receiving warfarin due to a combination of mechanical valve replacement and atrial fibrillation, and (4) patients receiving warfarin for indications other than mechanical valve replacement or atrial fibrillation.

The TTR was calculated using the Rosendaal method, which considers the time interval between consecutive INR measurements and the variations in INR values 11.

The data were analysed using the Kruskal-Wallis test to compare the TTR across the different indications for warfarin. Data analysis was performed using IBM SPSS Statistics software, version 28.0.1.1. Statistical significance was assessed with a threshold p-value of less than 0.05.

Results

DEMOGRAPHICAL INFORMATION

Among the 88 patients receiving warfarin at our institution, the median age at the start of warfarin therapy was 43 years (range: 19–80), with a predominantly female cohort, comprising 67% of the total population, as illustrated in Figure 1. Male patients had a median age of 49 years, while female patients had a median age of 41 years. However, the age range for female patients was broader, spanning from 19 to 80 years, compared to 20 to 75 years for male patients. The age distribution of the cohort at the start of warfarin therapy is summarised in Table 1.

Table 1 *Age Distribution at Start of Warfarin Therapy*

	Number of Patients	Median Age	Minimum Age	Maximum Age	Standard Deviation (Age)
Male	29	49	20	75	14.7
Female	59	41	19	80	13.4
All Patients	88	43	19	80	14.0

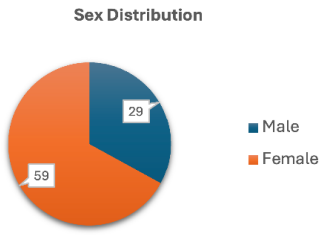

Figure 1

TTR FINDINGS

Among the patients included in this study, 28 were receiving warfarin due to mechanical valve replacement, 14 were treated with warfarin for atrial fibrillation, 12 were treated with warfarin for both mechanical valve replacement and atrial fibrillation, and the remaining 34 were prescribed warfarin for indications other than mechanical valve replacement and atrial fibrillation such as haematological disorders including Protein S deficiency, Protein C deficiency, Systemic Lupus Erythematosus, and others. The distribution of warfarin indications is summarised in Figure 2.

Table 2 presents the TTR values for patients receiving warfarin based on their indication group. The minimum TTR across all groups was 20.69%, while the maximum TTR reached 86.84%. The mean TTR was highest in patients with mechanical valves (58.93%) and lowest in those with atrial fibrillation (52.36%). Similarly, the median TTR was also highest among patients with mechanical valves (62.50%) and lowest for those with atrial fibrillation (50.18%). For the total cohort, the mean TTR was 55.79%, and the median TTR was 58.73%.

STATISTICAL ANALYSIS

The Kruskal-Wallis test, used to compare the TTR across all four groups, yielded a p-value of 0.101, indicating no statistically significant differences among the groups.

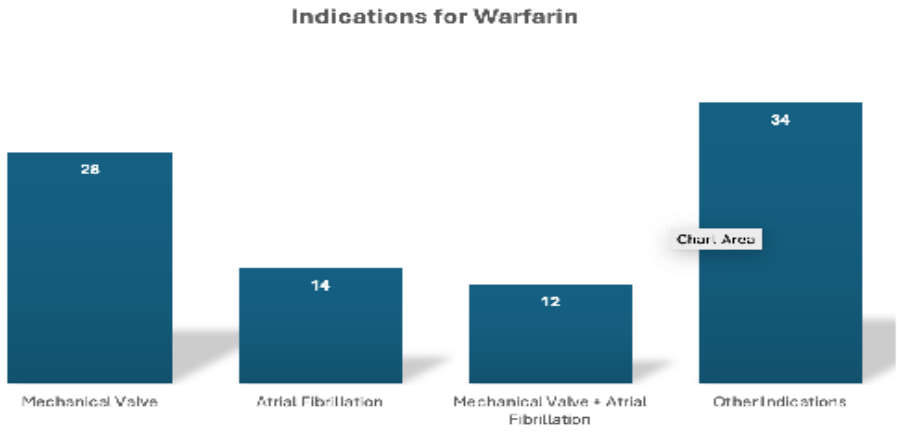

Figure 2

Table 2 *TTR for Patients Receiving Warfarin*

	Minimum TTR	Maximum TTR	Mean TTR	Median TTR
Mechanical Valve	20.69%	79.05%	58.93%	62.50%
Atrial Fibrillation	39.29%	66.44%	52.36%	50.18%
Mechanical Valve + Atrial Fibrillation	34.53%	78.74%	54.58%	54.61%
Other Indications	30.95%	86.84%	55.05%	55.11%
Total	20.69%	86.84%	55.79%	58.73%

Discussion

This study offers valuable insights into the indications for and quality of warfarin control at King Abdulaziz Hospital, categorising patients by indication into four distinct groups: mechanical valve replacement, atrial fibrillation, mechanical valve replacement combined with atrial fibrillation, and other indications.

The TTR has become the most widely accepted and validated method for assessing anticoagulation control and predicting adverse events 12. The overall median TTR for the cohort was 58.73%, falling short of the recommended threshold of 60% for adequate anticoagulation control 5. Among the groups, patients with mechanical valves demonstrated the highest median TTR at 62.50%, surpassing the threshold, whereas the atrial fibrillation group had the lowest median TTR at 50.18%.

The findings highlight variability in TTR control based on the indication for warfarin use, with patients treated for mechanical valves achieving relatively better outcomes. This may be due to structured follow-up care often associated with mechanical valve management. However, the median TTR for all groups, except mechanical valves, remained below the recommended threshold, indicating suboptimal anticoagulation control. The group with atrial fibrillation had particularly low TTR values, potentially reflecting challenges such as irregular follow-up, adherence issues, or the inherent difficulty in managing anticoagulation in this population.

The Kruskal-Wallis test, used to compare the TTR across all four groups, yielded a p-value of 0.101, indicating no statistically significant differences among the groups. However, the overall median TTR for the cohort (58.73%) was more favourable than a similar study conducted in Saudi Arabia, which reported a median TTR of 52% 6. This suggests that while anticoagulation control at King Abdul-Aziz Hospital is suboptimal, it compares relatively well to other regional findings, reflecting potential differences in patient care approaches or population characteristics.

Improving anticoagulation control in this setting requires multifaceted interventions, including improved patient education, regular INR monitoring, and leveraging alternative therapies such as DOACs for eligible non-mechanical valve replacement patients. Additionally, ensuring access to anticoagulation clinics and structured follow-up programs may help address the observed disparities.

A key strength of this study is its comprehensive analysis conducted over an extended period. However, there are some limitations. First, as a single-centre retrospective study, the findings should be validated in an independent prospective cohort. Second, while this study suggests satisfactory INR control at King Abdul-Aziz Hospital, further stratification is needed for patients with indications other than mechanical valve replacement and atrial fibrillation.

Conclusion

The median TTR among patients on warfarin at King Abdul-Aziz Hospital was suboptimal at 58.73% during this limited time, with only patients in the mechanical valve group achieving a median TTR exceeding 60%. These findings underscore the need for targeted interventions to enhance anticoagulation management. Key strategies include improving patient education, increasing access to INR monitoring services, and considering alternative therapies such as DOACs when appropriate. Further studies are necessary to explore the barriers to achieving optimal TTR and to develop tailored solutions for improving warfarin management in this population.

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Diversity and Cultural Differences in Preeclampsia Beliefs and Management Practices: A Narrative Review

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Abstract

Preeclampsia is a hypertensive disorder that poses significant risks to maternal and fetal health. Effective management is critical to minimize maternal and fetal morbidity and mortality. Preeclampsia management practices vary widely across different cultural and geographical settings. This review explores the cultural differences in the beliefs and management of preeclampsia. High income countries benefit from well-established diagnostic and treatment protocols however, low- and middle-income countries face challenges related to lack of knowledge, resources, and access to care. Cultural factors, including the use of traditional medicine and the influence of family decisions on healthcare, often delay receiving appropriate medical care. In some cultures, traditional birth attendants and community health workers are the primary antenatal carers, but their approaches can conflict with modern medical practices. By understanding these cultural influences in healthcare, it can improve maternal health outcomes. This review emphasizes the need for culturally competent healthcare, improved training for healthcare workers, and the implementation of standardized protocols globally. By integrating culturally competent practices into maternal healthcare systems and addressing the structural barriers to care, healthcare providers can optimize the diagnosis, treatment, and long-term outcomes for women with preeclampsia.

Introduction

Preeclampsia is the development of new onset hypertension that occurs during pregnancy, typically after the 20th week, with accompanying proteinuria1. If not properly managed, it can lead to severe maternal complications including organ damage, eclampsia, as well as fetal complications including fetal growth restrictions, and fetal demise1. Patients with preeclampsia typically have complaints of a new-onset headache that is not responsive to medication and may be accompanied by visual disturbances2. Other symptoms one may present with are nausea, vomiting, or epigastric pain1. In addition to new onset hypertension and proteinuria on urinalysis, assessments for preeclampsia includes an elevated protein to creatinine ratio and abnormal liver and kidney function tests1. Early interventions are crucial to mitigate complications however, practices surrounding management differ across cultures.

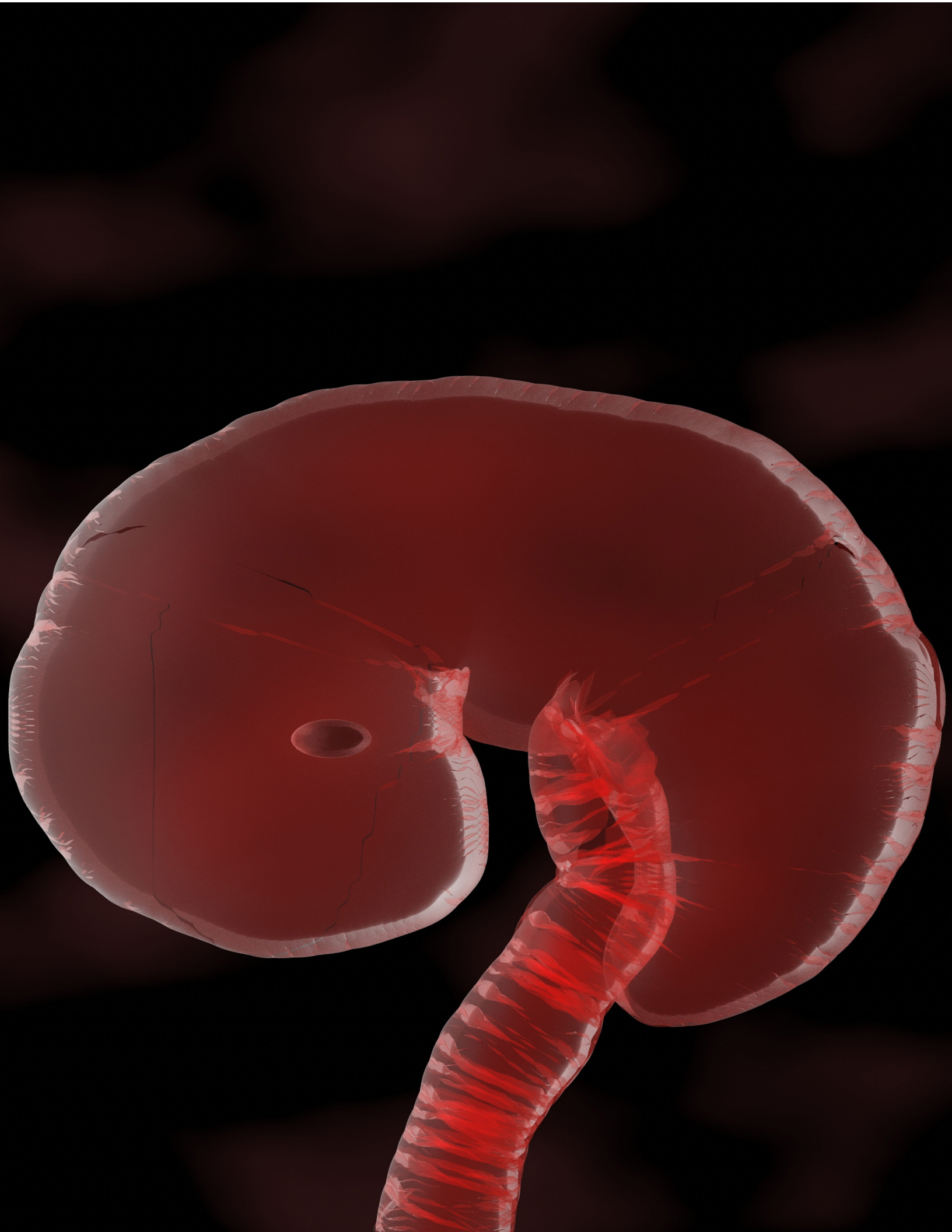
Different management practices can be attributed to a combination of healthcare system disparities, and socio-economic conditions, that influence healthcare-seeking behaviours and medical practices3,4. High-income countries have well-established clinical guidelines and the availability of advanced diagnostic tools which generally lead to early detection and intervention5. Many middle- and low-income countries face challenges including limited access to healthcare services, and inadequate infrastructure3.

Cultural perceptions play a key role in preeclampsia management6,7. For instance, some cultures prefer traditional or alternative treatments over medical interventions, which can delay or prevent women from seeking appropriate care6,7. By understanding the cultural context of preeclampsia management, it can improve health outcomes in diverse and underserved populations. This review examines how cultural differences influence the management of preeclampsia and discusses potential strategies to overcome these challenges.

Methods

A literature search was performed in December 2024 using PubMed, Academic Search Complete, and Google Scholar journals. Search terms included “preeclampsia”, “cultural beliefs”, “traditional medicine”, “low-income” and “management practices”. Boolean operators combined variations of the terms for a comprehensive retrieval. Inclusion criteria included peer reviewed studies published up until December 1, 2024 in English that addressed preeclampsia beliefs or management across diverse cultural settings. Studies that were published in a non-English language, did not directly discuss preeclampsia views or management, and lacking clear methodology were excluded. Data extraction of the eligible studies included study location, design, attitudes and management of preeclampsia.

Many studies were observational, qualitative, or cross-sectional, limiting causal inferences. Sample sizes in several low-middle income countries were small, reducing generalizability.



Most evidence for herbal therapies stemmed from small pilot studies or anecdotal reports. Overall, evidence supporting traditional practices is weak due to heterogenous methodologies and absence of standardized outcome measures.

Health Beliefs and Practices with Cultural Influences

The National Institute for Clinical Excellence (NICE) made recommendations for the development of guidelines in assessing risk and created a schedule to monitor women in the community after 20 weeks of gestation8. The guidelines recommend assessment of preeclampsia at 16, 28, 34, 36, 38, 40 and 41 weeks for healthy women8. The guidelines are followed in Western societies where there is greater availability to diagnostic tools and better healthcare infrastructure1.

In many non-Western societies, traditional medicine is commonly used for managing preeclampsia6,8. The term traditional medicine describes alternative medicine practices developed by cultures over time, and often emphasize the balance in mental, physical, and spiritual health10,11.

In South Asian culture, the use of Traditional Birth Attendants (TBA)'s is prevalent where they assist in childbirth based on cultural practices of the communities they serve, traditional knowledge, and experience, rather than formal medical training4,5. This includes using herbal remedies, dietary adjustments to manage hypertension due to the belief it is more natural or safer5. There are also Lady Health Workers (LHW) that work in the community and provide basic healthcare services to women for their antenatal care5. In terms of the beliefs surrounding preeclampsia, many women are aware of high blood pressure developing during pregnancy but did not recognize it as a distinct medical condition5. It was commonly believed that stress and weakness were the primary causes of high blood pressure during pregnancy, and that it led to symptoms like headaches5. The understanding of high blood pressure was largely symptom-based rather than being grounded in actual measurements5.

In several areas of Africa, traditional medicine plays a significant role in maternal health care6. Traditional healers are common as primary health care workers for pregnant women to promote a healthy pregnancy and to ensure a normal birth6. Studies done in Nigeria have shown the prevalence of herbal remedy use ranges from 12-67% during pregnancy13. This is because many perceive it as being safer to take during pregnancy and more effective9,13. In Ghana, medical recommendations provided during pregnancy may contradict the religious and cultural beliefs10. Women rely on socially spread misleading pregnancy beliefs, since many women do not receive clinical education in pregnancy10.

Cultural attitudes toward healthcare providers influence behaviour in seeking care and can be demonstrated by many countries in the Middle East14. Decisions are made as a family about medical interventions which may delay the care the women receive, since members of the family may prioritize traditional solutions over medical management14.

Traditional Chinese Medicine (TCM) considers concepts of cause, diagnosis, and treatment11. TCM holds that during pregnancy, the majority of a mother's blood is directed to the placenta to nourish the developing baby, which can make other maternal organs such as the liver, spleen, and kidneys are more susceptible to damage11. Spasms in the arterioles were identified by TCM as being the pathophysiological mechanism of preeclampsia11. Herbal treatments which are taken or made from plants are believed to help manage preeclampsia by promoting vasodilation and enhancing blood circulation11.

Healthcare Infrastructure and Barriers to Resources

As mentioned earlier, the NICE guidelines for preeclampsia monitoring had recommendations about how often and when women should be monitored for preeclampsia8. This has been implemented in developed countries that have adequate resources1. However, this demanding schedule of hospital visits may not be feasible in low – or middle-income communities, where health systems are already overwhelmed, and patients often struggle to access healthcare due to financial constraints and distance barriers3,8,16. Non-attendance at antenatal visits is a significant risk factor for the development of preeclampsia, as it often leads to failure of prevention and inadequate management5, 13.

Studies have also found that in low- or middle- income countries, women are not regularly screened at their antenatal visits for hypertension due to limited knowledge from healthcare providers3,5. In many developing countries, delays in seeking care during obstetric emergencies are common13. These delays are frequently due to insufficient knowledge about when and where to seek help13. Additional factors including limited decision-making power among women, poverty, and rising healthcare costs exacerbate this issue13. Socio-demographic factors, including education levels and marital status as well as cultural beliefs surrounding maternal health also play a significant role in shaping health seeking behaviours4,14. Social determinants have been identified as contributing up to 27% of maternal deaths17. For

example, in rural areas of South Asia where healthcare access is limited and due to low health literacy, many pregnant women rely on information from older women, friends, and family members, rather than consulting healthcare professionals5,17. In addition, personal, societal, and structural barriers such as feelings of shame or fear of stigma can prevent women from discussing their pregnancies openly with doctors10,14.

Treatment Approaches

Management of preeclampsia focuses on blood pressure control and preventing seizures1. Earlier diagnosis and intervention are the most beneficial in preventing complications from developing1. Antihypertensive medications that do not have adverse effects on the fetus and adequately control blood pressure, include beta blockers such as intravenous labetalol, vasodilators such as intravenous hydralazine and oral calcium channel blockers such as nifedipine1. Prophylaxis management in preventing the development of eclampsia, includes intravenous magnesium sulfate or levetiracetam if magnesium sulfate in contraindicated1. If eclampsia develops, intravenous benzodiazepine medication is administered such as diazepam1.

In Pakistan, studies have found misconceptions among health care providers in administering magnesium sulfate including, overestimating the toxicity risks of magnesium sulfate and the need for women to be admitted in the intensive care unit5,18. Doctors in Pakistan did not appreciate the importance of giving magnesium sulfate to reduce the morbidity or mortality risk5. This is because the providers mentioned that it is relatively uncommon for women to have preeclampsia in Pakistan, despite it globally being the second-leading cause of maternal mortality5. Due to the low prevalence of preeclampsia, doctors report to lacking the confidence in dealing with these patients, leading to women being untreated when referred to other healthcare facilities5,1.

In the community where Pakistani women are most treated by Lady Health Workers, it is reported that some of these providers give medications that they have learnt from interacting with doctors who have treated women with preeclampsia such as methyl-dopa along with advising a low salt and low-fat diet5. Another traditional birth attendant gave traditional medicine including Phakki which is an herbal remedy for constipation to manage blood pressure however, there is no rigorous evidence of antihypertensive efficacy5.

As mentioned earlier, women in South Asia are more likely to treat symptoms rather than treating the hypertension such as self-medicating for headaches5. Occasionally, women in rural areas believed home remedies and spiritual treatments can be beneficial for managing preeclampsia such as 'reciting holy verses or drinking holy water and are perceived as safe15. However, delays in seeking medical care are common when symptoms escalate15.

The current South African management guidelines recommend Aspirin as a preventative treatment for women at high risk of developing hypertension without proteinuria during pregnancy19. However, the use of herbal remedies in prevention and treatment are still commonly used in South Africa10. Healthcare providers including physicians and pharmacists have also been shown to lack the knowledge of the efficacy and safety profile of most herbal medications available in the country10. Hence, most healthcare providers do not recommend herbal products to their patients10. Many of the herbal remedies are self-prescribed based on the patient's own cultural beliefs and knowledge8. In addition, despite a caesarean section being the ideal mode of delivery when there is complication in preeclampsia, many cultures including African and Asian cultures have a strong preference for vaginal deliveries10.

In Chinese culture, Chinese herbal medicines are very popular and are reported to effective in treating preeclampsia11. Herbal remedies such as Chuan Xiong Qin which is known as ligustrazine that has been extracted from rhizome of Sichuan lovage, is thought to encourage vasodilation and increase blood flow11. Chuan Xiong Qin is commonly used in treating women with preeclampsia in China, where it is also suspected to cause a sustained reduction in blood pressure11. Other herbal medicines such as Dan Shen (saliva miltiorrhiza) is thought to dilate small arteries11. Yi Mu Cao (herba leonuri), Chuan Xiong and Dan Shen are thought to also decrease platelet aggregation11. These are some of the several Chinese herbal remedies that are prescribed for preeclamptic women and are taken based on the different symptoms they are experiencing11. Risks of traditional Chinese herbal medicine include herb-drug interactions. More research is needed in order to understand the safety profile and interactions of these herbal medicines.

Discussion

Preeclampsia is a dangerous medical condition and obstetric emergency since there are many complications associated with it to the mother and fetus1. By managing the condition early on, the risk of developing complications reduces, hence the need for a standardized treatment approach. It is essential for cultural competency in healthcare to address these challenges. By training healthcare providers in cultural differences, they will be able to improve communication and engagement with patients.

The management of preeclampsia varies over the world

where it is influenced by access to resources, cultural beliefs, and health care systems8. This article demonstrated the difference in terms of beliefs and management between cultures, especially between high and low-income countries. In well developed countries, the medical approaches to preeclampsia management are established with guidelines and recommendations, whereas in resource poor areas, there is often a delay in diagnosis and treatment, which can lead to poor maternal outcomes16. In resource poor areas, nifedipine can be administered orally, as opposed to the requirement of intravenous access for other antihypertensives treated in pregnancy. Therefore, oral administration provides the possibility of administration in the community.

Most countries have a strong area in midwifery, including low- and middle-income countries5. There is great importance in educating midwives on recognizing obstetrical emergencies, as midwives are likely the only point of care women may receive16. In rural areas, health workers such as LHW should receive training on understanding the importance of preeclampsia and be able to recognize it and how to manage it. By implementing standardized protocols and improving the training of all healthcare workers in obstetrics, clinicians can become more confident in prescribing essential medications such as magnesium sulfate.

Future research should focus on rigorous evaluation of commonly used herbal remedies and conduct randomized placebo-controlled trials to assess safety, dosing and efficacy of widely used preparations, along with detecting any adverse events. To address the lack of consistent cross-country comparisons, studies that enroll pregnant women across diverse cultural settings to document management pathways, outcomes and cultural influences, is important for a clear comparison. Lastly, future research can look into developing and testing educational interventions with local religious and community leaders to address any misconceptions surrounding preeclampsia and its management, and promoting evidence-based practice. This can then be measured in changes of care-seeking behaviour and clinical outcomes.

Conclusion

Preeclampsia is one of the leading causes of maternal morbidity and mortality. Cultural differences play a significant role in the management of preeclampsia where it influences patient outcomes and medical practices. By adopting culturally competent approaches to maternal care and enhancing cultural sensitivity, it can improve access to maternal healthcare and the health outcomes for women with preeclampsia. By enhancing healthcare access and providing maternal education through community-based healthcare workers in rural and underserved areas, it can help bridge the gap in healthcare access and enhance preeclampsia management.

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Evaluating the Efficacy and Safety of MDMA for the Treatment of Posttraumatic Stress Disorder: A Systematic Review

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Abstract

BACKGROUND: Posttraumatic stress disorder (PTSD) affects approximately 5-7% of the population, with conventional treatments often proving inadequate for some patients. Recent studies suggest that methylenedioxymethamphetamine (MDMA) combined with psychotherapy may offer a novel therapeutic approach. This systematic review evaluates the efficacy and safety of MDMA-assisted psychotherapy for the treatment of PTSD in individuals with chronic, treatment-resistant forms of the disorder.

METHODS: A comprehensive search was conducted in PubMed, OVID, Scopus, Cochrane databases, and select reference lists for randomized controlled trials (RCTs) evaluating MDMA as a treatment for PTSD. Eligibility criteria included RCTs with participants with confirmed PTSD diagnoses using standardized clinical assessments.

RESULTS: In the RCT studies, there are significant reductions in PTSD symptoms ($p<0.05$) in those with MDMA-assisted psychotherapy compared to those with placebo and psychotherapy; dose-dependent improvements were observed in various measurements scales (specifically in CAPS-IV/CAPS-5 scores). Open-label trials further demonstrated improvements in PTSD symptoms when given MDMA-assisted therapy ($p<0.05$) and long-term analyses of studies demonstrated that effects of MDMA-assisted therapy were maintained for a minimum of 12 months post-intervention($p<0.05$). Adverse effects were transient and mild to moderate, including anxiety, headache, fatigue, muscle tension, and insomnia.

CONCLUSION: Extant data suggests that MDMA-assisted psychotherapy for PTSD demonstrates significant symptom reduction, with sustained efficacy up to 12 months post-treatment. Functional unblinding is a major methodological challenge, which makes it difficult to interpret the magnitude of the effect MDMA has in the treatment of treatment-resistant PTSD. Future research should refine methodologies and explore long-term safety and efficacy in diverse populations.

Introduction

Posttraumatic stress disorder (PTSD) is a mental disorder that occurs in approximately 5-7% of the population, with higher rates in women than in men (1). Individuals can develop PTSD post-experiencing/witnessing a traumatic event, and their symptoms include, but are not limited to, hypervigilance, increased startle response, avoidance of traumatic triggers, anxiety, depression, and sleep disturbances (2). Conventional treatment for PTSD consists of psychotherapy (e.g., trauma-focused psychotherapy) and/or pharmacotherapy, which consists of therapy and medications (1,2). Currently, selective serotonin reuptake inhibitors (SSRIs), specifically paroxetine and sertraline, are FDA-approved treatments for PTSD; other medications such as venlafaxine, a serotonin-norepinephrine reuptake inhibitors, are used to treat PTSD off-label (2). However, extant literature indicates that monoamine-based pharmacotherapy is suboptimal in facilitating fear extinction emotional processing (3). Exposure-based psychotherapy is efficacious in improving PTSD symptoms broadly; however, patient adherence is low and is not generally accessible and/or available (3).

Methylenedioxymethamphetamine(MDMA) modulates serotonin, dopamine, and norepinephrine signaling (4). MDMA primarily acts by increasing the synaptic release and blocking the reuptake of serotonin, which is associated with feelings of euphoria, increased sociability, and decreased anxiety (5). In addition to the effects on serotonin, MDMA also increases levels of dopamine and norepinephrine in the brain (4). These neurotransmitters are involved in regulating mood, motivation, and attention, and MDMA-induced synaptic release of dopamine and norepinephrine can contribute to the drug's effects of elevated mood, decreased fear, altered perception of surroundings, and impaired memory (4). The foregoing points

provide the impetus to investigate the efficacy of MDMA-assisted psychotherapy as an alternative and novel treatment for PTSD. Herein, we aim to conduct a systematic review to comprehensively evaluate published clinical trials investigating MDMA for the treatment of PTSD. Notably, we delimited our search to studies that investigated MDMA-assisted psychotherapy as previous studies have reported additional therapeutic benefits of psychotherapy when integrated with MDMA compared to standalone MDMA treatment (6).

Materials and Methods

ELIGIBILITY CRITERIA

Any clinical trial that evaluates MDMA-assisted psychotherapy as an adjuvant or standalone treatment for PTSD. Only English-language articles were included. Studies must have included participants with a confirmed diagnosis of PTSD based on standard clinical assessments or structural interviews (i.e. Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) and Sheehan Disability Scale (SDS)) were included. Studies were excluded if they 1) described unpublished data sets, case reports, crossover studies, and observational studies, 2) did not have a clinical assessment of PTSD, 3) did not have MDMA as the treatment intervention, and 4) were animal studies. Papers were further divided based on whether they were randomized controlled trials (RCTs), open-label trials, and follow-up studies. Qualitative analyses were conducted on RCTs, open-label trials, and follow-up studies.

SEARCH STRATEGY

MK, HC, and CC conducted a search on PubMed, OVID, Scopus, and Cochrane databases for English-language articles published between database inception to June 15 2024, using the following search string: ((“MDMA” OR “Methylenedioxymethamphetamine” OR “Ecstasy” OR “Molly”) AND (“PTSD” OR “Post-traumatic stress disorder” OR “Combat disorder” OR “Post-traumatic stress syndrome” OR “Trauma stress disorder”)). Subsequent searches through previous systematic reviews were conducted manually. Zotero was used to conduct screening and remove duplicate papers. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and checklist was used to assess the reliability of included studies and the reporting of study methods and results. The titles, abstracts, and full text of the studies were screened by 3 reviewers (MK, HC, and CC) independently based on the eligibility criteria. The consensus for papers to include was based on follow-up discussions.

DATA EXTRACTION AND MANAGEMENT

The data to be extracted from studies was predetermined and included sample size, ethnicity, gender, mean age, clinical presentation, type of MDMA and psychotherapy intervention, PTSD assessment, endpoints (primary and secondary), study design, Quality Rating Scheme for Studies and Other Evidence, and main study findings. Missing data was noted in the tables. Data extraction was performed independently by MK and AA, and later reviewed and confirmed by HC and CC.

ASSESSMENT OF BIASES

Study quality assessments (i.e. risk of bias) were performed by HF and MK. Study quality was assessed using the revised Cochrane risk-of-bias tool for randomized trials (RoB2 tool). All the RCTs involved in the quantitative assessment would be assessed according to the six domains that evaluated the risk of bias, including randomization process, deviation from the intended interventions, missing outcome data, measurement of the outcome, selection of the reported result and other biases.

Results

SEARCH RESULTS

A total of 3363 studies were identified from the search on PubMed, OVID, Scopus, and Cochrane databases and previous systematic reviews. There were 2704 studies remaining after 659 duplicates were removed, of which 2677 were excluded following title and abstract screening. 27 studies were assessed in the full-text evaluation stage, of which 1 was removed for being a symposium abstract and 3 were removed for reporting on data from original studies already being assessed. A total of 23 studies were included in this review - 8 studies were found to be follow-up/long-term follow-up studies, 5 studies were open-label studies, and 10 studies were original RCTs. See supplementary materials for the PRISMA flow diagram.

RISK OF BIAS IN STUDIES

The Cochrane risk of bias assessment is displayed in Table 4. All included studies had minimal biases except for Bouso et al. (2008) which included more significant biases in the domains: randomization process, measurement of the outcome, and selection of the reported result. This study was halted due to political pressures, the original objective of the paper was altered and the reported data was only recorded from 6 individuals with variable follow-up times (7).

STUDY CHARACTERISTICS AND EFFICACY OF MDMA IN RCTS

The total sample of all the included RCTs included in the quantitative analysis (k=10) consisted of 530 participants. 335 participants received an active dose of MDMA (between 75-125 mg +/- optional half-dose) and psychotherapy, and 215 participants received a placebo/control dose (between 0-40 mg) of MDMA and psychotherapy.

A summary of all the major factors of each RCT is displayed in Table 1. Some studies included pooled data from multiple studies (8,9) or were conducted over multiple sites (8,10,11). One study was halted prior to full completion (7). Mean sample ages ranged between 35-45 years. All participants presented with chronic, treatment-resistant PTSD with CAPS-IV/CAPS-5 scores greater than 50. Evaluation of PTSD was conducted with CAPS-IV/CAPS-5 for the majority of studies, except for one study (7). The study designs also differed, some were randomized, double-blind, dose-response trials (6,12), others were randomized, double-blind, controlled trials (7–11,13–15), and one paper was a prospective, double-blind, crossover-design study (14). Some studies further included a placebo run-in component where the participants were unblinded to treatment allocation following the collection of outcome variables and prior to open-label trials (6,8,9,12–15). All studies, except one (7), consisted of a primary endpoint of change in CAPS-IV/CAPS-5 score from baseline (prior to MDMA administration) to at least a month after the 2nd/3rd treatment session. The secondary endpoint of the studies included changes in other domains of psychopathology (eg. depression, sleep, alcohol consumption, etc.).

Across the included RCTs, reductions in PTSD-related symptom severity scores were dose-dependent. The foregoing studies reported significant improvements in PTSD symptoms across various measurement scales, primarily focusing on CAPS-IV scores. In Mithoefer et al. (2018), the mean change in CAPS-IV total scores was –11.4 (standard deviation (SD) 12.7) for the 30 mg group, –58.3 (SD 9.8) for the 75 mg group, and –44.3 (SD 28.7) for the 125 mg group, with the 75 mg and 125 mg MDMA groups showing significantly greater improvements than the 30 mg group (6). Mithoefer et al. (2019) reported that the active group (75–125 mg) had a mean decrease of –30.4 (standard error (SE) 3.20) in CAPS-IV scores compared to the control group's drop of –10.5 (SE 4.46) ($P < 0.0001$) (8).

Mithoefer et al. (2019) reported a greater improvement in BDI-II scores in the active group, with a mean change of –12.4 (SE 1.84) versus –6.5 (SE 2.69) in the control group ($P = 0.053$) (8). Ponte et al. (2021) highlighted significant treatment effects in CAPS-IV scores (active group mean change –34.0, SD 26.46; control group mean change –12.4, SD 16.38, $p = .003$) and Pittsburgh Sleep Quality Index (PSQI) scores (mean change –3.53, SD 5.03, active group vs. 0.56, SD 3.05, control group, $p = .003$) (9). Mithoefer et al. (2011) found that the active group had a mean CAPS-IV change of -53.7 points compared to -20.5 points in the placebo group, with a higher response rate in the active group (14). In Ot'alora et al. (2018), it was observed that active dose groups had mean CAPS-IV reductions of –26.3 (SD 29.5) for 125 mg, –24.4 (SD 24.2) for 100 mg, and –11.5 (SD 21.2) for 40 mg (12). Oehen et al. (2013) demonstrated that the full-dose group, given 125mg of MDMA, had significantly greater reductions in CAPS-IV scores by -15.6 (18.1) compared to the active placebo group which only reduced by -3.2 (15.3); this study unlike others did not find a significant reduction in CAPS-IV score in the placebo group (15). The group that received full-dose MDMA also had reductions in CAPS scores (35% reduction) at the 12-month follow-up assessments compared to baseline. Changes in Posttraumatic Diagnostic Scale (PDS) scores were -8.6 (13.0) in the full MDMA dose group and +7.3 (6.2) in the active placebo group, an increases in the PDS score in the placebo group was not expected (15).

Mitchell et al. (2021) reported a mean change in CAPS-5 scores of -24.4 (SD 11.6) for the MDMA group and -13.9 (SD 11.5) for the placebo group, indicating the superior efficacy of MDMA-assisted therapy (10). Mitchell et al. (2023) revealed a mean CAPS-5 score change of -23.7 for the MDMA group compared to -14.7 for the placebo group (effect size 0.91, $p < 0.001$) (13). Bouso et al. (2008) suggested a dose-response relationship in PTSD symptom reduction, with low doses of MDMA showing promising efficacy compared to placebo, despite the study's small sample size of 6 individuals (7). Finally, Nicholas et al. (2022) reported that the MDMA treatment group demonstrated a greater improvement in Alcohol Use Disorders Identification Test (AUDIT) scores from baseline to study termination, although changes were not statistically significant (11).

STUDY CHARACTERISTICS AND EFFICACY OF MDMA IN OPEN-LABEL TRIALS

The specific information for each study is displayed in Table 2. Ching et al. (2022) reported mean adjusted changes in CAPS-IV scores in the MDMA group of –25.65 (SD 14.54) for Black, Indigenous, and people of color (BIPOC) participants and –25.95 (SD 13.16) for non-Hispanic White participants (16). In the Placebo group, the mean changes were –16.77 (SD 10.08) for BIPOC participants and –9.59 (SD 11.96) for non-Hispanic White/Caucasian participants (16). There was a greater mean improvement between treatment and placebo groups among Caucasian participants compared to BIPOC participants (16). This suggests that ethnicity may modulate MDMA treatment efficacy in persons with PTSD. Consistent with the foregoing trends, Jardim et al. (2021) observed that MDMA-assisted psychotherapy significantly reduced CAPS-IV scores, with all reductions greater than 30%, indicating clinically significant improvement (17). The baseline scores of 90, 78, and 72 dropped to 61, 27, and 8 at the primary endpoint, with reductions of 29, 51, and 64 points, respectively (Jardim et al., 2021). Wang et al. (2021) demonstrated a significant mean change in CAPS-5 scores of –29.89 (SD 13.45) at the primary endpoint, indicating an improvement in PTSD symptoms ($p < .0001$) (18). At the primary endpoint (Visit 19), 91.89% of participants had a clinically meaningful reduction (10 points or greater) in their CAPS-5 scores, and 75.68% no longer met PTSD criteria ($p < .001$) (18). Lewis et al. (2023) reported that in a sub-study sample, the MDMA group had a baseline CAPS-5 score of 44.2 (SD 6.16) and a final score of 17.94 (SD 14.28), with a mean

difference of 26.26 (SD 15.55) (19). The placebo group had a baseline score of 46.6 (SD 7.03) and a final score of 30.77 (SD 11.02), with a mean difference of 15.83 (SD 13.07) (19).

In addition, MDMA-assisted psychotherapy was evaluated for its effects on secondary outcomes. Specifically, MDMA treatment was significantly associated with both lower Beck Depression Inventory (BDI-II) scores and higher Post-Traumatic Growth Inventory and Global Assessment of Functioning scores (17). Christie et al. (2022) focused on chronic pain rather than PTSD (20). Significant reductions in Chronic Pain Grade Scale (CPGS) subscales for pain intensity and disability scores among participants in the highest pain cluster, and for pain intensity in the medium pain cluster post-treatment were reported, however, the small sample size limited the power of the analysis (20).

STUDY CHARACTERISTICS AND EFFICACY OF MDMA IN FOLLOW-UP STUDIES

The specific information for each study is displayed in Table 3. Jerome et al. (2020) reported a mean change in CAPS-IV total scores from baseline to the primary endpoint of -44.8 (SE 2.82) (21). Scores continued to decrease from the primary endpoint to the long-term follow-up of 12 months by -5.2 (SE 2.29) (21). The percentage of participants who no longer met PTSD criteria increased from 56.0% at treatment exit to 67.0% at long-term follow-up (LTFU) (21). Comparatively, Mithoefer et al. (2013) found no statistically significant change in mean CAPS-IV and IES-R scores at LTFU for the 16 study completers compared to their 2-month (short-term) mean scores (22). Barone et al. (2019) reported that all participants experienced lasting personal benefits and enhanced quality of life beyond quantifiable symptom reduction (23). Fifteen participants (79%) had prolonged therapeutic efficacy from MDMA therapy, but there were no changes in PTSD symptom severity at the one-year follow-up compared to the end of the study (23).

A secondary analysis of the study conducted by Wang et al. (2021), done by Godes et al. (2023), indicated that all seven participants reported a range of benefits during and at the end of treatment, including tolerance of conflict, processing trauma, positive emotions, interpersonal connections, and connection (24). The change in CAPS-5 from baseline to termination, after approximately 1 month after the last treatment session, for these seven participants was -34 (SD 8) (24). Van Der Kolk et al. (2024) considered data from the original study done by Mitchell et al. (2023) (25). They found significant improvements in alexithymia, self-compassion, and most IASC factors compared to the placebo group. Higher baseline alexithymia was associated with greater reductions in PTSD symptoms, with a notable decrease in CAPS-5 scores (-16.16; 95% CI: -28.80, -7.52) (25).

Zeifman et al. (2024) reported that therapeutic alliance, the relationship between a healthcare professional and a patient, significantly increased the explained variance in post-treatment PTSD severity, with session 4 adding 29% and session 9 adding 24% (26). Self-reported PTSD severity showed that therapeutic alliance at session 4 explained an additional 40% of the variance, and at session 9 it explained an additional 26% of the variance (26). Corey et al. (2016) did a further analysis of the study conducted by Mithoefer et al. (2011) and investigated the correlation between utterances, which were when patients initiated topics that were empathic, entactic, or ensuic, during psychotherapy sessions and change in their CAPS-IV score (27). Corey et al. (2016) observed that the MDMA treatment group produced significantly more utterances than the placebo group, and a higher number of scored utterances correlated with a lower post-treatment CAPS-IV score ($r = -0.506$, $p = 0.023$, $n = 20$) (27). The correlation remained significant when utterances were grouped into "many" (nine or more) and "few" (six or fewer) categories ($r = -0.596$, $p = 0.006$, $n = 20$) (27). The sub-group utterances correlated with an overall change in CAPS-IV scores ($r = 0.513$, $p = 0.021$, $n = 20$) (27). Wagner et al. (2017) observed a significant interaction between changes in Openness and CAPS-IV scores, with those showing the greatest increase in Openness also demonstrating the greatest decreases in PTSD symptom severity (28).

ADVERSE EFFECTS DUE TO MDMA THERAPY

The main adverse effects that were noted to have occurred or been contributed to by MDMA therapy compared to placebo in the RCTs are displayed in Table 5. The adverse effects did not significantly vary based on the dose of active MDMA individuals received (6). Most adverse events were transient with rates decreasing 7-10 days after treatment cessation (6,8,14). MDMA therapy did not increase in suicidal behavior, participants with pre-existing suicidal thoughts would report thoughts of suicide after sessions but this was not increased from baseline (10,12,13).

Discussion

Our synthesis of extant literature of MDMA-assisted psychotherapy in the treatment of PTSD demonstrates a significant reduction in PTSD psychopathology as measured by CAPS-5 score up to 1-month post-treatment as well as sustained efficacy with maintenance treatment for 12-months. All of the included RCTs were double-blinded until the end of the second/third treatment session, and all the RCTs (even if a placebo run-in trial component was incorporated) reported similar levels of efficacy of MDMA for treatment-resistant PTSD, through various measurement modalities. The RCTs demonstrated that MDMA-assisted therapy reduced PTSD symptoms more than placebo with psychotherapy ($p<0.05$) and did so in a dose-dependent manner. Open-label trials further demonstrated the benefits of MDMA-assisted therapy in

reducing PTSD symptoms. Moreover, Follow-up/Long-term trials observed that the beneficial effects of MDMA-assisted therapy on symptoms of PTSD are maintained for a minimum of 12 months post-treatment ($p<0.05$).

Our results reported herein align with previous reviews and research into this field (29). The implications of this review indicate that MDMA may be a useful therapy for treatment-resistant PTSD only after first and second-line treatments have been exhausted.

Notwithstanding the observed benefit, there are several methodological limitations that affect the interpretation of our findings. An overarching limitation is functional unblinding in the clinical trials investigating MDMA. Functional unblinding refers to the lack of concealment of group assignment as a consequence of the subjective effects of the intervention (6,8,10,12–15). In addition to participants knowing they were assigned to MDMA in most cases, they also reported a high level of confidence that they were taking this treatment. As MDMA has been combined with psychotherapy, it is not possible to discern the relative therapeutic contribution of MDMA. The aforementioned methodologic concerns have also been identified by an FDA Advisory Panel who were evaluating the efficacy of MDMA for PTSD (30).

Further limitations include the differences in the studies when it comes to the different dosages of MDMA used (the doses for the control groups ranged between 0-40 mg and in the treatment groups 70-180 mg), the number of therapy sessions (2 or 3 sessions) and the study design utilized (some studies included a placebo run-in trial). Other limitations mentioned from the RCT trials include: small sample sizes, study populations mainly consisting of Caucasians, study populations consisting predominantly of one gender, studies including a cross-over component at the end without a control group which prevented long-term results from being assessed, participants being on other psychotropic medications during trials, including subjective measures (questionnaire) for symptom measurement, evaluation of symptoms after a short assessment period and lack of long-term follow-up (although some studies are currently undergoing long-term follow-up), disclusion of those with imminent suicide risk, and placebo group drop-outs.

The implications of our analysis suggest that MDMA may have therapeutic benefits in the treatment of PTSD when combined with psychotherapy. There is, however inadequate, long-term data as well as suboptimal evaluation of the safety of this agent. The methodological aspects discussed above also hinder the ability to accurately evaluate the relative contribution of MDMA.

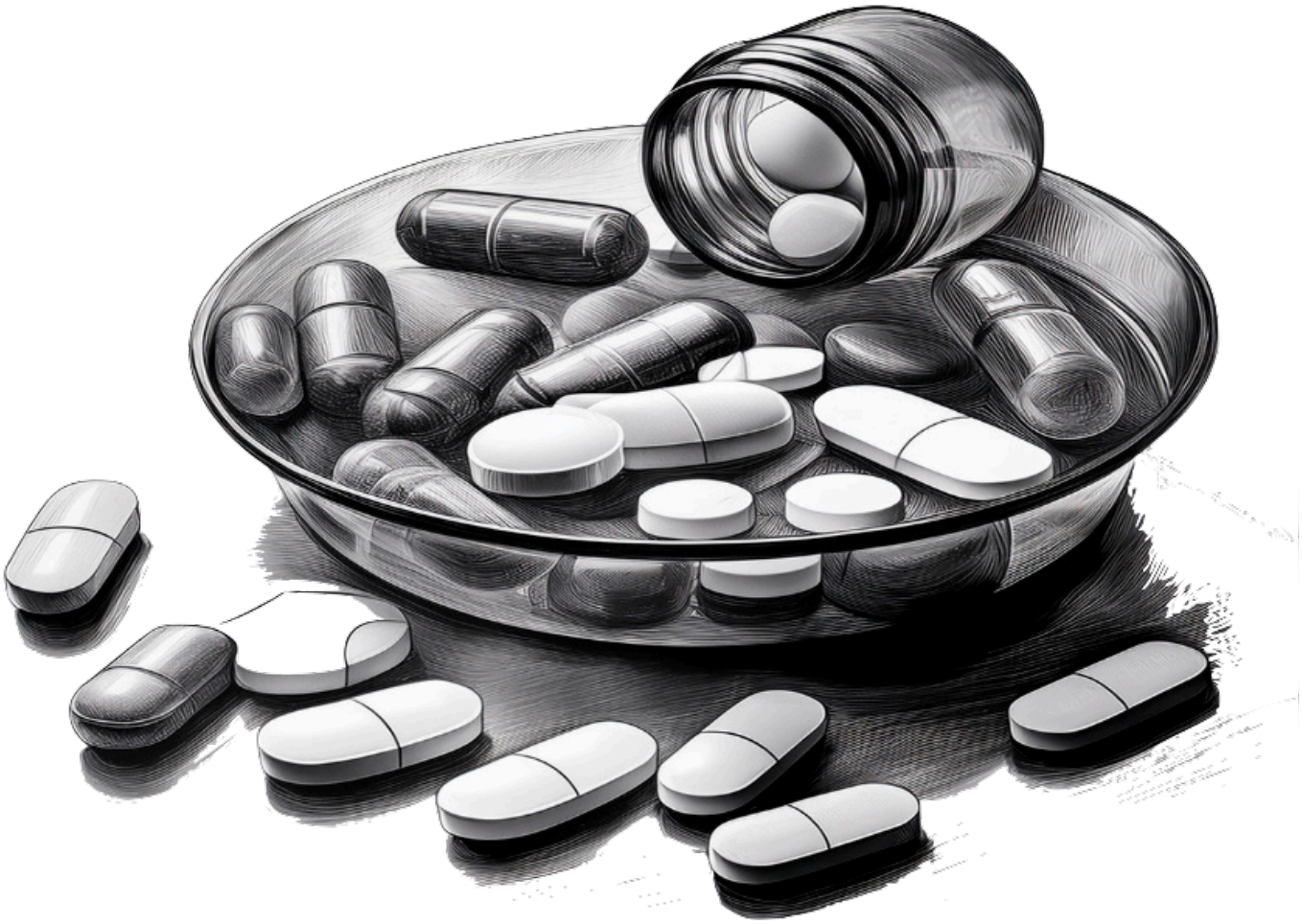

Table 1: RCTs

Source	Sample Size	Ethnicity	Gender	Mean Age (SD)	Clinical Presentation	Intervention	PTSD Assessment	Endpoints - Primary (P), Secondary (S)	Study Design	Quality Rating	Findings
Mithoefer et al. 2018.	26	85% Caucasian; 8% Hispanic/Latino; 4% Native American; 4% Mixed	73% M, 26% F	37.2 (10.3)	Chronic, treatment-resistant PTSD resulting from traumatic experiences during their service as military veterans, firefighters, or police officers	2× 8h MDMA-assisted psychotherapy sessions (30, 75, 125 mg) + optional half-dose; 2–3 weekly integration sessions; open-label phase followed	CAPS-IV	P: CAPS-5 change at 1 mo post-2nd session. S: BDI-II, PSQI, PTGI, NEO-PI-R, DES-II, GAF	RCT, double-blind, dose-response + open-label	1	Mean CAPS-IV change: –11.4 (30 mg), –58.3 (75 mg, p=0.0005), –44.3 (125 mg, p=0.004). 75 & 125 mg > 30 mg; no diff. 75 vs 125. Secondary outcomes also improved. Placebo group improved after open-label high-dose.
Mithoefer et al. 2019	105	87.6% White; 2.9% Hispanic; 1.9% Native Am.; 1.9% Middle Eastern; 5.7% Other	42% M, 58% F	40.5 (10.6)	Chronic, treatment-resistant PTSD related to various causes (e.g., combat, abuse, assault, accidents)	2× 8h MDMA-assisted sessions (0–40 mg vs 75–125 mg) + optional half-dose; 2–3 integration sessions; open-label crossover	CAPS-IV	P: CAPS-5 change after 2nd session. S: BDI-II change; CAPS-5 at 2 mo post-blind	6 RCTs, double-blind + open-label	1	Active (75–125 mg) group improved more than control (Δ –30.4 vs –10.5; p<0.0001). BDI-II change trended toward significance. Further gains in open-label active dose.
Nicholas et al. 2022	82	80% White; 6% Asian; 4% Native Am.; 2% Black; 7% Mixed	35% M, 65% F	41.42 (12.22)	Severe PTSD + alcohol/substance use disorder	3× 8h MDMA (80→120 mg + optional half-dose) or placebo; 3× 90-min integration sessions	CAPS-5	P: AUDIT, DUDIT change. S: CAPS-5, SDS, BDI-II, C-SSRS	RCT, double-blind	1	MDMA group had greater AUDIT improvement vs placebo (p=0.0436, g=0.45). No sig. DUDIT difference. MDMA also reduced PTSD severity, functional impairment, and depression.
Ponte et al. 2021	63	85% Caucasian; 4% Hispanic; 2% Native Am.; 9% Other	54% M, 46% F	40.80 (11.49)	Chronic, treatment resistant PTSD	3× 8h MDMA (75–125 mg) or placebo (0–40 mg) + half-dose option; integration; open-label	CAPS-IV	P: PSQI & CAPS-5 at 1–2 mo. S: 12-mo follow-up	RCT, double-blind + open-label	1	Significant treatment effect of change in CAPS scores (–34.0 vs –12.4; p=0.003) and PSQI (–3.53 vs +0.56; p=0.003). More pts in the active group improved ≥3 PSQI points than in the control group (53% vs 13%). Open-label active doses gave further benefit
Mitchell JM, Bogenschutz M, et al. 2021	90	77% White; 9% Mixed; 8% Asian; 3% Native Am.; 2% African	34% M, 66% F	41.0 (11.9)	Severe PTSD incl. commorbidities such as dissociation, depression, substance use, childhood trauma	3× 8h MDMA (80→120 mg + half-dose) or placebo; 3 integration sessions	CAPS-5	P: CAPS-5 at 8 wks post-3rd session. S: SDS at 18 wks	RCT, double-blind	1	CAPS-5 reduction greater with MDMA (–24.4 vs –13.9). SDS also improved (–3.1 vs –2.0). Equally effective in comorbid subtypes.
Mithoefer et al. 2011	20		15% M, 85% F	40.4 (7.2)	Chronic, treatment-resistant PTSD.	2× 8h MDMA (125 mg + half-dose) or placebo; integration; open-label	CAPS-IV	P: CAPS-5 at 2 mo post-2nd session. S: IES-R, SCL-90-R	RCT, double-blind + open-label	1	Active MDMA reduced CAPS more than placebo (–53.7 vs –20.5; p=0.015) and had a higher response rate (83% vs 25%). Open-label higher doses gave further benefit.
Mitchell JM, Ot'alora GM, et al. 2023	104	66% White; 11% Asian; 8% Black; 2% Native Am.; 1% Hawaiian; 12% Other	33% M, 67% F	39.1 (10.3)	Moderate–severe PTSD (mean CAPS 52.5)	3× 8h MDMA (80→120 mg + half-dose) or placebo; integration (CBT, psychodynamic, mindfulness)	CAPS-5	P: CAPS-5 change at 18 wks. S: SDS change at 18 wks	RCT, double-blind + open-label	1	CAPS-5 improvement greater with MDMA (–23.7 vs –14.7; ES=0.91, p<0.001). 67% vs 32% no longer met PTSD criteria (p=0.02). Also improved depression/anxiety.
Ot'alora et al. 2018	28	93% White; 4% Hispanic; 4% Native Am.	32% M, 68% F	42.0 (12.9)	Chronic, treatment resistant PTSD	2× 8h MDMA (40, 100, 125 mg) + half-dose option; placebo; integration; open-label	CAPS-IV	P: CAPS-5 at 1 mo. S: BDI-II, DES-II, PSQI at 1 mo	RCT, double-blind, dose-response + open-label	1	CAPS reduction larger in active dose groups (–26.3 at 125 mg; –24.4 at 100 mg; –11.5 at 40 mg). Placebo improved in open-label; 12-mo follow-up confirmed 125 mg benefit. 40 mg ≈ placebo. Well tolerated.
Oehen et al. 2013	12	Not reported	17% M, 83% F	41.4 (11.2)	Chronic, treatment-resistant PTSD (CAPS ≥50)	3× 8h MDMA (125 mg) or active placebo (25 mg) + half-dose; integration; open-label	CAPS-IV	P: CAPS at 3 wks post-2nd & 3rd sessions. S: PDS at same timepoints	RCT, double-blind + open-label	1	CAPS reduction greater with MDMA (–15.6 vs –3.2). 12-mo follow-up: 35% CAPS reduction in full-dose MDMA group. PDS improved with MDMA (–8.6 vs +7.3). 50% full-dose pts had clinical response.
Bouso et al. 2008	6	Not reported (All participants from Madrid)	100% F	35.6 (7.3)	Chronic, treatment resistent PTSD	6× 6h MDMA (50–75 mg) or placebo; pre/post non-drug therapy	SSPTSD, STAI, BDI, HAM-D, MSF III, Maladjustment Scale, RSE	P: safety of low-dose MDMA. S: alliance, side effects, subjective & physiological effects	Planned RCT (underpowered)	1	Low-dose MDMA were psychologically and physiologically safe. Signs of efficacy in reducing PTSD symptomatology: 75 mg > 50 mg > placebo. Too small for significance; larger/higher-dose studies needed.

Abbreviations: AUDIT = Alcohol Use Disorders IdentificationTest, BDI-II = Beck's Depression Inventory, C-SSRS = Columbia Suicide Severity Rating Scale, DES-II = Dissociative Experiences Scale, DUDIT = Drug Use Disorders Identifiction Test, GAF = Global Assessment of Functioning, HAM-D = Hamilton Rating Scale, IES-R = Impact of Event Scale, MSF II = Modified Fear Scale, NEO-PI-R = Revised NEO Personaility Inventory, PDS = Posttraumatic Diagnostic Scale, PSQI = Pittsburg Sleep Quality Index, PTGI = Posttraumatic Grwoth Inventory, RSE = Rosenberg Self-Esteem Scale, SCL-90-R = Symptom Checklist - 90 - Revised, SDS = Sheehan Disability Scale, SSSPTSD = Severity of Symptoms Scale for Post-traumatic Stress Disorder, STAI = State-Trait Anxiety Inventory

Table 2: OPEN LABEL TRIALS

Source	Sample Size	Race/Ethnicity Breakdown	Gender Breakdown	Mean Age (SD)	Clinical Presentation	MDMA and Psychotherapy Intervention	PTSD Assessment	Study Design	Quality Rating Scheme for Studies and Other Evidence	Study Findings
Ching et al. 2022	127	2.9% Native American, 9.5% Asian, 2.9% African American, 11.7% Hispanic, 65.7% White, and 7.3% Multiracial.	37% M, 63% F	40.0 (12.6)	Chronic, treatment resistant PTSD (CAPS-5 score 35<)	3x MDMA sessions and 9x integrative sessions. 80/40 mg for the first dosing session and increased to 120/60 mg for the second and third dosing sessions.	CAPS-IV	Secondary analysis of two Phase 2 open-label trials and a Phase 3 randomized, blinded placebo-controlled trial	2	In the MDMA-assisted psychotherapy group, both BIPOC and non-Hispanic White participants showed similar reductions in PTSD symptoms, with recovery rates of 65% and 71%, respectively. In contrast, the placebo group showed smaller improvements overall, though BIPOC participants trended toward greater symptom reduction than non-Hispanic White participants (p = 0.054), with recovery rates of 29% and 26%.
Wang et al. 2021	37	2.7% Native American, 16.2% Asian, 2.7% African American, 73.0% White, and 5.4% Mixed.	40.5% M, 59.5% F	35.6 (10.8)	Chronic, treatment resistant PTSD with associated suicidal ideation in most	3x sessions, with each session being 3 to 5 weeks apart. Initially were given 80 mg MDMA initial + 40 mg MDMA supplemental (United States) or 100 mg MDMA initial + 50 mg MDMA supplemental (Canada). The second and third experimental sessions utilized slightly higher divided doses of 120 mg MDMA + 60 mg MDMA (United States) and 125 mg MDMA + 62.5 mg MDMA (Canada).	CAPS-5	Multisite Open-Label Clinical Trial of MDMA-Assisted Therapy for Severe PTSD, conducted across 14 investigative sites	2	At the primary endpoint, there was a significant mean change in CAPS-5 scores of −29.89 (13.45), p < .0001 indicating improvement in PTSD symptoms. At the primary endpoint (Visit 19), 91.89% (n = 34) of all participants had a clinically meaningful reduction (10 points or greater) in their CAPS-5 scores (p < .0001) and 75.68% (n = 28) no longer met PTSD criteria (p < .001).
Jardim et al. 2021	3	Not provided	33% M, 64% F	40.3 (5.0)	Severe, chronic, treatment resistent PTSD resulting from sexual abuse	Multidisciplinary Association for Psychedelic Studies (MAPS) protocol consisting of 15 weekly therapy sessions: 3x with orally administered MDMA with concurrent psychotherapy and music, spaced approximately 1 month apart. Initially was 75 mg, and 75 or 125 mg in the second and third sessions. A supplemental dose of 50% the initial dose was offered 90 to 120 minutes after the initial dose.	CAPS-IV	The study design was an open-label pilot study.	2	The study found that MDMA-assisted psychotherapy could become a viable treatment in Brazil for PTSD. CAPS-IV reductions were 29, 51, and 64 points (z = 1.604, r = 0.924 and p = 0.108) for the participants, which is indicative of clinically significant improvement. Secondary outcomes included lower BDI-II scores, higher PTGI, and GAF scores.
Christie et al. 2022	32	72% Caucasian, 3% Native American, 16% Asian, 3% African American, 6% Mixed	41% M, 59% F	37.5 (IQR = 30.5–46.5).	Severe, chronic, treatment resistent PTSD and chronic pain.	3x experimental sessions 3 to 5 weeks apart. Initially given 80 mg MDMA, followed by a supplemental dose of 40 mg MDMA. In the second and/or third study drug sessions, participants received an increased dose of 120 mg MDMA followed by a supplemental dose of 60 mg MDMA.	CAPS-5	Exploratory data analysis of a subset of participants who completed chronic pain measures drawn from a Phase 2 open-label study	2	Significant reductions in CPGS subscales for pain intensity and disability score, and overall CPGS severity grade were observed among participants in the highest pain cluster (n = 9, p < 0.05), and for pain intensity in the medium pain cluster (n = 11, p < 0.05) post- vs. pre-treatment. However, the small sample size limited the power of the analysis, and further research with a larger sample in randomized, controlled trials is needed to investigate the role of MDMA-assisted psychotherapy as a treatment for chronic pain.
Lewis et al. 2023	23	Not provided	48% M, 52% F	42.4 (12.7)	Severe, chronic, treatment-resistent PTSD	Each experimental session was followed by three 90-min integration sessions that were spaced ~1 week apart to allow the participant to understand and incorporate their experience. The first integration session always occurred on the morning after the experimental session, and the remaining two integration sessions occurred over the following 3–4 weeks. Participants received a single divided dose of 80–180 mg MDMA or placebo.	CAPS-5	Pilot sub-study to the parent clinical trial (Phase 3). The study utilized a subsample of patients from the larger clinical trial who consented to participate in the epigenetic sub-study.	2	Baseline mean difference CAPS-V score in the MDMA group of the sub-study sample was 44.2 (6.16), and the final CAPS-V score was 26.26 (15.55). Baseline mean difference CAPS-V score in the placebo group of the sub-study sample was 46.6 (7.03), and the final CAPS-V score was 15.83 (13.07). Changes in DNA methylation of the NR3C1 and FKBP5 gene were associated with treatment response, with greater methylation changes associated with greater reductions in PTSD symptoms.

Abbreviations: BDI-II = Beck's Depression Inventory, BIPOC = Black, Indigenous, People of Colour, CPGS = Chronic Pain Grade Scale, C-SSRS = Columbia Suicide Severity Rating Scale, DES-II = Dissociative Experiences Scale, GAF = Global Assessment of Functioning, PSQI = Pittsburg Sleep Quality Index, PTGI = Posttraumatic Growth Inventory

Table 3: LONG TERM FOLLOW-UP AND ADDITIONAL FOLLOW-UP OF RCTS OF MDMA AND PTSD

Source	Sample Size	Ethnicity Breakdown	Gender Breakdown	Mean Age (SD)	Clinical Presentation	PTSD Assessment	Endpoints of Interest (Primary, Secondary)	Study Design	Quality Rating Scheme for Studies and Other Evidence	Study Findings	Extra Notes
Wagner et al. 2017	20	100% Caucasian	15% M, 85% F	40.4 (7.2)	Crime or war-related, chronic, treatment-resistent PTSD (CAPS score of ≥ 50)	CAPS-IV	**P**: NEO PI-R 2 months after blinded trials ended. **S**: CAPS score 2 months after blinded trials ended.	Randomized, double-blind, controlled trial followed by open-label sessions.	1	At two-month follow-up, increases in Openness and decreases in Neuroticism were significantly associated with greater reductions in PTSD symptoms, though the effect of MDMA-assisted therapy on CAPS scores was not significant after adjusting for Openness. Long-term data showed lasting changes in both traits, with Openness increasing and Neuroticism decreasing in the MDMA group, and an inverse correlation observed between the two traits.	Additional analysis and Follow-up of **Mithoefer et al. 2011**
Jerome et al. 2020	105	87.6% White, 2.9% Hispanic/Latino, 1.9% Native American, 1.9% Middle Eastern, and 5.7% Other/Biracial.	42% M, 58% F	40.5 (10.6)	Chronic, treatment resistent PTSD lasting more than 6 months with a CAPS-IV score of ≥50 (except for one study with ≥60). Average duration of PTSD at baseline was 214.1 months.	CAPS-IV	**P**: CAPS-5 score **S**: LTFU Questionnaire at least 12 months after final MDMA session, C-SSRS (n=68) at all visits	Long-term follow-up of six randomized, blinded with open-label crossover sessions, phase 2 trials	1	The mean change in the CAPS-IV total score from baseline to the primary endpoint was - 44.8 (SE 2.82). Scores continued to decrease from primary endpoint to LTFU by -5.2 (SE 2.29). Number of participants who no longer met PTSD criteria increased from treatment exit (56.0%) to LTFU (67.0%).	Follow-up of **Mithoefer et al. 2019**
Mithoefer et al. 2013	20	100% Caucasian.	15% M, 85% F	40.4 (7.2)	Chronic, treatment-resistant PTSD mostly resulting from sexual abuse or assault	CAPS-IV	**P**: CAPS-5 and IES-R score from 2-month follow-up to LTFU. **S**: LTFU questionnaire 10–74 months after final MDMA session	Long-term follow-up Randomized, double-blinded with open-label cross-over sessions	1	This study focused on long term follow up (LFTU) of participants in the original treatment group. No statistically significant change in mean CAPS-5 and IES-R scores at LTFU for the 16 study completers compared to 2-month (short-term) mean scores.	Follow-up of **Mithoefer et al. 2011**
Corey et al. 2016	20	100% Caucasian	15% M, 85% F	40.4 (7.2)	Chronic, treatment-resistant PTSD from crime or combat with CAPS score of ≥50.	CAPS-IV	**S**: Correlation between number of scored utterances and bimodal categories with overall change in CAPS score.	Additional evaluation of randomized, double-blind study	1	Participants in the MDMA group produced significantly more scored utterances, which were associated with lower posttreatment CAPS scores and greater overall symptom reduction when categorized as “many” vs. “few.” While the total number of utterances alone did not correlate with overall CAPS score change, the bimodal grouping showed a significant relationship with symptom improvement.	Additional analysis of **Mithoefer et al. 2011**
Barone et al. 2019	19	90% Caucasian, 5% Caucasian/Native American, 5% Native American	68% M, 32% F	24-56 years old. Original study reported Mean (SD) = 37.2 (10.3)	The study included military veterans, police, and firefighter with treatment-resistant PTSD with a CAPS-IV total score of ≥50.	CAPS-IV	**P**: Interpretative Phenomenological Analysis to semi-structured interviews to examine the meaning participants make of their experiences in the trial.	Long-term follow-up qualitative study of semi-structured interviews conducted one year post ending of randomized, double-blind, crossover phase 2 clinical trial.	1	All participants reported experiencing lasting personal benefits and enhanced quality of life that extend beyond quantifiable symptom reduction. 15 participants (79%) showed clinically significant decreases in PTSD symptoms at one-year follow-up (>30% reduction in CAPS-IV total scores from baseline), with average change in CAPS-IV total scores of 68% from baseline.	Follow-up of **Mithoefer et al. 2018**
Godes et al. 2023	7	85.7% Caucasian and 14.3% Asian	57.1% M, 42.9% F	36.3 (9.19)	The study included participants who met criteria for severe PTSD. Baseline CAPS-5 of 46.28 (5.72). Cause of PTSD development trauma (71.4%), veteran (28.6%), combat exposure (28.6%), and multiple trauma (57.1%).	CAPS-5	**P**: Interpretative phenomenological analysis. **S**: Change in CAPS-5 from baseline to termination.	Part of phase 2 open-label clinical trial - qualitative analysis of patients' experiences.	2	All seven participants reported experiencing a range of benefits during the course and at the end of the treatment. Coding scheme included tolerance of conflict, processing trauma, positive emotions, interpersonal, and connection. Change in CAPS-5 from baseline to termination for 7 participants −34 (8).	Additional analysis of **Wang et al. 2021**
van der Kolk et al. 2024	90	3.3% American Indian, 7.8% Asian, 2.2% African American, 76.7 % Caucasian, 8.9& Mixed, 1.1% Unknown	34.4% M, 65.6% F	41.0 (11.9)	Chronic (over 6 monthes) and severe PTSD (CAPS score of > 35)	CAPS-5, IASC, TAS-20, SCS	**P**: changes IASC score, TAS-20 score, and SCS score 2 monthes afetr last experimental session from baseline	Analysis of a multi-site double-blind, placebo-controlled randomized Phase 3 study	1	Reductions in alexithymia were significant, and participants with higher baseline alexithymia showed greater PTSD symptom improvement, especially in the MDMA-assisted therapy group. Notably, those with high alexithymia receiving MDMA had significantly larger reductions in CAPS-5 scores compared to the placebo group, suggesting MDMA therapy may enhance emotional regulation and self-awareness.	Additional analysis of **Mitchell JM, Ot'alora GM, et al. 2023**
Zeifman et al. 2024	22	100% Caucasian	28.7% M, 77.3% F	57.5 (7.5)	Chronic, treatment resistent, and severe/moderate PTSD (CAPS score of > 50)	WAI score for therapeutic alliance, CAPS-IV, IES-R	**P**: relationship between thearpautic alliance and cliniation and patient obsevred changes in PTSD symptoms.	Double-blind randomised controlled phase (Phase 1) followed by an open-label phase (Phase 2)	1	Therapeutic alliance at sessions 4 and 9 significantly predicted reductions in both clinician- and self-reported PTSD severity, explaining up to 40% of the variance in outcomes. No gender differences were found in alliance scores, and Bayesian analyses confirmed the strong predictive value of therapeutic alliance in MDMA-assisted therapy.	Additional analysis of **Mithoefer et al. 2011**

Abbreviations: C-SSRS = Columbia Suicide Severity Rating Scale, IASC = Inventroy of Altered Self Capacities, IES-R = Impact of Event Scale, LTFU = Long term follow-up, NEO-PI-R = Revised NEO Personaility Inventory, SCS = Self-Compassion Scale, TAS-20 = Toronto Alexithymia Scale, WAI = Work Ability Index

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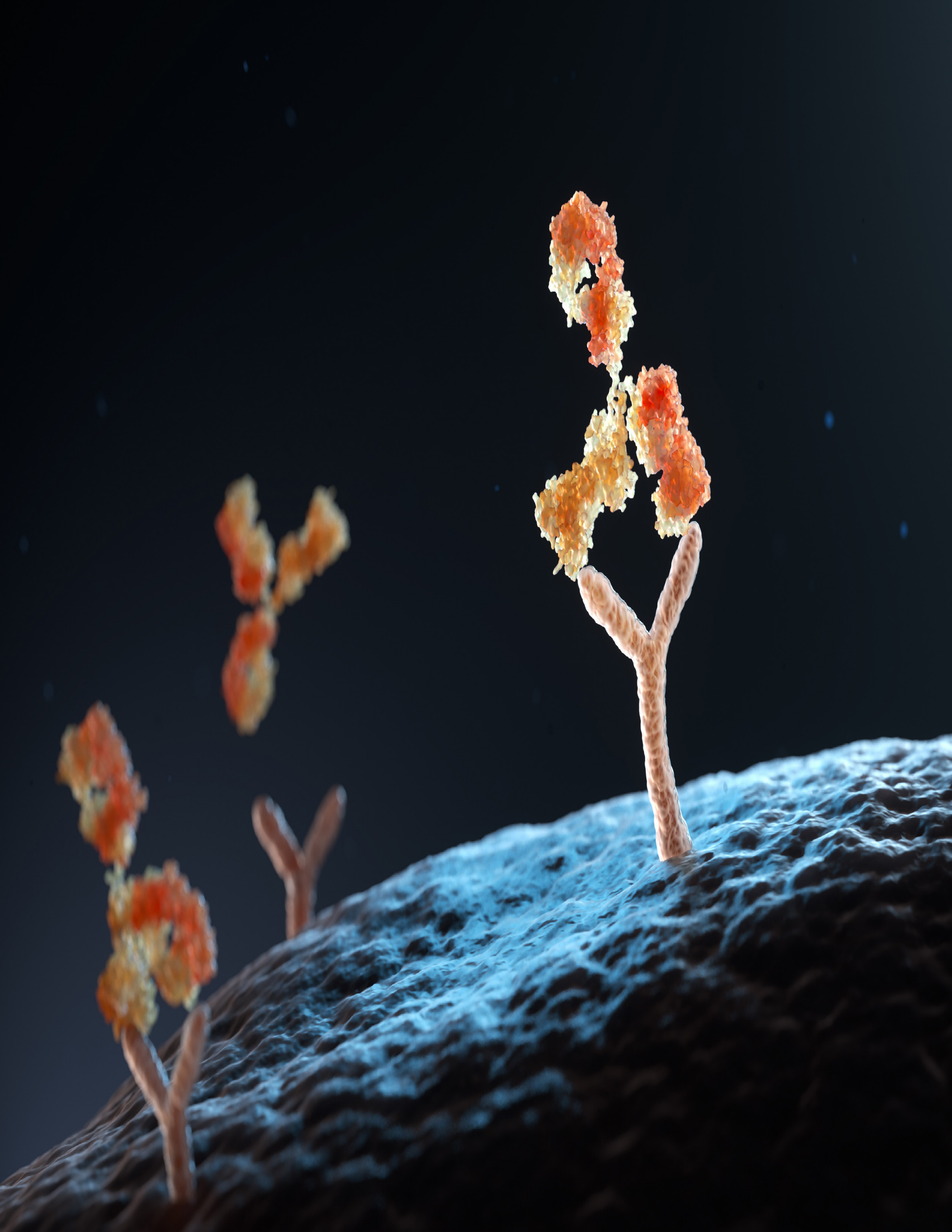

LTBP2: Bridging our Understanding of the Extracellular Matrix in Cardiac Fibrosis

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Abstract

Cardiac fibrosis is a major driver of heart failure, with complex mechanisms contributing to its progression. One such contributor is latent transforming growth factor-beta binding protein-2 (LTBP2), a protein significantly upregulated in fibrotic tissues. Unlike other TGF-β binding proteins, LTBP2 does not bind to TGF-β, and its role in cardiac fibrosis is largely unexplored. However, LTBP2 is involved in key profibrotic signaling pathways, including those related to TGF-β1, fibroblast growth factor-2 (FGF-2), caspase-3, and NF-κB, all of which are potential therapeutic targets. Notably, NF-κB signaling activation through LTBP2 in fibrosis progression has been identified as an important mechanism that warrants further investigation. In addition to its role in cell signaling, LTBP2 is essential for maintaining microfibril structural integrity, particularly in tissues such as the eye. However, the specific contributions of LTBP2 and microfibrils to cardiac fibrosis remain to be fully elucidated. Furthermore, LTBP2's early-stage upregulation and its presence in circulating serum highlight its potential as a biomarker for fibrotic diseases. Studies in pulmonary fibrosis and other organ systems have demonstrated that serum LTBP2 levels correlate with fibrosis progression and the differentiation of fibroblasts to myofibroblasts. These findings suggest that LTBP2 may serve as an early indicator of cardiac fibrosis. Overall, the investigation of LTBP2's role in cardiac fibrosis is crucial for understanding its therapeutic potential and for identifying new strategies to promote reparative fibrosis and prevent the progression to heart failure.

Background of Cardiac Fibrosis

Heart diseases are a leading cause of global morbidity and mortality, affecting over 523-million individuals annually, with a rising incidence and significant economic burden.1,2 Heart failure, a progressive condition where the heart fails to meet circulatory demands, often culminates in severe outcomes. Cardiac fibrosis, a key driver of heart failure, is characterized by the replacement of dead cardiomyocytes with stiff, collagen-rich scars, impairing cardiac function.2,3

Cardiac fibrosis involves pathological remodeling of the myocardium via excessive extracellular matrix (ECM) deposition by activated cardiac fibroblasts.3-6 This process reduces myocardial compliance and is observed in conditions like myocardial infarction, hypertensive heart disease, and cardiomyopathy, all marked by cardiomyocyte death.7 The initial fibrotic response serves to stabilize myocardial structure and prevent rupture after injury, but chronic ECM remodeling by myofibroblasts leads to stiffened scars and impaired cardiac function.2,4,7-9

Cardiac fibroblasts, essential for maintaining ECM integrity, provide structural support, mediate mechanical forces, and maintain electrophysiological homeostasis.2,9 Following injury, they differentiate into myofibroblasts, driving ECM deposition and scar formation.2-4,8 Chronic activation of these cells leads to pathological fibrosis, emphasizing the need to understand the cellular and signaling mechanisms involved, which may offer therapeutic targets.

LTBP2: An ECM-Specific Modulator of Cardiac Fibrosis

Cardiac fibrosis arises from diverse causes such as injury, aging, and disease, which are difficult to target therapeutically.9 However, the activation of myofibroblasts and excessive ECM protein deposition offers potential intervention points. Controlling fibrosis to preserve its reparative function, rather than progressing to stiff scar formation, could mitigate fatal outcomes.

In a myocardial infarction heart failure model, Shah et al. demonstrated widespread activation of cardiac fibroblasts and upregulation of Latent TGF-β Binding Proteins (LTBPs) in fibrotic regions.4,10-12,15 Notably, LTBP2 expression was significantly elevated, a finding corroborated by studies across various heart failure and fibrosis models.4,6,10-12 These findings underscore the need to explore the poorly understood role of LTBP2 in fibrosis.

Among LTBP isoforms, LTBP2 exhibits unique interactions, with potential roles in fibrotic signaling, microfibril structural integrity, and as a biomarker for cardiac diseases. Understanding these mechanisms may reveal therapeutic targets to reduce fibrosis-related complications and improve outcomes.12

TGF-β: A Primary Activator of Myofibroblasts After Cardiac Injury

Cardiomyocytes have limited regenerative capacity, necessitating a reparative process mediated by cardiac fibroblasts that form collagen-rich scars to preserve structural integrity and prevent rupture.2,4,8 While initially adaptive, this process can progress to pathological cardiac remodeling if unregulated. The balance between tissue repair and fibrosis depends on the activation of cardiac fibroblasts.

Resident fibroblasts are typically quiescent but become activated into myofibroblasts in response to various stimuli, including mechanical stretch, pathogens, necrotic cell mediators, and inflammatory signals.3-4,7,8 Post-cardiac injury, necrotic cardiomyocytes trigger inflammatory and healing responses, altering the matrix environment via growth factors and cytokines that induce myofibroblast transdifferentiation.7

Transforming growth factor-beta (TGF-β) is a well-studied pro-fibrotic cytokine implicated in fibroblast activation.7,8,10,13 It promotes ECM production and remodeling and is highly expressed in fibrotic tissues.8,10,13,15 Macrophages are a major source of TGF-β, which is stored in the ECM in its latent form, bound to large glycoproteins called LTBPs.8,13 Activation of latent TGF-β to its active form occurs via multiple mechanisms, with small quantities inducing significant cellular responses.7 The interaction between LTBPs and TGF-β underscores the role of LTBPs as key regulators in fibrogenesis.

The LTBP Family and Its Isoforms

Latent TGF-β Binding Proteins (LTBPs) are large extracellular glycoproteins structurally similar to fibrillin microfibrils, primarily regulating TGF-β bioavailability.14,15 LTBP-1, -3, and -4 bind to the latent associated peptide (LAP) of TGF-β through disulfide bonds, with LTBP-1 and -3 binding efficiently to all three TGF-β isoforms, while LTBP-4 binds weakly to TGF-β1.13,15 LTBPs facilitate LAP folding, secretion, and deposition in the ECM, as well as TGF-β activation.14,15

TGF-β activation mechanisms include shear forces, protease activity, pH extremes, and integrin interactions via the LAP's RGD site, with integrin-mediated activation being most crucial for fibrotic diseases.14,16 Integrins bind latent TGF-β, requiring LTBP-mediated ECM incorporation and traction forces to release active TGF-β by breaking LTBP-LAP disulfide bonds.14,16 The importance of integrins was confirmed in vivo, where RGD motif mutations or integrin deletions resulted in phenotypes mimicking TGF-β1-null mice and impaired fibrosis development in hepatic, pulmonary, and renal tissues.17,18

Proteases also aid in TGF-β activation by cleaving latent complexes, while reactive conditions, such as ischemia-induced acidic environments and reactive oxygen species, contribute to activation in cardiac pathologies like myocardial infarction and ischemic cardiomyopathy.8,9,14

Loss-of-function studies highlight LTBP isoforms' developmental roles. LTBP-1 and -3 knockouts result in reduced TGF-β signaling and connective tissue abnormalities, such as cardiac septation failure in LTBP-1-null mice.15 LTBP-4 deficiency leads to abnormal lung development, cardiomyopathy, and colorectal cancer.15

Unlike other isoforms, LTBP-2 does not bind TGF-β, leaving its role in cardiac fibrosis poorly understood.

LTBP2: A Unique Member of the LTBP Family

LTBP2 is distinct among its family as it does not bind TGF-β, suggesting a unique role in cardiac fibrosis. Shah et al. identified LTBP2 as significantly upregulated in a myocardial injury heart failure model, with fold changes far exceeding other LTBP isoforms, which remained at baseline expression levels.4 This dramatic upregulation highlights LTBP2's potential importance in fibrosis and heart failure. Similarly, other studies have reported elevated LTBP2 expression in fibrotic regions across various cardiac fibrosis models.6,10,19,20

Unlike LTBP-1, -3, and -4, which regulate latent TGF-β complexes by facilitating storage, activation, and release, LTBP2 may contribute to fibrosis through alternative mechanisms such as ECM remodeling, microfibril stabilization, or interactions with other profibrotic pathways like NF-κB and FGF-2.21-24 This functional divergence could explain why LTBP2 is highly upregulated in fibrotic tissues while other isoforms remain stable. Understanding how LTBP2 influences fibrosis independently of TGF-β activation could provide novel therapeutic avenues distinct from traditional TGF-β-targeted interventions.

While in vitro studies have provided insight into LTBP2's role in fibrosis, its function in vivo remains poorly characterized. Current in vivo models, including myocardial injury-induced fibrosis and transgenic knockout studies, suggest its importance, but further research is needed to confirm whether LTBP2 directly modulates fibrosis or acts through secondary mechanisms. This review explores LTBP2's role in cardiac fibrosis, focusing on its involvement in cell signaling, microfibril integrity, and biomarker potential.

Discussion

LTBP2 AND ITS ROLE IN CARDIAC FIBROSIS SIGNALING PATHWAYS

LTBP2 plays multiple roles in the signaling pathways associated with cardiac fibrosis. Although it does not bind TGF-β directly, LTBP2 upregulates TGF-β1 expression and secretion through Akt and p38 MAPK pathways, exacerbating myofibroblast activation and fibrosis.21 This pro-fibrotic effect requires further in vivo validation, as conflicting evidence about TGF-β1 binding persists.

LTBP2 also strongly binds fibroblast growth factor-2 (FGF-2), which influences fibroblast activity. While FGF-2 promotes healing in chronic fibrosis by reducing TGF-β1-induced collagen production and inducing myofibroblast apoptosis, LTBP2 inhibits FGF-2 function, perpetuating fibrosis.22-24 Modulating this interaction could serve as a therapeutic target to enhance FGF-2's anti-fibrotic effects.

Additionally, LTBP2 influences fibroblast apoptosis via caspase-3 activation. Shi et al. showed that ISO-treated cardiac fibroblasts with elevated LTBP2 levels experienced increased apoptosis.6 However, it remains unclear if this apoptosis is selective for reparative or myofibroblasts, a key distinction that requires further research.25

Pang et al. demonstrated that LTBP2 knockdown in a rat dilated cardiomyopathy model reduced fibrosis, oxidative stress, and inflammation via NF-κB signaling suppression.20 Similarly, in pulmonary fibrosis models, LTBP2 silencing reduced fibroblast-to-myofibroblast differentiation by attenuating NF-κB activation, both with and without TGF-β1 involvement.26 These findings suggest that LTBP2-targeted therapies, particularly through NF-κB inhibition, may mitigate fibrosis progression.

LTBP2 AND THE STRUCTURAL INTEGRITY OF MICROFIBRILS

LTBP2 plays a critical role in maintaining extracellular matrix (ECM) microfibril integrity, especially in elastic tissues. It serves as a bridging component of 10-nm microfibrils, structures present in various organs including the heart. While LTBP2's function is well-characterized in ocular and pulmonary tissues, its contribution to cardiac fibrosis remains underexplored.

In the eye, LTBP2 is essential for proper microfibril assembly and lens development. LTBP2-null mice exhibit disorganized microfibrils and phenotypic defects that can be rescued with recombinant LTBP2.27 Additionally, LTBP2 deficiency disrupts ciliary zonule formation, further supporting its structural role.27 Mutations in LTBP2 are also associated with primary congenital glaucoma due to trabecular meshwork malformation, raising the possibility that similar ECM defects could contribute to fibrosis in other organs, including the heart.28–29

LTBP2 also interacts with fibulin-5 (DANCE), a protein critical for elastogenesis. By regulating DANCE's binding to fibrillin-1 microfibrils, LTBP2 promotes elastic fiber deposition.30 This interaction may be relevant in the cardiac ECM, where elastic fiber remodeling is a key component of fibrosis.

In summary, LTBP2 is vital for ECM microfibril organization and elastic fiber formation. While evidence from ocular models suggests a structural role, further studies in cardiac tissues are needed to elucidate its contribution to fibrosis progression and scar stabilization in heart disease.

LTBP2 AS A POTENTIAL BIOMARKER FOR EARLY-STAGE FIBROSIS

LTBP2 has emerged as a promising biomarker for early-stage fibrosis across various organ systems. In pulmonary fibrosis, serum levels of LTBP2 have been shown to correlate with the differentiation of lung fibroblasts to myofibroblasts, especially following TGF-β1 induction.11 A study using the Cox hazard model found that serum LTBP2 levels could predict the prognosis of idiopathic pulmonary fibrosis.11 Furthermore, LTBP2 overexpression in bleomycin-induced pulmonary fibrosis models also led to myofibroblast differentiation via NF-κB signaling, even in the absence of TGF-β1.26 Notably, serum LTBP2 levels were elevated in COVID-19-related pulmonary fibrosis, suggesting its potential as a biomarker for fibrotic diseases.

While these findings are promising in pulmonary fibrosis, further research is needed to explore LTBP2's biomarker potential in cardiac fibrosis. In the context of cardiac fibrosis, LTBP2 is highly upregulated in fibrotic regions and secreted into the ECM. A 2018 study by Park et al. observed higher LTBP2 levels in isoproterenol-induced hypertrophic cardiomyopathy mice.10 However, they did not find significant differences in serum LTBP2 levels between heart failure patients and healthy controls. A follow-up study did show elevated serum LTBP2 in heart failure patients with reduced

ejection fraction, but the protein's localization to fibrotic regions and its expression in various types of fibrosis limited its effectiveness as a circulating biomarker.12,19

Future research should focus on developing more sensitive assays, such as using coronary sinus blood samples (which contain the highest concentration of LTBP2), and improving antibody specificity to enhance LTBP2's potential as a biomarker for cardiac fibrosis and heart failure.

Future Directions

Most of our current understanding of LTBP2 cell signaling in cardiac fibrosis originates from in vitro tests using isolated fibroblasts modeling fibrosis. However, these models fail to capture the full complexity of cardiac fibrosis, which involves dynamic interactions between fibroblasts, myocytes, immune cells, and extracellular matrix components. More in vivo studies are needed to clarify LTBP2's role in fibrosis progression and cardiac remodeling.

In addition to its use as a biomarker, LTBP2 holds potential as a therapeutic target for cardiac fibrosis. Given its involvement in key fibrosis-related signaling pathways such as NF-κB, TGF-β1, and microfibril integrity, targeting these pathways could provide a dual strategy in modulating LTBP2 expression. 6,20-26 For instance, downregulating NF-κB signaling reduced cardiac fibrosis in DCM rats, highlighting its potential as a target.20

Therapeutic interventions may include the use of small molecules or monoclonal antibodies to either inhibit LTBP2's pro-fibrotic effects or regulate its interactions with ECM components.26-30 Targeting receptors involved in LTBP2 signaling, such as integrins or proteases, could enable more precise interventions while minimizing off-target effects.27-30 Furthermore, viral gene delivery systems, such as adeno-associated viral vectors, could be explored for selective modulation of LTBP2 expression in cardiac tissue to promote reparative fibrosis.28

Future studies should refine these strategies using preclinical models to identify the most effective approaches. A deeper understanding of LTBP2 in cardiac fibrosis will be essential for developing targeted therapies to prevent heart failure and improve patient outcomes.

Study Limitations

While many cited studies provide valuable insights, most are limited to in vitro systems or animal models that may not fully replicate human cardiac fibrosis. The translational relevance of these findings remains uncertain, underscoring the need for more robust in vivo and clinical studies to validate LTBP2's role and therapeutic potential in humans.

Search Methods

A narrative literature review was conducted using the University of Toronto library databases. Keyword combinations such as "LTBP2," "fibrosis," and "ECM" were used. Articles were selected based on abstract relevance and peer-reviewed primary research, focusing on studies exploring LTBP2's role in fibrosis.

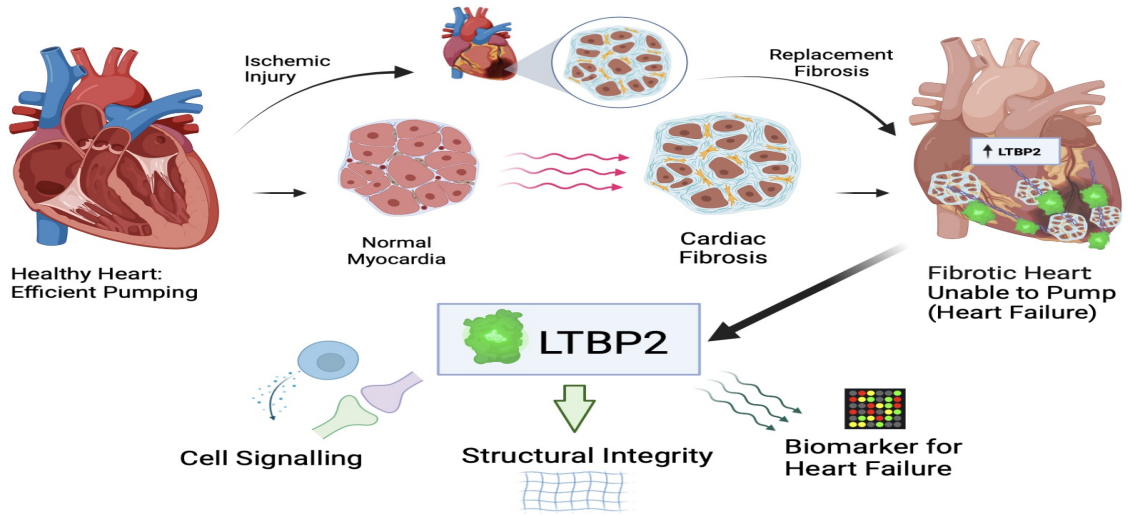

Figure 1. Progression of Cardiac Fibrosis and Potential Functions of LTBP2 31

LTBP2 is upregulated in cardiac fibrosis and may contribute to fibrosis progression through involvement in key cell signaling pathways and maintenance of microfibril integrity. Additionally, its early upregulation in fibrotic tissue and detection in serum suggest its potential as a biomarker for early-stage cardiac fibrosis.

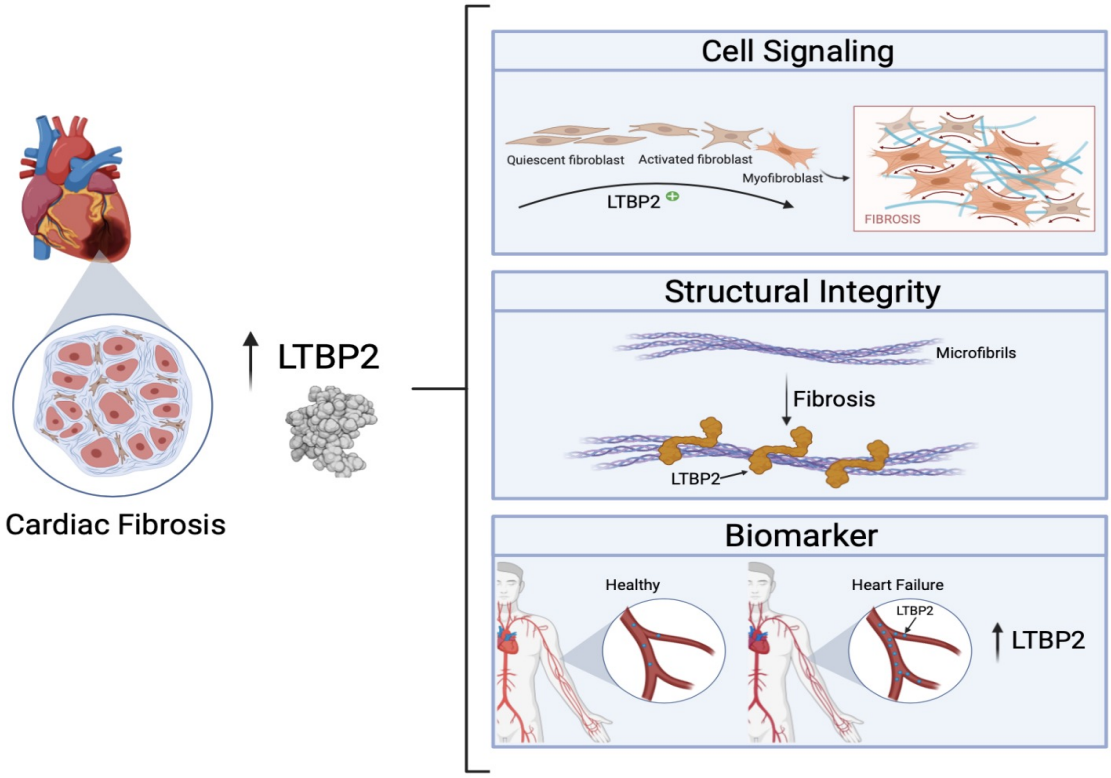

Figure 2. LTBP2 as a Tool for Understanding and Treating Cardiac Fibrosis 31

Exploring the role of LTBP2 in cardiac fibrosis through its involvement in cell signaling pathways, maintenance of microfibril integrity, and potential as a biomarker for early fibrosis and heart failure.

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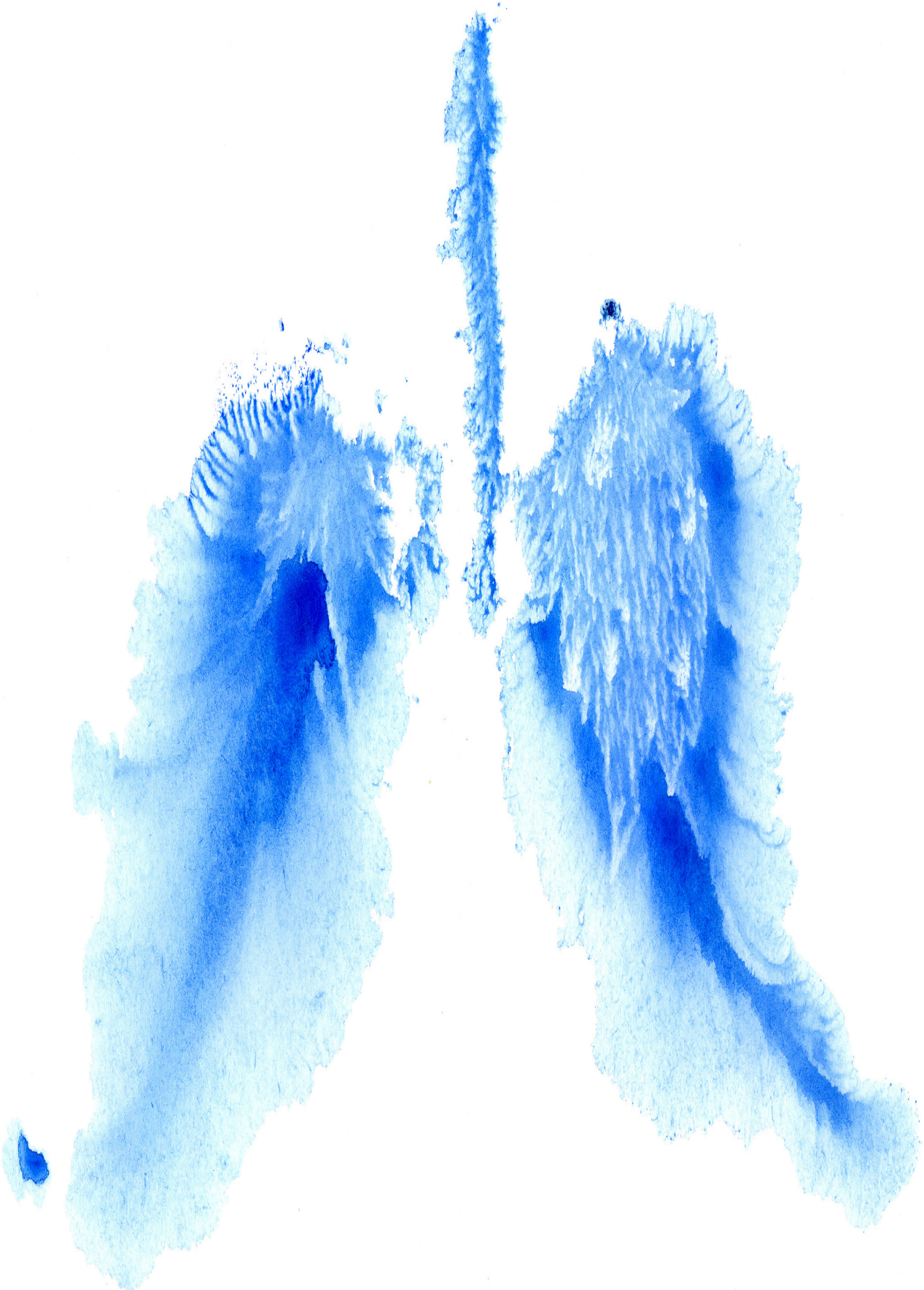

General Anesthesia for a Patient with Chronic Obstructive Pulmonary Disorder and Postoperative Respiratory Failure: A Case Report

ZAINEB HAMZA
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Abstract

INTRODUCTION: Chronic obstructive pulmonary disease (COPD) and other comorbidities, such as obesity and diabetes, significantly increase the risk of postoperative complications, including respiratory failure. This case concerns a 53-year--old male patient (BT) who presented to Cork University Hospital for rigid bronchoscopy for debulking of his carcinoid tumour obstructing the left main bronchus. Upon emergence from anesthesia, the patient (BT) suffered bronchospasm, which progressed into respiratory failure.

OBJECTIVES: The case study methodology involved a comprehensive review of the patient's medical history, family background, and clinical presentation. An evaluation of respiratory complications and contributing risk factors for general anesthesia was done through a thorough review of the literature. Consent was obtained prior to drafting the case report.

METHODS: Postoperatively, the patient developed bronchospasm, leading to respiratory failure. Immediate interventions included the administration of anesthetic agents, Magnesium, and Ventolin. Chest imaging revealed mediastinal widening, atelectasis, and poor inspiratory effort. The patient also experienced gagging and hemoptysis.

RESULTS: COPD is associated with increased postoperative complications, including prolonged mechanical ventilation. Low preoperative PaO_2 is a significant risk factor for postoperative respiratory failure. Additionally, airway hyper-reactivity and bronchospasm can be triggered by pharyngeal and tracheal stimulation during the procedure.

CONCLUSION: Preoperative evaluation of pulmonary risks, particularly in COPD patients, is crucial for identifying potential complications. Anesthesia management, tailored to the patient's unique conditions, plays a key role in reducing perioperative risks and improving outcomes in high-risk cases.

Case Background

The patient (BT) has a diagnosis of chronic obstructive pulmonary disorder (COPD) given his 30 pack-year history of smoking. Additionally, he has a high body mass index (121 kg weight) and a 9-year history of alcohol dependence which has resulted in him developing hepatic steatosis. A high smoking burden alone is a strong risk estimate for COPD[1]. He also suffers from hypertension and non-insulin-dependent diabetes mellitus. His family history is positive for cancer – his father had throat cancer and prostate cancer. Research shows a positive correlation between carcinoid tumours of the lung and a family history of cancer[2]. A few months prior, the patient (BT) suffered from type 2 respiratory failure as a result of an infection due to an obstructing left main bronchus lesion with ball valve physiology. It was supported with non-invasive ventilation. A cardiothoracic multidisciplinary meeting (MDM) was held to evaluate another suspected tumour/ or cancer. The MDM team concluded it was lymphadenopathy or possibly an abnormality of the left adrenal gland with nodular thickening but absence of discrete mass – thus not needing immediate intervention or resection. Before the decision to do debulking via rigid bronchoscopy under general anesthesia, an assessment was done a month ago for the tumour under conscious sedation via bronchoscopy. However, the patient (BT) developed a cough and expiratory dynamic airway collapse, rendering it difficult to evaluate the lesion properly. Thus, after a thorough evaluation, the decision was made to proceed with rigid bronchoscopy to manage the carcinoid tumour obstructing the left main bronchus.

Case Details

The patient was intubated, and surgery commenced. The procedure proceeded for longer than expected due to the snare needing replacement mid-procedure. The malignant airway obstruction was dealt with from the post-lateral wall, and the distal left main bronchus was debulked with a monopolar snare, flexible single-use cryoprobe and APC. Since the patient could not be kept on anesthesia longer, the team decided to finish the procedure – a residual obstruction of 20% remained, which was to be addressed later. The patient was intubated, and surgery commenced. The procedure proceeded for longer than expected due to the snare needing replacement mid-procedure. The malignant airway obstruction was dealt with from the post-lateral wall, and the distal left main bronchus was debulked with a monopolar snare, flexible single-use cryoprobe and APC. Since the patient could not be kept on anesthesia longer, the team decided to finish the procedure – a residual obstruction of 20% remained, which was to be addressed later.

Upon emergence from anesthesia, the patient (BT) devUpon emergence from anesthesia, the patient (BT) developed bronchospasm, which rapidly escalated to respiratory failure. The anesthesia team initially administered 20 mL of anesthetic induction agents to counteract the effect, followed by the administration of magnesium and Ventolin. The patient's power grip was also assessed to rule out a stroke. Additionally, an anteroposterior projection chest x-ray (AP CXR) was urgently done to rule out pneumothorax. It showed mediastinal widening, with a slight displacement of the inferior trachea to the right. There was poor inspiratory effort, with bilateral basal atelectasis being more pronounced on the right. His stats were elevated, particularly carbon dioxide levels, and the patient (BT) started to gag, which was associated with the expectoration of blood.

Discussion and Conclusion

Postoperative complications are heightened with COPD.3 Additionally, COPD is associated with prolonged mechanical ventilation after surgery. 4 Hou et al., in a retrospective study of 120 patients with COPD who underwent spinal surgery with general anesthesia, found that postoperative respiratory failure was not associated with the severity of COPD. Instead, lower preoperative partial pressure of oxygen in arterial blood (PaO_2) was identified as a significant risk factor for developing postoperative respiratory failure.5 In this patient's (BT) case, the PaO_2 was on the lower end prior to the procedure 10.23 and after the respiratory failure – which is consistent with the aforementioned research study.

Furthermore, the patient's obesity and diabetes mellitus added to the perioperative risks, as these conditions are also associated with higher rates of respiratory complications. His history of alcohol dependence and hepatic steatosis further complicated his metabolic status, making him a high-risk candidate for anesthesia and surgery. This multifactorial risk profile necessitates careful consideration of perioperative management strategies to minimize complications.

It is of note that in the case of the patient (BT) he has a carcinoid tumor and although still being explored, the need for caution in repeated anesthetic exposures for cancer management, particularly in high-risk patients like BT, who may require multiple procedures.

Bronchospasm is marked by heightened airway sensitivity, leading to severe respiratory distress, along with frequent coughing and wheezing. Pharyngeal and tracheal stimulation caused by secretions, aspiration, or suctioning can provoke bronchial smooth muscle constriction, resulting in bronchospasm.7

A key takeaway from this case is the importance of a comprehensive preoperative evaluation to assess pulmonary risks, particularly in patients with COPD and other co-morbidities like obesity, diabetes etc., which further complicated the management. Such evaluations are crucial to anticipate potential complications and guide the selection of appropriate anesthesia and surgical techniques. Furthermore, this case underscores the need for tailored perioperative management, including early intervention strategies to address bronchospasm and other respiratory complications, ensuring optimal outcomes in high-risk patients.

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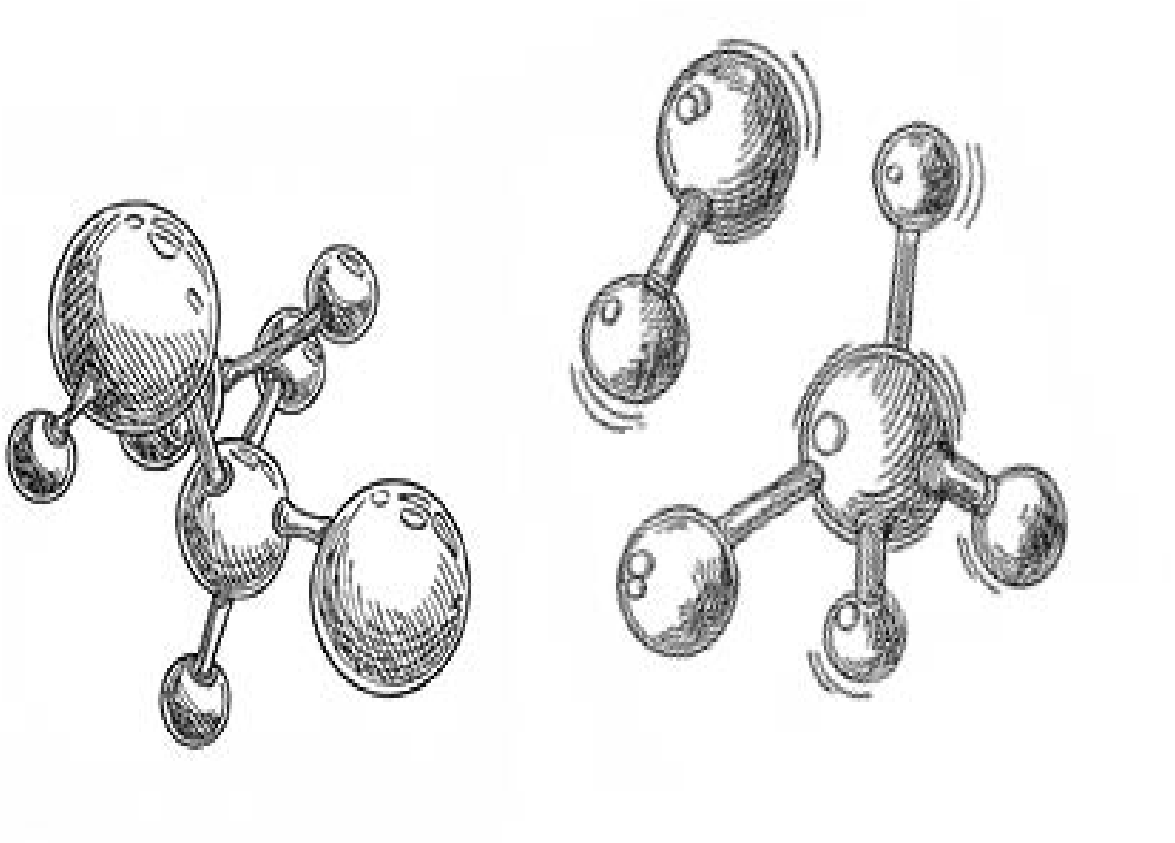

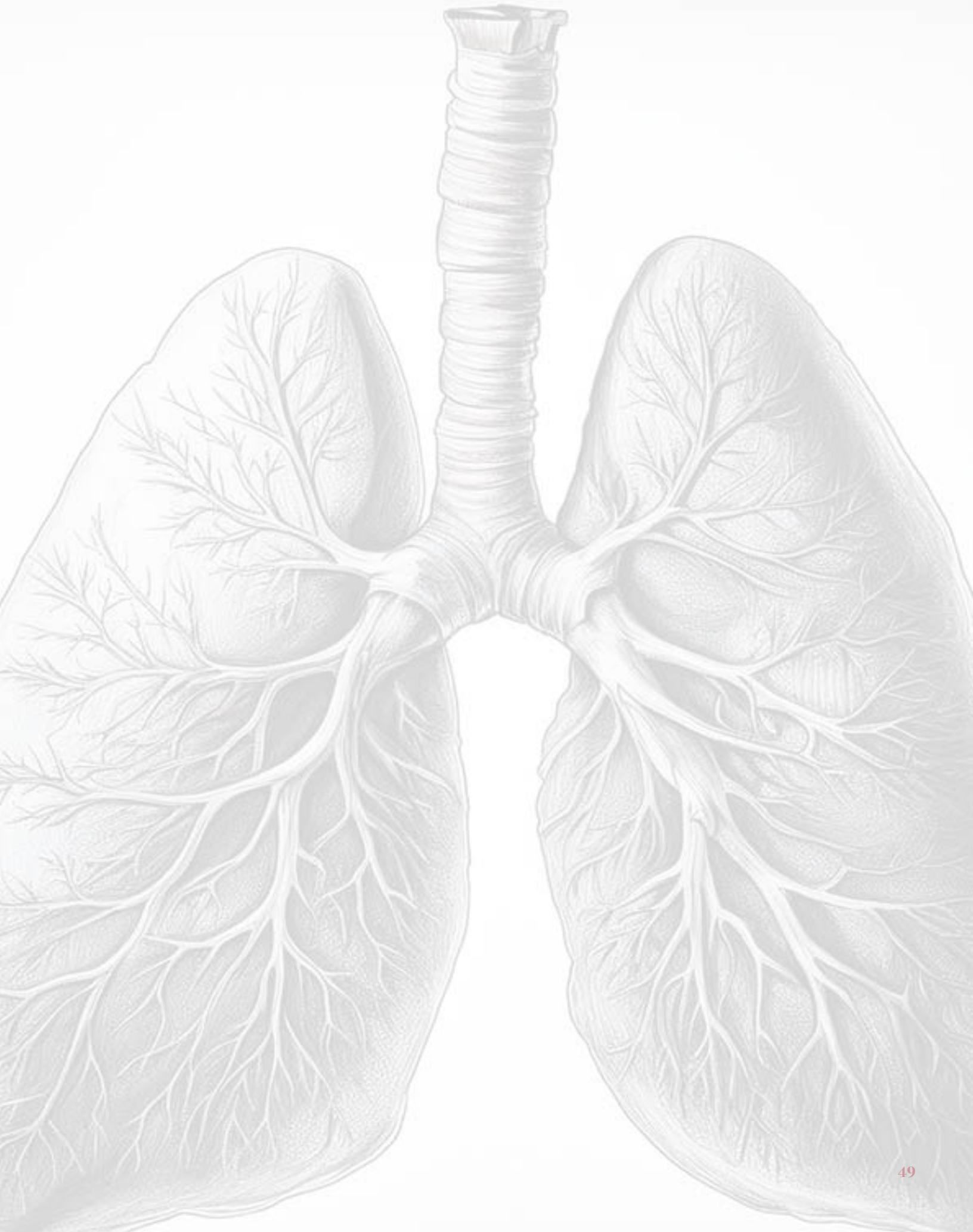

Public & Patient Involvement - A Moral Obligation In Medical Research

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PPI & The Patients Voice In Medical Research

Within recent decades medical research has advanced rapidly toward a future of personalised treatment. As the field progresses, medical management is being tailored to individual patients across the world, from wealthy 1st world nations to the poorer 3rd world, a population of over 7 billion people with individual experiences, values, cultural insights and religious backgrounds to account for. Within this context, the idea of a one size fits all approach to people ceases to work and this nuanced aspect of the modern patient comes to the fore. Leading the charge on this challenge of making medicine relevant to the individual is the concept of Public and Patient Involvement (PPI).

PPI is a research approach that can be defined as "with" or "by" the public as opposed to the conventional "on" or "to inform" them (1). PPI can involve members of the public throughout the research process from establishing research priorities, through co-designing research methodologies, all the way to outcome interpretation and dissemination (2). In this article we seek to examine why PPI is a critical piece of the medical research puzzle by improving research planning, as well as providing the patient with a voice to foster impactful outcomes, and demonstrate why it not only generates fruitful research despite additional steps in the research process, but is a moral obligation for the academic community.

Improve Research Planning

Medical research planning is a multi-step process requiring careful attention for successful outcomes. Without input from key stakeholders—patients, families, and caregivers—research may become unfeasible, lack inclusivity, and reduce engagement. Involving PPI throughout this cycle helps mitigate these risks by allowing the target group to shape the study design. From the outset, PPI can guide feasible methodologies, reduce participant burden, improve clarity of study materials, and ensure fair representation of the study population.

Influencing the language of study materials has been demonstrated to be of particular benefit in the early stages of research, such as questionnaires and recruitment documents, as it ensures the individual has a clear understanding of their involvement and improves the effectiveness of data capture through increased response (4). The lack of representation of minorities and societal subgroups within medical research is well documented and has been shown to hinder patient care (5), however PPI is a promising way of combating this issue. Whilst using PPI to address this issue does add layers to the research process and additional costs to projects, by the inclusion of a diverse panel within the early stages of project planning, research recruitment strategies can be better tailored to capture these groups at risk of underrepresentation.

Additionally, whilst this integration of PPI into research planning does call for structural changes to better facilitate individual involvement which can add time and necessary resources to research planning (6),, recent literature indicates the increased desire of the general public to get involved in this pursuit (7), and is likely to accelerate this transition to the person-centric model of medical research. This proven benefit of PPI to project planning, coupled with the public's desire to engage further in the studies which impacts them, demonstrates the moral obligation we have to facilitate it's inclusion in medical research.

Enhancing Research Relevance

Medical research is a process which involves many different individuals coming from diverse academic backgrounds, from scientists to engineers, clinicians to administrators, all synergising their various experiences and knowledge to bear on the problem being examined. However, in this process one viewpoint which is often neglected is that at the centre of the research endeavour itself, the patient. PPI is a powerful method of bringing the patient to the centre in medical research and establishing meaningful outcomes.

During the research planning phase, identifying the desired outcomes which will be most impactful to the individual can often prevent the delay in implementation of translational research into the clinical environment (8). A strong example of PPI in action is the Young Adult Panel (YAP), a group of eight young adults with Type 1 Diabetes. Founded at NUI Galway in 2014, YAP has helped guide diabetes research by offering insights on study materials, interpreting findings, and improving young patients' engagement with healthcare providers (9). Whilst originally based at one university site, this group has now expanded to an all-island clinical trial with the assistance of the Health Research Board Definitive Intervention and Feasibility Awards (10). Not limited to diabetes, PPI has also been demonstrated to promote study relevance amongst patients in mental health research (11), neurodegeneration (12), and cancer treatment (13).

Whilst it has been difficult historically to quantify the benefit of patient involvement in research due to the lack of reported literature on the topic, this is likely to become evident in the near future with the increased reference to PPI within research in recent publications (14), requirement from research councils to include PPI in grant applications, and the growing collection of published PPI evaluation frameworks to measure the impact of this research (15). This ability of PPI to ensure the patients voice is heard at the research team level ensures that the intended beneficiary is a core element of the research process, improving research relevance, meaningful outcomes, and demonstrating its role as a moral obligation in medical research.

Conclusion

As medical research continues to evolve and expand throughout the world, PPI is a valuable tool which advocates for the patient throughout the research process. This use of patient enhanced research gives the public a voice in the research sphere and helps guide the process to more meaningful outcomes which benefits the patient, their care network, and the wider medical community. The continued expansion of PPI into the grant review and ethical approval process throughout the academic structure ensures it's place in the future of medical research, cementing it's importance to patient outcomes, and indicating a bright future for the voice of the patient within medical research.

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Analgesic efficacy of a single dose intrathecal morphine in patients undergoing robot-assisted laparoscopic prostatectomy (RALP)

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Abstract

BACKGROUND: The World Federation of Societies of Anaesthesiologists has established guidelines for anaesthesia in laparoscopic surgery, but detailed protocols for perioperative pain management in Robot- Assisted Laparoscopic Prostatectomy (RALP) are lacking (1). This study evaluated the analgesic efficacy of a single intrathecal morphine (ITM) dose in RALP.

METHODS: Following Ethics Committee approval, a retrospective chart review of 79 patient charts that underwent RALP procedures between 01/01/2021 and 31/05/2023 was conducted. One patient was excluded due to regular codeine use. As this study was retrospective, confounding factors such as patient co-morbidity, intraoperative analgesia, operating time, could not be controlled for however all surgeries were performed by the same experienced surgeon. A power analysis was done to confirm the minimum sample size of 62 patients. Patients were divided into ITM (n=18) and non-ITM (NITM, n=60) based on whether patients had or had not received the injection. Outcomes included recovery room pain scores, opioid requirements, time to first opioid request, 24-hour postoperative opioid consumption, opioid- related side effects (including respiratory depression, pruritus, nausea and vomiting), and anti-emetic usage. The expertise of the consultant anesthesiologist determined the dose of ITM. Data was analyzed using SPSS. The normality of continuous variables was assessed using the Shapiro-Wilk test. Group differences were analyzed using independent sample t-tests for parametric data and Mann--Whitney U tests for non-parametric data. A P-value of <0.05 was considered significant.

RESULTS: The median [IQR] ITM dose was 200 [50] micrograms. Pain scores in the RR and 24-hour opioid consumption were similar between groups. However, the ITM group had a longer time to first opioid request compared to the NITM group (16.64 [22.9] vs. 1.32 [7.78] hours, P=0.05). Morphine- related side effects were more frequent in the ITM group (16.7% vs. 0%, P<0.001), as was anti-emetic usage (55.6% vs. 15.3%, P=0.001).

CONCLUSION: In conclusion, a single dose of intrathecal morphine delayed the time to first opioid request in RALP patients but was associated with higher rates of side effects and anti-emetic use. These findings highlight the need to weigh the benefits of analgesia against the potential for increased adverse effects in patients undergoing RALP. For further clinical implications, these findings may help to establish specific pain management guidelines for anaesthesiologists in RALP. Furthermore, due to the retrospective design limits and small ITM group, future studies should look to have randomized or prospective studies to confirm these findings.

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Rethinking Obesity Hypoventilation Syndrome: Is Obesity the Primary Driver of Hypoventilation?

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Abstract

INTRODUCTION: Obesity Hypoventilation Syndrome (OHS) is usually diagnosed following an acute admission with type 2 respiratory failure, or incidentally following overnight sleep studies in someone suspected of having Obstructive Sleep Apnoea. Obesity is widely considered to be the main causative factor in (OHS). It follows that with increasing Body Mass Index (BMI), evidence of nocturnal hypoxaemia would emerge strongly. We hypothesized that this assumption is not accurate and set out to investigate the relationship between BMI and nocturnal hypoventilation.

METHODS: We conducted a retrospective analysis of 770 bariatric patients with BMIs ranging from 35-82kg/m2..Using linear and multivariate regression analysis, we assessed the relationship between BMI and surrogate markers for nocturnal hypoventilation, including average SpO2, Lowest SpO2, Time spent with SpO2<90% (T90), AHI (Apnoea-Hypopnoea Index), and bicarbonate levels.

RESULTS: As expected, AHI increased with rising BMI, indicating a higher incidence and severity of Obstructive Sleep Apnoea as BMI increases. However, the correlation between BMI and hypoventilatory markers was weak: for instance, in BMI vs average SpO2 (r 2 =0.105, p=0). In Multivariate regression, BMI was only associated with AHI and Lowest SpO2, both of which are more characteristic of OSA rather than hypoventilation. Figure 1.

Univariate Regression Analysis				
BMI vs:	**R^2**	**Adjusted R^2**	**P value**	**Standard Error**
Age	0.0002	-0.0011	0.670	0.023
Gender	0.0001	-0.0012	0.781	0.590
Average SpO2	0.105	0.103	0.000	12.552
Lowest SpO2	0.1646	0.1626	0.000	3.636
T90	0.1022	0.0972	0.000	3.288
Log Transformed T90	0.127	0.1215	0.000	0.388
Venous Bicarbonate	0.0847	0.0657	0.040	0.259
AHI	0.114	0.1124	0.000	0.113
Supine AHI	0.061	0.0584	0.000	0.119
Anti-Depressant use	0.0012	-0.0002	0.349	0.580
Multivariate Regression Analysis				
Average SpO2	0.233	0.2227	0.137	19.90
Lowest SpO2	0.233	0.2227	**0.000**	6.134
AHI	0.233	0.2227	**0.033**	0.0297
Supine AHI	0.233	0.2227	0.106	0.022

Figure 1. Univariate and multivariate regression analyses showing that BMI was only associated with AHI and Lowest SpO2.

CONCLUSION: Our findings suggest that Obesity Hypoventilation Syndrome is not caused by obesity alone, as the name would suggest. Instead, it is likely to be due to a multitude of different factors, such as leptin resistance and variances in fat distribution. This study opens the door for further research to be done into the contributing causes of Obesity Hypoventilation Syndrome.

AFFILIATIONS: Dr. Liam Doherty, Department of Respiratory and Sleep Medicine, Bon Secours Cork, Mr. Colm O' Boyle, Department of General and Bariatric Surgery, Bon Secours Cork, UCC School of Medicine, Department of Research.

Osteomyelitis Treatment Plan – A Poem

NOORALHUDA ALSHAMI
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Our tale begins where trouble resides,
In the bone marrow Osteomyelitis hides.
But fear not the illness, for treatment is near,
And a healer whispers, "Have no fear."

Brave Antibiotic knights, with strength in their dose,
Marching in the blood as a formidable force.
They seek out the invaders in a relentless war cry,
A valiant quest to bid infection goodbye.

Surgeons, skilled performers in the healing arts,
With precision and care, they cut out the bad parts.
They cleanse the afflicted, with their expert hands
And from its throne, pain is driven from these lands!

Castles of calcium, protective and wise,
Guarding the fortress as the infection dies.
Patience, a potion where recovery brews,
A potent remedy, and at last, tissue renews.

Hyperbaric chambers, where oxygen dances,
A therapeutic waltz, as healing advances.
Pain's gentle whisper, managed with a grim face,
In the symphony of care, with a comforting embrace.

The treatment plan unfolds with strength it bestows,
And the Osteomyelitis chapter may close.
This symphony of care, a melody grand,
A healing poem written by the future physician's hand.

Purple Scrubs

ZAINEB HAMZA
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Hues of purple scurrying in the rain,
A buzz of energy and calm anticipation lingered in the air.
This was the day we all waited for
My thoughts drift back to years ago, same rain, another place -
Skipping my way onto the stage,
Stethoscope dangling around my neck,
My parents' laughter and cheers lighting the crowd.
Oh, the nostalgia of a "dress-up" day in kindergarten

Rows of purple now stretch endlessly,
Phones floating, ready to treasure this moment forever.
This was the day we all waited for
My mind, yet again, wanders to years ago,
My uncle's voice over the phone
"Try your best," he said with quiet pride,
Calling me "my future doctor."
Oh, the warmth of hopeful car ride calls

Silence settles as a stream of red fills the room,
Sheets of yellow passed hand to hand.
This was the day we all waited for
My heart and mind wander back precisely a year and a half,
Sitting in Brookfield G01,
Nearly the same seat, heart brimming with excitement.

The first day of medical school,
Oh, the tremble of first-day nerves
Now, voices of promise and commitment carry through the air,
Loved ones tune in from close and afar.
This was the day we all waited for
The beginning of our clinical years has commenced – our next chapter.

Repeating back in a single breath,
I will…

Special Edition

Diversity & Cultural Differences in Medicine

Cultural and Ethical Considerations in Obstetrics & Gynaecology: A Narrative Review

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Abstract

The field of obstetrics and gynecology (OBGYN) is integral to women's health, encompassing preventive care, pregnancy, and reproductive health. However, significant cultural, racial, and ethical challenges persist, impacting patient outcomes and equity. This narrative review highlights key issues in OBGYN care, including disparities driven by communication barriers, racial bias, and restricted access to reproductive services. The relationship between language discordance and obstetric trauma for non-English speakers, emphasizes the need for interpreter services and bilingual proficiency among providers. Racial bias manifests in higher maternal mortality rates for Black women and inadequate pain management due to unfounded beliefs about biological differences. Ethical challenges also arise, concerning access to abortion and prenatal screening services, with wide global variation in legislation and implementation. In Ireland, restrictive laws and a lack of universal non-invasive prenatal testing (NIPT) highlights barriers to informed decision-making. Future directives emphasize fostering diversity in healthcare teams, implementing educational programs to address stigma, and advocating for inclusive policies that ensure equitable care. By addressing these challenges, OBGYN care can evolve to reflect the principles of equity, representation, and inclusivity, ultimately improving outcomes for diverse patient populations.

Introduction

Obstetrics and Gynecology (OBGYN) is a medical specialty focused on the health of the female reproductive system, pregnancy, and childbirth. It encompasses a broad range of care, from preventive screenings and hormonal management to surgical interventions and prenatal care. In the dynamic landscape of healthcare, cultural awareness plays a pivotal role in ensuring effective, equitable, and compassionate care. The World Health Organization's (WHO) "Health for All" mandate emphasizes universal access to quality healthcare, equity in health opportunities, and the elimination of disparities in care, regardless of socioeconomic status, gender, or cultural background.1 In the field of OBGYN, this principle underscores the need to address inclusivity limitations by ensuring that all individuals can access comprehensive and respectful reproductive healthcare. However, many cultural and ethical challenges persist in the field of OBGYN. In this narrative review, we discuss cultural and racial considerations in OBGYN care, OBGYN policies restricting patient access to reproductive care, and future directives in the field. More specifically, this article describes communication barriers influenced by cultural and linguistic differences, disparities in provider-patient dynamics, racial bias, and restricted access to abortion services and prenatal screening.

Cultural and Racial Considerations in OBGYN Care

Cultural and racial awareness is crucial in the field of OBGYN to ensure the delivery of quality care while respecting the unique needs of diverse populations. Effective communication between patients and physicians is critical for quality care and safety. Language discordance significantly impacts outcomes, with non-English speakers facing double the risk of obstetric trauma and increased high-risk deliveries compared to English speakers.[2] Additionally, a systematic review of patient experiences during childbirth reported that patient satisfaction during childbirth is more influenced by support from caregivers through open communication and inclusion in decision making than medical interventions.[3] Strategies to improve communication in OBGYN at the individual level are gaining awareness including providing care in languages with professional proficiency via interpreter services and incentivizing staff to obtain qualified bilingual certifications.[4] Community collaborations and national-level language policies are also necessary to drive diversity, equity, and inclusion in OBGYN.

Provider gender is another topic that intersects with patient preferences and culture. Some patients associate care with opposite-gender providers as uncomfortable or inappropriate. Individuals of the Islamic faith minimize eye and physical contact with providers of the opposite sex in accordance with their religious guidelines, and have reported poor maternity care indicated by stereotypical and discriminatory behaviour.[5] Understanding the unique values of patients in OBGYN is a step towards improving patient rapport and outcomes.

Racial bias in OBGYN is a well-documented issue, manifesting in disparities in care, treatment outcomes, and patient experiences. Research indicates that racial and ethnic minority groups face inequities due to biases among healthcare providers and systemic factors. In the United States in 2021 the maternal mortality for Black women was 2.[6] times higher than that for non-Hispanic White women.[6] Another racial discrepancy is inadequate pain management among patients of colour. Healthcare providers have been shown to underestimate the pain of Black and Hispanic patients compared to White patients because of perceived biological differences among races.[7] Another study, found that White medical students and residents incorrectly believed that Black patients have a higher pain tolerance than White patients, suggesting biased medical judgement even among early medical trainees.[7] It is important to actively work against personal and systemic racial biases as it can affect morbidity and mortality of patients.

Ethical Challenges in OBGYN Care

While reproductive health and access to safe termination of pregnancy (TOP) services are widely recognized as basic human rights, enormous variation exists with regards to access to contraception and abortion services.[8-10] The global discourse surrounding ethical principles governing pregnancy and TOP has largely been divided between protecting or restricting reproductive services. The US has enacted state-specific legislation restricting or criminalizing TOP, whereas France has entrenched the right to abortion services in their constitution.[11] National differences in legislation, policies and standards of care are key determinants affecting access to reproductive healthcare.

In Ireland, as of December 2018 under The Health (Regulation of Termination of Pregnancy) Act, TOP was made legal under the following circumstances: up to 12 weeks gestation, fatal fetal anomaly present, and/or risk to life or health of the pregnant woman.[12,13] With regards to a fatal fetal anomaly, specific criteria requires one obstetrician and one other medical practitioner to agree the anomaly would result in death within 28 days of life.[12] Following implementation of this in clinical practice, research revealed clinician fear of persecution for sub-fatal diagnoses, strained interprofessional communications, and conflicting personal and psychological challenges faced by practitioners.[14] This highlights that legislation alone does not equate to clear clinical decision making - clinician support must follow.

Furthermore, in the context of TOP, concerns have been raised regarding prenatal screening in Ireland. There is no national program for non-invasive prenatal testing (NIPT), however, in certain centres the Health Service Executive (HSE) offers blood tests and fetal anatomy ultrasound scans at 18-20 weeks gestation for a fee.[15] This screening identifies physical and chromosomal abnormalities. However, screening is not foolproof, as certain fatal conditions may not be detectable until later in gestation. This presents a potential barrier to fully informed decision making. Governing bodies, such as the American College of Obstetricians and Gynecologists, and the Royal College of Obstetricians and Gynaecologists, agree that there is a lack of universal access to prenatal screening.[16-19] Additionally, surveys in Ireland have shown a desire for NIPT to be included as part of prenatal care.[20] Conversely, there are divided opinions between healthcare providers and pregnant people with regards to routinization of NIPT.[21] Further discussion to address the controversy of opinions must take place, with considerations to the ethical impacts of NIPT routinization.[21]

Future Directives

Improving care in OBGYN is an ongoing effort that includes enhancing representation, education, and policy. Lack of inclusive representation in healthcare settings deters patients from accessing reproductive care. A study of fertility centers in Europe found that clinic websites often fail to reflect the racial, gender, and class diversity of their patient populations.[22] Efforts to address this issue include programs aimed at recruiting and supporting underrepresented minorities in the medical profession, and increasing the diversity of clinical staff.[23,24] These measures aim to improve accessibility and outcomes in reproductive care by fostering diversity in both patient populations and clinical settings.

A handful of educational programs have been put forward in OBGYN to address the discrimination and stigma often faced by patients of minority. Some centers have successfully implemented diversity-based grand rounds and curriculum changes in OBGYN clerkships, which increased providers' knowledge of sexual and ethnic minorities.[25,26] However, these initiatives are limited, and a broader push for such programs in healthcare institutions is necessary to make a lasting impact on accessibility.

Policy changes also hold great potential to improve inclusive care for underrepresented OBGYN patients. In the US, sexual minorities are less likely to seek prenatal care in states lacking legal protections, while the reverse occurs in states with such protections.[27] This highlights the importance of policies that foster trust and reduce fear among patients. Research has also suggested improvements such as better referral methods for ethnic minorities, access to interpreters, and physical accommodations for patients with disabilities.[28,29] Future directives in inclusive OBGYN care should focus on more than just bedside care, by prioritizing representation, education, and policy to improve accessibility for diverse populations.

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Impact of Cultural Biases and Language Barriers in Emergency Care

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Abstract

As patient populations continue to diversify, the need for culturally competent medical care is increasingly import Emergency departments serve diverse populations, making it essential to deliver equitable, high-quality care to all patients, regardless of their cultural or ethnic backgrounds. However, the fast-paced, high-stress environment of EDs, combined with challenges such as language barriers and cultural biases, often impedes this goal. These obstacles have been widely recognized as significant barriers to effective care. Addressing these challenges, as highlighted in the literature, can empower EDs and emergency care providers to enhance patient care quality, promote equity, and ultimately reduce adverse patient outcomes.

Introduction

As patient populations continue to diversify, the need for culturally competent medical care is increasingly important, especially in settings where prompt and accurate care is critical. Emergency departments (ED) often serve as the first point of contact for vulnerable populations, including those from different cultural and linguistic backgrounds. However, language barriers and cultural differences in marginalized groups may create significant delays in care, leading to miscommunication and less favourable health outcomes. Furthermore, implicit biases shaped by cultural stereotypes can complicate care in these high-stakes environments, leading to poorer outcomes. It is crucial to address these challenges and find solutions beyond point-of-care services like simple translation—and instead, find ones that encourage trust and improve communication, equity, and cultural knowledge among healthcare providers. Addressing research gaps by including culturally diverse populations in research can help ensure that emergency care is equitable to all screening.

Cultural Biases in Emergency Care

"Medical intuition", a key feature utilized for diagnosing in clinical practice, is, by nature, highly subject to the implicit biases of an examining practitioner. Implicit bias concerns the influence of unconscious attitudes and associated stereotypes that alter an individual's judgement, behaviour and decisions.[1] While unconscious biases regarding race and cultural norms are not limited to a single medical speciality or level of experience, emergency medicine requires physicians to treat patients under conditions that have been shown to exacerbate this bias. This includes conditions such as significant time constraints, fatigue, increased cognitive stressors and diagnostic uncertainty, which in turn increases the incidences of racial stereotyping and prejudice.[2,3]

A study by Johnson et al. found that the cognitive "overload" experienced by physicians during an ED shift was associated with increased implicit bias, particularly with ED overcrowding.[4] However, this paper did not investigate how situational factors in the ED influenced the application of bias through mediums, including poor communication or diagnostic errors. While no current studies conclusively indicate how implicit bias directly relates to poor patient outcomes in minority groups, there are many studies noting overarching racial disparities in ED care.[5,6] Given the implications of practitioner bias in patient outcomes, further investigation of the racial and cultural biases in emergency medicine is important, considering that EDs are often the primary treatment centres accessed by vulnerable populations with varying ethnic and socioeconomic backgrounds.

The Health Service Executive (HSE) currently delivers intercultural awareness training through online learning modules.[7] However, these programs lack direct educational strategies to address or assess healthcare professionals' implicit biases related to cultural norms. Instead, the focus remains on promoting cultural sensitivity within patient-centered care. Although there is limited literature evaluating the effectiveness of these specific modules, a systematic review has shown that patient-centered care models incorporating cultural competence enhance practitioners' knowledge, awareness, and cultural sensitivity but no significant improvements in patient health outcomes were observed.[8]

Language Barriers

Communication is key in medicine, especially emergency medicine. However, communication is limited when the patient and healthcare provider do not share the same language. As countries become increasingly multicultural, language barriers pose an additional challenge to providing prompt medical care.

Studies have shown that individuals who speak languages other than English (LOE) will experience longer hospital stays, more misdiagnoses and are more likely to revisit the hospital.[9,10] Barriers imposed by language differences can also affect the status of a pre-alert. 999 calls are made in high-stress situations, but with the additional challenge of language nuances and interpretation, critical information can be missed. In an Australian study, where English is spoken predominantly, dispatchers were more likely to miss critical cardiac arrest signs if the caller were LOE speakers, which delayed care.[11] This is a significant concern, given the time-sensitive nature of treating a cardiac arrest. Which is one of many reasons why non-English speakers are more hesitant to attend the hospitals and thus have poorer health outcomes.[12]

Although professional translators are an option, this is limited by funds and time. EDs are one of the highest users of translation services, with 25% of hospital requests10; however, not all requests are fulfilled in a timely manner. Thus, digital systems such as Tranlatly have emerged. Tranlatyl is a digital real-time translator covering over 20 languages, including Farsi and Arabic. Unlike Google Translate, its accuracy is higher. When Tranlatyl is paired with medical students or professionals, patients report feeling more informed about their care.10 Although in-person interpreters are often preferred, the use of online translation tools may enhance healthcare quality and increase satisfaction for both patients and providers.[13]

Gaps in Research & Future Directives

Existing research has highlighted global health inequities in emergency care for racially and ethnically marginalized individuals, particularly in areas such as pain management, diagnosis, and transport.[14] Yet, few studies have explored strategies to reduce disparities in prehospital care based on patient demographics (e.g., underrepresented race, ethnicity, sex, gender, or sexual orientation) and addressed clinician bias to ensure high-quality, equitable care for all patient populations. These gaps often stem from the underrepresentation and limited participation of marginalized groups in research. For instance, ethnic minorities and those from lower socioeconomic backgrounds are more likely to be lost to follow-up, which can introduce bias into data analysis.[15,16] Hence, clinical research in prehospital care is essential for developing evidence-based guidelines; however, significant gaps persist due to limited resources, ethical considerations, and prioritizing patient care over research. All these complexities hinder the ability to conduct high-quality studies in emergency medicine, particularly for marginalized groups.

Emergency care is frequently the first point of medical contact for many seriously ill or injured patients, making it an essential link in the healthcare delivery continuum. Evidence suggests that care from physicians who share a patient's racial and cultural background may enhance exam participation, self-advocacy, and doctor-patient trust.[17] The rapport established in these interactions can improve communication, resulting in more accurate diagnoses and tailored treatment plans. Thus, increasing diversity among healthcare practitioners can help marginalized groups increase their trust and use of such services, which improves health outcomes and reduces disparities.

Conclusion

Emergency medicine operates under time pressures that can exacerbate implicit biases in clinicians, particularly in environments with cognitive overload and diagnostic uncertainty. These biases often lead to inequities in care, leaving marginalized groups facing miscommunication, diagnostic errors, and worse health outcomes. While existing research highlights these disparities, there is still a need to explore solutions which address the underlying causes. Increasing diversity within healthcare teams is one potential step, as shared cultural perspectives can foster trust and improve patient-provider communication. Another major challenge is language barriers, which can delay critical care and lead to misunderstandings, especially for non-English speakers. Tools like real-time translation systems offer ways to bridge these gaps and enhance the patient experience. Addressing bias, improving diversity, and adopting innovative technologies are all critical to making emergency care more equitable and accessible for everyone.

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Cultural Impacts on Psychiatric Care for Pre- and Post-Diagnosed Patients and their Respective Health Outcomes

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Abstract

Given the cultural influences and perceptions surrounding psychiatry, this has led to hesitancy and delays in seeking mental health services and treatment. Even the process of being diagnosed is affected by cultural perceptions and physician bias. Symptomatology differs between various minority groups, resulting in misdiagnoses and further delays. Compounded with pre-existing disparities and a perception that mental health conditions are inferior to other medical conditions, cultural minorities have experienced poorer health outcomes and a reduction in quality of life. Only with a better understanding of the cultural impacts on pre- and post-diagnosis and treatment can psychiatry better serve its patients and provide effective care.

Introduction

Global statistics show that one in four individuals will be diagnosed with a mental health disorder.1 However, 20-50% of these individuals who come from ethnic and racial minorities will not pursue mental health services.2 This is attributed to the cultural perceptions and stigmas surrounding mental health disorders.2 Each culture has its own beliefs around psychiatric conditions, which in turn can lead to variations in condition presentation, delays in seeking care, and treatment adherence.2,3 Historically, those with delayed diagnoses have experienced poorer health outcomes and reductions in quality of life (QOL), which, given the literature, places marginalized populations and ethnic minorities at a higher risk.2,3 Therefore, this paper will explore various cultures' impacts on the psychiatric pre- and post-diagnostic process and treatment outcomes.

Pre-Diagnosis Process

Cultural factors in psychiatry significantly impact symptom presentation and help-seeking behaviours.4 For instance, one study found that the majority of Latino participants initially sought support from social networks (e.g. friends or family members) as opposed to formal mental health services.5 Cultural stigma also plays a role in shaping patients' perceptions of their illness and how they seek help.3 In Arab cultures, where psychiatric conditions can be associated with spiritual conflict, patients are more likely to seek spiritual help first and then proceed to traditional treatments.3 Such stigmas can delay access to care, worsen symptoms and reduce QOL3

Another critical role of culture in psychiatric care is how it can affect patient presentation. Culture-bound syndromes are defined as "a combination of psychiatric and somatic symptoms that are considered to be a recognizable disease within specific cultures".3 For example, "Ghost sickness", a culture-bound syndrome in some Indigenous American (e.g. Navajo, Muscogee) and Polynesian populations, is characterized by severe anxious and fearful thoughts regarding the supernatural presence.6

There should also be an understanding of how racism impacts the social determinants of mental health and the specific mental health needs associated with racial discrimination.7 Identifying the impacts of culture and race on condition presentation and help-seeking behaviours can allow physicians to provide more effective support for patients. In turn, patient-physician interactions will be grounded in an improved understanding of a patient's concerns and treatment options, which ultimately enhances care and treatment adherence.4

Diagnosis Process

Cultural perceptions have a significant impact on the diagnosis of mental health conditions, leading to delays in care.8 Primary care is the first point of contact for most ethnic and racial minorities seeking mental health care, but it faces challenges in recognizing and diagnosing mental health conditions.10 This increases the risk that patients of minority backgrounds remain undiagnosed in primary care settings.8

Different cultural beliefs, values, and stigmas surrounding mental illness influence how patients describe their symptoms to clinicians.8 For example, Asian patients will selectively report symptoms focusing on somatic symptoms like dizziness, as opposed to their emotional symptoms.10 Similarly, South Asians with mental health illnesses do not seek psychological help and instead go to their primary care physicians and present initially with somatic symptoms rather than depressive symptoms.9

When clinicians and patients come from different cultural

backgrounds, there is a greater potential for misunderstandings, as clinicians may overlook symptoms important to the patient or misinterpret their concerns.8. Additionally, clinician biases' and stereotypes about ethnic and racial minorities can contribute to misdiagnoses, such as over diagnosing schizophrenia in African Americans11 or underdiagnosing mental health conditions in Asian Americans.8 Thus, cultural competence among healthcare providers is essential to mitigate cultural stigmas and barriers to care.

Treatment and Healthcare Outcomes

The impacts of culture and ethnicity heavily influence treatment adherence and psychiatric outcomes, with ethnic minorities disproportionately being more negatively affected.2 Medication compliance is one factor that significantly affects treatment success. One systematic review stated that up to 60% of individuals from racial or ethnic minorities will not fill their psychiatric prescriptions.2 Concerningly, 40-80% of these patients will prematurely terminate their treatment, especially if their diagnosis is mood or anxiety-related.2 Decreased drug compliance is attributed to multiple beliefs. However, the overarching concern claimed by minorities such as African Americans, Hispanics, and Latinos is the belief that mental health medications are not effective.12,13,14 This stems from the cultural perception that mental health disorders are not as severe as other medical conditions and are highly stigmatized.12,13,14 These beliefs contribute to delays in care and ultimately impact a patient's QOL.3 Coupled with cultural stigmatization of mental health disorders and pre-existing health disparities, ethnic minorities are more vulnerable and place themselves at a higher risk for condition relapses.2,3

To address these concerns, physicians should adopt their patients' cultural perspectives.2 Being culturally sensitive, empathetic, and cognizant of a patient's perception of their illness and the associated stigmas can lead to earlier treatment and better health outcomes.

Conclusion

In summary, cultural diversity plays a critical role in psychiatric care by influencing the recognition, diagnosis, and treatment of mental health conditions from both the patient and physician's perspective. Cultural beliefs, values, and stigmas shape how patients perceive mental illness, describe their symptoms, and their approach to seeking help. These factors can result in delays in care, misdiagnoses, and suboptimal treatment outcomes, particularly for ethnic and racial minorities. For instance, culture-bound syndromes and somatic symptom presentation reflect the intricate ways culture impacts mental health narratives. Additionally, systemic issues like disparities and cultural stigmas further exacerbate the adverse outcomes that marginalized populations experience.

To address these barriers, culturally competent care is essential. Understanding cultural contexts allows physicians to engage patients more effectively, encourage trust, and tailor treatments to individual needs as relevant to their cultural background. By acknowledging the unique cultural factors that shape psychiatric care, physicians can improve diagnostic accuracy, treatment adherence, and overall health outcomes. Bridging the gap between diverse cultural perspectives and clinical practices is crucial for effective mental health care, and emphasizing cultural competence and systemic reforms can pave the way for more inclusive psychiatric care.

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From Bias to Better Care: Cultural Competency in Primary Care

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Cultural Implicit bias in healthcare presents a serious problem with potential profound implications for patients. As Ireland's population continues to diversify, so too does the need to address the consequences brought forth by implicit bias. There are particularly high chances that the general practitioner is taken as the first point of contact for many patients with various complaints. Implicit bias can influence clinical judgment in a very significant way due to unconscious attitudes or stereotypes that influence decisions made between doctor and patient. As indicated by recent works, such as that by FitzGerald and Hurst (2017), investigating implicit bias within the healthcare setting, it is unconscious stereotypes that act to influence clinicians' perceptions and behaviours. These manifest themselves in many ways, such as in diagnostic evaluations, in treatment recommendations, and even in the amount of empathy provided to patients from diverse backgrounds (Blair et al., 2013). While much of the existing literature focuses on the United States and other contexts, unique cultural and systemic features within Ireland's healthcare landscape raise specific reasons to take a closer look at implicit bias among Irish GPs.

Marginality and implicit biases in healthcare contribute to significant disparities in patient care and health outcomes. Disparities related to marginality can explain differences in health outcomes and quality of life (Havranek et al., 2015). Hall et al. (2015) found that implicit biases harm patient–provider interactions, treatment decisions, and patient adherence. Cooper et al. (2012) reported that physician bias consistently leads to discriminatory care, with patients rating physicians who have higher implicit bias as less patient-centered. Blanchard & Lurie (2004) showed that patients who felt they would have received better treatment if they were another race were less likely to get recommended chronic disease screenings, follow medical advice, or seek care promptly. Furthermore, Blair et al. (2013) found that higher provider bias correlated with lower patient ratings of interpersonal treatment, knowledge of patient context, communication, and trust. In England, ethnic minority patients have repeatedly reported lower satisfaction with primary care, mainly due to service-related factors rather than patient characteristics (Magadi & Magadi, 2022). This spotlights the need to address structural and contextual issues in healthcare to improve patient experiences and outcomes.

The dilemma in primary-care disparities in underserved communities has given rise to different solutions to be enacted to varying levels of success (Vanderbilt, Dail, & Jaberi, 2015); one being the targeted recruitment of medical students likely to practice in rural areas (Evans et al., 2020; Vanderbilt, Dail, & Jaberi, 2015). However, literature shows students' idealistic inclinations toward the service of underserved communities decline during education and training (Smith & Weaver, 2006). A factor being the lack of early exposure and training, given the positive correlation between rural medical electives and students' attitudes in practicing in under-resourced areas (Smith & Weaver, 2006; Kutob et al., 2013). However, nearly half of U.S. family physicians have not received formal cultural/linguistic training in medical school/residency (Mainous et al., 2020). Practical training requires research evidently lacking in underserved communities due to insufficient resources/time, inconsistent global methodology, and lack of community participation (Kumar et al., 2019; Kutob et al., 2013). This cascade of systemic deficiencies is a barrier to bridging the gap in health care for the underserved. Establishing systemic change requires the collective effort of individual physicians, associations, and journals to develop culturally sensitive practices and systems, eventually inducing policy-level change (Kumar et al., 2019; Kutob et al., 2013).

An understanding of various cultures is of particular importance for primary care physicians who are often the patient's first point of contact with healthcare (Rothlind et al., 2021). Failing to appropriately incorporate culture into patient-care and treatment discussions can lead to lower quality care, poorer patient outcomes, and reduced treatment adherence (Brottman et al., 2020; Giger & Davidhizar, 2002). This contributes to health inequities (Brottman et al., 2020). Furthermore, literature shows that many primary care physicians and residents view intercultural interactions as challenging and feel unprepared (Rothlind et al., 2021). Consequently, there is an increasing demand for training (Brottman et al., 2020). This need has further been voiced by education boards such as the Liaison Committee on Medical Education, Accreditation Council for Graduate Medical Education, Institute of Medicine, and World Health Organization (Brottman et al., 2020). The Liaison Committee on Medical Education has proposed four major pillars of cultural education which include skills, attitudes, awareness, and knowledge (Brottman et al., 2020; Association of American Medical Colleges,

2003). Although exact training schemes and methods are still an area of active exploration, one proposed method of training is the use of virtual patient simulations (Rothlind et al., 2021). Ultimately, there is a need for primary care physicians to undergo formal training and teaching in intercultural care in order to provide appropriate, holistic, patient-centered care.

Primary care physicians hold an important role in health-promotion and equity in healthcare (Williamson, 2024). In marginalized communities, they perform the vital role of promoting health screenings and treatment compliance (Hall et al., 2015). However, despite their importance in these communities, disparity in quality of this care can have significant effects on health-related quality of life (Havranek et al., 2015). Furthermore, while initiatives like targeted medical student recruitment aim to fill this gap, they have not been entirely successful. This is largely due to a lack of formal training for both students and physicians in how to provide culturally competent care (Smith & Weaver, 2006; Kutob et al., 2013; Brottman et al., 2020). Many physicians feel unprepared to provide this type of care, highlighting the need for adequate training on this topic (Rothlind et al., 2021). Although there is no consensus on what type of training is best, greater investment into these training programs is necessary to provide better quality healthcare to minority groups. For the future, we must continue to examine the importance of primary care in marginalized communities, and the efficacy of initiatives to promote this care and cultural competency at large. Through this understanding we can ensure better access and quality of primary care to communities that need it most.

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Cultural Neuroscience and its Implications in Healthcare - a Narrative Review

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Introduction

Culture provides a framework in which individual cognitions and behaviours are understood, realized and made meaningful.1 Cultural influences, including language, shared values and social structures, play a critical role in shaping neural organization and brain development. For instance, reading difficulties such as dyslexia manifest differently across cultures, shaped by the characteristics of the writing system used. In alphabetic systems like English, where letters correspond to sounds, dyslexia is linked to dysfunction in the left temporoparietal and occipitoparietal regions2,3, areas essential for phonological processing and decoding written language. In contrast, in logographic systems such as Chinese, which rely on symbols representing words or concepts, dyslexia primarily affects the left middle frontal gyrus,4 a region involved in visuospatial and motor processing.

Differences in information processing also arise from shared values and beliefs, which differ significantly across societies. For example, East Asian cultures – rooted in collectivism – tend to process information holistically, prioritising context and intuitive reasoning.5,6 In contrast, Western cultures – characterized by individualism – focus on specific objects in visual stimuli and rely on formal reasoning.5 Functional differences in visual stimuli processing have been observed in the ventral visual cortex, where evidence suggests that Western individuals exhibit greater activation in object-processing regions.5

Previous reviews on cultural neuroscience have highlighted the importance of integrating culture into the study of brain and development1, and posit that neural connectivity is likely modified through sustained engagement in cultural practices.7,8 This narrative review aims to explore new findings in the emerging field of cultural neuroscience, focusing on how an individual's culture and environment influences their neurocognitive processes, and how this understanding can be applied to advance community-based, inclusive research.

Methods

ELIGIBILITY CRITERIA

All study methodologies were included in this review in order to capture a complete picture of the existing literature. Studies included any modality of assessing structural or functional brain differences, including but not limited to magnetic resonance imaging, computed tomography, and voxel-based morphometry. Specific inclusion criteria were: 1) studies published in English 2) studies will the full text available 3) studies comparing cultural (i.e. linguistic and sociological) differences as opposed to difference in race or ethnic background.

INFROMATION SOURCES

Searches were completed on PubMed, Cochrane Library, Embase and Academic Search Complete from 2000 to December 8th, 2024. Database searches included synonyms of the following terms: race, culture, ethnicity, neural changes and cortical changes. This search was adequately reproduced on all databases included in the review. Furthermore, references listed in the included studies were also searched for eligibility based on the eligibility criteria outlined above.

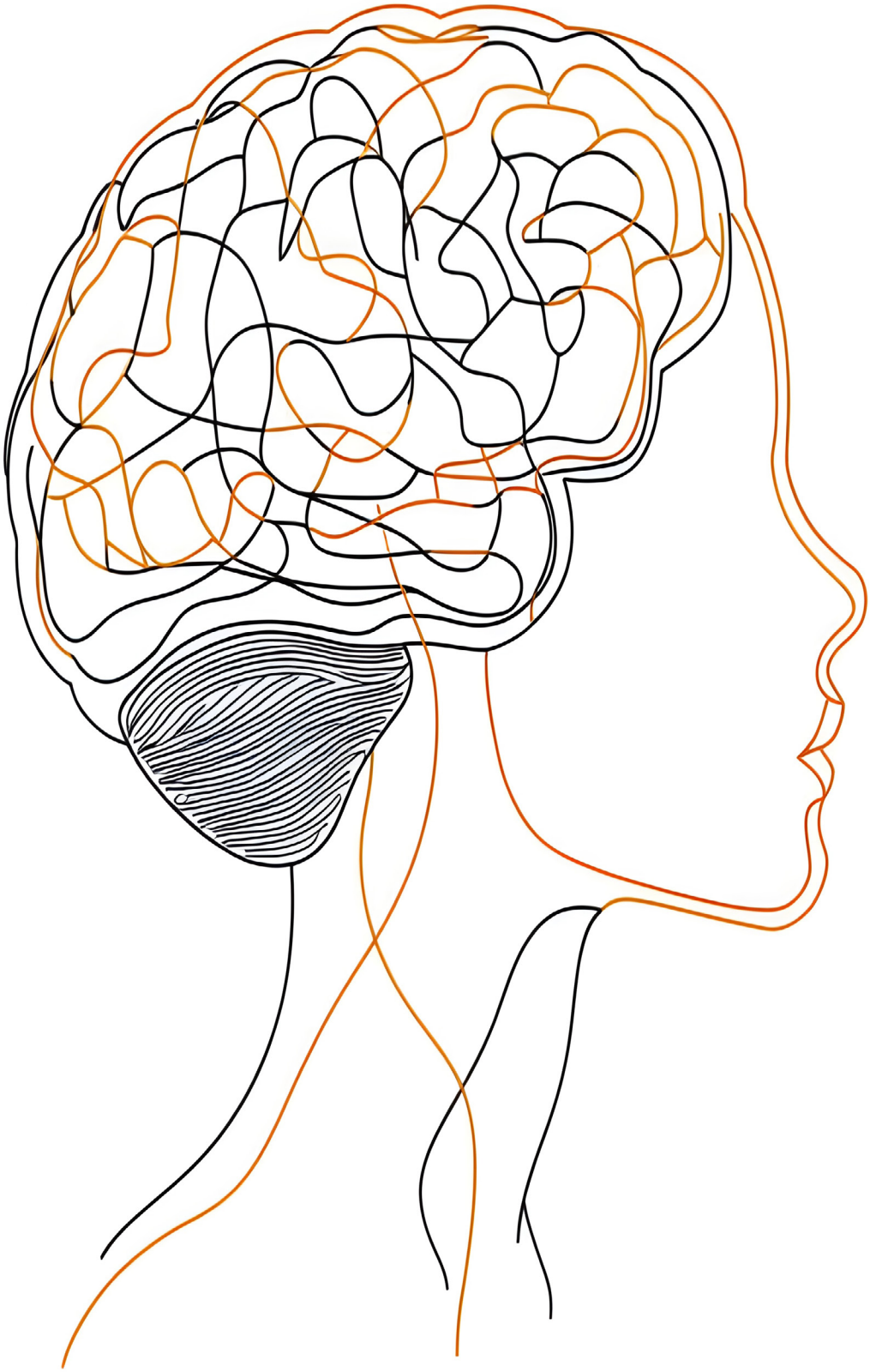
Results

Our search ultimately yielded 7 articles published from 2004 to 2024 included in this review and summarized below. The articles included a wide variety of study methodology, target population and outcome measures, but all attempted to differentiate between cultural (i.e. language, shared values, etc.) vs. racial or ethnic explanations for their findings.

DIFFERENCES IN NORTH AMERICAN VS EAST ASIAN POPULATIONS

Five studies (Table 1) found noticeable differences in structure, cognitive processing and underlying neural networks across Western and East Asian cultures.

Mechelli et al. (2004)9, Wang et al. (2017)10, Huang et al. (2019)11, and Yu et al. (2019)12 all employed voxel-based



morphometry (VBM) in combination with a variety of genetic and cultural factors. Mechelli et al. found Chinese speakers had significant enhancement of grey matter density in the right and left superior temporal gyrus, right inferior frontal gyrus, and left middle temporal gyrus. This study found the same structural differences in Chinese speakers who learned it as both their first and second language, thereby confirming the effect was as a result of language rather than ethnicity.

Yu et al. found that individuals who carried the 7- or 2-repeat allele of the dopamine D4 receptor gene were more sensitive to environmental and cultural influences. They found that grey matter volume was significantly higher in both Caucasian Americans and DRD4 variant carriers. Additionally they found that, among East Asian carriers, the number of years spent in the US predicted increased grey matter volume, supporting the finding that culture shapes the brain by mobilizing epigenetic pathways that are gradually established through socialization and enculturation.

Both Wang et al. and Huang et al. found that individuals who displayed independence (vs. collectivist) traits had increased grey matter volume in a number of brain regions associated with self-relation, including the ventromedial prefrontal cortex. This is consistent with other findings in Western populations, which are associated with independent cultural orientations, in cross-cultural comparisons by Masuda & Nisbett (2006)6, Chee et al. (2011)13 and Tang et al. (2018)4.

Hisanaga et al. (2016)14 found that English speakers process multisensory speech more efficiently than auditory only, and the reverse was true for Japanese speakers. They suggest these results indicate that cultural and linguistic experiences lead to the development of unique neural systems for audiovisual speech perception. These cross-linguistic effects are also supported by previous findings in a review by Green et al. (2007)15.

DIFFERENCES IN NORTH AMERICAN VS LATINX POPULATIONS

Only two studies examined difference between Latinx and North American/Caucasian populations (Table 2).

In an fMRI study of adolescents, Telzer et al. (2011)16 found that Caucasian participants displayed more mesolimbic (reward) activity when gaining a monetary reward for themselves, while Latino participants showed similar or increased activity during costly donations to their family rather than their own gain. The authors posited that these findings were consistent with the cultural emphasis placed on family obligation from Latino families and cultures, and possibly with a stronger importance of family identity to their sense of self.

Ferjan Ramírez et al. (2016)17 found that Spanish-English bilingual infants displayed increased magnetoencephalograpy (MEG) activity in the prefrontal and orbitofrontal cortex when compared to English monolingual infants. This increased activity in areas linked to executive functioning is theorized to arise as a result of a constant need to resolve conflict at a linguistic level, which then translates to the ability to resolve non-linguistic conflict.

Limitations

Firstly, the majority of the studies available to include in this review compare East Asian and English-speaking Western populations. The findings' generalizability is limited by this restrictive scope, which excludes other ethnic and cultural groups such as Indigenous communities, Middle Easterners, and Africans. Given the steady global increase in multiculturalism, a more thorough study spanning a range of cultural backgrounds is necessary to completely comprehend the wider influence of culture on neural development.

Secondly, even though this analysis highlights the influence of culture, it's crucial to acknowledge that other elements like nutrition, exposure to the environment, socioeconomic status, and heredity also affect the structure and development of the brain. The intricate relationship between these elements and cultural effects is not adequately covered in the examined studies.

Finally, cross-sectional approaches, which might show correlations but not causality, are used in the majority of the included studies. To ascertain whether observed changes are due to cultural exposure or other underlying variables, as well as how cultural influences impact brain anatomy over time, longitudinal studies are required.

Conclusion

The emerging concept of cultural neuroscience aids the ever-evolving understanding of how we develop thinking and learning skills, and particularly how these are reflected differently in various cultures. A greater understanding of how cultural differences affect neurocognitive development affords us the opportunity to approach neuroscience in a culturally sensitive manner, rather than as a one-size-fits-all endeavor. Understanding the neuroanatomical and neurophysiological differences that manifest across cultures can help to improve myriad aspects of neuroscience and healthcare, including tailored neuroimaging protocols, improved specificity of clinical

trials and interventions, and providing a biological basis for understanding cultural differences across groups.

Future advances in this field might involve the inclusion of other ethnic groups to ensure greater diversity and provide a more detailed view of cultural differences beyond an Eastern versus Western cultural comparison. Additionally, it would be of value to consider other cultural factors together with language systems when exploring the cultural underpinnings of neuroconnectivity, as well as individual differences in experience and how these may impact neurocognitive development.

The increasing emphasis on cultural differences in brain anatomy remind us that medicine cannot be practised in a vacuum independent of lived experience. Rather, the way our brains are shaped is to some degree dependent on the context in which we experience life, which is strongly influenced by our cultural setting.

Table 1. Studies examining East Asian vs. Western populations

Study	Methodology	Sample Size	Primary Outcomes	Findings
MECHELLI ET AL. (2004)	Case Control	83	VBM of grey matter density	Increased grey matter density in left posterior supramarginal parietal region in bilinguals
HISANAGA ET AL. (2016)	Case Control	39	RT, ERP and eye tracking in syllable identification task	English-speakers: visual speech facilitates auditory speech Japanese-speakers: visual speech does not facilitate auditory speech
WANG ET AL. (2017)	Cross Sectional	265	VBM	A relative focus of independence (vs. interdependence) was associated with increased gray-matter volume in a number of self-related regions, including vmPFC, right DLPFC, and right RLPFC
HUANG ET AL. (2019)	Case Control	113	VBM and SCS	VBM results demonstrated that Western participants showed greater gray matter volume in the fronto-parietal network, whereas Taiwanese participants showed greater regional volume in temporal and occipital regions
YU ET AL. (2019)	Case Control	132	VBM and DRD4 allele carrier status	VBM Grey matter volume of the medial prefrontal cortex and the orbitofrontal cortex was significantly greater among European Americans than among East Asians. The difference in volume was significantly more pronounced among carriers of the 7/2-R allele of DRD4 than among non-carriers

DLPFC = dorsolateral prefrontal cortex, DRD4 = dopamine D4 receptor gene, ERP = event-related brain potentials, RLPFC = rostrolateral prefrontal cortex, RT = response time, SCS = Singelis Self-Construal Scale, VBM = voxel-based morphometry, vmPFC = ventromedial prefrontal cortex

Table 2. Studies examining Latinx vs. Western populations

Study	Methodology	Sample Size	Primary Outcomes	Findings
TELZER ET AL. (2011)	Cross Sectional	28	fMRI of reward system activation	White participants: Increased VS, DS and VTA activity during self gain Latino participants: Increased activity during sacrifice for benefit of family
FERIAN RAMIREZ ET AL. (2016)	Case Control	35	MEG of neural activity	Bilingual infants show increased brain activity in bilateral brain areas, with significant right hemisphere bias, and extension into prefrontal and orbitofrontal cortices

DS = dorsal striatum, fMRI = functional magnetic resonance imaging, MEG = magnetoencephalography, VS = ventral striatum, VTA = ventral tegmental area

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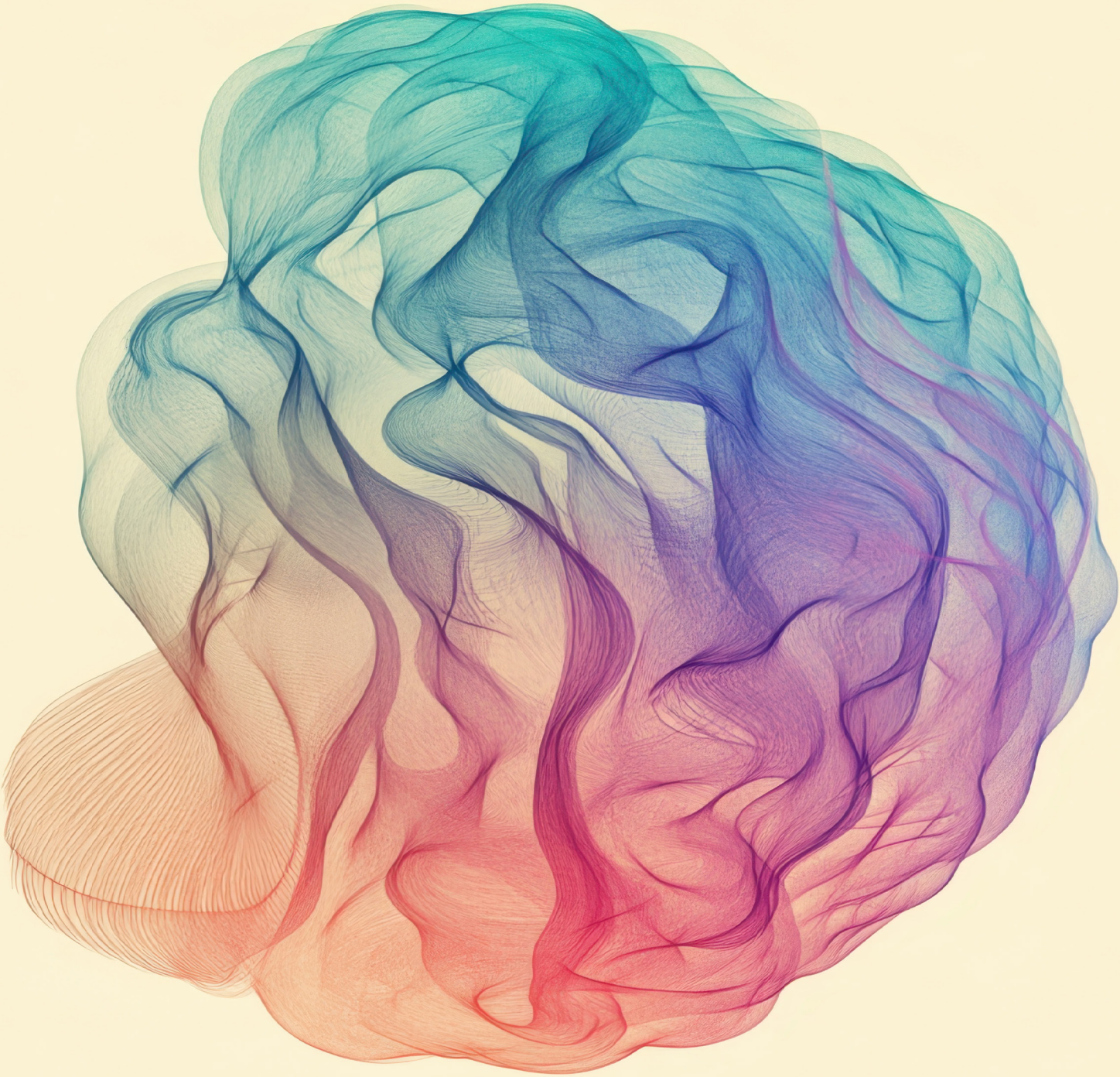

Breaking Barriers: Addressing Stigma and Cultural Taboos in Global Health Initiatives by Médecins Sans Frontières (MSF)

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Abstract

Médecins Sans Frontières (MSF) addresses the impact of cultural stigma and taboos on mental health, sexual and reproductive health (SRH), and vaccine hesitancy. Stigma and taboos, rooted in cultural and societal norms, hinder equitable access to care, erode trust in healthcare, and perpetuate misinformation. MSF employs culturally sensitive, community-centered strategies, including education campaigns, local partnerships, and psychosocial support, to combat these barriers. Initiatives such as tele-Mental Health services, Teen Mums' Clubs, and vaccine education programs foster awareness, normalize care, and dismantle misconceptions. By integrating advocacy and research, MSF champions global health equity and drives sustainable progress in humanitarian healthcare.

Introduction

Médecins Sans Frontières (MSF) is an independent humanitarian organization that has, since 1971, strived to provide medical aid to communities impacted by conflicts and disasters, among other issues.[1] At its core, MSF is committed to promoting diversity, equity, and inclusion in both its operations and healthcare practices. However, these principles can be influenced by cultural stigma and taboos across communities. Stigma involves dehumanizing and shaming individuals by labelling them with undesirable traits, leading to exclusion and denial of care. In contrast, taboos refer to societal silences that can suppress open dialogue or, at times, provide mechanisms of resistance or avoidance.[2] While stigma and taboos differ across cultures, they are deeply interlinked. This article will explore how cultural stigma and taboos impact mental health, sexual and reproductive health, and vaccine hesitancy, and will examine MSF's strategies to address these issues at a global scale.

Mental Health

In the United States, 20% of adults or 44 million people live with mental illnesses. However, mental health (MH) continues to be overlooked due to stigma.[3] For a large group of people, mental illnesses are considered "a sign of weakness" and get minimized due to a lack of visible symptoms, unlike physical illnesses.3 Over the past decade, MSF has prioritized MH, increasing the number of MH consultants by 230% and integrating these services into its global initiatives.[4] The aftermath of the COVID-19 pandemic paved the way for Tele-Mental Health (tele-MH) services, due to COVID-19 travel restrictions. MSF had to adapt and reorganize MH care remotely. However, although successful in developed countries, most tele-MH care proved unaccommodating to low-income areas due to lack of access to technology and poor network coverage.[4] Therefore, in low- and middle-income countries, fewer than 10% of those needing mental health care receive adequate treatment, with even lower rates in regions where mental health remains taboo.[4] Many fear a lack of acceptance and understanding from their community and are wary of being labelled by their mental health issues.[5]

To combat stigma, MSF employs culturally sensitive and community-centred education campaigns. This education comes from medical professionals who help to break down taboos about mental health and increase awareness about the availability of counselling services. Educational campaigns normalize seeking help and underscore the treatability of mental health conditions, fostering greater awareness. By training local staff, i.e., the educational staff and counsellor of the area and collaborating with communities, MSF builds trust and ensures cultural relevance, reducing stigma in familiar settings. In crisis zones, MSF reframes mental health needs as natural responses to trauma, encouraging acceptance, and fosters a safe space for dealing with mental illnesses like refugee camps.[6]

Additionally, psychosocial support, including group therapy, addresses both individual and social recovery aspects, alleviating isolation.

Women's Sexual and Reproductive Health

Sexual and reproductive health (SRH), as defined by the WHO, encompasses physical, emotional, mental, and social well-being; beyond the absence of illness or dysfunction, it necessitates respecting, protecting, and upholding the sexual rights of all individuals.[7] Taboos and stigma significantly impact SRH at both an individual and community level, driven by societal, cultural, and religious beliefs and values.[8] The taboos are deeply rooted in historical and religious foundations which persist in some way to date - for instance, menstruation is surrounded by notions of "purity" and "impurity" in many communities.[9] Gender roles also influence SRH such that in a patriarchal society women have limited autonomy in their reproductive decisions hindering their access to contraception or safe abortion services, thus, increased rates of unplanned pregnancies contribute to higher maternal morbidity and mortality rates.[10]

Moreover, policies also tie into cultural context such as in the form of sex education in schools being 'abstinence-only' or 'comprehensive'.[8] At an individual level these taboos result in reduced access to health services, impact mental health, result in inadequate menstrual hygiene management, and are a barrier to sexual and reproductive autonomy. Various research studies highlight how stigma acts as a barrier for adolescents seeking care at sexual health clinics. This leads to higher rates of untreated sexually transmitted diseases (STDs) and unintended pregnancies, as shown in a study by Baigry et al. focusing on Pacific Island countries and territories.[8,11]

MSF has taken the initiative to tackle these taboos at multiple levels, in various communities. Sex workers in San Pedro Sula are shackled by social stigma and a lack of inclusive services to access medical and psychological care - MSF clinics served as a "blessing" for many, catering to prevention and control of STDs, family planning, psychological help etc.[12]

Additionally, in Zimbabwe, teenage pregnancy is a taboo. These young girls have no access to appropriate information, and have minimal say in decisions about their body. To address this,

MSF formed the Teen Mums' Club to facilitate conversation and provide information to teenage girls in the same boat, with lessons about contraception, safe sex, and pregnancy.12

Between 20-40% births are unintended, there are 50 million induced abortions out of which about 20 million are done in an unsafe manner, 600 thousand women die annually due to pregnancy related complications, and STDs are on the rise with 333 million new cases each year.[13] Thus, globally, SRH is compromised and the lack of attention poses multiple challenges in the form of increasing maternal mortality, poor health and marginalization of women and girls - deeming utmost attention and care.

Vaccination Tendency

Effective provision of vaccines is one of the cornerstones of MSF's strategies to combat rampant preventable diseases. In 2023 alone, MSF administered 4,623,700 routine vaccines globally.14 In spite of the cost-effectiveness and success of vaccines, there are numerous barriers to their provision, including but not limited to logistical challenges and vaccine hesitancy in treating populations, which varies across different cultures.[14]

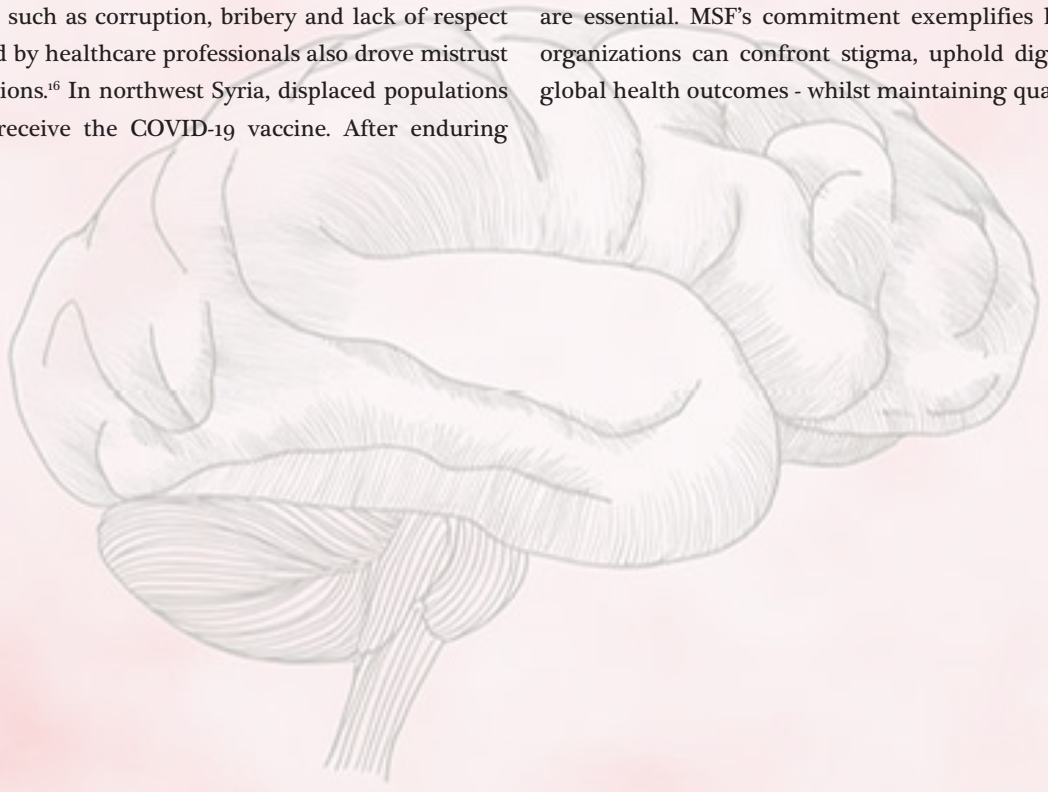
A study on vaccine hesitancy in a population in Yaoundé, Cameroon, identified vaccine hesitancy in 26% of parents/guardians.[15] The oral polio vaccine was the most affected, with the primary underlying cause of this being a lack of trust. This was less prevalent in wealthy households compared to poorer households.[15] Another study on medical mistrust identified that in sub-Saharan Africa, skepticism towards preventative healthcare measures stemmed from a culture and deep history influenced by colonialism. Additional factors, such as corruption, bribery and lack of respect when being treated by healthcare professionals also drove mistrust in African populations.[16] In northwest Syria, displaced populations were hesitant to receive the COVID-19 vaccine. After enduring periods of fear, violence, and hunger, they did not they did not feel the imminent life-threatening risk of the virus, nor experienced the need for the vaccine.[17]

During MSF's measles vaccination program in Tillabéri, Niger[18] and the distribution of COVID-19 vaccines in northwest Syria[17], MSF additionally dispatched health promotion teams. Through community engagement and outreach, they combatted vaccine hesitancy by highlighting their importance and dismantling misconceptions.

The factors and cultural beliefs that influence vaccine hesitancy are multifaceted and complex. For this reason, the administration of vaccines accompanied by educational measures highlighting their importance and dismantling fears of adverse effects is crucial in ensuring the effectiveness of vaccine campaigns.[15]

Conclusion

To conclude, cultural taboos and social stigma significantly impact mental health, sexual and reproductive care, and vaccine acceptance, creating barriers to treatment, eroding trust in healthcare, and fostering misinformation. These challenges hinder equitable access to quality care and leave communities vulnerable to preventable health crises. MSF's culturally sensitive, community-centred approaches address these issues by integrating mental health services, challenging sexual health taboos, and combating vaccine hesitancy through education and advocacy. These efforts provide immediate relief and drive long-term change by normalizing critical health conversations and dismantling misconceptions. To ensure sustainable progress, further research and tailored interventions are essential. MSF's commitment exemplifies how humanitarian organizations can confront stigma, uphold dignity, and improve global health outcomes - whilst maintaining quality medical care.



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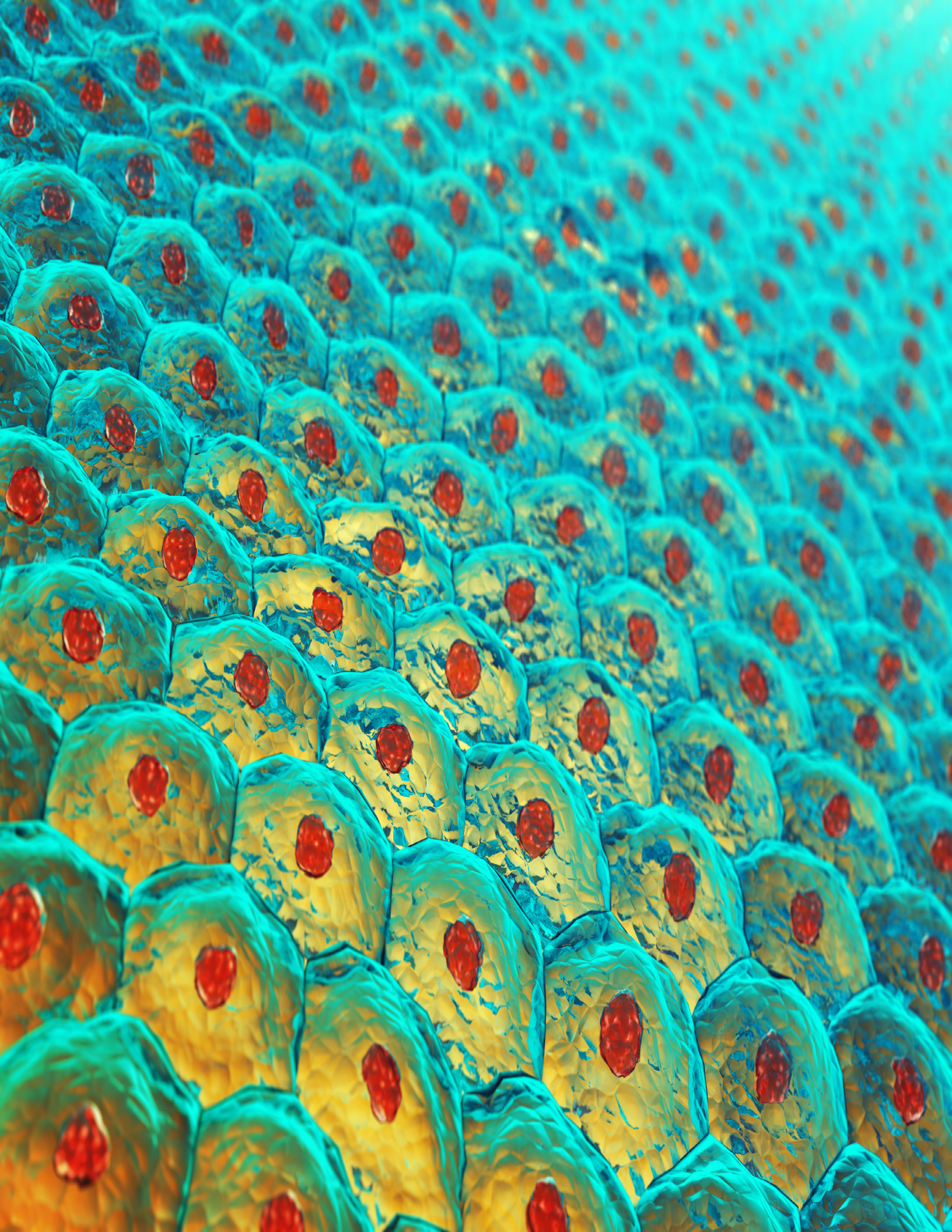

Exploring the Biopsychosocial Impact of Recalcitrant Eczema in a 13-Year-Old Patient: A Case Report

GHUFRAN BANDER, ALEXANDER JOHNSON, NORA SKURIDINA, & MAHEEN JUNAID
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https://doi.org/10.33178/SMJ.2025.1.18

Abstract

INTRODUCTION: A 13-year-old female patient presents with a complex case of severe eczema ongoing for over a year. This case report integrates the biopsychosocial model, focusing on the biological, psychological, and social determinants affecting flare onset and guiding the treatment plan.

METHODS: Consent was obtained from the patient and her mother. A comprehensive review of the patient's medical file, including past medical and surgical history, family, and social history was conducted. A multidisciplinary approach drawing on opinions from dermatology, primary care, and social work, was used to optimize treatment.

RESULTS: Through a biological perspective, the patient has widespread excoriation and lichenification throughout the body, likely attributed to hormonal changes associated with menarche and family history. Psychologically, the patient described a shift from her previously calm demeanor to a more agitated and anxious state. Socially, the patient reports social withdrawal and the stigma associated with her flares.

DISCUSSION: This case highlights the importance of incorporating the biopsychosocial model when treating severe and relapsing cases of eczema in pediatric populations. Dealing with chronic, worsening flares, as reported in the case, highlights the vital need for a multidisciplinary approach to address the emotional and physical impacts.

CONCLUSION: The patient's case represents a common pediatric presentation in general practice and illustrates the necessity of incorporating the biopsychosocial model when addressing treatment options for chronic skin conditions such as eczema.

Introduction

One of the main principles in primary care is treating patients with a holistic approach. While several models have been developed to improve patient outcomes, the biopsychosocial model has shown superior outcomes and a stronger doctor-patient relationship.1 First introduced by George Engel in 1977, this model marked a major shift in the treatment of chronic diseases by emphasizing the interplay of biological, psychological, and social dimensions in health and healing.1 In Ireland, skin conditions account for 15-20% of cases encountered daily in general practice.2 Many of these skin conditions have a biological basis that is closely linked to mental health, stigma and long-term social isolation. Therefore, understanding and applying the biopsychosocial model is crucial to enhance patients' quality of life.

Recent literature continues to support the biopsychosocial model in managing chronic conditions in pediatric populations, particularly where psychosocial stressors exacerbate biological symptoms. For example, a study on pediatric sickle cell disease found that parenting stress is influenced by a combination of child pain frequency, missed school days, and caregiver mental health, underscoring the need for comprehensive care approaches.3

Case Background

A 13-year-old female Irish-Caucasian patient with treatment-resistant eczema presented to general practice in Mallow.

FROM A BIOLOGICAL PERSPECTIVE, the patient began experiencing severe, itchy, episodic flares on the face and body since menarche, which worsened over 12 months. These episodes are likely attributed to both immunological and genetic factors.

FROM A PSYCHOLOGICAL PERSPECTIVE, the patient reports persistent daytime fatigue as her eczema has affected her quality of sleep. This fatigue has negatively impacted her performance in school and increased irritability and anxiety.

FROM A SOCIAL PERSPECTIVE, the patient reports social anxiety and withdrawal due to a lack of confidence in her body image. This has led her to avoid certain activities such as shopping with her family and participating in physical education classes.

Case Details

PRESENTING COMPLAINT

A 13-year-old female presents with severe, episodic flares of eczema, unresponsive to topical treatments, persisting since the onset of menarche 12 months ago. These flares are characterized by intense pruritus and a widespread distribution across the face and body, and have significantly impacted her self-esteem and daily activities. She previously had eczema as a toddler, which resolved by age four with topical treatments.

FAMILY HISTORY

Family history reveals a strong predisposition to atopic conditions, including asthma in her father and younger sister.

PAST MEDICAL HISTORY

The patient's medical history is significant for other atopic conditions, including asthma and hay fever.

PREMORBID BEHAVIOR

The patient states that “since the flares started, I am not the same person I used to be.” She reports increased agitation and withdrawal, in contrast to her previously energetic and happy personality.

ENVIRONMENTAL AND SOCIAL FACTORS

The patient reports having a supportive family and school counselor; however, she experiences a sense of isolation as she struggles with her flares, leading to increased withdrawal and concern about peer judgment. This is further highlighted by her avoidance of physical education classes to prevent exposing her skin, which suggests underlying social anxiety and concerns about stigma.

CURRENT MANAGEMENT

Her treatment regimen includes topical therapies coupled with antihistamines and inhalers. She was admitted for one week at the South Infirmary Victoria University Hospital to begin treatment with Methotrexate at 10mg that was later reduced to 7.5mg due to deranged liver function tests (LFTs).

Clinical Findings

PHYSICAL EXAMINATION

Severe eczema affecting the limbs, torso, legs, and face. On examination, there is diffuse facial erythema resembling a sunburn, along with widespread excoriation and lichenification, particularly on the legs and ankles. Lesions are non-purulent and non-edematous.

LABORATORY FINDINGS

Routine blood test was normal. LFTs were normal.

Biological Considerations

There is a complex interplay of genetic, hormonal, and immunological factors. A strong family history of atopic conditions is noted, as her father and younger sister both have asthma, coupled with her own past medical history of asthma and hay fever. This suggests a hereditary component closely linked to atopy.5 The onset of the patient’s symptoms coinciding with menarche suggests the possibility of hormonal influence. Hormones such as estrogen and progesterone can play a role in the pathogenesis of eczema, as they impact the integrity of the skin barrier.5 Additionally, the patient’s episodic history of widespread excoriations, lichenification, and intense pruritus could indicate a skewed immunological profile.6 Particularly, an overactive Th2 response has been linked to eczema, as it can lead to chronic inflammation and poor wound healing.6 This immunological dysfunction is the basis for systemic therapies for eczema, such as methotrexate, which is an effective treatment option7; however, the patient’s deranged LFTs underscore the challenges of balancing efficacy and safety in managing her condition.7

Psychological Considerations

From a psychological perspective, atopic dermatitis is associated with sleep disturbances and impaired daytime functioning, leading to compromised function and mood.8 The impact of sleep disruption on this patient is seen as she navigates through life challenges, like school and puberty. Frustration and anxiety are experienced by those with chronic skin conditions due to itching, discomfort, and perceived social stigma.9 This may further contribute to, or be exacerbated by, sleep disturbances, resulting in changes in behavior and social interactions.9

Moreover, the patient reports feeling agitated due to her perceived social stigmatization linked to her skin. She experiences difficulties coping with her condition, mentioning a loss of her previous “cheerful” identity. This shift can worsen her stress and reduce her quality of life, further contributing to the disease state.10 Additionally, she perceives her treatment-resistant eczema as a personal inadequacy and a drastic shift in her life, leading to feelings of frustration, social isolation, and diminished day-to-day life satisfaction.

Social Considerations

The patient’s struggles with her treatment-resistant eczema highlights the significant social challenges faced by

many patients with chronic dermatological conditions which can impact a patient's social interactions, their relationships, and ultimately their self-perception. There is also frequent stigma associated with visible chronic eczema, which can lead to bullying and social isolation as a result.11 In this case, the patient reports avoiding certain activities like shopping and physical exercise in order to hide her skin, which raises concerns about the long-term effects on her social development and peer relationships. This pattern of withdrawal is well-documented in patients with chronic skin conditions, particularly those that are visible.12

Peers may harbor negative perceptions, often incorrectly associating dermatological conditions with poor hygiene or contagiousness.13 Although this patient reports having a supportive family and access to a school counsellor, she expresses feelings of isolation, as she lacks someone who fully understands and shares her experiences. This feeling of perceived solitude is only further compounded by the disruptive nature of her flare ups. The stress of living with treatment-resistant eczema, combined with the repetitive frustration of ineffective treatment, can lead to a vicious cycle that negatively affects mental health.11,12

Conclusion

This case highlights the importance of the biopsychosocial model in managing chronic skin conditions in the pediatric population. A multidisciplinary team, including dermatologists, primary care physicians, and school counselors, is essential to improve psychological and social outcomes for childhood skin conditions.9

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Conference Abstracts

NEUROVISION 2024 Abstracts

Walter E Dandy Neurosurgical Society (WEDNS) Student Chapter - Ireland

Date: June 26th, 2024

Location: Albert Hall, RCSI, 123 St. Stephen's Green, Dublin.

EVENT DESCRIPTION

The Neurovision Case Competition was an intercollegiate event open toall medical students in Ireland with an interest in neurology and neurosurgery. Students submitted abstracts describing a case of personal interest, and the most promising entrants were invited to present their case in a head-to-head battle judged by a panel of Irish neurosurgeons, as well as a live audience. The competition was organized by a committee comprised of students from medical schools across Ireland.

ACKNOWLEDGEMENTS

Event Organizers - Dandy Ireland Committee

George-Paul O'Byrne - Y3 - GEM University of Limerick
Michael O'Connor - Y4 - GEM RCSI
Arianna Gholami - Y3 - GEM RCSI
Jaifar Alomairi - Y4 - GEM RCSI
Samin Abrar - Y4 GEM - University College Cork
Michael O'Connor - RCSI
Jaifar Alomari - RCSI

RCSI Surgical Society

Mohammad Alabdulrahman - Y4 GEM - University College Cork
Mohammed Alrtam
Arianna Gholami - Y3 GEM - RCSI

Photographers

Dr. Ailish Bradley - HSE Intern - University College Cork
Dr. Lena Dablouk - HSE Intern Cork - University Hospital

Judges

Ms. Suzanne Murphy - Neurosurgical Registrar - Temple St Children's Hospital
Dr. Jack Henry - Neurosurgical SHO - Cork University Hospital

A Rare Case Of Paediatric Meningioma

JUDITH ESTHER LINARES GOMEZ
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COMPETITION WINNER
https://doi.org/10.33178/SMJ.2025.1.19

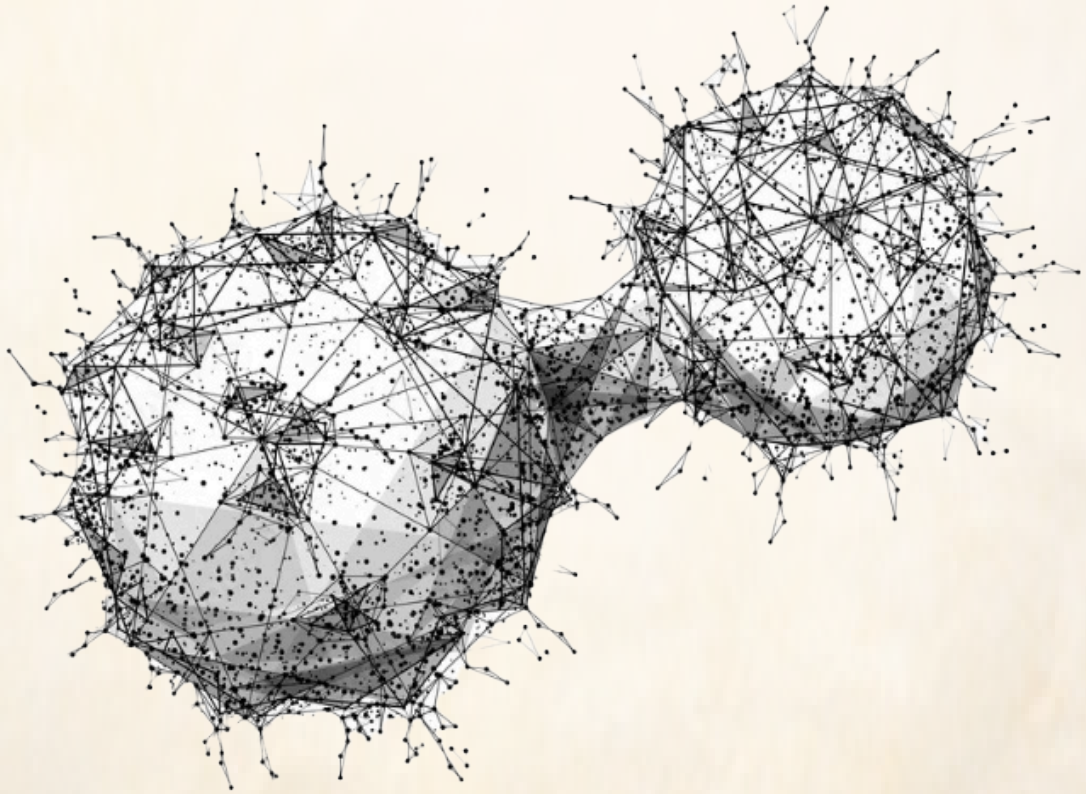
Abstract

BACKGROUND: Meningiomas are arachnoid cell-originating tumours which rarely present in the paediatric population. Characteristic symptoms include focal or generalised seizures, although many patients are asymptomatic. These tumours are commonly seen in patients suffering from neurofibromatosis type 2, and almost half of patients presenting with meningiomas have allele losses in the DAL-1 and NF2 genes.

CASE DESCRIPTION: A 3-year-old female patient presented with a bony protuberance on the apex of her cranium. As part of her investigations, computed tomography imaging was performed, which showed a large intracranial calcified mass arising from the falx cerebri in the interhemispheric fissure, invading the overlying bone. As part of her treatment, a complete resection of the tumour was done, along with the surrounding dura mater and the overlying bone in June of 2023. During the postoperative recovery period, the patient developed an infection in the dural graft and cranioplasty with a cerebrospinal fluid leak. This was managed by the patient undergoing a staged cranial reconstruction 10 months after her original operation, with hopes of discharging her on the first anniversary of her original resection surgery.

CONCLUSION: We present an atypical case of paediatric meningioma originating from the falx cerebri and a review of literature which explores the occurrence of meningiomas in the paediatric population, its aetiology, presentation and management. The final objective of the surgery should be tumour resection using the Simpson Grade and management using systemic approaches such as mTOR inhibitors or antiangiogenic treatments have also shown promising results.

KEYWORDS: Meningioma, paediatric brain tumour, paediatric meningioma, complete resection, staged cranial reconstruction.



Visualizing Facial Distortions In Prospometamorphopsia

RHIEYA RAHUL
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https://doi.org/10.33178/SMJ.2025.1.20

Abstract

BACKGROUND: Prosopometamorphopsia is a specific type of visual distortion where patients perceive distortions when viewing the faces of others. It is an extremely rare condition, with less than 100 cases being reported since 1904. Not to be confused with prosopagnosia which is a condition in which patients cannot recognize faces, in prosopometamorphopsia patients can still identify faces even while being distorted. The cause of this is unknown, however this case in particular sheds more light on the condition and the potential aetiology behind this condition. Lesions in the posterior section of the corpus callosum, specifically the splenium have been linked to visual distortions (prosopometamorphopsia) and reading difficulties such as alexia.

CASE DESCRIPTION: This case explores a 62 year old right handed Caucasian male presenting with alexia and prosopometaphoprasia affecting the lower part of the face after suffering an infarction in the left splenium of the corpus collosum. The patient reported distorted perception specifically of people's mouths while other facial features appeared normal, he also reported difficulty in reading but his writing remained unaffected. The patient's opthalmic examination revealed normal visual acuity, color vision and ocular motility with no apparent abnormalities on retinal examination. Neuroimaging disclosed a late subacute infarction in the left splenium which is crucial for the interhemispheric transfer of visual information and is a part of the Papez circuit involved in memory function.

CONCLUSION: The findings from this case emphasize the importance of comprehensive neuroimaging in patients who present with unusual combinations of visual and cognitive disturbances.

Intracranial Vein of Galen Malformations and Its Management

JUBRAN AL-BALUSHI
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https://doi.org/10.33178/SMJ.2025.1.21

Abstract

BACKGROUND: Vein of Galen Malformation (VOGM) is a rare congenital arteriovenous malformation affecting the paediatric population, characterized by a fistula between the diencephalon and a dilated vein of Galen.

CASE DESCRIPTION: This report presents the case of a 6-month-old male infant referred for developmental delays and abnormal head circumference. Clinical examination revealed macrocephaly, dilated scalp veins, and neurological abnormalities. Neuroimaging, including CT, MRI and MRA, confirmed a large VOGM with associated hydrocephalus. Furthermore, an echocardiography revealed a high-flow cardiac murmur, confirming the hemodynamic impact of the VOGM. A multidisciplinary team devised a treatment plan involving a combined transvenous and trans-arterial endovascular embolization method using a "kissing microcatheter technique" and ventriculoperitoneal shunt placement. Postoperative recovery showed improvement in neurodevelopmental milestones and reduced head circumference. VOGM management requires a comprehensive approach, including early diagnosis, precise imaging, and timely intervention.

CONCLUSION: This is a novel case because the interventional radiology speciality approach demonstrates the optimum diagnostic and preplanning investigations for cases of vascular origin. In addition, the kissing microcatheter endovascular embolisation technique highlights the importance of considering this innovative surgical option in complex vascular cases.

KEYWORDS: Paediatric Intracranial Vein of Galen Malformation, trans-arterial endovascular embolization, kissing microcatheter technique.

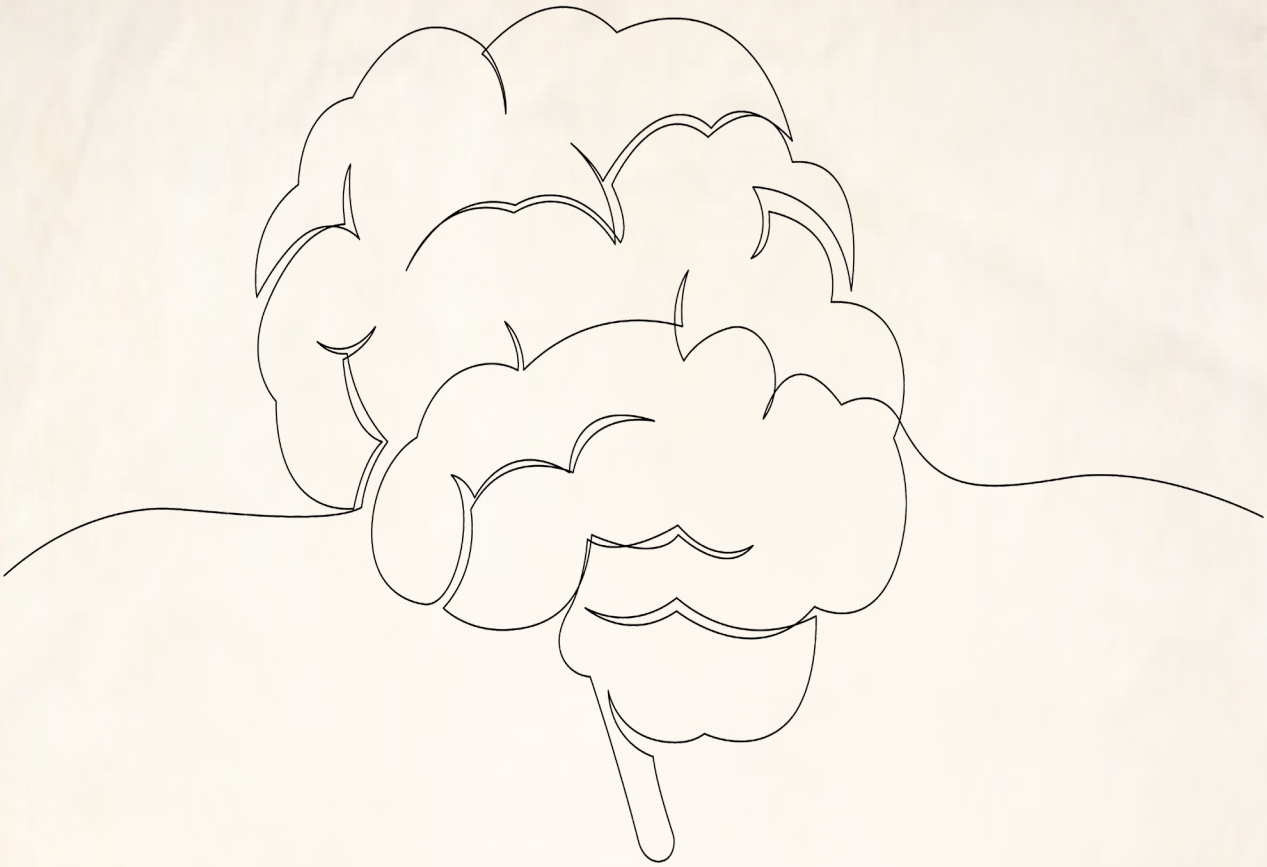
A Rasmussen Encephalitis in an Adolescent Girl

SHREYA SANKAR
2nd Year MBBS Student, Royal College of Surgeons Ireland (RCSI), Dublin
https://doi.org/10.33178/SMJ.2025.1.22

Abstract

INTRODUCTION: A 12-year-old female presented to clinic with various features of cognitive decline, including headaches, worsening academic performance, and decline in writing abilities and social skills. On neurological examination, she was found to have intrinsic muscle weakness in the right hand, reduced grip and wrist extension of the right arm, pronator drift of the right arm, and left hemiglossal atrophy, along with lessened spontaneous speech abilities. She had no dysarthria, sensory loss, or reduction of tone. The differential diagnoses considered for this patient were chronic viral encephalitis and autoimmune encephalitis. Initial tests included serology (Full Blood Count and IgG Antibody) and cerebrospinal fluid (CSF) analysis, both of which were unremarkable. Angiography results were also normal. Magnetic Resonance Imaging (MRI) depicted left cerebral hemisphere atrophy and T2 hyperintensity in the frontal lobe. Electrophoresis and flow cytometry were not indicative of oligoclonal bands or NMDA-receptor antibodies. Most interestingly, routine EEG did not demonstrate epileptic activity (the hallmark sign of RE), but right-sided amplitude predominance indicated left hemispheric dysfunction. Surgical intervention involved a biopsy of the anterior middle frontal gyrus. The biopsy depicted CD45+ T-cell lymphocyte infiltration, microglial nodules, cortical atrophy, neuronal loss, and cytomegalic dysplastic neurons, which altogether are indicative of Rasmussen Encephalitis. The patient was started on immunosuppressive therapy, including tacrolimus, methylprednisolone, and Intravenous Immunoglobulin (IVIG). 6-month follow-up demonstrated interval progression of atrophy, and 15-month follow-up demonstrated improvement in right extremity strength. Immunosuppression was continued, and the patient continues to be seizure- free with no further worsening of cognitive abilities.

KEYWORDS: Paediatric Rasmussen encephalitis, immunosuppressive therapy.



A Retelling of the First Successful Treatment of Total Posterior Craniopagus

AURA ILOVAN
1st Year MBBS Student, Royal College of Surgeons Ireland (RCSI), Dublin
https://doi.org/10.33178/SMJ.2025.1.23

Abstract

INTRODUCTION: The case of the first total posterior craniopagus twins in the Central African Republic highlights the complex challenges and remarkable outcomes in paediatric neurosurgery, particularly in resource-limited settings.

OBJECTIVES: The twins underwent a meticulous separation process at Bambino Gesù Hospital in Rome. A three-step separation was performed in order to construct two independent venous systems—the first part involving the separation of the tent and the first of the two common transverse sinuses. The second surgery scheduled was the separation of the upper sagittal sinuses and the junction point of the cerebral venous sinus, with the use of a neuronavigation. The final operation performed was the separation of the second transverse sinus and its tentorium and the reconstruction of the brain envelope. In total, the three-part surgery was spread over the time frame of 13 months.

CONCLUSION: The results of this surgery reaffirm that early surgical intervention combined with post- operative care and rehabilitation can optimise outcomes for complex congenital conditions. It also emphasises the importance of detailed pre-surgical planning, advanced imaging techniques, and a multidisciplinary approach in achieving a successful separation. Finally, this case underscores the critical role of neuroplasticity in children, where the brain's remarkable ability to reorganise and adapt facilitates recovery post-surgery. Neuroplasticity was pivotal for the twins' cognitive and motor development, resulting in a favourable clinical prognosis and quality of life.

Medical Research and Technology Society's Student Research Conference

Date: March 22nd, 2025

Location: Western Gateway Building, Western Road, Cork

EVENT DESCRIPTION

The Student Research Conference, hosted annually by the Medical Research and Technology (MRT) Society, is a student-led medical research conference which brings together research being conducted at the undergraduate level into place to demonstrate the wide variety of skills and cutting edge research being performed at UCC. Through oral and poster presentations, keynote speakers, and mentorship opportunities, the SRC allows students to gain valuable experience in research dissemination while enhancing their skills in research methodology, statistical analysis, and scientific communication. By uniting students, faculty, and researchers under the shared goal of advancing medical and scientific knowledge, the Student Research Conference stands as a cornerstone event at UCC that embodies the values, mission, and objectives of the MRT Society.

ACKNOWLEDGEMENTS

Event Organizers - MRT Society Committee

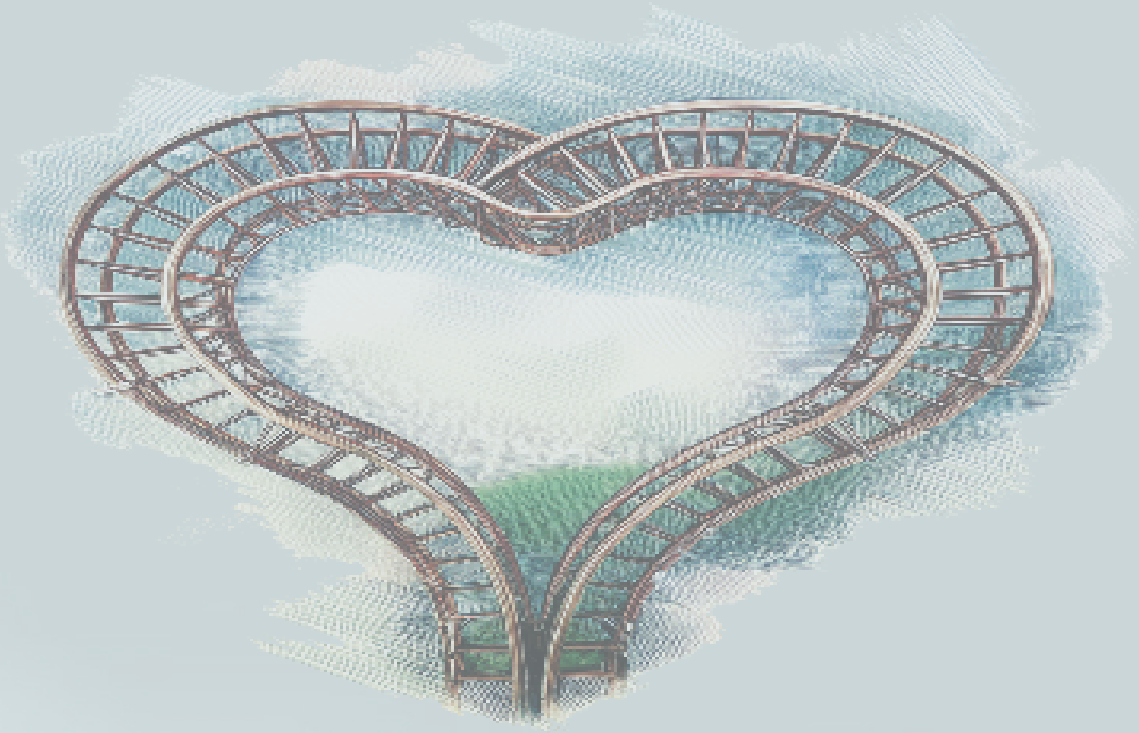
Wesley Chorney - SRC Lead
Kimya Ghaffarian - SRC Officer
Sten Kajitani - SRC OCM

Keynote Speakers

Dr. Gabriella Rizzo - Clinical Tutor, UCC & Specialist in Infectious Diseases
Prof. Jack Gleeson - Professor of Oncology, UCC & Consultant Medical Oncologist, CUH
Prof. Roisin Connolly - Professor Gerald O'Sullivan Chair in Cancer Research, UCC & Medical Oncologist, CUH
Prof. Brian Sweeney - Honorary Clinical Professor, UCC & Consultant Neurologist, Bon Secours Hospital Cork

Judges

Prof. Gerard Clarke - Professor of Neurobehavioural Science in the Department of Psychiatry and Neurobehavioural Science
Dr. Barry Boland - Researcher & Lecturer in the Department of Pharmacology and Therapeutics
Shobha Mehta, MSc
Pádraig Cronin



Amusement Park Rides and Cardiac Devices: Heart Dropper or Device Stopper?

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https://doi.org/10.33178/SMJ.2025.1.24

Abstract

BACKGROUND: Cardiac implantable electronic devices (CIEDs) are essential for managing cardiac conditions, but may malfunction due to magnetic fields >10,000mG. Roller coasters using linear induction motors (LIMs) generate magnetic fields, yet their potential for electromagnetic interference (EMI) with CIEDs is unclear. This study assesses magnetic field exposure on amusement rides and examines healthcare provider recommendations.

METHODS: Magnetic field strength was measured using gaussmeters placed at shoulder and abdomen levels, representing pediatric CIED sites. Rides at an amusement park were tested at least four times, recording median and maximum magnetic field strengths per second throughout the ride. Magnetic field strengths were compared between rides with health advisory messages (HAMs) and without (NHAMs). A survey was distributed to the Pediatric and Congenital Electrophysiology Society (PACES) and the Canadian Council of Cardiovascular Nurses to assess healthcare provider recommendations.

RESULTS: A total of 15 rides were sampled: 11 with HAMs and 4 with NHAM. The median magnetic field strength was higher for HAM rides (2.9mG) than NHAM rides (1.6mG; p=0.05). Maximum field strength was also greater in HAM rides (46.4mG vs. 6.5mG; p<0.001), and in rides using LIMs (n=2) compared to those using other mechanisms (211.7mG vs. 7.8mG; p<0.001). Only 18.1% (n=13) of healthcare providers relied on published resources for amusement park ride recommendations, while 58.3% (n=42) advised patients to consider HAMs.

CONCLUSION: Magnetic field strengths on all rides were clinically insignificant, posing minimal EMI risk for CIED patients. Further validation and standardized guidelines are needed to inform healthcare recommendations for patients with CIEDs.

Predictive Markers for Treatment Response in Metastatic KRAS-mutant Non-Small Cell Lung Cancer.

EMILY RYAN, DEARBHAILE COLLINS
https://doi.org/10.33178/SMJ.2025.1.25

Abstract

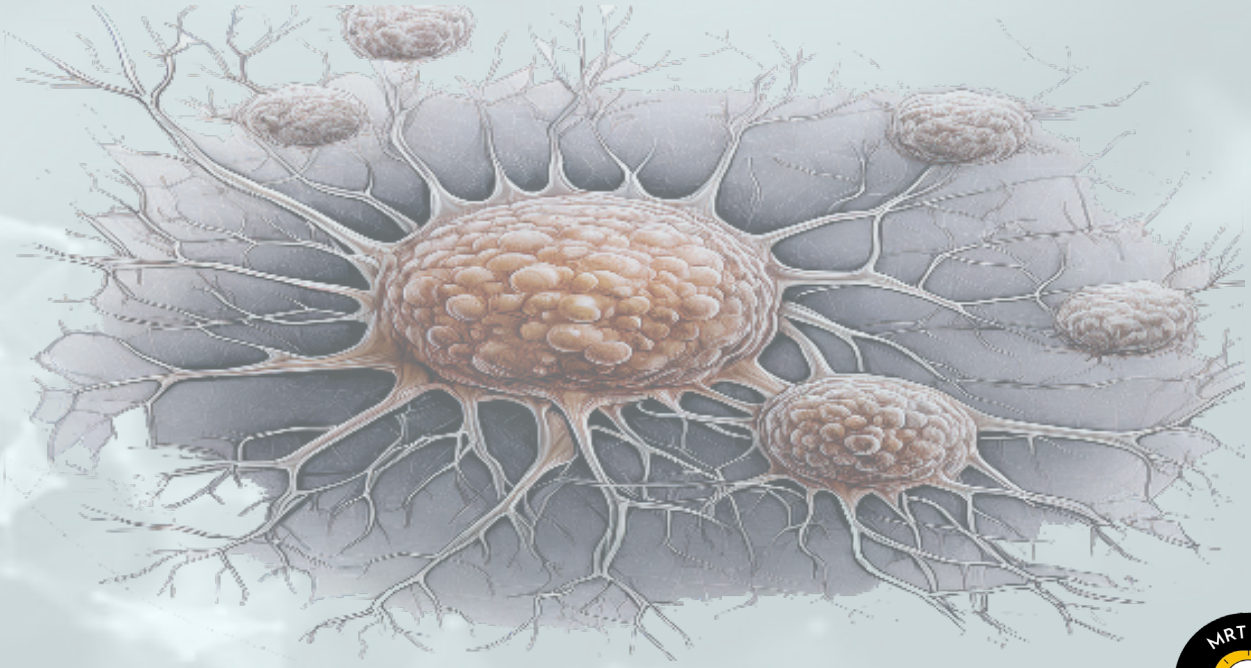
BACKGROUND: Non-small-cell lung carcinoma (NSCLC) represents 85% of all lung cancer cases, with Kirsten Rat Sarcoma Virus (KRAS) being the most commonly detected mutation.

AIMS: This study retrospectively reviews patient charts and databases to identify specific markers linked to favorable and poor responses to treatment in a tertiary care setting.

METHODS: Pre-treatment hematological, pathological, and biochemical data were gathered from 70 patients diagnosed with KRAS--mutant NSCLC at Cork University Hospital between January 1, 2017, and December 31, 2021. Patients were categorized by radiological response to treatment and progression-free survival (PFS). Statistical analysis was performed using SPSS v29, with parametric data expressed as mean (SD) and nonparametric data as median [IQR]. T-tests, Chi-squared tests, and Mann-Whitney U tests were employed, with a significance level of $p < 0.05$.

RESULTS: The average age of patients was 66 years (10.2), with an age range of 36-86 years. The median PFS was 36 weeks [74.5], and overall survival (OS) was 55.6 weeks [88.3]. Patients with progressive disease (PD) had higher levels of neutrophils ($p = 0.015$), neutrophil-to-lymphocyte ratio (NLR) ($p = 0.04$), and platelet-to-lymphocyte ratio (PLR) ($p = 0.026$) compared to those with partial response (PR) to treatment. Patients with poor PFS showed increased platelet counts ($p = 0.047$, 95% CI [-112.3, -0.796]), NLR ($p = 0.001$), and PLR ($p = 0.004$), as well as reduced serum albumin ($p = 0.022$, 95% CI [1.06, 13.25]) and lymphocytes ($p = 0.010$, 95% CI [0.121, 0.879]) in comparison to those with good PFS. KRAS mutation subtype and tumor pathology had no significant effect on treatment response. Chemotherapy treatment was associated with significantly longer PFS compared to other treatment types ($p < 0.001$).

CONCLUSION: Certain patient-specific biomarkers were associated with poorer radiological response to treatment and reduced PFS. These biomarkers could be useful for clinicians when assessing treatment plans and for prognostication of these patients.



Hypertensive Disorders In Pregnancy and Cognitive outcomes in childhood and adolescence.

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Abstract

BACKGROUND: Hypertensive disorders in pregnancy (HDP), including preeclampsia, have been linked to lower cognitive scores in offspring, but findings remain inconsistent. This study examines the relationship between maternal HDP and cognitive development in offspring aged 3–17 years.

METHODS: We conducted a cohort study using data from the UK Millennium Cohort Study (2001). Maternal HDP was examined as an exposure factor in relation to children's cognitive abilities, including verbal and visuospatial outcomes. Cognitive delay was defined as scoring >1 SD below the mean and classified as "never delayed," "delayed only once," "persistent delay," "early childhood delay," or "adolescent onset delay."

RESULTS: Among 5,994 singleton pregnancies, 460 were affected by maternal HDP. Mothers were primarily aged 30–39 years (51.6%) and predominantly Caucasian (86.2%). Adjusted odds ratios (OR) controlled for maternal characteristics (age, ethnicity, BMI, alcohol use, smoking, education, income) and offspring gender. No significant association was found between maternal HDP and verbal delay at 3 years (OR: 1.008, 95% CI: 0.783–1.297), 5 years (OR: 0.864, 95% CI: 0.659–1.133), or 7 years (OR: 1.034, 95% CI: 0.800–1.336). Similarly, visuospatial delay at 7 years (OR: 0.863, 95% CI: 0.679–1.097) and adolescence (14 years: OR: 0.871, 95% CI: 0.688–1.101; 17 years: OR: 1.069, 95% CI: 0.856–1.336) showed no significant association.

CONCLUSION: Maternal HDP does not appear to significantly impact offspring cognitive development. Further research with larger cohorts is needed.

Reaching the 6-hour target: a comparative analysis of patient characteristics and outcomes in the emergency department.

KELSEY TIMONEY
https://doi.org/10.33178/SMJ.2025.1.27

Abstract

OBJECTIVES: Prolonged Emergency Department (ED) visits lead to overcrowding, compromising safe provision of care. To improve patient outcomes, the Emergency Medicine Programme for Ireland set a national target that 95% of ED attendees should be admitted or discharged within 6 hours. This study aims to define the characteristics of patients attending the ED and compare these characteristics for patients whose episode of care was or was not concluded within the 6-hour target.

DESIGN, SETTING & PARTICIPANTS: A cross-sectional study was conducted at Cork University Hospital (CUH), a level one major trauma centre. A total of 2,166 adult patients (aged ≥ 16 years) were included from the iPatient Manager database.

RESULTS: Overall, 50.9% (n = 1,103) of patients had an episode of care lasting less than 6 hours. Over 75s were more likely to stay over 6 hours (n = 300, 68%). The most frequent presenting complaints were 'limb problems' (n = 218, 69%) under 6 hours and 'shortness of breath' (n = 73, 66%) over 6 hours. Most episodes of care concluded under 6 hours for self referrals and over 6 hours for 999 calls and GP referrals. Triage categories 1, 4 or 5 were more likely to stay in ED under 6 hours. Admitted patients were more likely to stay in ED over 6 hours (n = 606, 74%).

CONCLUSION: This study suggests national targets are not being met, indicating the need for better streamlined outpatient services and further resourcing for urgent care service planning and provision in the future.

Understanding the Impact of Palliative and Ablative Radiotherapy (RT) on Health-Related Quality of Life (HRQOL) in Patients with Metastatic Disease.

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https://doi.org/10.33178/SMJ.2025.1.28

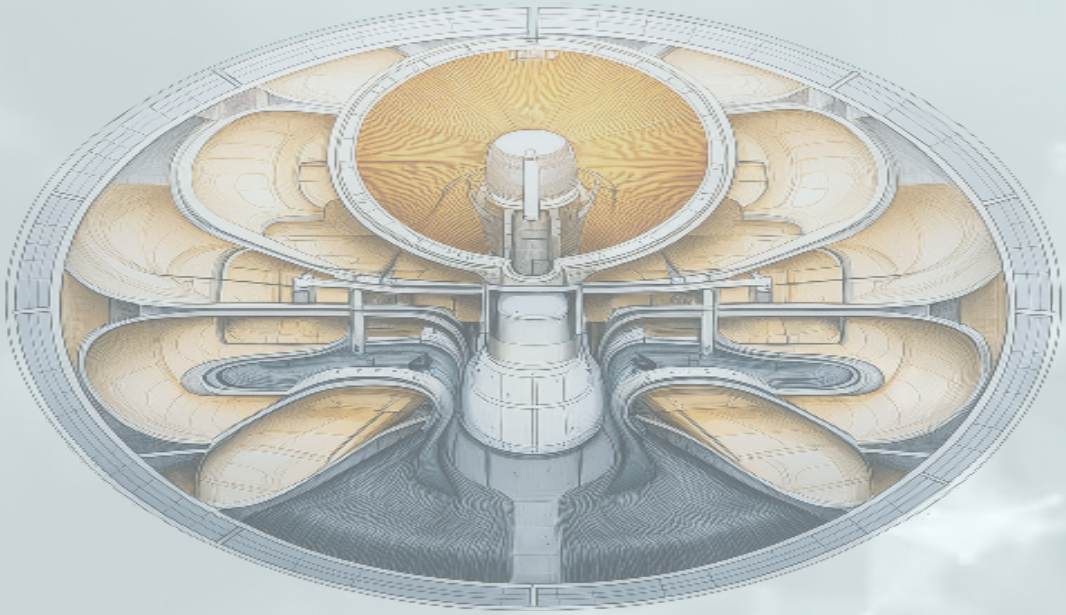
Abstract

BACKGROUND: Radiotherapy (RT) is an effective but underutilized treatment option for patients with metastatic cancer. While studies have examined RT's impact on health-related quality of life (HRQOL) internationally, there is limited data on Irish patients. Some research suggests aspects of quality of life may dip after RT but eventually return to baseline, though this varies depending on prognosis. Since healthcare systems, cultural factors, and socioeconomic conditions differ across countries, these findings may not be easily generalizable to the Irish population. This study aims to explore the feasibility of the use of electronic patient-reported outcomes (ePROs) to assess HRQOL in Irish patients receiving palliative or ablative RT.

METHODS: This single-institution observational study at Cork University Hospital utilizes the ePRO application, ONCOpatient, to administer pre-validated HRQOL questionnaires including the EORTC-QOL-C30, EORTC-QOL-C15 PAL, and EQ-5D-5L to patients or their caregivers via their smartphone at four-timepoints: baseline, final treatment, and 4- and 12-weeks-post-treatment. Descriptive statistics were used to summarize engagement and compliance. Longitudinal analysis will be conducted to evaluate HRQOL changes over time, and regression models will be used to identify predictors of HRQOL outcomes.

RESULTS: From October 2024 to March 2025, 22 participants were onboarded (mean age 63.23 years, 40.9% male, 59.1% female), with various cancer subtypes (breast n=7, lung n=5, renal n=3, other n=7). Overall app engagement was 54.5% (9/14 patients and 3/8 caregivers). Compliance declined over time: 40.9% at baseline, 25% at final treatment, 15% at 4-weeks post-RT, and 0% at 12-weeks post-RT. Barriers to app engagement included licensing issues, syncing delays and difficulty locating assessment dates. Limited provider engagement regarding patient identification and onboarding also presented challenges. Further results to follow.

CONCLUSION: This study highlights feasibility challenges in integrating ePROs for metastatic cancer patients receiving RT. While engagement was moderate, declining compliance indicates barriers to data collection. Addressing technical and app usability issues may improve long-term implementation. Future analyses will further assess HRQOL changes over time and identify predictors of patient-reported outcomes to enhance RT decision-making and patient-centered care.



Differences Between the Clinical Manifestation of Adult-onset and Childhood-onset Systemic Lupus Erythematosus.

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https://doi.org/10.33178/SMJ.2025.1.29

Abstract

INTRODUCTION: Systemic lupus erythematosus is a multi-system autoimmune disorder that affects approximately 1500 people in Ireland. The cause of SLE is multifactorial and involves genetic, environmental, and hormonal influences. Most commonly diagnosed in women (10:1) and between ages 15–44, international studies have shown differences between childhood-onset SLE (COS) and adult-onset SLE (AOS), however, no such research exists in Ireland.

METHODS: This retrospective cohort study analysed patient records from Cork University Hospital's (CUH) Rheumatology Department (November 2023-June 2024). A convenience sampling method was used, and eligible participants were identified from the hospital database of referral letters. Categorical variables of symptoms and autoantibodies were analysed using Fisher's exact test and logistic regression for significant findings.

RESULTS: A total of 71 patients (COS = 24, AOS = 47) were included in this study. The mean age at diagnosis was 28.01 ± 11.57 years. Malar rash was significantly more common in COS (17, 70.8%) compared to AOS (17, 36.2%). Polyarthritis/polyarthralgia was significantly more prevalent in AOS (43, 91.5%) than in COS (7, 70.8%). While autoantibody profiles revealed no significant differences, low complement C_4 levels were significantly more prevalent in COS (16, 66.7%) compared to AOS (15, 31.9%). Finally, Lupus Nephritis, while also insignificant, was also more prevalent in COS (11, 45.8% vs 17, 35.2%).

CONCLUSION: The higher prevalence of malar rash and complement deficiency in COS suggests a more pronounced immune response in younger patients. Although statistically insignificant, trends such as higher fever incidence increased lupus nephritis rates in COS highlight areas for further research. These findings increase the understanding of SLE in Ireland and underscore the importance of age-specific considerations in diagnosis and management. Future multicenter collaboration could offer deeper insights into regional variations and help refine treatment approaches.

A Rare Cause of Otalgia - Langerhans Cell Histiocytosis Case Report.

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Abstract

BACKGROUND: Langerhans Cell Histiocytosis (LCH) is a myeloid neoplastic disorder with a rare prevalence of one case per million adults. LCH has a complicated etiology that presents as lesions composed of proliferative 'LCH cells'. These lesions can affect different organ systems including the lungs, skin, liver, and bone. This study reports the steps toward LCH diagnosis in an adult, the current state of literature in regards to LCH of the temporal bone, and important takeaways for ENT physicians.

CASE REPORT: We describe the case of a 52 year old woman with a two year history of seemingly idiopathic Central Diabetes Insipidus (CDI) complaining of right otalgia for two weeks unresponsive to antibiotic therapy. The patient has a normal otoscopy and audiogram, and an elevated CRP test (22 mg/dl). Further investigations with CT and MRI confirmed destruction of the right mastoid air cells and enhancing tissue respectively. Cholesteatoma was ruled out with diffusion weighted imaging on MRI. Cortical mastoidectomy was performed and histopathological examination of biopsy confirmed the diagnosis of LCH. The patient has a final multisystem (Temporal bone and Pituitary gland) low-risk LCH diagnosis with a great prognosis through chemotherapy and corticosteroid treatment.

CONCLUSION: Temporal bone and craniofacial manifestations of LCH are often managed by ENT physicians. A plethora of pathologies present with otalgia in ENT practice, but symptoms such as CDI and otalgia with lack of findings on otoscopy should raise suspicion for LCH.

Lithium-Induced Cardiotoxicity Mimicking Acute Coronary Syndrome: A Case Report

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https://doi.org/10.33178/SMJ.2025.1.31

Abstract

INTRODUCTION: Lithium toxicity, a complication of chronic lithium therapy used in the treatment of bipolar disorder (BPD), commonly presents with gastrointestinal and neurological symptoms. However, rare cardiac manifestations of lithium cardiotoxicity can occur. This case describes a 51-year-old woman with BPD on long-term lithium therapy who developed neurological symptoms (confusion, resting tremor, dysarthria). Investigations were notable for elevated troponin levels and transthoracic echocardiogram revealed a novel reduced left ventricular ejection fraction. Coronary artery disease and other potential causes were ruled out, and lithium-induced cardiotoxicity was determined to be the etiology of the patient's presentation.

METHODS: A thorough clinical evaluation was conducted, including history, physical examination, and diagnostic testing. Investigations included an electrocardiogram (ECG), transthoracic echocardiogram (TTE), coronary angiography, chest X-ray, neuroimaging (CT and MRI brain), and blood tests (troponins, lithium levels, thyroid panel). The patient declined a CT angiogram of the head, leading to an alternative MRI assessment.

RESULTS: The patient presented to the emergency department with confusion, bilateral resting tremors, gait instability, and dysarthria. Non-contrast CT and MRI of the head ruled out hemorrhagic and ischemic stroke, respectively. Chest X-ray confirmed mild pulmonary congestion. ECG showed bradycardia with 1st-degree atrioventricular block and TTE revealed global systolic dysfunction with a reduced ejection fraction 35-40%. Laboratory findings indicated elevated high sensitivity troponin I of 105 ng/L. Coronary angiography showed no evidence of significant coronary artery disease. Lithium levels were elevated at 3.3mmol/L on admission. The patient remained conscious and interactive, with no indications for emergent hemodialysis. This resulted in the diagnosis of acute-on-chronic lithium neuro- and cardiotoxicity. Cardiac function improved with standard lithium toxicity management, including lithium cessation, IV hydration, and monitoring.

CONCLUSION: This case describes lithium-induced cardiotoxicity, a rare yet critical differential diagnosis in patients with suspected coronary artery syndrome in the context of lithium treatment. Unlike ischemic cardiac disease, it presents with global rather than regional myocardial dysfunction. Early recognition and lithium cessation are essential for management.

A Case Study on Suboptimal Asthma Control in a Pediatric Patient: Addressing Adherence and Caregiver Concerns

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https://doi.org/10.33178/SMJ.2025.1.32

Abstract

This case study presents an 8-year-old male patient, B.M., admitted to Cork University Hospital with symptoms of cough, wheezing, shortness of breath, and fever (38.5°C). With a history of recurrent asthma exacerbations requiring hospitalization, B.M. has suboptimal asthma control due to poor adherence to inhaled corticosteroids, primarily driven by parental concerns about potential side effects, such as growth stunting. His exacerbations are primarily triggered by viral infections, with recent exposure to a family member with a viral illness. Clinical examination revealed wheezing on expiration, prolonged expiration, and stable vital signs, suggesting a mild to moderate exacerbation.

The literature review highlights asthma as a prevalent pediatric condition, influenced by genetic, environmental, and immunological factors. Although not curable, the symptoms of asthma can be well controlled with effective treatment. However, as present in the case, adherence to asthma treatment remains a significant challenge, with one study reporting mean adherence rates as low as 36% to ICS in children –thus hindering the treatment effectiveness. Poor health literacy and side effect anxiety are two reasons for the poor adherence relevant to this case.

To tackle unique difficulties in adhering, the case emphasizes the importance of personalized asthma action plans (PAAPs), which are individualized plans catered to the patients needs/concern. Studies have shown that increased patient involvement in decision making regarding their health results in an increase in the effectiveness of care. It can be discussed with the patient's caregiver that although some research suggests that ICS may temporarily slightly impact growth, the benefits in preventing severe exacerbations outweigh these risks. This case emphasizes the importance for patient/caregiver engagement, healthcare literacy and tailored treatment plans to optimize asthma management in pediatric populations and prevent long-term consequences.

A Re-Audit of Polypharmacy Recognition in Older Patients on Admission to an Acute Hospital.

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Abstract

BACKGROUND: Polypharmacy has a high overall prevalence of approximately 37%. Left unrecognised, polypharmacy can increase the risk of drug-drug interactions and lead to prescribing cascades. Prompt recognition and management of polypharmacy is essential as it may represent a reversible cause of a patient's symptoms.

METHODS: A re-audit of polypharmacy recognition in Bantry General Hospital was performed. Patients were included if they were aged seventy-five years or older, prescribed 5 or more medications on admission and were in-patients during a 24-hour period on the 10th of September 2024. The presence or absence of polypharmacy as a diagnosis was recorded.

RESULTS: 25 patients were identified as eligible for inclusion. 17 male patients (68%) and 8 female (32%) were included. The median age was 82 years old and ages ranged from 75-99. Polypharmacy was included as a diagnosis in only one of the 25 patients' admissions (4%), this is a marginal increase from 0 (0%) in the previous audit. The mean number of medications observed was 8.76 (2.7% less than the previous audit). The number of medications prescribed ranged from 5 – 15. The maximum number of prescribed medications reduced from 21 to 15 in the re-audit.

CONCLUSION: Marginal improvements in the volume of polypharmacy and polypharmacy documentation were observed in this re-audit, however, further efforts are required to reduce this problem. It is important to recognise and document polypharmacy in older patients to reduce the potential for adverse outcomes.

Ramsay Hunt Syndrome Misdiagnosed as Bell's Palsy: A Case Report.

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https://doi.org/10.33178/SMJ.2025.1.34

Abstract

INTRODUCTION: Ramsay Hunt Syndrome (RHS) is a neurological disorder caused by the reactivation of latent varicella-zoster virus in the facial nerve. It often presents with ipsilateral facial palsy, otalgia, and vesicular eruptions. RHS is often misdiagnosed as Bell's palsy, which results in delayed treatment and increases the risk of long-term complications. This case highlights a 38-year-old male initially diagnosed with Bell's palsy whose symptoms persisted despite standard therapy. He later developed ear pain, discharge, vesicles, and gait instability, prompting a revised diagnosis of RHS.

METHODS: A comprehensive clinical assessment was conducted, including a detailed patient history, neurological and otologic examination, and laboratory investigations. Diagnostic imaging and serological tests confirmed varicella-zoster virus reactivation. The patient was treated with antiviral therapy (acyclovir), corticosteroids, and symptomatic pain management.

RESULTS: The patient initially presented with progressive facial nerve dysfunction refractory to Bell's palsy treatment, and subsequently developed vesicular ear lesions and balance disturbances. Examination revealed asymmetric facial weakness, inflamed auricular vesicles, and an unsteady gait. Laboratory results confirmed RHS. Following initiation of antiviral and steroid therapy, symptoms improved, though residual facial weakness persisted.

CONCLUSION: This case underscores the importance of early diagnosis of RHS in order to prevent long term complications. When diagnosing idiopathic Bell's palsy, RHS should be considered, particularly when new otologic symptoms emerge. Unlike Bell's palsy, RHS is associated with a lower rate of full recovery due to greater nerve degeneration. Clinicians should maintain a high index of suspicion for RHS in cases of persistent facial palsy, ensuring timely diagnosis and intervention in order to improve patient outcomes.

Proton Pump Inhibitors as Chemoprophylaxis Against the Progression of Barrett's Esophagus: A Literature Review.

TOUQA ABDELSAMAD, ALLY O'BRIEN DAVIS

https://doi.org/10.33178/SMJ.2025.1.35

Abstract

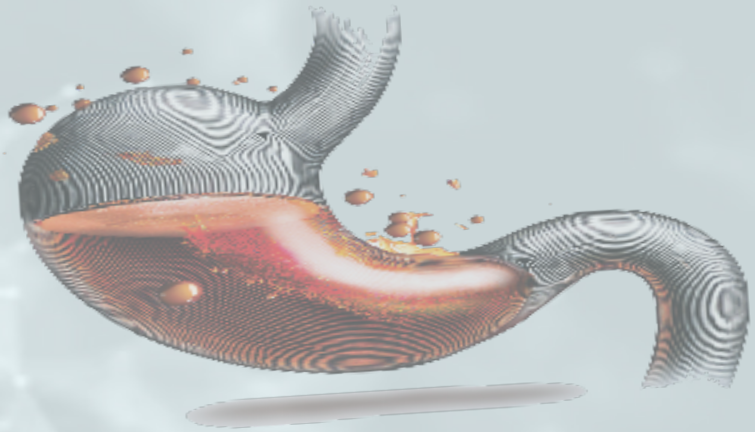
BACKGROUND: Barrett's Esophagus (BE) is a premalignant condition with a strong association with an increased risk of Esophageal Adenocarcinoma (EAC). Due to this established progression, management strategies focus on symptom control with acid suppression therapy via proton pump inhibitors (PPIs), and endoscopic surveillance using advanced imaging techniques to detect neoplastic progression early, despite its small association with decreased mortality. These approaches emphasize early detection rather than preventing malignant transformation. A case described in The New England Journal of Medicine highlights a 56-year-old obese man with a 4-cm segment of non-dysplastic BE who was managed with PPIs for reflux control and endoscopic surveillance. This case exemplifies a key gap in standard clinical practice - BE management relies on PPIs and surveillance rather than chemoprevention. Given this, optimizing PPI dosage as a targeted pharmacological intervention could offer a minimally invasive alternative to more resource-intensive endoscopic interventions, reducing procedural burden on healthcare systems. However, the role of PPIs in chemoprophylaxis remains unclear, necessitating further investigation into their efficacy in preventing neoplastic progression.

OBJECTIVES: Evaluate the efficacy of PPIs as a chemopreventive strategy by establishing the optimal dosage and duration required and assess whether PPIs, either alone or in combination with other pharmacological agents will effectively interrupt the progression of BEs from high-grade dysplasia to EAC.

METHODS: To address this gap, a systematic search was performed using PubMed with MeSH terms. Exclusion and inclusion filters were applied, yielding 49 articles. Studies focusing on PPI use alone or with other pharmacological agents were prioritised with title/abstract screening conducted to assess eligibility. This generated the 14 articles used in this review.

RESULTS: The literature review found strong evidence supporting the chemopreventive role of PPIs in the neoplastic progression of Barrett's esophagus (BE). Long-term PPI use has been shown to reduce the risk of high-grade dysplasia and esophageal adenocarcinoma (EAC), with some studies even demonstrating a significant reduction in all-cause mortality and neoplastic progression in BE patients. The greatest benefit was observed at higher PPI doses, and this was further enhanced combined with NSAIDs or statins, suggesting potential synergistic chemopreventive properties. Despite these promising findings, variability in individual patient responses, coupled with concerns regarding the long term risk of PPI therapy, has fueled ongoing debate about the safety and efficacy of prolonged use. This confers the need for a tailored, individualized approach to BE chemoprophylaxis strategies. These findings highlight the necessity for updated clinical guidelines to optimize PPI dosing, treatment duration and potential adjunctive therapies in the prevention of BE progression.

CONCLUSION: The available evidence suggests that while long-term, high-dose PPI therapy may be an effective chemopreventive strategy, its ability to completely prevent neoplastic progression remains uncertain. Future research should focus on determining the optimal PPI dosage, duration, and potential synergistic effects with other chemopreventive agents. Simultaneously, standardizing these approaches through refined treatment protocols could improve clinical practice and help reduce the burden of EAC.



Melatonin as a Reactive Treatment for Post-operative Delirium in Patients in the Cardiac ICU: A Retrospective Cohort Study.

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https://doi.org/10.33178/SMJ.2025.1.36

Abstract

INTRODUCTION: ICU delirium is a significant problem in post-operative cardiothoracic patients, contributing to prolonged ICU and hospital stays and increased mortality. Current pharmacological treatments, such as benzodiazepines and antipsychotics, have notable adverse effects, leading to interest in safer alternatives. A systematic review has shown melatonin's effectiveness as a prophylactic agent for delirium in surgical and ICU patients. This study aims to assess the use of melatonin as a reactive therapeutic agent in post-operative delirium in cardiac ICU patients.

METHODS: This retrospective cohort study analysed data from 127 patients diagnosed with delirium, confirmed through a positive CAM-ICU score. Patients were divided into two groups: one that received melatonin (n=57) as part of their delirium management and another that did not (n=70). The primary outcome was delirium regression, measured by a negative CAM-ICU score during the ICU stay. Secondary outcomes included ICU length of stay, hospital length of stay, and duration of mechanical ventilation. Statistical analyses included the Mann-Whitney U test for continuous variables, the Chi-square test for categorical variables, and binomial regression analysis to determine predictors of delirium regression.

RESULTS: Delirium regression was slightly lower in the non-melatonin group (23/57, 32.9%) compared to the melatonin group (24/70, 42.1%), though this difference was not statistically significant (p=0.356). Binomial regression revealed an odds ratio of 0.845 (95% CI: 0.329-2.172, p=0.727) for melatonin's effect on delirium regression. Statistically significant predictors of delirium regression included ICU length of stay (1.126, 95% CI: 1.041-1.219, p=0.003) and mechanical ventilation (0.897, 95% CI: 0.833-0.965, p=0.004).

CONCLUSION: Melatonin showed a loose association with delirium regression but did not demonstrate significant effectiveness as a reactive treatment for post-operative delirium in cardiac ICU patients. Larger studies with more controlled environments are needed to better assess its potential as a treatment for ICU delirium.

Impact of Opioid-Free Anaesthesia on Postoperative Opioid Consumption: A Systematic Review and Meta-Analysis

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https://doi.org/10.33178/SMJ.2025.1.37

Abstract

BACKGROUND: The main objective was to assess the effects of opioid-free versus opioid-based anaesthesia on postoperative opioid use.

METHODS: A systematic review and meta-analysis were conducted using MEDLINE, SCOPUS, Cochrane Library, Web of Science, and Embase. Inclusion criteria consisted of randomised control trials published from 2004–2024 on adult surgical patients undergoing opioid-free or opioid-based general anaesthesia. Studies with regional anaesthesia, ICU, or pregnant patients were excluded. The primary outcome measure was postoperative opioid consumption at 24 hours. Subgroup analysis was performed on studies measuring the postoperative period as 1-3 hours, 12 hours, 24 hours, and 48 hours. Secondary outcome measures were postoperative nausea and vomiting, Post-Anaesthesia Care Unit discharge time, and pain scores. The Cochrane Risk of Bias (RoB-2) tool assessed the risk of bias, and a meta-analysis was performed using Cochrane RevMan software.

RESULTS: The search included 26 RCTs with 2,370 patients undergoing various surgeries, predominantly gastric bypasses, and cholecystectomies. The patients varied in age, BMI, and ASA grade. Opioid-free anaesthesia was associated with a decrease of 11.55 [18.91, 4.20] mg oral morphine equivalents postoperatively. There was also a statistically significant decrease in postoperative nausea and vomiting (RR=0.62 [0.55, 0.71]), and pain scores (0.49 [0.83, 0.15]) in the opioid free anaesthesia group. PACU discharge time was slightly longer in the opioid free group (5.32 [0.11, 10.53] minutes).

DISCUSSION: Our systematic review and meta-analysis found a decrease in postoperative opioid consumption in those receiving opioid-free anaesthesia versus opioid-based anaesthesia. We also found that opioid-free anaesthesia can decrease postoperative nausea and vomiting and pain scores. These findings suggest that opioid-free anaesthesia can improve patient outcomes. Limitations include variability in opioids between studies, extrapolated dosage conversions, and non-opioid analgesic use. High heterogeneity across analyses reflects these differences.

Hyperlipidaemia in Primary Care: Management Challenges for GPs and Patients

JAGATJIT GARHA, DIARMUID QUINLAN

https://doi.org/10.33178/SMJ.2025.1.38

Abstract

OBJECTIVES & AIM: This project aims to assess the management of patients with hyperlipidaemia in a General Practitioner (GP) setting. The project will evaluate current care practices, identify gaps in care, and explore barriers to delivering patient care.

DESIGN: This was a cross-sectional study involving a retrospective review of patient data and an interview with the clinic GPs.

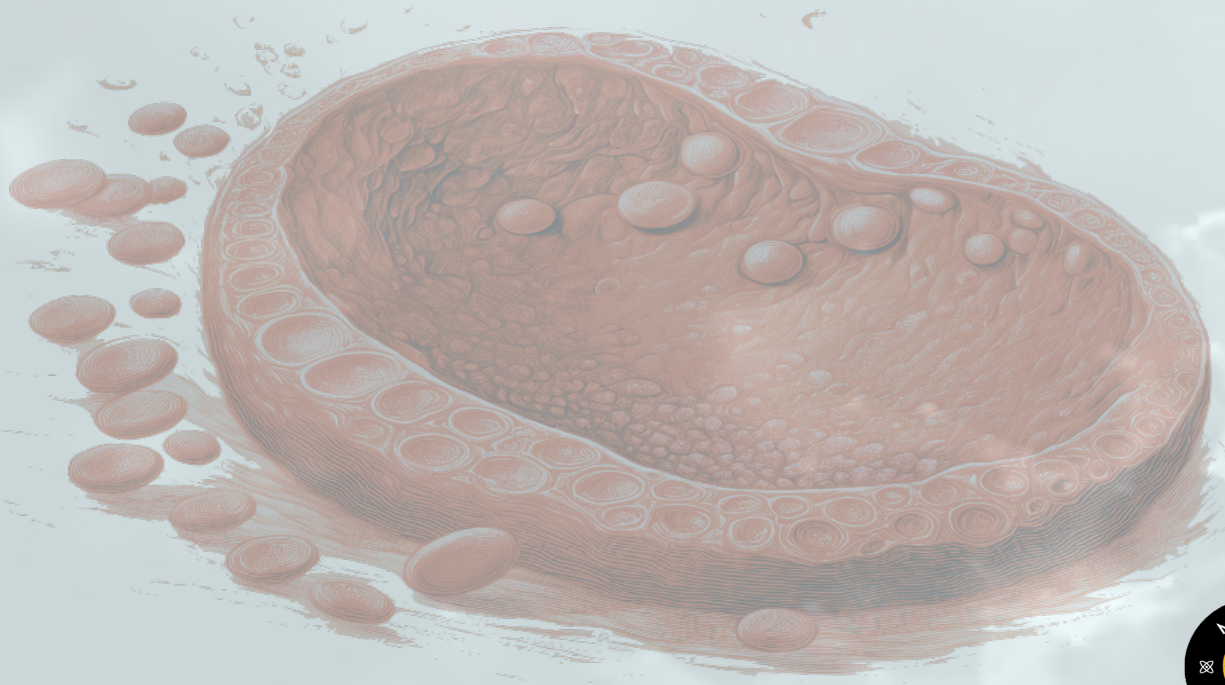
SETTING: The project was conducted at Woodview Family Doctors clinic, in Glanmire, Co. Cork, Ireland.

PARTICIPANTS SELECTION & CRITERIA: The study included 70 patients aged 50-55 years with a diagnosis of hyperlipidaemia, identified through elevated lipid panel results (LDL-C ≥ 4 mmol/L). Participants were randomly selected from the patient lists of seven GPs at the clinic, 10 patients each.

PRIMARY & SECONDARY OUTCOMES: The study primarily assessed patient health and care as determined by relevant factors including total cholesterol, LDL-C, HDL-C, triglycerides, smoking and drinking status, BMI, adverse cardiovascular events, and referral to dietician or cardiologist. Secondary outcomes explored via interviewing the clinic GPs were barriers to delivering optimal patient care.

RESULTS: The baseline data was assessed in regard to the number of patients with Max LDL > 2.6 mmol/L, Max Chol > 5.17 mmol/L, and BMI > 25, which were present in over 27% of males and females. All other risk factors were found to be present or above advisable levels in less than 27%. The interview with GPs also revealed significant barriers to effective hyperlipidaemia management, including limited consultation time, patient non-compliance, and resource constraints. A review of literature showed that statin therapy was questionable in efficacy.

CONCLUSION: This study highlighted substantial challenges in managing hyperlipidaemia in a GP setting. Despite adherence to guidelines, practical barriers hinder optimal care. Future initiatives should focus on addressing these barriers through targeted and personalized interventions and measuring long-term outcomes through follow-up.



Generative AI's performance on emergency medicine boards questions: observational study

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Abstract

BACKGROUND: The evolving field of medicine has introduced ChatGPT as a potential assistive platform, though its use in medical board exam preparation remains debated [1-2]. This study aimed to evaluate the performance of a custom-modified version of ChatGPT-4, tailored with emergency medicine board exam preparatory materials (Anki deck), compared to its default version and previous iteration (3.5) [3]. The goal was to assess the accuracy of ChatGPT-4 answering board- style questions and its suitability as a tool for medical education.

MATERIALS & METHODS: A comparative analysis was conducted using a random selection of 598 questions from the Rosh In--Training Exam Question Bank [4]. The subjects of the study included three versions of ChatGPT: the Default, a Custom, and ChatGPT-3.5. Accuracy, response length, medical discipline subgroups, and underlying causes of error were analyzed.

RESULTS: Custom ChatGPT-4 did not significantly improve accuracy over Default ($p>0.05$), but both significantly outperformed ChatGPT-3.5 ($p<0.05$) (Table 1). Default produced longer responses than Custom ($p<0.05$). Subgroup analysis showed no significant difference across medical sub-disciplines ($p>0.05$). ChatGPT-4 had a 99% probability of passing, while ChatGPT-3.5 had 85%.

	Custom ChatGPT-4 (n=598)	Default ChatGPT-4 (n=598)	Default ChatGPT-3.5 (n=269)
Number of Correct Questions	481	480	169
Correct (%)	80.4	80.3	62.8

Table 1. The performance of 3 language models on American Emergency Board Exam using Rosh Review.

CONCLUSIONS: The findings suggest that while newer versions of ChatGPT exhibit improved performance in emergency medicine board exam preparation, specific enhancements do not significantly impact accuracy. The study highlights the potential of ChatGPT-4 as a tool for medical education, capable of providing accurate support across a wide range of topics in emergency medicine.

Research on Antibiotic Producing Bacteria in Irish Soil

JONE MARTINEZ, JUNE NARAVAITE & CONOR SHANAHAN
https://doi.org/10.33178/SMJ.2025.1.40

Abstract

For the past decade, the School of Microbiology of University College Cork has conducted an annual project with Antibiotics Unearthed, which aims to isolate and study antibiotic-producing bacteria from soil environments. The Small World Initiative and Tiny Earth Project were established globally in 2015 to encourage biologists and STEM students to participate in active research against infectious diseases and aid in antibiotic discovery. Both programs aim to integrate student learning into fields of research that address the crisis of dwindling supply of antibiotics.

The Microbiology society within the EU established Antibiotics Unearthed, inspired by Small World Initiative, to provide training and support in order to continue this important research and raise awareness about AMR. This project was conducted over the course of 6-8 weeks of research at a third- year undergraduate level. This poster presents data from 3 out of over 40 students on a small-scale research project.

Management of Neonatal Abdominal Immature Teratoma in a Resource-Limited South African Hospital: A Case Report

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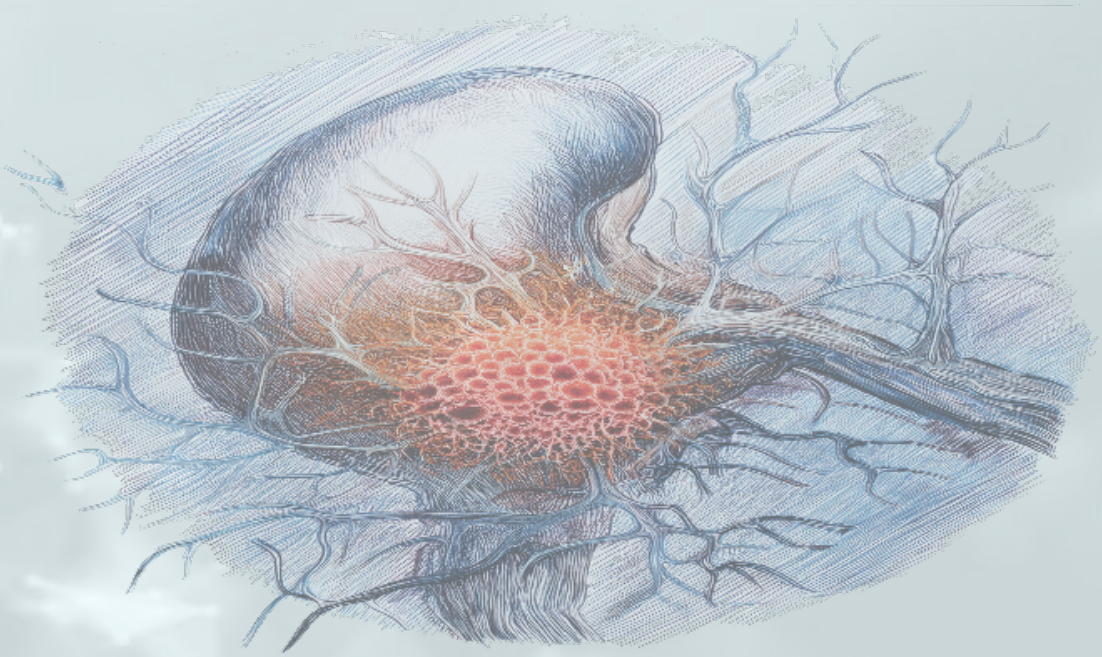
Abstract

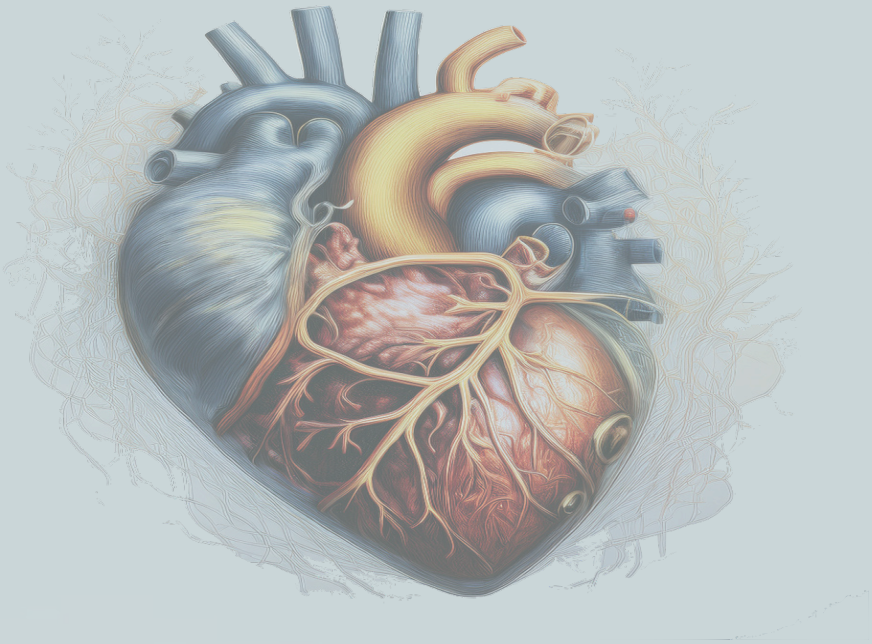
INTRODUCTION: Abdominal immature teratomas, rare congenital tumors, primarily originate from the gonads but can also present in extragonadal locations. Typically identified prenatally, these tumors carry a high risk of in-utero complications, often leading to fetal demise. This case report details the successful management of an abdominal immature teratoma in a neonate at a resource-limited hospital in South Africa, highlighting unique treatment adaptations for such complex cases in low-resource settings.

METHODS: A 28-day-old neonate with abdominal distention underwent initial imaging, revealing a heterogeneous mass in the left retroperitoneum. Following a multidisciplinary evaluation, the patient was initially managed with chemotherapy based on a differential diagnosis including neuroblastoma. However, a biopsy confirmed an immature teratoma, necessitating a shift in management to surgical resection. The neonate underwent a left nephrectomy and excision of the tumor, followed by postoperative intensive care to address complications from both chemotherapy and surgery.

RESULTS: The patient faced significant challenges, including nosocomial infections, neutropenic sepsis, and respiratory issues requiring prolonged ventilation. Despite these obstacles, the tumor was successfully excised, and postoperative complications were managed with targeted therapies, including antibiotic and antifungal treatments, blood transfusions, and hemodynamic support. The patient's condition stabilized postoperatively, and she is currently stable.

CONCLUSION: This case demonstrates the feasibility of managing complex congenital tumors like abdominal immature teratomas in resource-limited settings. Multidisciplinary collaboration and flexible treatment protocols were essential to achieving a positive outcome. The case offers valuable insights into adaptable management strategies that may be applied in similar cases within low-resource environments, expanding the understanding of congenital tumor care in underserved regions.





When STEMI Isn't STEMI: A Case of Severe Aortic Stenosis Masquerading as Acute Coronary Syndrome.

NOORALHUDA ALSHAMI AND ZAINEB HAMZA

Internal medicine society Case competition Abstract 1
https://doi.org/10.33178/SMJ.2025.1.42

Abstract

BACKGROUND: Aortic stenosis (AS) is a progressive valvular heart disease that, in severe cases, can present with angina, syncope, and heart failure. Severe aortic stenosis can mimic acute coronary syndromes but rarely presents with ST-elevation myocardial infarction (STEMI)-like features, which presents a diagnostic challenge. This case emphasizes the importance of considering valvular pathology in patients with ischemic ECG changes and non-obstructive coronary arteries.

CASE PRESENTATION: We describe a 69-year-old female who presented to the emergency department (ED) with acute chest pain, progressive dyspnea, and transient loss of consciousness episodes. Her medical history included Type II diabetes mellitus, hypertension, hypercholesterolemia, and a history of smoking. Initial electrocardiography (ECG) revealed ST-elevation in leads V_2-V_5, prompting concern for anterior STEMI. However, a coronary angiogram showed non-obstructive coronary disease, and bedside transthoracic echocardiography confirmed the presence of severe AS.

INVESTIGATIONS & DIAGNOSIS: The patient's physical examination findings included an S_4 gallop, a grade III-IV harsh systolic ejection murmur radiating to the base, and bibasilar crackles. Laboratory investigations revealed an elevated N-terminal pro-brain natriuretic peptide (NT-proBNP) level of 290 pg/mL, with otherwise normal blood counts and urinalysis. Echocardiographic Doppler imaging demonstrated heavily calcified aortic valve leaflets, ventricular hypertrophy, increased left atrial volume, and elevated right-sided pressures consistent with critical AS.

MANAGEMENT & OUTCOMES: The patient was initially managed for a STEMI with dual antiplatelet therapy before echocardiographic findings led to a shift in diagnosis and management thereafter. Once severe AS was identified, an intra-aortic balloon pump was inserted, which resulted in rapid disease improvement. She subsequently underwent aortic valve replacement (AVR), and was symptom-free at 8 weeks.

DISCUSSION & CONCLUSION: This case underscores the importance of considering AS as a differential diagnosis in patients presenting with STEMI-like ECG findings, particularly in those without significant coronary artery disease. Echocardiography is pivotal in distinguishing AS from myocardial infarction, preventing unnecessary thrombolysis or percutaneous interventions. The definitive treatment for severe AS remains AVR, either via surgical or transcatheter approaches. Clinicians should maintain a high index of suspicion for valvular heart disease in atypical STEMI presentations to ensure timely and appropriate intervention.

Immunosuppression, a Double-Edged Sword: Sepsis, Skin Cancer Risk, and Potential Multiple Sclerosis Stabilization.

MIHIKA MULL AND ILEESHA SINGH
Internal medicine society Case competition Abstract 2
https://doi.org/10.33178/SMJ.2025.1.43

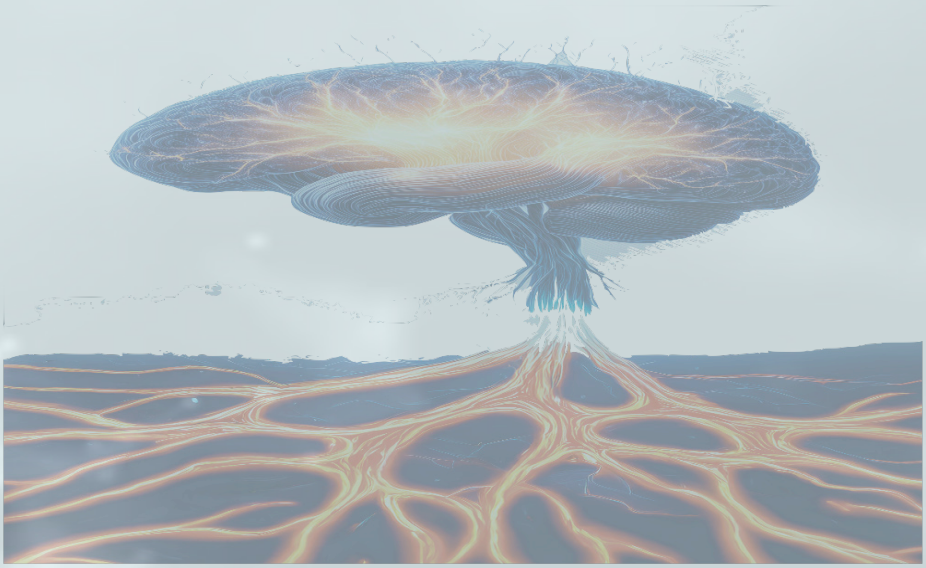
Abstract

BACKGROUND: Immunosuppression remains an essential component in post-transplant care but carries significant risks, including infection and malignancy. However, post-transplant immunosuppressants may have a role in stabilising multiple sclerosis (MS), despite not being first-line therapy.

CASE PRESENTATION: A 65-year-old female with a history of autosomal dominant polycystic kidney disease and associated polycystic liver disease underwent a deceased-donor renal transplant in 1998. Her long-term maintenance immunosuppressive regimen included tacrolimus, low-dose prednisolone, and azathioprine (discontinued in 2024). She was diagnosed with MS in 1990. In July 2024, she was hospitalised for sepsis, with an enhancing hepatic cyst being the presumed source. Blood cultures grew Enterococcus faecium, which was treated with IV vancomycin. This occured on the background of recurrent gram-negative bacteraemias and non-melanoma skin cancers since 2020. These complications were attributed to long-term immunosuppression. Nonetheless, her MS has remained clinically stable for over 20 years. She reported no relapses or neurological deficits, and an MRI in September 2024 showed no new demyelinating lesions.

DISCUSSION: This case highlights the double-edged nature of immunosuppressive therapy. While tacrolimus and azathioprine are associated with increased risk of infections and malignancies, particularly skin cancers, they may also modulate autoimmune neuroinflammation. Although evidence for tacrolimus use in MS treatment remains limited, some studies suggest possible neuroprotective effects. Conversely, while azathioprine has shown potential benefits in relapse reduction in controlled trials, further research is needed to establish its full utility in MS management. Short-term high-dose prednisolone is effective in acute exacerbations but lacks evidence for long-term MS stabilisation.

CONCLUSION: This is a unique case of long-term immunosuppressants resulting in recurrent severe infections and malignancies, yet coinciding with sustained MS stabilisation. This raises the hypothesis that certain non-first-line agents may contribute to MS modulation, warranting further investigation.



Thank you to MRT Society Members

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