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Union Health Minister Shri Jagat Prakash Nadda Addresses 23rd Convocation Ceremony of NBEMS in New Delhi

The Union Health Minister expressed satisfaction that NBEMS qualifications have emerged as symbols of quality, excellence and trust in medical education. He noted that the NBEMS brand today commands national recognition for producing highly competent medical specialists dedicated to patient care and professional excellence.

Addressing the gathering, Shri J.P. Nadda, Union Health Minister, stated that the Convocation was not merely a ceremony for conferment of degrees, but a celebration of the dedication, perseverance and hard work of students, teachers and parents

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EDITORIAL

The Impact of National Healthcare Policies on Increasing NBEMS-Accredited Hospital Space & Improving Public Healthcare Outreach

Minu Bajpai[1,*] and Abhijat C. Sheth[2]
[1]*Vice-President & Honorary Executive Director, National Board of Examinations in Medical Sciences, New Delhi*
[2]*Chairman of National Medical Commission & President, National Board of Examinations in Medical Sciences, New Delhi*

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Over the past decade, India's healthcare reforms have increasingly recognised that expanding medical education capacity and improving healthcare access are interdependent goals. The policy ecosystem led by the Ministry of Health and Family Welfare has created favourable conditions for the expansion of accreditation by the National Board of Examinations in Medical Sciences, thereby strengthening both postgraduate medical education and healthcare service delivery. NBEMS accreditation has emerged as a strategic mechanism for converting service-delivery hospitals into training institutions, particularly in underserved regions.

*Corresponding Author: Minu Bajpai
Email: bajpai2b@gmail.com

Policy Shift: From Medical Colleges Alone to a Distributed Training Ecosystem

Historically, postgraduate medical education was concentrated in government and private medical colleges. National healthcare policies have increasingly promoted a broader training architecture by recognizing:

- District hospitals
- Corporate hospitals
- Trust hospitals
- Specialized institutions
- Public sector hospitals

as potential postgraduate training sites.

Impact on NBEMS Accreditation

- Significant increase in DNB and DrNB training institutions.
- Expansion of training opportunities beyond traditional medical colleges.
- Improved geographic distribution of specialty training.

Public Health Impact

- Specialists are trained closer to the populations they serve.
- Improved retention of healthcare professionals in non-metropolitan regions.
- Strengthening of secondary and tertiary care services.

Expansion of Medical Education Capacity Through National Policies

Several national initiatives emphasised increasing the healthcare workforce

Policy Drivers

- Expansion of postgraduate seats.
- Strengthening district hospitals.
- Promotion of competency-based education.
- Public-private partnership models.

NBEMS Contribution

NBEMS offers a flexible accreditation framework allowing hospitals with adequate patient load and faculty to become teaching institutions without requiring full-fledged medical colleges.

Outcomes

- Rapid expansion of postgraduate training capacity.
- Reduced dependence on conventional medical colleges.
- Enhanced utilization of existing healthcare infrastructure.

In the last 10 years, NBEMS accreditation has evolved from an educational mechanism into a powerful instrument of healthcare system strengthening.

National healthcare policies that expand accreditation opportunities simultaneously increase specialist training capacity, improve hospital quality, strengthen district-level healthcare services, and enhance public access to advanced medical care.

As India moves toward universal health coverage and a larger healthcare workforce, NBEMS-accredited hospitals will remain critical pillars linking education, service delivery, quality improvement, and public health outreach.

Every new NBEMS-accredited hospital is not merely a training centre—it is a multiplier of healthcare capacity, quality, and access for the nation.

District Hospitals as Academic and Service Hubs

NHM guidelines and recent healthcare strengthening initiatives have emphasised district hospitals as:

- Centres for secondary care.
- Training sites for doctors, nurses, and allied health professionals.
- Referral hubs within integrated healthcare networks.

Impact on Accreditation

NBEMS accreditation has enabled district hospitals to initiate:

- DNB programs
- Diploma programs
- Fellowship programs

Public Healthcare Benefits

- Improved specialist availability at district level.

- Reduced referral burden on tertiary hospitals.
- Lower out-of-pocket expenditure for patients.
- Enhanced emergency and trauma care services.

Ayushman Bharat and Increased Clinical Exposure

The implementation of Ayushman Bharat Pradhan Mantri Jan Arogya Yojana substantially increased access to secondary and tertiary care.

Impact on Accredited Hospitals

- Higher patient volumes.
- Greater case diversity.
- Improved opportunities for clinical training.

Educational Impact

NBEMS trainees gain exposure to:

- Complex disease management.
- Surgical procedures.
- Critical care services.
- High-volume clinical practice.

Public Outreach Impact

- More patients receive specialist care.
- Enhanced quality of treatment in accredited centres.

National Digital Health Ecosystem and Accreditation

The emergence of digital health initiatives has improved institutional readiness for accreditation.

Benefits for NBEMS Hospitals

- Electronic health records.
- Digital logbooks.
- Online assessments.
- Tele-education.
- Quality monitoring systems.

Public Health Impact

- Better continuity of care.
- Improved referral pathways.
- Enhanced data-driven quality improvement.

Emergency and Trauma Care Strengthening

Recent national initiatives to strengthen emergency and trauma care at district hospitals have created new opportunities for accreditation.

Emerging Areas

- Emergency Medicine
- Critical Care Medicine
- Trauma Surgery
- Anaesthesia
- Emergency Nursing

NBEMS Role

Accreditation provides:

- Structured specialist training.
- Faculty development.
- Quality assurance mechanisms.

Public Health Impact

- Better management of time-sensitive emergencies.
- Reduced mortality from trauma, stroke, cardiac emergencies, poisoning, and obstetric emergencies.

Public–Private Partnerships and Corporate Hospital Accreditation

National policies increasingly encourage public-private collaboration in healthcare delivery and education.

Advantages

Corporate hospitals often possess:

- Advanced technology
- High patient volumes
- Specialized expertise
- Strong quality systems

Impact on NBEMS Accreditation

- Significant expansion of DNB and DrNB seats.
- Development of super-specialty programs.
- Enhanced exposure to advanced clinical practice.

Public Healthcare Benefits

- Increased national specialist workforce.
- Dissemination of best practices across the healthcare system.

Strategic Outcomes for India

Healthcare Workforce

- Expanded specialist production.
- Increased availability of trained healthcare professionals.

Healthcare Access

- Enhanced access to specialty care outside metropolitan areas.

Quality

- Standardization of training and clinical practice.

Equity

- Reduced urban-rural disparities.

System Strengthening

- Integration of service delivery with education and research.

Improving Healthcare Outreach Through Academic Accreditation

A frequently overlooked benefit of accreditation is its impact on service quality.

Accredited hospitals are required to maintain:

- Faculty standards.
- Clinical protocols.
- Academic activities.
- Audits and quality assurance systems.

Result

Training requirements drive service improvements.

Public Impact

Patients benefit from:

- Better clinical governance.
- Evidence-based care.
- Improved patient safety.
- Continuous quality improvement.

Key takeaways:

1. Universal DNB Accreditation Pathway

All eligible district hospitals and large public hospitals should be encouraged to pursue NBEMS accreditation.

2. Explore Accreditation Incentivisation feasibility.

Provide financial and infrastructure support for first-time accredited institutions.

3. Integration with National Workforce Planning

Use NBEMS accreditation as a tool to address speciality shortages.

4. Digital Accreditation Platform

Create real-time monitoring of training quality, outcomes, and workforce deployment.

5. Academic Health System Model

Develop a national framework linking:

- **Medical colleges**
- **NBEMS hospitals**
- **District hospitals**
- **Corporate hospitals; into a unified academic healthcare network.**

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ORIGINAL ARTICLE

Accuracy of Estimated GFR: Addressing the Elephant in the Room

Nisha Jose,[1,*] Jayaprakash V,[2] Indhumathy E,[3] Thenmozhi Mani,[4] Venkatachalapathy E[5] and M Jayakumar[6]

[1]*Associate Professor, Department of Nephrology, Christian Medical College, Vellore, Tamil Nadu*
[2]*Professor, Department of Nephrology, SRM Medical College Hospital and Research Center (SRMIST), Kattankulathur, Chengalpattu, Tamil Nadu*
[3]*Professor, Department of Nephrology, Saveetha Institute of Medical Sciences, Kanchipuram, Tamil Nadu*
[4]*Department of Biostatistics, Christian Medical College, Vellore, Tamil Nadu*
[5]*Professor, Department of Nuclear Medicine, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu*
[6]*Professor, Department of Nephrology, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu*

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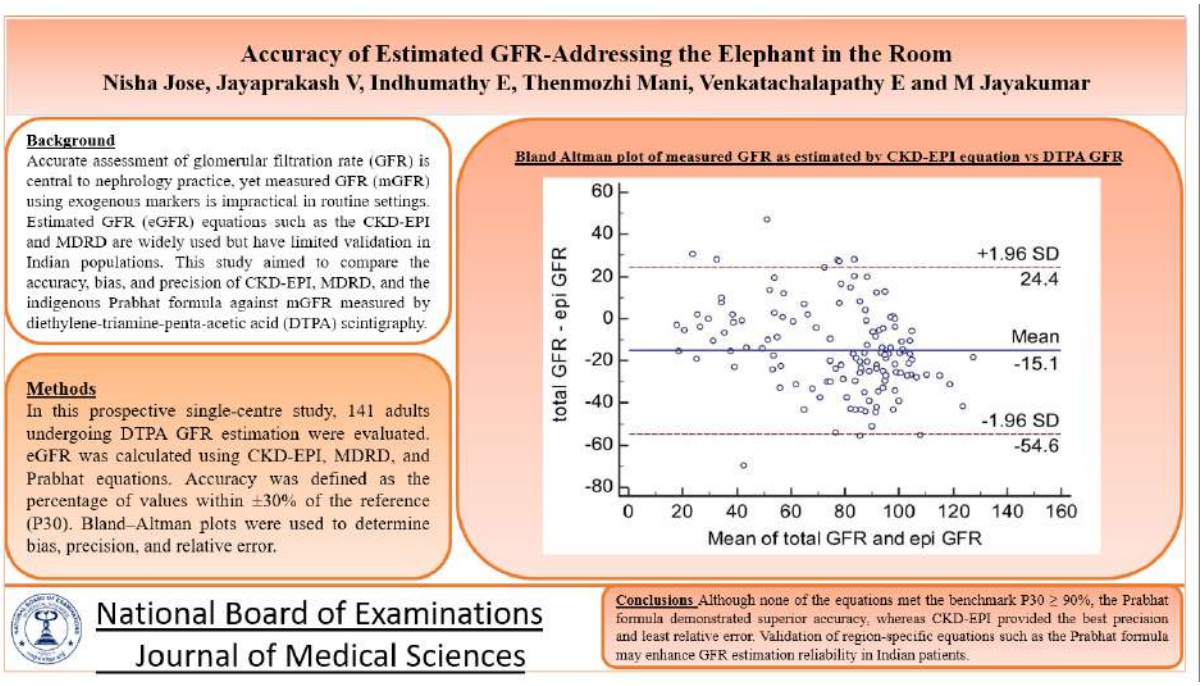
Abstract

Background: Accurate assessment of glomerular filtration rate (GFR) is central to nephrology practice, yet measured GFR (mGFR) using exogenous markers is impractical in routine settings. Estimated GFR (eGFR) equations such as the CKD-EPI and MDRD are widely used but have limited validation in Indian populations. This study aimed to compare the accuracy, bias, and precision of CKD-EPI, MDRD, and the indigenous Prabhat formula against mGFR measured by diethylene-triamine-penta-acetic acid (DTPA) scintigraphy. **Methods:** In this prospective single-centre study, 141 adults undergoing DTPA GFR estimation were evaluated. eGFR was calculated using CKD-EPI, MDRD, and Prabhat equations. Accuracy was defined as the percentage of values within ±30% of the reference (P30). Bland–Altman plots were used to determine bias, precision, and relative error. **Results:** The mean DTPA-GFR was 71.2 ± 23.5 mL/min. Mean eGFRs were 85.9 ± 29.4 mL/min for CKD-EPI, 83.9 ± 34.4 mL/min for MDRD, and 68.2 ± 26.4 mL/min for Prabhat. The Prabhat formula showed the highest accuracy (P30 = 74.6%), followed by MDRD (61.1%) and CKD-EPI (57.5%). Bias was lowest with Prabhat (2.5 mL/min), while CKD-EPI demonstrated the best precision (38.5). All three equations correlated strongly with DTPA-GFR (r = 0.65–0.73). **Conclusions:** Although none of the equations met the benchmark P30 ≥ 90%, the Prabhat formula demonstrated superior accuracy, whereas CKD-EPI provided the best precision and least relative error. Validation of region-specific equations such as the Prabhat formula may enhance GFR estimation reliability in Indian patients.

Keywords: eGFR, CKD-EPI, MDRD, Prabhat formula, DTPA, accuracy, bias, precision

*Corresponding Author: Nisha Jose
Email: josenisha2000@gmail.com

Graphical Abstract



Key Points

- Estimated GFR equations such as CKD-EPI and MDRD were developed in Western populations and show reduced accuracy in Indian adults.
- In this cohort of 141 individuals, the indigenous Prabhat equation demonstrated the highest accuracy (P30 = 74.6%) and the lowest bias compared with DTPA-measured GFR.
- CKD-EPI and MDRD significantly overestimated renal function, leading to potential misclassification of CKD stage.
- Population-specific calibration of GFR estimation equations is necessary in regions with different anthropometry and dietary patterns.
- Inaccurate GFR estimation may affect CKD staging, drug dosing, donor evaluation, and clinical decision-making.

Introduction

The estimation of glomerular filtration rate (GFR) through various equations is integral to routine nephrology practice. Because direct measurement of GFR (mGFR) using exogenous filtration markers is impractical in most clinical settings, estimated GFR (eGFR) is widely preferred. Among the available equations, the Modification of Diet in Renal Disease (MDRD) formula was long regarded as the standard, but it has largely been superseded by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, which offers greater accuracy at GFR values above 60 mL/min/1.73 m². However, the CKD-EPI equation has not been extensively validated across diverse populations, and data from the Indian subcontinent remain limited.

The present study aimed to assess the accuracy and precision of commonly used eGFR equations compared with mGFR determined by diethylenetriaminepentaacetic acid (DTPA) scintigraphy and to evaluate an indigenous simplified equation, the Prabhat formula.

Methods

This single-centre, prospective study was conducted over two years (October 2018 – October 2020) and included 141 consecutive patients who attended the nephrology outpatient clinic, in whom accurate assessment of GFR was considered clinically necessary by the treating physician. Eligible participants were adults aged ≥ 30 years and included renal donors, patients with single kidneys, congenital anomalies of the kidney and urinary tract, or established chronic kidney disease (CKD). Exclusion criteria comprised pregnancy, acute kidney injury (AKI) with unstable renal function, kidney transplant recipients, and patients on dialysis. Demographic and clinical data—including age, sex, comorbidities, underlying renal diagnosis, and serum creatinine—were recorded for all participants. All subjects underwent GFR measurement using technetium-99m diethylenetriaminepentaacetic acid (Tc-99m DTPA) scintigraphy.

Method of creatinine estimation

Serum creatinine was measured using kinetic compensated Jaffe assay traceable to isotope dilution mass spectrometry determination in Cobas 8000 analyzer (Roche Diagnostics GmbH Mannheim, Germany).

Method of dynamic renal scintigraphy

Following breakfast, patients were instructed to drink 300–500 mL of water. A bolus of 185 MBq (megabecquerels) of technetium-99m-labelled diethylenetriaminepentaacetic acid (Tc-99m DTPA) was then administered intravenously. The syringe containing Tc-99m DTPA was measured for radioactivity before and after injection, and the total injected dose was calculated. The injection site was scanned using a gamma camera, and dynamic scintigraphy images were acquired over 30 minutes at 2-minute intervals. At the 20-minute mark, furosemide (0.5–1 mg/kg body weight, maximum 40 mg) was injected intravenously, followed by immediate post-void and delayed (2-hour) imaging. GFR values (mL/min) were derived using the Gates method, applying the equation:

GFR = 9.75621 × Fractional unit − 6.19843. Measured GFR obtained from Tc-99m DTPA scintigraphy was expressed as absolute GFR (mL/min). Estimated GFR values derived from the CKD-EPI, MDRD, and Prabhat equations were compared directly with these measured values without body surface area normalization.

Equations used for GFR estimation

CKD -EPI Formula used – calculated using NKF online calculator

- $GFR = 141 * \min(Scr/\kappa,1)^{\alpha} * \max(Scr/\kappa, 1)^{-1.209} * 0.993^{Age} * 1.018$ [if female] * 1.159 [if black]

Scr is serum creatinine (mg/dL), κ is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.

CKD MDRD 4 variable formula used – calculated using NKF online calculator

GFR in mL/min per 1.73 m^2 = 175 x $SerumCr^{-1.154}$ x $age^{-0.203}$ x 1.212 (if patient is black) x 0.742 (if female)

The equation Prabhat's formula is expressed as:

- CrCl = 100/(1.3 × S. Creatinine) × (0.8 if female) if age is between 30 and 40 years
- CrCl = 100/(1.5 × S. Creatinine) × (0.8 if female) if age is between 41 and 50 years
- CrCl = 100/(1.8 × S. Creatinine) × (0.8 if female) if age >50 years.

Statistical analysis

Statistical analysis was performed using SPSS version 17.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD). The performance of the different eGFR equations was evaluated in terms of accuracy, bias, and precision. Accuracy was defined as the proportion of eGFR values falling within ± 30% of the measured GFR by Tc-99m DTPA (P30). Agreement between eGFR and mGFR values was assessed using Bland–Altman plots. Bias was defined as the mean difference between estimated and measured GFR values. Precision was assessed by the standard deviation of the bias, reflecting the spread of differences around the mean bias. Relative error was calculated as twice the standard deviation of the bias divided by the mean measured GFR.

Results

Complete paired DTPA and estimated GFR data were available for 139 participants for CKD-EPI and MDRD analyses and 138 participants for the Prabhat formula. A total of 141 patients met the inclusion criteria and were included in the analysis. The mean age of the cohort was 47.3 ± 11.0 years, and 53.2% were male. The most common comorbidity was chronic kidney disease (52.4%), followed by diabetes mellitus (17.0%) and hypertension (14.9%). The mean serum creatinine was 1.04 ± 0.66 mg/dL. In most patients, renal function was marginally higher in the right kidney than in the left (50.4% vs 49.5%, respectively). The most frequent indication for DTPA evaluation was renal donor assessment (16.3%), followed by pelvi-ureteric junction obstruction (8.5%) and renal stone disease (6.4%) (Table 1).

The mean total GFR measured by DTPA was 71.2 ± 23.5 mL/min. Among the estimation equations, the CKD-EPI equation produced the highest mean eGFR (85.9 ± 29.4 mL/min), followed by the MDRD (83.9 ± 34.4 mL/min) and Prabhat (68.2 ± 26.4 mL/min) equations. The mean difference from the reference standard was smallest for the Prabhat formula (2.5 mL/min) and greatest for the CKD-EPI equation (−15.1 mL/min), with MDRD showing an intermediate bias of −13.1 mL/min.

Table 1. Baseline characteristics of the study population

Characteristic	Value (Percentage/ SD) (n=141)
Mean age of study population	47.26 (SD 10.96)
Sex	
Male	75 (53.2%)
Female	66 (46.8%)
Co-morbidities	

Chronic Kidney disease	74 (52.4%)
Diabetes	24 (17%)
Hypertension	21 (14.9%)
Coronary artery disease	9 (6.3%)
Hypothyroidism	5 (3.5%)
COPD (chronic obstructive	1 (0.7%)
Pulmonary disease)	2 (1.4%)
Malignancy	1 (0.7%)
Obstructive Sleep Apnea	1 (0.7%)
Chronic gastritis	1 (0.7%)
Cervical spondylosis	1 (0.7%)
Amyloidosis	
Mean creatinine	1.04mg/dl (SD 0.66)
Differential renal function (DTPA)	
Left mean function	49.53% (SD 23.25)
Right mean function	50.38% (SD 23.24)
Disease	Value (percent)
Renal donor	23 (16.3%)
PUJ (pelvi-uretric junction)	12 (8.5%)
obstruction	9 (6.4%)
Renal stone disease	5 (3.5%)
Chronic kidney disease unknown	5 (3.5%)
Pyelonephritis	2 (1.4%)
Renal artery stenosis	3 (2.1%)
Stricture ureter	2 (1.4%)
Single Kidney	2 (1.4%)
Non-functioning kidney	1 (0.7%)
Congenital Mega-ureter	1 (0.7%)
Horseshoe kidney	1 (0.7%)
Crossed ectopic kidney	1 (0.7%)
Bladder neck hypertrophy	1 (0.7%)
Xanthogranulomatous pyelonephritis	1 (0.7%)
Carcinoma Bladder	1 (0.7%)
RCC kidney (Renal Cell Carcinoma)	1 (0.7%)
Genito-urinary tuberculosis	1 (0.7%)
Vesico-ureteric reflux	1 (0.7%)
Hydro-ureteronephrosis without	1 (0.7%)
obstruction	
Vesical calculus	

Table 2. Mean GFR estimated by different methods

GFR estimation method	Mean GFR (SD) N=141	Difference between the means from DTPA (SD)
DTPA mean total GFR	71.21ml/min (23.46)	
Left kidney	34.59ml/min (18.06)	
Right kidney	36.63ml/min (18.94)	
Mean GFR by CKD-EPI equation	85.89ml/min (29.38)	-15.09 (20.17)
Mean GFR by MDRD	83.87ml/min (34.37)	-13.07 (26.09)
Mean GFR by Prabhat formula	68.15ml/min (26.37)	2.53 (19.98)
Mean difference for overestimation from DTPA		**Significance – (2 tailed) for t test equality of means**
GFR (Standard Deviation)	13.68 (11.31)	
CKD-EPI GFR	15.50 (12.47)	
GFR – MDRD	16.43 (13.10)	0.00
Prabhat formula		0.00
		0.00
Mean difference for under-estimation from DTPA		
GFR (Confidence Intervals)	-23.01 (13.86)	
CKD-EPI GFR	- 23.05 (21.88)	0.00
GFR – MDRD	-14.02 (12.83)	0.00
Prabhat formula		0.00

Table 3. Correlation, bias, precision and accuracy between the different GFR estimation equations using DTPA as the gold standard

	CKD-EPI	MDRD GFR	Prabhat formula GFR
Total GFR (DTPA)			
Pearson correlation	0.73	0.65	0.68
Significance 2-tailed (significant at 0.01)	0.00	0.00	0.00
ICC (95% CI)	0.83 (0.77-0.88)	0.76 (0.66-0.83)	0.81 (0.73-0.86)
Bias	-15.09 (20.171)	-13.07 (26.01)	2.52 (19.98)
Precision	38.54	51.14	39.16
Relative error	0.512	0.67	0.57
Accuracy p30	57.55%	61.1%	74.63%

Table 4. Reclassification of CKD stages using CKD-EPI, MDRD, and Prabhat equations compared with DTPA-derived CKD stage

	Stage 1 (n= 34)	**Stage 2 (n=67)**	**Stage 3 (n=28)**	**Stage 4 (n=8)**	**Stage 5 (n=2)**	**Overall 139**
Percentage retained in same stage CKD-EPI	25 (73.5%)	13 (19.4%)	13 (46.4%)	4 (50%)	0	55 (39.56%)
Percentage moved up CKD-EPI	0	51 (76.2%)	13 (46.4%)	4 (50%)	2 (100%)	70 (50.3%)
Percentage moved down CKD-EPI	9 (26.5%)	3 (4.5%)	2 (7.1%)	0	0	14 (10.1%)
Percentage retained in same stage MDRD equation	22 (64.7%)	27 (40.3%)	14 (50%)	5 (62.5%)	0	68 (48.9)%
Percentage moved up MDRD equation	0	33 (49.3%)	11 (39.2%)	3 (37.5%)	2 (100%)	49 (35.2%)
Percentage moved down MDRD equation	12 (35.3%)	7 (10.4%)	3 (10.71%)	0	0	22 (15.8%)
Percentage retained in same stage	9 (27.3%)	43 (64.2%)	15 (53.6%)	6 (75%)	0	73 (52.9%).

Prabhat formula						
Percentage moved up Prabhat formula	24 (72.7%)	10 (14.9%)	5 (17.9%)	0	0	39 (28.3%)
Percentage moved down Prabhat formula	0	14 (20.9%)	8(28.6%)	2 (25%)	2 (100%)	26 (18.8%)

The CKD-EPI equation demonstrated the strongest correlation with DTPA-GFR (r = 0.73), followed by the Prabhat (r = 0.68) and MDRD (r = 0.65) equations (Table 3). In terms of accuracy, defined by P30, the Prabhat formula performed best (74.6%), followed by MDRD (61.1%) and CKD-EPI (57.6%). Bland–Altman analysis showed that the Prabhat formula exhibited the lowest bias (2.5 ± 20.0 mL/min), whereas CKD-EPI demonstrated marginally better precision than the Prabhat formula. MDRD showed the greatest imprecision and the widest limits of agreement (−64.2 to 38.1). Relative error values were lowest for CKD-EPI (0.51), followed by the Prabhat formula (0.57) and MDRD (0.67) (Figure 2a, b and c).

Based on DTPA-derived GFR, most patients were classified as having CKD stage 2 (Figure 1). When eGFR was determined using CKD-EPI or MDRD, many patients originally classified as stage 2 were reclassified as stage 1. Conversely, use of the Prabhat formula resulted in more patients being shifted from stage 1 to lower CKD stages. Overestimation of GFR occurred in 77% of cases using CKD-EPI and 73% using MDRD, whereas the Prabhat formula demonstrated greater concordance with DTPA staging, with 52.9% of patients remaining within the same CKD stage (Table 4).

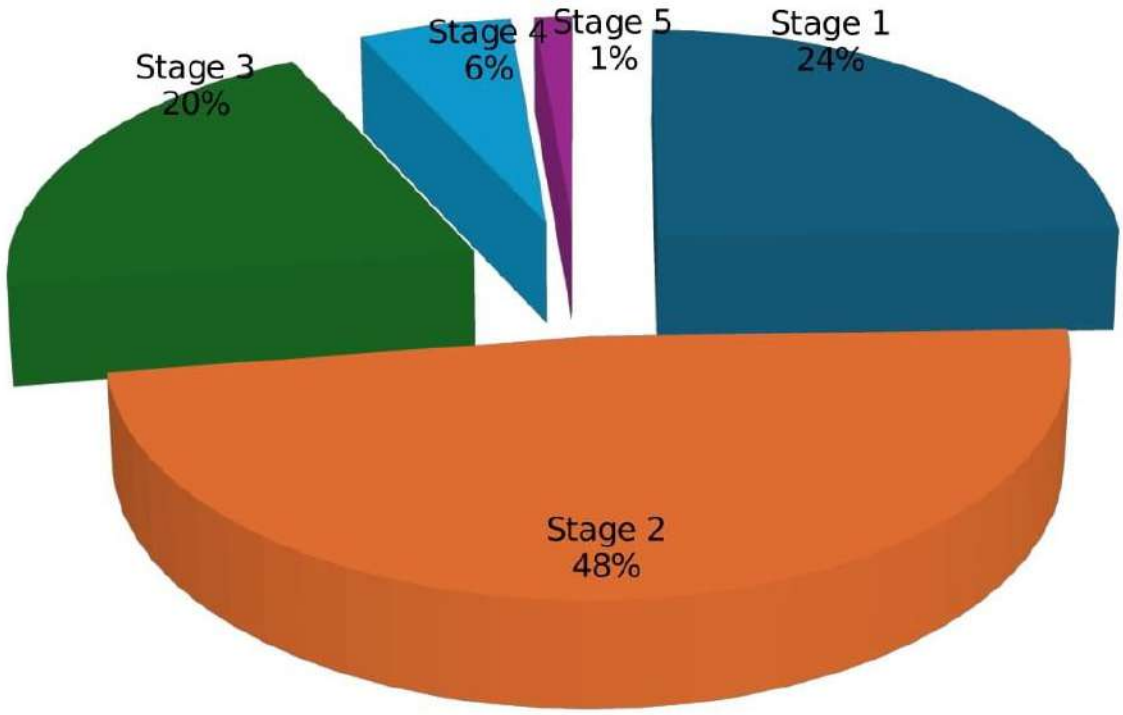


Figure 1. Pie chart with frequency of patients according to CKD Stage as classified by DTPA

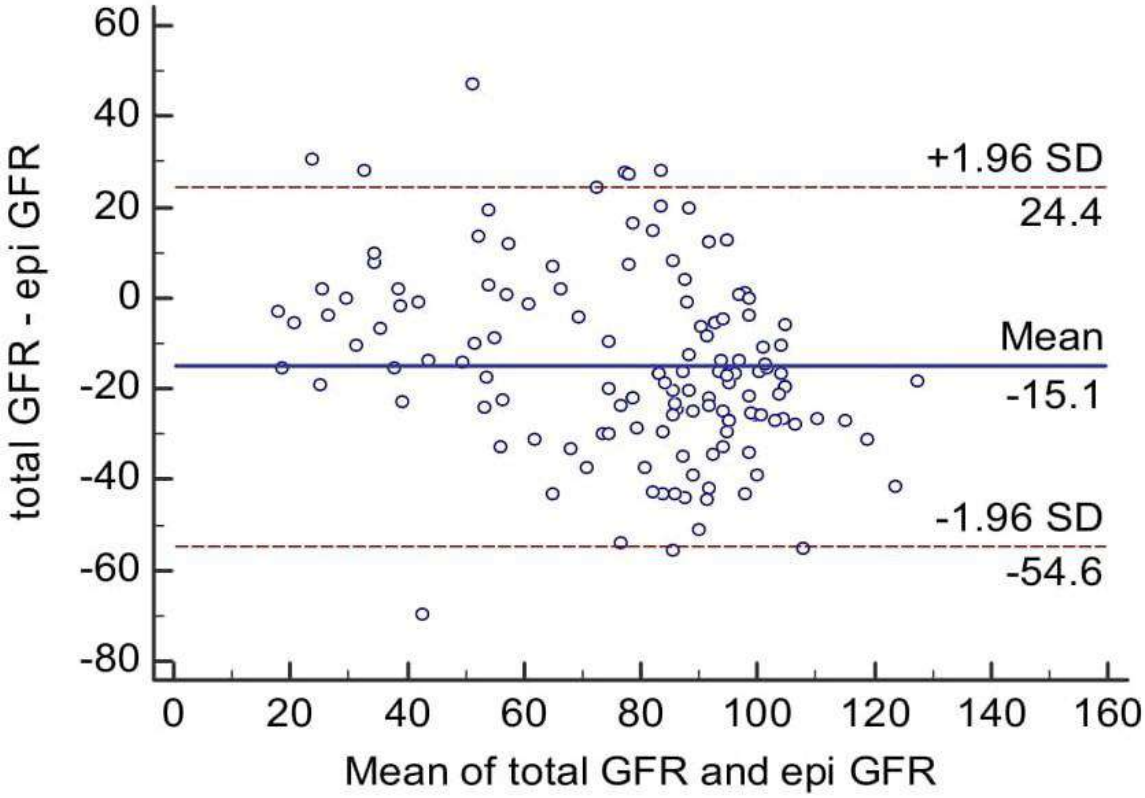


Figure 2a. Bland Altman plot of measured GFR as estimated by CKD-EPI equation vs DTPA GFR

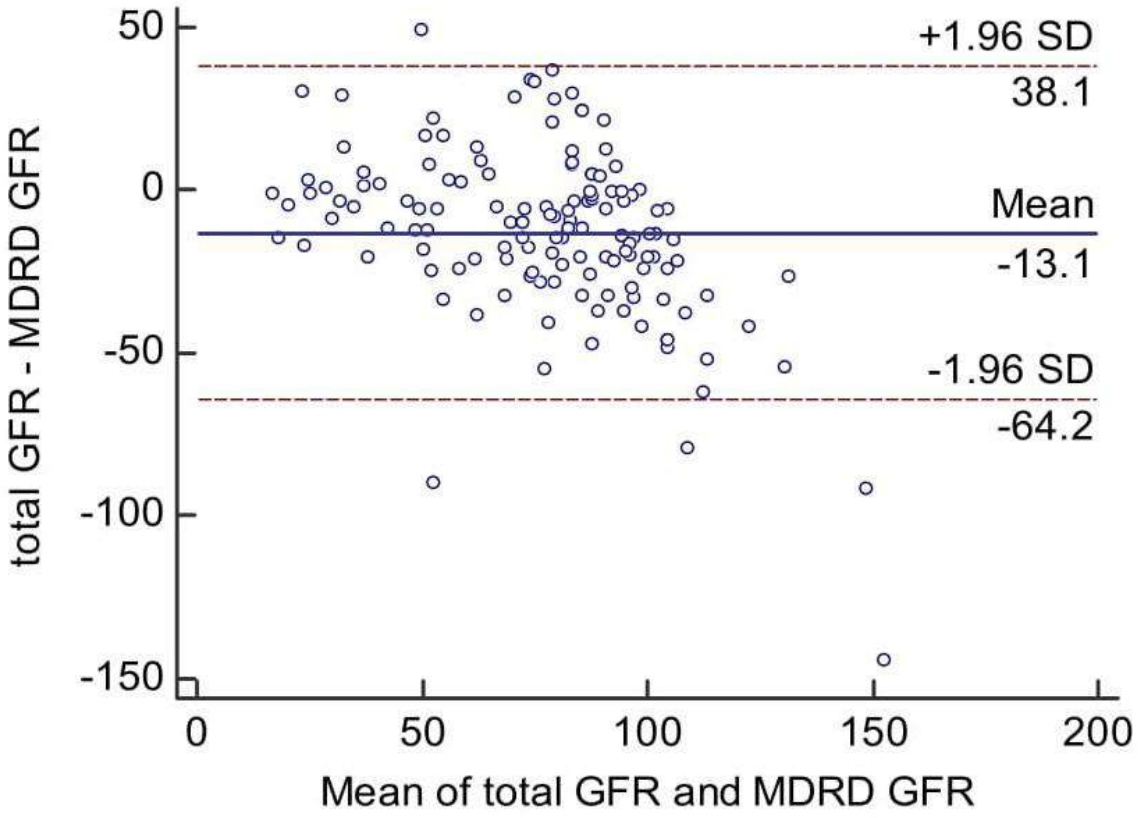


Figure 2b. Bland Altman plot of measured GFR as estimated by MDRD equation vs DTPA GFR

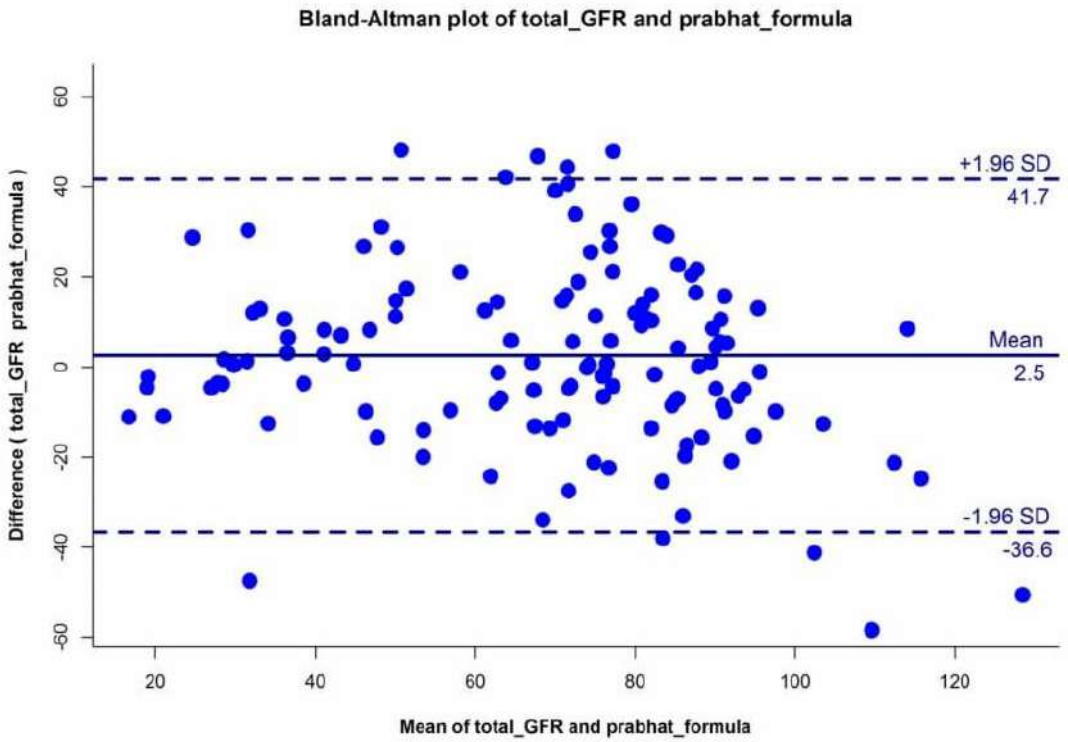


Figure 2c. Bland Altman plot of measured GFR as estimated by Prabhat formula vs DTPA GFR

Discussion

Why the need for a new formula for GFR estimation and what is the Prabhat formula?

Over the past several decades, more than 70 equations for estimating glomerular filtration rate (eGFR) have been developed. As described by Porrini et al. although these equations have evolved, their accuracy and precision have not markedly improved [1]. Most existing formulas achieve a P30—defined as the proportion of values lying within 30% of the reference standard—of only around 40%. Despite these limitations, the MDRD and CKD-EPI equations remain the most widely used worldwide. However, each has inherent shortcomings related to population specificity, bias, and precision [2]. Ethnic and environmental factors also affect equation performance, prompting the development of region-specific modifications.

The Prabhat formula was proposed as a simplified, indigenous alternative designed to make GFR estimation easier in clinical settings [3]. Its simplicity and local derivation are appealing features, but it has not previously undergone formal validation.

In addition, all creatinine-based estimation equations share certain intrinsic limitations. Serum creatinine is influenced by non-GFR determinants such as muscle mass, diet, age, sex, and medication use [4]. Alternative filtration markers like cystatin C, while promising, are themselves affected by inflammatory states and certain drugs, limiting their reliability in routine clinical use.

The study population

Cohorts of patients undergoing DTPA studies are often heterogeneous, comprising both renal donors and individuals with kidney disease. In the study by Ocampo et al., which compared various GFR estimation methods, the most common indication for DTPA scanning was donor evaluation [5]. In our study, the mean age of participants was 47.2 years—approximately a decade older than those in other reported cohorts. This difference likely reflects the inclusion of both healthy and diseased individuals, rather than a purely donor population. Data from a South Indian centre evaluating renal donors have previously demonstrated laterality differences in renal function, with mean GFRs of 47.7 mL/min on the right and 43.4 mL/min on the left [6]. A similar finding was observed in our cohort, with slightly higher function on the right side.

Difference between mean GFR estimated by various equations and measured GFR

In this study, the mean GFR estimated by the CKD-EPI equation was higher than that derived from both other estimation methods and the measured DTPA GFR. The mean difference between the DTPA GFR (reference standard) and each estimation equation was smallest for the Prabhat formula, followed by the MDRD and CKD-EPI equations (Table 2).

Both the CKD-EPI and MDRD equations frequently overestimated GFR when compared with DTPA measurements, whereas the Prabhat formula more often underestimated GFR. The degree of overestimation by CKD-EPI was greatest among patients with CKD stages II, IV, and V, and a similar trend was noted with the MDRD equation. In contrast, the Prabhat formula demonstrated a distinct pattern, with underestimation in CKD stages I and III and overestimation in stages IV and V.

These findings were unexpected, as the MDRD equation is generally known to

underestimate GFR in individuals with preserved renal function (GFR > 60 mL/min/1.73 m²)—a limitation that led to the widespread adoption of the CKD-EPI equation. One possible explanation is that the accuracy of an equation may vary according to the underlying clinical profile of the population. Murata et al. reported that CKD-EPI had lower bias than MDRD in potential kidney donors, whereas MDRD performed better among patients with CKD [7]. Because the present cohort included both donors and patients with kidney disease, this heterogeneity may have influenced the results.

Additionally, racial and dietary factors could contribute to discrepancies between measured and estimated GFR. Both CKD-EPI and MDRD equations were developed primarily in Western populations and have not been extensively validated in Indian cohorts. Variations in body composition and habitual low protein intake in Indian populations may partially explain the differences observed when these equations are applied locally.

Correlation, accuracy, precision and bias between DTPA GFR and estimation equations

In this study, all three equations—CKD-EPI, MDRD, and the Prabhat formula—demonstrated good correlation with measured DTPA GFR. The CKD-EPI equation showed the highest Pearson correlation coefficient (r = 0.73), followed by the Prabhat (r = 0.68) and MDRD (r = 0.65) equations (Table 3). Similarly, Malik et al. reported comparable findings, with r values of 0.40 for CKD-EPI, 0.39 for MDRD, and −0.03 for the Cockcroft–Gault equation [8].

Although correlation was good in this cohort, it is not the ideal metric for assessing the performance of GFR estimation equations. For such comparisons, accuracy, precision, and bias are more relevant indicators. Accuracy refers to the closeness of an estimated value to the true value. In this study, accuracy was expressed as the proportion of eGFR results within ± 30% of the DTPA-measured GFR (P30). By international convention, a P30 ≥ 90% is considered the benchmark for acceptable accuracy, although this threshold is largely based on expert opinion [9]. Some researchers have proposed adopting a stricter criterion, such as P10, which would require 90% of estimates to fall within 10% of the reference value.

In the present study, the Prabhat formula demonstrated the highest accuracy (P30 = 74.6%), followed by the MDRD (61.1%) and CKD-EPI (57.5%) equations. These findings are comparable to previously published data: Jeong *et al.* reported P30 values of 60.7% for CKD-EPI at mGFR < 60 mL/min and 91.7% at higher GFRs [10], while a Congolese cohort showed P30 values of 86% for CKD-EPI and 81.7% for MDRD [11]. In an Indian study by Kumar et al., the CKD-EPI and MDRD equations had P30 values of 22.3% and 25.4%, respectively [8].

Bland–Altman analysis further quantified the degree of agreement between the equations and the reference method. The limits of agreement that were published by Kakde et al earlier for a cohort of Indian donors showed limits of agreement and accuracy similar to this study [12]. The Prabhat formula exhibited the narrowest limits of agreement and the lowest bias (2.52 mL/min), followed by MDRD (−13.07 mL/min) and CKD-EPI (−15.09 mL/min). The biases reported in this study were larger than those in other Asian cohorts—for example, Teo et al. found a

bias of −1.17 mL/min in a Singapore population that included patients of Indian origin [13].

Precision, which reflects reproducibility, was highest for the CKD-EPI equation (38.54) and lowest for the MDRD equation (51.14), with the Prabhat formula showing intermediate precision (39.16). The degree of imprecision observed here is greater than that reported in most East Asian studies, where interquartile ranges (IQRs) for precision typically fall between 15 and 20. In the Singapore study including Indian participants, the IQR was 13.7, indicating substantially better reproducibility.

The relative error in this study was 0.51 for CKD-EPI, 0.67 for MDRD, and 0.57 for the Prabhat formula. Among the evaluated equations, CKD-EPI demonstrated the lowest relative error, suggesting comparatively better consistency despite its larger bias.

Strengths and limitations of the current study

The principal strength of this study is that it evaluates and compares three commonly used eGFR equations—including an indigenous formula— against the reference DTPA method within the same patient cohort. To our knowledge, this is one of the few Indian studies to directly assess the performance of the Prabhat equation. The sample size of 141 participants provides adequate statistical power to identify clinically meaningful differences between estimation methods. Furthermore, by including both healthy renal donors and patients with varying degrees of kidney disease, the study captures a broad spectrum of GFR values, thereby improving generalizability to real-world nephrology practice.

However, several limitations should be acknowledged. First, the study was conducted at a single centre, which may limit external validity. Second, the heterogeneous nature of the cohort, which included both healthy renal donors and patients with diverse renal pathologies, may also have influenced the performance characteristics of the individual estimation equations across subgroups. Third, although DTPA scintigraphy is an accepted reference method, it is less precise than inulin or iothalamate clearance, which are considered the definitive gold standards for measuring GFR. Fourth, because the study excluded individuals with acute kidney injury, the results may not apply to patients with rapidly changing renal function. Finally, muscle mass, dietary factors, and body surface area were not uniformly quantified, all of which can influence creatinine-based estimates.

Despite these limitations, the findings highlight the potential clinical relevance of region-specific equations, such as the Prabhat formula, in improving the accuracy of GFR estimation among Indian patients.

Conclusion

The current study demonstrates that while all three estimation equations—CKD-EPI, MDRD, and the Prabhat formula—correlate reasonably well with measured GFR, their accuracy and precision remain suboptimal when compared with the reference DTPA method. Among them, the Prabhat formula showed the highest overall accuracy (P30 = 74.6%), whereas the CKD-EPI equation demonstrated the best precision and lowest relative error. None of the equations, however, achieved the internationally accepted accuracy threshold of P30 ≥ 90%.

These findings underscore the need for continued refinement and validation of GFR estimation equations in diverse ethnic and geographic populations. Given that creatinine-based equations are influenced by multiple non-GFR determinants—including muscle mass, diet, and medication use—future work should explore combined creatinine–cystatin C models or incorporate novel biomarkers and machine-learning approaches for better precision.

The results of this study support the concept that locally derived, population-specific equations, such as the Prabhat formula, may improve the accuracy of renal function assessment in Indian patients. Multicentric studies with larger sample sizes and direct comparison against inulin clearance are warranted to confirm these observations and to establish optimal tools for clinical application.

Statements and Disclosures

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Conflict of Interest

The authors declare that they have no conflicts of interest relevant to this article.

Ethical Approval

The study was approved by the Institutional Ethics Committee of Sri Ramachandra Institute of Higher Education and Research, Chennai (Approval No. CSP-MED/19/FEB/50/24).

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AI Usage Declaration

Artificial intelligence tools were not used for data analysis or content generation. Language refinement and formatting assistance were provided using ChatGPT (OpenAI, USA) under the supervision of the corresponding author.

Author Contributions

NJ, Conceptualization, study design, data collection, data analysis, interpretation of results, manuscript drafting, and final approval; JV, Conceptualization, supervision, critical revision of the manuscript, and final approval; IE, Data interpretation, assistance in study conduct, and review of the manuscript; TM, Statistical analysis, data interpretation, and review of the manuscript; VE, Contribution to DTPA GFR methodology and data acquisition, and review of the manuscript; MJ, Critical revision of the manuscript, intellectual input, and final approval. All authors have read and approved the final manuscript.

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ORIGINAL ARTICLE

Postpartum Depression and Anxiety: Prevalence and Associated Factors Across the Perinatal Period in a Tertiary Care Hospital

Selva Sruthi T,[1] Rajeshwari S,[2] Vanitha Nallathambi[3] and Jeevithan Shanmugam[4,*]
[1]*Assistant Surgeon, Government Hospital, Tiruchendur 15.*
[2]*Assistant Professor in OBG, Thoothukudi Medical College and Hospital, Thoothukudi-8*
[3]*Consultant OBGYN, KMCH Sulur Hospital, Coimbatore – 641402*
[4]*Professor in Community Medicine, KMCH Institute of Health Sciences and Research, Coimbatore – 14*

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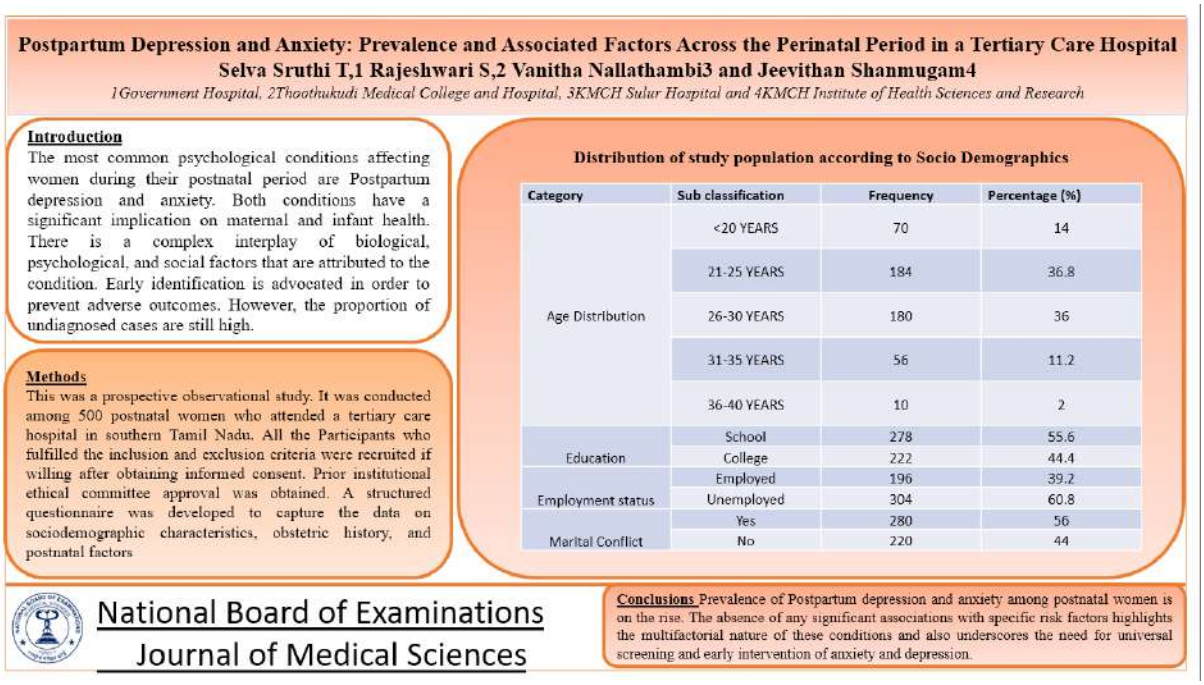
Abstract

Introduction: The most common psychological conditions affecting women during their postnatal period are Postpartum depression and anxiety. Both conditions have a significant implication on maternal and infant health. There is a complex interplay of biological, psychological, and social factors that are attributed to the condition. Early identification is advocated in order to prevent adverse outcomes. However, the proportion of undiagnosed cases are still high. **Materials and Methods:** This was a prospective observational study. It was conducted among 500 postnatal women who attended a tertiary care hospital in southern Tamil Nadu. All the Participants who fulfilled the inclusion and exclusion criteria were recruited if willing after obtaining informed consent. Prior institutional ethical committee approval was obtained. A structured questionnaire was developed to capture the data on sociodemographic characteristics, obstetric history, and postnatal factors. **Results:** Most participants were in the age group of 21–30 years (72.8%). A High risk of depression was noted among 35.4% of participants, while another 30.4% and 34.2% had moderate risk and low risk, respectively. When applied State-Trait Anxiety Inventory (STAI), we observed that 30.6% had high levels, another 37.4% had moderate, and 32% had low levels of anxiety. Psychological distress (moderate to high) was observed among a substantial proportion of women. However, there was no statistically significant association between sociodemographic, obstetric, or postnatal factors and Depression/Anxiety. **Conclusion:** Prevalence of Postpartum depression and anxiety among postnatal women is on the rise. The absence of any significant associations with specific risk factors highlights the multifactorial nature of these conditions and also underscores the need for universal screening and early intervention of anxiety and depression so to improve maternal and neonatal outcomes.

Keywords: Postpartum depression, Postpartum anxiety, EPDS, STAI, Maternal mental health

*Corresponding Author: Jeevithan Shanmugam
Email: dr.jeevithan@gmail.com

Graphical Abstract



Introduction

Postpartum depression (PPD) is one of the most frequently observed psychiatric disorder in the postnatal period. The symptoms of PPD are persistent low mood, loss of interest in previously pleasurable activities, disturbances in sleep, myalgia, fatigue and impaired mother–baby bonding, usually within the first year following childbirth, most common till the 3rd month following delivery. Post partum depression is classified under the broader category of peripartum depression, encompassing depressive episodes that begin during pregnancy or within four weeks after delivery by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [1,2]. Postpartum depression is different from transcient "baby blues," as PPD is more severe, prolonged, and if not treated, can cause significant functional impairment.

Post partum depression affects women of all age groups, from all cultures and ethnicities, irrespective of their socioeconomic strata. The incidence of PPD globally is 6.5% to 20% among all post partum women, with higher percentages reported in low- and middle-income countries [3]. Along with depression, anxiety symptoms are also being recognized as an important part of postpartum psychological morbidity, with prevalence rates of postpartum anxiety disorders ranging from 8.4% to 13.7% [4]. These are frequently found together and may have a compounded effect on maternal well-being. Maternal depression and anxiety can adversely affect infant growth, neurodevelopment, feeding practices, and emotional bonding and hence extends the impact, further to the family unit from the mother and child [4].

Post partum depression has a multifactorial causation, with a complex play of biological, psychological, and social factors. A sudden hormonal fluctuation following delivery characterised by the decline in estrogen and progesterone levels is postulated. It plays

an important role in precipitating depressive symptoms in susceptible women. In addition, the dysregulation of neuroendocrine pathways namely the hypothalamic–pituitary–adrenal (HPA) axis and neurotransmitter systems such as gamma-aminobutyric acid (GABA), has shown to affect the pathophysiology [5]. History of depression in earlier age, lack of social support, presence of familial conflicts, financial burden, and any prior adverse life events aggravates the risk of developing postpartum mental health disorders [6–8].

Underlying risk factors for postpartum depression could be present pre pregnancy, start during pregnancy, or begin in the postpartum period. The Pre-pregnancy risks include poor education, low socioeconomic conditions, and any previous history of psychiatric diseases. During pregnancy, co existing illnesses like diabetes, hypertension, fetal abnormalities, and high-risk obstetric conditions are likely to cause increased psychological distress. Postnatal factors include complications during birthing, neonatal intensive care unit (NICU) admission, breastfeeding problems, and inadequate social support [6,7]. The additive effect of these risk factors highlights the need for a comprehensive assessment across all stages of the perinatal period.

Recognising the danger signs early with timely intervention are very important to counteract the adverse consequences of postpartum depression and anxiety. For routine screening of perinatal women, Edinburgh Postnatal Depression Scale (EPDS) is one of the many screening tools which are advocated by American College of Obstetricians and Gynaecologists (ACOG), the American Academy of Pediatrics (AAP) and also the American Academy of Family Physicians (AAFP) [4]. Inspite of multiple effective screening and treatment methods being available, a higher percentage of mothers still remain undiagnosed due to stigma, lack of awareness, and restricted access to mental health services [9]. This necessitated the need for understanding distribution and determinants of postpartum psychological morbidity which is essential for planning any targeted interventions.

In this context, the present study was done to assess postpartum depression and anxiety among mothers, to understand potential risk factors occurring before, during, and after pregnancy among post natal mothers attending a tertiary care hospital.

Materials and Methods

After approval from the Institutional Ethics Committee, the patients were recruited for the study at Government Thoothukudi Medical College Hospital. This study was conducted between November 2022 and November 2023 in the department of OBGYN. All the ethical principles as explained in the Declaration of Helsinki were followed. Postnatal mothers between the age group of 18 to 40 years of any gravida, with singleton or even multiple pregnancies, who delivered in our Institution were included. Women who had been diagnosed with psychiatric or neurological illness, hypothyroidism, those who delivered in other institution and came for higher level of care were excluded from the study.

All the eligible participants who satisfied the inclusion and exclusion criteria were approached in the postnatal ward and outpatient follow-up clinic by the principal investigator and the participant information sheet was handed over to them. The aim,

purpose and the study procedure, rights of the participants, option to withdraw at any stage, voluntariness were detailed in their local vernacular language. Written informed consent was obtained from each participant after they gave their oral consent and were enrolled to our study. Confidentiality and privacy of the study participants were strictly maintained.

A total of five hundred postnatal women were included in this study. A structured and pretested proforma was instituted to collect a detailed information from each participant. Sociodemographic data including age, educational status, employment status, and marital conflict if any were recorded. Obstetric and pregnancy-related variables such as parity, planned or unplanned pregnancy, presence of hyperemesis gravidarum, medical disorders, fetal complications, bad obstetric history, and frequency of antenatal admissions were asked and documented. Postnatal factors including gender of the newborn, any admissions, complications if any, mode of delivery, and feeding satisfaction were also recorded.

To assess the psychological outcome, Edinburgh Postnatal Depression Scale (EPDS), Tamil version was used. It consisted of 10 items evaluating depressive symptoms experienced over the previous one week. Anxiety among post natal was assessed using the State-Trait Anxiety Inventory (STAI). Study participants were evaluated during the postnatal period, and their responses were recorded systematically. Based on the EPDS scores calculated, participants were categorized into low, moderate, and high risk for depression. Similarly, the STAI scores were also categorized into low, moderate, and high levels of anxiety. For inferential analysis, both depression and anxiety variables were further categorized into binary outcomes (present/absent) by combining moderate and high categories as "present" and low category as "absent".

All the data collected were coded in Microsoft Excel and was analyzed using Statistical Package for Social Sciences (SPSS) version 27. Descriptive data were expressed as frequencies and percentages. For categorical variables and Mean ± SD for continuous variables. Chi-square test was conducted to assess the association between categorical variables. Binary logistic regression analysis was applied to identify predictors for depression and anxiety. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 500 participants were included in the study. The majority of women belonged to the 21–25 years age group (36.8%, n=184) and 26–30 years (36%, n=180), together accounting for 72.8% of the study population, indicating that most participants were in the early reproductive age group. Only 14% (n=70) were below 20 years and 13.2% (n=66) were above 30 years. More than half of the participants had education up to school level (55.6%, n=278), while 44.4% (n=222) had college-level education. A higher proportion of women were unemployed (60.8%, n=304) compared to employed (39.2%, n=196). Marital conflict was reported by 56% (n=280) of participants, indicating a considerable psychosocial burden in the study population (Table 1).

Table 1. Distribution of study population according to Socio Demographics

Category	Sub classification	Frequency	Percentage (%)
Age Distribution (years)	<20	70	14
	21-25	184	36.8
	26-30	180	36
	31-35	56	11.2
	36-40	10	2
Education	School	278	55.6
	College	222	44.4
Employment status	Employed	196	39.2
	Unemployed	304	60.8
Marital Conflict	Yes	280	56
	No	220	44

Among the 500 participants, primigravida constituted 51.4% (n=257) and multigravida 48.6% (n=243), showing a nearly equal distribution. Unplanned pregnancy was observed in 49.4% (n=247) of cases. Hyperemesis gravidarum was reported by 50.2% (n=251) of women. Regarding medical disorders, 52.2% (n=261) had no associated illness, while gestational diabetes mellitus (21.2%, n=106) and gestational hypertension (16.6%, n=83) were the most common conditions, followed by anaemia (4.2%, n=21) (Table 2).

Table 2. Distribution of study population according to obstetrics and Pregnancy factors

Category	Sub classification	Frequency	Percentage (%)
Parity	Primi	257	51.4
	Multi	243	48.6
Unplanned pregnancy	Yes	247	49.4
	No	253	50.6
Hyperemesis gravidarum	Yes	251	50.2
	No	249	49.8
Medical disorders	Anaemia	21	4.2
	Chronic hypertension	12	2.4
	Gestational diabetes	106	21.2
	Gestational Hypertension	83	16.6
	Heart disease	11	2.2

	Overt Diabetes	6	1.2
	Normal	261	52.2
Bad obstetric history	Yes	233	46.6
	No	267	53.4
Frequent antenatal admission	Yes	250	50
	No	250	50

Postnatal characteristics showed that 51.8% (n=259) of newborns were female and 48.2% (n=241) were male. Nearly half of the neonates required NICU admission (48%, n=240), reflecting a substantial level of neonatal morbidity. Delivery complications were reported in 52.2% (n=261) of cases, while 47.8% (n=239) had no complications. Birth outcomes were equally distributed between normal vaginal delivery (50%, n=250) and lower segment caesarean section (50%, n=250). Feeding satisfaction was reported by 48.6% (n=243) of mothers, whereas a slightly higher proportion (51.4%, n=257) experienced feeding dissatisfaction (Table 3).

Table 3. Distribution of study population according to Post natal factors

Category	Sub classification	Frequency	Percentage (%)
Child gender	Male	241	48.2
	Female	259	51.8
Nicu admission	Yes	240	48
	No	260	52
Delivery complications	Yes	261	52.2
	No	239	47.8
Birth outcome	Labour natural	250	50
	LSCS	250	50
Feeding satisfaction	Yes	243	48.6
	No	257	51.4

With respect to psychological outcomes, 35.4% (n=177) of participants were classified as having a high risk of depression, while 30.4% (n=152) and 34.2% (n=171) had moderate and low risk, respectively. Thus, nearly two-thirds of the participants (65.8%) exhibited moderate to high risk of depressive symptoms. Similarly, for anxiety, 30.6% (n=153) had high levels and 37.4% (n=187) had moderate levels, whereas 32% (n=160) had low levels of anxiety. Overall, 68% of participants demonstrated moderate to high anxiety levels, indicating a considerable burden of postpartum psychological distress in the study population (Table 4).

Table 4. Distribution of study population according to Outcome Variables

Risk of Depression	Low	171	34.2
	Moderate	152	30.4
	High	177	35.4
Risk of Anxiety	Low	160	32
	Moderate	187	37.4
	High	153	30.6

Inferential analysis using chi-square test and binary logistic regression was performed to assess the association between sociodemographic, obstetric, and postnatal factors with depression and anxiety. However, none of the variables demonstrated statistically significant association with depression or anxiety.

Discussion

The present study was conducted to assess the distribution of postpartum depression and anxiety and to evaluate their association with various sociodemographic, obstetric, and postnatal factors. The findings of our study demonstrated a considerable burden of psychological morbidity among postnatal women - 35.4% of participants categorized as having a high risk of depression and a substantial proportion exhibiting moderate to high levels of anxiety. Similar reports has been reported by other studies that have reported a significant prevalence of postpartum psychological disorders among post natal mothers, emphasizing that postpartum depression and anxiety are major public health concerns affecting the maternal well-being [3].

Majority of our participants were in 21–30 years age group, which is the peak reproductive age. Though many studies indicate younger maternal age as a potential risk factor for postpartum depression 20-23, no statistically significant association was observed in our present study. This finding contrasts with an earlier report which observed that younger mothers may be more vulnerable to psychological distress. Poor coping mechanisms and social support has also been observed [10]. Lack of association in our study shall be attributed to relatively homogeneous age distribution and similar sociodemographic characteristics among the study participants.

Educational status of the mother and employment status are often considered important determinants of maternal mental health. In our study, a higher proportion of women had education up to school level and were unemployed. Previous studies have demonstrated that poor education and unemployment are associated factors for postpartum depression and anxiety, possibly due to financial dependency on others and reduced autonomy [6–8,10]. However, in this present study, no significant association has been observed.

More than half of the mothers reported Marital conflict which indicates a substantial psychosocial burden. Previous studies has consistently identified poor support from partner and marital disharmony as significant predictors

[10,11]. Although a higher proportion of women in our study with marital conflict exhibited depressive and anxiety symptoms, the association was not statistically significant. Independent effect could have been influenced by other unmeasured psychosocial factors such as family support or cultural coping mechanisms.

Nearly half of the pregnancies were reported as unplanned, and hence a considerable proportion of women experienced various medical disorders and fetal complications. Unplanned pregnancy, high-risk pregnancy conditions, and adverse outcomes of pregnancy are associated with increased psychological distress [6,7,10].

Postnatal factors such as NICU admission, delivery complications, and feeding difficulties are known to influence maternal psychological health. In this study, nearly half of the neonates required NICU admission, and more than half of the mothers experienced delivery complications or feeding dissatisfaction. Previous studies have reported that NICU admission and breastfeeding difficulties are associated with increased maternal anxiety and depressive symptoms, primarily due to concerns regarding neonatal health and impaired mother–infant bonding [12,13].

A high prevalence of both depression and anxiety among postnatal women were observed in our. Similar studies have reported coexisting anxiety and depressive symptoms during the postpartum period, which highlights the need for comprehensive screening strategies [4,13]. Despite the presence of multiple potential risk factors, inferential analysis using chi-square test and logistic regression did not demonstrate statistically significant associations. Since the study population was homogenous, a relatively high baseline prevalence of psychological distress, and a complex interplay of biological, psychological, and social determinants underlying postpartum mental health disorders can be attributed to.

Conclusion

A high prevalence of postpartum depression and anxiety among postnatal women were observed in our study, which highlights a substantial burden of psychological morbidity during the postpartum period. Though no risk factors can be attributed in our study, the study findings necessitates the importance of Structured screening for post natal depression and anxiety is advocated since multifactorial cause is involved. Early identification and intervention is a must to improve the maternal and neonatal outcomes.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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ORIGINAL ARTICLE

Study of Methylene Tetrahydrofolate Reductase (MTHFR C677T) Single Nucleotide Polymorphism in Preeclampsia

S. Vinitha,[1,*] B.Anitha,[2] Vasmathie S[1] and Saravanan T[3]
[1]*Assistant Professor, Department of Biochemistry, Government Medical College and ESI Hospital, Coimbatore*
[2]*Assistant Professor, Department of Biochemistry, Coimbatore Medical College, Coimbatore*
[3]*Professor & HOD, Department of Biochemistry, Government Medical College and ESI Hospital, Coimbatore*

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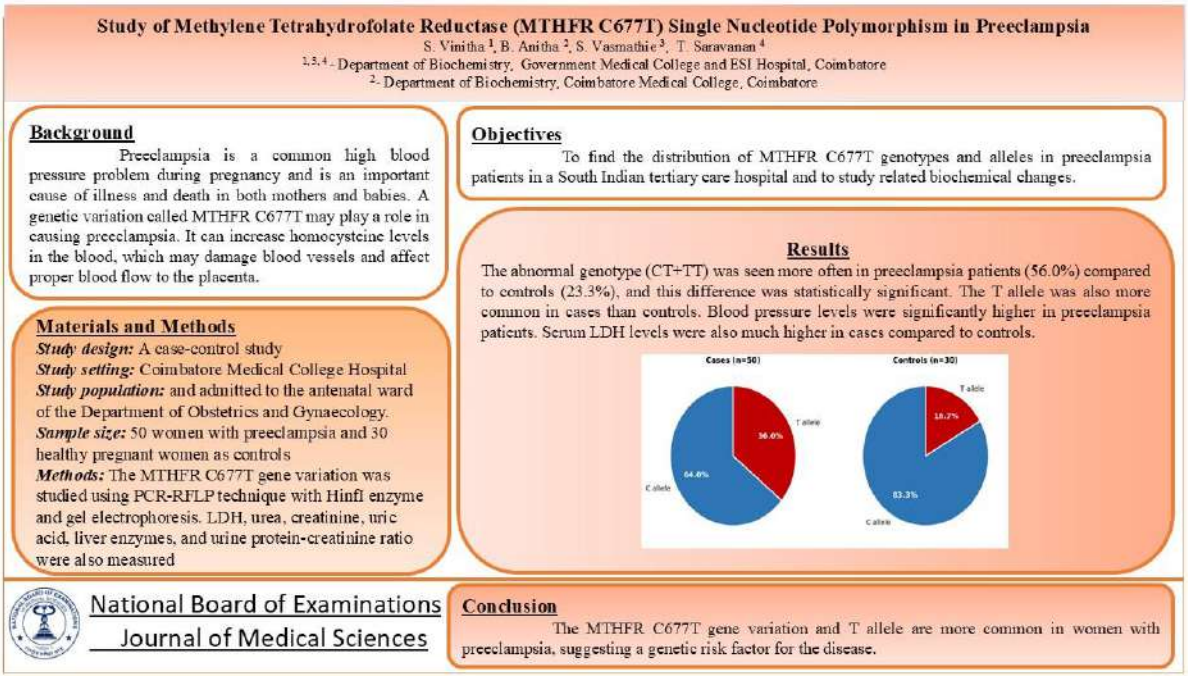
Abstract

Background: Preeclampsia is a common high blood pressure problem during pregnancy and is an important cause of illness and death in both mothers and babies. A genetic variation called MTHFR C677T may play a role in causing preeclampsia. It can increase homocysteine levels in the blood, which may damage blood vessels and affect proper blood flow to the placenta. **Methods:** This study was a hospital-based case-control study conducted at Coimbatore Medical College Hospital from May 2019 to February 2020. It included 50 women with preeclampsia and 30 healthy pregnant women as controls. The MTHFR C677T gene variation was studied using PCR-RFLP technique with HinfI enzyme and gel electrophoresis. Blood tests such as LDH, urea, creatinine, uric acid, liver enzymes, and urine protein-creatinine ratio were also measured. Statistical tests like Chi-square, Fisher's exact test, and odds ratio with confidence interval were used for analysis. **Results:** The abnormal genotype (CT+TT) was seen more often in preeclampsia patients (56.0%) compared to controls (23.3%), and this difference was statistically significant. The T allele was also more common in cases than controls. Blood pressure levels were significantly higher in preeclampsia patients. Serum LDH levels were also much higher in cases compared to controls. **Conclusion:** The MTHFR C677T gene variation and T allele are more common in women with preeclampsia, suggesting a genetic risk factor for the disease. Serum LDH can be used as a helpful marker to assess disease severity. Further studies with larger samples are needed to better understand the relationship between this gene variation and homocysteine levels.

Keywords: MTHFR, C677T Polymorphism, Preeclampsia, Hyperhomocysteinaemia, PCR-RFLP, Hypertension in Pregnancy

*Corresponding Author: S. Vinitha
Email: vini.somasekar@gmail.com

Graphical Abstract



Introduction

Preeclampsia (PE) is a condition in pregnancy where a woman develops high blood pressure (systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg) along with protein in urine after 20 weeks of pregnancy, and it is one of the most serious complications of pregnancy [1]. It affects about 5–8% of pregnancies worldwide and is responsible for 10–15% of maternal deaths globally [2]. In India, preeclampsia occurs in about 8–10% of pregnancies and is a major cause of illness and death in both mothers and babies [3].

The cause of preeclampsia involves problems in the blood vessels, including damage to the inner lining of blood vessels, poor invasion of placental cells into uterine arteries, and increased inflammation in the body [4]. It is caused by multiple factors, including genetics. Women whose mothers had preeclampsia have about a 3 times higher risk of developing the condition, showing the role of genetic factors [5]. Many genes related to blood clotting, blood vessel function, immune system, and metabolism have been studied in relation to preeclampsia [6].

The Methylene Tetrahydrofolate Reductase (MTHFR) gene, located on chromosome 1p36.3, produces an important enzyme involved in folate and homocysteine metabolism [7]. A common genetic change called C677T (change from cytosine to thymine at position 677 in exon 4) leads to a less active enzyme. In people with TT genotype, enzyme activity is reduced by about 75%, causing increased levels of homocysteine in the blood [8]. High homocysteine levels can damage blood vessels, increase clot formation, cause oxidative stress, and lead to thrombosis, all of which are important in the development of preeclampsia [9]. Many meta-analysis studies have shown a strong link between MTHFR C677T variation and preeclampsia, especially in Caucasian and Asian populations [10].

However, there is limited information about this genetic variation in

South Indian populations. Therefore, this study was done to find the distribution of MTHFR C677T genotypes and alleles in preeclampsia patients in a South Indian tertiary care hospital and to study related biochemical changes.

Materials and Methods

Study Design and Setting

This was a hospital-based case-control study carried out at Coimbatore Medical College & Hospital, Coimbatore, Tamil Nadu, India from May 2019 to February 2020. Approval was obtained from the Institutional Ethics Committee, and written informed consent was taken from all participants before including them in the study.

Study Population

As this was an exploratory hospital-based genetic association study, a formal sample size calculation was not performed. The sample size was based on the number of eligible participants recruited during the study period and feasibility considerations

Cases: 50 pregnant women diagnosed with preeclampsia and admitted to the antenatal ward of the Department of Obstetrics and Gynaecology.

Controls: 30 healthy pregnant women (first pregnancy) beyond 20 weeks of gestation with normal blood pressure and no other medical problems.

Inclusion and Exclusion Criteria

Inclusion: Pregnant women aged 15–45 years; first pregnancy; gestational age more than 20 weeks; diagnosis of preeclampsia based on blood pressure ≥140/90 mmHg recorded twice at least 6 hours apart, along with urine protein (protein-creatinine ratio >0.3 or ≥+1 on dipstick) after 20 weeks.

Exclusion: Women with chronic hypertension, multiple pregnancy, molar pregnancy, hydrops fetalis, diabetes, kidney disease, liver disease, autoimmune disorders, or other systemic illnesses were excluded.

Sample Collection

A total of 5 mL of venous blood was collected under sterile conditions. Out of this, 2 mL was collected in an EDTA tube for DNA extraction, and 3 mL was collected in a plain tube for biochemical tests.

DNA Extraction and MTHFR C677T Genotyping

DNA was extracted using the salting-out method. Red blood cells were first broken down using TKM1 buffer and Triton-X, followed by cell lysis using TKM2 buffer with SDS and sodium chloride. DNA was then precipitated using isopropanol, washed with ethanol, dried, and dissolved in buffer. The quality of DNA was checked using spectrophotometry.

The MTHFR gene (exon 4) was amplified using PCR with specific primers. The PCR product (198 base pairs) was then cut using HinfI enzyme and analysed on agarose gel. Based on the band pattern: normal (CC) showed one band at 198 bp; heterozygous (CT) showed three bands (198, 175, 23 bp); and mutant (TT) showed two bands (175 and 23 bp) [11].

Biochemical Parameters

Blood tests were done using an automated analyser (XL 640). These included urea, creatinine, uric acid, LDH, ALP, SGOT, and SGPT using standard laboratory methods. Urine protein-creatinine ratio was measured using

standard methods, and platelet count was assessed using an automated cell counter.

Statistical Analysis

Data were analysed using IBM SPSS version 20. Continuous data were expressed as mean ± standard deviation and compared using Student's t-test. Categorical data were analysed using Chi-square test or Fisher's exact test. Odds ratios with 95% confidence intervals were calculated. Hardy-Weinberg equilibrium was checked using Chi-square test. A p-value less than 0.05 was considered statistically significant.

Results

Demographic and Clinical Parameters

The average age of women in both groups was similar, with cases having a mean age of 27.26 ± 4.12 years and controls 26.37 ± 3.76 years (p = 0.33), showing that both groups were well matched for age. The average gestational age and haemoglobin levels were also similar in both groups.

However, systolic and diastolic blood pressure were significantly higher in women with preeclampsia compared to controls (SBP: 147.60 ± 5.55 vs 118.87 ± 5.72 mmHg; DBP: 86.32 ± 4.61 vs 74.33 ± 4.37 mmHg), and this difference was statistically significant (p = 0.001 for both). Clinical parameters between cases and controls are compared and displayed in Table 1.

Table 1. Comparison of Clinical Parameters between Cases and Controls

Parameter	**Cases Mean ± SD**	**Controls Mean ± SD**	**t value**	**P value**	**Sig.**
Age (years)	27.26 ± 4.12	26.37 ± 3.76	0.96	0.33	NS
Gestational Age (weeks)	28.14 ± 4.27	28.57 ± 3.70	0.45	0.65	NS
SBP (mmHg)	147.60 ± 5.55	118.87 ± 5.72	22.1	0.001	S
DBP (mmHg)	86.32 ± 4.61	74.33 ± 4.37	11.47	0.001	S
Hb (g/dL)	11.11 ± 1.24	11.14 ± 1.12	0.08	0.92	NS

S = Significant; NS = Not significant

Biochemical Parameters

Serum LDH levels were much higher in women with preeclampsia (553.66 ± 195.31 U/L) compared to controls (247.57 ± 53.77 U/L; p = 0.001), indicating damage to the placenta and blood vessel lining. Liver enzymes SGOT (p = 0.049) and SGPT (p = 0.05) were also significantly higher in cases.

Urea levels were significantly lower in preeclampsia cases (20.46 ± 4.18 vs 25.23 ± 5.41 mg/dL; p = 0.045). However, there was no significant difference between cases and controls in ALP, uric acid, creatinine, platelet count, and urine protein-creatinine ratio. Biochemical parameters between cases and controls are compared and displayed in Table 2.

Table 2. Comparison of Biochemical Parameters between Cases and Controls

Parameter	**Cases Mean ± SD**	**Controls Mean ± SD**	**t value**	**P value**	**Sig.**
LDH (U/L)	553.66 ± 195.31	247.57 ± 53.77	8.3	0.001	S
SGOT (U/L)	22.92 ± 9.36	27.33 ± 7.09	2.22	0.049	S
SGPT (U/L)	19.46 ± 6.66	24.67 ± 7.56	3.2	0.05	S
ALP (U/L)	159.20 ± 72.45	141.07 ± 29.77	1.3	0.19	NS
Urea (mg/dL)	20.46 ± 4.18	25.23 ± 5.41	4.42	0.045	S
Creatinine (mg/dL)	0.82 ± 0.15	0.77 ± 0.12	1.54	0.12	NS
Uric Acid (mg/dL)	5.30 ± 1.14	5.25 ± 0.90	0.20	0.83	NS
Platelet ($\times 10^3/\mu L$)	183.72 ± 57.82	203.93 ± 55.57	1.5	0.12	NS
Spot Urine PCR	0.20 ± 0.13	0.15 ± 0.05	1.8	0.07	NS

S = Significant; NS = Not significant; PCR = Protein:Creatinine Ratio

MTHFR C677T Genotype Distribution

Among the 50 women with preeclampsia, 22 (44.0%) had the normal CC genotype, 13 (26.0%) had CT, and 15 (30.0%) had TT. Among the 30 control women, 23 (76.7%) had CC, 4 (13.3%) had CT, and 3 (10.0%) had TT. Distribution of *MTHFR C677T* Genotype between cases and controls compared and displayed in Table 3.

When CT and TT were grouped together as mutant types and compared with the normal CC type, the mutant genotype was seen more often in preeclampsia cases (56.0%) than in controls (23.3%). This difference was statistically significant (p = 0.004), and women with the mutant genotype had about 4 times higher risk of developing preeclampsia (OR = 4.18; 95% CI: 1.51–11.49) (Table 4). Distribution of *mutant and wild* Genotype between cases and controls compared and displayed in Table 4.

Table 3. Genotype Distribution of MTHFR C677T between Cases and Controls

Genotype	**Cases n (%)**	**Controls n (%)**	**Total**
Wild-type CC	22 (44.0%)	23 (76.7%)	45
Heterozygous CT	13 (26.0%)	4 (13.3%)	17
Homozygous TT	15 (30.0%)	3 (10.0%)	18
Total	50 (100%)	30 (100%)	80

Table 4. Mutant (CT+TT) vs Wild-Type (CC) Genotype — Cases vs Controls

Genotype	**Cases n (%)**	**Controls n (%)**	**P value**	**OR (95% CI)**
Wild-type CC	22 (44.0%)	23 (76.7%)	0.004	Reference
Mutant CT+TT	28 (56.0%)	7 (23.3%)	0.004	4.18 (1.51–11.49)

Allele Frequency Distribution

The T allele was found more often in women with preeclampsia (83.3%) compared to controls (16.7%), and this difference was statistically significant (p = 0.04). Women carrying the T allele had about 2.84 times higher risk of developing preeclampsia (OR = 2.84; 95% CI: 1.55–4.13).

The C allele frequency was 64% in cases and 36% in controls. The distribution of both alleles and genotypes followed Hardy-Weinberg equilibrium which is displayed in Table 5 and Figure 1.

Table 5. Allele Frequency Distribution of MTHFR C677T — Cases vs Controls

Allele	**Cases n (%)**	**Controls n (%)**	**P value**	**OR (95% CI)**
C allele	64 (64.0%)	36 (36.0%)	0.04	Reference
T allele	50 (83.3%)	10 (16.7%)	0.04	2.84 (1.55–4.13)

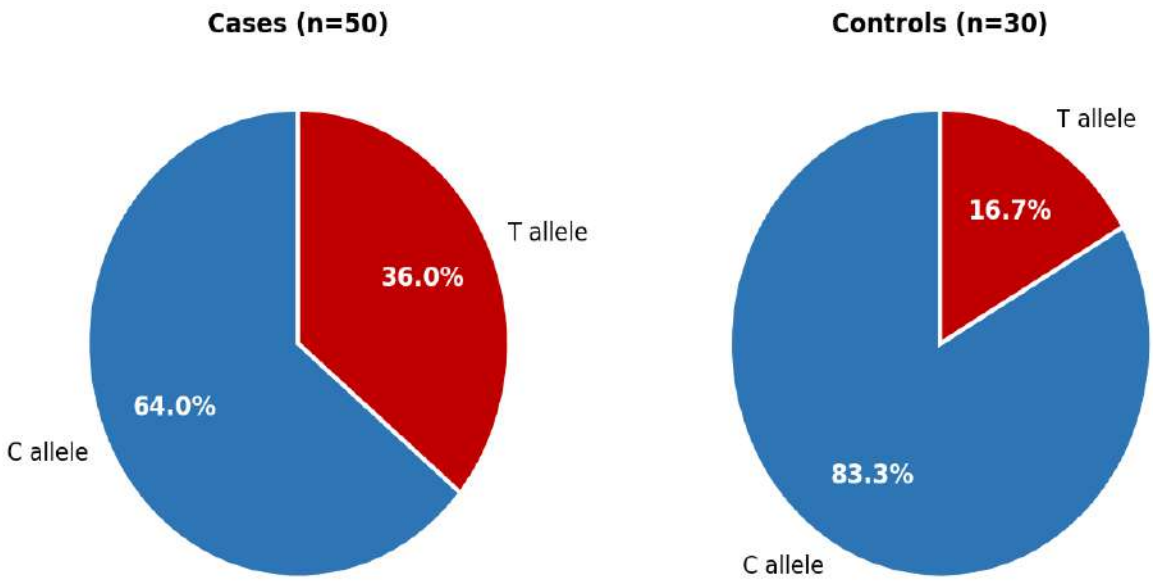


Figure 1. Allele Frequency Distribution (%) in Cases and Controls.

Discussion

Preeclampsia is a condition in pregnancy caused by a combination of genetic and environmental factors [12]. It affects about 2–8% of pregnancies worldwide, and its genetic causes have been widely studied in recent years [13]. One important genetic factor is the MTHFR C677T variation, which can increase homocysteine levels in the blood due to reduced enzyme activity, especially in people with the TT type [8].

In this study, the abnormal genotype (CT+TT) was found in 56.0% of preeclampsia cases compared to 23.3% of controls, showing a significantly higher risk (OR = 4.18; p = 0.004). This finding is similar to the results of Wu et al. [10], who showed a significant association between MTHFR C677T and preeclampsia in both Caucasian and Asian populations. They found that this mutation was about 1.37 times more common in preeclampsia cases. Merviel et al. [14] also reported a higher frequency of this mutation in pregnant women with hypertension, especially in early-onset cases. Yang et al. [15] supported these findings in a large meta-analysis of over 15,000 cases, confirming the link between MTHFR polymorphism and hypertension in pregnancy.

In our study, the T allele was much more common in cases (83.3%) than in controls (16.7%), with about 2.84 times higher risk (p = 0.04). El Baz et al. [16] reported a much higher risk (OR = 21.7), which may be due to differences in population, sample size, and genetic background. Salimi et al. [17] also found a strong association between MTHFR C677T and early-onset preeclampsia in an Iranian population, supporting its role in Asian groups.

The link between MTHFR C677T and preeclampsia is mainly due to increased homocysteine levels [18]. High homocysteine can reduce nitric oxide, increase oxidative stress, promote clot formation, and affect normal placental development, all of which contribute to preeclampsia.[9] This mutation may also lead to poor blood vessel formation in the placenta by causing small clots and affecting trophoblast invasion [19].

Serum LDH levels were much higher in preeclampsia cases (553.66 ± 195.31 vs 247.57 ± 53.77 U/L; p = 0.001), indicating cell damage, liver involvement, and placental injury. LDH is an important marker of disease severity and is also used in diagnosing HELLP syndrome.[20] The slight increase in SGOT and SGPT may suggest early liver involvement that has not yet progressed to severe disease.

In South India, Radha Rama Devi et al. [21] reported the presence of MTHFR polymorphism and its association with pregnancy-related complications, showing its importance in this region. The present study adds further evidence by studying this gene variation specifically in preeclampsia patients from Tamil Nadu.

One limitation of this study is that homocysteine levels were not measured, so a direct link between gene variation, homocysteine levels, and disease severity could not be established. The small sample size, single-centre design, and inclusion of only first-time pregnant women also limit how widely these results can be applied. Future studies should include larger and more diverse populations, measure homocysteine levels over time, assess enzyme activity, and study other related genetic factors.

Conclusion

The MTHFR C677T mutant genotype (CT+TT) and T allele were found more often in women with preeclampsia compared to healthy pregnant women, with risks increased by about 4.18 times and 2.84 times respectively. This shows that this gene variation may play a crucial role in preeclampsia in the South Indian population. Serum LDH levels were also significantly higher in preeclampsia patients, making it a useful test to assess how severity of the disease. Further large studies involving multiple centres are needed to better understand the role of this gene variation by studying its relationship with homocysteine levels in preeclampsia.

Limitations

Single-centre study; small sample size; serum homocysteine not measured; restricted to primigravidae. A formal sample size estimation was not performed prior to study initiation, which may limit the statistical power and generalisability of the findings.

Future Scope

Multicentre studies correlating MTHFR C677T genotype with serum homocysteine, folate, and vitamin B12 levels; extension to multigravidae and other hypertensive disorders of pregnancy; pharmacogenomic studies examining periconceptional folate supplementation in T allele carriers.

Conflicting Interest

The authors declare that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

Data availability statement

The datasets generated and analysed in this study are available from the corresponding author on reasonable request. They are not publicly shared because they contain sensitive information that could indirectly identify participants.

Ethical considerations

This study has been approved by the Institutional Human Ethics Committee of Coimbatore Medical College, Coimbatore carrying certificate number 0172/2018, dt 15.12.2018

Informed Consent

Written informed consent was obtained from all participants after explaining the study procedures, potential risks and benefits. Consent covered both participation and publication of anonymised findings, with assurance of confidentiality and data privacy.

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ORIGINAL ARTICLE

The Effect of Covid-19 Pandemic in Hand Hygiene Behaviour Among Elderly Persons in Chennai District

Sai Sanjith Raaghav Ramakumar,[1] Lakshmi Priya Navaneetha Krishnan,[2] Sopia Abigail,[3] Ananthi B,[4] Sivaharivelan Thiagarajan[5,*] and Balakumar M[5]

[1]*Department of Microbiology, Madras Medical College, Chennai, Tamil Nadu, India*
[2]*Associate Professor, Govt Omandurar Medical College, Chennai, Tamil Nadu, India*
[3]*Associate Professor, Department of Microbiology, A.C.S. Medical College and Hospital, Dr. M.G.R. Educational and Research Institute, Chennai, Tamil Nadu, India*
[4]*Professor & HOD, Department of Microbiology, A.C.S. Medical College and Hospital, Dr. M.G.R. Educational and Research Institute, Chennai, Tamil Nadu, India*
[5]*Assistant Professor, Department of Community Medicine, A.C.S. Medical College and Hospital, Dr. M.G.R. Educational and Research Institute, Chennai, Tamil Nadu, India*

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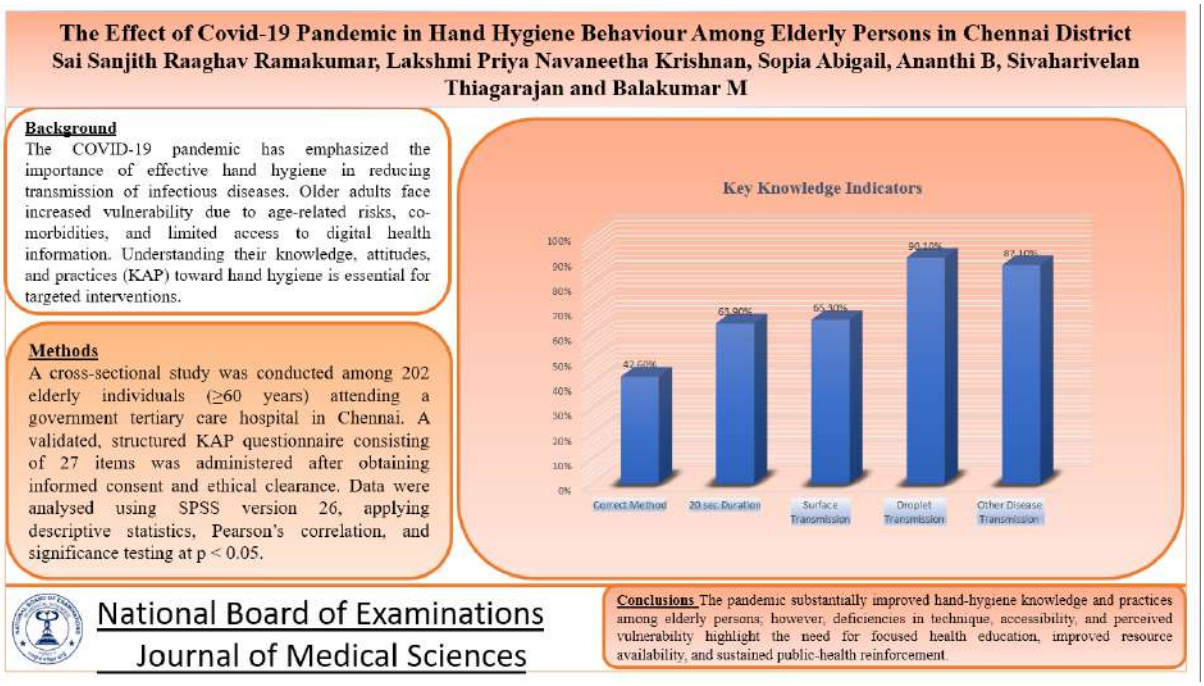
Abstract

Background: The COVID-19 pandemic has emphasized the importance of effective hand hygiene in reducing transmission of infectious diseases. Older adults face increased vulnerability due to age-related risks, co-morbidities, and limited access to digital health information. Understanding their knowledge, attitudes, and practices (KAP) toward hand hygiene is essential for targeted interventions. **Materials and Methods:** A cross-sectional study was conducted among 202 elderly individuals (≥60 years) attending a government tertiary care hospital in Chennai. A validated, structured KAP questionnaire consisting of 27 items was administered after obtaining informed consent and ethical clearance. Data were analysed using SPSS version 26, applying descriptive statistics, Pearson's correlation, and significance testing at $p < 0.05$. **Results:** The mean participant age was 68.87 years; 52% were males. Most participants demonstrated adequate knowledge of COVID-19 transmission, with 82.7% reporting exposure to government awareness initiatives. Knowledge scores negatively correlated with age ($r = –0.167$, $p = 0.018$). Positive attitudes were reported by the majority, and significant behavioural improvements were observed after the pandemic, including increased handwashing frequency (48.2%), greater use of liquid soap, and higher adoption of hand sanitiser use. However, gaps persisted in correct technique, recommended duration, and key hand-hygiene moments. **Conclusion:** The pandemic substantially improved hand-hygiene knowledge and practices among elderly persons; however, deficiencies in technique, accessibility, and perceived vulnerability highlight the need for focused health education, improved resource availability, and sustained public-health reinforcement to protect high-risk elderly populations.

Keywords: COVID-19, Hand hygiene, Elderly population, Behavioural changes

*Corresponding Author: Sivaharivelan Thiagarajan
Email: sivaharivelantry@gmail.com

Graphical Abstract



Introduction

The SARS-CoV-2 (COVID-19) pandemic has had a profound impact on the health, well-being and economy of people all over the world. Globally, as of 26th October,2022, 625,740,449 confirmed cases of COVID-19, including 6,563,667 deaths, were documented by WHO [1]. India is the world's second-most populous and the second-worst affected country by COVID-19 to date (in terms of the total number of confirmed COVID-19 cases). In India as of 26th October,2022 44,645,768 confirmed cases of COVID-19 including 528,981 deaths has been documented by WHO [2]. While significant amount of investment has been made in the development and roll out of vaccines for COVID-19, behavioural prevention continues to be critical in reducing COVID-related morbidity and mortality. Hand-washing is an important and the most cost-effective strategy for minimising transmission of COVID-19 and other respiratory viruses, diarrhoeal diseases and outbreaks of viral hemorrhagic fevers like Ebola [3].

The current COVID-19 pandemic has brought an increased focus on the importance of hand-washing aimed both at people working within the health sector as well as to the general public. There has been promotion of awareness raising initiatives through various means about the importance and correct techniques of hand-washing. Memes, messages and short videos directed at reaching people on their handheld devices including through social media, and mainstream television, print advertisements, radio and billboards are all in use, and all with the same message that effective hand- washing is crucial to stop the spread of COVID-19 [4].

When policies and public health interventions aim to secure health for all, due prudence need to be given to vulnerable populations. The issue of health inequalities unfolding during disease outbreaks has been extensively investigated across pandemics [5,6].

Elderly people are at a higher risk of COVID-19 infection and the course of the disease tends to be more severe in them resulting in higher mortality [7][8]. Hence awareness and practices on hand-washing strategy is very important among the elderly. However, there is insufficient data to know if the importance of hand-washing has sufficiently reached the elderly people, who have lower exposure to digital and mass media and may find the concept of using hand sanitisers unusual [9].

The study design we have opted for in this research is questionnaire-based Cross- sectional study using the KAP survey model. This design is observational in nature and is also known as descriptive research. This study design can provide a useful jumpstart to further researches.

While the importance of hand-washing has been identified in multiple publications [10], there is limited empirical evidence on hand-washing knowledge, attitude and practices especially in India in the context of the COVID-19 pandemic. It is important to address the deficiencies in KAP literature on Hand-washing at the community level. To fill this gap and aid in the ongoing and future pandemic prevention efforts, this study examines the determinants and trends of hand-washing knowledge, attitude and practices among elderly persons, who are a particularly vulnerable population, in Chennai, a major cosmopolitan city in India.

The findings can be used to design a health educational program to promote effective hand-washing practices among elderly persons.

Materials and methods

Study design: Cross-sectional study

Study setting: Government tertiary care hospital in Chennai.

Study population: Elderly persons of 60 years or more

Study period: August 20,2022 to October 20,2022

Sample size: 202 study participants

Inclusion Criteria & Exclusion Criteria

Elderly persons aged 60 years and above who were willing to participate were included in the study, while individuals below 60 years of age or unwilling to participate were excluded.

Questionnaire Preparation and Statistical Analysis

A self-administered, expert-validated KAP questionnaire comprising 5 sociodemographic items and 27 questions on knowledge, attitude, and handwashing practices was used. The questionnaire was expert-validated, involving subject experts from microbiology and community medicine who assessed content relevance, clarity, and comprehensiveness. Necessary modifications were made based on expert feedback before data collection Data from 202 participants were analyzed using SPSS version 26, with normality testing performed and $p < 0.05$ considered statistically significant.

Results

Table 1. Distribution of Sociodemographic Characteristics among Study Participants

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	Mean ± SD	68.87 ± 6.59	—
	Median	67	—
	Range	60 – 87	—
Sex	Male	105	52.0%
	Female	97	48.0%
Educational Qualification	10th grade or lower	115	56.9%
	12th grade	49	24.3%
	Undergraduate	22	10.9%
	Postgraduate	16	7.9%
Co-morbid Conditions	Diabetes/Hypertension	83	41.4%
	Multiple co-morbidities	65	32.2%
	Other co-morbidities	11	5.4%
	No co-morbidities	43	21.3%

Table 1 shows that the mean age of participants was 68.87 ± 6.59 years with nearly equal gender distribution (52% males, 48% females). Most participants (56.9%) had education up to 10th grade or below. A large proportion had co-morbidities, with 41.4% having diabetes/hypertension and 32.2% having multiple co-morbid conditions.

Knowledge

Most participants demonstrated good awareness of COVID-19 transmission and hand hygiene, with high recognition of droplet (90.1%) and surface transmission (65.3%). While 63.9% knew the recommended 20-second handwashing duration, only 42.6% correctly identified liquid soap as ideal. Knowledge scores were higher among females and those with higher education and showed a significant negative correlation with age.

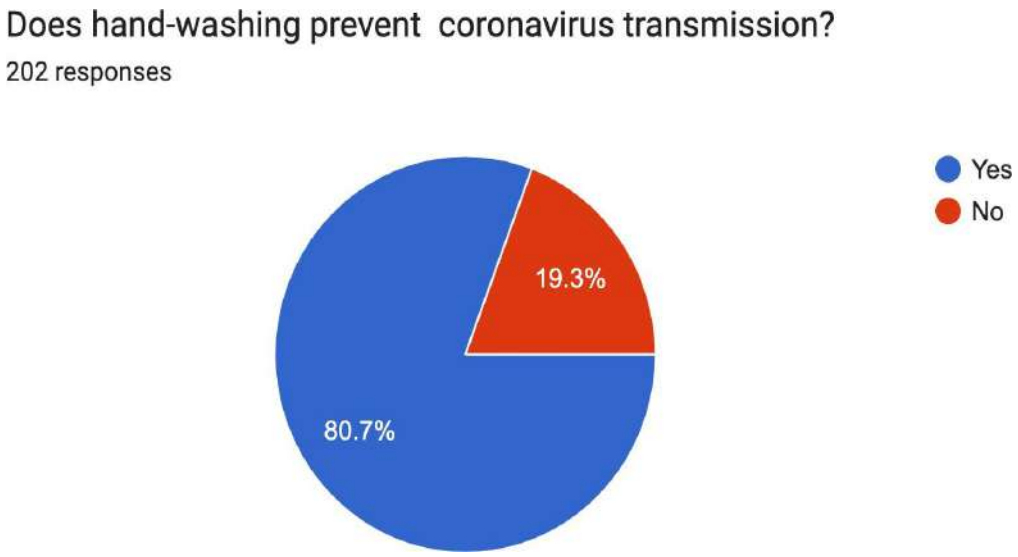


Figure 1. Participants on whether hand-washing prevents coronavirus transmission

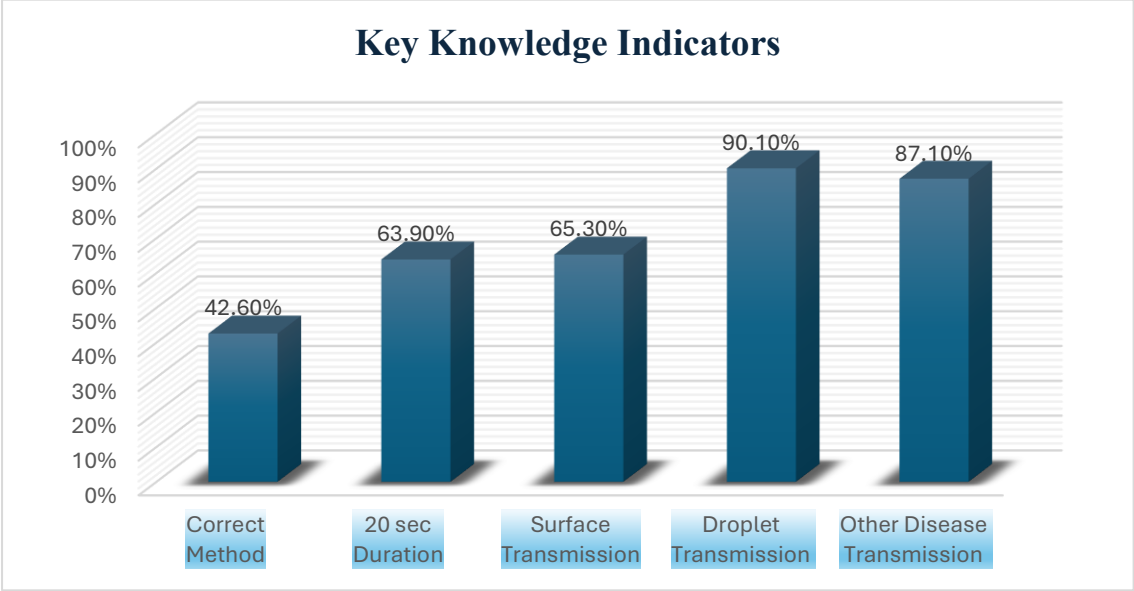


Figure 2. Knowledge Indicators Related to Hand Hygiene Practices

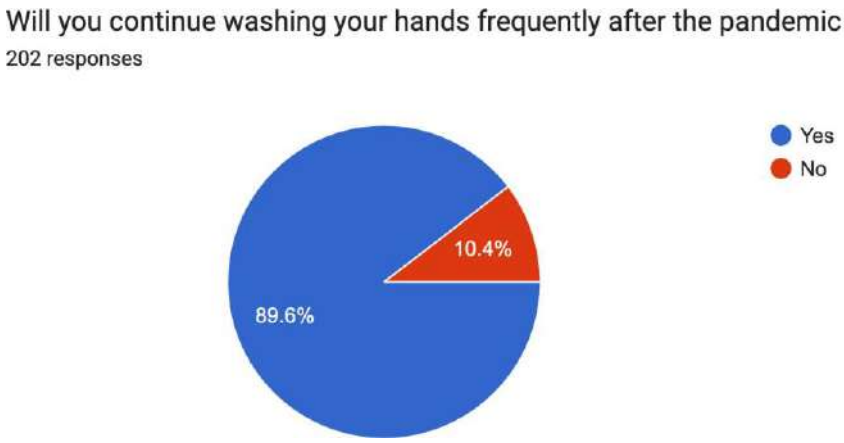


Figure 3. Answers of the participants on whether they will continue to wash their hands frequently after the pandemic is over

A positive attitude toward hand hygiene was observed: 73.8% felt vulnerable to COVID-19, 96% believed hand hygiene should be routine, and 89.6% intended to continue frequent hand-washing post-pandemic. No significant correlation existed between age and attitude scores.

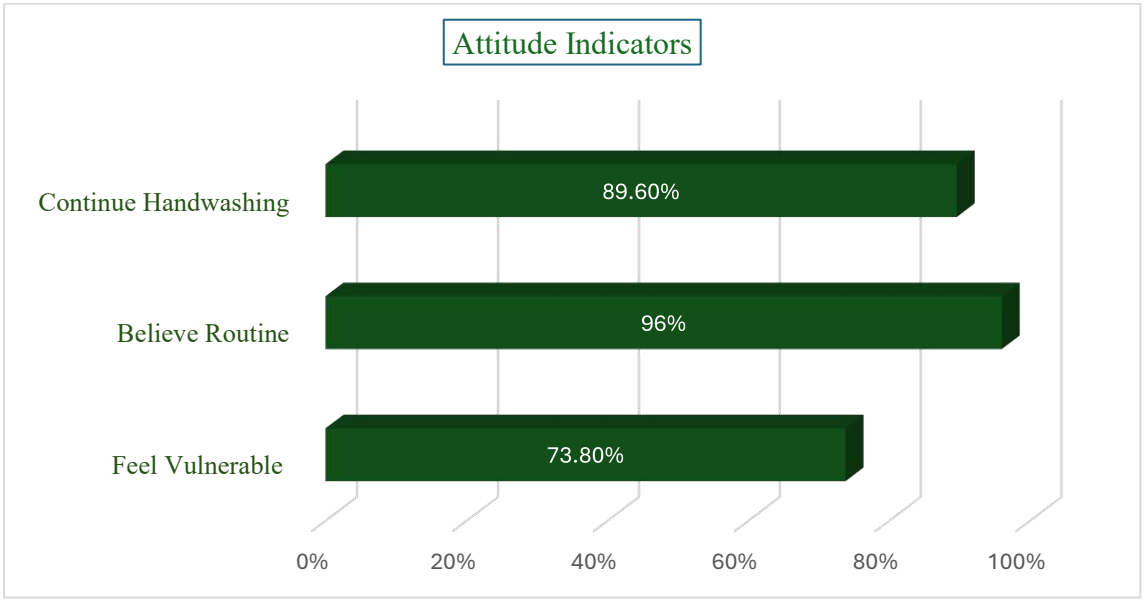


Figure 4. Attitude Levels Toward Hand Hygiene Among Elderly Participant

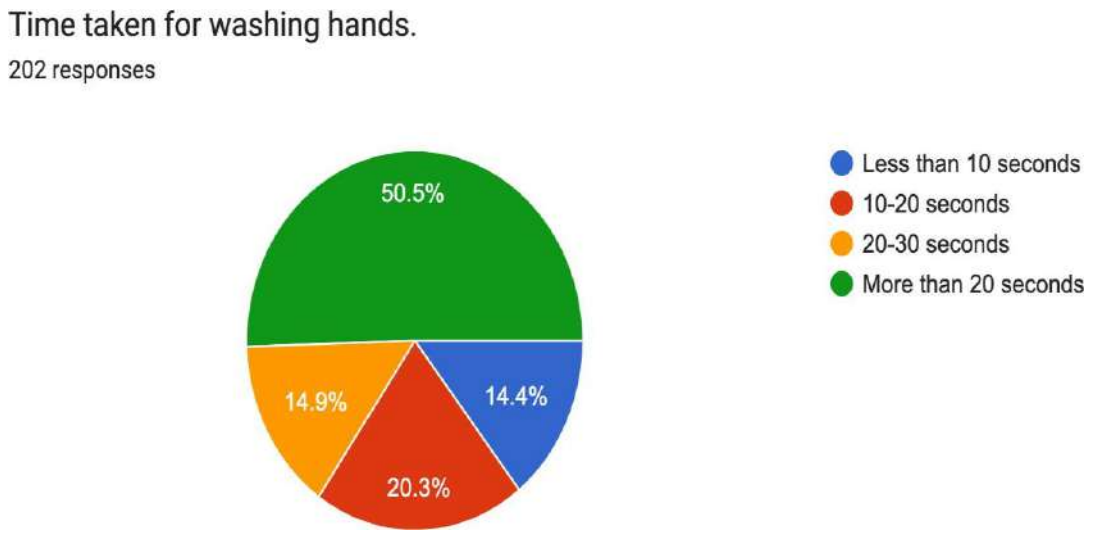


Figure 5. Time taken for washing hands but the participants

A marked improvement in hand hygiene behavior was observed after the COVID-19 pandemic, with liquid soap use increasing to 38.6% and non-use declining to 14.9%, while hand-sanitizer use rose from 2% to 12.9%, with 42% initiating use post-pandemic. Nearly 48.2% reported increased handwashing frequency and 50.5% washed hands for more than 20 seconds; mass media was the main awareness source (56.9%), though only 28.9% practiced handwashing before and after mask use.

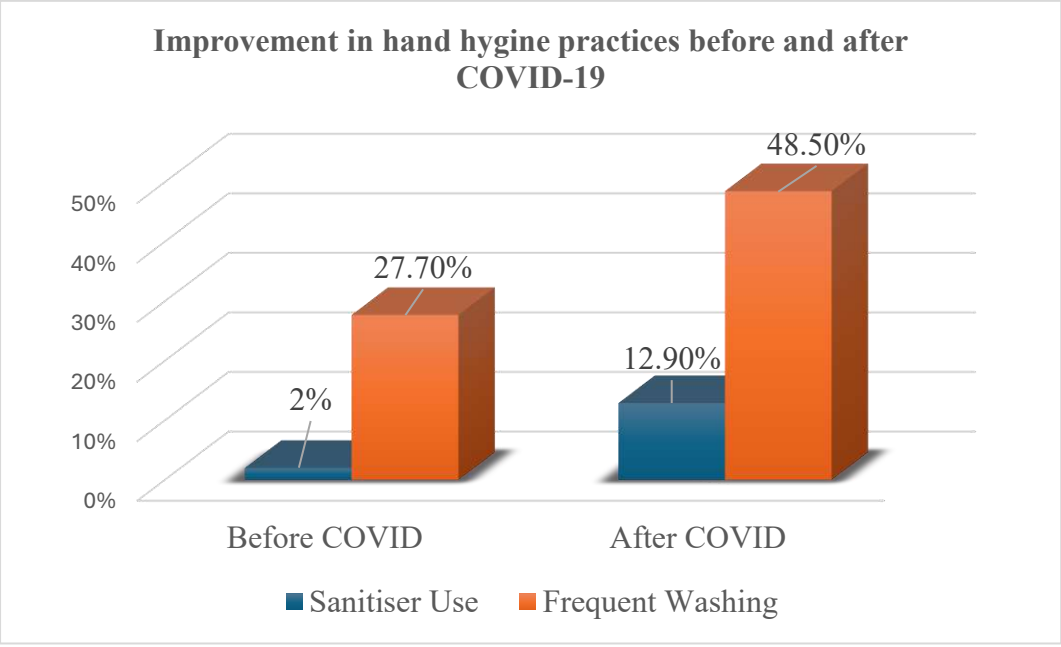


Figure 6. Correlation Between Age and Knowledge Score Among Elderly Participants (N = 202)

Table 2. Correlation Between Age and Knowledge Score on Hand Hygiene Among Elderly Participants (N = 202)

Variables	**Age**	**Knowledge Score**
Age	1.00	**–0.167***
Knowledge Score	**–0.167***	1.00
Significance (2-tailed)	—	0.018
N	202	202

***Correlation is significant at the 0.05 level.

The observed negative correlation between age and knowledge score (r = –0.167, p = 0.018) may be attributed to multiple factors. Increasing age is often associated with a decline in cognitive processing and memory retention, which can affect the ability to comprehend and recall newly disseminated health information. Additionally, older elderly individuals may have limited exposure to digital media and modern communication platforms, which were the primary channels for COVID-19 awareness campaigns. This digital divide likely contributed to relatively lower knowledge levels among higher age groups.

Discussion

This study was done to find out the determinants and trends in Knowledge, attitude and practices on Hand hygiene behaviour in the context of the COVID-19 pandemic among persons older than 60 years, who are at a greater risk of both severe COVID-19 and other infectious diseases due to their lower immunity and other co- morbid factors.

There is a significant negative correlation between age and the mean knowledge score of the respondent. As age increases from 60, the mean knowledge score decreased. This could be attributed to decline in an old adult's cognitive ability which hampers one's ability to comprehend and/or to recall new health information as well as a lower exposure to digital and mass media. However, there was no co-relation between age and the mean attitude score of the respondents. This finding is consistent with other similar studies.[11][12] while contradicting the study done by Kartheek et al. in Andhra Pradesh in 2022 [13], which suggested that age of the participant had no co-relation with their knowledge on hand-hygiene practices.

It is also observed that the respondents of the female sex scored a higher mean knowledge score and higher mean attitude score than their male counterparts. This finding is consistent with the Al-Wutayd et al. 2021's study [11]. Aunger et al. in their study [14] reported that factors such as business, tiredness or hunger can discourage male respondents from performing HH behaviour. Another possible explanation is that, females' high compliance can be also associated with their tendency to practice socially acceptable behaviour [15].

While there was no significant co-relation between presence of co-morbidities and the mean attitude score, it is observed that persons with no-co morbid factors had the highest mean knowledge score and

persons with multiple co-morbidities the least mean knowledge score. This could be because individuals who actively consume health related information and follow healthy habits continue their discipline in keeping themselves healthy. This finding is in concordance with the study done by Nshimyiryo et al. [16].

Although 82.7% of the participants in the study had been exposed to the awareness raising initiatives on hand-hygiene practices by the government, it is still concerning that 17.3% of the study population has not even been exposed to the importance of hand-hygiene during this critical pandemic. This suggests that more targeted and specific initiatives and policies should be implemented for the elderly population.12.8% of the study participants previously did not wash hands regularly but since the COVID-19 outbreak started have started washing regularly. 42% of the study participants who had not used hand-sanitisers before the COVID-19 have since the outbreak started using them.

Likewise, 48.2% of the study participants have increased their frequency of hand- washing and 48.1% have maintained their frequency of hand-washing after the pandemic. These findings are consistent with other similar studies [11] and reflect the significant amount of progress done in inculcating good hand hygiene behaviour due to the increased public awareness campaigns, initiatives and policies implemented during the pandemic.

Mass media like TV, radio and Newspapers have made the biggest impact in ensuring that awareness on hand-hygiene behaviour has reached the elderly population substantiated by 57% of the study population answering mass media as the cause of their awareness, 23,3% of the study population have stated that their reason for skipping hand-washing is due to the inability to afford hand-washing products and a further 7.9% of the study population citing inability to go to the shop and get it.

This implies that accessibility to hand-washing products still remains a major hurdle in our country, and policymakers must take not of it and ensure that good hand- hygiene practices is accessible to all.

The knowledge and practice of correct hand hygiene technique (duration of handwash, ideal hand wash product and indications for hand wash) is still lacking with only 50-60% of the study participants answering correctly. Inadequate handwashing can have the same effects of not handwashing [17]. Therefore, this is another critical aspect of hand-hygiene that needs to be prioritised in the public health initiatives and awareness.

25.9% of the study population believe they are not vulnerable to COVID-19. While this is concerning, it is lower than the 58% seen among the general population in the study conducted by Al-Wutayd et al. in 2021[11]. This finding might be due to the participants wanting to think positively or due to their perception of total immunity after completing their COVID-19 vaccination dose.

Conclusion

The COVID-19 pandemic is a still ongoing pandemic that has affected the entire world for more than 2 years and good hand-hygiene behaviour still remains the most cost-effective method to fight against it. The COVID-19 pandemic has brought an increased focus on the importance of hand-washing among both health care workers and the general public. The handwashing frequencies, soap and hand- sanitisers

usage and also knowledge on handwashing has increased among the elderly persons in Chennai. This is in concordance with multiple similar researches conducted across the world. Our study has also found that younger participants have a higher awareness correlating with better handwashing practices and therefore to create better awareness among the elderly population, especially the older elderly population, specific and targeted initiatives and policies incorporating their daily activities must be created for them.

This study contributes to public health by:

- Providing evidence on behavioural changes in a high-risk population
- Identifying gaps in knowledge and practice despite high awareness
- Highlighting age-related disparities in health literacy
- Supporting policy formulation for vulnerable groups
- Reinforcing the importance of hand hygiene as a cost-effective preventive strategy.

The study highlights several important policy implications:

- Need for targeted health education programs specifically designed for elderly populations
- Strengthening non-digital communication strategies (TV, radio, community outreach)
- Improving accessibility and affordability of hand hygiene products
- Incorporation of behavioural change communication (BCC) tailored to elderly needs
- Development of community-based interventions focusing on correct hand hygiene techniques

Recommendation

- Longitudinal studies to assess sustained behavioural changes post-pandemic
- Interventional studies evaluating effectiveness of targeted education programs
- Research exploring barriers to proper hand hygiene practices among elderly
- Studies assessing rural vs urban differences in hygiene behaviours
- Qualitative research on behavioural and psychosocial determinants

Acknowledgment

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Generalizability

The findings should be interpreted with caution. As the study was conducted in a single tertiary care hospital in Chennai, generalizability may be limited. However, the results provide valuable insights applicable to similar urban elderly populations in India, particularly in healthcare-access settings. Further multicentric studies are recommended for broader generalization.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

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ORIGINAL ARTICLE

Impact of Specimen Weight and Body Mass Index on Surgical Site Infection following Mastectomy in a South Indian Tertiary Care Center

Karthikhaeyan TR,[1] Prateek Gourav,[2] Dhivya M,[3] Jeevithan Shanmugam[4,*] and Rajasenthil V[5]

[1]*Associate Professor, Department of General Surgery, KMCH Institute of Health Sciences and Research, Coimbatore*
[2]*Senior Resident, Department of General Surgery, SCB Medical College & Hospital, Cuttack*
[3]*Assistant Professor, Department of General Surgery, KMCH Institute of Health Sciences and Research, Coimbatore*
[4]*Professor, Department of Community Medicine, KMCH Institute of Health Sciences and Research, Coimbatore*
[5]*Professor, Department of General Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai*

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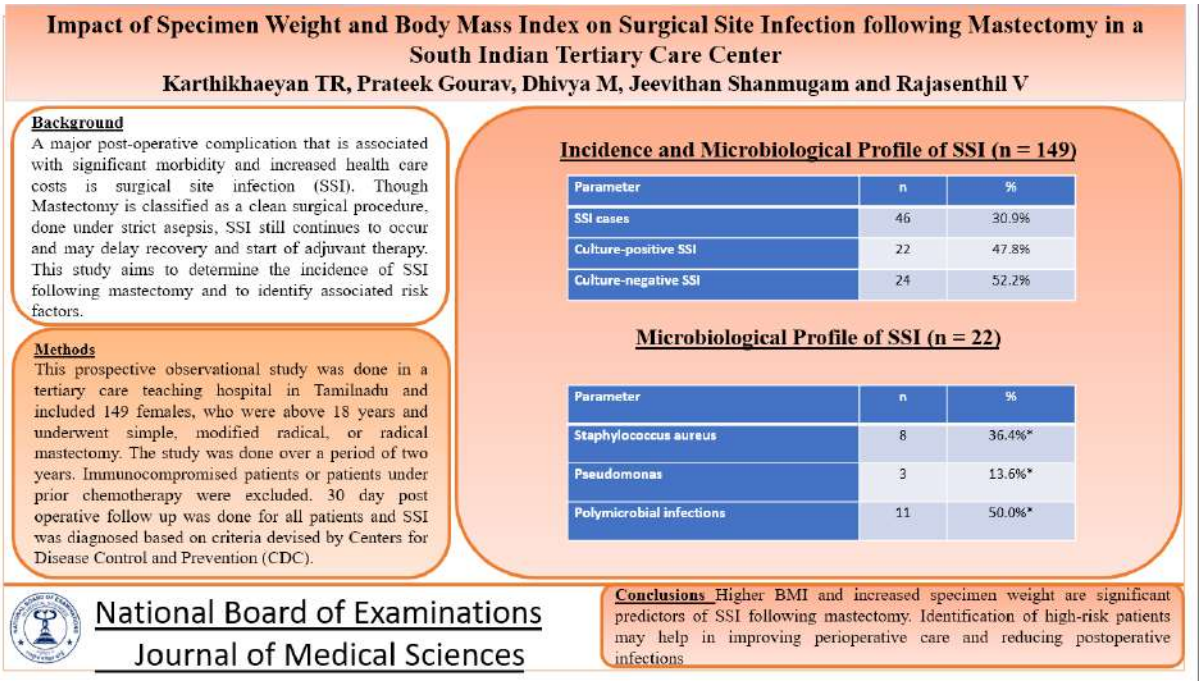
Abstract

Background: A major post-operative complication that is associated with significant morbidity and increased health care costs is surgical site infection (SSI). Though Mastectomy is classified as a clean surgical procedure, done under strict asepsis, SSI still continues to occur and may delay recovery and start of adjuvant therapy. This study aims to determine the incidence of SSI following mastectomy and to identify associated risk factors. **Materials and Methods:** This prospective observational study was done in a tertiary care teaching hospital in Tamilnadu and included 149 females, who were above 18 years and underwent simple, modified radical, or radical mastectomy. The study was done over a period of two years. Immunocompromised patients or patients under prior chemotherapy were excluded. 30 day post operative follow up was done for all patients and SSI was diagnosed based on criteria devised by Centers for Disease Control and Prevention (CDC). **Results:** SSI was noted in 46 patients, with an incidence of 30.9%. Culture was positive in 22 cases (47.8%), while 24 cases (52.2%) were culture-negative. *Staphylococcus aureus* was the most common organism isolated. Higher BMI and greater specimen weight showed significant association with SSI. Other factors such as age, diabetes mellitus, serum albumin, type of mastectomy, and hospital stay did not show significant correlation. **Conclusion:** Higher BMI and increased specimen weight are significant predictors of SSI following mastectomy. Identification of high-risk patients may help in improving perioperative care and reducing postoperative infections.

Keywords: Surgical site infection, Mastectomy, Body mass index, Specimen weight, Breast cancer, Postoperative complications

*Corresponding Author: Jeevithan Shanmugam
Email: dr.jeevithan@gmail.com

Graphical Abstract



Introduction

A major post operative complication that is associated with significant morbidity, prolongation of hospital stay and increased health care costs is surgical site infection [1]. Though there is significant advance in aseptic techniques, perioperative care, and the routine use of prophylactic antibiotics, SSIs still occurs across all types of surgeries, including breast surgery [2,3].

Mastectomy is usually categorized as a clean surgical procedure. Postoperative wound complications like surgical site infections, formation of seromas and flap necrosis are still seen frequently [4]. The reported incidence of SSI following breast surgery differs widely, ranging from 3% to 15%, and depends on patient characteristics, surgical technique, and Institutional practices [5,6]. These infections can affect overall treatment outcomes by delaying wound healing and delay of start of adjuvant therapy.

Risk factors that are associated in the formation of SSIs need to be identified early to implement preventive strategies and to have better surgical outcomes. Patient-related factors like obesity and diabetes mellitus are important contributors to postoperative infections [7,8]. In addition, operative factors like the extent of dissection and mastectomy specimen weight have been known to influence wound healing and infection risk [9]. However, the relative contribution of these factors remains variable across different clinical settings.

Hence, this present study was done to determine the incidence of surgical site infection following mastectomy and to evaluate the association of patient-related and operative factors, particularly body mass index and specimen weight, with the occurrence of SSI.

Materials and Methods

This was a prospective observational study conducted in the Department of General Surgery of a tertiary care teaching hospital in South India. It was done over a period of two years. 149 females aged above 18 years who underwent mastectomy were included in the study. All types of mastectomy including simple mastectomy, modified radical mastectomy, and radical mastectomy were included. Patients who had received neoadjuvant chemotherapy, immunosuppressed patients and those undergoing immediate breast reconstruction were excluded from the study.

Approval was obtained from the Institutional Ethics Committee before the start of the study. All patients had the nature, purpose, and procedures of the study explained to them in their native language, and written informed consent was obtained from each patient before enrolment. All patient details were handled strictly confidential throughout the study. All procedures were carried out ethically.

Baseline clinical details like age, weight, height, body mass index (BMI), blood glucose and preoperative serum albumin levels were noted before the start of the study. Strict aseptic precautions were followed throughout surgery for all patients and prophylactic antibiotics were administered at induction. The choice of antibiotic was based on the institutional antibiogram. After mastectomy, two closed-suction drains were placed and the excised specimen was weighed and recorded in grams, intraoperatively, using a calibrated digital scale.

Postoperatively, all patients were followed up for a period of 30 days to assess for the occurrence of surgical site infection. SSI was defined according to the criteria established by the Centers for Disease Control and Prevention (CDC). Features like presence of purulent discharge, erythema, warmth, and tenderness at the surgical site were assessed for. In suspected infection, wound swabs or fluid samples were collected under strict aseptic precautions and sent for microbiological analysis. Processing was done using routine microbiological techniques by inoculation and incubation on appropriate culture media, followed by identification of organisms. Identification was done based on the morphological and biochemical characteristics of the colonies.

The data collected was compiled and analysed using IBM SPSS Statistics for Windows, Version 27.0 (Armonk, NY: IBM Corp). Categorical variables were analysed using descriptive statistics with frequencies and percentages. Mean and standard deviation was calculated for continuous variables. The association between categorical variables and SSI was evaluated using the Chi-square test, and continuous variables were assessed using the independent samples t-test. A p-value of less than 0.05 was considered statistically significant.

Results

149 females were included in the present study. The mean age of the patients was 52.2 years. The overall incidence of surgical site infection (SSI) in this study was 30.9%, which indicates a high incidence of postoperative infections following mastectomy. Among patients with SSI, 22 (47.8%) were culture-positive, while more than half (52.2%: n=24) were culture-negative, which suggests a possible role of prior antibiotic use or low bacterial load. Among the

culture-positive cases, the complex microbial etiology of SSIs are explained by the presence of polymicrobial infections (50.0%). This was followed by *Staphylococcus aureus* (36.4%) and *Pseudomonas spp.* (13.6%), indicating that both Gram-positive and Gram-negative organisms contribute significantly to postoperative infections (Tables 1 and 2).

Table 1. Incidence and Microbiological Profile of SSI (n = 149)

Parameter	**n**	**%**
SSI cases	46	30.9
Culture-positive SSI	22	14.77
Culture-negative SSI	24	16.11

Table 2. Microbiological Profile of SSI (n = 22)

Parameter	**n**	**%**
Staphylococcus aureus	8	36.4
Pseudomonas	3	13.6
Polymicrobial infections	11	50.0

Among the categorical risk factors, body mass index (BMI) showed a statistically significant association with SSI ($p = 0.038$). The incidence of SSI was highest among obese patients, with 10 out of 16 patients (62.5%) developing SSI, compared to 31 out of 114 (27.2%) in the normal BMI group, indicating obesity as a strong predictor of postoperative infection. In contrast, diabetes mellitus was not significantly associated with SSI ($p = 0.828$), with comparable rates observed among diabetics (21/70; 30.0%) and non-diabetics (25/79; 31.6%). Similarly, the type of mastectomy did not show a significant association ($p = 0.467$), although SSI was slightly more frequent in modified radical mastectomy (38/115; 33.0%) compared to simple (2/12; 16.7%) and radical procedures (6/22; 27.3%) (Table 3).

Table 3. Association of Categorical Risk Factors with SSI

Risk Factor	**SSI Present (n=46)**	**SSI Absent (n=103)**	**Total (n=149)**	**P-Value**
Body Mass Index (BMI)				
Underweight (<18.5)	2 (28.6%)	5 (71.4%)	7	0.038
Normal (18.5–24.9)	31 (27.2%)	83 (72.8%)	114	
Overweight (25–29.9)	3 (25.0%)	9 (75.0%)	12	
Obese (≥30)	10 (62.5%)	6 (37.5%)	16	
Diabetes Mellitus				
No	25 (31.6%)	54 (68.4%)	79	0.828
Yes	21 (30.0%)	49 (70.0%)	70	
Type of Mastectomy				
Simple	2 (16.7%)	10 (83.3%)	12	0.467

Modified Radical Mastectomy	38 (33.0%)	77 (67.0%)	115	
Radical	6 (27.3%)	16 (72.7%)	22	
**Statistically Significant (p < 0.05) (Statistical Test: Chi-Square Test)*				

Among the continuous variables, specimen weight demonstrated a statistically significant association with SSI (p = 0.016), with a higher mean weight observed in the SSI group (1347.7 ± 337.4 g) compared to the non-SSI group (1217.2 ± 282.8 g). Although patients with SSI had slightly lower mean serum albumin levels (3.4 ± 0.6 g/dL) compared to those without SSI (3.6 ± 0.5 g/dL), this difference was not statistically significant (p = 0.065). Similarly, age (51.8 ± 12.3 vs 52.6 ± 11.9 years; p = 0.482) and duration of hospital stay (8.0 ± 5.2 vs 8.0 ± 4.8 days; p = 0.989) were comparable between the two groups, indicating no significant association with SSI (Table 4).

Table 4. Comparison of Continuous Variables

Variable	**SSI Present (Mean ± SD)**	**SSI Absent (Mean ± SD)**	**P-Value**
Specimen Weight (grams)	**1347.7 ± 337.4**	**1217.2 ± 282.8**	**0.016***
Age (years)	51.8 ± 12.3	52.6 ± 11.9	0.482
Serum Albumin (g/dL)	3.4 ± 0.6	3.6 ± 0.5	0.065
Hospital Stay (days)	8 ±5.2	8 ± 4.8	0.989
**Statistically Significant (p < 0.05) (Statistical Test: Independent Samples T-Test)*			

Discussion

Surgical site infection (SSI) remains a significant postoperative complication following breast surgery and contributes to increased morbidity, prolonged recovery, and higher healthcare costs [10-13]. Although mastectomy is considered a clean surgical procedure, the incidence of SSI reported in the literature ranges from 3% to 15% [5,6]. In the present study, the incidence of SSI was found to be 30.9%, which is considerably higher than previously reported rates. Recent studies have shown that surgical site infections remain a significant concern in breast surgery, particularly in low- and middle-income settings, where the incidence can be substantially higher due to patient-related and healthcare system factors [14]. This variation may be attributed to differences in patient characteristics, tumour burden, perioperative factors, and Institutional practices. Along with that, addition of clinically diagnosed infections, including culture-negative patients, may have contributed to the higher incidence that was observed. Tertiary care settings in

India, similar to developing countries reported similar high rates, which can be attributed due to delay in presentation, larger tumour burden, and resource-related factors, which can influence postoperative outcomes [15,16].

In our study, obesity was identified as a significant risk factor for SSI as it was observed more in obese individuals than in people in a normal BMI range, similar to earlier studies which showed an increased risk of postoperative infections in overweight individuals [8]. The higher incidence could be due to reduced vascularity of adipose tissue and impaired oxygen delivery along with technical challenges during surgery which can all negatively impact wound healing. Seroma formation is another risk factor than can be attributed to increased subcutaneous tissue thickness escalating pre existing infection. Xue et al. in their meta analysis, done for many surgical procedures observed that obesity significantly increases the risk of SSIs, re emphasizing BMI as an important modifiable risk factor for SSIs [17].

A significant association was also noted between SSI and specimen weight after mastectomy in this study. Women whose specimen weight was higher had a higher chance of developing an infection, which adds to the hypothesis that larger breast size and wider surgical dissection may lead to increased dead space and fluid accumulation, which predispose bacterial proliferation and cause an impairment in wound healing. Similar observations were noted in many other previous studies done to analyse risk factors for development of post operative infections [9]. In clinical practice, the importance of meticulous planning and surgical technique is re inforced and adequate drainage with close postoperative monitoring in patients with larger specimen weights is mandated. It has also been noted that a higher breast volume and specimen weight were associated with higher rates of seroma formation and wound complications thereby causing an increased susceptibility to post operative infection [18].

On the other hand, in the present study there was no significant association between SSI and diabetes mellitus. This finding is different from many other older studies that proved that diabetes is an independent risk factor for postoperative infections [7]. The lack of association in the present study may be because of excellent perioperative glycemic control or the relatively balanced proportion of diabetics and non-diabetics in the study group. This underlines the significance of good metabolic control in reducing risk of infections in diabetics. Few studies have shown that well-controlled diabetes may not increase SSI risk, stating the importance of optimisation of glycemia control perioperatively [19].

Likewise, other factors like age, serum albumin levels, type of mastectomy, and duration of hospital stay were not associated with SSI significantly in the present study. Hypoalbuminemia is frequently regarded as an indicator of inadequate nutritional status and compromised wound healing; however, the absence of statistical significance in this study may be attributed to the limited number of patients exhibiting mild to severe hypoalbuminemia. The type of mastectomy also did not influence rate of infection significantly, which recommends that patient-related factors and extent of tissue dissection may play a more important role than the actual surgical technique.

As for the microbiological profile of the organisms causing SSI, Staphylococcus aureus was the most common, followed by *Pseudomonas* species, with a remarkable proportion of cases showing polymicrobial infections. These findings are in line with older studies that observed that skin flora was a main source of infection in mastectomy [11,12]. Similar findings have been reported in a recent study, where Staphylococci account for the majority of surgical site infections in breast surgery, followed by Gram-negative organisms and polymicrobial infections [20]. Appropriate empirical antibiotic coverage is needed and is highlighted by the presence of polymicrobial infections. Also, the emergence of resistant organisms highlights the importance of continuous microbiological surveillance and judicious antibiotic use [13]. The synergistic interaction of aerobic and anaerobic organisms cause polymicrobial infections in surgical wounds, which can increase virulence and complicate the management post operatively [21].

The relatively high percentage of culture-negative SSI cases seen in the present study can be due to previous antibiotic administration, low bacterial load, or the presence of sterile inflammatory conditions like a seroma. This highlights that clinical diagnosis is mainstay and we should not be dependent on microbiological confirmation alone. Prior studies done have reported similar findings where previous antibiotic exposure and low bacterial load cause culture-negative infections despite clinical evidence of SSI [22].

Limitations

This study has certain limitations. Being conducted in a single tertiary care centre, the findings may reflect local patient characteristics and may not be generalizable to other settings. The sample size was moderate, and multivariate analysis was not performed, thereby limiting the ability to identify independent predictors of surgical site infection. In addition, the follow-up period was restricted to 30 days, which may have led to underestimation of late-onset infections. Furthermore, a significant proportion of cases were culture-negative, which may have influenced the observed microbiological profile.

Conclusion

There was a 30.9% incidence of surgical site infection following mastectomy in our present study. Higher body mass index and increased specimen weight were significantly associated with SSI, while other factors did not show any significant association. These results highlight the importance of targeted perioperative care in high-risk patients. Sharp surgical technique, efficient dead space management along with immediate identification and treatment of seromas may reduce the risk of post op infections. More larger multicentric studies with multivariate analyses are necessary to validate these findings and design reliable predictive factors for surgical site infection (SSI) following mastectomy.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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ORIGINAL ARTICLE

A Clay-Based Puzzle Icebreaker for Integrated Problem-Based Learning: An Educational Innovation

Divyashanthi Chellathambi Malathi,[1,*] Niraimathi Manickam,[2] Sevitha Venkatesan,[3] Radha Sugumaran,[3] Abinaya Ramachandran,[4] Rishiraj Bhatt,[3] Jeyakumari Duraipandian[3] and Balamurugan Madasamy[3]

[1]*Department of Pharmacology, Jawaharlal Institute of Postgraduate Medical Education and Research, Karaikal*
[2]*Department of Pathology, Jawaharlal Institute of Postgraduate Medical Education and Research, Karaikal*
[3]*Department of Microbiology, Jawaharlal Institute of Postgraduate Medical Education and Research, Karaikal*
[4]*Department of Anesthesiology, Jawaharlal Institute of Postgraduate Medical Education and Research, Karaikal*

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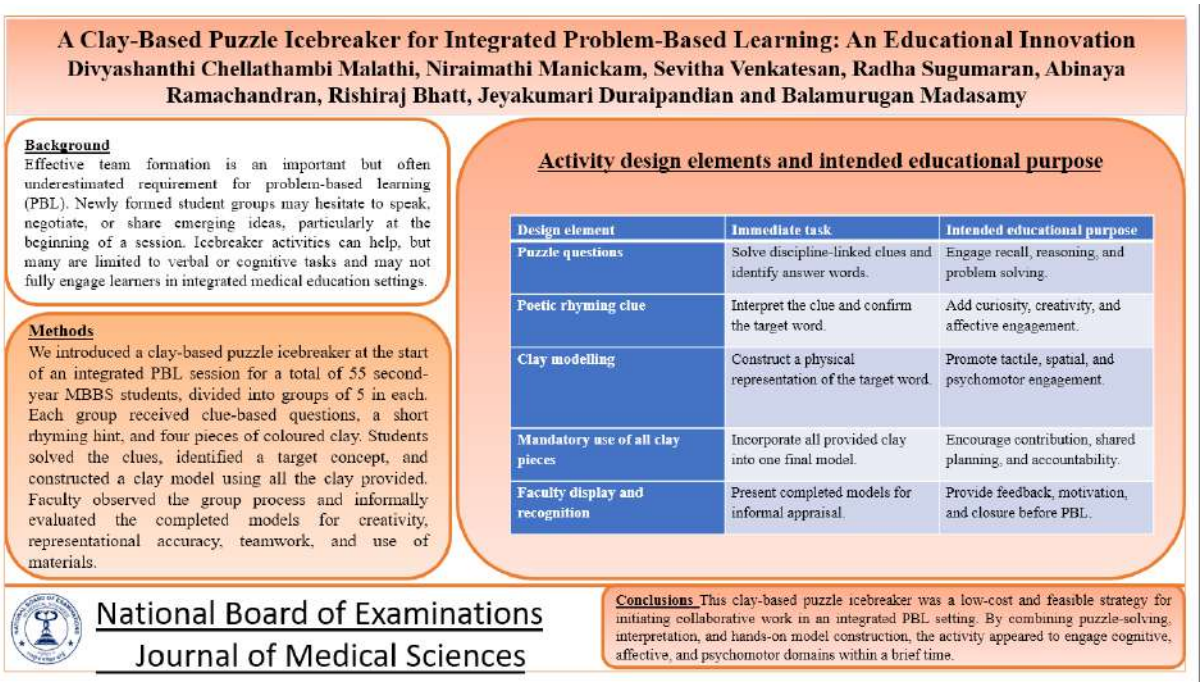
Abstract

Background: Effective team formation is an important but often underestimated requirement for problem-based learning (PBL). Newly formed student groups may hesitate to speak, negotiate, or share emerging ideas, particularly at the beginning of a session. Icebreaker activities can help, but many are limited to verbal or cognitive tasks and may not fully engage learners in integrated medical education settings. **Methodology:** We introduced a clay-based puzzle icebreaker at the start of an integrated PBL session for a total of 55 second-year MBBS students, divided into groups of 5 in each. Each group received clue-based questions, a short rhyming hint, and four pieces of coloured clay. Students solved the clues, identified a target concept, and constructed a clay model using all the clay provided. Faculty observed the group process and informally evaluated the completed models for creativity, representational accuracy, teamwork, and use of materials. **Results:** The activity appeared to promote early interaction among students who were initially unfamiliar with one another. Groups began discussing the clues, sharing construction ideas, and negotiating roles within the first few minutes. Faculty observed increased peer communication, reduced hesitation among quieter students, visible psychomotor engagement, and a more energetic learning climate before the main PBL discussion. **Conclusion:** This clay-based puzzle icebreaker was a low-cost and feasible strategy for initiating collaborative work in an integrated PBL setting. By combining puzzle-solving, interpretation, and hands-on model construction, the activity appeared to engage cognitive, affective, and psychomotor domains within a brief time. Further studies using structured learner feedback, validated engagement measures, and comparison groups are needed before stronger conclusions about effectiveness can be drawn.

Keywords: Icebreaker, Tuckman's framework, Team dynamics, Problem-based learning, Bloom's taxonomy

*Corresponding Author: Divyashanthi Chellathambi Malathi
Email: dishanthii@gmail.com

Graphical Abstract



Introduction

Small-group learning is central to many health professions education formats, including PBL tutorials, clinical case discussions, and simulation-based teaching. The educational value of these formats depends not only on the case or task, but also on the quality of interaction within the group. When students participate actively, listen to one another, and build on each other's ideas, group work can support deeper learning and skill development [1].

PBL is particularly dependent on such interaction. It asks learners to reason through uncertainty, articulate tentative explanations, question assumptions, and learn with and from peers [2, 3]. However, this level of participation cannot be assumed at the start of a session, especially when groups are newly formed. In Tuckman's model of group development, early group behaviour is characterized by caution, dependence on structure, and uncertainty about roles [4]. In a short PBL session, a group that remains in this "forming" stage may lose valuable time before meaningful discussion begins.

Icebreaker activities are commonly used to reduce this initial hesitation. Their value lies in giving students a shared task before the main learning activity begins. However, many icebreakers rely mainly on introductions, conversation prompts, or simple quizzes. Such formats may be useful, but they often engage only one dimension of learning. Bloom's revised taxonomy provides a helpful way to view this limitation, as learning may involve cognitive, affective, and psychomotor domains [5]. An opening activity that brings these domains together may create stronger engagement than an activity based only on verbal exchange.

Kolb's experiential learning cycle also supports the use of brief, hands-on tasks in group learning [6]. A concrete shared experience can prompt discussion, reflection, interpretation, and subsequent application. Clay modelling has been described as a tactile learning tool in

medical education and may support spatial thinking, creativity, and active participation [7,8]. It is inexpensive, easy to organize, and suitable for group use.

Based on these considerations, we designed a clay-based puzzle icebreaker for second-year MBBS students during an integrated PBL session. The aim was to help students move quickly into collaborative work, reduce early social inhibition, and prepare the group for the case discussion that followed. This article describes the design, implementation, observed outcomes, and educational interpretation of the activity.

Materials and Methods

Setting and participants

The activity was conducted during an integrated PBL session for a total of 55 second-year MBBS students at a medical college. The session drew content from pharmacology, microbiology, and pathology. Students were arranged into six groups, with five to six members in each group.

Before the task began, each group was assigned a subject-themed name: *Colony Counters, Slide Survivors, Pink and Purple Squad, Therapeutic Window, Half-Life Hustlers, and Invisible Invaders.* This was intended to provide a simple team identity and create an early sense of belonging before the main task started.

Activity design

Each group received a standardised activity packet. The packet contained clue-based questions, a two-line rhyming clue, and four pieces of coloured modelling clay, each approximately 2 × 2 cm.

The activity was designed to engage three learning domains. The clue-based questions required recall and reasoning, thereby addressing the cognitive domain. The rhyming clue added interpretation, curiosity, and an element of play, contributing to affective engagement. The clay model required students to manipulate materials, make spatial decisions, and construct a physical representation of the target concept, thereby engaging the psychomotor domain [5].

A deliberate rule was added: all four pieces of clay had to be used in the final model. (Table 1). This small constraint encouraged shared planning, reduced the chance that only one or two students would complete the task, and made the group responsible for the final product.

Procedure

The activity was completed in 15 minutes. Groups first solved the clue-based questions and used the initial letters of the answers to identify the target word. They then used the rhyming clue to confirm or refine their interpretation. After this, they constructed a clay model representing the target word and presented the completed model to the faculty panel.

The sample clue card and representative student outputs are shown in Figures 1 and 2.

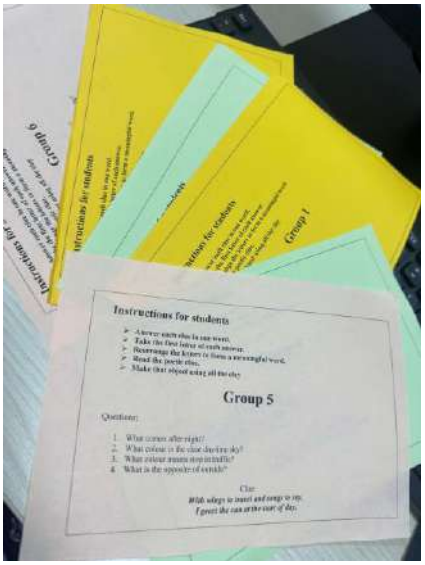


Figure 1. The sample Clue cards

Figure 2. Clay models prepared by students

Evaluation approach

Faculty members observed the group process during the activity and informally reviewed the completed models. The models were appraised using four broad criteria: creativity of representation, accuracy in depicting the target word, evidence of teamwork during construction, and efficient use of the materials provided. The purpose of the appraisal was formative. It was used to provide feedback, recognition, and closure before the PBL discussion, rather than to assign marks.

Table 1. Activity design elements and intended educational purpose

Design element	Immediate task	Intended educational purpose
Puzzle questions	Solve discipline-linked clues and identify answer words.	Engage recall, reasoning, and problem solving.
Poetic rhyming clue	Interpret the clue and confirm the target word.	Add curiosity, creativity, and affective engagement.
Clay modelling	Construct a physical representation of the target word.	Promote tactile, spatial, and psychomotor engagement.
Mandatory use of all clay pieces	Incorporate all provided clay into one final model.	Encourage contribution, shared planning, and accountability.
Faculty display and recognition	Present completed models for informal appraisal.	Provide feedback, motivation, and closure before PBL.

Results

The observed group processes during the ice breaker activity is explained in Table 2.

Rapid team formation

Students began interacting within two to three minutes of receiving the activity materials. The shared task gave each group an immediate focus and appeared to reduce the usual hesitation seen at the beginning of newly formed group work. Students moved quickly from reading the clues to discussing possibilities, assigning small roles, and making construction decisions. This pattern suggested an early shift from social caution toward purposeful collaboration.

Psychomotor engagement

All groups handled the clay actively and worked toward a visible shared product. Students leaned forward, exchanged clay pieces, tested possible shapes, and modified their models based on peer suggestions. The requirement to use all four pieces of clay appeared to increase participation because the group had to decide how every piece would contribute to the final representation.

Peer communication

The activity generated spontaneous peer discussion. Students debated clue answers, interpreted the rhyming hint, and negotiated how the target concept could be shown through clay. Much of this communication occurred without direct faculty prompting, suggesting that the structure of the task itself encouraged interaction.

Reduced social inhibition

Some students who were initially quiet became more involved as the activity progressed. The informal and creative nature of the task appeared to lower the threshold for participation. Because the task was group-based and formative, students could contribute ideas without feeling individually evaluated.

Learning climate before PBL

At the end of the icebreaker, the classroom atmosphere was more energetic and collaborative. Faculty facilitators

observed that students entered the subsequent PBL discussion with greater readiness to speak, share ideas, and respond to case-based questions. These observations should be interpreted cautiously, as they were based on faculty perception and not on a formal comparison with a control group.

Table 2. Observed group processes during the clay-based icebreaker

Observed domain	What was observed	Educational interpretation
Team formation	Students began interacting within two to three minutes and organized around the task.	Suggests an early transition from forming toward collaborative working.
Psychomotor engagement	All groups manipulated clay and worked toward a visible shared product.	Indicates hands-on participation and purposeful use of materials.
Peer communication	Students discussed clues, negotiated ideas, and made shared construction decisions.	Reflects peer-supported problem solving and collaborative learning.
Social inhibition	Initially, quiet students became more comfortable contributing.	Suggests that the creative format may have reduced hesitation.
Learning climate	The room became more active and collaborative before the PBL discussion.	Supports the role of the icebreaker as a preparatory group activity.

Discussion

This educational innovation was developed in response to a common challenge in PBL facilitation: students may need time to become comfortable with one another before they can engage meaningfully with a case. In the present activity, a brief clay-based puzzle task appeared to help groups begin working together quickly. The findings are best understood as preliminary observations from a single implementation, but they offer useful insights for educators designing short preparatory activities for small-group learning.

Relevance to Tuckman's group development model

Tuckman's model describes the early "forming" stage as a period in which group members are cautious, uncertain about expectations, and dependent on external structure [4]. This stage can limit the discussion expected in PBL. The clay-based task provided a defined goal, shared materials, and a short time frame. These features appeared to help students move from hesitation to interaction more quickly. The observed behaviours, including spontaneous discussion, role negotiation, and shared decision-making, are consistent with early movement toward more functional group processes.

Engagement across learning domains

The activity was intentionally designed to include cognitive, affective, and psychomotor elements [5]. The puzzle questions required students to recall and reason through discipline-linked clues. The

rhyming hint introduced curiosity and interpretation. The clay model required physical construction and spatial representation. This combination may explain why students remained engaged throughout the short activity. However, because formal engagement measures were not used, this interpretation should be viewed as a plausible explanation rather than a measured outcome.

Experiential learning perspective

Kolb's experiential learning cycle provides another useful lens for interpreting the activity [6]. The clay construction served as a concrete experience. The discussion around the clues and model encouraged reflection and interpretation. The subsequent PBL discussion allowed students to apply the collaborative ease developed during the icebreaker. In this sense, the activity acted not as a separate game but as a bridge into the main learning task.

Peer scaffolding and collaborative learning

The activity also created opportunities for peer scaffolding. Students with stronger spatial, creative, or verbal skills naturally supported others, while quieter students found smaller but meaningful ways to contribute. The rule that all clay pieces had to be incorporated into the model promoted interdependence, as the final product required collective planning. This aligns with the broader principle that well-structured group tasks can make peer contribution necessary rather than optional [2, 3,10,11].

Practical value for educators

The practical strengths of the activity are important. It required inexpensive materials, minimal preparation, and no specialised equipment. It could be completed within 15 minutes and adapted to different subjects by changing the clues and target words. For resource-limited settings, these features make the activity feasible. The use of team names, faculty display, and informal recognition also added motivation without making the task high-stakes.

Limitations

This report has several limitations. It describes a single implementation at one institution and is based mainly on faculty observation. There was no control group, no validated tool to measure engagement or team development, and no structured pre- and post-activity comparison. Faculty interpretation may have been influenced by observer expectations, and student perceptions were not systematically collected. Therefore, the findings should be interpreted as early observations from an educational innovation rather than evidence of effectiveness. Future work should include structured student feedback, validated engagement or teamwork measures, and implementation across different learner groups and institutions.

Conclusion

A clay-based puzzle icebreaker may be a useful and feasible strategy for preparing students for integrated PBL. In this implementation, the activity appeared to promote early interaction, hands-on participation, peer communication, and a more collaborative classroom climate. Its value lies in its simplicity: a short, low-cost task can give students a shared experience before they begin the main case discussion. Further research using structured outcome measures and comparison groups is needed

to determine whether such activities consistently improve engagement and team functioning in PBL settings.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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ORIGINAL ARTICLE

Study of Natural Death in Prisoners: An Autopsy Based Cross Sectional Study Conducted in a Tertiary Care Hospital

K. Rajesh,[1] V. Ajoy Kumar Ghosh,[1] K. Priyatharsini[2,*] and M. Kumaran[3]

[1]*Assistant Professor, Department of Forensic Medicine and Toxicology, Government Stanley Medical College, Chennai*
[2]*Professor and Head, Department of Forensic Medicine and Toxicology, Government Stanley Medical College, Chennai*
[3]*Associate Professor, Department of Forensic Medicine and Toxicology, Jawaharlal Institute of Postgraduate Medical Education and Research, Karaikal*

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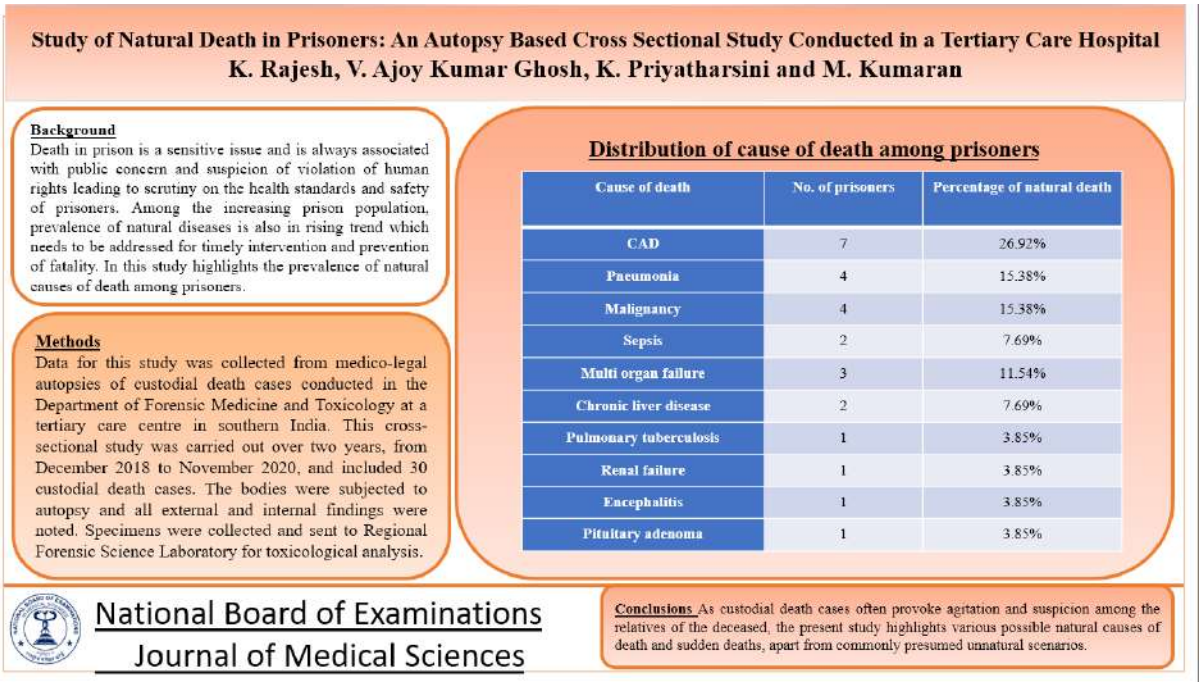
Abstract

Background: Death in prison is a sensitive issue and is always associated with public concern and suspicion of violation of human rights leading to scrutiny on the health standards and safety of prisoners. Among the increasing prison population, prevalence of natural diseases is also in rising trend which needs to be addressed for timely intervention and prevention of fatality. In this study highlights the prevalence of natural causes of death among prisoners. **Methods:** Data for this study was collected from medico-legal autopsies of custodial death cases conducted in the Department of Forensic Medicine and Toxicology at a tertiary care centre in southern India. This cross-sectional study was carried out over two years, from December 2018 to November 2020, and included 30 custodial death cases. The bodies were subjected to autopsy and all external and internal findings were noted. Specimens were collected and sent to Regional Forensic Science Laboratory for toxicological analysis. **Results:** In this study out of the total 30 deaths among prisoners, 26 cases were natural deaths and 4 were unnatural. Among the natural deaths, the most common system involved is the circulatory followed by the respiratory involvement. The most common non-communicable disease prevalent in prisoners were hypertension and diabetes. Sudden death in prison is an entity which can trigger restlessness among the relatives raising suspicion of custodial torture. Five cases sustained sudden death without any previous medical illness. In our study we found that this pattern of sudden death was not uncommon among the prisoners. Out of the seven cases of death due to cardiovascular complications, three cases were not exposed to any pre-existing illness and were apparently normal. The forensic pathologist can consider these natural causes to clear the air of all suspicion and give a clear idea about the cause of death. **Conclusion:** As custodial death cases often provoke agitation and suspicion among the relatives of the deceased, the present study highlights various possible natural causes of death and sudden deaths, apart from commonly presumed unnatural scenarios.

Keywords: Custodial death, Natural diseases, Sudden death, Prisoners

*Corresponding Author: K. Priyatharsini
Email: dr.priyatharsini@gmail.com

Graphical Abstract



Introduction

Death in prison is a sensitive issue and is always associated with public concern and suspicion of violation of human rights leading to scrutiny on the health standards and safety of prisoners. Apart from the allegation of torture, deprivation of medical care is of considerable importance. Owing to the increase in the prison population, there is a significant increase in the death rate among prisoners. In legal terms, custody is defined as any point in time when a person's freedom of movement is denied by law enforcement agencies such as during arrest, transportation to remand, prosecution, sentencing and confinement [1]. Death occurring in some form of custodial detention such as police cell or prison is commonly known as death in custody or custodial death [2]. In other words, death at any point ranging from arrest of a person, imprisonment including transit of prisoners to court. Everyone in prison or custody has the right to proper health care and to be treated humanely. Although there is no suspicion about the circumstances, death in prison raises the suspicion of torture and human rights violations among the relatives, the public and the media. Relatives of the deceased may express concerns about the propriety of police behaviour, and this anxiety may generate additional public disquiet.

According to section 196(2) of BNSS, Magistrate inquest should be carried out in cases of deaths in Police custody. During this inquest the body of the deceased is autopsied, and the process is video graphed. The National Human Rights Commission (NHRC) in India contends that a team of forensic experts conduct the autopsy and deposit the postmortem examination report [3].

The prison population comprises people of various ages, socio-economic and educational status. The prevalence and duration of chronic diseases among the prisoners vary grossly. Some may have initiated treatment before coming to the

prison while some may be screened and started treatment in the prison hospital. But poor knowledge about the usefulness of regular and continuous treatment for their diseases or early reporting of health issues and morbidity among prisoners increase despite adequate medical facilities round the clock. In this study we have analysed the natural death among prisoners and its correlation with demographic profile, prevalence of communicable and non-communicable disease, lifestyle medical and autopsy records. The forensic pathologist can consider these causes to clear the air of all suspicion and give a clear idea about the cause of death.

Aims and Objectives

1. To study the natural causes of death in prisoners.
2. To assess the prevalence of communicable and non-communicable diseases in cases of natural death in prisoners.

Materials and Methods

Data for the present study was collected from the medico-legal autopsies of custodial death cases conducted in the Department of Forensic Medicine and Toxicology in a tertiary care setup in southern-India. This cross-sectional study was undertaken for a period of two years from December 2018 to November 2020 and 30 cases of custodial death were examined. The bodies were subjected to autopsy and all external and internal findings were noted. Specimens were collected and sent to Regional Forensic Science Laboratory for toxicological analysis. Tissue bits from various organs were preserved and sent to Department of Pathology for histopathological examination. For all the cases informed consent was taken from the next of kin. For all the cases studied, medical history and details of the case were collected from the hospital records, prison records and from relatives of deceased prisoner. All cases of unnatural death in jail or police custody, prison or judicial custody and convict ward were excluded from the study. Descriptive data in the present study was expressed as frequency/percentage.

Results

Out of the 30 cases autopsied during the study period, 26 cases had natural cause of death. The details pertaining to these cases were collected from the Magistrate inquest report, prison record furnished during autopsy, hospital records from Medical Records Department, autopsy report, photographs taken at autopsy, chemical analysis report and histopathological examination report. These data were recorded in the proforma for each prisoner and tabulated in the master chart. The master chart was analysed, and results were tabulated category wise. In the present study, among the 30 cases of custodial death, 26 were natural deaths and 4 were unnatural deaths, majority of the natural deaths occurred in the age group of 51–70 years (n=12, 46.16%) followed by 31 to 40 years (n=5, 19.23%), 41 to 50 years (n=4, 15.38%), 19 to 30 years (n=2, 7.69%), 71 to 80 years (n=2, 7.69%). Least number of cases were found in the age group of 81 to 90 years (n=1, 3.85%). Male preponderance was noted in this study contributing to 92.31% (n=24) of natural deaths in the prisoners and females contributing to 7.69% (n=2).

Among the 26 cases of natural death, majority of them were unskilled workers (n=7, 26.92%), four cases were semiskilled (15.38%), four cases were

clerks (15.38%), four cases were semi-professionals (15.38%), three cases were skilled workers (11.54%), two of them were professionals (7.69%) and two of them were unemployed (7.69%).

Considering the scores of modified Kuppuswamy classification for education, occupational and income status the socioeconomic class was calculated. Most of the cases belonged to the 'upper lower' socioeconomic class with 11 cases, contributing to about 42.31% of natural death cases in prisoners. Seven cases belonged to the 'lower middle' class (26.92%), six cases belonged to the 'upper middle' class (23.08%) and the least number of cases belonged to 'upper' and 'lower' socioeconomic status with 1 case, contributing 3.85% each.

On account to the place of death of the prisoners, 20 prisoners died during treatment in the hospital (76.92%), five prisoners died en-route to the hospital (19.23%) and one person died in a private hospital (3.85%).

Out of 30 cases examined 26 cases had natural causes of death (86.67%). Majority of the prisoners died due to complications of coronary artery disease (n=7, 26.92%). Four prisoners died due to pneumonia (15.38%), four individuals died due to complications of malignancy (15.38%) which included a case of squamous cell carcinoma of larynx, squamous cell carcinoma of tongue, adenocarcinoma of gall bladder and pituitary adenoma. Two individuals died of sepsis (7.69%), three died due to multi organ failure (11.54%), two died of chronic liver disease (7.69%), one person died due to pulmonary tuberculosis (3.85%), one died due to renal failure (3.85%), one person died due to encephalitis (3.85%) (Table 1)

.

Table 1. Distribution of cause of death among prisoners.

Cause of death	No. of prisoners	Percentage of natural death
CAD	7	26.92%
Pneumonia	4	15.38%
Malignancy	4	15.38%
Sepsis	2	7.69%
Multi organ failure	3	11.54%
Chronic liver disease	2	7.69%
Pulmonary tuberculosis	1	3.85%
Renal failure	1	3.85%
Encephalitis	1	3.85%
Pituitary adenoma	1	3.85%

In studying the prevalence of non-communicable diseases among the prisoners, isolated systemic hypertension was noted in three individuals (11.5%), isolated diabetes mellitus was present in three individuals (11.5%), and a combined prevalence of diabetes and hypertension was present in six people (23.08%). Respiratory ailments such as bronchial asthma or COPD were prevalent in 2 prisoners (7.69%), two cases were known epileptic patients (7.69%), four prisoners had malignancy (15.38%%), two of them had chronic kidney disease (7.69%) and two prisoners (7.69%) were suffering from decompensated liver disease with portal hypertension (Table 2). In the study nine prisoners died within 24 hours of the terminal event, two between 24-48 hours, one survived for 2-3 days, four survived for 4-5 days and nine survived for a week (Table 3). In five prisoners' sudden death occurred within 24 hours without any pre-existing medical illness. Out of five prisoners with sudden death one died of chronic pyelonephritis three died of coronary disease and one due to organising pneumonia.

Table 2. Distribution of non-communicable diseases among prisoners.

Non-communicable diseases	No. of prisoners	Percentage
Isolated systemic hypertension	3	11.5%
Isolated diabetes mellitus	3	11.5%
Hypertension with diabetes	6	23.08%
Bronchial asthma/COPD	2	7.69%
Epilepsy	2	7.69%
Cancer	3	11.54%
Chronic kidney disease	2	7.69%
DCLD with portal hypertension	2	7.69%

Table 3. Period of survival from onset of terminal event to death

Duration	No. of prisoners	Percentage
<24 hours	9	34.62
24 – 48 hours	2	7.69
2 – 3 days	1	3.85
3 – 4 days	0	0.00
4 – 5 days	4	15.38
5 – 6 days	0	0.00
6 – 7 days	0	0.00
>7 days	9	34.62

On studying the prevalence of communicable diseases among the natural deaths, six prisoners were infected with HIV (23.08%), one person was infected with tuberculosis (3.85%) and four cases suffered from pneumonia (15.38%). In the present study, all cases of natural death in prisoners with HIV infection had been diagnosed before imprisonment and were on Anti-retroviral therapy. But there was history of irregular treatment in 2 cases. Identifying the prevalence of HIV-AIDS among prisoners is critical in preventing spread of other opportunistic infection due to their immune-compromised state.

Discussion

Treatment for critical illness of prisoners in this central prison is usually given at our hospital in a separate convict ward. This had helped us to analyse various cases of custodial deaths. In the study period of 2 years, a total of 30 cases of custodial death were autopsied and natural cause was noted in 26 cases with a prevalence of 86.67%. This is in concordance with the studies conducted by Satinder pal Singh et al. [4], Bansal et al. [5] and Volkanunal et al. [6] with a prevalence of 80%-90%. This implies that death due to natural cause is more frequent than unnatural causes in custodial deaths. In the present study, natural deaths were more in the age group of 51 to 70 years. This is in concordance with the study conducted by Fazel et al. [7] where most cases of natural death occurred in the age group between 50–59 years. This can be related to the fact that natural deaths are more common in elderly prisoner population. In the present study, percentage of natural deaths in males was 92.31% and percentage of natural deaths in females was 7.69% which is in concordance to the study conducted by Sharad Kuchavar et al. [8]. This indicates the preponderance of male population indulging in crimes. In the present study, about 5 cases (19.23%) died while transporting the patient to the hospital and were declared brought dead to the hospital. The remaining 20 natural deaths (76.92%) died in the convict ward of our hospital. This is contradictory to a study conducted by Kuchavar et al. [8] where 31.59% of

cases were natural deaths which occurred inside prisons. In the present study, prevalence of HIV was noted in 6 cases (23.08%) of cases. This is high when compared to Indian study conducted by Bansal et al.(5) which included only 11% of natural death cases died of AIDS. In an USA based study conducted by Okoye et al. [9] the prevalence of death due to AIDS among prisoners was very low such as 2%. In our study, among the cases with single system involvement, majority of cases had cardiovascular system involvement with 26.92% prevalence followed by 19.23% with respiratory system involvement. This is in concordance with studies conducted by Okoye et al. [9], Wu et al.(10) and Aline Desesquelles et al. [11]. But few Indian studies such as Kulkarni et al. [12], Jadhao et al. [13], had proved respiratory diseases are more common than cardiovascular diseases followed by other system involvement. This indicates the need for screening and follow up of cardiovascular and respiratory diseases among prisoners to prevent mortality. Sudden death in prison is an entity which can trigger restlessness among the relatives raising suspicion of custodial torture. In our study we found that this pattern of sudden death was not uncommon among the prisoners. 5 cases sustained sudden death without any previous medical illness. The cause of deaths in these cases are attributed to coronary disease, pneumonia and renal failure United States is the leading country with high numbers of incarceration. In a recent study conducted by the Leonard Davis Institute of Health Economics (LDI) it was established that 30 % of cardiac patients did not receive any diagnostic tests and presented as sudden death in prisons [14]. In the present study, most common cause of death was coronary artery disease (26.92%) followed by pneumonia (15.38%). This is in concordance with a Chinese study conducted by Wu et al. [10] where the author reported coronary artery disease (26.23%) as the most common cause of death followed by pneumonia (13.93%). Indian studies conducted by Kuchavar et al. [8] and Vijaykumarvohra et al. [15] also imply that coronary artery disease is the most common cause of natural death among prisoners. Coronary artery disease stands the commonest cause of natural death among in India and worldwide. This indicates the necessity of intense healthcare and follow up of prisoners with risk factors or history of coronary artery disease. In the present study, all cases of death due to coronary artery disease were males and were in the age group of 35 to 55 years of age.–The youngest man to die of coronary artery disease was 39 years of age. Of the seven cases of death due to coronary artery disease, all cases had history of mixed diet, smoking, alcohol abuse and one case had history of tobacco intake.

In the present study, death due to cancer was noted in three cases (11.54%). All cases of death due to malignancy were males and were in the age group of 60 to70 years of age. This denotes the need for increased cancer screening and management among elderly prisoners. Similar results were observed in the studies conducted by Fazel et al. [7] Aline Desesquelles et al. [11], and Okoye et al. [9].

Wendy L. Wobeser et al. [16] conducted a Canadian study in which death due to malignancy was only second to cardiovascular diseases which analogized with our study.

Conclusion

According to 'article 21' of constitution of India, every person has right to life. In the event of conviction and imprisonment the freedom of a person is restricted by the government, and it becomes the duty of the government to protect his/her human rights and health. Also, regular medical check-up in prison from time to time to review the prisoner's disease status and monitoring intake of prescribed medications will help greatly in controlling the disease and preventing mortality. The National Human Right Commission has prescribed a formal medical screening format for the prison authorities to follow whenever a new prisoner arrives.

This study reveals a different perspective on the causes of death among prisoners. Even the prisoner may sustain sudden death due to a natural cause. As custodial death cases often provoke agitation and suspicion among the relatives of the deceased, the present study highlights various possible natural causes of death and sudden deaths, apart from commonly presumed unnatural scenarios. Forensic pathologists should always consider these possibilities while evaluating and interpreting cases of custodial death.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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Ethical approval

Ethical approval was obtained from institutional ethics committee, Govt. Stanley Medical College & Hospital Chennai-01

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ORIGINAL ARTICLE

Prevalence of Plantar Fasciitis Among Operation Theatre Personnel: A Cross-Sectional Study

Santhosh S,[1,*] T. Gunasekar,[1] and D. Balamurugan[2]
[1]*Assistant Professor, Department of Orthopaedics, Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur– 621 113. Tamil Nadu*
[2]*Assistant Professor, Department of Orthopaedics, Kanyakumari Medical Mission Research Centre, Kanyakumari, Tamil Nadu*

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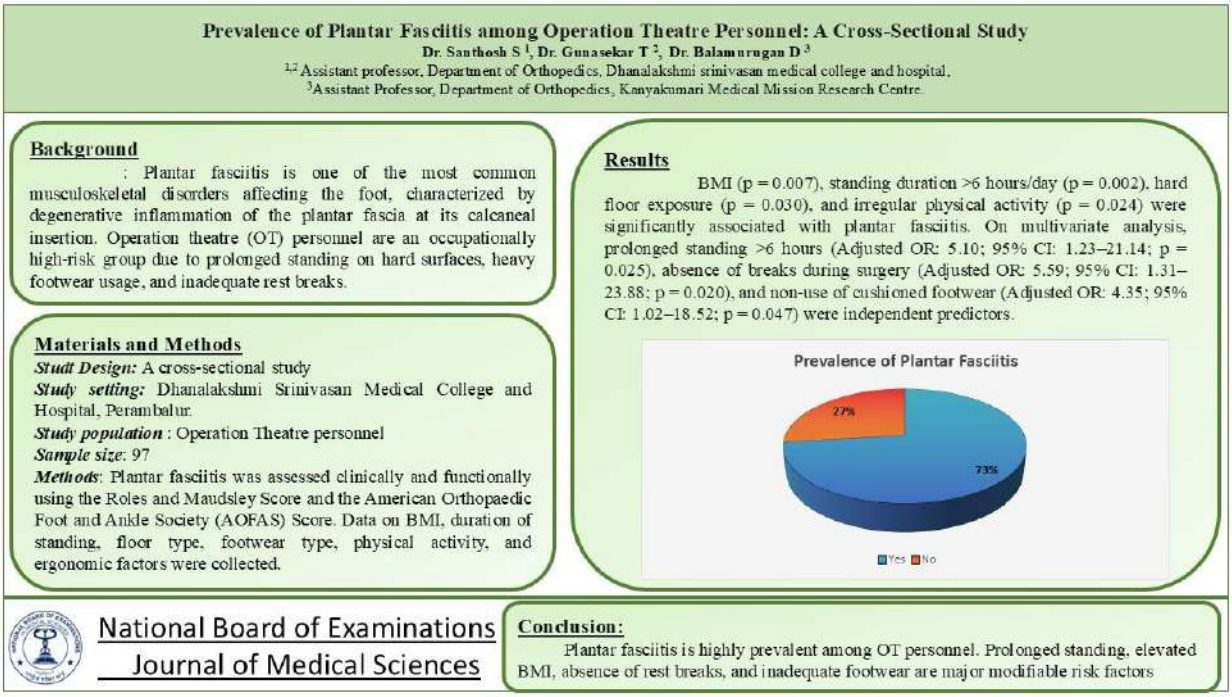
Abstract
Background: Plantar fasciitis is one of the most common musculoskeletal disorders affecting the foot, characterised by degenerative inflammation of the plantar fascia at its calcaneal insertion. Operation theatre (OT) personnel are an occupationally high-risk group due to prolonged standing on hard surfaces, heavy footwear usage, and inadequate rest breaks. However, published data on the prevalence of plantar fasciitis specifically among OT staff remain limited. **Methods:** A cross-sectional study was conducted among 97 operation theatre personnel at Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur. Plantar fasciitis was assessed clinically and functionally using the Roles and Maudsley Score and the American Orthopaedic Foot and Ankle Society (AOFAS) Score. Data on BMI, duration of standing, floor type, footwear type, physical activity, and ergonomic factors were collected. Statistical analysis included Chi-square test for categorical associations and multivariate logistic regression for independent predictors. **Results:** The overall prevalence of plantar fasciitis was 73.2% (71/97). BMI ($p = 0.007$), standing duration >6 hours/day ($p = 0.002$), hard floor exposure ($p = 0.030$), and irregular physical activity ($p = 0.024$) were significantly associated with plantar fasciitis. On multivariate analysis, prolonged standing >6 hours (Adjusted OR: 5.10; 95% CI: 1.23–21.14; $p = 0.025$), absence of breaks during surgery (Adjusted OR: 5.59; 95% CI: 1.31–23.88; $p = 0.020$), and non-use of cushioned footwear (Adjusted OR: 4.35; 95% CI: 1.02–18.52; $p = 0.047$) were independent predictors. **Conclusion:** Plantar fasciitis is highly prevalent among OT personnel. Prolonged standing, elevated BMI, absence of rest breaks, and inadequate footwear are major modifiable risk factors. Workplace ergonomic interventions including scheduled breaks, cushioned footwear, and anti-fatigue matting are urgently needed.

Keywords: Plantar fasciitis, Operation theatre personnel, Occupational health, AOFAS score, Roles and Maudsley Score, Ergonomics, Risk factors

*Corresponding Author: Santhosh S
Email: ssanthosh152@gmail.com

Graphical Abstract



Introduction

Plantar fasciitis is the most common cause of heel pain in adults and accounts for nearly 80% of cases seen by foot and ankle specialists [1]. It develops due to repeated small injuries at the point where the plantar fascia attaches to the medial calcaneal tuberosity of the heel bone. This leads to a long-term degenerative change marked by disturbed collagen fibres, fibrocyte proliferation, and myxoid degeneration, rather than a true inflammatory process [2]. The annual incidence is around 2 million cases in the United States, and the lifetime prevalence is about 10% in the general population [3].

Operation theatre (OT) personnel, including surgeons, anaesthetists, nurses, and technicians, are considered a high-risk group for this condition. Their work often requires standing continuously for long hours, sometimes more than six hours at a time, on hard floor surfaces [4]. These stresses are increased by the use of formal or poorly cushioned footwear and the difficulty of taking breaks during surgical procedures. Obesity can further increase strain on the plantar fascia because of excess body weight and abnormal loading forces [5].

Although these risk factors are common among OT staff, there are only a few studies measuring the prevalence of plantar fasciitis in this group. Most previous research has focused on the general population, runners, or military personnel, with less attention given to healthcare workers working in operation theatres [6,7]. In addition, functional assessment tools such as the Roles and Maudsley Score and the American Orthopaedic Foot and Ankle Society (AOFAS) Score have rarely been used in occupational studies, so the level of disability among affected OT staff is not well understood [8].

Because of this lack of evidence, the present study was planned to determine the

prevalence of plantar fasciitis among operation theatre personnel, assess functional impairment using validated scoring systems, and identify modifiable occupational and body-related risk factors that independently predict the condition. The results may help in developing evidence-based ergonomic policies in hospital workplaces.

Materials and Methods

Study Design and Setting

A cross-sectional study was conducted in the operation theatres of Dhanalakshmi Srinivasan Medical College and Hospital, Siruvachur, Perambalur, Tamil Nadu, India. Ethics approval was obtained from the Institutional Ethics Committee on Human Subjects (Reg. No. IECHS/IRCHS/DSMCH/Cert/1037, dated 27 January 2026) in accordance with the Standard Operating Procedures of the IECHS. Written informed consent was obtained from all participants prior to enrolment.

Study Population

All operation theatre personnel actively working in the OT complex were considered for inclusion. Eligible participants included nurses, technicians, surgeons, and anaesthetists. Personnel who had sustained a lower limb fracture or injury within the preceding six months, those with rheumatological disorders, peripheral vascular disease, or peripheral neuropathy, and those who were pregnant were excluded. Of 112 OT personnel approached, 97 fulfilled the inclusion criteria and consented to participate.

Sample Size

The sample size was calculated using the formula $n = Z^2pq/d^2$, assuming a reference prevalence of plantar fasciitis of 50% ($p = 0.50$), a precision of 10% ($d = 0.10$), and a 95% confidence level ($Z = 1.96$), yielding a minimum of 96 participants. A total of 97 were enrolled.

Clinical Assessment

Plantar fasciitis was diagnosed clinically based on the presence of all three of the following criteria: (a) heel pain that was maximal with the first steps in the morning or after prolonged rest, (b) localised tenderness over the medial calcaneal tuberosity at the origin of the plantar fascia, and (c) pain aggravation on passive dorsiflexion of the toes (Windlass test). Each participant's anthropometric data (height, weight, BMI) were recorded. BMI was classified as normal (<25 kg/m²), overweight (25–29.9 kg/m²), and obese (≥30 kg/m²) per WHO criteria.

Functional Outcome Scoring

Functional impairment was assessed using two validated instruments:

Roles and Maudsley Score (RMS)

A 4-point ordinal scale where 1 = excellent (no pain, full activity), 2 = good (occasional pain, full activity), 3 = fair (pain limiting some activities), and 4 = poor (pain markedly limiting activity). Scores of 3–4 indicate clinically significant functional impairment.

American Orthopaedic Foot and Ankle Society (AOFAS) Ankle-Hindfoot Scale

A 100-point composite score encompassing pain (40 points), function (50 points), and alignment (10 points). Scores below 75 indicate impaired function.

Exposure Variables

Occupational and lifestyle exposure data were collected through a structured interviewer-administered questionnaire. Variables assessed included: duration of daily standing in the OT (categorised as <2, 2–4, 4–6, and >6 hours per day); floor type (hard surface, anti-fatigue mat, or both); type of footwear (cushioned versus non-cushioned); use of shoe inserts or insoles; frequency of breaks during surgery; and level of physical activity outside work (regular versus occasional, defined as exercise on <3 days per week). Foot pain affecting work performance and history of leave taken due to foot pain were also documented.

Statistical Analysis

Data were entered in Microsoft Excel 2019 and analysed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation and compared using the independent samples t-test or Mann-Whitney U test as appropriate after checking for normality using the Shapiro-Wilk test. Categorical variables were expressed as frequencies and percentages and compared using the Chi-square test. Variables with $p < 0.20$ on univariate analysis were entered into a forward conditional multivariate logistic regression model to identify independent predictors of plantar fasciitis. Results are presented as adjusted odds ratios (OR) with 95% confidence intervals (CI). A two-tailed p value of <0.05 was considered statistically significant.

Results

Participant Characteristics and Prevalence

A total of 97 operation theatre personnel were enrolled in the study. The overall prevalence of plantar fasciitis was 73.2%, with 71 participants (73.2%) affected and 26 (26.8%) unaffected (Figure 1). Occupation-wise distribution showed plantar fasciitis in 28 of 37 nurses (75.7%), 15 of 21 technicians (71.4%), 14 of 19 surgeons (73.7%), and 14 of 20 anaesthetists (70.0%). The condition was prevalent across all occupational categories, with nurses contributing the largest number of absolute cases (Figure 2).

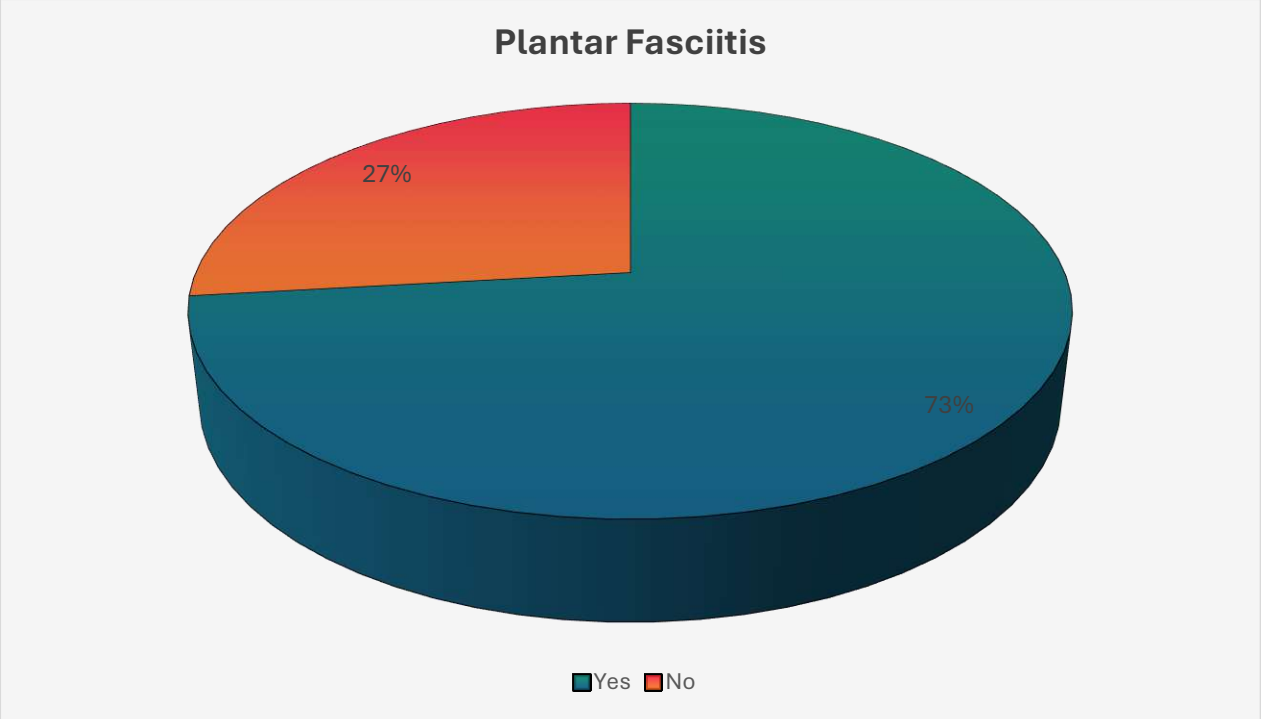


Figure 1. Overall prevalence of plantar fasciitis among operation theatre personnel

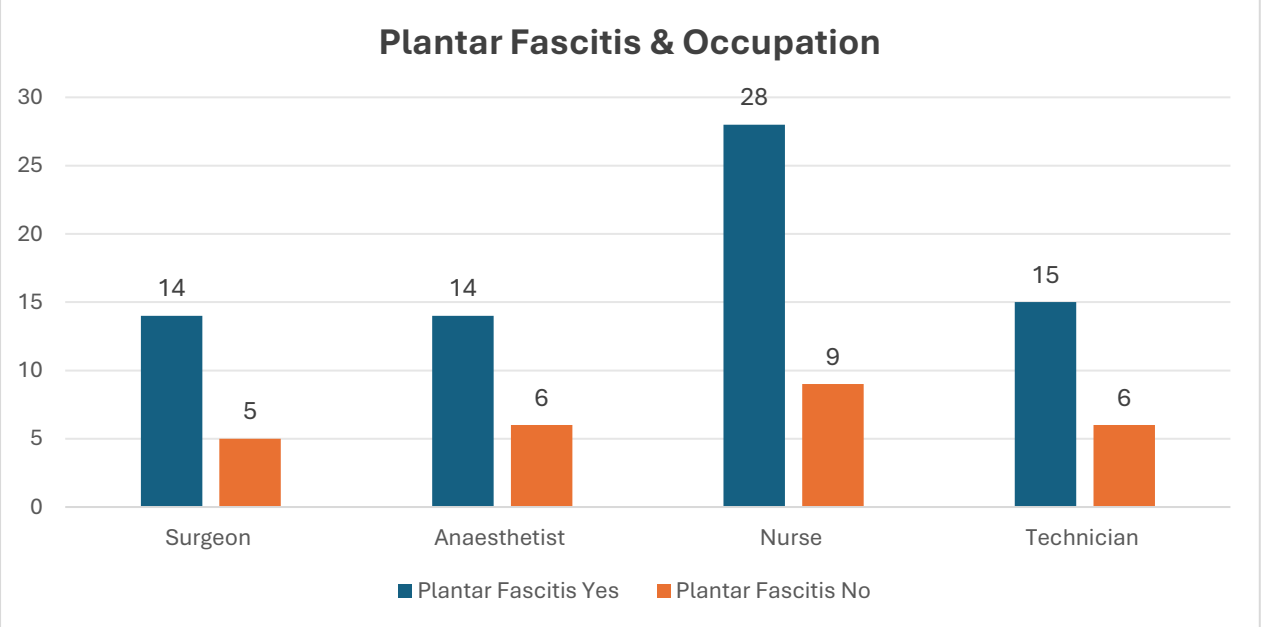


Figure 2. Occupation-wise distribution of plantar fasciitis among operation theatre personnel

Table 1. Comparison of demographic and clinical scores between participants with and without plantar fasciitis

Variable	PF: Yes	PF: No	p-value
Age (years)	31.14±5.34	28.81±5.76	0.06
	31.00 (28.00–36.00)	28.00 (24.00–32.50)	
BMI	27.66±4.07	24.26±3.09	<0.001*
	27.20 (24.40–30.75)	24.15 (22.65–25.48)	
Roles & Maudsley Score (1-4)	3.10±0.72	1.31±0.47	<0.001*
	3.00 (3.00–4.00)	1.00 (1.00–2.00)	
AOFAS Score (0-100)	58.89±7.21	89.85±6.10	<0.001*
	60.00 (53.00–64.00)	90.00 (85.50–94.75)	

** Statistically significant ($p < 0.05$); NS = Not significant; PF = Plantar fasciitis*

Association of Occupational and Anthropometric Factors with Plantar Fasciitis

BMI was significantly associated with plantar fasciitis ($\chi^2 = 9.85$, $p = 0.007$). The prevalence was highest among obese participants (22/24; 91.7%), followed by overweight participants (24/30; 80.0%), and those with normal BMI (25/43; 58.1%). Duration of daily standing in the OT was significantly associated with plantar fasciitis ($\chi^2 = 15.4$, $p = 0.002$), with the highest prevalence among those standing for more than six hours per day (40/46; 87.0%). Floor type was significantly related ($\chi^2 = 6.985$, $p = 0.030$), with participants working predominantly on hard surfaces showing the highest prevalence (48/58; 82.8%). Participants who engaged only in occasional physical activity had a significantly higher prevalence compared to those with regular activity ($\chi^2 = 5.096$, $p = 0.024$). Work-related functional factors — including absence of breaks during surgery ($p = 0.003$), non-use of cushioned footwear ($p = 0.002$), and non-use of shoe inserts or insoles ($p = 0.009$) — were all significantly associated with plantar fasciitis. Foot pain affecting work performance and leave taken due to foot pain were the most strongly associated factors (both $p < 0.001$) Association of BMI, occupational exposure, and lifestyle factors with plantar fasciitis are given in Table 2.

Table 2. Association of occupational and anthropometric factors with plantar fasciitis

Variables		**PF: Yes n (%)**	**PF: No n (%)**	**Chi-square Value**	**p value**
BMI	Normal	25 (58.1%)	18 (41.9%)	9.85	0.007*
	Obese	22 (91.7%)	2 (8.3%)		
	Overweight	24 (80.0%)	6 (20.0%)		
Standing Hours/Day (OT)	2-4 hours	7 (46.7%)	8 (53.3%)	15.4	0.002*
	4-6 hours	24 (70.6%)	10 (29.4%)		
	Less than 2 hours	0 (0.0%)	2 (100.0%)		
	More than 6 hours	40 (87.0%)	6 (13.0%)		
Floor Type	Anti-fatigue mat	7 (53.8%)	6 (46.2%)	6.985	0.03*
	Both	16 (61.5%)	10 (38.5%)		
	Hard surface	48 (82.8%)	10 (17.2%)		
Physical Activity	Occasional	29 (74.4%)	10 (25.6%)	5.096	0.024*
	Regular	10 (45.5%)	12 (54.5%)		
Functional Factors	Breaks During Surgery	25 (58.1%)	18 (41.9%)	8.925	0.003*
	Cushioned Footwear	17 (53.1%)	15 (46.9%)	9.805	0.002*
	Shoe Inserts/Insoles	14 (53.8%)	12 (46.2%)	6.779	0.009*
	Foot Pain Affects Work	58 (93.5%)	4 (6.5%)	36.278	<0.001*
	Leave Taken Due to Foot Pain	35 (94.6%)	2 (5.4%)	13.961	<0.001*

***** *Statistically significant ($p < 0.05$)*

Multivariate Logistic Regression Analysis

Multivariate logistic regression identified three independent predictors of plantar fasciitis (Table 3). Prolonged standing for more than six hours per day carried the highest odds of plantar fasciitis after adjustment (Adjusted OR: 5.10; 95% CI: 1.23–21.14; p = 0.025), followed by the absence of breaks during surgery (Adjusted OR: 5.59; 95% CI: 1.31–23.88; p = 0.020), and the non-use of cushioned footwear (Adjusted OR: 4.35; 95% CI: 1.02–18.52; p = 0.047). Non-use of shoe inserts, hard floor exposure, and use of formal footwear were associated with increased odds but did not attain statistical significance after adjustment.

Table 3. Multivariate logistic regression analysis of predictors of plantar fasciitis

Predictor	**B (SE)**	**Adjusted OR (95% CI)**	**p-value**
Standing > 6 hours/day	1.629 (0.726)	5.10 (1.23–21.14)	0.025*
Absence of breaks during surgery	1.721 (0.741)	5.59 (1.31–23.88)	0.020*
Non-use of cushioned footwear	1.470 (0.739)	4.35 (1.02–18.52)	0.047*
Non-use of shoe inserts	0.705 (0.718)	2.02 (0.50–8.27)	0.326 (NS)
Hard floor exposure	1.267 (0.686)	3.55 (0.93–13.61)	0.065 (NS)
Formal footwear	0.493 (0.910)	1.64 (0.28–9.74)	0.588 (NS)

** Statistically significant (p < 0.05); NS = Not significant; OR = Odds ratio; CI = Confidence interval; SE = Standard error*

Discussion

The present study showed a high prevalence of plantar fasciitis (73.2%) among operation theatre personnel. This is much higher than the prevalence reported in the general adult population (around 10%) and is similar to other occupations involving prolonged standing, such as military recruits and distance runners [3,7]. A cross-sectional study among street vendors in Delhi where they are exposed to prolonged standing, reported heel pain among 46.1% of workers who had higher BMI and longer standing hours as significant risk factors [9]. These findings show that workers in standing-intensive jobs carry a high and often neglected musculoskeletal burden. The comparatively high prevalence noted in this study may attributed to the occupational bunching of multiple risk factors among OT personnel, comprising prolonged standing on hard surfaces, limited rest breaks, and defective footwear support. Furthermore, diagnosis was based on a rigorous combination of clinically typical symptoms

and examination findings, which may have augmented case detection even among mild symptomatic people routinely exposed to these workplace stressors.

High BMI was noted in affected participants which supports the known association between obesity and plantar fasciitis. Excess body weight increases strain on the plantar fascia during walking that leads to degenerative changes at its calcaneal attachment [5]. In this study, plantar fasciitis prevalence increased from 58.1% in normal-weight participants to 80.0% in overweight and 91.7% in obese participants. This pattern is similar to the dose-response relationship reported by Riddle and Schappert [10]. Irving et al. also confirmed that BMI is one of the most consistent factors linked with chronic plantar heel pain in non-athletic populations [11].

Prolonged standing was the strongest predictor in the multivariate model (Adjusted OR: 5.10). Continuous standing places creates repeated stress on the plantar fascia which reduces tissue recovery and promotes small tears [12]. The six-hour threshold seen in this study is similar to the occupational threshold reported by Werner et al. in assembly plant workers [13]. Irving et al. also found moderate evidence linking prolonged standing with chronic plantar heel pain [11].

Lack of intraoperative breaks was independently associated with plantar fasciitis (Adjusted OR: 5.59). This is important because it is a modifiable workplace factor. In operation theatres, long procedures often discourage breaks due to sterility and continuity of surgery. However, planned rest breaks may help reduce fatigue and also protect the plantar fascia [14].

Not using cushioned footwear was another independent predictor (Adjusted OR: 4.35). Reviews have shown that cushioned insoles and anti-fatigue mats reduce discomfort in workers who stand for long periods [15]. Anti-fatigue mats also reduce low back discomfort [16]. Heel cups, heel pads, viscoelastic insoles, rocker-sole shoes, and foot orthoses have all been shown to reduce pain and improve function in plantar fasciitis [17–21]. These findings support the use of cushioned or orthotic footwear for all OT staff.

The mean AOFAS Ankle-Hindfoot Score of 58.89 indicates significant functional limitation in affected participants. Madeley et al. confirmed the validity of this score by showing good response measures and correlation with SF-36 [22]. The Roles and Maudsley Score of 3.10, mainly in the fair-to-poor range which further shows that plantar fasciitis reduces work performance and also their quality of life. Frequent pain-related sick leave also increases institutional burden.

The protective effect of regular physical activity observed in this study is supported by Plesek et al., who found that moderate weekly running reduced the risk of plantar fasciitis compared with inactivity or excessive running [23]. Therefore, regular low-impact exercise can help prevent plantar fasciitis among the study participants.

Plantar fasciitis prevalence was high across all occupational groups—nurses (75.7%), surgeons (73.7%), technicians (71.4%), and anaesthetists (70.0%). This suggests that the common OT environment, standing hours, and footwear are the main causes rather than specific job roles.

Preventive measures should therefore target all OT staff. The Windlass

test used in this study has proven biomechanical validity. Alshami et al. showed that extension of the MTP joint significantly increases plantar fascia strain [24]. Although diagnosis was clinical without imaging, the symptom combination of first-step morning pain, local heel tenderness, and positive Windlass test is accepted in guidelines [25]. Limitations of this study include its cross-sectional design, which cannot prove causation, and its single-centre setting, which may limit generalisability. Furthermore, as participation was voluntary, the likelihood of selection bias cannot be ruled out, as personnel experiencing typical symptoms may have been more persuaded to participate in the study. In addition, certain occupational exposure details were self-reported, which is prone for recall bias and the diagnosis of plantar fasciitis was based on clinical assessment without any imaging confirmation which may have resulted in an overt diagnosis. Future studies should assess new cases after ergonomic interventions and estimate the economic burden on healthcare institutions.

Conclusion

Plantar fasciitis is highly prevalent among operation theatre personnel, affecting nearly three-fourths of this occupationally exposed cohort and causing clinically significant functional impairment as quantified by validated scoring instruments. Prolonged standing exceeding six hours per day, absence of intraoperative rest breaks, and non-use of cushioned footwear are independent and modifiable occupational risk factors. Institutional preventive strategies — including the mandate of viscoelastic footwear, scheduled intraoperative micro-breaks, and the installation of anti-fatigue flooring — are strongly indicated to reduce the musculoskeletal burden on OT personnel.

Conflict of interest

The authors declare that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

Data availability statement

The datasets generated and analysed in this study are available from the corresponding author on reasonable request. They are not publicly shared because they contain sensitive information that could indirectly identify participants.

Ethical Approval

This study has been approved by the Institutional Ethics Committee on Human Subjects, DSMCH, Certificate No. IECHS/IRCHS/DSMCH/Cert/1037, dated 27 January 2026.

Informed Consent

Written informed consent was obtained from all participants after explaining the study procedures, potential risks and benefits. Consent covered both participation and publication of anonymised findings, with assurance of confidentiality and data privacy.

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ORIGINAL ARTICLE

Effect of Antioxidants in Arresting the Progression of Diabetic Retinopathy and Ascertaining the Morphological Changes in the Red Blood Cells as Oxidative Stress Marker: A Pilot Study

Lavanya R,[1,*] Archana Settu[2] and R Kavitha[3]
[1]*Assistant Professor, Department of Pharmacology, Faculty of Medicine, Sri Lalithambigai Medical College and Hospital, Dr M.G.R. Educational and Research Institute, Chennai-600095, Tamil Nadu, India*
[2]*Assistant Professor, Department of Pharmacology, Vels Medical College and Hospital, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Tiruvallur -601102, Tamil Nadu, India*
[3]*Assistant Professor, Department of Pharmacology, Government Medical College and Hospital, Tiruppur-641604, Tamil Nadu, India*

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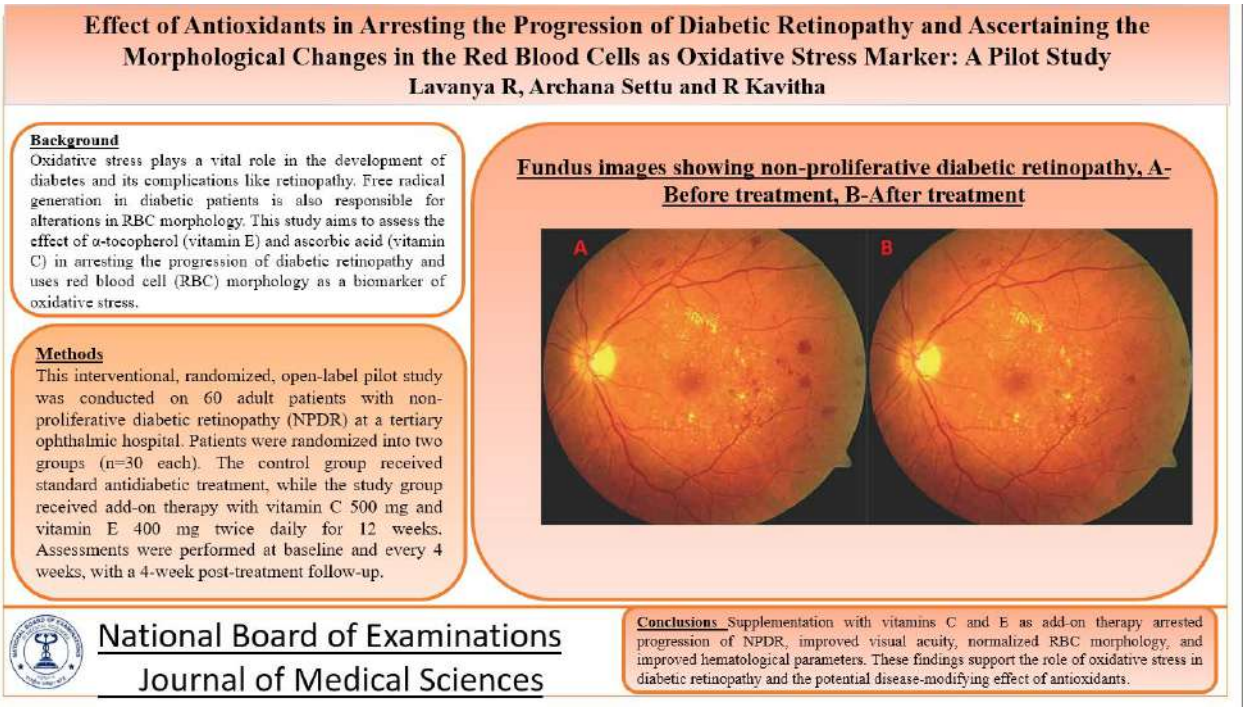
Abstract
Background: Oxidative stress plays a vital role in the development of diabetes and its complications like retinopathy. Free radical generation in diabetic patients is also responsible for alterations in RBC morphology. This study aims to assess the effect of α-tocopherol (vitamin E) and ascorbic acid (vitamin C) in arresting the progression of diabetic retinopathy and uses red blood cell (RBC) morphology as a biomarker of oxidative stress. **Materials and methods:** This interventional, randomized, open-label pilot study was conducted on 60 adult patients with non-proliferative diabetic retinopathy (NPDR) at a tertiary ophthalmic hospital. Patients were randomized into two groups (n=30 each). The control group received standard antidiabetic treatment, while the study group received add-on therapy with vitamin C 500 mg and vitamin E 400 mg twice daily for 12 weeks. Assessments were performed at baseline and every 4 weeks, with a 4-week post-treatment follow-up. **Results:** There was a statistically significant reduction in fasting blood glucose in the study group compared to control at 12 weeks (ANCOVA $p<0.001$). The study group showed a highly significant reduction in crenated RBCs with Heinz bodies (from 80.40% to 7.20%, $p<0.001$) versus minimal change in control (82.57% to 82.33%). Hemoglobin and total RBC count increased significantly in the study group only ($p<0.001$). **Conclusions:** Supplementation with vitamins C and E as add-on therapy arrested progression of NPDR, improved visual acuity, normalized RBC morphology, and improved hematological parameters. These findings support the role of oxidative stress in diabetic retinopathy and the potential disease-modifying effect of antioxidants.

Keywords: Diabetic retinopathy, Oxidative stress, Antioxidants, Vitamin C, Vitamin E, Red blood cell morphology, Heinz bodies

*Corresponding Author: Lavanya R
Email: rlavanyadr@gmail.com

Graphical Abstract



Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycemia, glycosuria, hyperlipidemia, and negative nitrogen balance due to defects in insulin secretion and/or action. Globally, an estimated 422 million adults are living with diabetes mellitus, of which type-II diabetes makes up about 85–90% of all cases [1–3]. In India, diabetes affects more than 62 million people, which is more than 7.1% of the adult population [4–6]. Among its complications, diabetic retinopathy is a major sight-threatening condition leading to blindness [7]. Nearly all patients with type I diabetes develop retinopathy within 15 years, while in type II diabetes the prevalence increases with disease duration: approximately 50% after 10 years, 70% after 20 years, and 90% after 30 years [8–10].

Oxidative stress, defined as an imbalance between free radical production and antioxidant defence [11,12]. Free radicals are products of normal cellular metabolism and can oxidize biomolecules leading to tissue injury [13,14]. Chronic hyperglycemia increases reactive oxygen species (ROS) generation [15,16], which triggers lipid peroxidation and produces inflammatory mediators such as F2-isoprostanes [17-19]. These isoprostanes promote insulin resistance, antagonize insulin action, and reduce nitric oxide bioavailability, leading to vasoconstriction and tissue ischemia [20, 21].

Red blood cells (RBCs), being enucleated and highly susceptible to oxidative damage, undergo membrane alterations, crenation, and hemolysis, contributing to anaemia. ROS also denatures hemoglobin, forming Heinz bodies and impairing oxygen-carrying capacity[22]. These changes, along with hyperglycemia-induced polyol pathway activation and sorbitol accumulation, exacerbate retinal ischemia, hypoxia, and the characteristic lesions of diabetic

retinopathy (microaneurysms, hemorrhages, exudates, neovascularisation, and macular edema) [23–26].

α-Tocopherol (vitamin E) is a potent lipid-soluble antioxidant that inhibits membrane lipid peroxidation, protects RBC integrity against hemolysis, and reduces retinal hypoxia [27–29]. Ascorbic acid (vitamin C) scavenges superoxide radicals, suppresses isoprostane formation, improves insulin sensitivity, reduces protein glycosylation and sorbitol accumulation, and enhances nitric oxide-mediated vasodilatation [30,31]. By mitigating oxidative stress and associated vascular events, early supplementation with vitamins C and E may arrest or reverse early signs of diabetic retinopathy [32–35]. The present study was conducted to evaluate the effect of vitamins C and E on insulin resistance, glycemic control, progression of diabetic retinopathy, and hemolytic anemia (using RBC morphology as a biomarker of oxidative stress) in a randomized, open-label, comparative pilot study.

Objectives of this study

Primary objective

To evaluate the efficacy of antioxidants (vitamin C and E) as add-on therapy in arresting the progression of diabetic retinopathy.

Secondary objectives

To evaluate morphological changes in red blood cells due to oxidative stress and their reversal with vitamins C and E; to assess improvement in hemoglobin and RBC count.

Materials and Methods

The study was conducted at the Regional Institute of Ophthalmology and Government Ophthalmic Hospital, Egmore, Chennai, and the Institute of Diabetology, Rajiv Gandhi Government General Hospital, Chennai from June 2016-January 2017.

Study Design

Open-label, randomized, comparative pilot study with 60 patients (30 per group). Total duration per patient was 16 weeks (12 weeks intervention + 4 weeks post-treatment follow-up).

Inclusion Criteria

Patients of either sex aged 40-70 years, diagnosed with diabetic retinopathy (very mild to very severe NPDR), type-II diabetes mellitus for >5 years, on standard treatment, and willing to give informed consent.

Exclusion Criteria

Proliferative diabetic retinopathy, previous ocular surgery or injections, other ocular diseases, uncontrolled hypertension, renal or hepatic dysfunction.

Study Procedure

Out of 134 patients screened, 60 eligible patients with non-proliferative diabetic retinopathy (NPDR) were enrolled after obtaining written informed consent. Participants were randomised (1:1) using simple randomisation into two groups. The control group (n=30) received standard antidiabetic therapy (oral hypoglycemic agents and/or insulin). The study group (n=30) received standard antidiabetic therapy plus ascorbic acid (vitamin C) 500 mg and α-tocopherol (vitamin E) 400 mg twice daily for 12 weeks. Compliance was monitored using empty blister packs at 4-weekly follow-up visits (weeks 4, 8, and 12). After completion of the 12-week

intervention, all patients were followed up for an additional 4 weeks without study medication to assess the sustainability of effects on diabetic retinopathy grading and RBC morphology.

Assessments

Diabetic retinopathy grading (ETDRS scale), RBC morphology (% crenated RBCs with Heinz bodies), fasting blood glucose, hemoglobin, RBC count, and visual acuity at baseline, 4, 8, and 12 weeks.

Statistical Analysis

Data were analyzed using SPSS version 21. Within-group changes were assessed by paired t-test/Wilcoxon signed-rank test. Between-group comparisons used independent t-test/Mann-Whitney U test and ANCOVA. A p-value <0.05 was considered statistically significant.

Results

The mean duration of diabetes in the control group was 9.97 years and the study group was 10.07 years, which was statistically insignificant (P=0.924). There was no significant statistical difference between the groups. Intergroup analysis showed that both the groups were comparable at 0 weeks (P=0.370), but at the end of 12 weeks there was a greater reduction in fasting blood glucose level in the study group (176.60 to 105.77 mg/dL) compared to the control group (172.17 to 150.80 mg/dL) and this was found to be statistically significant (P<0.001). There was no significant difference between the control and study group at 0 weeks (P=0.253), whereas, at the end of 12 weeks, the study group showed a significant decrease in the percentage of crenated RBCs (P<0.001).

The mean hemoglobin (Hb) was below average in both the control (11.25 gm/dl) and study group (10.8 gm/dl) at 0 weeks. After 12 weeks, the study group showed a significant increase in Hb (12.27gm/dL, P<0.001), while the control group did not show any significant difference (11.16 gm/dL, P=0.228). Between the groups, at 0 weeks there was no statistical difference (P=0.138) but at the end of 12 weeks, the study group showed a significant increase in hemoglobin than the control group (P=0.001). The mean total RBC count significantly increased in the study group from 3.94 million/µL at 0 weeks to 4.58 million/µL at 12 weeks (P=<0.001), while there was no statistically significant difference in the control group (0 weeks-4.02 million/µL, 12 weeks-4.01 million/µL, P=0.491).

The two groups were comparable at the beginning of the study (P=0.393). But at the end of the 12 weeks, the study group showed a significant increase in RBC count (P=<0.001). The morphology of RBCs before (crenated RBC) and after (normal RBC) is shown in Figure 1. The number of patients with the grading of diabetic retinopathy among study participants is depicted in Table 1.

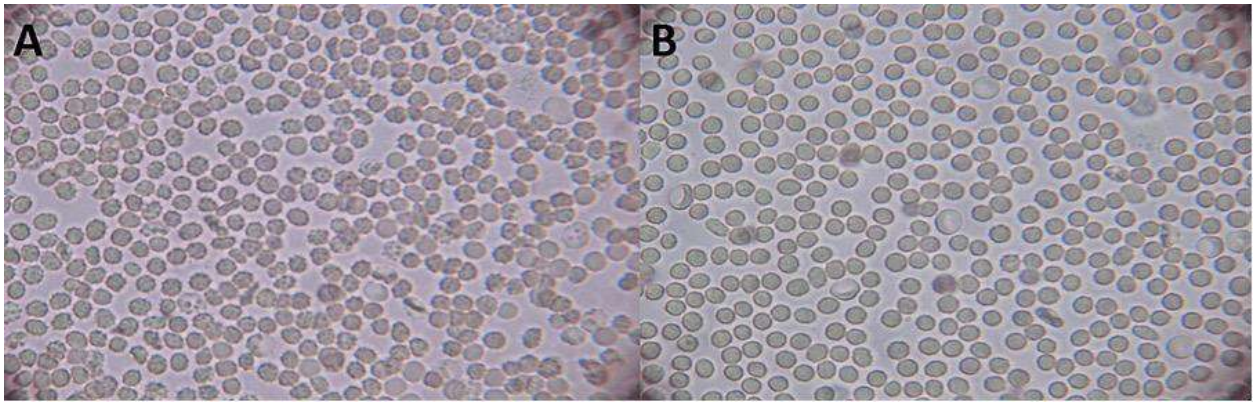


Figure 1. Morphology of RBCs, A-Before (crenated RBC), B-After (normal RBC)
RBC-Red blood cells

Table 1. Grading of diabetic retinopathy among study participants

Study population	**Grading**	**0 week**	**At the end of 12 weeks**	**P-value**
Control group (n=30)	Normal	0	0	0.09
	Very mild	0	1	
	Mild	3	0	
	Moderate	9	10	
	Severe	12	12	
	Very severe	6	7	
Study group (n=30)	Normal	0	1	0.001 (Significant)
	Very mild	0	13	
	Mild	0	14	
	Moderate	3	2	
	Severe	12	0	
	Very severe	15	0	
P-value		0.665	0.019 (Significant)	

Intergroup analysis at 12 weeks showed a statistically significant improvement in DR grading in the study group (p=0.019).

Visual status and complications among the study participants at the end of 12 weeks is shown in Tables 2 and 3 respectively. The fundus images of non-proliferative diabetic retinopathy are shown in Figure 2.

Table 2. Visual status among study participants at the end of 12 weeks

Visual acuity	**Control group (n=30)**	**Study group (n=30)**
	Number of patients (%)	Number of patients (%)
Improved ≥6/12	1 (3.33%)	6 (20%)
Stable 6/18–6/36	20 (66.67%)	23 (76.67%)
Deterioration ≤6/60	9 (26.67%)	1 (3.33%)

Table 3. Complications among the study participants

Adverse events	Control group (n=30)	Study group (n=30)	P-value
Nausea	3	1	-
Abdominal pain	1	1	-
Diarrhea	2	0	-
Hypoglycemia	2	1	-
Metallic taste	1	1	-
Incidence	30%	13%	**0.209***

*P-value calculated using Fisher's Exact Test for overall incidence between groups. Individual event frequencies were too small for independent robust statistical comparison. The difference in overall incidence is not statistically significant ($p > 0.05$).

All events were mild. Beneficial effects on DR grading, visual acuity, and RBC morphology were sustained during the 4-week post-treatment follow-up.

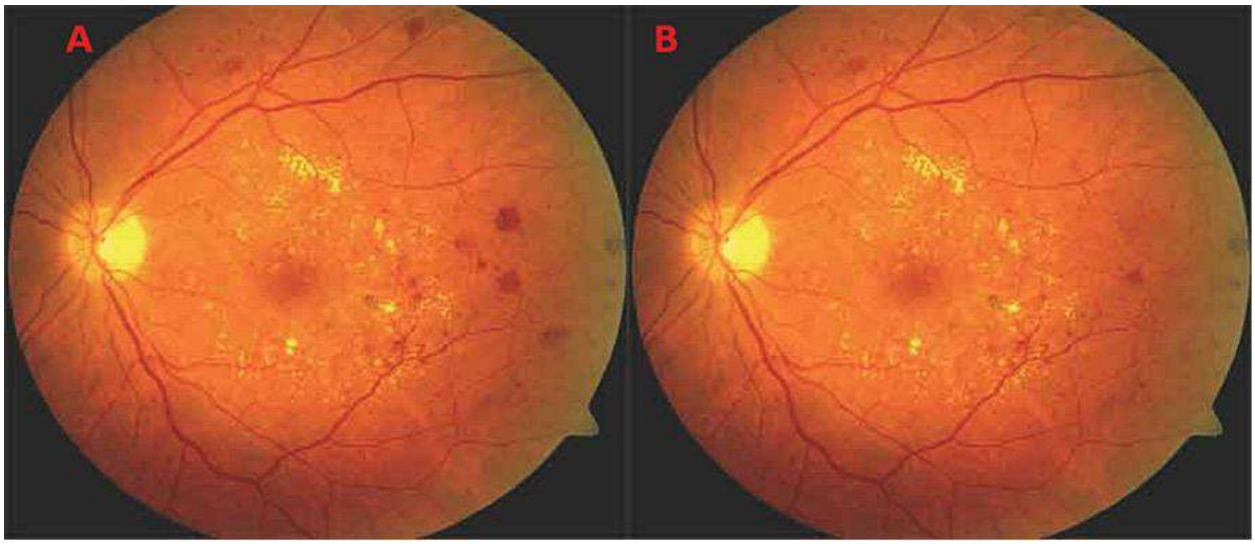


Figure 2. Fundus images showing non-proliferative diabetic retinopathy, A-Before treatment, B-After treatment

Discussion

Diabetic retinopathy is a microangiopathy characterized by microaneurysms, retinal hemorrhages, hard exudates, and cotton wool spots. Complications of proliferative diabetic retinopathy, including vitreous hemorrhage, neovascular glaucoma, and tractional retinal detachment, remain major causes of blindness [36]. Approximately 50% of diabetic patients develop retinopathy after 10 years and 90% after 30 years of disease onset [37].

In diabetes, hyperglycemia-driven excess free radical production coupled with antioxidant deficiency leads to oxidative tissue damage. Oxidative injury to RBC membranes results in crenated cells with loss of biconcave shape, while hemoglobin denaturation produces Heinz bodies [22]. These damaged RBCs undergo accelerated destruction in the spleen, causing hemolytic anemia [38,39]. Reactive oxygen species (ROS) also reduce nitric oxide bioavailability, promoting vasospasm [40], while lipid peroxidation of cell membranes

increases arachidonic acid and generates inflammatory isoprostanes [41]. Collectively, hemolytic anemia, vasospasm, and chronic inflammation contribute to retinal ischemia and progression of diabetic retinopathy[41].

The present study evaluated the efficacy of antioxidants α-tocopherol (vitamin E 400 mg) and ascorbic acid (vitamin C 500 mg) twice daily as add-on therapy to standard antidiabetic treatment in patients with non-proliferative diabetic retinopathy (NPDR) of more than five years duration. Sixty patients were randomized into control (standard therapy) and study groups (n=30 each) and followed for 12 weeks of treatment plus 4 weeks post-treatment.

Both groups had comparable baseline characteristics (mean age ≈53 years, mean diabetes duration ≈10 years). After 12 weeks, the study group showed significantly greater reduction in fasting blood glucose (176.60 to 105.77 mg/dL, P<0.001) compared to the control group (172.17 to 150.80 mg/dL, P=0.025), with intergroup difference P<0.001, indicating improved glycemic control with antioxidant supplementation.

Oxidative stress markers improved markedly in the study group. The percentage of crenated RBCs with Heinz bodies decreased dramatically from 80.40% to 7.20% (P<0.001), while no significant change occurred in the control group. Reticulocyte count fell from 2.50% to 0.40% (P<0.001) in the study group only. Hemoglobin rose from 10.8 to 12.27 g/dL (P<0.001) and total RBC count increased from 3.94 to 4.58 million/μL (P<0.001) in the study group, confirming that antioxidant therapy reduces free radical-induced RBC damage, hemolysis, and associated anemia [33,44].

Regarding retinopathy, ETDRS grading by fundus examination showed statistically significant regression in the number of patients with very severe, severe, and moderate NPDR in the study group (P=0.001) but not in the control group (P=0.09). Intergroup analysis confirmed greater reduction in retinopathy severity (P=0.019). Visual acuity improved in 20% of the study group versus 3.33% in the control group.

Antioxidants exert these benefits by scavenging ROS, preserving nitric oxide bioavailability to prevent vasospasm, reducing isoprostane-mediated inflammation, protecting RBC membrane integrity, and improving tissue oxygenation. Mild adverse effects (nausea, abdominal pain, diarrhea, hypoglycemia, metallic taste) were less frequent and less severe in the study group. Beneficial effects on glycemic control, RBC morphology, anemia, retinopathy grading, and visual acuity were sustained at the 4-week follow-up in the study group.

These findings are largely consistent with previous study reports on antioxidant therapy in diabetic retinopathy, although the magnitude and rapidity of improvement observed here appear more pronounced. Sanz-González et al. demonstrated that long-term supplementation with a multi-antioxidant formulation (including vitamins C and E) significantly slowed the progression of diabetic retinopathy over 60 months in patients with mild-to-moderate NPDR [34]. Similarly, Chatziralli et al. reported reduced oxidative stress markers and improved outcomes with vitamin E supplementation in insulin-dependent type 2 diabetes patients with retinopathy [29]. However, several other randomized controlled trials have demonstrated only

modest or inconsistent benefits on retinopathy progression with shorter durations or single-antioxidant regimens, while some studies found no significant structural improvement.

In conclusion, the addition of vitamins C and E to standard therapy resulted in superior glycemic control, normalization of RBC morphology, correction of hemolytic anemia, arrest/regression of NPDR, and better visual outcomes. These findings highlight the central role of oxidative stress in diabetic retinopathy and support RBC morphology as a simple, accessible biomarker of oxidative damage.

Limitations

Small sample size, short duration, open-label design. Larger, double-blind, randomized controlled trials with longer follow-up and inclusion of HbA1c and masked fundus photography grading are warranted.

Conclusions

Free radicals contribute significantly to the complications of diabetes. Antioxidants like α-tocopherol (vitamin E) and ascorbic acid (vitamin C) act as disease-modifying agents by reducing oxidative stress and insulin resistance. This pilot study demonstrates their potential in arresting diabetic retinopathy progression, normalizing RBC morphology, and improving quality of life in type-II diabetic patients.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

Funding

No funding was received for conducting this study.

Competing Interests

The authors have no relevant financial or non-financial interests to disclose. The authors have no competing interests to declare that are relevant to the content of this article.

Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Institutional Ethics Committee approval was obtained (ECR/270/Inst./TN/2013/14051016). The study followed the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines. Written informed consent was obtained from all individual participants included in the study.

Informed Consent

Informed consent was obtained from all individual participants included in the study. The authors affirm that human research participants provided informed consent for publication of the images in Figure 1 (RBC morphology) and Figure 2 (fundus images), where applicable.

Data Availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' Contributions

LR: Conceptualization, Methodology, Investigation, Data Curation, Writing – Original Draft, Writing – Review & Editing, Visualization, Supervision, Project Administration. AS: Methodology, Formal Analysis, Investigation, Data Curation, Writing – Review & Editing. RK: Investigation, Resources, Writing – Review & Editing.

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ORIGINAL ARTICLE

Impact of Lipid Status on Environmental Quality of Life and Mood Disorders Among Diabetic Cohorts

B.S. Suganya Priyadharshini,[1] Ramesh A,[2] Srinithi Rajendran,[3] Ashwin Samilal[4] and Jeevithan Shanmugam[5,*]
[1]*Associate Professor, Department of Psychiatry, KMCH Institute of Health Sciences and Research, Coimbatore -14*
[2]*Assistant Professor, Department of Urology, KMCH Institute of Health Sciences and Research, Coimbatore – 14*
[3]*Assistant Professor, Department of Psychiatry, KMCH institute of Health Sciences and Research, Coimbatore – 14*
[4]*Fellow Trainee, The Royal Australian and New Zealand College of Psychiatrists (RANZCP)*
[5]*Professor, Department of Community Medicine, KMCH Institute of Health Sciences and Research, Coimbatore – 14*

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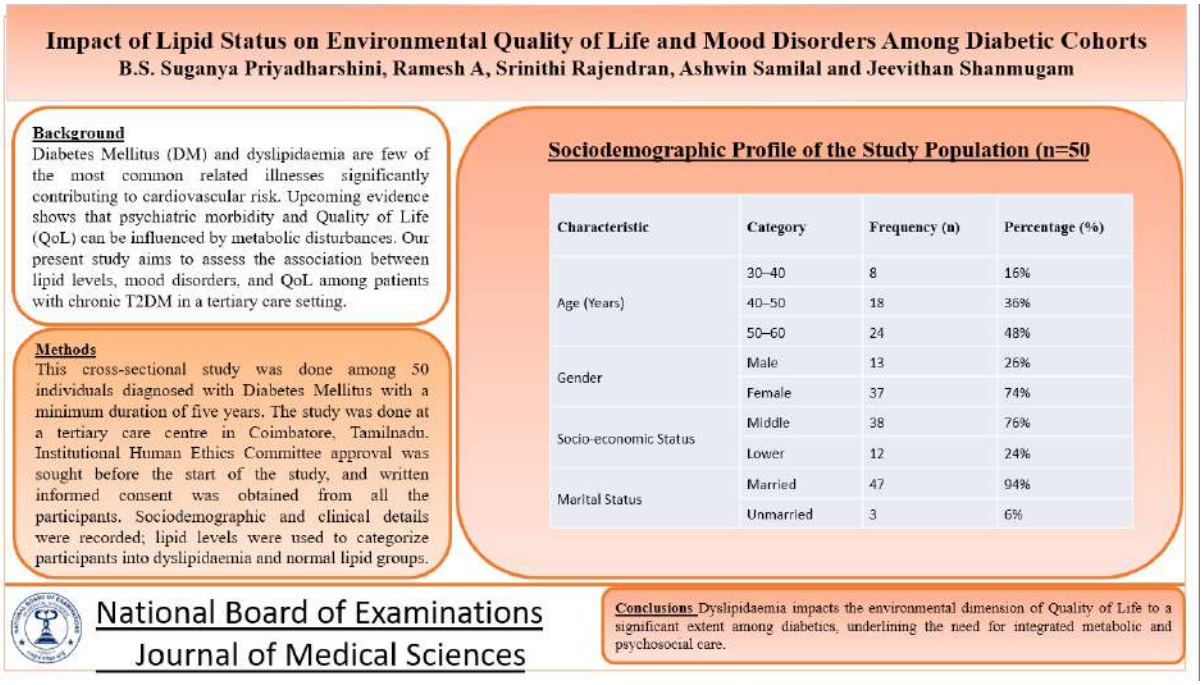
Abstract

Introduction: Diabetes Mellitus (DM) and dyslipidaemia are few of the most common related illnesses significantly contributing to cardiovascular risk. Upcoming evidence shows that psychiatric morbidity and Quality of Life (QoL) can be influenced by metabolic disturbances. Our present study aims to assess the association between lipid levels, mood disorders, and QoL among patients with chronic T2DM in a tertiary care setting. **Materials and Methods:** This cross-sectional study was done among 50 individuals diagnosed with Diabetes Mellitus with a minimum duration of five years. The study was done at a tertiary care centre in Coimbatore, Tamilnadu. Institutional Human Ethics Committee approval was sought before the start of the study, and written informed consent was obtained from all the participants. Sociodemographic and clinical details were recorded; lipid levels were used to categorize participants into dyslipidaemia and normal lipid groups. The M.I.N.I. Plus 5.0 structured diagnostic interview was used to assess psychiatric co morbidities. Quality of Life was evaluated using the WHOQOL-BREF questionnaire. **Results:** Dyslipidaemia was seen in 68% of the study group. Although patterns of mood disorders varied between groups, the association between lipid status and psychiatric diagnosis was not statistically significant (P = 0.068). A significant difference was seen in the Environmental domain of QoL (P = 0.018), with lower scores reported in dyslipidaemia patients. **Conclusion:** Dyslipidaemia impacts the environmental dimension of Quality of Life to a significant extent among diabetics, underlining the need for integrated metabolic and psychosocial care.

Keywords: Diabetes Mellitus, Dyslipidaemia, Quality of Life, Mood Disorders, WHOQOL-BREF

*Corresponding Author: Jeevithan Shanmugam
Email: dr.jeevithan@gmail.com

Graphical Abstract



Introduction

Diabetes Mellitus (DM) and dyslipidaemia are one of the commonest metabolic disorders that can be related. The concurrent presence of both significantly worsens the global burden of non-communicable cardiovascular diseases. India is presently in a period of an acute epidemiological transition due to growing urbanization, non active lifestyle added with change in dietary habits, leading to a startling increase in the diagnosis of type 2 diabetes. The ICMR-INDIAB study highlights the increasing incidence of prediabetes leading to diabetes across the country underscoring the importance of the enormous public health challenge [1]. Taking into consideration of this fact, the classical pattern of "diabetic dyslipidaemia"— is characterised by triglyceridemia, reduced high-density lipoprotein (HDL) and increase in LDL levels. This has emerged as a very frequent metabolic phenotype among Indians [1,2]. This atherogenic lipid profile significantly increases risk of cardiovascular events, leading to long term and chronic complications.

Along with proven cardiovascular interference, recent new evidence underscores that metabolic changes like dyslipidaemia can also influence neuropsychiatric wellness. Advances in neurobiological research highlight that metabolic and psychiatric disorders have common pathophysiologies, including low-grade inflammation, oxidative stress, insulin resistance, and dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis [3]. These pathways are associated and put forward that metabolic instability is not an isolated phenomenon but can interfere with functioning of the central nervous system, inclining patients to mood disorders. Along with that, the "cholesterol–serotonin hypothesis" brings up the idea that changes in serum cholesterol levels may affect serotonergic

neurotransmission which can modulate mood regulation and behavioral outcomes [4]. Biological interconnections like these provide a reasonable mechanistic framework relating lipid abnormalities with depressive symptoms.

Biological mechanisms along with psychosocial and environmental determinants may worsen the symptoms of patients with dyslipidaemia and diabetes. Long term and chronic illnesses require proper and regular self-management with proper compliance to medication, diet and follow up. All these can significantly impact an individual's perceived quality of life. The World Health Organization sequentiates that Quality of Life (QoL) is a multidimensional variable influenced by physical, environmental, social and psychological well-being [5]. While many studies have explored psychiatric morbidity in diabetes and the impact of metabolic control on QoL, very few researches have examined how lipid status specifically impacts both psychiatric comorbidities and the different domains of QoL within the Indian clinical setting.

Our study aims to substantiate the association between lipid status, mood disorders, and the multidimensional aspects of Quality of Life among patients with chronic diabetes Mellitus. By exploring these interrelationships in a tertiary care context, this study looks to contribute to a more holistic understanding of integrated metabolic and mental health in chronic disease management.

Materials and Methods

The study protocol was reviewed and approved by the Institutional Human Ethics Committee (IHEC) of the institute (IEC Approval Number: 14/405). The study was ethically conducted in according to the Declaration of Helsinki. All eligible participants were administered a detailed Participant Information Sheet (PIS) explaining the objectives, procedures, benefits and risks of the study. Adequate time was given for clarification of doubts, and written informed consent was obtained from all participants before inclusion. Confidentiality of personal and clinical information was strictly maintained by anonymizing data using unique identification codes, and participants were assured of their right to withdraw from the study at any stage without affecting their ongoing treatment.

This cross-sectional study was conducted in the Departments of Medicine and Endocrinology at a tertiary care teaching hospital in Coimbatore between January 2014 and June 2014. The study population comprised patients diagnosed with Diabetes Mellitus attending outpatient and inpatient services during the study period. Participants were selected using purposive sampling based on predefined eligibility criteria.

Patients aged between 30 and 60 years, of either gender, with a documented diagnosis of Diabetes Mellitus for at least five years were included in the study. Patients with juvenile-onset diabetes mellitus, intellectual disability, comorbid neurological disorders such as cerebrovascular accidents or neurodegenerative diseases, acute exacerbations of chronic illnesses, terminal conditions including malignancy, or those currently receiving psychotropic medications were excluded to minimize confounding factors in psychiatric assessment. Individuals unwilling to provide informed consent were also excluded.

After enrollment, sociodemographic details including age, gender, marital status, and socioeconomic status were recorded using a structured proforma. Clinical details related to duration of diabetes and relevant medical history were obtained from medical records and patient interviews. Metabolic assessment was carried out through evaluation of fasting lipid profiles obtained from hospital laboratory records. Based on lipid parameters, participants were categorized into two groups: those with elevated lipid levels (dyslipidaemia) and those with normal lipid profiles, as per standard laboratory reference values.

Psychiatric assessment was done using the Mini International Neuropsychiatric Interview (M.I.N.I.) Plus 5.0 which is a structured diagnostic interview tool designed to identify major Axis I psychiatric disorders according to DSM-IV criteria. Quality of Life was assessed using the World Health Organization Quality of Life–BREF (WHOQOL-BREF) questionnaire. It evaluates four domains - Physical, Psychological, Social Relationships, and Environmental Health. It was administered in the local vernacular language and standard scoring procedures were used to calculate domain-specific mean scores.

All data collected was entered and cross-verified and statistical analysis was performed. Descriptive statistics were used to sum-up sociodemographic and clinical characteristics. Categorical variables were expressed as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. The association between lipid status and psychiatric diagnoses was analyzed using the Chi-square test. Independent sample t-tests were applied to compare mean Quality of Life domain scores between dyslipidemic and non-dyslipidemic groups. A P value of less than 0.05 was considered statistically significant.

Results

The study cohort comprised of 50 participants. A majority of the population (74%), were females, with nearly half falling within the 50–60-year age group (48%). 76% of the study population were in the middle-income group and a significant proportion of participants (94%) were married. All participants had a primary diagnosis of Diabetes Mellitus for a minimum of five years (Table 1).

Table 1. Sociodemographic Profile of the Study Population (n=50)

Characteristic	**Category**	**Frequency (n)**	**Percentage (%)**
Age (Years)	30–40	8	16%
	40–50	18	36%
	50–60	24	48%
Gender	Male	13	26%

Characteristic	**Category**	**Frequency (n)**	**Percentage (%)**
	Female	37	74%
Socio-economic Status	Middle	38	76%
	Lower	12	24%
Marital Status	Married	47	94%
	Unmarried	3	6%

Comorbid dyslipidaemia was detected in 68% of the study participants and 32% had normal lipid levels. Psychiatric assessment was done using the The Mini-International Neuropsychiatric Interview Plus (M.I.N.I. Plus 5.0) and it identified the presence of mood disorders within the study population. Out of the participants in the group with dyslipidaemia, 2.9% fulfilled the criteria for a Major Depressive Episode (MDE). Notably, patients with normal lipid levels showed a higher incidence of MDE with melancholic features (12.5%) and Dysthymia (6.3%). Though the prevalence highlighted a probable association between lipid status and psychiatric illnesses, there was no significant association (P = 0.068) (Table 2).

Table 2. Psychiatric comorbidities and dyslipidaemia of the study sample

Dyslipidaemia	None	Major depressive episode	Major depressive episode with melancholia	Dysthymia	P value
Elevated	33(97.1%)	1(2.9%)	0(0%)	0(0%)	0.068
Normal	13(81.3%)	0(0%)	2(12.5%)	1(6.3%)	

The influence of the lipid levels on patient-reported outcomes was evaluated among the four domains of the WHOQOL-BREF. Analysis of the results highlighted that physical and psychological health scores were comparable between the two groups; though, environmental quality of life varied. There were no statistically significant differences between the Physical, Psychological, or social domains ($P > 0.05$), which shows that both groups perceived similar levels of physical burden and social support within the cohort with diabetes. However, the environmental domain showed a statistically significant difference ($P = 0.018$). Patients with increased levels of lipids showed a lower mean Environmental QoL score (64.03 ± 7.2) when compared to people with normal lipid levels (69.00 ± 5.4). (Table 3).

Table 3. Comparison of Quality of Life (QoL) Scores by Lipid Status

Quality of life	Dyslipidaemia	Mean ± SD	P Value
Physical	Elevated	58.65± 7.7	0.710
	Normal	59.50± 7.3	
Psychological	Elevated	58.91±8.6	0.591
	Normal	60.31±8.6	
Social	Elevated	67.76±8.3	0.459
	Normal	69.56±7.3	
Environmental	Elevated	64.03±7.2	0.018
	Normal	69.00±5.4	

Discussion

Our study explored the multi interactions between Diabetes Mellitus, dyslipidaemia, psychiatric comorbidities, and Quality of Life, among adults in a tertiary care centre in Western Tamilnadu. Majority of the study population were women (74%), and most of them were in the age group of 50-60 year. This above pattern highlights the already proven propensity of middle aged individuals, especially women to metabolic and endocrine disturbances associated with long term diabetes mellitus. The presence of a long term illness in our study population, with the minimum duration of 5 years further underlines the added metabolic stress influencing physical, mental and psychological outcomes.

There was a high prevalence of dyslipidaemia in our study population showing the very frequent association of metabolic risk factors in people with long standing and chronic Type 2 diabetes mellitus. This is in accordance with the already proven physiological link between insulin resistance and an abnormal lipid metabolism. As suggested by the American Diabetes Association in 2024, diabetic dyslipidaemia is a classic feature of T2DM, usually characterised by increased triglycerides and reduced HDL levels. The abnormal lipid levels contribute in high levels to cardiovascular morbidity among patients with long standing diabetes [6]. Similar observations were noted by Rubin and Peyrot, who showed that diabetes and its metabolic complications negatively affected overall Quality of Life in many domains, underscoring the need for comprehensive metabolic control [7].

An interesting yet statistically non-significant trend came up in relation to psychiatric comorbidities. Very few (2.9%) patients in the dyslipidemic group fulfilled the criteria for Major Depressive Episodes (MDE) but then, the group with normal lipid levels showed a relatively higher proportion of MDE with melancholic features (12.5%) and Dysthymia (6.3%), with the association

not statistically significant (P = 0.068). The "cholesterol–serotonin hypothesis" proposes that lower serum cholesterol levels may influence serotonergic neurotransmission, predisposing individuals to few depressive subtypes. Huang (2005) showed associations between serum lipid levels and specific subtypes of major depression, especially melancholic presentations of major depression [8]. Also, Anderson et al. in their study showed that depression is significantly more present among diabetics than in the general population, supporting the bidirectional relationship between metabolic and psychiatric disorders. Though dyslipidaemia is usually considered as a negative factor to physical health, lower lipid levels may not necessarily confer psychological protection. Additionally, people with normal lipid profiles may be under stringent lifestyle modifications, which could cause increased stress and thereby cause emotional burden. However, given the small sample size, these findings should be interpreted with caution necessitating further research in larger groups [9].

The statistically significant finding of our present study was the difference observed in the Environmental domain of the WHOQOL-BREF (P = 0.018). Patients with high levels of lipids reported significant lowering of environmental Quality of Life scores, when compared to people with normal lipid levels. According to the World Health Organization (1998), the Environmental domain of health includes financial resources, physical safety, health care accessibility, and aspects of the home environment [10]. The lesser scores in this domain among patients with dyslipidaemia may show the effect of cumulative socioeconomic strain due to the burden of multiple chronic conditions. The dual effect of diabetes and dyslipidaemia often requires more medications, laboratory investigations, dietary adjustments, and frequent medical consultations, which can increase healthcare-related expenditures and perceived financial insecurity.

Similar findings were observed by Wexler et al., who showed that an increasing burden of comorbid conditions in T2DM is significantly associated with reduced Quality of Life in relation to health. This was more seen in domains associated to environmental and economic factors [11]. Vahedi showed that increased burden of comorbidities is postulated to a decrease in perceived Quality of Life, especially in the environmental dimension. [12]. Our study puts forward that physical, psychological, and social perceptions may remain relatively stable across lipid level categories but environmental stressors play an important role in deciding overall well-being. These findings underline the importance of socioeconomic determinants of health along with clinical parameters in management of chronic diseases.

Conclusion

The study results highlight the need for an integrated and holistic approach to management of diabetes. Management should include measures above lipid and sugar control and should include routine screening for psychiatric comorbidities and evaluation of environmental stressors that may compromise Quality of Life. Socioeconomic challenges should be looked into and combining mental health assessment into routine metabolic care may result in better overall patient well being and long-term outcomes.

Statements and Declarations

Conflicts of interest

The authors declare that they do not have conflict of interest.

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CASE SERIES

Clinical and Immunohematological Significance of Anti-Le^a, Anti-Le^b, and Anti-E Antibodies in Pre-Transfusion Testing

Anandan S,[1,*] Ashwin A,[2] Niranj Rathan R,[2] Krishnamoorthy R[3] and Sampat Kumar M[4]

[1]*Postgraduate, Department of Immunohematology and Blood Transfusion Medicine, Sri Ramachandra Medical College, Porur, Chennai*

[2]*Associate Professor, Department of Immunohematology and Blood Transfusion Medicine, Sri Ramachandra Medical College, Porur, Chennai*

[3]*Head of the Department, Department of Immunohematology and Blood Transfusion Medicine, Sri Ramachandra Medical College, Porur, Chennai*

[4]*Assistant Professor, Department of Immunohematology and Blood Transfusion Medicine, Sri Ramachandra Medical College, Porur, Chennai*

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Abstract

Background: Unexpected red cell antibodies detected during pretransfusion testing can pose significant challenges in transfusion management, particularly in obstetric patients. While some antibodies are clinically insignificant, others may lead to hemolytic transfusion reactions, necessitating careful immunohematological evaluation. **Case Presentation:** We report three cases of unexpected red cell antibodies detected during routine pretransfusion testing. In Case 1, a 28-year-old gravida 3 para 1 female with no prior transfusion history showed incompatible crossmatches, and further workup identified an Anti-Le^b antibody, with no transfusion required due to minimal blood loss. In Case 2, a 26-year-old primigravida at term with fetal distress demonstrated Anti-Le^a antibody during antibody screening. Despite its presence, one unit of PRBC compatible was transfused uneventfully during cesarean section, consistent with the typically clinically insignificant nature of Lewis antibodies. In Case 3, a 46-year-old multiparous female with a history of prior transfusions presented with abnormal uterine bleeding and was found to have anti-E alloantibody. **Results:** Two cases showed positive direct antiglobulin test (DAT) with negative autocontrol, suggesting alloimmunization. Lewis antibodies (anti-Le^a and anti-Le^b) were clinically insignificant and did not impact transfusion outcomes, whereas anti-E, a clinically significant Rh antibody, required careful antigen-matched transfusion support. **Conclusion:** These cases highlight the importance of comprehensive antibody screening and identification in pretransfusion testing. While Lewis system antibodies are usually benign, clinically significant antibodies such as anti-E necessitate antigen-negative blood selection to prevent hemolytic complications. Early detection and appropriate transfusion strategies are essential for ensuring patient safety.

Keywords: Alloantibodies, Anti-Lewis, Anti-E, Transfusion, Pregnancy

*Corresponding Author: Anandan S
Email: arunanandhan95@gmail.com

Introduction

Alloantibody formation following transfusion of blood products remains a clinically significant concern. Red blood cell (RBC) alloantibodies are particularly important, as they can adversely affect future transfusions by causing incompatibility. These antibodies may lead to acute or delayed hemolytic transfusion reactions and can also contribute to hemolytic disease of the fetus and newborn [1]. The Lewis blood group system is unique because its antigens are passively adsorbed onto red blood cells from plasma, leading to variable antigen expression [2]. Antibodies such as anti-Le^a and anti-Le^b are usually naturally occurring IgM antibodies that react at temperatures below 37 °C and are generally considered clinically insignificant [3]. Lewis antibodies can induce red cell agglutination and activate the complement cascade, leading to hemolysis. Importantly, they may demonstrate clinical significance even when they are not reactive at 37 °C. Notably, there is emerging evidence that anti-Lewis antibodies, although often considered clinically insignificant, can occasionally result in hemolytic transfusion reactions. The Rh blood grouping system is the second most clinically important blood system following the ABO group system. The major antigens of this blood grouping system, which include D, C, E, c, and e, are highly immunogenic and have the ability to induce HTR and HDFN [4]. Anti-E is a common, clinically significant Rh alloantibody frequently identified among alloimmunized patients across diverse populations and has been implicated in DHTR [5,6].

Case Presentation

Case 1

A 28-year-old female, gravida 3 para 1 living 1 (G3P1L1), presented with complaints of lower abdominal pain of one-day duration, with a history of a previous normal vaginal delivery two years prior and no prior history of blood transfusion. She was admitted and planned for normal vaginal delivery. Routine laboratory investigations revealed hemoglobin of 11.9 g/dL, total leukocyte count of 11,830 cells/mm^3, and platelet count of $3.40 \times 10^5/mm^3$. Blood grouping performed using column agglutination technology (CAT) identified her as O, RhD positive. In anticipation of obstetric blood loss, a requisition for one unit of packed red blood cells was received; however, major crossmatching of three units was found to be incompatible with agglutination strengths of 1+, 1+, and 3+ by CAT. Further immunohematological workup showed a positive direct antiglobulin test (DAT) with a negative autocontrol. Antibody screening using a three-cell panel demonstrated reactivity with Cell I (3+), Cell II (1+), and non-reactivity with Cell III, suggesting the presence of an unexpected alloantibody. Subsequent antibody identification using a 11-cell panel confirmed the specificity as an Anti-Le^b antibody. In view of the minimal intra operative blood loss,transfusion support was not indicated.

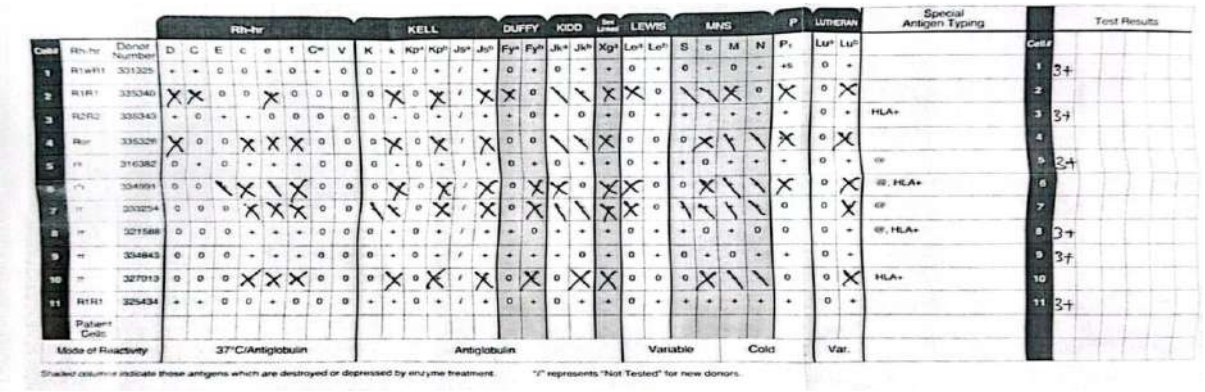

Figure 1. Antibody identification panel findings indicate presence of Anti-Le^b Antibody

Case 2

A 26-year-old primigravida at 37+3 weeks of gestation presented with complaints of reduced fetal movements for one day, with no associated comorbidities. Obstetric evaluation with ultrasonography and Doppler revealed a cerebroplacental ratio below the 5th percentile, suggestive of fetal hypoxia with a brain-sparing effect, necessitating emergency obstetric intervention. As part of preoperative preparation, one unit of PRBC was requisitioned for transfusion support. Initial crossmatching demonstrated compatibility with one unit. The patient had no prior history of blood transfusion. Immunohematological workup showed blood group B RhD negative, determined by column agglutination technology (CAT) Compatibility testing revealed one unit was crossmatched and compatible. Antibody screening performed using both CAT and manual gel card method demonstrated reactivity with Screening Cell I (2+), while Screening Cells II and III were non-reactive. Direct antiglobulin test (DAT) was negative, with a negative autocontrol, suggesting the presence of an alloantibody. Subsequent antibody identification using a panel revealed the presence of anti-Le^a antibody. Lower segment cesarean section (LSCS) was performed, delivering a baby with low Apgar score, with an estimated blood loss of 800 mL, for which one unit of PRBC was transfused and transfusion was completed uneventfully. Anti-Le^a antibodies generally do not affect transfusion outcomes, as they are usually naturally occurring IgM antibodies that react at cold temperatures and are rarely clinically significant.

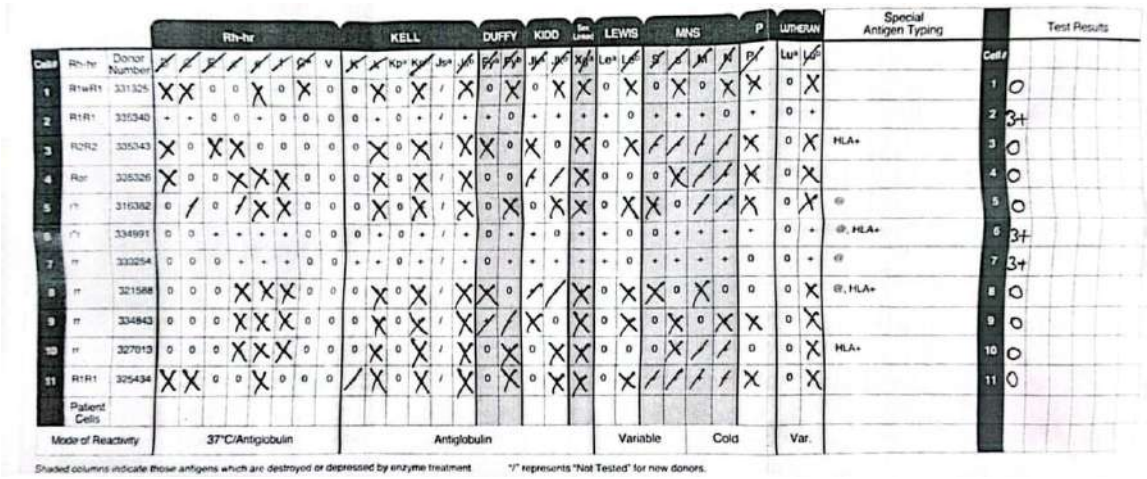

Figure 2. Antibody identification panel findings indicate presence of Anti-Le^a Antibody

Case 3

A 46-year-old female, with obstetric score of para 2 live 2, presented with complaints of amenorrhea for last 12 months, after which she developed heavy menstrual bleeding lasting 15-20 days associated with 4-5 fully soaked cloths per pad per day and previous history of 3 units of PRBC was transfused. Routine laboratory investigations revealed hemoglobin of 9.5 g/dL, total leukocyte count of 5060 cells/mm^3, and platelet count of 2.30 × 10^5/mm^3. Blood grouping performed using column agglutination technology (CAT) identified her as O RhD positive. In anticipation of potential perioperative blood loss, a requisition for one unit of packed red blood cells was received; however, major crossmatching of one unit was found to be compatible by both CAT and manual gel card methods. Further immunohematological workup showed a positive direct antiglobulin test (DAT) with a negative autocontrol. Antibody screening using a three-cell panel demonstrated reactivity with Cell I (0), Cell II (3+), Cell III (0), suggesting the presence of an unexpected alloantibody. Subsequent antibody identification using an 11-cell panel confirmed the specificity as anti-E (anti-E) antibody, one unit of PRBC was transfused and transfusion was completed uneventfully.

Figure 3. Antibody identification panel findings indicate presence of Anti-E Antibody

Discussion

Case 1

The Le-a and Lewis-b (Le-b) antigens are not expressed on RBCs and are adsorbed from plasma [6]. Generally, the clinically significant antibodies are those that agglutinate at 37 °C under in-vitro conditions and also during the IAT phase, usually classified as IgG antibodies. But the antibodies of the Lewis blood group system are normally considered to be naturally occurring and also fall into the IgM antibodies' classification [7]. Such antibodies usually agglutinate below 37 °C and are generally not considered to be clinically significant [8]. The antibodies of the Lewis blood group are commonly found in the serum of pregnant women and those having Le (a−b−) phenotype [9]. However, pregnancy-induced suppression of Lewis antigens may lead to a transient Le(a−b−) phenotype, predisposing to antibody formation. In the present case, crossmatch incompatibility with variable agglutination strengths [1+ to 3+] and a positive direct antiglobulin test (DAT) with negative autocontrol suggests alloimmune sensitization, likely pregnancy-related in the absence of prior transfusion. Similar observations have been reported by Mustafa et al. and Arthi et al., where Lewis antibodies were detected in patients without transfusion history, highlighting pregnancy as a potential immunizing factor [10]. Overall, in comparison with similar case reports, this case reinforces that while Lewis antibodies are usually benign, they can occasionally present with clinically relevant serological challenges, particularly in antenatal patients, warranting thorough immunohematological evaluation and selection of crossmatch-compatible blood units.

Case 2

Anti-Lewis antibodies are commonly seen in the serum of pregnant women and individuals possessing Le a− and Le b− antigens [9]. Among the various types of Lewis antibodies, is the most frequently encountered one. The most common form of Lewis antibodies, anti-Lea, anti-Le^a is often observed at room temperature, although it may react either with the indirect antiglobulin test or at 37 °C [8,9]. It is more common for anti-Le^a to cause acute HTR compared to anti-Le^b antibodies. Delayed HTR is another form of HTR that has been reported before [11]. In the present case, transfusion of crossmatch-compatible blood in a pregnant patient with anti-Lewis antibodies was uneventful. In contrast, Rajeswari et al. reported a delayed hemolytic reaction following transfusion of but crossmatch-incompatible blood in a similar setting. This highlights that Lewis antibodies are usually clinically insignificant but may cause hemolysis if incompatible units are transfused [6]. In the present case, transfusion of crossmatch-compatible blood in a patient with anti-Lewis antibody was uneventful, supporting their generally benign nature in transfusion practice. However, Lewis antigens are expressed on renal tissues and can induce cytotoxic immune responses. As reported by Spitalnik et al., Lewis-incompatible renal transplants may lead to graft rejection, indicating their potential clinical significance in transplantation settings [12].

Case 3

The present case, a multiparous woman with a history of prior transfusion, was found to have anti-E alloantibody. Despite the presence of this clinically significant antibody, transfusion was successfully completed using E antigen negative, crossmatch-compatible packed red blood cell units, with no evidence of hemolytic transfusion reaction. In contrast, Panja et al. reported a case of anti-E mediated delayed hemolytic transfusion reaction with acute kidney injury, despite initial compatibility, attributed to antigen exposure and an anamnestic immune response. Both cases showed DAT positivity, indicating in vivo sensitization; however, the difference in clinical outcomes highlights the critical importance of antigen-negative blood selection and comprehensive antibody screening in preventing transfusion-related complications [13].

Conclusion

In the present study, although Lewis antibodies (anti-Le^a and anti-Le^b) are generally considered clinically insignificant, their reactivity at room temperature and occasionally at 37 °C warrants careful consideration during pretransfusion testing. Provision of Le^a antigen-negative red blood cell units, crossmatched at 37 °C, may be beneficial in minimizing the risk of hemolytic transfusion reactions, particularly in cases demonstrating reactivity at body temperature. Thus, appropriate antibody identification and selection of antigen-negative, crossmatch-compatible units remain essential to ensure safe transfusion practices. This case highlights the clinical importance of detecting anti-E alloantibody during pretransfusion testing in a previously transfused multiparous patient. Despite crossmatch compatibility, the presence of a clinically significant Rh antibody underscores the limitation of compatibility testing alone. The likely transfusion of E antigen-negative red cell units contributed to the absence of any hemolytic transfusion reaction. Therefore, comprehensive antibody screening and identification, along with provision of antigen-negative, crossmatch-compatible blood, are essential to ensure safe transfusion and to prevent delayed hemolytic complications in sensitized individuals.

Statements and Declarations

Conflicts of interest

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CASE REPORT

An Unexpected Diagnosis: Intramuscular Myxoma of Biceps Brachii

Kaushik Bhattacharya,[1,*] Sharad Syangden,[2] Mahesh Kumar,[2] Asitava Deb Roy,[3] Babai Halder[4] and Aarzoo Nagpal[5]

[1]*Associate Professor, Department of Surgery, Mata Gujri Memorial Medical College and LSK Hospital, Kishanganj - 855107, Bihar, India*
[2]*Assistant Professor, Department of Surgery, Mata Gujri Memorial Medical College and LSK Hospital, Kishanganj -855107, Bihar, India*
[3]*Professor and HOD, Department of Pathology, Mata Gujri Memorial Medical College and LSK Hospital, Kishanganj -855107, Bihar, India*
[4]*Professor, Department of Pathology, Mata Gujri Memorial Medical College and LSK Hospital, Kishanganj -855107, Bihar, India*
[5]*Postgraduate, Department of Surgery, Mata Gujri Memorial Medical College and LSK Hospital, Kishanganj -855107, Bihar, India*

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Abstract

A 50-year-old woman presented with a longstanding, painless right upper arm swelling. Imaging and FNAC suggested a spindle cell neoplasm. Surgical excision revealed a well-circumscribed intramuscular mass. Histopathology and immunohistochemistry confirmed myxofibroma (intramuscular myxoma). The postoperative course was uneventful, with no recurrence at one-year follow-up. Intramuscular myxomas are rare benign tumors requiring surgery only for symptomatic relief. Long-term follow-up is essential due to recurrence risk and to exclude misdiagnosed myxofibrosarcoma.

Keywords: Intramuscular Myxoma, Soft Tissue Neoplasms, Upper Extremity

*Corresponding Author: Kaushik Bhattacharya
Email: kbhattacharya10@yahoo.com

Case report

A 50-year-old lady presented with a hard, non-tender swelling of 9cm X 8 cm fixed to the underlying muscle over the right upper arm with occasional pain over the swelling for more than 3 years (Figure 1). Fine needle aspiration cytology was reported as a spindle cell neoplasm. X-ray of the right upper arm showed no bony involvement. CT scan of the lesion showed a large hypodense, well-defined soft-tissue density involving the intermuscular plane over the right proximal forearm, with a provisional diagnosis of either a soft tissue sarcoma or a peripheral nerve sheath tumour (Figure 2).

Figure 1. Intramuscular myxoma right upper arm

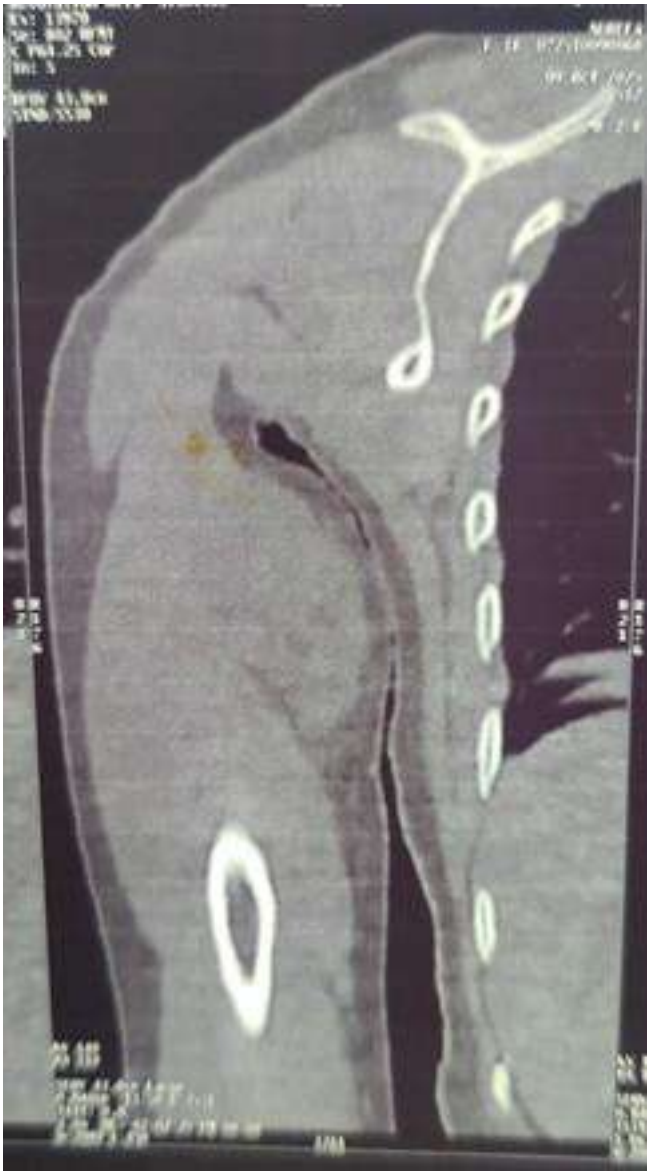

Figure 2. CT scan showing a hypodense lesion of intramuscular myxoma

The patient underwent surgery under general anaesthesia, and the entire swelling in the muscular plane of the short head of the biceps brachii was excised and sent for histopathology (Figure 3). The lesion appeared as a solid, well-circumscribed, encapsulated mass, and it was easily removed during surgery (Figure 4). The postoperative course was uneventful. The histopathology report was a myxoma of the right upper arm, which on immunohistochemistry showed Alpha-smooth muscle actin (SMA) diffusely positive, while S100 was negative (Figure 5). The final diagnosis was myxofibroma of the upper limb extremity. The patient has been followed up for 1 year.

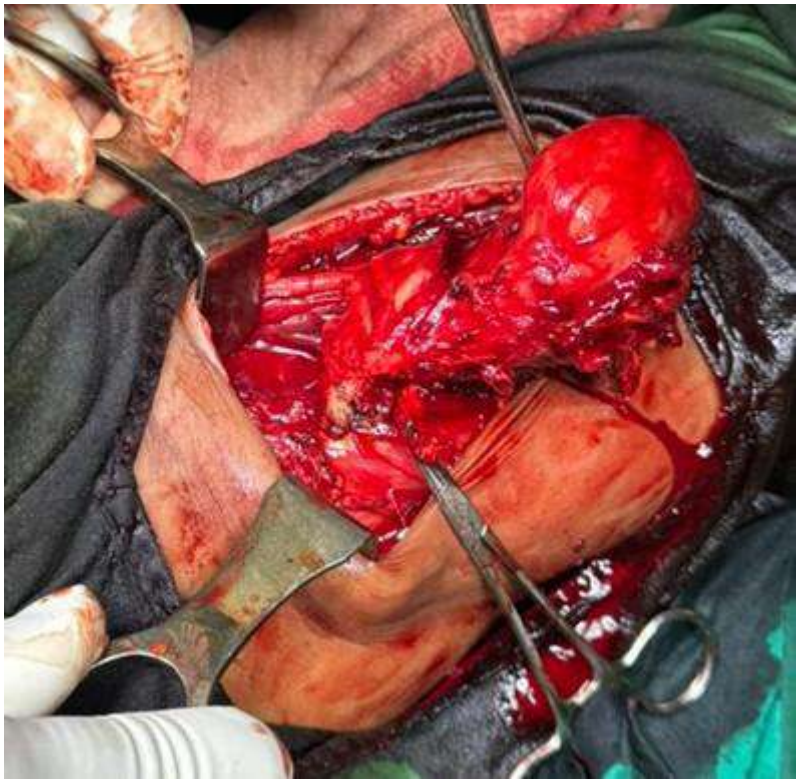

Figure 3. Intraoperative pic of Intramuscular myxoma excision from Biceps brachii

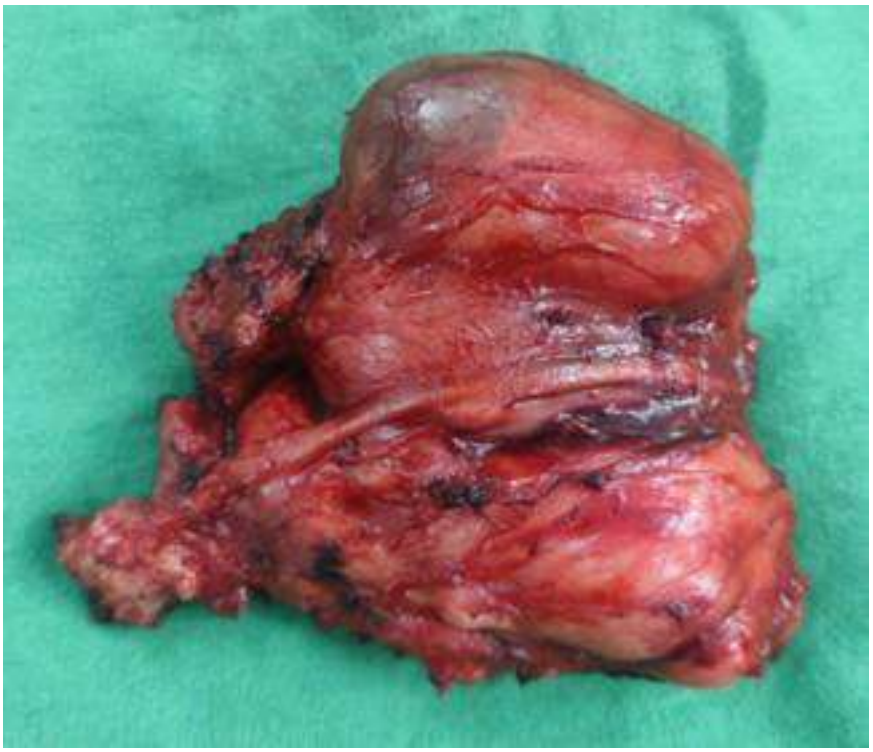

Figure 4. Resected specimen of Intramuscular myxoma

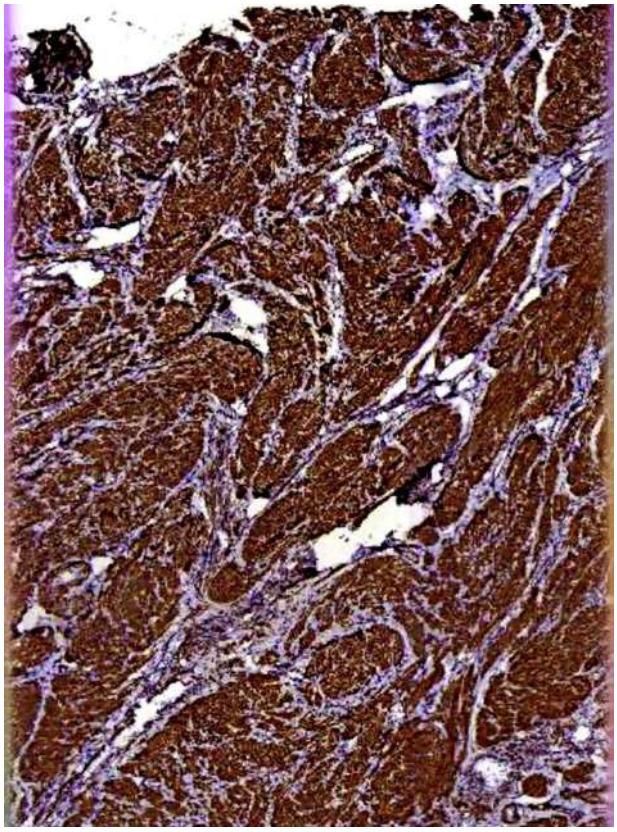

Figure 5. Immunohistochemistry showing SMA diffusely positive and S100 negative

Discussion

Intramuscular myxoma (IMM) is an extremely rare, benign soft-tissue tumor with a reported incidence of 0.1 to 0.13 per 100,000 population [1]. This is a very rare benign soft tissue tumour originating from mesenchymal tissue and confined within skeletal muscle. It is a hypocellular, hypovascular neoplasm composed of bland spindle or stellate cells embedded in abundant myxoid stroma without nuclear atypia, mitotic figures, or necrosis. It is often referred as Cellular Myxoma**.** The incidence is mostly seen over the large muscles of the thigh in 50–60% of cases and over the shoulder and upper arm in 9% to 11% cases. IMM can be solitary or multiple, but when associated with fibrous dysplasia, it is called Mazabraud syndrome [2]. Mazabraud syndrome is associated with postzygotic mutations in the GNAS1 gene on chromosome 20q13.2-q13.3. The management of IMM is usually conservative, and surgery is indicated only if they cause pain, pressure symptoms, neurological symptoms, or interferes with functionality. The most common postoperative complication of myxomatous surgical excision is recurrence, which occurs in more than 30% of cases at a median of 8.5 years, which mandates a long-term follow-up.

The differential diagnosis of IMM is low-grade myxofibrosarcoma, which has characteristic curvilinear vessels with perivascular condensation of cells around vessels. Distinction may be very challenging in small biopsy specimens. There may be variable nonspecific cytogenetic aberrations (83%), no *GNAS1* activating mutations.

Another differential diagnosis is Nerve sheath myxoma, which is typically superficial, not intramuscular. The periphery has parallel rows of spindle cells with wavy nuclei representing the nerve. Typically has diffuse expression of S100, SOX10

Rudolf Ludwig Carl Virchow was the first person to use the term 'myxoma' in 1871 when he found that the pathology resembled the mucinous substance of the umbilical cord [3]. Arthur Purdy Stout defined the strict histological criteria for these tumors in 1948, describing them as neoplasms composed of undifferentiated stellate cells in a hypovascular, myxoid stroma. The long-term follow-up is necessary in view of the recurrence or an error in the initial histopathology report, missing out myxofibrosarcomas [4]. The duration between the initial excision and recurrence in benign cases is generally 2 years, but if it occurs early, a more aggressive pathology has to be ruled out. It is widely established in medical literature that IMM do not show potential for malignant transformation and do not have a tendency to metastasize.

The case report gains importance as IMMs are rare benign tumors that often are missed, being diagnosed with fine needle aspiration cytology, and should be subjected to immunohistochemistry and GNAS mutation analysis for the final result. A complete excision, along with long-term follow-up, is mandatory to prevent recurrence.

Conclusion

Intramuscular myxoma of the biceps brachii is a rare benign entity that can mimic malignant soft tissue tumors on clinical and radiological evaluation. This case highlights the limitations of FNAC and the importance of complete surgical excision followed by definitive histopathology and immunohistochemistry. Awareness of this entity helps avoid overtreatment. Although prognosis is excellent, long-term follow-up remains essential to detect recurrence and to exclude misdiagnosis of low-grade myxofibrosarcoma.

Authors contribution

Conception and design of the study, KB, SS, MK; Acquisition of data, KB, AN; Drafting of the article, KB, AD, BH; Critical revising; KB, SS, MK, AD; Final approval, KB, SS, MK, AD, BH, AN

Statements and Declarations

Conflicts of interest

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Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Informed Consent

Informed consent has been taken from the patient for publication of the case for academic interest only.

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LETTER TO THE EDITOR

Antimicrobial Resistance (AMR) Prevention is a Shared Responsibility: Superbug Menace is a One Health Challenge

Kattamreddy Ananth Rupesh[1,*]

[1]*Assistant Professor of Forensic Medicine, Government Medical College, Ongole*

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Keywords: Antibiotic resistance, One health, Superbugs, Plastisphere, Co-selection, Microplastics

Dear Editor,

Apropos your timely and highly relevant editorial [1], one critically important but often underemphasized area in India's antimicrobial resistance (AMR) crisis is its environmental dimension. The menace of multidrug-resistant "superbugs" is not merely a clinical or prescribing issue; it represents a profound *One Health* challenge linking human health, animal health, agriculture, and also our interaction with the larger environment.

AMR is frequently attributed to irrational antibiotic use — such as self-medication, overprescribing, and incomplete treatment courses. While these factors are significant, growing scientific evidence demonstrates that the environment plays a major role in the emergence, amplification, and dissemination of resistant organisms [2]. As rightly pointed out in the editorial, antibiotics and resistant bacteria do not remain confined to hospitals or households. They circulate through sewage, wastewater, rivers, soil, agricultural fields, and even air, creating reservoirs where resistance genes can persist and evolve [2].

A major driver is inadequate liquid waste management in healthcare facilities. Hazardous liquid biomedical waste from intensive care units, operation theatres, mortuaries, and laboratories is often discharged into municipal sewage systems without adequate on-site effluent treatment. At the same time, wastewater from patients often contains both unmetabolized antibiotic residues and resistant bacteria. Together, these biologically rich effluents become a favourable medium for the survival and exchange of resistance genes among microbes [3].

*Corresponding Author: KA Rupesh
Email: ananth.kattam@gmail.com

Urban sewage treatment plants, many of which operate sub optimally, receive mixed effluents from households, hospitals, slaughterhouses, and industries. When treatment is incomplete, antibiotic residues and resistant organisms enter surface waters and groundwater. Even low concentrations of antimicrobials exert selective pressure, enabling bacteria to acquire and exchange resistance genes, thereby transforming treatment plants into resistance-amplification hubs [4].

Pharmaceutical manufacturing units represent another ignored critical concern. Industrial effluents may contain high concentrations of active drug compounds. When these are discharged without proper treatment in to the environment, the residues contaminate soil and water bodies, exposing environmental microbes to sustained antibiotic pressure. This resistance can then enter the food chain through contaminated irrigation water, crops, fish, livestock, and ultimately humans [5].

Improper disposal of unused and expired antibiotics further compounds the problem as mentioned in the editorial. Medications discarded into household garbage, sinks, or toilets leach into landfills, soil, and water systems, maintaining low-level environmental antibiotic exposure. These residues persist in soil microbiomes, where resistance genes can be transferred to human and animal pathogens, creating long-term ecological reservoirs of resistance [6].

Environmental co-selection agents such as heavy metals, biocides, pesticides, and microplastics contribute significantly to antimicrobial resistance by exerting selective pressure on microbial populations. These agents often co-select for antibiotic resistance genes located on mobile genetic elements, enabling the persistence and spread of multidrug-resistant organisms even in the absence of antibiotic exposure. Microplastics further facilitate biofilm formation and horizontal gene transfer in aquatic and terrestrial ecosystems, reinforcing environmental reservoirs of resistance [7].

Thus, AMR must be recognized not merely as a clinical failure but as an environmental governance challenge. Effective mitigation requires strengthening hospital effluent treatment systems, enforcing stringent regulation of pharmaceutical and industrial discharges, upgrading sewage treatment infrastructure, promoting safe antibiotic disposal practices, and ensuring rational antimicrobial use across human and veterinary medicine. Without safeguarding environmental pathways, improvements in prescribing practices alone will be insufficient to curb antimicrobial resistance.

While current awareness campaigns represent a positive and necessary first step, substantial and sustained efforts will be required to achieve meaningful and long-term impact.

Statements and Declarations

Conflicts of interest

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