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July - September 2024 | Vol XVII | Issue 3

Integration of AI in Healthcare

Continuous Glucose Monitoring in India

Acute Disseminated Encephalomyelitis

Case of Bilateral Pheochromocytoma

Adolescent Idiopathic Scoliosis (AIS)

Spontaneous Arterial Dissection

Stereoscopic Visualization

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Focus and Scope of IMA KMJ

IMA Kerala Medical Journal is the academic journal published by Indian Medical Association Kerala State Branch. The journal is published online and in print form and has 4 issues per year. Articles are selected in original research in clinical medicine, public health and clinical epidemiology and undergo a strict process of peer review before confirmation. Authors are to pay publishing charges on acceptance. The journal access is fully open online.

The following are the guiding principles of IMA KMJ

- To promote and p ublish original research in all areas of modern medicine
- To create active discussions and initiate debates on topics of importance in health policy and health decision making
- To propagate safe, evidence based and ethical practice of modern medicine popularising guidelines for management.

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Preparing the manuscript for submission to IMA Kerala Medical Journal (IMA KMJ) is a process that requires meticulous planning, diligent writing and attention to details.

The following word processor file formats are acceptable for the main manuscript document typed in unjustified format, using Arial font size 11 and 1.5 line spacing.

- Microsoft Word (DOC, DOCX)
- Rich Text Format (RTF)
- Open Document Format (ODT)

General Guidelines for Manuscript Preparation

1. The title page should be a separate document that contains the title of the paper, the category of submission, detailed author information, and full contact details of corresponding author. Full names of authors must be used with initials expanded. Any one author can be corresponding author. The title page should be uploaded as a supplementary file while submitting the manuscript
2. The first page of the main document should contain the title, abstract and keywords followed by the full text of the article. The full text should incorporate everything including images, tables and references in appropriate places. This helps to provide our reviewers with a single file and avoiding them the trouble of searching through multiple documents.
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6. Graphs and Charts should use simple, two dimensional styles without any designer effects. We recommend MS Excel for creating charts.
7. Tables should use simple wireframe styles without any colours or effects and should be editable. Best created in the word processor programme itself.
8. Original full resolution jpeg versions of photographs (if any) should be uploaded as supplementary files while submitting the manuscript.
9. Endnotes section should contain List of abbreviations with expansions, Explanations of terminologies as required, Conflicts of Interest statement, Acknowledgements and Financial Support.

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10. References should be created in the International Committee of Medical Journal Editors (ICMJE) format also known as the Vancouver style. We recommend using the free reference management programme Zotero for creating references.
11. Format used for data collection should be uploaded as supplementary file while submitting the manuscript.

Additional Guidelines for Research Articles

1. Word limit is 6000 for Original Research and 2500 for Brief Communication.
2. Title should be descriptive and should contain enough information for readers to understand what the study is about.
3. Abstract should not be of more than 400 words and should be structured, containing background, objectives, methods, results and conclusions.
4. Keywords – four to eight comma separated keywords representing the topic of the article.
5. Full text should contain Background and Rationale, Objectives, Methods, Results, Discussion, Conclusions, End Notes and References.
6. Background – elaborating the existing knowledge scenario with regard to the research question and how this study would add to it.
7. Objectives of the Study – Numbered output indicators that the study tries to look into (aims of the study).
8. Methods – includes study design, study subjects, inclusion and exclusion criteria, sample size and sampling methods, materials used, duration, data collection, data analysis and ethical considerations.
9. Results – the findings of the study presented in the form of statistical indicators, figures and tables.
10. Discussion – Evaluation of the results in the light of existing evidence.
11. Conclusions – Final deductions arrived at and new knowledge obtained at the end of the study.
12. Limitations – describes the limitations of the study.
13. Endnotes section should contain List of abbreviations with expansions, Explanations of terminologies as required, Conflicts of Interest statement, Acknowledgements and Financial Support.
14. References should be in Vancouver style.

Message from State President

Dr Joseph Benaven
State President
IMA Kerala State Branch

Dr Sasidharan K
State Secretary
IMA Kerala State Branch

The Indian Medical Association, Kerala State Branch, proudly acknowledges and appreciates the outstanding contributions of Dr. Kavitha Ravi and the editorial team for their tireless efforts in publishing four issues of the Kerala Medical Journal this year, in addition to a previous issue. The journal was a masterpiece showcasing cutting-edge medical research, innovation and advancements in medical science and has significantly enhanced the journal's reputation and value to the medical community.

I would note the main achievements of the year as;

1. Consistent publication of high-quality issues.

2. Showcasing innovative medical research and advancements.

3. Submission for indexing, expanding the journal's reach.

I express my deepest appreciation to team for their commitment to excellence and maintaining rigorous editorial standards. Your efforts has elevated the journal's stature and it occupies a pride of place among the many publications of the Indian Medical Association.

I extend my sincere gratitude to Dr. Kavitha Ravi and her team and also Dr. Anooplal for your remarkable contributions to the Kerala Medical Journal.

Message from the Editor

As we approach the end of this IMA year, I take great pride and satisfaction in signing off as the editor of the Kerala Medical Journal. The scientific community has warmly received all the issues with enthusiasm. I extend my sincere thanks to the authors and readers for their invaluable contributions. Special gratitude goes to IMA Kerala State President Dr. Joseph Benaven, State Secretary Dr. Sasidharan, Dr. Anooplal, and Mrs Sree, whose unwavering support has been instrumental in the successful and timely publication of each issue.

I wish the future team continued success and growth.

Sincerely,

Dr Kavitha Ravi
Chief Editor

Dr Prakash V
Secretary Cum Treasurer

Kerala Medical Journal IMA KMJ

July - September 2024 | Vol XVII Issue 3

TABLE OF CONTENTS

continued..

Kerala Medical Journal IMA KMJ

July - September 2024 | Vol XVII Issue 3

TABLE OF CONTENTS

The Integration of Artificial Intelligence in Healthcare: Ethical Considerations and Future Prospects

Kavitha Ravi[a]

a. Department of Pathology, Government Medical College, Thiruvananthapuram*

Published on 21st October 2024

Artificial Intelligence (AI) has emerged as a transformative force across various sectors, including healthcare. AI's promise in medical field is vast and multifaceted with unprecedented gains in productivity, therapeutic results, treatment personalization, and diagnostic research.[1] As we get closer to this significant shift, it is crucial to thoroughly examine ethical concerns and possible future uses of AI integration.

There are many ways in which artificial intelligence (AI) can transform healthcare. Machine learning is capable of quickly analysing medical data, yielding insights and patterns that human practitioners may not have realized. These benefits of AI have already been demonstrated in fields such as Radiology, where it can detect abnormalities in medical imaging with remarkable accuracy.[2] Similarly the AI driven predictive analytics facilitate early diagnosis and thus intervention strategies for chronic diseases such as Diabetes and Heart disease.

AI also has the potential to democratize healthcare. AI-powered telemedicine solutions help bridge gaps in access to healthcare by bringing medical expertise to remote and underserved regions. AI's ability to analyse personalized genetic lifestyle data supports personalized medicine, opening the door to treatments that meet each patient's unique needs, maximize outcomes and reduce side effects.[3]

But with great power comes important moral responsibility. One particular concern is data storage. AI systems require large amounts of data to be effective, raising concerns about patient data security and privacy. Strong data protection measures and transparent data governance structures are essential to maintaining patient confidence and complying with regulatory requirements. Another serious problem is bias in AI algorithms. AI programs that have been educated on past medical data could unintentionally reinforce current healthcare inequities. An AI system's diagnosis accuracy for other demographics, for example, may be harmed if it is primarily trained on data from a specific population. To reduce bias and advance equitable healthcare, it is essential to ensure diversity in training datasets and to put strict testing procedures in place.

It's also important to take into account how AI might alter the conventional doctor-patient interaction. AI should not take the role of human practitioners' compassionate and nuanced care, even while it can improve treatment planning and diagnostic precision. Preserving the human element in healthcare requires a balanced integration in which AI is used as a supplementary tool rather than as a substitute.

In the future, the use of AI in healthcare is expected to increase due to ongoing technological developments and rising professional acceptability. To successfully navigate the challenging terrain of AI implementation, cooperation between AI developers, healthcare professionals, and regulatory agencies will be crucial.[4] Investing in healthcare professionals' AI education and training will promote an innovative culture and enable even more seamless integration.

Research and development in AI should prioritize not only technological advancements but also ethical frameworks that ensure, patient welfare remains paramount. Policies and procedures that protect ethical integrity will be shaped in large part by interdisciplinary approaches that integrate knowledge from computer science, ethics, law, and medical. To summarize, the integration of AI in healthcare is a double-edged sword, providing dramatic benefits while

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raising severe ethical challenges. Harnessing AI's full potential for improving global health will need a commitment to ethical considerations and collective governance.

END NOTE

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Conflict of Interest: None declared

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Safety During Night Duty: Survey of 3885 Doctors Across India

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Published on 21st October 2024

ABSTRACT

Background: Reports of violence against doctors at the workplace are on the rise. In August 2024, a young female doctor was raped and murdered during night duty at her workplace in Kolkata, India. This incident prompted nationwide protests and a service shutdown by doctors' organizations advocating for improved workplace safety.

Aim: This survey was undertaken by the Indian Medical Association to evaluate safety concerns during night shifts among doctors. With 3,885 individual responses, it is the largest study from India on this topic.

Methods: An online survey was sent to doctors across India through a Google form. There were 3885 responses. In addition to seeking suggestions to improve safety, three separate parameters were assessed:

1. 0-10 numeric rating scale of perception of safety
2. Availability of duty room
3. Access to bathroom while on night duty

Results:

1. Respondents were from several states. 85% were under 35 years. 61% were interns or postgraduate trainees. Women constituted 63%, aligning with the gender ratio in some MBBS courses.
2. Several doctors reported feeling unsafe (24.1%) or very unsafe (11.4%), totalling one-third of the respondents. The proportion of those feeling unsafe was higher among women.
3. A duty room was not available to 45% of respondents during night shifts.
4. Those with access to a duty room had greater sense of safety.
5. Duty rooms were often inadequate due to overcrowding, lack of privacy and missing locks, forcing doctors to find alternative rest areas.
6. One-third of available duty rooms did not have an attached bathroom.
7. In more than half the instances (53%), duty room was located far from the ward/casualty area.
8. Suggestions to enhance safety included increasing the number of trained security personnel, installing CCTV cameras, ensuring proper lighting, implementing the Central Protection Act (CPA), restricting bystander numbers, installing alarm systems, and providing basic amenities such as secure duty rooms with locks. For detailed information, refer to **Table 12**, the synopsis and the verbatim comments section.

Conclusions: Doctors across the country, particularly women, report feeling unsafe during night shifts. There is substantial scope for improving security personnel and equipment in healthcare settings. Modifications to infrastructure are essential to ensure safe, clean, and accessible duty rooms, bathrooms, food, and drinking water. Adequate staffing, effective triaging, and crowd control in patient care areas are also necessary to ensure that doctors can provide the required attention to each patient without feeling threatened by their work environment.

Keywords: Healthcare Violence, Attack, Rape, Workplace Violence, Occupational Hazard, Security, Duty Room, Perception of Safety, Mental Health, Night Duty, Infrastructure, Healthcare Policy, Night Shifts

*See End Note for complete author details

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INTRODUCTION

Background

Healthcare professionals are required to take night shifts as part of their training during internships and postgraduate studies, and they continue to work night duties in both private and public sectors throughout their careers. This aspect of the profession makes them vulnerable to various forms of workplace violence.

Public anger is frequently directed at doctors, who are perceived as the leaders in a healthcare team. In crowded settings like outpatient facilities, emergency rooms, or ICU waiting areas, doctors on the frontline are particularly vulnerable to sudden and unprovoked attacks. Violence can be triggered by perceived or real deficiencies in healthcare delivery, adverse outcomes, payment disputes, and substance abuse. While most instances of violence are spontaneous, some cases, such as the recent incident in Kolkata, are premeditated. These acts often result in more severe and sometimes fatal outcomes due to the advanced planning involved and the backgrounds of the perpetrators.

Although targeted at doctors, workplace violence ultimately impacts the quality of care provided to the public. For example, doctors may become hesitant to undertake potentially risky life-saving procedures and may prefer to refer patients to other centres. Night shifts increase doctors' vulnerability to violence due to reduced staff, the cover of darkness, and the presence of individuals under the influence of alcohol or drugs. Factors such as the lack of dedicated and secure duty rooms, their distance from the workplace, and the need to walk a significant distance to access facilities further heighten their risk. Women doctors face greater risks in these situations.

Globally, workplace violence is a known issue. A 2017 study by the Indian Medical Association found that over 75% of doctors in the country have experienced workplace violence, while 62.8% are unable to see their patients without any fear of violence.[1,2] Another study reported that 69.5% of resident doctors encounter violence while at work.[3] Exposure to violence is known to lead to fear, anxiety, depression, and post-traumatic stress disorder among doctors.[4]

Healthcare related violence is a worldwide problem. In China, a survey among medical staff in children's hospitals revealed that 68.6% had suffered verbal or physical violence in the past year.[5]

Perceptions of safety significantly influence job satisfaction among doctors.[6] The recent rape and murder of a young woman doctor in Kolkata India triggered widespread protests among the medical fraternity.[7]

This survey was conducted to address the following research question: "How do doctors in India perceive their safety during night shifts? What environmental factors influence their sense of safety, and what suggestions do they have for improving their safety?"

OBJECTIVE

1. To assess three safety parameters pertaining to night duty
   a. 0-10 scale of perception of safety
   b. availability of duty room
   c. Access to bathroom while on night duty
2. To collect suggestions from individual doctors about how their personal safety can be improved.

METHODOLOGY

Study Design:

An online survey of 10 questions was sent to doctors across India through Google form. There were 3885 responses. The survey was cross-sectional and anonymous, which was to encourage individual doctors to provide their frank opinion. Data was collected through a Google form on 17 August 2024, and the results were accessed on a Microsoft Excel spreadsheet.

Parameters Assessed:

1. **Perceived Safety:** Participants chose a number on a numeric rating scale of 0-10 indicating their sense of safety, with 0 being the worst and 10 being the best. A score of 0-3 was classified as unsafe, while 810 was interpreted as safe. 0 was called very unsafe, while 10 was termed safest. Those who scored 4-7 were classified as "uncertain".
2. **Duty Room Availability:** Yes/No question about whether they have a duty room.
3. **Bathroom Accessibility:** Yes/No question about whether the duty room has an attached bathroom.
   Distance to bathroom: to see if it was nearby or otherwise.
4. Suggestions from individual doctors about how their personal safety can be improved.

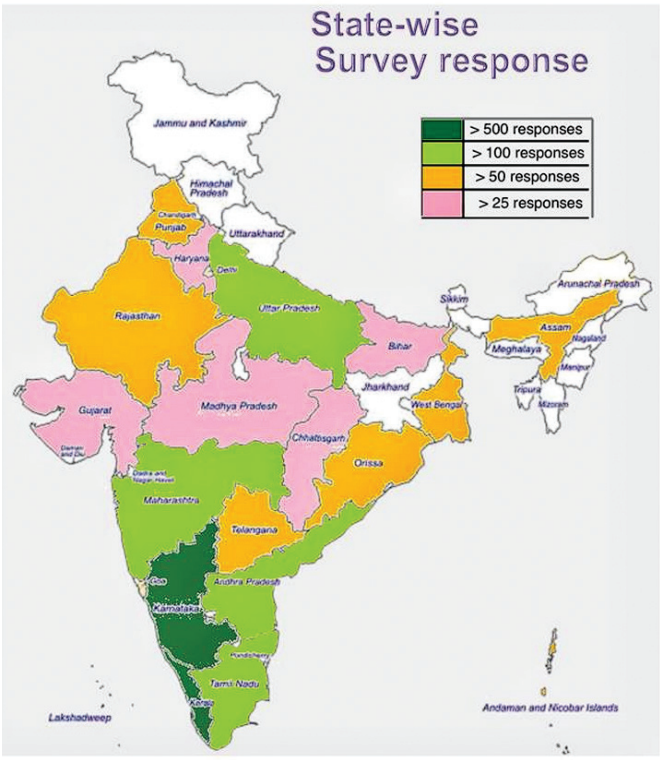

Figure 1. **State-wise Survey Response**

STATISTICAL ANALYSIS

Descriptive statistics were employed to evaluate the baseline characteristics of the survey population, using counts and percentages for qualitative variables, with bar charts and pie charts for visual representation. To assess the association between safety perceptions and other variables, chi-square tests or Fisher's exact tests were applied, depending on cell counts. The analysis was conducted with a 95% confidence interval, setting the significance level at 5%. Data were entered into Microsoft Excel and analysed using SPSS version 20.0.

RESULTS

The Survey conducted by IMA Kerala State Branch in August 2024, captures data from 3,885 respondents from various states across India, providing insights into gender, age, designation, duty room availability, and safety perceptions during night duty.

Table 1. Gender distribution

Gender	Frequency	Percentage
Male	1425	36.7%
Female	2460	63.3%
Total	3885	100%

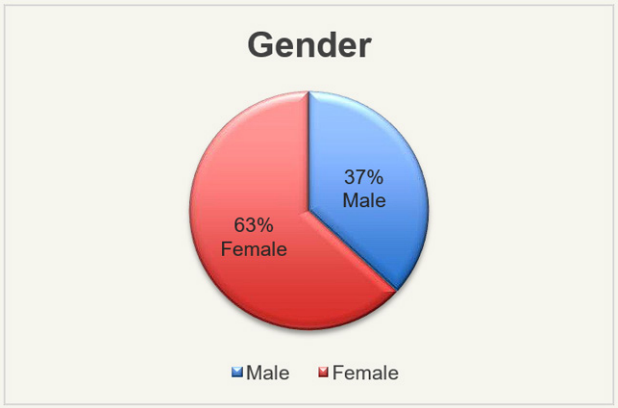

Figure 2. **Gender distribution**

The survey received 3885 responses from doctors across India. The states are colour-coded according to the number of responses received **(Figure 1)**. See **table 10** for details.

Table 2. Age distribution

Age	Frequency	Percentage
20-25	948	24.4%
26-30	1795	46.2%
31-35	580	14.9%
36-40	245	6.3%
41-45	112	2.9%
46 and above	205	5.3%
Total	3885	100%

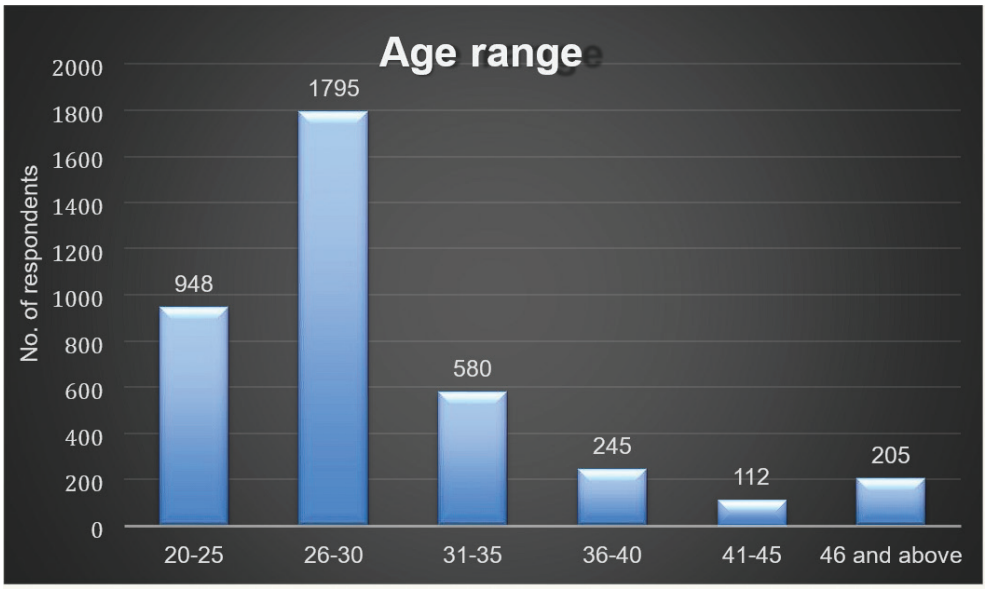

Figure 3. **Age distribution of survey respondents**

Table 3. Distribution of designation of the doctors

Designation	Category	Frequency	Percentage
Government Hospital	Senior Doctors	184	4.70%
	Junior Doctors	407	10.50%
	Medical College Faculty	201	5.20%
Private Hospital	Senior Doctors	224	5.80%
	Junior Doctors	332	8.50%
	Medical College Faculty	168	4.3%
Intern		750	19.3%
Postgraduate		1619	41.70%
Total		3348	100%

Figure 6 shows the assessment of duty room availability among the participants shows that 55.2% have access to a duty room, while 44.8% do not.

Among the 2,145 participants with access to a duty room, 67.6% reported having a duty room with an attached washroom/restroom, while 31.4% did not. A small percentage (1.03%) gave invalid responses **(Figure 7)**.

Among the participants with access to a duty room, 52.9% reported that their duty room was located far away from the ward or casualty area (100-1000 meters).

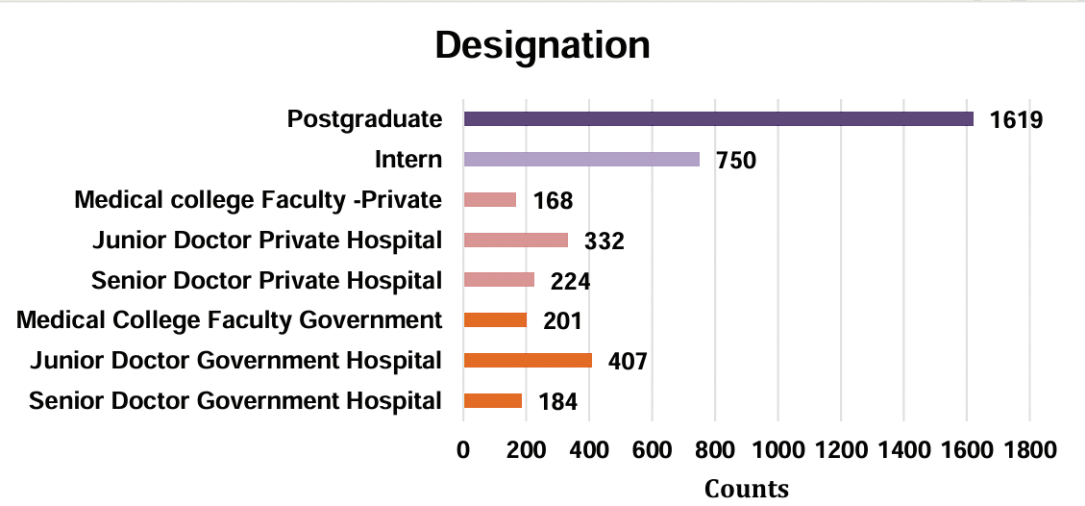

Figure 4. **Designation of doctors who took the survey**

Figure 2 shows the majority of the 3,885 respondents, were women, (63%) reflecting current gender distribution trends among MBBS students in certain states such as Kerala[8]

Figure 3 shows, 85% of the respondents were at or below age 35. Two-thirds were aged 30 or below. The majority (46.2%) fall within the 26-30 year age range, with 24.4% in the 20-25 year group. Smaller proportions are seen in older age categories, with just 5.3% aged 46 years and above.

Figure 4,5 shows the designation distribution among study participants shows that the largest group consists of postgraduates (41.7%), followed by interns (19.3%), with a combined representation of 61%.

Junior doctors in government hospitals make up 10.5%, while their counterparts in private hospitals account for 8.5%. Senior doctors and medical college faculty were evenly distributed, with senior doctors from private hospitals at 5.8%, government hospitals at 4.7%, and medical college faculty at 5.2% in government and 4.3% in private institutions. The distribution reveals that a majority of participants (80%) are junior doctors. This indicates that the survey primarily captured the perspectives of those in relatively junior positions.

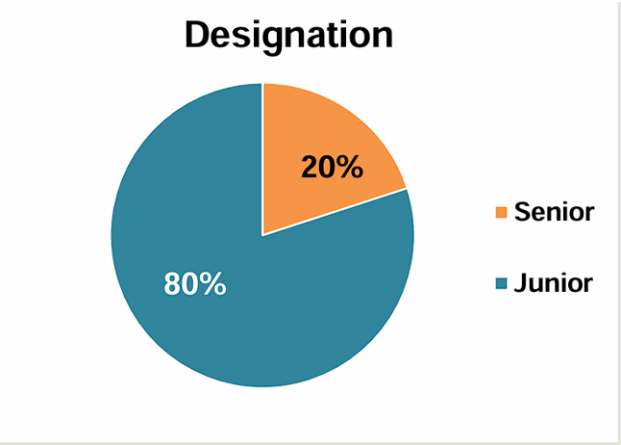

Figure 5. **Professional seniority status**

Table 4. Assessment of duty room availability

Availability of duty room	Frequency	Percentage
Yes	2145	55.20%
No	1740	44.80%
Total	3885	100%

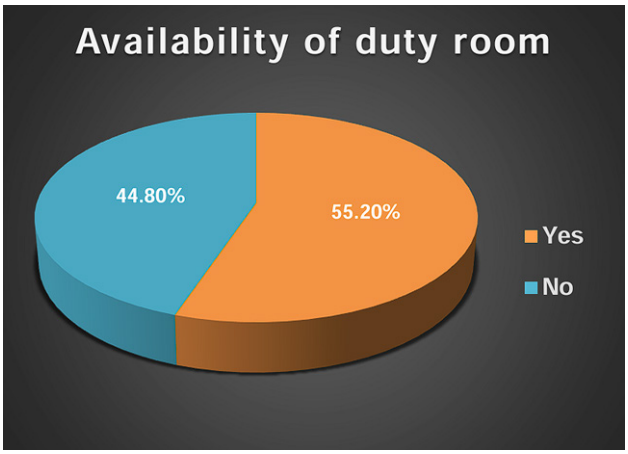

Figure 6. **Duty room availability**

A majority of doctors must walk a significant distance from their duty rooms to reach the ward or casualty area, which can pose a safety risk at night if the path is not well-lit and secure **(Figure 8).**

Table 7 shows the participants chose a number on a numeric rating scale of 0-10 indicating their sense of safety, with 0 being the worst and 10 being the best. A score of 0-3 was classified as unsafe, while 8-10 was interpreted as safe. 0 was called very unsafe, while 10 was termed safest. Those who scored 4-7 were classified as "uncertain".

Figure 9 shows the subjective assessment of safety during duty hours shows that a significant portion, 24.1%, felt unsafe, and 11.4% considered their situation very unsafe, with a total of 35.5% feeling unsafe to various degrees. On the other hand, 14.1% felt safe and 4% felt it was the safest. 46.5% of respondents reported "Uncertain Safety", reflecting mixed feelings or uncertainty about their safety.

The data shows significant variation in safety perceptions during duty across different demographics and environmental factors **(Table 8).**

Women report higher levels of feeling unsafe or very unsafe (36.7%) compared to men (32.5%), with this finding being statistically significant ($p < .0001$). Age also plays a role, with younger respondents (20-25 years) feeling less safe compared to older groups, and this age-based difference is significant ($p < .0001$).

Table 5. Duty room with attached washroom facility

Duty Room with Attached washroom	Frequency	Percentage
Yes	1449	67.55%
No	674	31.42%
Invalid	22	1.03%
Total	2145	100%

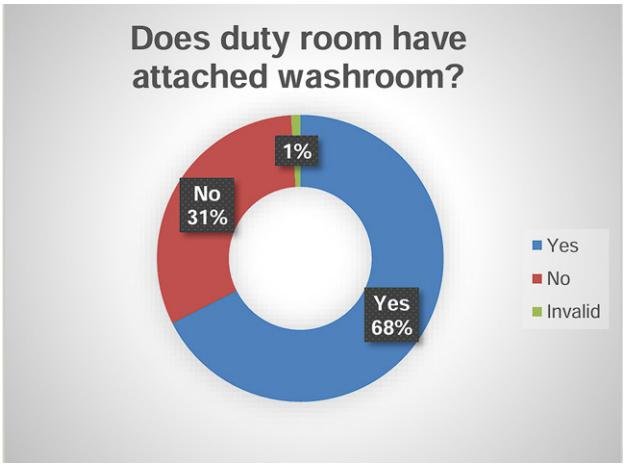

Figure 7. **Duty Room with attached washroom/restroom**

Regarding designation, juniors generally feel less safe compared to seniors, with this discrepancy also being significant ($p < .0001$).

Table 6. Distance of duty room from Ward/Casualty

Distance from Duty Room and Ward/Casualty	Frequency	Percentage
Very Near	262(<50 metres)	12.21%
Near	549(50-100 metres)	25.59%
Far	1135(100-1000 metres)	52.92%
Very Far	199 (>1000 metres)	9.28%
Total	2145	100%
Total	2145	100%

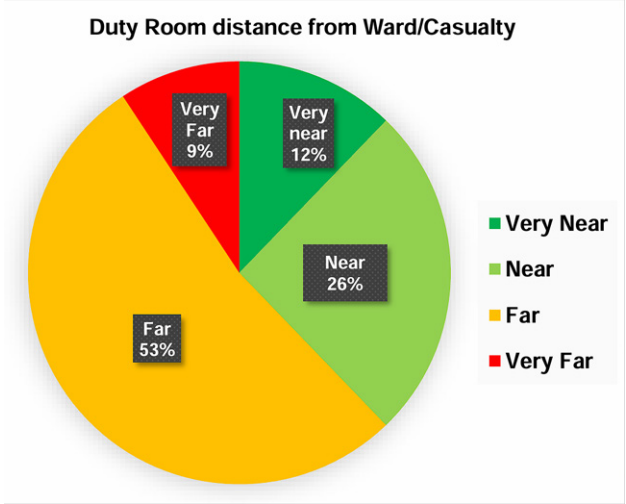

Figure 8. **Distance of duty room from ward/casualty**

Table 7. Subjective assessment of safety during duty hours		
Rating safety	Frequency	Percentage
Very unsafe	442	11.40%
Felt Unsafe	936	24.10%
Uncertain Safety	1805	46.50%
Safe	546	14.10%
Safest	156	4%
Total	3885	100%
Total	2145	100%

only 1.89% of government workers shared this level of confidence in their safety.

Adding up, 38.3% felt safe in the private sector, while only 10.6% shared the same sense of safety in the government sector.

This section of analysis did not include interns or postgraduate trainee doctors, as they were not subclassified into public or private sector in the survey.

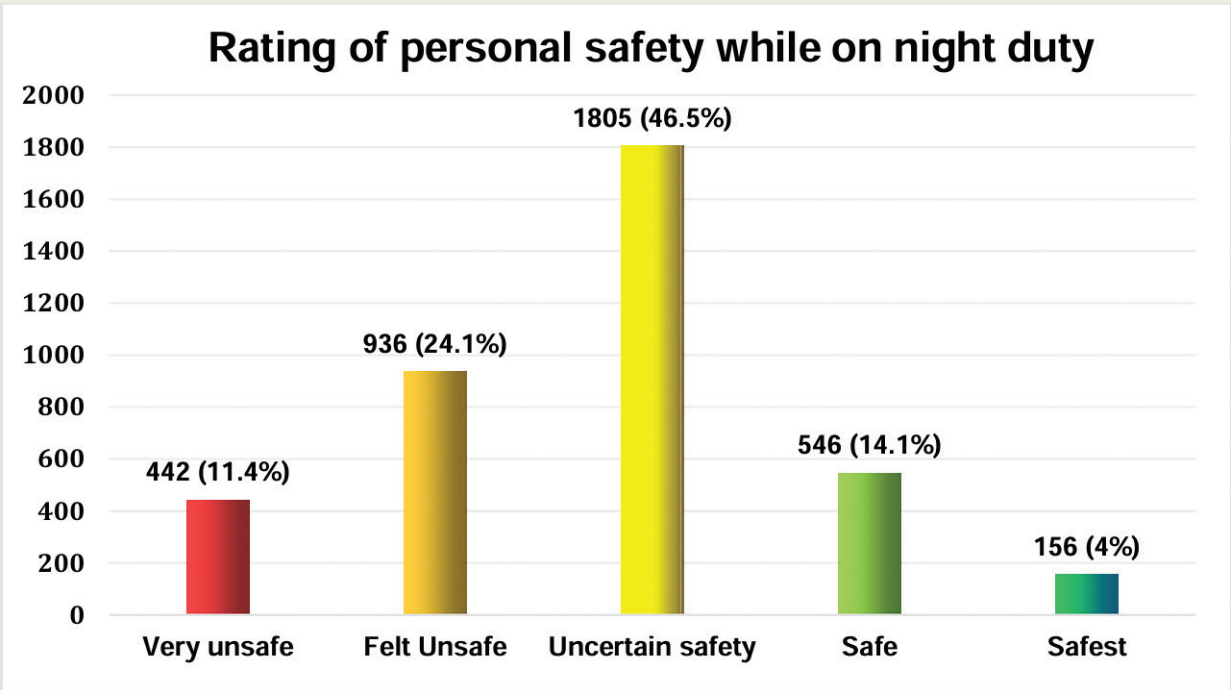

Figure 9. **Self-Reported Safety Level in workplace**

Figure 10 shows association between duty room and sense of safety: Two parameters relating to safety perception are displayed here. The red bar is the proportion of those who felt unsafe, scoring 0-3 on a numeric rating scale of 0-10, while the green bar represents those who felt safe, with a score of 8-10.

When duty room was not available, more doctors felt unsafe (tall red bar) and fewer doctors felt safe (short green bar).

This shows that availability of a duty room significantly impacts safety perceptions, with those without access feeling unsafe (50.9%) compared to those with a duty room (22.9%) ($p < .0001$). Similarly, 26.4% of those with a duty room reported feeling safe compared to only 7.8% without.

Likewise, the presence of a duty room with an attached washroom is associated with better safety perceptions; more of those without such facilities feel unsafe (44.8%) compared to those with the facility (20.2%) ($p < .0001$). Similarly, more of those with an attached washroom felt safe (30%) compared to only 10.8% without. This shows a clear correlation between the availability of basic facilities and safety perception.

Table 9 shows the distribution of statewide responses reveals that the largest representation comes from Kerala (27.7%) and Karnataka (21.1%). More than a hundred individual responses each came from U.P (4.4%), Andhra Pradesh (7.2%) Maharashtra (9.2%), and Tamil Nadu (11.1%). More than 50 responses each were obtained from Assam, Delhi, Odisha, Puducherry, Punjab, Telangana and West Bengal. More than 25 responses each came from Haryana, Madhya Pradesh, Chhattisgarh, Bihar and Gujarat.

Table 10 shows that safety perception trends are comparable across regions in India, with minor differences

Table 8. Safety perceptions during duty hours by demographic and facility parameters

Parameter		Very Unsafe	Felt Unsafe	Uncerta in safety	Safe	Safest	Significance
Gender	Male	12.00%	21.30%	44.40%	16.60%	5.60%	Significant (p < .0001)
	Female	11.00%	25.70%	47.60%	12.60%	3.10%	
Age	20-25 Years	11.30%	29.30%	45.10%	11.60%	2.60%	Significant (p < .0001)
	26-30 Years	10.50%	24.20%	49.90%	12.40%	3.10%	
	31-35 Years	12.90%	21.70%	43.30%	16.90%	5.20%	
	36-40 Years	18.40%	16.70%	42.40%	16.70%	5.70%	
	41-45 Years	10.70%	17.90%	44.60%	20.50%	6.20%	
	46 and above	7.30%	18.00%	37.10%	25.40%	12.20 %	
Designation	Senior	11.70%	16.30%	43.80%	21.10%	7.10%	Significant (p < .0001)
	Junior	11.30%	26.00%	47.10%	12.30%	3.20%	
Duty Room Available	Yes	5.60%	17.30%	50.70%	20.20%	6.20%	Significant (p < .0001)
	No	18.40%	32.50%	41.30%	6.50%	1.30%	
Duty Room with Attached Wash Room Facility	Yes	5.60%	14.60%	49.80%	22.70%	7.30%	Significant (p < .0001)
	No	14.90%	29.90%	44.40%	8.80%	2.00%	

Chi square test, p<0.0001 shows significance

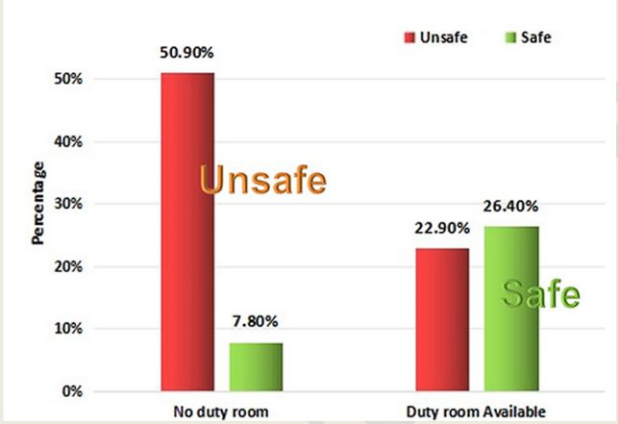

Figure 10. **Duty room and sense of safety**

that can be expected due to sample size from each region.

Table 11 shows subjective safety perceptions among healthcare workers in the government and private sector, revealing a significant difference between the two groups (Chi-square test, $p < 0.0001$).

Government healthcare workers reported higher levels of insecurity, with 17.05% feeling "Very Unsafe" and 27.4% feeling "Unsafe", totalling 44.5%. In contrast, only 5.52% and 12.02% of private healthcare workers reported feeling "Very Unsafe" and "Unsafe," respectively, totalling 17.5%. The classification was described earlier, in methodology.

Similarly, a larger percentage of private healthcare workers felt "Safe" (28.04%) compared to those in government institutions (8.71%). Additionally, 10.22% of private healthcare workers felt the "Safest," whereas

SUGGESTIONS TO IMPROVE SAFETY

Numerous suggestions were raised by 3885 respondents. Some individuals contributed several, while others mentioned one or two key points. All of these were individually read by the study authors in repeated sittings, categorised according to the theme and quantified by frequency. All of this qualitative analysis was done manually using pencil and paper. The reasons for doing this manually was to acquire a deeper understanding as well as to eliminate any misreading due to language limitation. Subsequently, a statistical analysis was performed.

The following are suggestions ranked according to frequency of keyword use. Those which were mentioned the most are given on top. Details are given in the subsequent section.

Synopsis of suggestions:

The following synopsis summarizes the numerous comments in each category. A verbatim comments section is provided further below, offering an unfiltered view of the concerns raised.

Security: Inadequate security at hospital premises was reported by a large number of doctors. Hospitals often employ low-wage security personnel to reduce costs. Many commented that the available security personnel were weak and frail individuals who themselves seemed to need protection and were the first to run away at the first sign of trouble. Doctors have expressed a preference for ex-servicemen as security guards, and able-

Table 9. Statewise distribution of responses

State	Frequency	Percentage
Kerala	1078	27.75%
Karnataka	764	19.67%
Tamilnadu	430	11.07%
Maharashtra	356	9.16%
Andhra Pradesh	302	7.77%
Uttar Pradesh	172	4.43%
West Bengal	86	2.21%
Puducherry	74	1.90%
Punjab	70	1.80%
Odisha	64	1.65%
Assam	58	1.49%
Rajasthan	56	1.44%
Delhi	51	1.31%
Telangana	51	1.31%
Gujarat	45	1.16%
Chattisgarh	39	1%
Andaman and	36	0.93%
Bihar	36	0.93%
Haryna	36	0.93%
Madhya	28	0.72%
Utarakhand	21	0.54%
Sikkim	14	0.36%
Jharkhand	5	0.13%
Tripura	5	0.13%
Himachal	3	0.08%
Daman and Diu	1	0.03%
Goa	1	0.03%
Jammu and	1	0.03%
Manipur	1	0.03%
Meghalaya	1	0.03%
Total	385	100%

bodied men in their 30's to 40's as bouncers in high-risk areas such as casualty and ICU lobby where skirmishes are common. Some women doctors indicated the need for female security personnel. Having a police checkpost is ideal. Security is particularly lacking in smaller peripheral hospitals where doctors may be alone with limited staff. Security personnel must be proportional to the size of the hospital and conduct regular rounds of the premises. Doctors who need to walk to different areas of the hospital during late hours—such as the blood bank, scan room, ward, lab, duty room or parking lot—should be accompanied by a security escort.

1. **CCTV camera:** Functioning cameras are required in multiple areas of healthcare establishments, and they must be manned by trained personnel who have the resources to take action should a potential problem be detected.

2. **CPA (National Law that protects healthcare workers)** Doctors were emphatic about the need for a CPA or Central Protection Act that enables them to work safely in any healthcare establishment. The absence of such a law encourages unscrupulous behaviour. It is equally important to file an FIR on time and to enforce the law when violence occurs. Awareness of such a law will deter violence. The presence of a grievance redressal forum at each facility will prevent minor discontent from escalating into violence.

3. **Duty Room:** Inadequate facilities were widely reported. When a doctor takes a night call, they need a place where they can rest for some time. The duty room must be secure and clean, with bolts on the door and an accessible, secure bathroom. Many suggested that women and men have different duty rooms and bathrooms. Interns as well as postgraduates must have duty rooms, and these must not be shared by other hospital staff. The room must be located away from where bystanders are waiting, but not in dark, isolated and deserted parts of the building. Currently, in the absence of duty rooms, many doctors are forced to go to insecure places like a seminar room or an empty cot on a ward or OPD

Table 10. Safety perceptions during duty hours by region

Region	Very Unsafe	Felt Unsafe	Intermediate	Safe	Safest	Total
Central India	8 (11.9%)	15 (22.4%)	28 (41.8%)	14 (20.9%)	2 (3.0%)	67 (100.0%)
Eastern India	37 (18.0%)	47 (22.9%)	89 (43.4%)	26 (12.7%)	6 (2.9%)	205 (100.0%)
Islands and UTs	3 (8.1%)	10 (27.0%)	17 (45.9%)	6 (16.2%)	1 (2.7%)	37 (100.0%)
North-Eastern India	8 (12.3%)	10 (15.4%)	36 (55.4%)	6 (9.2%)	5 (7.7%)	65 (100.0%)
Northern India	40 (11.3%)	95 (26.8%)	173 (48.9%)	38 (10.7%)	8 (2.3%)	354 (100.0%)
Southern India	315 (11.4%)	679 (24.6%)	1258 (45.7%)	388 (14.1%)	115 (4.2%)	2755 (100.0%)
Western India	31 (7.7%)	80 (19.9%)	204 (50.7%)	68 (16.9%)	19 (4.7%)	402 (100.0%)
Total	442 (11.4%)	936 (24.1%)	1805 (46.5%)	546 (14.1%)	156 (4.0%)	3885 (100.0%)

Fishers Exact Test, p=0.024*

Table 11. Safety perceptions during duty hours by work sector

Safety Perception	Government (N=792)	Private (N=724)	Total (N=1516)
Very Unsafe	135(17.05%)	40(5.52%)	175 (11.5%)
Felt Unsafe	217(27.4%)	87(12.02%)	304 (20.1%)
Uncertain Safety	356(44.95%)	320(44.20%)	676 (44.6%)
Safe	69(8.71%)	203(28.04%)	272 (17.9%)
Safest	15(1.89%)	74(10.22%)	89 (5.9%)
Total	792 (52.2%)	724 (47.8%)	1516 (100.0%)

Chi Square Test, $p<0.0001$ shows significance

Table 12. Suggestions for better workplace safety from individual doctors, ranked by frequency

1	Duty room with bathroom, close to work location*
2	Adequate number of professional security personnel
3	CCTV camera 24/7 to monitor key areas
4	CPA Central Protection Act, and its enforcement
5	Secure locks/bolts on all duty room doors
6	Restrict the number of bystanders/attendants with each patient
7	Adequate lighting to be ensured
8	Panic button/alarm system/code grey in case of emergency
9	Food and water to be made available nearby during night duty
10	Do not allow drunk bystanders in casualty

*As the questionnaire directly mentioned duty room, ranking of this parameter is not possible. The other parameters were derived from individual comments and ranked according to frequency of use.

to lie down, which occasionally leads to experiences such as theft and even assault.

4. **Lighting** is required throughout the areas where doctors and staff are expected to be using while doing night calls. Doctors reported several instances of dark unlit corridors, duty rooms located in isolated parts or floors of the building and parking lots without security or lights.

5. **Restricting the number of bystanders** is essential in healthcare settings. Doctors reported instances of being surrounded by crowds while attending to road accident victims or performing procedures in the casualty area. This is both unnecessary and dangerous, as some individuals may be under the influence of alcohol or drugs, increasing the risk of violence due to ignorance or aggression. Ideally, only female bystanders should be permitted in wards at night. All building entrances must be secure and monitored to prevent unauthorized access to patient care areas or isolated sections of the facility. Construction workers should not be present on the premises at night. Bystanders should be given wristbands for identification and should not be allowed entry without them.

6. **The absence of locks and bolts** of duty rooms was highlighted by many doctors, a problem that does not require a large investment to fix. Doctors said that they often do not know who is knocking on their duty room door until they open it, this poses a significant security risk. Some duty rooms do not have complete walls, a few others only had tinted glass partitions that did not provide adequate privacy.

7. **Panic Button:** Despite substantial investment in infrastructure and personnel, violence can occur at any time in healthcare settings. In such situations, there must be a panic button, emergency helpline, or specialized alarm system to summon immediate assistance. Known as code grey or code white in various facilities, this practice is already implemented in several tertiary care centers and should be made universal.

8. **Alcohol and drugs** play a major role in healthcare violence. Bystanders who are inebriated should not be allowed to enter casualty, and this requires protocols and manpower in the security/triage department.

9. **Food and Water:** Food and water are fundamental needs for doctors on night shifts. Providing these essentials near their work areas eliminates the need for doctors to walk through dark and unsecured parts of the campus to obtain them. Additionally, vending machines for sanitary napkins should be installed, and designated rooms should be provided for doctors who are nursing mothers.

10. **Grievance Redressal or Helpdesk:** A help desk should be established outside casualty areas or wards where bystanders can direct their questions, rather than interrupting doctors. This also protects doctors from becoming convenient targets for even minor grievances. Additionally, having trained staff available for counselling can reduce some of the doctors' workload in crowded settings.

11. **The support of administration** is essential to promote a safe and secure work environment. Interns and postgraduates highlighted the need to reduce the toxicity at the workplace, emphasising their right to be treated fairly. Periodic audits and appraisal meetings of workplace safety will help reduce the sense of fear that doctors feel while taking night calls.

12. **Animal attacks** were mentioned by several doctors. Stray dogs and snakes were the most common. A

well-maintained, walled, clean campus will eliminate such threats.

13. **Non-clinical night duty:** Some trainee doctors questioned the necessity of performing night duties in non-clinical departments such as pathology and microbiology.

A sample of comments verbatim: they provide insight into individual doctors' concerns

1. "I have felt bad touches many times working in crowded casualty"
2. "Have worked as a faculty in two private medical colleges. The duty rooms were at the end of a deserted corridor without much light, always felt unsafe and always carried a pepper spray and foldable knife in my bag."
3. "I don't feel safe."
4. "Security personnel run away when any situation arises."
5. "Only one bystander to be allowed per patient."
6. "Anyone can knock on the duty room door. We open without knowing who the person outside is."
7. "Providing security alone is not enough, need law which punishes culprits."
8. "Implement CPA" (Central Protection Act)
9. "If ESMA applies to us, protection too should." (Essential Services Maintenance Act)
10. "I am concerned about my female colleagues."
11. "We need an airport-like safe zone."
12. "During 70% of my duty days, I had to handle drunk mobs at night."
13. "10 people (bystanders) stand around me when I take RTA (road traffic accident) patient's history."
14. "Institutions must have written policy on safety at workplace."
15. "Doctors have to do ward boy work due to lack of labour force."
16. "I am a senior resident at a private hospital where I feel safe while taking night duties; but I did my undergraduate and MD at government hospitals where I would rate the safety feeling at 2 to 3 out of 10."
17. "Security is an old, short, skinny man most of the times."
18. "We have CCTV cameras everywhere and security personnel too, so no issues."
19. "I do need a place to rest, somewhere with a lock and a place to use as a restroom."
20. "Training of postgraduates to be non-toxic."
21. "We are just provided some unused ward for all female duty doctors with one untidy washroom, and that ward is barely cleaned."
22. "We often get attacked by patient bystanders in casualty and ICU."
23. "We have faced atrocities of patient bystanders."
24. "Provide a gun to all the doctors, and guards of younger age."
25. "Security Jo Jagada Hone per sabse Pehle nahin Bhaage." (We need security who do not run away at the first sign of trouble.)
26. "I have faced serious security threats as a woman doing night duties."
27. "If we need to use the washroom, we need to go to hostels in the middle of the night when it is pitch dark, no security."
28. "Postgraduates sleep in OPD as no room available."
29. "I have faced exhibitionism from a 56-year-old male in an outpatient department."
30. "It is scary to run to different wards for code blue at night."
31. "Approval for use of Self Defence tool for health-care workers."
32. "If we scream, no one will hear."
33. "OPD's should have a double door system. One for entry and one for escaping violent attacks from patients or bystanders."
34. "Authorities don't take our complaints seriously, they act as if this is how universally things are."
35. "Do not make us go to deserted places and corridors at night."
36. "Pls give a room with locks"
37. "A wearable panic button for every doctor on call"
38. "As I am working in a private setup, things are better"
39. "Just one duty room provided for all female PG's and interns which will eventually become crowded, and we search for some other places to take rest which is unsafe"
40. "Though we don't have a great duty room, we feel pretty safe, mainly because our seniors are open to

our concerns and show genuine interest when we raise an issue. We also have good security guards."

41. "Periodic safety audit to be done"
42. "…we are human beings, can't work 36-48 hours without rest"
43. "Let security staff accompany the doctor at odd hours"
44. "Security needed in all ward/ICU/red zone, wherever doctor need to disclose death"
45. "Security guards looks not so strong."
46. "Avoid more than 24 hours duty….one will be very weak physically and mentally to overcome any stressful situations"
47. "Most unsafe are the rural postings"
48. "I work in emergency medicine. I feel safe"
49. "One patient, one relative policy"
50. "Security to patrol isolated corridors. Lifts to have 24/7 security"
51. "Department is cool and safe, but rural posting hard to imagine"
52. "Not just tertiary care hospitals/medical colleges, doctors are working at peripheral hospitals as a part of bond service or training or DRP, so, security and safety should be provided at every work place"

DISCUSSION

This is the largest study on healthcare violence done among doctors in India. Over one-third of the doctors reported feeling unsafe while doing night duty. More than one out of ten felt totally unsafe, giving the lowest score of zero out of ten for sense of safety. The feeling of being unsafe was worse among women, and among younger doctors. Doctors of age 20-30 years had the lowest sense of safety ($p < 0.001$, **Table 8**), this group largely consists of interns and postgraduates.

The survey identified several rectifiable reasons for this.

The availability of duty room and facilities was limited, with only 55% being provided a duty room. Thus, 45% of doctors are compelled to find less secure places such as empty outpatient beds or seminar rooms to sit down or lie down. Nearly one-thirds of the available duty rooms did not have an attached bathroom, which means that the doctors needed to step outside during late hours to access these facilities.

Where available, duty rooms were often reported to be inadequate in size, safety, comfort, privacy, location and upkeep – all of which are factors that necessitate doctors to venture out to less secure places at night. Providing a safe place for doctors to rest during night duty is a basic necessity and does not come at great cost to any healthcare establishment. The survey unearths the lack of attention to this aspect of healthcare.

The data indicate that the presence of a duty room with an attached bathroom significantly improved the sense of safety. This correlation might be attributed to the possibility that hospitals with wellequipped duty rooms are also more likely to have invested in comprehensive security measures.

Apart from being a basic necessity, the availability and adequacy of these facilities translates into better patient care as doctors feel secure, safe and well-cared for.

Several additional factors were highlighted by doctors who participated in the survey. The lack of sufficient numbers of trained security personnel, inadequate lighting of the corridors, absence of CCTV cameras and unrestricted entry of unauthorised individuals into patient care areas were among the most frequent remarks. Providing basic facilities like clean and accessible bathrooms, drinking water and food for those who work through the night are expected of any healthcare establishment. When these are not provided, doctors are forced to walk through dark and insecure areas of the building or premises that are often not walled or fenced from the public road outside.

Some doctors indicated the need to start carrying weapons for self-defence. One doctor admitted that she always carried a foldable knife and pepper spray in her handbag because the duty room was located at the far end of a dark and deserted corridor. Doctors who worked in casualty reported verbal and physical threats from people who were drunk or under the influence of drugs. Another doctor reported that she repeatedly experienced bad touch or inappropriate contact in a crowded emergency room. The situation is worse in some smaller hospitals where there is limited staff and no security.

Several doctors reported apathy from the administrators when security concerns were raised, a common excuse being that the seniors also had endured similar working conditions. It is noteworthy that violence is predominantly experienced by junior doctors, who, being on the frontline, are particularly vulnerable but have limited involvement in administration or policy-making. Senior faculty members bear the responsibility of implementing policies to improve patient care delivery as well as enhancing security measures, thereby creating a safer work environment for junior doctors.

Doctors across the country have called for a Central Protection Law to prohibit violence in all healthcare settings and enforce airport-like security measures, ensuring a safer working environment and better patient care. Such a law would standardize security arrangements across the sector, ultimately benefiting patients as well as doctors.

The survey findings have significant implications for broad policy changes, some of which have already been addressed by the Government of India in response to the Kolkata incident. The Supreme Court of India took suo motu cognizance, assuring that "doctors and medical professionals shall stand assured that their concerns are receiving the highest attention from the highest court, with input from a diverse range of experts."[9,10] The multiple factors that contribute to healthcare violence in India have been analysed earlier.[11]

The large number of respondents with representation from multiple states in India from both public and private sector, across a broad range of age and professional seniority are the strengths of the study. All studies have limitations. While the anonymity offered by the online survey encouraged doctors to be frank and open about their concerns, individual comments cannot be verified. A significant limitation of any survey is the potential for sampling bias. Participation may have been skewed towards doctors with strong opinions or personal experiences related to safety. However, the clear differences observed between public and private sectors, as well as by professional seniority, suggest that the survey captured genuine and relevant responses. The findings may be supplemented with in-person interviews by trained professionals.

CONCLUSION

Doctors across the country report feeling unsafe during night shifts. This survey, the largest of its kind in India, identifies several modifiable risk factors contributing to violence in healthcare settings. There is significant potential for enhancing security personnel and equipment. Infrastructure improvements are needed to ensure that duty rooms, bathrooms, food, and drinking water are safe, clean, and accessible. Adequate staffing, effective triaging, and crowd control are essential in patient care areas to ensure that doctors can provide necessary attention to each patient without feeling threatened. The extensive and diverse suggestions from individual doctors, summarised and quoted in this article, will provide valuable insights for administrators and policymakers.

END NOTE

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Vision Related Quality of Life in patients with Diabetic Macular Edema receiving Intravitreal Ranibizumab

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ABSTRACT

Introduction: Diabetic macular edema is the most common cause of vision impairment in individuals with diabetic retinopathy. Diabetic macular edema develops due to leakage of fluid from diseased microvasculature in the retina. Various treatment modalities exist for diabetic macular edema, the present gold standard being the use of intravitreal anti-VEGF agents.

Aim: To assess the changes in vision-related quality of life among patients with diabetic macular edema receiving intravitreal Ranibizumab.

Materials and Methods: A hospital-based observational longitudinal study was conducted.

Demographic details as well as details about the disease were collected. A validated National Eye Institute Visual Function Questionnaire (using the interviewer-administered format of the questionnaire) was administered by a single interviewer, on the day before the scheduled intravitreal Ranibizumab injection and again repeated over a period of 3 months at 2, 6 and 12 weeks from the date of the first injection.

The overall composite score and the various subscale scores for visual function were computed using a validated scoring method for each patient based on their response to the questionnaire.

Analysis of data was done using Statistical Packages for Social Sciences Version 24 software. Changes in the various parameters contributing to the vision-related quality of life were studied using analysis of variance for repeated measures. The level of significance was determined by the p-value. A p-value less than 0.05 was considered statistically significant.

Results: The baseline composite score was found to be 38.2±9.1, at 2 weeks 41.0±10.3, at 6 weeks 48.2±14 and at 12 weeks 51.1±15.2. Data analysis showed the increase in the mean value of the baseline composite score to be statistically significant with a p value of 0.000.

All subdomains except general health also showed statistically significant improvement.

Conclusion: Patients diagnosed with diabetic macular edema were shown to have an improvement in their vision-related quality of life following a single injection of intravitreal Ranibizumab. Various subdomains of vision which contribute to the vision-related quality of life except general health were also noted to show statistically significant improvement.

Keywords: Diabetic Macular edema, Ranibizumab, Vision-Related Quality of Life, Diabetes Mellitus, Diabetic Retinopathy

*See End Note for complete author details

INTRODUCTION

Diabetes mellitus is a metabolic disease, known to be a major cause of concern for healthcare systems around the globe. According to World Health Organization statistics, more than 422 million adults globally were suffering from diabetes mellitus in 2014 and a continuous rise in diabetes mellitus prevalence is expected.[1] Diabetic retinopathy is one of the microvascular complications of the disease and among individuals suffering from diabetic retinopathy, diabetic maculopathy has been found to be the leading cause of vision loss. Diabetic maculopathy encompasses focal maculopathy, diffuse maculopathy and ischaemic maculopathy. The prevalence of diabetic macular edema in patients with diabetic retinopathy is 2.7% to 11%.[2-6] In diabetic macular edema, the retinal capillaries become hyperpermeable, due to which fluid extravasates out of the capillaries and accumulates within the macula. The pathogenesis behind diabetic macular edema involves

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a complex interplay of various pathways. The final cause for macular edema could be either a breakdown of the inner blood retinal barrier which occurs due to increased levels of vascular endothelial growth factor (VEGF) or due to vitreomacular traction.

VEGF was first described in 1983 and was initially named vascular permeability factor. It acts as an endothelial-specific mitogen and is able to induce angiogenesis in vivo. VEGF is not a single chemical substance, but rather a group of seven secreted glycoproteins namely VEGF-A, VEGF-B, VEGF-C, VEGF-D, VEGF-E and placental growth factors 1 and 2. Among these, VEGF-A, a 45 kilo Dalton homodimer glycoprotein has been known to play a vasoproliferative role in the pathogenesis of proliferative diabetic retinopathy and at the same time it also acts as a potent vasopermeability factor and plays a key role in the pathogenesis of diabetic macular edema. Both the retinal pigment epithelium as well as the neurosensory retina are known to release VEGF.

Clinically significant macular edema (CSME) has been defined in the Early Treatment for Diabetic Retinopathy Study (ETDRS)[7] as either retinal thickening within 500 micrometres of the centre of the macula or when hard exudates are noted within 500 micrometres of the centre of the macula and with an associated retinal thickening or when there is a retinal thickening of one disc area or larger, of which a part needs to lie within one disc diameter of the centre of the macula. Diabetic macular edema (DME), on the other hand, has been defined by the American Academy of Ophthalmology (AAO), as the presence of any retinal thickening or hard exudates within 1 disc diameter of the centre of the macula. Whichever is the definition used to diagnose macular edema in the context of diabetic retinopathy, treatment is imperative to improve the vision of the patient. Various modalities of treatment exist for diabetic macular edema. Laser photocoagulation of the retina served as the mainstay of treatment for diabetic macular edema till recently but has now largely been replaced by the use of intravitreal anti-VEGF agents.

Anti-VEGF agents belong to the group of monoclonal antibodies, which are engineered from mouse antibodies and have the majority of the mouse genetic sequence replaced by human gene sequence to reduce immunogenicity. Ranibizumab, an anti-VEGF agent, is the antigen-binding fragment of a recombinant humanized monoclonal antibody and it specifically binds to VEGF, thereby preventing the interaction between VEGF molecule and its receptor. Ranibizumab has a molecular weight of 48,000 Daltons and has demonstrated good penetration into the retinal pigment epithelium when administered intravitreally.

As per the Diabetic Retinopathy Clinical Research Network (DRCR.net) Protocol I, intravitreal Ranibizumab more effectively improves visual acuity than focal or grid laser treatment for centres involving diabetic macular edema.[8] No difference in visual acuity was noted at 5 years irrespective of whether aflibercept, bevacizumab or ranibizumab is used in patients with diabetic maculopathy and a visual acuity of better than 6/15.[8]

METHODOLOGY

Study Design: Hospital-based observational longitudinal study

Study Setting: A tertiary eye care hospital at Trivandrum, Kerala

Study Population: Patients diagnosed with diabetic macular edema and admitted for intravitreal Ranibizumab injection at a tertiary eye care hospital in Trivandrum, Kerala.

Study Subjects: Consecutive patients diagnosed with diabetic macular edema, who fulfil the eligibility criteria were recruited into the study, after receiving their informed consent.

Eligibility Criteria

1) Inclusion Criteria: Patients diagnosed with diabetic macular edema in the outpatient department (OPD) at a tertiary eye care hospital at Trivandrum and admitted by their treating ophthalmologist for intravitreal Ranibizumab injection. Diabetic macular edema is defined as the presence of retinal thickening or hard exudates within 1 disc diameter of the centre of the macula. (Definition by American Academy Of Ophthalmology)

2) Exclusion Criteria: Patients having other ocular pathology which can interfere with their vision related quality of life - viz central corneal ulcer, central corneal opacity, glaucoma and mature cataract.

Patients not willing to give consent for the study.

Patients less than 18 years of age.

Sample Size Calculation

Based on the study conducted by Elif Betel Turkoglu, Erkan Celic,. et al[9] change in the NEI VFQ 25

Table 1. Descriptive statistics showing score and corresponding SD for the overall vision-related quality of life during the period of study

Time of the study at which the scores where calculated	Score for the overall vision related quality of life	Standard Deviation
Baseline	38.2	9.1
At 2 weeks	41.0	10.3
At 6 weeks	48.2	14.0
At 12 weeks	51.1	15.2

Composite score was 12.4 with a standard deviation of the difference between the pairs being 18.2.

Substituting these values in the formula

$$N = (Z_{\alpha} + Z_{\beta}\left(\frac{\delta}{\sigma}\right)^2$$

$2 \propto = 1.96$

$Z\beta = 0.84$ σ = Standard deviation of difference between pair δ = Effect size (change in mean)

N = 17

Since the parent study I have analysed[9] is analysing changes in the value of a particular variable, hence the above formula was used for sample size calculation.

As per the sample size calculation, only 17 participants were needed. However analysing the patient load at the study centre, the time period for which my study had gained clearance and to strengthen the output of my study, I enrolled 40 participants for the study.

Table 2. Showing test of within subject effects for the overall vision related quality of life score

Source	Type III Sum of Squares	dF	Mean Square	F	p value
Overall vision related quality of life score	4353.606	3	1451.202	37.110	0.000

Sampling Technique

Consecutive patients satisfying the eligibility criteria were recruited into the study.

Method of Data Collection

Patients diagnosed with diabetic macular edema and admitted for intravitreal Ranibizumab injection, who fulfil the eligibility criteria, were recruited into the study. Demographic details like age and gender, as well as, details about the disease like duration of diabetes mellitus, type of diabetes mellitus, treatment currently taken by the patient for diabetes mellitus was collected. Visual acuity for distance was recorded using the Snellen distance visual acuity chart and expressed as log MAR. Baseline value of the central macular thickness in micrometres from optical coherence tomography report was recorded. Indirect Ophthalmoscopy with a +20 dioptre lens was done to find out the type of diabetic retinopathy in the eye planned for injection prior to the procedure. A validated National Eye Institute Visual Function Questionnaire (using the interviewer administered format of the questionnaire) was administered by a single interviewer, after obtaining

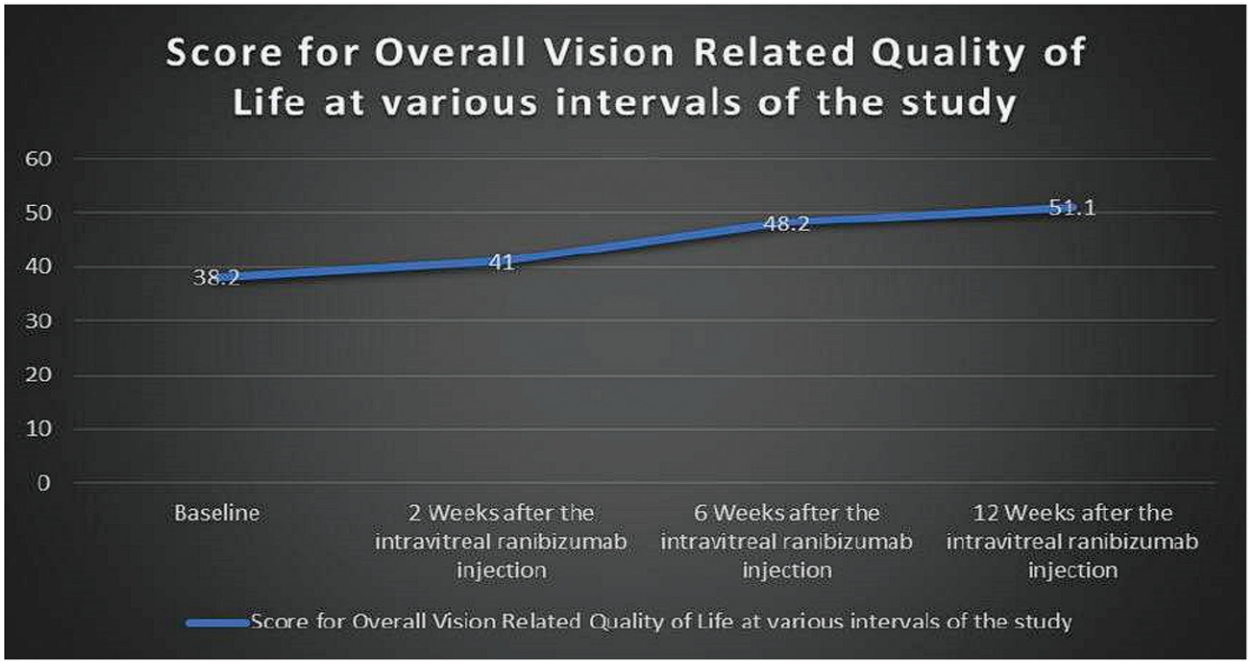

Figure 1. **Changes in the score for the overall vision related quality of life during the period of study**

Table 3. Table showing a test of pairwise comparison for overall vision-related quality of life score

Time interval at which the score for the overall vision related quality of life was measured (A)	Time interval at which the score for the overall vision related quality of life was measured (B)	Mean Difference (A) - (B) Mean Difference (A) - (B)	Standard Error	p Value
Baseline	At 2 weeks	-2.787	0.986	0.044
Baseline	At 6 weeks	-9.979	1.620	0.000
Baseline	At 12 weeks	-12.882	1.943	0.000
At 2 weeks	Baseline	2.787	0.986	0.044
At 2 weeks	At 6 weeks	-7.192	1.212	0.000
At 2 weeks	At 12 weeks	-10.095	1.554	0.000
At 6 weeks	Baseline	9.979	1.620	0.000
At 6 weeks	At 2 weeks	7.192	1.212	0.000
At 6 weeks	At 12 weeks	-2.903	0.690	0.001
At 12 weeks	Baseline	12.882	1.943	0.000
At 12 weeks	At 2 weeks	10.095	1.554	0.000
At 12 weeks	At 6 weeks	2.903	0.690	0.001

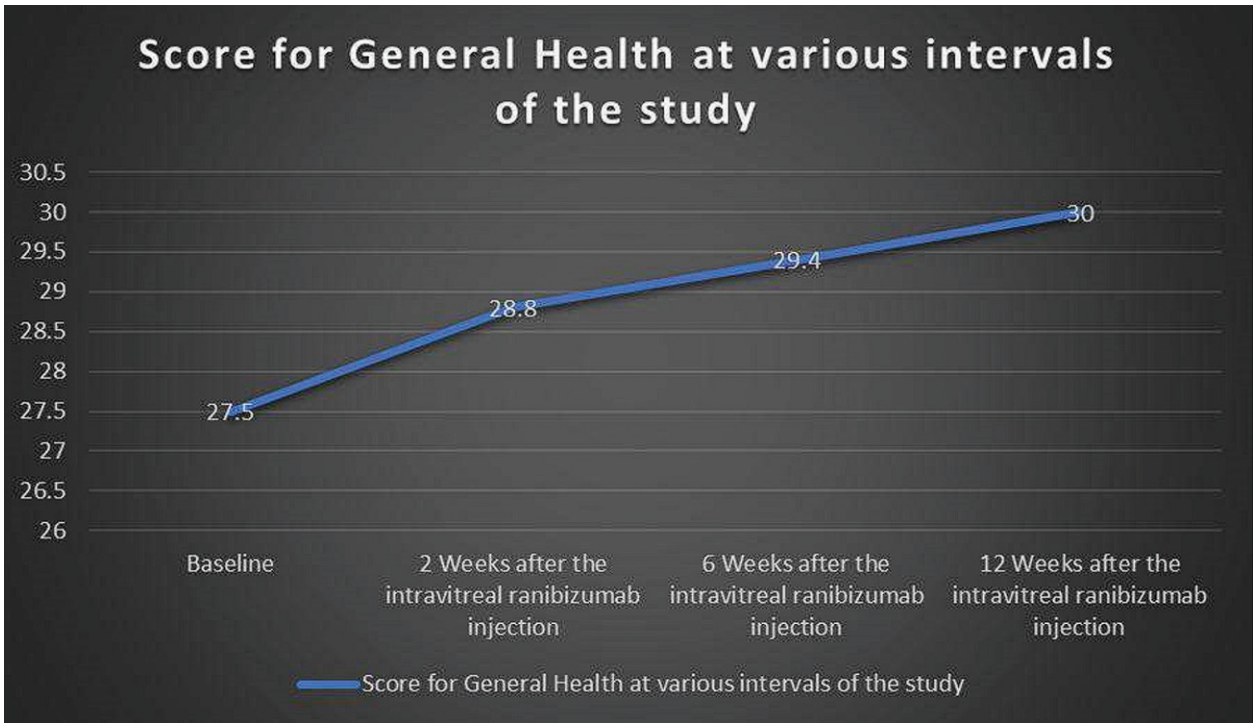

Figure 2. **Changes in the score for general health during the period of study**

informed consent from the patient, on the day prior to the scheduled intravitreal Ranibizumab injection and again repeated over a period of 3 months at 2, 6 and 12 weeks from the date of first injection – either when the patient reported for follow up to the hospital or over the telephone. Out of the 25 questions in the National Eye Institute Visual Function Questionnaire 25, 5 questions were eliminated (2 questions pertaining to driving, 1 question regarding vision specific social functioning, 1 question regarding distance vision activity and 1 question regarding ocular pain) from my study, as these questions are not applicable to my study subjects. Hence, I have administered 20 questions in the questionnaire for my study.

Method of Outcome Measurement

The overall composite score and the various subscale scores for visual function were computed using a validated scoring method for each patient based on their response to the questionnaire.

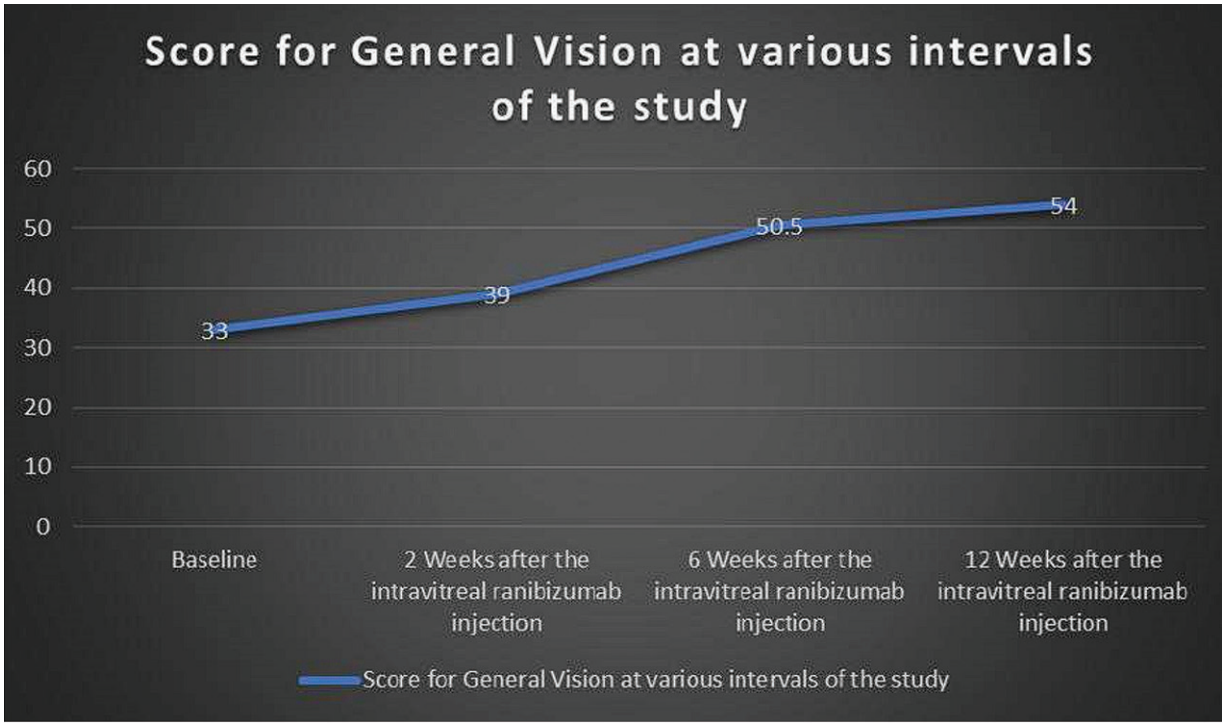

Figure 3. **Changes in the score for general vision during the period of study**

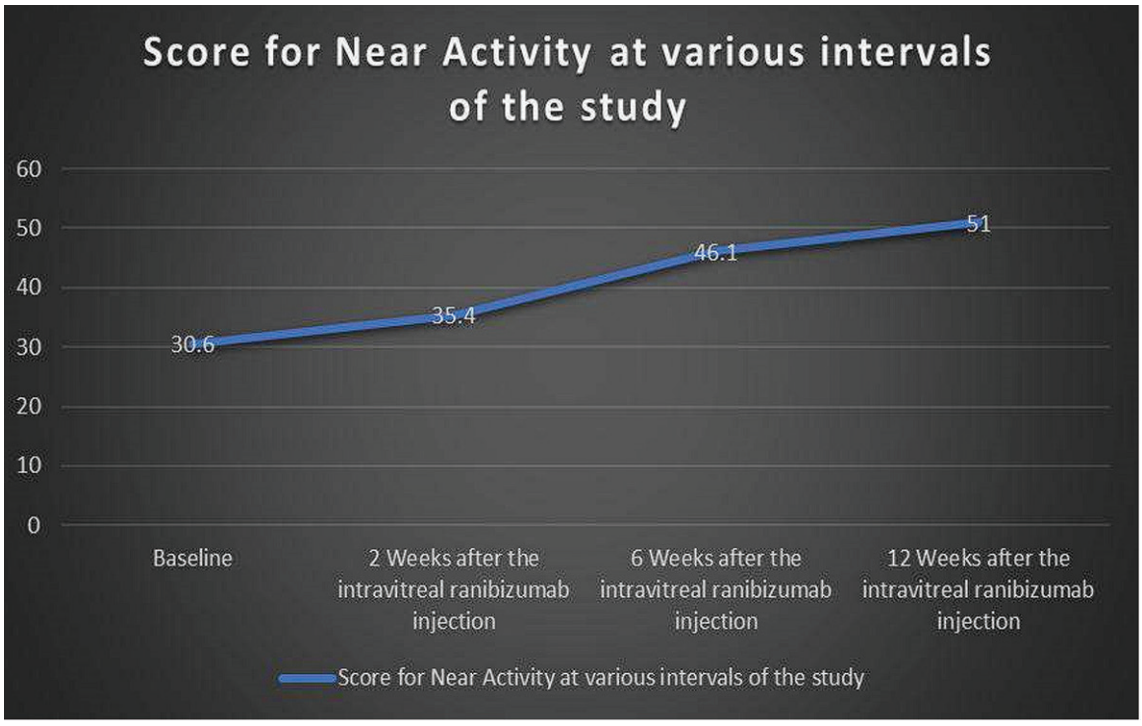

Figure 4. **Changes in the score for near activity during the period of study**

Method of Data Analysis

All statistical data collected was entered into Microsoft Excel Sheet. Qualitative variables were expressed as proportion while quantitative variables were expressed as mean with standard deviation. Analysis of data was done using Statistical Package for Social Sciences (SPSS) Version 24 software. Change in various parameters of vision related quality of life was studied using repeated measures of Analysis of Variance (ANOVA). The level of significance was determined by the p-value. A p-value less than 0.05 was considered statistically significant.

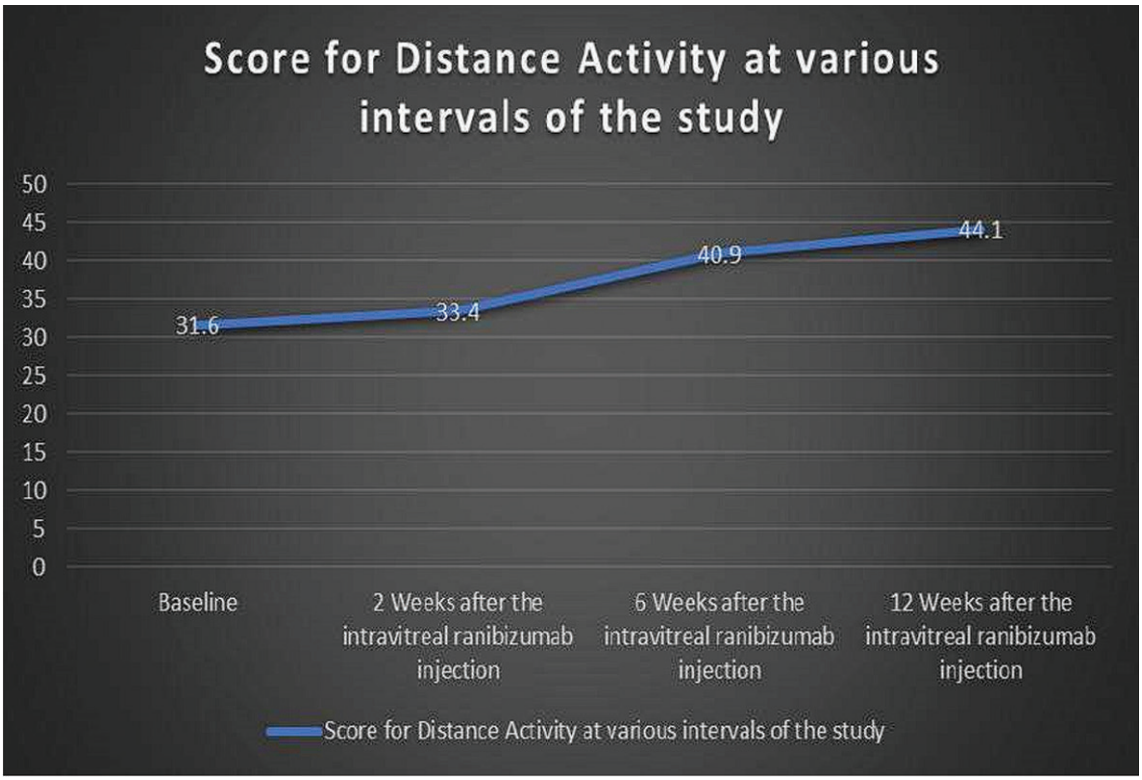

Figure 5. **Changes in the score for distance activity during the period of study**

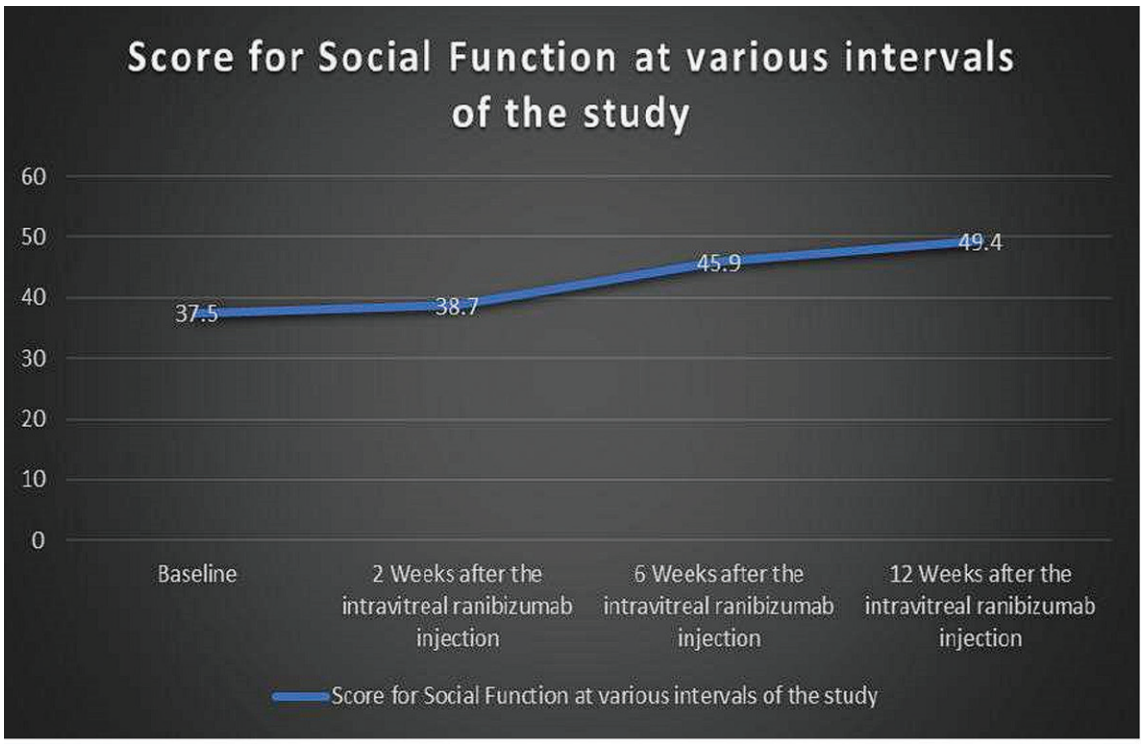

Figure 6. **Changes in the score for social function during the period of study**

RESULTS

40 patients were enrolled for the study of which 16(40%) were males and 24(60%) were females. 16(40%) of the subjects received the intravitreal Ranibizumab injection in the right eye while 24(60%) of them received the injection in the left eye. 18(45%) subjects belonged to the age group of 45 – 60 years while 22(55%) of them were aged above 60 years. 15(37.5%) of the subjects were homemaker, 10(25%) were professionals, 8(20%) were skilled workers while 7(17.5%) were clerical workers. 17 (42.5%) of the subjects had an income

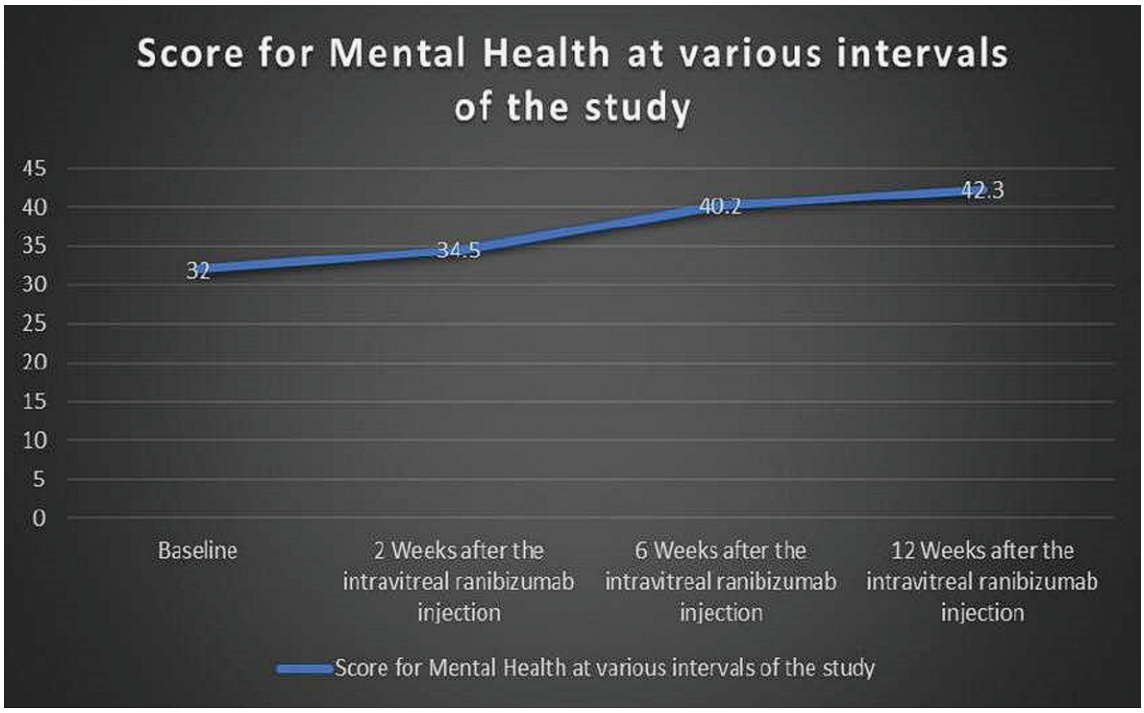

Figure 7. **Changes in the score for mental health during the period of study**

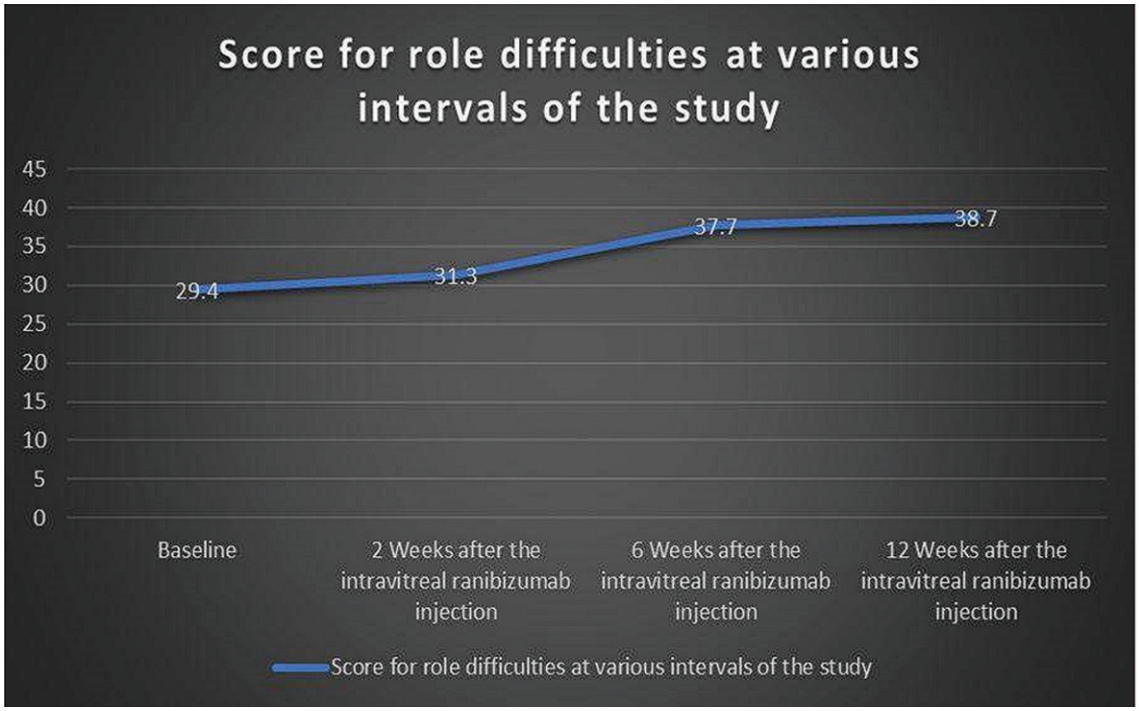

Figure 8. **Changes in the score for role difficulties during the period of study**

between 1000 to 3000 Indian Rupees, 10(25%) subjects each had an income less than 500 Indian Rupees and between 500 to 1000 Indian Rupees, and 3(7.5%) had their income between 3000 to 6000 Indian Rupees. 21(52.5%) of the study participants had a duration of diabetes mellitus between 5 to 10 years, 15(37.5%) had diabetes mellitus for a duration of more than 10 years and 4(10%) had the disease for a duration of less than 5 years. 19(47.5%) of the subjects received oral hypoglycaemic agents (OHA) alone as part of treatment for diabetes mellitus, 17(42.5%) received both insulin and OHA while 4(10%) received insulin alone. 11(27.5%) patients had a baseline central macular thickness as measured by the optical coherence tomography report of the macula to be between 600-700 micrometres, 10(25%) patients had a value of 500 – 600microme-

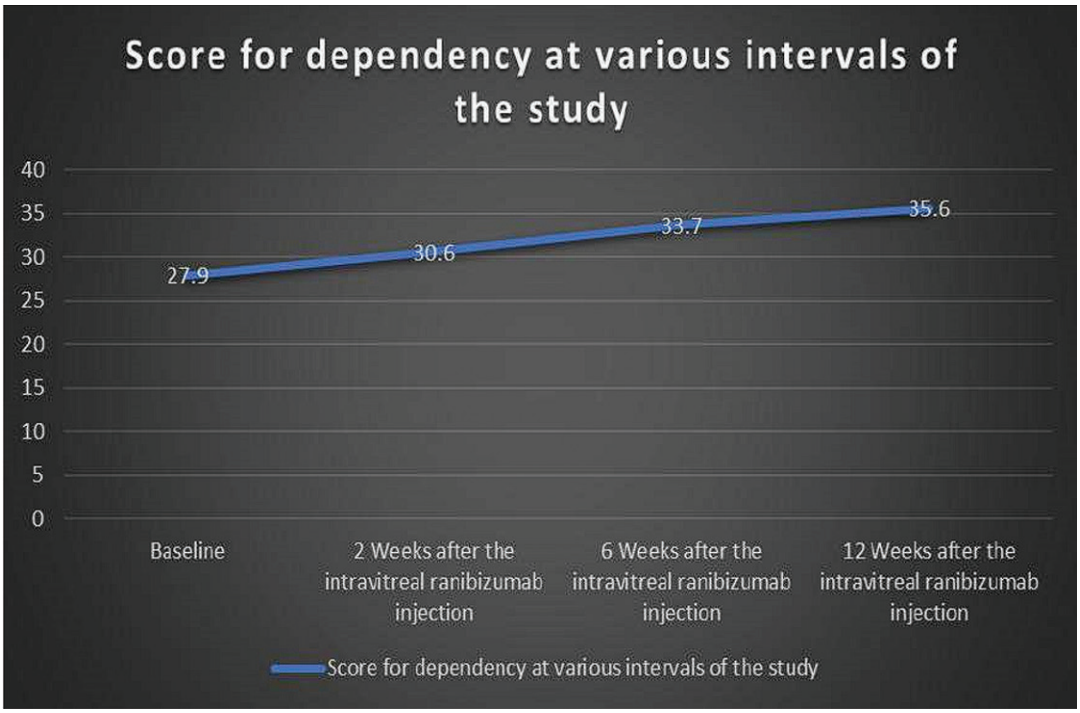

Figure 9. **Changes in the score for dependency during the period of study**

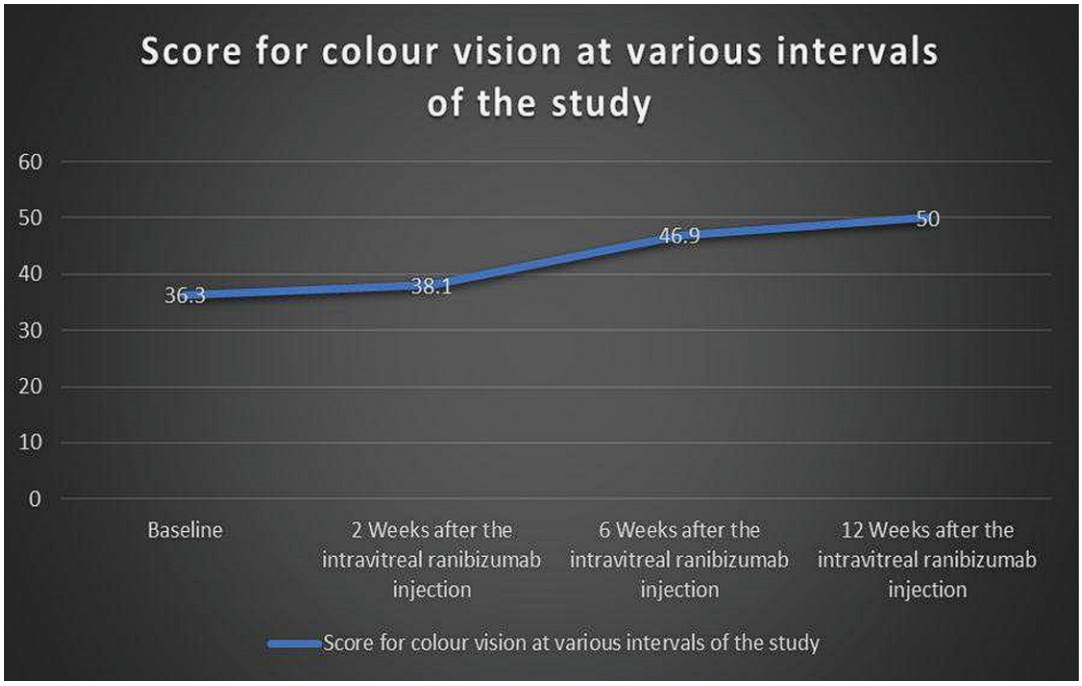

Figure 10. **Changes in the score for colour vision during the period of study**

tres, 8(20%) patients had a value of 400-500 micrometres, 7(17.5%) patients had a value between 300-400 micrometres and the remaining 4(10%) had a value more than 700 micrometres. The evaluation of the retina of the subjects, with a +20 Dioptre lens using an indirect ophthalmoscope, who were to undergo the intravitreal Ranibizumab injection showed that 14(35%) patients had severe non-proliferative diabetic retinopathy, 13(32.5%) had moderate non-proliferative diabetic retinopathy, 9(22.5%) had mild to moderate proliferative diabetic retinopathy, 3(7.5%) had mild non-proliferative diabetic retinopathy and 1(2.5%) patient had high risk proliferative diabetic retinopathy.

The following **Table 1** and **Figure 1** shows the descriptive statistics regarding the scores for the overall vision-related quality of life during the period of study.

Analysis of variance (ANOVA) for repeated measures

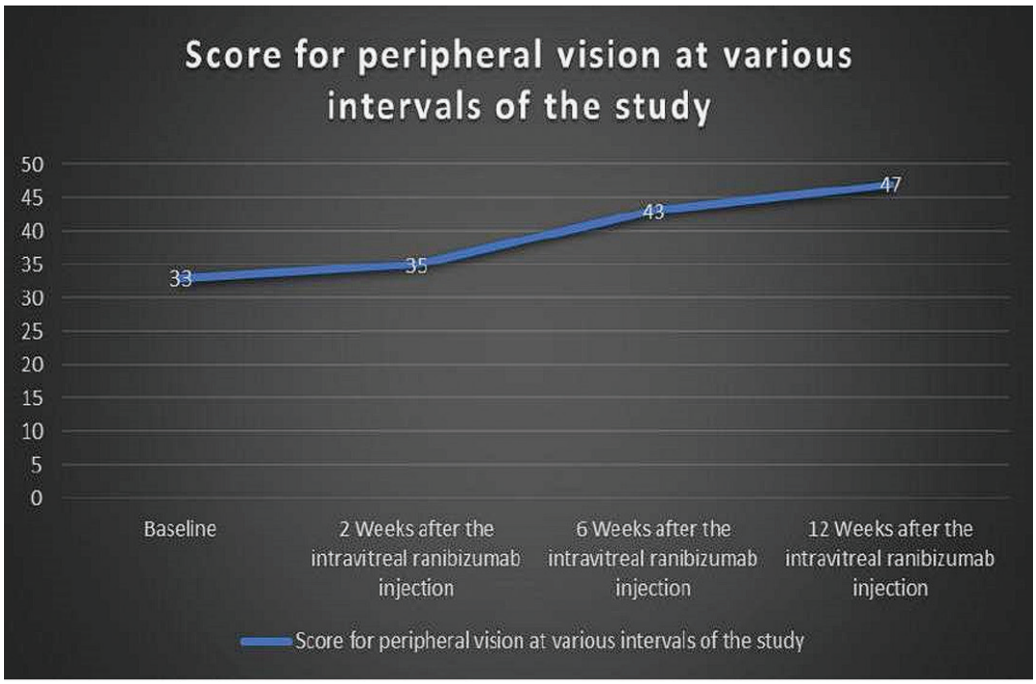

Figure 11. **Changes in the score for peripheral vision during the period of study**

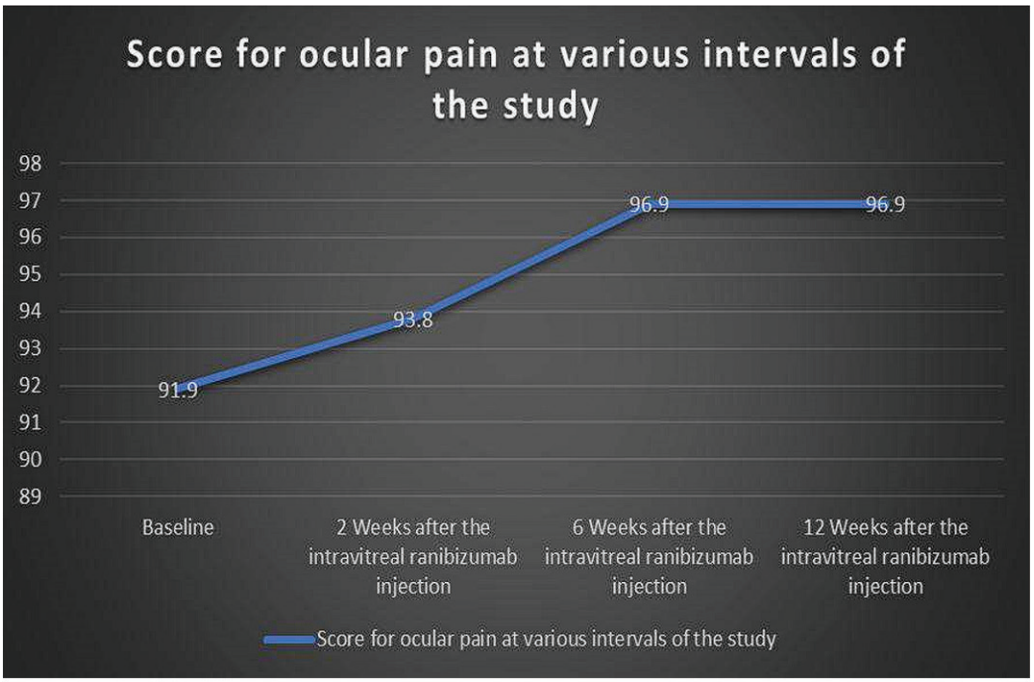

Figure 12. **Changes in the score for ocular pain during the period of study**

was utilized for the statistical analysis and the adjustment used for multiple comparisons was Sidak. The p value was kept significant at 0.05. The following tables **(Table 2 and Table 3)** depict the results of the statistical analysis.

The following figures **(Figures 2-12)** shows the descriptive statistics regarding the scores for various subdomains of vision related quality of life during the period of study.

DISCUSSION

The main objective of this study was to assess the changes in the overall vision-related quality of life among patients with diabetic macular edema who were receiving intravitreal ranibizumab injections at a tertiary eye care hospital in Trivandrum.

The mean score for the overall vision-related quality of life in the study was found to be 38.2±9.1 at baseline

which improved to 41.0±10.3 at 2 weeks, 48.2±14.0 at 6 weeks and 51.1±15.2 at 12 weeks following the single injection of intravitreal ranibizumab. Statistical analysis was done using ANOVA for repeated measures and the p-value was kept significant at a value less than 0.05. The p-value obtained on statistical analysis was 0.000 and this showed that there was a statistically significant improvement in the overall vision-related quality of life among patients with diabetic macular edema receiving intravitreal ranibizumab injection. The result obtained in this study was similar to other studies done elsewhere such as the study done by Elif Betul et al[9] where at 6 months following the intravitreal ranibizumab injection, they found the improvement in the overall vision-related quality of life scores was significantly higher for the group that received intravitreal ranibizumab than the group that received the focal or grid laser. Also, the RIDE and RISE studies showed improvement in the overall vision-related quality of life irrespective of whether 0.3mg or 0.5mg ranibizumab was used.[10]

The secondary objective of the study was to analyse the changes in the various subdomains that contribute to vision related quality of life viz general vision, general health, distance vision, near vision, peripheral vision, colour vision, ocular pain, social function, role difficulties, mental health and dependency.

All subdomains of vision related quality of life showed a statistically significant improvement except the score for general health.

The baseline score for general health was 27.5±7.6, which at 2 weeks improved to 28.8±9.0, at 6 weeks was 29.4±9.6 and at 12 weeks was 30.0±11.6. However, statistical analysis showed the improvement in scores was not statistically significant and the p-value was 0.062. In the study conducted by Elif Betul et al,[9] the baseline score for general health was 48.6 and in 6th month following intravitreal ranibizumab it was 51. The p-value in their study was 0.22. Their study also did not get any statistically significant improvements in the general health subscale following the intravitreal ranibizumab injection.

CONCLUSION

The study was undertaken to analyse what changes were being brought about in the vision-related quality of life of individuals with diabetic macular edema who were receiving intravitreal ranibizumab injections. Diabetic macular edema has been identified as the most common cause of defective vision in patients with diabetic retinopathy. Many modalities of treating the same have been identified, of which the current mainstay treatment is pharmacotherapy using intravitreal anti-VEGF agents. The study showed that the overall vision-related quality of life showed a statistically significant improvement following an injection of intravitreal ranibizumab thereby helping in decreasing the burden of the disease. This shows that the intravitreal ranibizumab injection not only brings about anatomical improvements in the thickness of the macula but also translates into better vision-related quality of life for the patients receiving the intravitreal ranibizumab injection.

The various subdomains of vision-related quality of life were also analysed in the study. All subdomains of vision-related quality of life except general health viz general vision, distance vision, near vision, peripheral vision, ocular pain, colour vision, social function, role difficulties, mental health and dependency also showed statistically significant improvement in scores during the period of study.

The general health subscale did not show any statistically significant improvement following the intravitreal ranibizumab injection in this study.

No studies were done in Kerala that analysed the qualitative changes brought about by the intravitreal ranibizumab injection in patients with diabetic macular edema and this study shows that similar to studies done elsewhere, intravitreal ranibizumab can bring about an improvement in the vision-related quality of life of individuals with diabetic macular edema.

END NOTE

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Conflict of Interest: None declared

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Body Surface Topography and Radiology in Adolescent Idiopathic Scoliosis (AIS): Is there a Correlation? : A Pilot Study Based on Clinical Photographs

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ABSTRACT

Background: Cosmesis is of paramount importance in adolescent idiopathic scoliosis. Conventional evaluation of scoliotic deformity is based on radiological parameters like Cobbs angle. However aesthetic parameters are the ones that are readily perceived by the patients, peers and parents. Patient Reported Outcome measures and self-image perception of these patients may not be dependent on radiological parameters alone. So there is a need to know whether there is a correlation between body surface topography and radiology in these patients.

Material and Methods: Cross-sectional, pilot study of 15 patients (10 thoracolumbar/lumbar and 5 thoracic curves. Clinical evaluation was done via Spinal Appearance Questionnaire, SRS 22 r questionnaire. Surgeon evaluation is done via the POTSI app and TRACES index. Body Surface Metrics were also calculated. Radiological parameters studied were Cobbs angle, apex deviation, Clavicle angle, Coracoid angle First Rib angle, T1 tilt and C7 Plumbline deviation.

Results

- POTSI had a strong correlation between SAQ (r value 0.735, p value 0.002).
- SAQ has a moderate correlation with cobbs angle of main curve (r value 0.519 p,0.047) and secondary curve (r value 0.539 p 0.038)
- SAQ had a moderate inverse correlation with SRS22r (r value-0.560, p =0.030).
- LWA-RWA has a moderate inverse correlation with Main Cobbs angle (0.551 p 0.033). WHA has a moderate correlation with Cobbs angle of main curve (0.545, p=0.036)
- However there was also a moderate correlation between apex deviation of the lumbosacral fractional curve with the WHA (0.567, p value 0.035).
- AHA has a moderate correlation between clavicle angle (0.523, p value 0.046) and mild correlation with FRA (0.390) and coracoid angle (0.393)

SHA had no significant correlation between any of the parameters studied.

Conclusion: Trunk aesthetic parameters should be given due importance in assessing children with Adolescent idiopathic Scoliosis. They have only moderate correlation with Cobbs angle. However, patients and surgeons perception of deformity has strong correlation. Studies on larger cohorts will be useful to validate the findings of the present study. Shoulder balance continues to be an enigma that requires further studies

Keywords: Surface Topography, Adolescent Idiopathic Scoliosis, POTSI, TRACES, SAQ, Shoulder Balance

*See End Note for complete author details

BACKGROUND AND RATIONALE

Scoliosis is defined as a lateral curvature of the spine more than 10 degrees.[1] (Scoliosis Research Society SRS definition). Though there are various etiologies of scoliosis, those that occur during the adolescent growth spurt are by far the most common. Scoliosis is a three-dimensional deformity with deformity occurring in coronal, transverse and sagittal plane. Traditionally, the measurement of AIS is quantified

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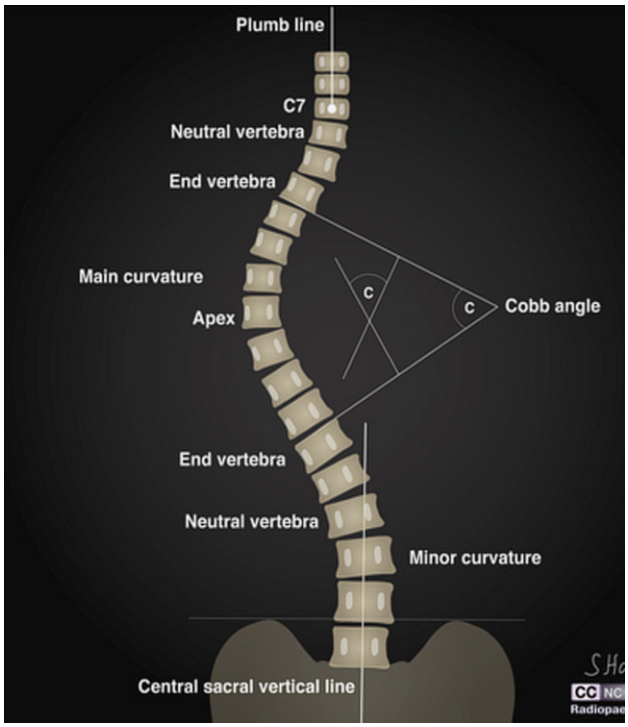


Figure 1. **Demonstrates the method of measurement of Cobbs angle**

using a radiological parameter known as Cobb's angle **(Figure 1)**.

However, Cobbs angle measures only one component of the 3D deformity. It is only a shadow of the two limit vertebra according to Kotwicki.[2]

However Cobbs angle has a dogmatic halo in measuring the degree of scoliosis and also assessing progression as most orthopedic surgeons are familiar with this measurement.

However, patients with AIS are quite concerned about their cosmesis and Cobb's measurement seems only to be a surrogate measure of their own physical assessment. Authors have noticed that the following features are very important for a patient in their own assessment of their body shape. They are symmetry of shoulders, symmetry of axillary folds, symmetry of waist folds, scapular prominence, pelvic symmetry, limb length equality and neck tilt. This applies well to parents perspective of their childs body shape as well.

The cosmetic improvement of the trunk after any treatment for scoliosis is the pinnacle that any child undergoing such treatments will expect. The symmetry of the trunk is what is seen and applauded by the patients, parents and peers. Sometimes, the surgeon is faced with the blooper situation where a good radiological outcome may not guarantee the same cosmetic outcome. Obviously, this would mean that other radiological parameters have an interplay in achieving a satisfactory cosmetic outcome.

The goal of any surgical correction for scoliosis is three fold 1. to prevent worsening and to correct the deformity as much as possible

- with minimal morbidities (Safety)

- to fuse shortest possible
  - preserving maximum mobility (Function)
- to achieved a well balanced and less deformed spine (Cosmetic).

In recent years, many authors from Asia[3-5] have emphasised on the need for achieving spinal balancing rather than a pure radiological correction. A balanced spine would mean a symmetric shoulder, axillary fold , waist and pelvis. Many of us have also observed that often two equal and opposite curves cancel out each other and achieves a certain symmetry – traditionally called as compensated deformity.

Various Spinal topographic measures[6] are in vogue. However, all of them are limited in their clinical use by inter and intraobserver errors due to the fact that landmarks used for measurement suffer from lack of concurrence. However, these are the only quantifiable markers of aesthesis and it would be prudent to know whether there exists a correlation between these aesthetic parameters and radiological parameters. One also need to assess the cosmesis from patients perspective and Patient Reported Outcomes. (Spinal Appearance Questionnaire[7] and SRS 22r.[8] Also of importance is Surgeons perspective in the assessment of cosmesis (TRACE[9] and POTSI[10]). A good correlation between patient and surgeons perspective will guarantee satisfaction for both parties at the end of long and arduous course of treatment.

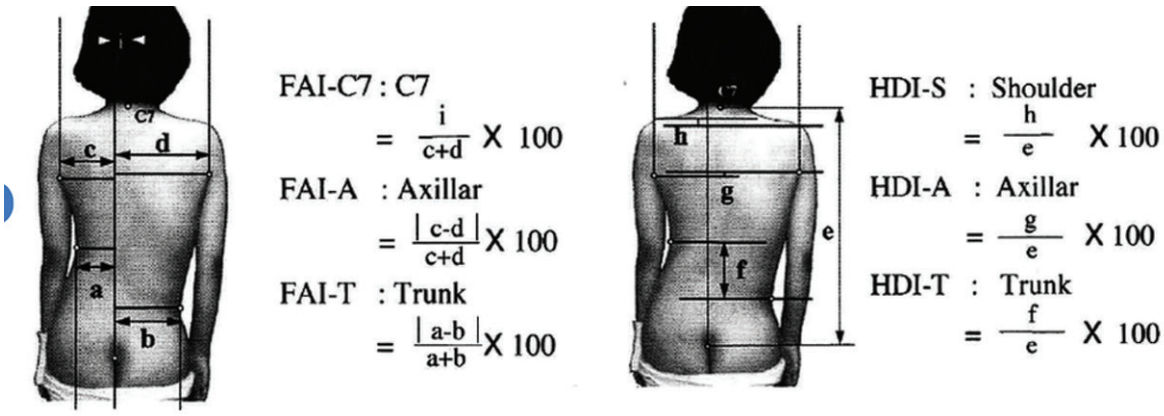
Hence we conducted a pilot study to look at their correlation.

MATERIALS AND METHODS

Study design: Cross sectional , Pilot Study.

Inclusion criteria: Patients with adolescent idiopathic scoliosis between 10 to 20 years. Non idiopathic causes were excluded.

15 patients with AIS who visited the Outpatient at Department of Orthopedics, GMC, Thiruvananthapuram were chosen. All patients were photographed from the back as per standard protocol. All patients filled the Appearance part of SAQ, SRS 22 r,. TRACES was calculated by two investigators who were adequatedly trained, FAI, HAI and POTSI index was calculated using software POTSI app using digital photographs. Standard technique of taking Xrays were followed and following



POsterior Trunk Symmetry Index (POTSI) after [56,61]. The POsterior Trunk Symmetry Index (POTSI) is computed as a sum of the 6 indices: POTSI = (FAI-C7 + FAI-A + FAI-T) + (HDI-S + HDI-A + HDI-T).

Figure 2. **Showing how POTSI index is calculated**

radiological parameters were recorded—cobbs angle, apical vertebra translation, clavicle angle, first rib angle, Coracoid angle and C7 plumbline deviation.

Spinal Appearance Questionnaire: SAQ[7]

The SAQ is a 33-question assessment broken down into different sections. There are 11 pictorial questions the individual identifies what most looks like themselves. This is the Appearance part of the questionnaire. Questions 13 through 32 (expectation part) are rating questions where the individual rates each item out of 5 ratings these include: not true, a little true, somewhat true, Fairly true, or very true. We have considered only the questions relevant to appearance from the back in this study.

SRS 22r[8] is a widely used tool for assessing outcome in AIS. It is a PROM.

The SRS-22r contains 22 questions in five domains:

- function (5 items),
- pain (5 items),
- self-image (5 items),
- mental health (5 items),
- satisfaction with management (2 items). Each item contains a 5-level Likert scale ranging from worst (1 point) to best (5 point); results are expressed as the mean score of each domain, and total score of the scale. The functional domain of SRS 22r questionnaire will be used to assess the change in function

A higher total score indicates a higher level of quality of life. In this study, we have taken into account the self image, mental status and total SRS score.

TRACE[9] is based on four sub-scales: shoulders, scapulae and waist (which were already present in the AI), and the hemi-thorax. Shoulder ranged for 0-3, Waist from 0-4, scapula from 0-2, hemithorax from 0-2 thus forming a maximum total score of 12.

POTSI Index[10]

The Potsi Index is the sum of two variables Height Asymmetry Index (HAI) and Frontal Asymmetry Index (FAI). Height asymmetry indexes are obtained as the sum of height differences of the shoulders, axillary folds, and waist creases, and it is normalized with the division of its value by the vertical distance from the C7 vertebra to the baseline of the gluteal cleft **(Figure 2).**

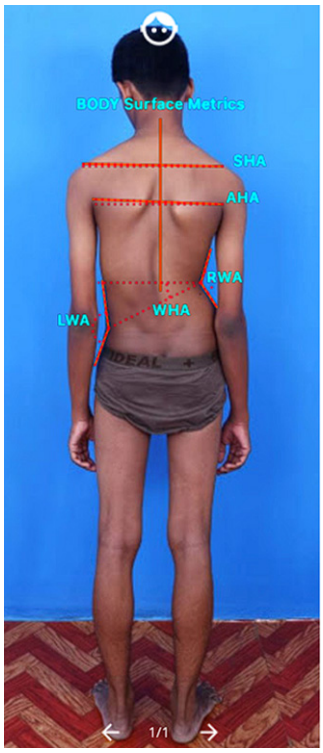


Figure 3. **Points taken to calculate the Body Surface Metrics**

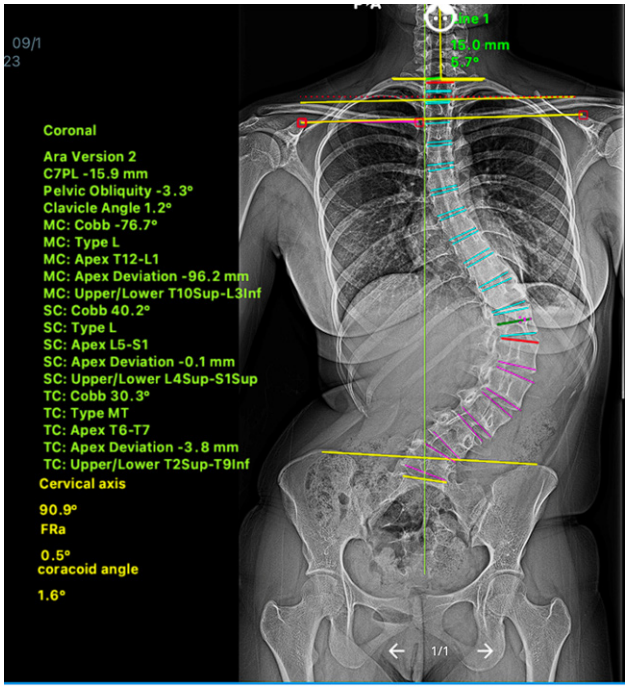


Figure 4. **Calculation of various radiological parameters**

The POTSI index will be calculated by the POTSI app from the clinical photographs of the patient.

Body Surface metrix is calculated from a digital photograph from the back. The following measures are taken LWA, RWA, WHA, AHA, SHA **(Figure 3).**

Radiological outcome

Is assessed by full length erect radiographs of spine with posteroanterior views and lateral views.

Xray protocol

- Whole spine Scanogram extended from (but not limited to) bilateral External Auditory Meatus to bilateral femoral heads. Anteroposterior and lateral.
- The patient will be positioned at a distance of 72 inches from the X-ray tube with the central ray targeting at the T6–T7 area.
- X-Rays will be taken with patient in standing position with neck neutral flexed and both the arms in 90* flexion, elbows and wrists flexed such that the fingers touch the ipsilateral shoulders.
- Preoperative radiographs include Supine right side bending and left side bending anteroposterior x-rays to assess curve flexibility.
- No fulcrum x-rays are assessed. The typical radiographic exposure factors were 25 mAs and 100 kVp.
- **Figure 4** showing representative image of how the radiological parameters were calculated.

How to take Clinical photographs for the study?[11]

Figure 5. **Method to take the clinical photograph**

Figure 5

- Wears underpants for photo from back
- Stands against a blank wall
- Arm by the sides, hair put-up
- Shot with mobile camera from 2 m centering inter-scapular area

All data will be entered in an excel file. Following correlations were assessed

1. POTSI vs cobbs angle
2. POTSI vs SAQappearance score
3. POTSI vs Srs 22
4. POTSI vs TRACE
5. POTSI VS APEX DEVIATION OF MC,SC,TC
6. SAQ VS COBBS ANGLE
7. SAQ VS APEX DEVIATION
8. SAQ VS SRS22
9. SAQ VS TRACE
10. LWA-RWA VS COBBS
11. WHA vs cobb's, Apex deviation
12. AHA vs cobbs, Apex deviation
13. SHA Vs cobbs , Apex deviation
14. WHA vs Pelvic obliquity
15. SHA vs coracoid angle
16. SHA Vs FRA
17. SHA vs clavicle angle

Table 1. Descriptive

	Mean±SD
POTSI	35.17±13.74
SRS22-Self image	2.85±0.44
SRS22-Mental health	3.32±0.66
SRS22-Total	3.54±0.47
SAQ Appearance score	2.85±0.61
Trace score	6.4±1.76
Cobb Angle (º)- MC	58.19±12.55
Apex Deviation (mm)- MC	92.77±47.61
Cobb Angle (º)- SC	34.65±11.47
Apex Deviation (mm)- SC	17.09±12.27
Cobb Angle (º)- TC	20.71±6.86
Apex Deviation (mm)- TC	9.35±11.39
LWA-RWA	20.85±29.03
WHA (º)	8.69±6.63
AHA (º)	3.09±3.3
SHA (º)	1.67±1.73
Pelvic Obliquity (º)	3.39±2.16
Corocoid Angle (º)	1.83±1.62
First Rib Angle (º)	2.78±3.75
Clavicle angle (º)	1.85±1.97
T1 TILT (º)	5.91±7.49
C7PL(mm)	28.95±12.77

Table 2. Correlation between POTSI and other outcome measures

	POTSI r value	95% Confidence Intervals		P value
		Lower	Upper	
SAQ Appearance score	.735**	0.358	0.906	0.002
SRS22-Self image	-0.359	-0.736	0.188	0.189
SRS22-Mental health	-0.246	-0.673	0.305	0.377
SRS22-Total	-0.425	-0.770	0.112	0.114
Trace score	0.428	-0.108	0.771	0.111
Cobb Angle (º)- MC	0.299	-0.251	0.704	0.278
Apex Deviation (mm)- MC	0.014	-0.502	0.522	0.961
Cobb Angle (º)- SC	0.170	-0.375	0.628	0.544
Apex Deviation (mm)- SC	-0.388	-0.751	0.155	0.153
Cobb Angle (º)- TC	-0.203	-0.662	0.367	0.486
Apex Deviation (mm)- TC	0.297	-0.278	0.715	0.303

18. SHA vs T1 tilt
19. AHA vs coracoid angle
20. AHA Vs FRA
21. AHA vs clavicle angle
22. AHA vs T1 tilt

The results are shown below in the following **tables (Tables 1-7).** There were 11 females and 4 males in the cohort. 5 cases were thoracic scoliosis and 10 were thoracolumbar/lumbar scoliosis.

Table 3. Correlation between SAQ score and other outcome measures

	SAQ Appearance score r value	95% Confidence Intervals		P value
		Lower	Upper	
Cobb Angle (º)- MC	.519*	0.009	0.815	0.047
Apex Deviation (mm)- MC	0.059	-0.467	0.554	0.835
Cobb Angle (º)- SC	.539*	0.037	0.824	0.038
Apex Deviation (mm)- SC	-0.001	-0.513	0.511	0.996
Cobb Angle (º)- TC	-0.096	-0.596	0.458	0.745
Apex Deviation (mm)- TC	0.267	-0.307	0.699	0.355
SRS22- Self image	-0.262	-0.683	0.289	0.346
SRS22- Mental health	-0.410	-0.762	0.130	0.129
SRS22-Total	-.560*	-0.833	-0.067	0.030
Trace score	0.491	-0.029	0.802	0.063

Table 4. Correlation between LWA-RWA and other outcome measures

	LWA-RWA r value	95% Confidence Intervals		P value
		Lower	Upper	
Cobb Angle (º)- MC	.551*	0.054	0.829	0.033
Apex Deviation (mm)- MC	-0.155	-0.618	0.388	0.581
Cobb Angle (º)- SC	0.327	-0.223	0.719	0.235
Apex Deviation (mm)- SC	-0.344	-0.728	0.204	0.209
Cobb Angle (º)- TC	0.139	-0.423	0.623	0.637
Apex Deviation (mm)- TC	-0.215	-0.669	0.356	0.461

Table 5. Correlation between WHA and other outcome measures

	WHA (º) r value	95% Confidence Intervals		P value
		Lower	Upper	
Cobb Angle (º)- MC	.545*	0.045	0.826	0.036
Apex Deviation (mm)- MC	0.411	-0.128	0.763	0.128
Cobb Angle (º)- SC	.523*	0.015	0.817	0.045
Apex Deviation (mm)- SC	-0.068	-0.561	0.461	0.811
Cobb Angle (º)- TC	-0.255	-0.692	0.319	0.379
Apex Deviation (mm)- TC	.567*	0.052	0.844	0.035
Pelvic Obliquity (º)	-0.101	-0.583	0.433	0.719

Figures 6 to figures 9 show representative cases and their radiology. (case numbers 11,12,13,14 in the series. For their individual parameters refer Appendix: supplementary material - data for pilot study.

RESULTS

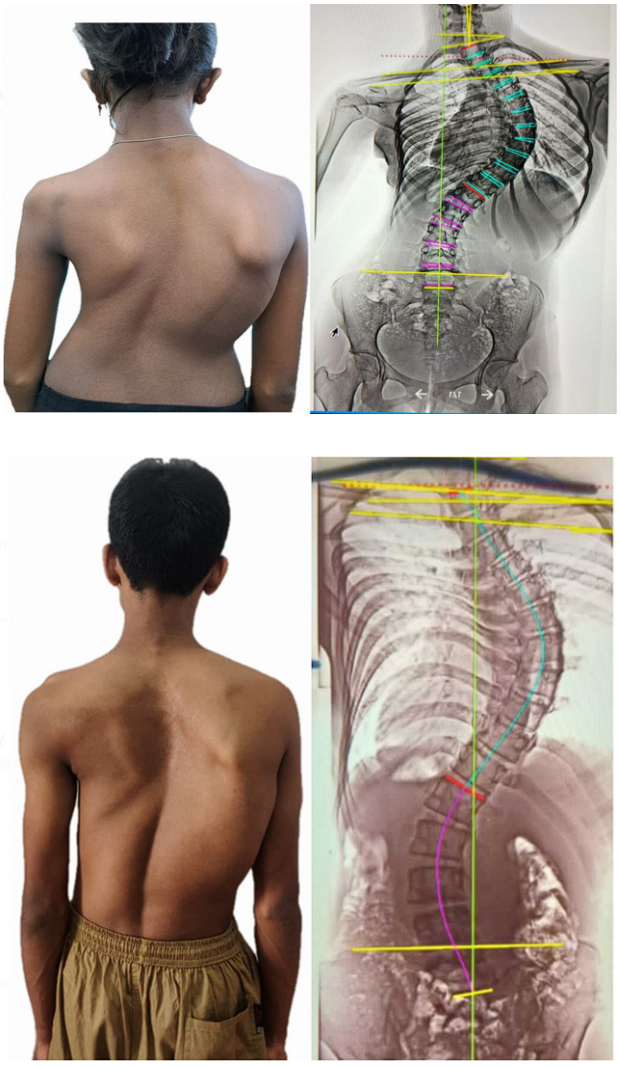
- POTSI had a strong correlation between SAQ (r value 0.735, p value 0.002).
- SAQ has a moderate correlation with cobbs angle of main curve (r value 0.519 p,0.047) and secondary curve (r value 0.539 p 0.038).

Table 6. Correlation between AHA and other outcome measures

	AHA (º) r value	95% Confidence Intervals		P value
		Lower	Upper	
Cobb Angle (º)- MC	0.215	-0.334	0.655	0.442
Apex Deviation (mm)- MC	-0.170	-0.628	0.375	0.545
Cobb Angle (º)- SC	0.302	-0.248	0.705	0.273
Apex Deviation (mm)- SC	-0.254	-0.678	0.296	0.360
Cobb Angle (º)- TC	-0.234	-0.680	0.339	0.421
Apex Deviation (mm)- TC	0.068	-0.480	0.578	0.818
Corocoid Angle (º)	0.393	-0.149	0.754	0.147
First Rib Angle (º)	0.390	-0.153	0.752	0.151
Clavicle angle (º)	.523*	0.014	0.816	0.046
T1 TILT (º)	0.118	-0.420	0.594	0.675

Table 7. Correlation between SHA and other outcome measures

	SHA (º) r value	95% Confidence Intervals		P value
		Lower	Upper	
Cobb Angle (º)- MC	0.250	-0.301	0.675	0.370
Apex Deviation (mm)- MC	0.065	-0.463	0.559	0.818
Cobb Angle (º)- SC	0.124	-0.414	0.598	0.659
Apex Deviation (mm)- SC	-0.191	-0.641	0.356	0.495
Cobb Angle (º)- TC	-0.106	-0.603	0.450	0.718
Apex Deviation (mm)- TC	0.142	-0.420	0.625	0.628
Corocoid Angle (º)	0.201	-0.347	0.647	0.472
First Rib Angle (º)	0.382	-0.162	0.748	0.160
Clavicle angle (º)	0.330	-0.219	0.720	0.230
T1 TILT (º)	0.133	-0.407	0.604	0.636



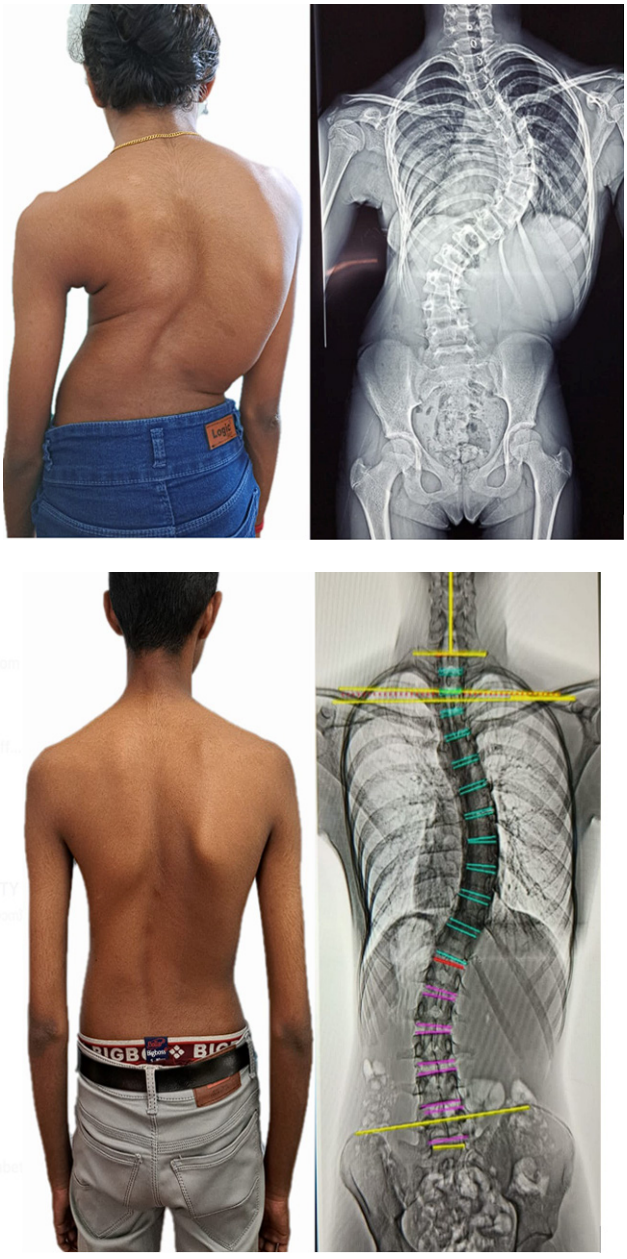


Figure 6-9. **Showing representative clinical photos and their x-rays**

- SAQ had a moderate inverse correlation with SRS22r (r value-0.560, p =0.030).
- LWA-RWA has a moderate inverse correlation with Main Cobbs angle (0.551 p 0.033). WHA has a moderate correlation with Cobbs angle of main curve (0.545, p=0.036)
- However there was also a moderate correlation between apex deviation of the lumbosacral fractional curve with the WHA (0.567, p value 0.035).
- AHA has a moderate correlation between clavicle angle (0.523, p value 0.046) and mild correlation with FRA (0.390) and coracoid angle (0.393)
- SHA had no significant correlation between any of the parameters studied.

DISCUSSION

Patients with Adolescent Idiopathic Scoliosis seek treatment largely for their body disfigurement. However radiological parameters are given great importance conventionally. However, there are many body topographic parameters that are very important for the patients in their own self assessment of body image. The concept of spinal balancing aims to provide the patient with the best possible aesthetic outcome and not just rely on radiological parameters alone. This pilot study was undertaken to assess the feasibility of a larger study assessing patients aesthesis, function and radiological improvement following corrective surgery for scoliosis. The study will assess many factors like shoulder balance, pelvic symmetry, rib coplanarity, neck tilt etc which are of paramount importance to the patients undergoing surgical correction. The pilot study shows that patients perception of deformity (SAQ) and surgeons perception (POTSI) has a strong correlation. However patients perception of deformity and PROM like SRS 22r has only a moderate correlation with radiological Cobbs angle. This has been emphasised by many authors in the past.[6,2] Extent of correction of Main Curve and its effect on subsidiary curves should be carefully taken into account while planning surgical correction to achieve a good spinal balance. However in lumbar/thoracolumbar curves, the lumbosacral fractional curve is important in achieving a symmetric pelvis and waist. However, surgeon needs to balance between losing of flexibility at the expense of a better cosmetic correction.

Achieving a balanced shoulder is a critical component of any AIS surgery. However, till date there are no specific parameters that can be used intraoperatively with high success rate in achieving this goal. This may be because shoulder is not directly connected to the spine though it is an important component in the perception of deformity. Should balance is contributed by spine, rib cage and shoulder girdle. In this pilot study also, no significant correlation existed between any of the parameters studied and achievement of shoulder balance. However, due to small number of thoracic curves in the pilot study, it is not prudent to make a passing conclusion. Also axillary height has a moderate correlation with clavicle angle. This would imply a role in adaptive changes in shoulder suspensory complex in patients with scoliotic deformities.

LIMITATIONS OF THE STUDY

Our study is only a pilot study in 15 preoperative patients. We have not included the effect of neck tilt or medial shoulder balance in this study. Our pilot study is also limited by fewer number of thoracic curves in the study population. However, the study gives a rough idea of how the larger study with more number of cases will span out.

CONCLUSION

Trunk aesthetic parameters should be given due importance in assessing children with Adolescent idiopathic Scoliosis. They have only moderate correlation with Cobbs angle. However , patients and surgeons perception of deformity has strong correlation. Studies on larger cohort will be useful to validate the findings of the present study. Shoulder balance still continues to be an enigma which requires further studies.

END NOTE

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List of Abbreviations

SAQ	Spinal Appearance Questionnaire	WHA	Waist Height Angle
SRS	Scoliosis Research Society	AHA	Axillary Height angle
FAI	Frontal Asymmetry Index	SHA	Shoulder Height Angle
HAI	Height Asymmetry Index	FRA	First Rib angle
POTSI	Posterior Trunk Symmetry Index	MC	Main curve
TRACES	Trunk Aesthetic Clinical Evaluation	SC	Secondary Curve
LWA	Left Waist Angle	TC	Tertiary Curve
RWA	Right Waist Angle		600

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Conflict of Interest: None declared

Appendix: Data Chart Pilot study

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Influence of Risk Perception and Physician Recommendations on the Adoption of Examinations for Early Detection of Breast, Cervical, Oral and Colon Cancers in Rural Thiruvananthapuram

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ABSTRACT

Early cancer detection is crucial in reducing mortality rates, especially in rural areas with limited healthcare access. This cross-sectional study investigates how risk perception and physician recommendations influence the adoption of screening practices for breast, cervical, oral, and colon cancers among 160 women aged 30-65 years in rural Thiruvananthapuram. The findings show that a significant proportion of participants perceived their cancer risk as low, which correlates with lower screening rates. Physician recommendations played a key role in motivating patients to undergo screening, but many did not receive such advice. This highlights the need for enhanced communication between healthcare providers and patients to improve risk awareness and increase cancer screening uptake.

Keywords: Risk Perception, Physicians Recommendation, Early Detection, Breast Cancer, Cervical Cancer, Oral Cancer, Colon Cancer

*See End Note for complete author details

INTRODUCTION

Cancer remains one of the leading causes of death worldwide,[1] with late-stage diagnoses significantly contributing to high mortality rates.[2,3] In India, cancer detection often occurs at advanced stages, particularly in rural areas where access to healthcare facilities and awareness about preventive measures are limited.[4] Early detection of cancers such as breast, cervical, oral, and colon cancers can greatly improve the chances of successful treatment and survival.[4]

"Risk perception plays a pivotal role in individuals' decisions to undergo cancer screening.[4] Many rural residents may underestimate their cancer risk due to a lack of knowledge or cultural beliefs, leading to low participation in screening programs. Physician recommendations are crucial in motivating patients to engage in cancer screening, particularly in low-literacy settings. However, when physicians fail to provide these recommendations, opportunities for early detection are missed.[5]

This study aims to explore the influence of risk perception and physician recommendations on the adoption of cancer screening practices in rural Thiruvananthapuram. By understanding the barriers to screening, we can develop targeted interventions to improve early detection rates.

MATERIALS AND METHODS

This cross-sectional study aimed to assess factors influencing the adoption of cancer screening among 160 female patients aged 30-65 years attending outpatient departments in rural Thiruvananthapuram. Participants were selected from four government-run primary care centers and one private facility, focusing on their cancer risk perception and physician recom-

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mendations. This age group was specifically chosen as the Priority Screening Group due to their higher risk of developing breast, cervical, oral, and colon cancers.

Ethical approval for the study was obtained from the Institutional Ethics Committee of Sree Gokulam Medical College. All participants were interviewed after obtaining written informed consent, ensuring that they were fully informed about the study's purpose and procedures before participation.

Inclusion Criteria:

Patients aged 30-65 years who had visited the same healthcare provider within the past six months were included in the study. Those who had undergone cancer screening within the previous six months were excluded to focus on individuals who were not already engaged in screening.

Data Collection:

Data were collected using a self-administered questionnaire that gathered information on demographic characteristics, health history, perceptions of cancer risk, and whether participants had received cancer screening recommendations from their healthcare providers. Barriers to screening were also explored, such as a lack of awareness about the need for screening, perceived low risk, fear of the disease, and logistical challenges.

Study Variables:

Study variables included demographic characteristics such as age, educational status, self-perceived risk of cancer, physician recommendations for cancer screening and the actual uptake of screening tests for diabetes, hypertension, breast, cervical, oral, and colon cancers. Barriers to screening were also explored, with participants identifying factors such as a lack of awareness about the need for screening, perceived low risk of developing cancer, fear of the disease, lack of nearby screening facilities, and personal factors like embarrassment or indifference.

Statistical Analysis:

Descriptive statistics, including frequencies and percentages, were used to summarize the socio-demographic characteristics and key study variables.

RESULTS

The study included 160 participants aged 30-65 years from rural Thiruvananthapuram. The socio-demographic characteristics, cancer risk perception, physician recommendations, and cancer screening practices are summarized below.

Socio-demographic Characteristics and Cancer Risk Perception

Table 1 presents the socio-demographic characteristics and self-perceived likelihood of developing cancer among participants. The majority (51.25%) had completed high school, and a significant proportion (53.12%) perceived their cancer risk as "very low" or "somewhat low."

Table 1. Socio-demographic Characteristics and Cancer Risk Perception

Priority Screening Group (Aged 30–65) (n=160)	
Age Group	
30-45	40%
46-65	60%
Educational Status	
Illiterate	3.75%
Literate	17.5%
High School	51.25%
Graduate	23.13%
Postgraduate	4.37%
Self-perceived Likelihood of Cancer	
Very Low	53.12%
Somewhat Low	14.3%
Moderate	21.8%
Somewhat High	7.5%
Very High	1.8%
Could early detection help outcome?	
Yes	84.3%

Physician Recommendations and Screening Practices

Physician recommendations were a key factor in determining screening uptake. Among participants, 56.25% reported not receiving any recommendation for cancer screening from their physician. However, 84.5% of those who received a recommendation proceeded with screening, underscoring the importance of physician involvement.

The rates of physician recommendations and subsequent screenings for diabetes and hypertension were notably higher than those for cancer, particularly for oral and colon cancers, where uptake was significantly lower **(Figure 1).** This discrepancy highlights the need for physicians to prioritize cancer screening recommendations in routine consultations. If physicians place the same emphasis on cancer screening as they do for other non-communicable diseases like diabetes

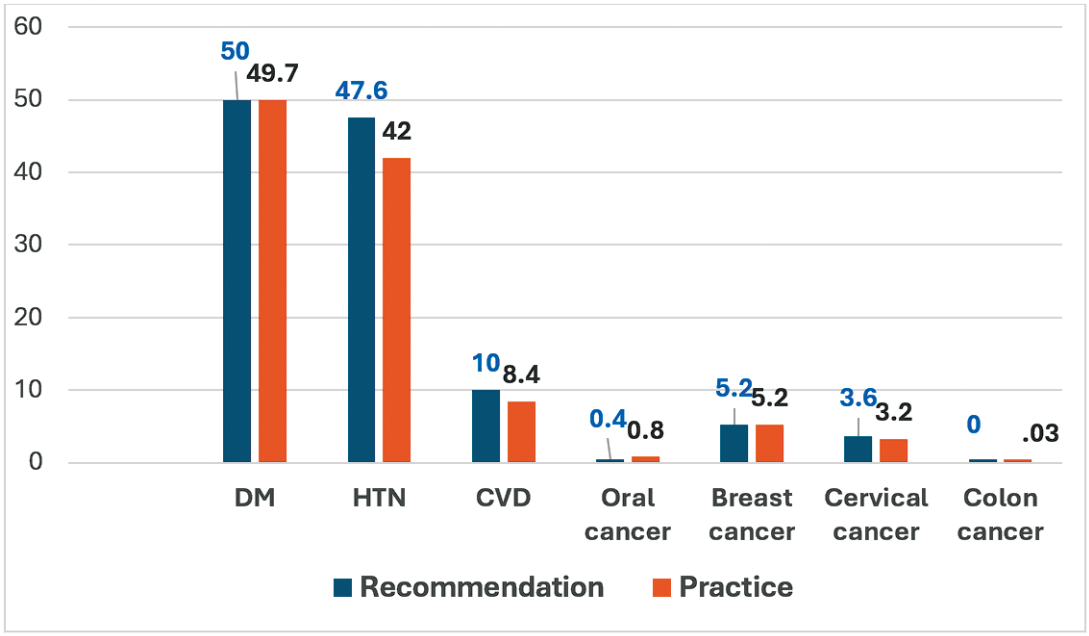

Figure 1. **Physicians' Recommendation and screening practices of NCDs**

and hypertension, it could significantly improve cancer screening rates and lead to earlier detection and better outcomes.

Barriers to Cancer Screening

Several barriers contributed to the low uptake of cancer screening **(Table 2).** The most common were lack of knowledge (38.75%) and fear of disease (10.62%).

Table 2. Barriers to Cancer Screening

Priority Screening Group (Aged 30–65) (n=160)	
No recommendation from physician	56.25%
Didn't know that screening was needed	38.75%
Thought I would never get the disease	10%
Fear of disease	10.62%
No screening facilities nearby	3.75%
Not going to worry until it happens	6.25%
Embarrassment	2.5%
Other	1.87%

The study also assessed the likelihood of participants undergoing regular cancer screening if recommended. Those who perceived their risk as low were less likely to engage in regular screening, even if they received a physician's recommendation. Conversely, participants with a higher perception of risk were more inclined to adhere to screening protocols.

DISCUSSION

The results of this study highlight the critical role of physician recommendations and risk perception in cancer screening uptake among women in rural Thiruvananthapuram.[6] A significant portion of participants underestimated their risk of developing cancer, which contributed to low screening rates. This finding is consistent with previous studies showing that individuals with low perceived risk are less likely to participate in screening programs.[7,8] Physician recommendations emerged as a powerful motivator for screening, with 84.5% of those who received a recommendation proceeding with screening. However, over half of the participants reported not receiving such recommendations, revealing a gap in clinical practice that needs to be addressed.

Impact of Perceived Cancer Risk on Screening Uptake

The results show that over 67% of the participants perceived their risk of developing cancer as "very low" or "somewhat low." This low risk perception is a key barrier to the adoption of screening practices, as those who perceived themselves as being at low risk were less likely to undergo regular screening, even if recommended by a physician. Previous studies have shown similar patterns, where lower perceived cancer risk is associated with reduced participation in screening programs.[7] Addressing this gap in awareness is crucial, as improving individuals' understanding of their actual cancer risk could help motivate them to adopt early detection practices.

Barriers to Cancer Screening

Several barriers to screening were identified in this study,

with lack of knowledge (38.75%) and fear of disease (10.62%) being the most commonly cited reasons. These findings are consistent with research conducted in similar low-resource settings, which found that lack of awareness about the importance of early detection is a major barrier to cancer screening.[8] Additionally, psychological barriers such as fear of diagnosis or treatment contribute significantly to patients avoiding screening, even when facilities are available. A small proportion of the participants (3.75%) also cited logistical issues, such as the absence of nearby screening facilities, which is a common challenge in rural areas.[9]

Role of Physician Recommendations

Physician recommendations emerged as a strong motivator for cancer screening, as evidenced by the fact that 84.5% of those who received a recommendation proceeded with the screening. This finding aligns with existing literature, which indicates that physician-initiated conversations about cancer screening significantly increase screening rates, particularly in populations with low health literacy.[5] However, the study also revealed that a large proportion of participants (56.25%) did not receive any recommendation for cancer screening, suggesting that opportunities for early detection may be missed during routine medical visits. Training healthcare providers to actively discuss cancer risk and screening options with their patients, especially in rural settings, could significantly enhance cancer screening rates.[3]

The Snehita Risk Calculator, designed for breast cancer risk assessment, is an effective tool that physicians can use to enhance perceived cancer risk among women.[10] By incorporating this tool into routine consultations, healthcare providers can raise awareness and motivate women to undergo early detection tests, such as Clinical Breast Examinations (CBE).[11-13] In addition to CBE for breast cancer, the HPV DNA test for cervical cancer and cost-effective methods like Fecal Occult Blood Test (FOBT) and Fecal Immunochemical Test (FIT) for colorectal cancer should be promoted. Opportunistic screening, such as oral cavity examinations during routine visits, is also an effective, low-cost approach that can significantly reduce cancer-related deaths and improve quality of life.

Comparison to Screening for Other Non-Communicable Diseases

The disparity between cancer screening and screening for other non-communicable diseases (NCDs), such as diabetes and hypertension, was also evident in this study. While many individuals in rural areas undergo regular screening for NCDs and receive appropriate treatment, cancer screening remains neglected despite its potential for early diagnosis and improved outcomes. This discrepancy may be partly due to the emphasis placed on NCD management in public health campaigns, with less focus on cancer screening.[14] There is a clear need to integrate cancer screening into routine NCD management programs to ensure that individuals receive comprehensive preventive care.

Implications for Public Health Interventions

The findings of this study have significant implications for public health policy, particularly in rural areas where cancer screening uptake remains low. One of the key barriers identified is the lack of physician recommendations, which are known to be a strong motivator for patients to undergo cancer screening. Many participants in this study did not receive such advice, pointing to a gap in clinical practice. Strengthening physician-patient communication through targeted interventions could play a crucial role in addressing this issue. Training programs for healthcare providers, especially primary care physicians, should focus on the importance of discussing cancer risks and providing clear, actionable recommendations during routine consultations. This would ensure that opportunities for early detection are not missed.

Public awareness is another critical area for intervention. Many individuals in rural areas underestimate their cancer risk, resulting in low participation in screening programs. Community-based educational campaigns can be instrumental in raising awareness about the importance of early detection and dispelling myths surrounding cancer. Programmes addressing psychological barriers, such as fear and embarrassment, is essential for improving screening uptake.

In summary, improving cancer screening rates in rural populations requires a multi-pronged approach. This includes enhancing physician-patient communication, training healthcare providers to routinely discuss cancer risks, and implementing public awareness campaigns that target psychological barriers.[5] By addressing these barriers, healthcare providers and policymakers can improve early detection rates and reduce cancer-related mortality in rural communities.

CONCLUSION

This study underscores the need to improve cancer screening uptake in rural Thiruvananthapuram by

focusing on enhancing physician recommendations and raising awareness about cancer risk. Targeted interventions, such as incorporating tools like the Snehita Risk Calculator and promoting opportunistic screening, can lead to earlier cancer detection. By addressing barriers to screening through improved physician-patient communication and public health campaigns, healthcare providers and policymakers can significantly reduce cancer-related mortality and improve health outcomes in rural areas.

END NOTE

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REVIEW ARTICLE KERALA MEDICAL JOURNAL

20 Years of Continuous Glucose Monitoring in India: Options and Indications

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ABSTRACT

The increasing prevalence of diabetes worldwide is a major concern, especially in developing countries where achieving optimal glycemic control is challenging. Continuous Glucose Monitoring (CGM) systems have revolutionized diabetes management by providing detailed and real-time insights into glucose fluctuations. Over the past 20 years, CGM technology has significantly evolved with improved accuracy, user-friendliness, and clinical utility. This review discusses the progressive development of CGM systems in India, types of CGM systems including professional, real-time, intermittently scanned, and integrated CGMs, and their specific indications. The review also highlights novel innovations in CGM and explores the importance of metrics such as Time in Range (TIR) and Time in Tight Range (TITR) in glycemic management. By enhancing patient and healthcare provider decision-making, CGM systems have become an inevitable part of diabetes care, offering a more comprehensive and effective approach to managing the condition.

Keywords: Diabetes, CGM, Technology, RT-CGM, P-CGM, Glucose Monitoring, Time in Range, Time in Tight Range

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INTRODUCTION

Continuous Glucose Monitoring (CGM) is an innovative technology used in diabetes management that provides detailed information about the direction, magnitude, duration, frequency, and causes of fluctuations in glucose levels throughout the day.[1] It is exciting that the global estimate of CGM users is now greater than seven million.[2] Continuous glucose monitoring allows people with diabetes to determine whether their glycemic targets are being safely met and analyze the response to a therapy on an individual basis. Incorporating these findings into diabetes care might be helpful in facilitating optimal treatment decision-making, avoiding hypoglycemia.[3]

BASIC DESIGN OF A CGM

A CGM system typically comprises three parts: a tiny sensor inserted subcutaneously (disposable sensors) or placed inside the body (implantable sensor), a transmitter that sends the information wirelessly to a software program stored on a smartphone, insulin pump, or a separate device called a receiver.[3] Currently available CGMs measure glucose level in the interstitial fluid (ISF) through a tiny sensor inserted subcutaneously under the skin, usually on the abdomen or arm. The sensor measures glucose level every few minutes and transmits the information wirelessly to a monitoring device.[4] The accuracy of CGM is generally assessed using a metric called Mean Absolute Relative Difference (MARD). MARD is a statistical measure used to evaluate the accuracy of glucose readings from CGM devices by comparing them to reference glucose measurements. Lower MARD values indicate higher accuracy of the CGM system.[5] Implementing CGM as a vital element in diabetes management aids both patients and healthcare professionals (HCPs) in making timely decisions, and in improving the quality of life (QoL).

EVOLUTION OF CGM

The development of implantable glucose sensors and sensor technologies began in the early 1980s,

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contributing to the development of CGM devices. Initially, CGM was used as a research tool. Until the FDA approved the first MiniMed Continuous Glucose Monitoring System (CGMS), CGMS Gold (Medtronic MiniMed, CA, USA), in 1999, this technology was not commercially accessible.[6] The first professional CGM for glucose monitoring was a blinded system, meaning the patient was unaware of the glucose data acquired for three days. The data was extracted and reviewed at the healthcare provider's office. The system includes a glucose sensor, a monitor, a connecting cable, a Com-Station compatible with Windows 95 that allowed glucose readings to be stored as data, and a test plug to assess the function of the sensor. The device measured the glucose levels of the interstitial fluid every 10 seconds, over 5-minute intervals. CGM readings alone were not suitable for the therapeutic decision-making and required a confirmatory finger-pick test. The main advantage of CGMS Gold was its ability to unveil patterns that are missed by conventional blood glucose monitoring.

When CGM was first commercially available, its measurement error was more than ± 20%. Technological advancements have reduced measurement errors (±10%) and improved accuracy. Furthermore, improvements in the size, weight, complexity, and cost of CGM sensors/devices contributed to better performance of these devices in terms of duration of use, specificity, user-friendliness, user interface and displays, and data analysis and management. Based on their intended use, four types of CGM systems have been developed: Professional/Blinded CGM (P-CGM), Intermittently scanned CGM (isCGM), Real-time CGM (rt-CGM), and Integrated CGM (iCGM).[7]

In India, the evolution of CGM started with the availability of CGMS Gold in 2005.[6,8] iPro2 (Medtronic), the professional CGM introduced in India in 2016, was popular for nearly a decade.[9] The iPro2 collects and stores data from a glucose sensor that can be uploaded into CareLinkiPro® Therapy Management Software for Diabetes (CareLinkiPro, MMT-7340), to generate reports and store data. The device can store data up to 144h (6 days). In 2015, Abbott received FDA approval in India for FreeStyle® Libre Pro Flash Glucose Monitoring System. India was the first country to launch this professional CGM that does not require user calibration with finger-prick blood glucose.[10] The FreeStyle Libre Pro Flash Glucose Monitoring System comprises a handheld reader, a disposable sensor, and FreeStyle Libre Pro software. The device is indicated only for HCPs for use in people aged 18 years and older with diabetes. FreeStyle Libre Pro System provides HCPs with an Ambulatory Glucose Profile (AGP), a report produced from comprehensive glucose data that offers a visual snapshot of a person's typical daily glucose level and reveals hypoglycemic and hyperglycemic trends, facilitating better patient therapy and education. Healthcare providers can link an individual's glucose trends from AGP for more personalized and informed treatment decisions and enhanced communication between HCPs and patients.[11]

In 2020, Abbott launched FreeStyle Libre in India.[12] FreeStyle® Libre has a sensor and reader that provides real-time glucose readings upon scanning the sensor with the reader/smartphone app, offering a complete picture of a person's glucose levels without painful finger sticks. The system has a sensor wear time of 14 days and a warmup period of I hr.

Guardian Connect, the first real time CGM (RT-CGM) in India, utilizes Guardian Sensor 3, the Guardian Connect transmitter, and the Guardian Connect app to transmit data via Bluetooth every 5 minutes to the user's smart phone or device via the Guardian Connect App via CareLink personal and professional software. Approved by FDA in 2018, the Guardian Connect system is indicated for the periodic monitoring of glucose levels in the interstitial fluid in patients aged 14 to 75 years. Guardian Sensor 3 is indicated for 7 days of continuous use and is approved for use as an adjunctive device to complement information obtained from standard blood glucose monitoring devices and requires 2 daily finger stick calibrations. It is a stand-alone system which displays past glucose data from the previous 3, 6, 12, or 24 hours. The system has personalized alerts and alarm features, including adjustable volume settings at night and throughout the day, and snooze feature to silence CGM alerts for a period. The Guardian Connect transmitter powers the sensor, collects and calculates sensor data, and transmits the data via Bluetooth version 4.0 to the Guardian Connect app installed on a compatible mobile device. The transmitter is only compatible with the Guardian Sensor 3. The app displays the data, provides a user interface for sensor calibration, enters data such as exercise and meals, and uploads information to the CareLink Personal website.[13]

Guardian 4 Sensor

The Guardian 4 sensor is part of the CGM system and is compatible with the MiniMed™ 780G system that uses the Guardian 4 transmitter. Guardian 4 sensor is used in conjunction with the Guardian App.

Many CGM systems are widely used in countries other than India. Some recently introduced CGM systems include Dexcom G7, FreeStyle Libre 3 etc. Dexcom G7 is CGM with a MARD of 8.2% in adults measures interstitial glucose levels and sends the data to compatible devices including smart phones and the G7 receiver every 5 minutes. The all-in-one sensor/transmitter, which has a 10-day lifespan, can be worn on the upper buttocks and back of arm in children 2–6 years old and on the back of the arm in people aged 7 years and older. The data can be tracked by the users using the G7 app, support personnel on the Follow app, and by health care professionals on the Clarity app. FreeStyle Libre 3 is the latest generation of iCGM from Abbott which has the smallest, thinnest and most discreet glucose sensor. The FreeStyle Libre 3 reader is a small handheld device that displays real-time glucose readings directly from a small sensor worn on the back of a person's upper arm on an easy-to-see screen.

NOVEL INNOVATIONS IN CGM SYSTEMS

Dexcom ONE+

The Dexcom ONE+ system consists of a water-resistant sensor to measure blood glucose, a transmitter that sends CGM readings and a Dexcom One smartphone-compatible app. The system allows for real-time monitoring of blood glucose by both the user and up to ten additional people to allow for shared monitoring. Dexcom ONE+ can be worn at three different locations – abdomen, back of upper arms, or upper buttocks (only in children aged 2-17 years). The device also has a 'delay first high' option to avoid repeated high-reading alerts and, thereby, help avoid alert fatigue that demotivates a user and reduces compliance.[14]

Simplera

Simplera Sync (Medtronic) is a disposable, all-in-one continuous glucose monitor. It features an improved user experience at half the size of previous Medtronic sensors with a simple, two-step insertion process. In 2024, the MiniMed™ 780G system with Simplera Sync™ sensor received CE approval. MiniMed™ 780G system with Simplera Sync™ sensor is indicated for people aged 7 years and older and compatible with iOS and Android. The Simplera™ CGM for integrated use with the InPen™ smart insulin pen received CE Mark in September 2023.[15]

CareSens Air Real-Time CGM

The CareSens Air is the first CGM device developed by i-sens, Inc. (Incheon, South Korea) that has been approved by the South Korean Ministry of Food and Drug Safety as an adjunctive use device. It can be used for 15 consecutive days and features a calibration mechanism for reliability. The CGM continuously measures glucose levels in interstitial fluid, providing data on trends in glucose changes to the users' smartphone every 5 minutes. It is ergonomic and easy to use. Real-time glucose fluctuations and various events can be seen at a glance, and data can be shared through the Sens365 app and website.[16]

Dexcom Stelo

The Dexcom Stelo Glucose Biosensor System is the first over-the-counter (OTC) iCGM, approved by the FDA, intended for individuals aged 18 years and older who are non-insulin users, or those without diabetes. This 15-day CGM uses a wearable sensor, paired with an application installed on a user's smartphone or other smart device, to continuously measure, record, analyze and display glucose values. Glucose measurements and trends will be presented to the corresponding apps every 15 minutes.[17]

Eversense E3

Eversense E3 is the world's first and only long-term implantable CGM system with six months of glucose real-time readings and only two sensors per year. The sensor is inserted by an Eversense Inserter in the upper arm and continuously measures glucose for up to 6 months. Worn over the sensor, the transmitter wirelessly sends data to user's mobile device. It is removable and rechargeable and provides unique on-body vibe alerts. The Eversense app receives and displays data in easy to-read charts and graphs. There is no need to carry a separate receiver. Instead, the users can discreetly check the information on an Android™ or iOS® smartphone or Apple Watch®. Remote real-time monitoring capability for up to 5 people is also a smart feature of the CGM.

Eversense 365-day system

The Eversense 365-day system, the upgraded version of the E3 system is another breakthrough innovation from Senseonics. The 365 days accuracy of the next-generation Eversense Sensor was proved in clinical trials including ENHANCE. This is a major technological leap towards offering the differentiated benefits of implantable CGM for one full year with a single sensor.[18]

FreeStyle Libre 2 and FreeStyle Libre 3 Sensors

The US FDA has cleared FreeStyle Libre 2 and FreeStyle

Figure 1. **Types of CGM systems (((a) Guardian Connect (b) Dexcom G6 (c) Dexcom G7 (d) FreeStyle Libre 3 (e) Eversense (rt-CGMs)) (f) FreeStyle Libre Pro (P-CGM) (g) FreeStyle Libre (isCGM)))**

Libre 3 iCGM system sensors for integration with the automated insulin delivery (AID) system. They are also cleared for use by children as young as two years old, for use by women with diabetes who are pregnant. The senor has a wear time of 14 days. FreeStyle Libre 3 sensor also integrates with CamDisb's CamAPS FX mobile app and Ypsomed's mylife YpsoPump.[19] FreeStyle Libre 2 Plus sensor is the modified version of FreeStyle Libre 2 sensor cleared in 2023 by the FDA for use with AID systems. It is the first and only CGM available in the United States with a wear time of 15 days for people with diabetes aged 2 years and older. FreeStyle Libre 2 Plus sensor can be integrated with the t:slim X2 insulin pump.

Table 1 and Table 2 demonstrate the currently available real time and professional CGM systems. **Figure 1** depicts different types of currently available CGMs.

CONTINUOUS GLUCOSE MONITORING AND TIME-IN-RANGE

Time-in-range (TIR)

TIR is defined as the percentage of time an individual spends with their blood glucose levels in the target range. It includes three key CGM measurements: time spent within target glucose range (TIR), time spent below target glucose range (TBR), and time spent above target glucose range (TAR). For instance, if a person's TIR is 50%, it can be explained as of the 24 hrs duration of a day, the person spent 12 hours within the target glycemic range. The target range varies depending upon the individual, but general guidelines suggest the range as 70 to 180 mg/dL. TIR can be measured accurately by using a CGM device. These devices are equipped with software/apps that automatically record the TIR that helps both patients and health care professionals to derive a clearer picture of their glycemic profile on a timely basis.[20,21]

IC-TIR recommendations for Time-in-range

The IC-TIR (International Consensus on Time-in-Range) expert panel recommends a target range of 70-180 mg/dL [3.9-10.0 mmol/L] for individuals with type 1 diabetes and type 2 diabetes, and 63-140 mg/dL [3.5-7.8 mmol/L] during pregnancy, along with a set of targets for the time per day [% of CGM readings or minutes/hrs]. TIR simplifies the significance of these values such that a patient with diabetes should aim to spend at least 17 hours a day or more than 70% of their time in the blood glucose range of 70-180 mg/dL. However, the target range was lowered for pregnant women to 63-140 mg/dL as the blood glucose levels are lower in pregnancy. The recommendations also outline fixing targets for people with diabetes who are older and/or considered high-risk and the time-in-range bar was set at 50% for these categories. The guidelines also suggest that for patients with diabetes, the time spent below 70 mg/dL (TBR) should be less than 1 hour a day or under 4% of the time and time spent at or above 180 mg/dL (TAR) should be less than 6 hours a day or 25% of the time. For people with serious hypoglycemia, the time spent below 54 mg/dL should be less than 15 minutes a day or 1% of the time and the time spent above 250 mg/dL should be less than 1 hour and 15 minutes a day or 5% of the time.[22]

TIR – South Asia Recommendations

There are a number of roadblocks for the employment of CGM devices in South Asia such as illiterate patients, incompetency with the use of CGM devices, non-reimbursable market, overcorrection or under correction of potential hyperglycemia/hypoglycemia

Table 1. Currently available RT-CGMs

System Type	Device	Age	Wear time duration of sensor	Calibration required	Alarms for highs/ lows	Data accession Software/ devices	Arrows	iCGM designation
Real-time CGM	Freestyle Libre 3	4+ years	14 days	No	Yes	FreeStyle Libre Link, LibreView	Glucose is rising quickly (>2 mg/dL/ minute) ↑ Glucose is rising (1–2 mg/dL/ minute) ↗ Glucose is changing slowly (>1 mg/dL/minute) → Glucose is falling (1–2 mg/dL/ minute) ↘ Glucose is falling quickly (>2 mg/dL/minute) ↓	Yes
	Dexcom G6	2+ years	10 days	No	Yes	Dexcom CLARITY software for data analysis. Data visualization in Android and iPhone apps, smartwatches, Tandem t: slim X2 pump	Glucose is rapidly rising (>3 mg/dL/ minute) ↑↑ Glucose is rising (2–3 mg/dL/ minute) ↑ Glucose is slowly rising (1–2 mg/dL / minute) ↗ Glucose is steady (not increasing or decreasing >1 mg/dL/ minute) → Glucose is slowly falling (1–2 mg/dL /minute) ↘ Glucose is falling (2–3 mg/dL/minute) ↓ Glucose is rapidly falling (>3 mg/dL/minute) ↓↓	Yes
	Dexcom G7	2+ years	10 days	No	Yes	Dexcom Clarity Dexcom Follow app for friends & family	Glucose is rising (30.6-45 mg/dL in 15 minutes)↑ Glucose is falling (30.6-45 mg/dL in 15 minutes) ↓ Steady (<14.4 mg/dL in 15 minutes) → Glucose is slowly rising (14.4-30.6 mg/dL in 15 minutes) ↗ Glucose is slowly falling. (14.4-30.6 mg/dL in 15 minutes) ↘ Glucose is rapidly rising. (> 45 mg/dL in 15 minutes) ↑↑ Glucose is rapidly falling. (>45 mg/dL in 15 minutes) ↓↓	Yes
	Dexcom ONE+	>2 years	10 days	No	Yes	Dexcom ONE+ mobile app	Steady (Changing less than 30 mg/dL in 30 minutes) → Slowly rising (Changing 30–60 mg/dL in 30 minutes) ↗ Slowly falling (Changing 30–60 mg/dL in 30 minutes ↘ Rising (Changing 60–90 mg/dL in 30 minutes) ↑ Falling (Changing 60–90 mg/dL in 30 minutes) ↓ Rapidly rising (Changing more than 90 mg/dL in 30 minutes) ↑↑ Rapidly falling (Changing more than 90 mg/dL in 30 minutes) ↓↓	No
	Guardian Connect	14+ years	7 days	Twice per day	Yes	Guardian Connect Android and iPhone apps.	Glucose is rising at a rate of ≥3 mg/dL/minute↑↑↑ Glucose is rising at a rate of ≥2 but <3 mg/dL/minute↑↑ Glucose is rising at a rate of ≥1 but <2 mg/dL/minute↑ Glucose is falling at a rate of ≥1 but <2 mg/dL/ minute↓ Glucose is falling at a rate of ≥2 but <3 mg/dL/ minute↓↓ Glucose is falling at a rate of ≥3 mg/dL/minute↓↓↓	No
	Eversense	18+ years	90 days	Twice per day	Yes	Android and iPhone apps	Gradually falling or rising glucose level at a rate between 0.0 mg/dL-1.0 mg/dL/ minute → Moderately rising glucose level at a rate between 1.0 mg/dL-2.0 mg/dL/minute ↗ Moderately falling glucose levels at a rate between 1.0 mg/dL-2.0 mg/dL/minute↘ Very rapidly rising glucose levels at a rate more than 2.0 mg/dL/ minute ↑ Very rapidly falling glucose levels at a rate more than 2.0 mg/dL/ minute↓	No
	Eversense E3	18+ years	180 days	Yes	Yes	Eversense® CGM app. Monitor glucose levels on Android™, iOS™ smartphone or Apple Watch.	Gradually rising or falling glucose levels (falling or rising at a rate between 0.0 mg/dL and 1.0 mg/dL per minute) → Moderately rising glucose levels, (rising at a rate between 1.0 mg/dL and 2.0 mg/dL per minute) ↗ Moderately falling glucose levels, falling at a rate between 1.0 mg/dL and 2.0 mg/dL per minute) ↘ Very rapidly rising glucose levels (rising at a rate more than 2.0 mg/dL per minute) ↑ Very rapidly falling glucose levels (falling at a rate more than 2.0 mg/dL per minute) ↓	
	Simplera	7+ years	7 days	No	Yes	iOS, Android	-	No

Table 2. Currently available Professional CGMs

System Type	Device	Wear time duration of sensor	Calibration required	Frequency of glucose readings	MARD	Data accession Software/devices	Arrows
Professional CGM	Libre Pro	14 days	No	Every 15 minutes	12.3%.	Data can be downloaded using Care-Link™ iPro software	No

Table 3. Proposed modifications to the established TIR targets for South Asian Population

S.No.	Target limits	Proposed modifications in CGM target limits
1	Change of lower limit in older and high-risk population.	Recommendation 1.1: TIR buffer can be of 90-180 mg/dL. The lower limit of TIR can be fixed as 90 mg/dL instead of 70 mg/dL. Recommendation 1.2: TIR above 50%, and considering limited life expectancy or limited functional age, gradually aim above >55%, >60% and >65% as appropriate with an optimal target of >60%.
2	Change of TAR upper limit	Recommendation 2: TAR is categorized into three levels: Level 1:180-249 mg/dL, Level 2: >250-349 mg/dL, and Level 3: >350 mg/dL
3	Revisal of percentage of time spent in TAR upper limit for pregnant women (GDM, T2DM with pregnancy)	Recommendation 3.1: Clear recommendation for GDM is needed for South Asians. For this more research is required. Recommendation 3.2: Flexibility in the percentage spent in TAR limit: <15% TAR for >140mg/dL
4	Recommendations on the frequency to repeat CGM in routine clinical practice	Recommendation 4: Considering the limitations and advantages of CGM, we are recommending a minimum frequency for the assessment of TIR in T2D. For those patients achieving a desirable TIR with minimal time below range, the frequency of repeating the test is minimal and vice versa. The treating physician can make individualised personalised clinical decisions.

(Adapted from Kesavadev J, Misra A, Saboo B, Agarwal S, Sosale A, Joshi SR, Hussain A, Somasundaram N, Basit A, Choudhary P, Soegondo S. Time-in-range and frequency of continuous glucose monitoring: Recommendations for South Asia. Diabetes Metab Syndr. 2022 Jan;16(1):102345)

etc., Considering the importance of the factors such as inadequate diabetes education, problem in accessing emergency medical facilities in case of hypoglycemia, and lack of awareness and training of health care professionals in South Asia that inhibits the wider access and use of CGM, it is essential that the established metrics by the IC-TIR panel should be looked upon critically in the safe interest of people with diabetes.[23] **Table 3** describes the suggested recommendations for TIR targets for South Asian patients with T2D.

Time in Tight Range (TITR)

Time in Tight Range is an emerging metric, defined as the percentage of time a person spends in the glucose range of 70-140 mg/dL. (or) Time in tight range describes the time an individual spends in normoglycemia. TITR lowers the upper threshold of Time in Range from 180 mg/dL to 140 mg/dL. The specified goal is to maintain a TITR> 50%. It can be implemented in clinical practice for timely therapy intensification and optimization. Even though achieving time in tight range is more challenging than achieving time in range, diabetes technologies such as automated insulin delivery (AID) and continuous glucose monitoring aid people with diabetes in accomplishing the goal.[24]

Recommendations on the Frequency to Repeat CGM in Clinical Practice

The IC-TIR does not have recommendations on the frequency of CGM use. In a nonreimbursable market such as in South Asia, people with diabetes need to spend out of their pocket and hence lack long-term sustained CGM use. In type 1 diabetes and gestational diabetes, it is always recommended to have continuous use of CGM if the resources are adequate. In the case of people with type 2 diabetes in South Asia, sustainability of CGM use is not feasible.

Considering the limitations and advantages of CGM, the expert panel recommends a minimum frequency for the assessment of TIR in T2D. For those patients achieving a desirable TIR with minimal time below range, the frequency of repeating the test is kept minimal and vice versa.The treating physician can make individualised clinical decisions.[23] **Figure 2** shows the recommended frequency for repeating CGM/TIR assessment in patients with type 2 diabetes in South Asia based on previous AGP report of the patient (non-pregnant).

SIGNIFICANCE OF CHOOSING THE RIGHT CGM

People with type 1 diabetes have to frequently monitor their blood glucose levels for optimal glycemic management. Real-Time CGM will be the wiser choice for people with type 1 diabetes compared to other CGM systems. Current RT-CGM systems automatically transmit a continuous stream of glucose data to the user in real time, provide alerts and active alarms,

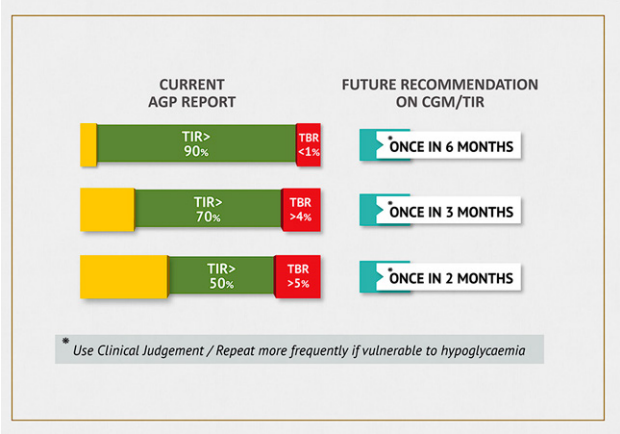

Figure 2. **Recommended frequency for repeating CGM/TIR assessment in patients with type 2 diabetes in South Asia based on previous AGP report of the patient (non-pregnant)**
(Adapted from Kesavadev J, Misra A, Saboo B, Agarwal S, Sosale A, Joshi SR, Hussain A, Somasundaram N, Basit A, Choudhary P, Soegondo S. Time-in-range and frequency of continuous glucose monitoring: Recommendations for South Asia. Diabetes Metab Syndr. 2022 Jan;16(1):102345)

and transmit glucose data (trend and numerical) to a receiver, smart watch, or smartphone. According to the American Diabetes Association, RT-CGM or is-CGM should be offered to youth and adults with type 1 and type 2 diabetes on intensive insulin therapy or continuous subcutaneous insulin infusion who are able to use the devices safely.[25]

Mounting evidence supports the multitude of benefits people with T1D my harness with the use of RT-CGM systems. For instance, a study by Hásková et al., compared the efficacy of RT-CGM (Guardian Connect Mobile) or isCGM (FreeStyle Libre) in maintaining optimal glycemic control in type 1 diabetes revealed that RT-CGM was superior to isCGM in reducing hypoglycemia and improving time in range in adults with T1D.[26] Rubelj et al., in their study confirmed that CGM is effective in achieving better control of type 1 diabetes by significantly improving HbA1c levels in a popula-

Table 4. Recommendations for CGM use by international organizations

RSSDI	ADA	AACE
CGM should be considered in conjunction with SMBG and HbA1C for glycemic status assessment in those T2DM individuals treated with intensive insulin therapy and who are not achieving glucose targets.	Real-time CGM (rtCGM) or intermittently scanned CGM (isCGM) should be offered for diabetes management in adults with diabetes on multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII) who are capable of using the devices safely (either by themselves or with a caregiver). rtCGM or isCGM should be offered for diabetes management in adults with diabetes on basal insulin who are capable of using the devices safely (either by themselves or with a caregiver).	rtCGM should be recommended over isCGM to persons with diabetes with problematic hypoglycemia (frequent/severe hypoglycemia, nocturnal hypoglycemia, hypoglycemia unawareness) who require predictive alarms/alerts. However, the lifestyle of persons with diabetes and other factors should also be considered.
In well-controlled T2DM, professional CGM once in 6 months could be sufficient irrespective of the treatment regimen.	rtCGM or isCGM should be offered for diabetes management in youth with type 1 diabetes on MDI or CSII who are capable of using the devices safely (either by themselves or with a caregiver). rtCGM or isCGM should be offered for diabetes management in youth with type 2 diabetes on MDI or CSII who are capable of using the devices safely (either by themselves or with a caregiver).	When used as an adjunct to preprandial and postprandial BGM, CGM can help to achieve A1C targets in diabetes and pregnancy.
CGM may be considered in women with GDM or pregnant women with T2DM and as a supplemental tool to SMBG in individuals with hypoglycemia unawareness and/or frequent hypoglycemic episodes.	In people with diabetes on MDI or CSII, rtCGM devices should be used as close to daily as possible for maximal benefit. isCGM devices should be scanned frequently, at a minimum once every 8 hours to avoid gaps in data.	isCGM should be considered for persons with diabetes who meet 1 or more of the following criteria: Newly diagnosed with T2D, Treated with non-hypoglycemic therapies, Motivated to scan device several times per day, At low risk for hypoglycemia, although desire more data than SMBG provides
	People with diabetes should have uninterrupted access to their supplies to minimize gaps in CGM.	
	Periodic use of rtCGM or isCGM or use of professional CGM can be helpful for diabetes management in circumstances where consistent use of CGM is not desired or available	
	Skin reactions, either due to irritation or allergy, should be assessed and addressed to aid in successful use of devices.	
	People who wear CGM devices should be educated on potential interfering substances and other factors that may affect accuracy.	

tion of highly motivated families, diseased children, adolescents and young adults.[27] The DIAMOND trial showed that use of RT-CGM improved HbA1c and reduced the time spent in the hypoglycemia in the T1D cohort.[28] A recent head-to-head comparative study demonstrated that use of Dexcom G5 RT-CGM is potentially beneficial in reducing time spent in hypoglycemia in MDI-treated T1D adults with impaired hypoglycemia awareness compared with isCGM use which supports the use of RT-CGm use in T1D.[29] It is also well-documented that current RT-CGM devices offer alarm functions, with individualized upper and lower limits, and rapidity of change alerts as well. This is particularly crucial for those who experience frequent episodes of severe hypoglycemia, frequently experience nocturnal hypoglycemia, or have poor awareness of hypoglycemia.[30]

People with type 2 diabetes also prefer CGM systems in this digital era. The ADA and AACE recommendations also support the use of CGM in type 2 diabetes. In prediabetes, the use of CGM aids people to make lifestyle modifications by displaying real-time glucose information that associates their behaviors to glycemic outcomes, providing information about how diet and exercise affects their blood glucose. Access to this information provides opportunities for people with prediabetes to be aware of the glycemic impact of previous behaviors and make more informed decisions in their daily lives. In a recent single-arm prospective study by Lee et al., investigated the feasibility and acceptability of CGM use in 32 individuals with prediabetes reported that majority of the participants were satisfied with the use of CGM.[31] Yost et al. assessed patient satisfaction and feasibility in 15 adults with prediabetes who used CGM in combination with a low-carbohydrate diet. The investigators observed a multitude of benefits including significant reductions in HbA1c and a high rate of satisfaction (93%) among participants.[32]

CGM also is found to be beneficial in managing diabetes therapy. A consensus recommendation from an expert panel with respect to the role of CGM in maintaining TIR among patients using OHAs, suggests that the use of CGM with TIR metric included for 2 weeks will help in readjustment or modification of treatment in these patients and waivers the need to wait for the 3-month duration to check the HbA1c status and efficacy of the treatment. Routine use of TIR is recommended for patients on basal insulin.[33]

Table 4 describes recommendations for CGM use by international organizations.[34-36]

CONCLUSION

CGM has revolutionized glucose (in the interstitial fluid) monitoring by providing multifarious benefits that, before its advent, were impossible to realize for people with diabetes. CGM addresses and alleviates many challenges patients and HCPs face in achieving glycemic targets, making it an inevitable part of diabetes management. It is now well-established that CGM is beneficial in substantially reducing hospitalizations, hypoglycemia, and the overall cost of diabetes care. Currently, CGM is more expensive when compared to conventional monitoring with a blood glucose meter, but it is more cost-effective in the long run.

END NOTE

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Spontaneous Arterial Dissection Secondary to Graves' Disease: A Possible Association

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ABSTRACT

Arterial dissection is one of the common etiologies of young ischemic strokes. We report a case of Graves' disease presenting as isolated spontaneous cervical internal carotid artery dissection followed by subarachnoid haemorrhage. A young female in her early 40s presented with 3-day history of headache and left hemiparesis. MRI of the Brain showed acute right hemispheric watershed infarcts. CT Angiogram showed a short segment right cervical internal carotid artery dissection. Her serum TSH was markedly reduced with an elevated free T3/free T4 ratio (1.78) and strongly positive Anti TSH-R antibodies. She was treated with anticoagulants and antithyroid medications. Still, later she developed an episode of focal seizure following right frontal subarachnoid hemorrhage, when anticoagulation was stopped and started on a single antiplatelet, with which she recovered well. Spontaneous cervical internal carotid artery dissection and focal subarachnoid haemorrhage presenting secondary to Graves' disease without any other symptomatic systemic manifestations of hyperthyroidism is probably rare.

Keywords: Carotid Dissection, Subarachnoid Haemorrhage, Hyper Dynamic Flow, Hyperthyroidism

*See End Note for complete author details

INTRODUCTION

Carotid artery dissection accounts for about 10-25% of ischemic strokes in the young population.[1] Headache, ipsilateral facial or eye pain, neck pain and neurological deficits are the usual presenting features. Arterial dissection occurs due to multifactorial aetiology and implies a tear in the intimal layer usually occurring spontaneously or secondary to trauma, leading to mural thrombus formation and distal ischemic symptoms or as a tear in the tunica adventitia, causing aneurysmal dilatation or subarachnoid haemorrhage.[2] About 61% of carotid dissections occur spontaneously secondary to multiple aetiologies, but that secondary to Graves' disease is uncommon.[3] We report a patient with newly detected Graves' hyperthyroidism presenting as acute ischemic stroke due to unilateral cervical carotid artery dissection and later had a focal seizure due to focal subarachnoid haemorrhage.

CASE PRESENTATION

A young female in her early 40s, without any known prior co-morbidities presented with sudden onset left upper and lower limb weakness along with deviation of her mouth towards the right for 3 days duration. She had difficulty in doing her routine household chores due to left upper limb weakness and was able to walk without support. She had a mild headache 3 days back at the onset of symptoms, which subsided gradually over 1-2 days. She did not have vomiting, neck pain, trauma, loss of consciousness or bleeding from nose, ear or mouth. She was neither a smoker nor an alcoholic. She had no history of migraine or significant family history. Her clinical presentation was suggestive of an acute vascular event in the right MCA territory. On examination, she had no markers of hypercholesterolemia or connective tissue disorder. Her blood pressure was within normal range and her pulse

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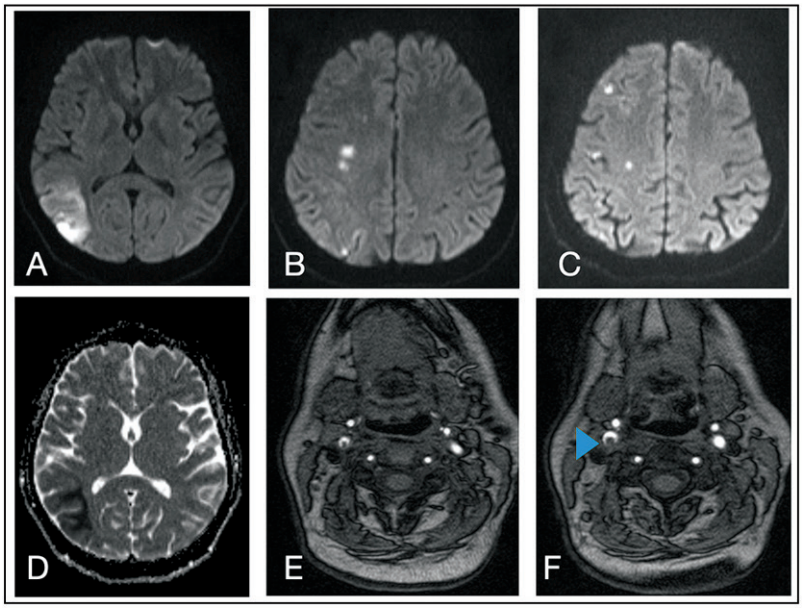

Figure 1. **MRI Brain Axial DWI showing acute infarcts (A-D) MR Angiography showing carotid dissection (E-F)**

was regular and equally felt on both sides. She had no carotid bruit or cardiac murmur. There were no signs of Horner's syndrome. She was alert and oriented, had mild dysarthria, left UMN facial palsy, left upper limb power 3/5 and left lower limb drift, without sensory dulling, ataxia or visual disturbances. Her NIHSS score was 5 and her mRS was 3.

INVESTIGATIONS

MRI Brain showed multiple patchy acute infarcts in the right MCA-PCA cortical watershed region and right MCA-ACA internal watershed region. MR Angiography showed dissection in the right internal carotid artery at its origin extending for about 2 cm and causing significant luminal narrowing **(Figure 1).** CT Angiography also showed similar findings and there was no evidence of large artery atherosclerotic disease in other vessels **(Figure 2).**

Routine haematological and biochemical investigations including a lipid profile, HbA1C and serum homocysteine levels were normal. Serum TSH was 0.005 miIU/mL (normal 0.5-5 mIU/L), free T3 was 11.25 pg/mL (normal 2.3-4.1 pg/mL) and free T4 was 6.32 ng/dL (normal 0.8-1.8 ng/dL). Free T3/Free T4 ratio was 1.78. TSH Receptor Antibody was strongly positive, suggestive of Graves' disease. ANA-IF was 2+ and ANA profile was negative. ECG showed normal sinus rhythm and 2D ECHO showed normal ejection fraction with grade 1 diastolic dysfunction.

TREATMENT

She was managed conservatively with anticoagulation. She was started on methimazole 5mg/day and slowly up titrated to 20mg/day. She was also started on propranolol as she had persistent resting tachycardia, though asymptomatic.

OUTCOME AND FOLLOW-UP

On day 7 of hospitalization, our patient developed a brief episode of left-sided focal motor seizure with impaired awareness. Imaging showed subarachnoid hemorrhage in the right frontal region **(Figure 3).** Anticoagulation was stopped and she was initiated on levetiracetam and a single antiplatelet. She had no further seizures and her neurological deficits improved. She was advised to avoid activities predisposing to cervical injury for at least 6 months. On follow-up after 1 month, she had improvement in neurological deficits with only residual dysarthria. Her NIHSS was 0 and mRS was 0. She is kept on regular follow-ups with an endocrinologist for the management of hyperthyroidism.

DISCUSSION

Arterial dissection accounts for about 1-2% of all ischemic strokes and is more common in younger individuals. About 7% of young ischemic strokes were secondary to arterial dissection in an Indian study.[4]

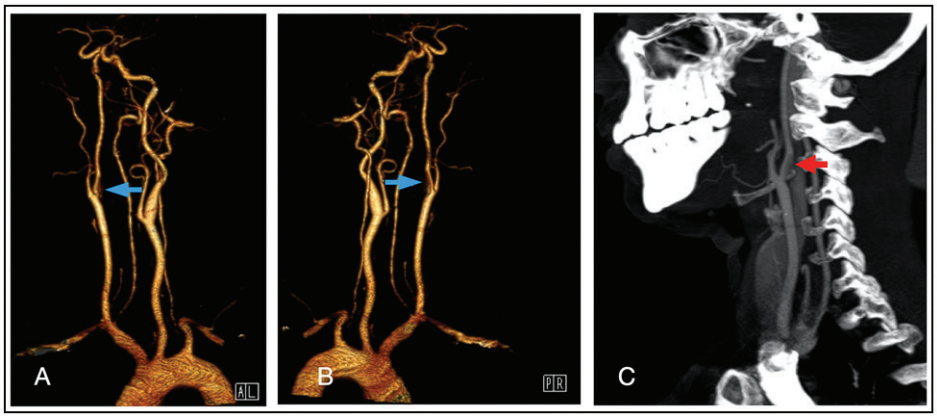

Figure 2. **CT Angiography showing right internal carotid dissection at its origin (A-C)**

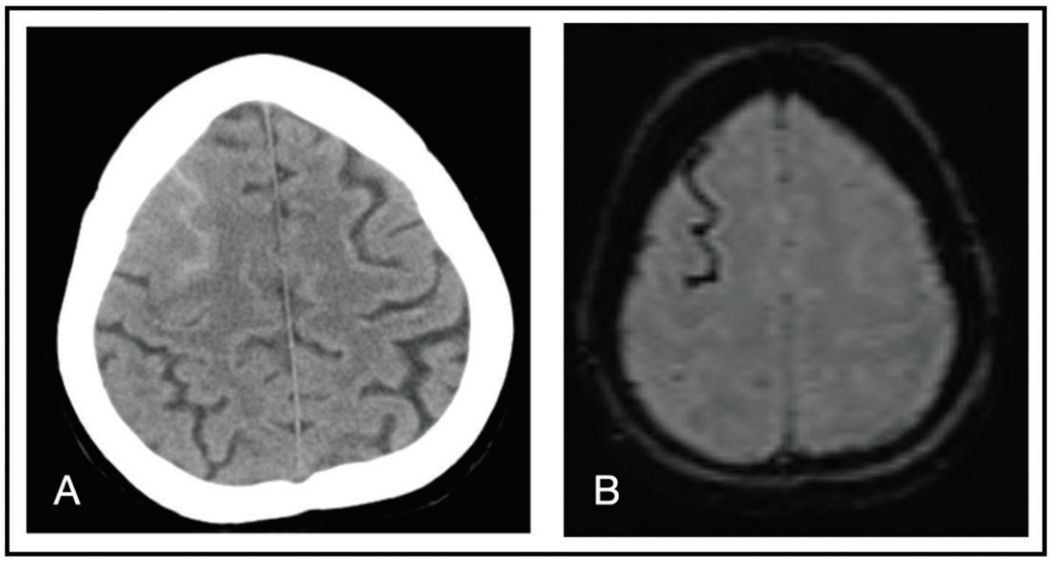

Figure 3. **A) CT Brain showing right frontal subarachnoid hemorrhage. B) Axial SWI sequence showing blooming in the same region**

Carotid artery dissections are multifactorial but are usually either traumatic or spontaneous. The carotid and vertebral arteries are more prone to dissection as compared to other arteries of similar size like coronary or renal arteries, probably due to their greater mobility and the propensity to get injured by contact with surrounding bony structures like cervical vertebrae and styloid process.[6-8] The tears in arterial walls are notoriously difficult to identify but a sub-intimal tear leads to intramural hematoma causing stroke either due to ischemia or embolic phenomenon and a sub-adventitial tear leads to aneurysmal dilatation of the artery or subarachnoid haemorrhage.[8] **(Figure 3).** In addition to classical presenting features of dissection like headache, facial pain and neck pain, the other reported features are Horner's syndrome, cranial nerve palsies especially lower nerves and pulsatile tinnitus.[9]

Spontaneous internal carotid artery dissection causes ischemic strokes in the majority like our patient, while other presentations include transient ischemic attacks, ischemic optic neuropathy, amaurosis fugax and retinal infarct.[9] Traumatic arterial dissection can occur due to significant insults following motor vehicle accidents, falls or direct blunt injuries to the neck. Though spontaneous dissections are attributed to variety of genetic (Ehlers-Danlos syndrome type IV, Marfan's syndrome, autosomal dominant polycystic kidney disease, Osteogenesis imperfecta I) and environmental factors (minor precipitating events like dancing, practicing yoga, coughing, vomiting, sneezing, anesthesia recipient, amusement park rides or chiropractic neck manipulations), the etiology is usually speculative and definite precipitant remains elusive in most cases as in our patient.[5,6]

The association of carotid dissection with thyroid dysfunction is a rarely reported entity. Campos et al first reported two cases with bilateral carotid dissection with Graves' disease who eventually succumbed, and postmortem evaluation of one of those patients showed segmental medial arteriopathy, which was a

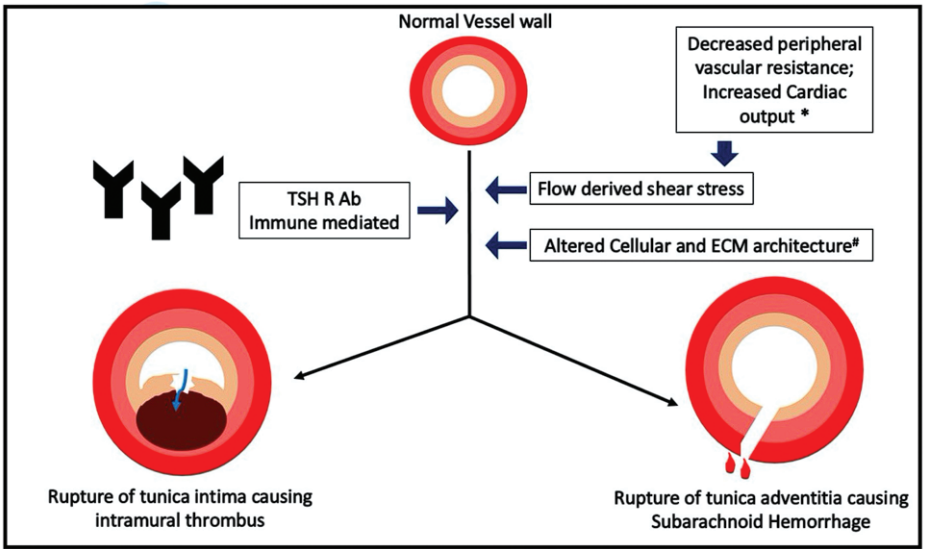

Figure 4. **Proposed mechanisms of arterial dissection due to Graves' disease.**

*Thyroid hormones cause pe-ripheral vasodilatation by direct effect causing decreased peripheral resistance, which activates renin-angiotensin system to increase sodium and water retention, which along with the direct iono-tropic effect of thyroid hormones causes increased cardiac output. # Thyroid hormones have a di-rect effect on vascular smooth muscles, endothelial cells and extracellular connective tissue; TSH R Ab - Thyroid Stimulating Hormone Receptor Antibody. (Illustrated by author L Priya)

lytic process involving tunica media and was attributed to be an immune mediated mechanism similar to the prior reported case with SLE and similar histopathological findings.[10,11] Pezzini et al conducted a retrospective study among 58 spontaneous carotid artery dissection patients and found that antithyroid antibodies were present in 31% of those patients and proposed a hypothesis that arterial disease might be one of the phenotypic expressions of generalized immune activation.[12] Another retrospective study by Shi Z et al showed that antithyroid peroxidase antibodies to be significantly elevated in young ischemic stroke patients with intracranial large artery stenosis (16.5% out of 121 patients), proposing an immune mediated pathogenesis.[13] Thyroid hormone has a direct effect on vascular smooth muscles causing vasodilation, that activates renin-angiotensin system to increase the plasma volume, which in addition to its transcriptional and non-transcriptional effects on cardiac myocytes increases the cardiac output, thereby creating a hyper dynamic circulatory state.[14] Although Graves' disease can be coincidentally detected along with carotid dissection in our patient, we consider it to be less likely in view of the support from existing literature. In our patient, we hypothesize that the hyper dynamic flow state in Graves' disease causes sheer stress on the vessel wall, which is already in a state of altered microstructure (vascular smooth muscle cells, endothelium and connection tissue) due to both direct and probable immune mediated mechanism, making the vessel vulnerable to dissection and perhaps this alteration occurs prior to the manifestation of overt clinical signs and symptoms of hyperthyroidism like ophthalmopathy or dermopathy **(Figure 4).** There had been a report of familial association of Graves' Disease with subarachnoid haemorrhage which had hypothesized hyper dynamic flow state as one of the predisposing mechanisms.[15] However, based on the available literature currently, we neither confirm nor disprove the association between Graves' Disease and spontaneous arterial dissection, but rather speculative.

Our patient had tapering occlusion and vessel wall irregularity on CT angiogram **(figure 2),** which was correlating with clinical picture to conclude carotid dissection. However, an MR Angiogram with fat-suppressed images would have helped to identify intramural hematoma if no clues had been obtained on CT Angiogram.[16] We propose that in our patient hyperthyroidism would have caused a tear in tunica adventitia also leading to subarachnoid hemorrhage, though anticoagulant use may account for rare instances. DSA was deferred to further characterise the aetiology given the risks associated with already existing occlusive thrombus in cervical ICA. Genetic testing is not routinely recommended to patients with carotid dissection, but may be useful in patients with recurrent dissections, positive family history and patients with physical signs suggestive of connective tissue disorders.[17]

As this patient had an occlusive thrombus with no other significant bleeding tendencies initially, she was treated with anticoagulation, but later when she developed subarachnoid hemorrhage, single anti platelet was considered the treatment of choice as per recent AHA guidelines. The risk of recurrent dissections are usually higher in the initial few months after first event.[17] Management of hyperthyroidism is crucial as early and appropriate management prevents further vessel damage.

LEARNING POINTS/TAKE HOME MESSAGES

- There must be a high index of suspicion of carotid dissection in young patients presenting with acute ischemic stroke though the classical symptoms of dissection like headache or neck pain are vague.
- Young females with arterial dissection must be evaluated for Graves' disease even though clinical signs and symptoms of thyroid dysfunction are absent.
- Hyperthyroidism may predispose to arterial dissection at two independent sites causing an occlusive thrombus and subarachnoid hemorrhage.

END NOTE

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Abbreviations

TSH-R: Thyroid Stimulating Hormone Receptor

ANA: IF Anti nuclear antibody - Immunofluorescence

CT: Computed Tomography

MRI: Magnetic Resonance Imaging

MRA: Magnetic Resonance Angiography

ICA: Internal Carotid Artery

MCA: ACA Middle Cerebral Artery - Anterior Cerebral Artery

MCA: PCA Middle Cerebral Artery - Posterior Cerebral Artery

ECG: Electrocardiogram

ECHO: Echocardiography

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LP, PR, AM, BKK - data collection and drafting of manuscript

PTA, JVM - revision and final drafting the manuscript

Data Availability: All data has been presented in this manuscript

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A Case of Pyloric Web with Fenestration

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ABSTRACT

Congenital gastric outlet obstruction can be caused by pre pyloric or pyloric abnormalities. Pyloric atresia is a rare congenital anomaly that causes partial or complete obliteration of the gastric lumen. It constitutes about 1% of all intestinal atresias. The pyloric web is the most common type of pyloric atresia which presents in the neonatal period with nonbilious vomiting just like more common conditions like idiopathic hypertrophic pyloric stenosis.[1] We report a case of a newborn with a pyloric web detected within the first week of life.

Keywords: Pyloric web, Pyloric atresia, Gastric outlet obstruction, Low birth weight

*See End Note for complete author details

CASE PRESENTATION

Term, Low birth weight (1.98kg) baby delivered normally (mother primi, PIH) who passed meconium and urine on the first day of life, developed non-bilious vomiting on the third day of life. The baby was treated conservatively. On the fourth day baby had further vomiting. The baby was moderately active with normal vitals and the upper abdomen was distended with visible gastric peristalsis. Other systems were within normal limits.

Sepsis screening was negative. A plain X-ray abdomen showed a dilated gastric shadow **(Figure1).** Ba meal follow-through showed gastric outlet obstruction **(Figure 2).** A laparotomy was done by Paediatric surgeon. The baby was found to have a partial pyloric web with fenestrations at the fundus of the pylorus **(Figure 3).** Pyloroplasty was done. The Baby improved, gained weight and was discharged.

DISCUSSION

Congenital pyloric atresia is a rare condition. Incidence is approximately 1 in 1 lakh newborns. It constitutes about 1% of all intestinal atresias.[2] It has three anatomic types, type A (membranous or web), type B (solid cord), and type C (gap between stomach and duodenum).[3] Clinical presentation: A maternal history of polyhydramnios is often reported. Affected infant presents in the first few days of life with non-bilious vomiting and features of gastric outlet obstruction.

Abdominal radiography: single gastric bubble with no air visible beyond the pylorus in complete atresia. In the pyloric web there may be distal air in the intes-

Figure 1. **Plain x-ray abdomen : Dilated gastric shadow**

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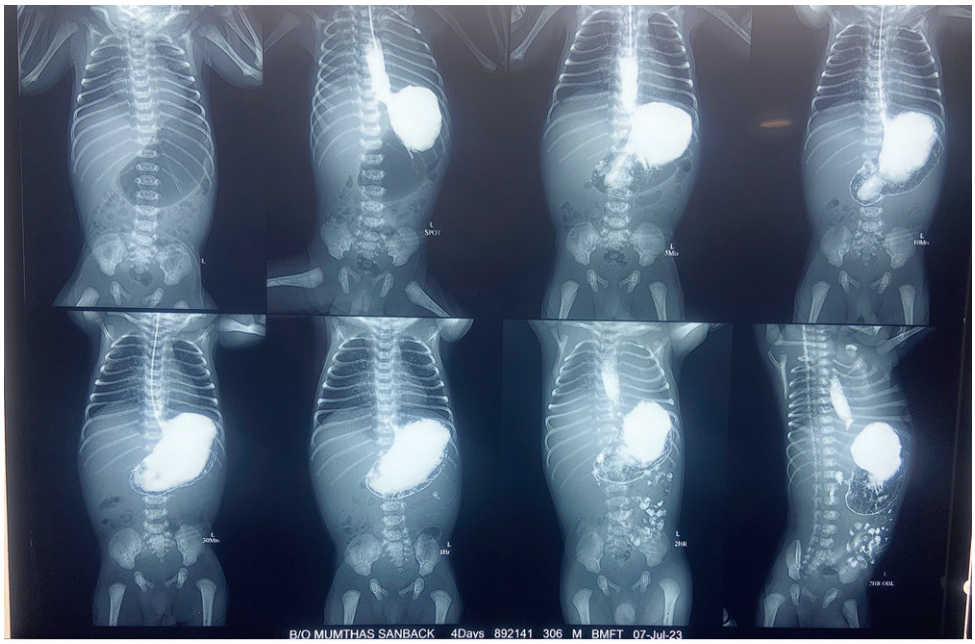

Figure 2. **Ba meal follow through : Gastric outlet obstruction**

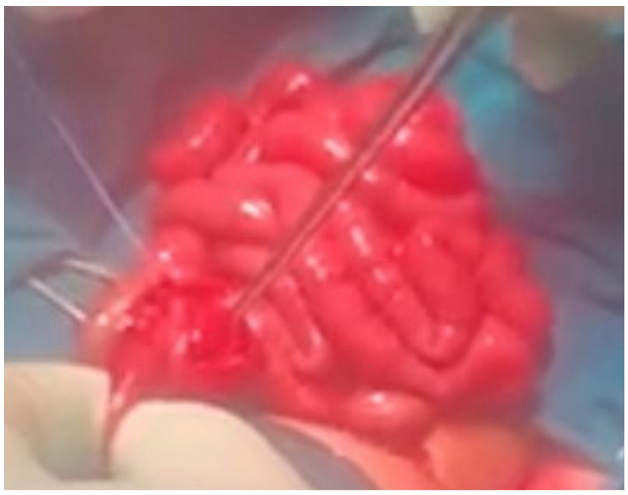

Figure 3. **Preoperative picture: Pyloric web**

tines. Symptoms of non bilious vomiting, a distended stomach and air noted distal to the stomach, dilute barium or soluble contrast is required for the diagnosis of an incomplete pyloric membrane. Treatment: Gastrotomy and distal passage of catheter may be required to detect membranous obstruction. Excision of a complete or partial diaphragm with Heineke-Mikulicz or Finney pyloroplasty is the procedure.

END NOTE

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Linezolid In Filariasis

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ABSTRACT

Two cases of filariasis responding well to the drug Linezolid are presented.

Keywords: Adenolymphangitis, Diethylcarbamazine, Linezolid, Lvermectin

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INTRODUCTION

Wuchereria bancroft is the common filarial parasite that infects humans in this part of the world. The thread-like adult parasites reside in lymphatic channels or lymph nodes. Adult worms can cause lymphatic dilatation and thickening of the vessel walls. Lymphoedema and chronic stasis changes occur as complications. These are due to the direct effect of worms and the inflammatory effect of the host on the parasite.[1,3] The inflammatory responses are believed to cause enhanced granulomatous reactions and fibrosis. Lymphatic obstruction results. Acute adenolymphangitis and chronic lymphatic disease are the two varieties of the disease.[2,4] Acute adenolymphangitis is characterized by high fever, lymphatic inflammation, and transient oedema. Linezolid is a synthetic Oxazolidinone antimicrobial drug, and it is indicated for gram-positive infections.

CASE HISTORY

Case 1

A 27-year-old lady presented with swelling of the distal part of her left leg for the past one week. She was a known case of filariasis and had an episode of pain and swelling in the left foot before, and that has subsided with a course of tablet Diethylcarbamazine.

Clinical examination showed swelling in the left foot mainly confined to the ankle and the lower end of the leg. There was little redness and mild tenderness.

A peripheral night blood smear and the tests for detection of antibodies were not done because she was a known case of filariasis. Doppler test was not done. Blood results of the tests done before treatment showed Hb 14 gm/ dL, WBC count-TLC 6200/cmm, DLC-P 64%, L 32%, E 4%, ESR 6 mm/hr, Random Blood sugar 122 mg/dL, Serum creatinine 0.8 mg/dL. There were no significant changes in the blood results of the tests done after treatment.

Case 2

A senior citizen aged 78 presented with body aches, feverishness, and mild chills for the past 2 weeks. He has been a known case of filariasis for the past 5 decades. He used to get chills and body aches frequently since the onset of the filarial infection, and every time these symptoms subsided with the drug Diethylcarbamazine. This time the symptoms do not subside with Diethylcarbamazine and with the drugs Albendazole and Ivermectin.

Clinical examination showed that he was febrile, and he had no swelling or tenderness in the legs. Routine blood examination did not show any leukocytosis or

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eosinophilia. The Widal test was normal. The blood culture did not grow any microorganisms. Peripheral night blood smear and indirect fluorescence test and Elisa test for detection of antibodies were not done because he was a known case of filariasis. A Doppler test was not done. Blood results of the tests done before treatment showed 13. 2 gm/dL, WBC TLC 5800/ cmm, DLC P 58%, L40%, E 2%; ESR 14mm/ hr, Random Blood sugar 134 mg/dL, Serum creatinine 1mg/ dL. There were no significant changes in the blood results of the tests done after treatment.

TREATMENT

These two patients were given Tablet Linezolid 600 mg twice daily for 7 days. Both of them had a dramatic recovery. All the symptoms, including the oedema, subsided completely after 7 days of treatment. None of them showed any side effects of the drug.

Follow up

Close observation for 6 months did not show any abnormality. They are perfectly alright.

DISCUSSION

Both patients were known cases of filariasis, and hence tests were not done to find microfilaria in the peripheral night blood or to detect antibodies. In the second case, bacterial infection was ruled out by the blood tests. The second case was a case of chronic filariasis. Because he was taking regularly Diethylcarbamazine, he did not develop oedema, and when it was developed, it was suppressed by medication. Diethylcarbamazine 2 mg/kg orally 3 times daily for 12 days or as a single dose, killed the adult worms. The repeated occurrence of fever was due to the direct effect of worms and the inflammatory effect of the host on the parasite. He has come to a stage where he became resistant to the drugs Diethylcarbamazine and the combination of the drugs Albendazole and Ivermectin. Linezolid is basically effective in skin and skin structure infections. It is thought that the drug acts on the lymphatic channels and the adult worms. This study is the first to show that Linezolid is effective in the treatment of filariasis. Further studies on the effect of Linezolid in filariasis are recommended with a large number of patients.

CONCLUSION

The drug Linezolid is found effective in filariasis, especially in resistant types of filarasis.

END NOTE

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CASE REPORT KERALA MEDICAL JOURNAL

A Rare Infectious Trigger for Acute Disseminated Encephalomyelitis

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ABSTRACT

Acute disseminated encephalomyelitis (ADEM) is an infrequent demyelinating disorder of the central nervous system precipitated by infections and immunizations. ADEM following scrub typhus infection is a rare manifestation. Here, we are reporting a case of ADEM triggered by Scrub Typhus infection.

Keywords: Scrub Typhus, ADEM

*See End Note for complete author details

INTRODUCTION

Neurological features accompany 20% of scrub typhus infections and may affect the central or peripheral nervous system and may even occur in combination. Multiple mechanisms underlie neurological involvement, including direct invasion (meningitis, encephalitis), vasculitis (myositis) or immune-mediated mechanisms (opsoclonus, myoclonus, optic neuritis, Guillain–Barre syndrome).[1] Scrub typhus infection is associated with a broad spectrum of neurological complications ranging from aseptic meningitis, meningoencephalitis, AIDP, multiple cranial nerve palsies, venous sinus thrombosis, transverse myelitis and cerebellitis. Acute disseminated encephalomyelitis [ADEM] is an immune-mediated demyelinating disorder affecting the brain and spine. Only a few cases of ADEM have been described in the literature. Chen et al. described a case of ADEM following scrub typhus infection with extensive periventricular white matter lesions.[2] We are reporting this case because of its rarity **(Figure 1).**

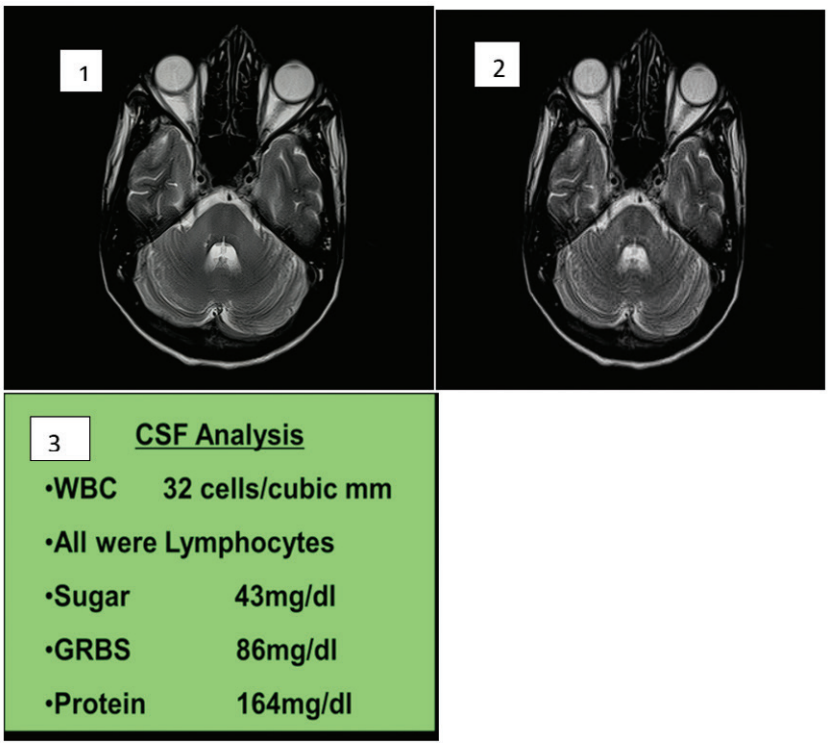

Figure 1. **MRI Brain suggestive of ADEM (Images 1&2); CSF Analysis (Image 3)**

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CASE REPORT

A 27 year male forest worker, an ethanolic, presented to the casualty with fever and myalgia of 7 days, followed by breathlessness and altered sensorium. He was referred from a local hospital as a case of short febrile illness with pseudo-hepato-renal dysfunction with pancreatitis. Because of oliguric acute kidney injury, haemodialysis was initiated. Workup for tropical fever syndrome revealed IgM Scrub Typhus ELISA as positive. Serology for dengue and leptospirosis was negative. Nasopharyngeal swab PCR was negative for influenza and SARS-CoV-2 infection. Three days later he progressed to hypoxaemia and became drowsy which necessitated endotracheal intubation and mechanical ventilation. Three days post-intubation, the patient developed flaccid quadriparesis. CSF study showed elevated protein with lymphocytic pleocytosis. Hypoglycorrhachia was absent. CSF neuroviral panel by Film array was negative. Serum ELISA for Hanta, Japanese encephalitis, West Nile and Kyasanur Forest Disease were negative. MRI BRAIN showed T2/FLAIR hyperintensities involving the periventricular, subcortical and deep white matter of frontal lobes bilaterally, middle cerebellar peduncle and posterior limb of the internal capsule with no diffusion restriction or enhancement, suggestive of ADEM. MRI Spine was normal. The patient was treated with intravenous methylprednisolone pulse for ADEM and a combination of intravenous doxycycline and azithromycin for scrub typhus infection. He was successfully weaned off the ventilator and his sensorium improved. Following the steroid pulse he regained upper limb power (grade 5/5) bilaterally in 5 days. Lower limb power remained grade 3/5 bilaterally initially. NCS showed features of critical illness polyneuropathy. He underwent nutritional and physical rehabilitation and completely recovered in 3 months.

CONCLUSION

Most common infectious triggers for ADEM are viral infections. Viral-induced autoimmunity can be activated through multiple mechanisms including molecular mimicry, epitope spreading and bystander activation. A bacterial infection like scrub typhus triggering ADEM is very rare and should be considered in endemic areas.

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Conflict of Interest: None declared

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CASE REPORT KERALA MEDICAL JOURNAL

Case of Bilateral Pheochromocytoma in a Young Female with VHL Mutation - A Glance into Novel Insights on Genetics of Pheochromocytoma

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ABSTRACT

Pheochromocytoma is a tumour of chromaffin cells arising in the adrenal medulla, for which genetic susceptibility is the only known causative factor. Here we describe a case of a 15-year-old girl who presented with hypertension and associated symptoms like headache and chest tightness lasting for nearly one month. On evaluation, she was found to have bilateral Pheochromocytoma, following which she underwent bilateral adrenalectomy and the diagnosis was confirmed by histopathology. Being a bilateral tumor we proceeded with further genetic studies. Clinical exome sequencing revealed a VHL gene mutation. Management of Pheochromocytoma Paraganglioma (PPGL) has now taken new turns which is based on molecular classification that groups them into three specific gene clusters based on underlying gene mutations, which have definite clinical, biochemical, imaging and prognostic significances. Molecular characterization of Pheochromocytoma hence becomes of utmost importance in the era of personalized patient management plans.

Keywords: Pheochromocytoma, VHL, Gene Clusters

*See End Note for complete author details

BACKGROUND

Pheochromocytoma is a tumour of chromaffin cells that arises in the adrenal medulla. It is important to recognize these tumours as they are rare causes of hypertension that can be surgically corrected. Genetic susceptibility is the only known causative factor for the development of this tumor[1] and nearly 70% of these have underlying gene mutations.[2] Many familial syndromes are also associated with the development of the same. Recent updates on molecular classification cluster these tumours into 3 groups which aid personalized patient management plans.[2–11]

CASE PRESENTATION

A 15-year-old girl presented with complaints of episodes of palpitations, breathlessness, chest tightness, and headache, followed by diaphoresis and a feeling of impending doom, altogether lasting for around 10 to 15 minutes. These symptoms would then resolve spontaneously. She had 8 to 10 such episodes each day, for nearly one month, by the time she was brought to the clinician. She also had a history of giddiness while getting up from bed. She didn't have any such symptoms in the past. She also didn't have any family history of young hypertension, premature CAD or CVA.

On evaluation, she was found to have hypertension, 180/100 mm of Hg and postural fall in BP. Her pulse rate was normal with regular rhythm. She did not have pallor/ plethora/ thyroid nodule/ galactorrhea/ or virilizing features. There were no lesions suggestive of neurofibromatosis or tuberous sclerosis. She had BMI of 24kg/m^2. All other systems were within normal limits. So, a clinical suspicion of Pheochromocytoma was made.

Routine blood investigations showed Hb-12.1gm/dl, a total count of 9600 cells/mm^3, N75L25. Renal function tests, liver function tests and serum electrolytes revealed normal study. Further, ECG, chest X-ray, and USG neck were done, which all turned out to be unremarkable. A CECT abdomen was done, which

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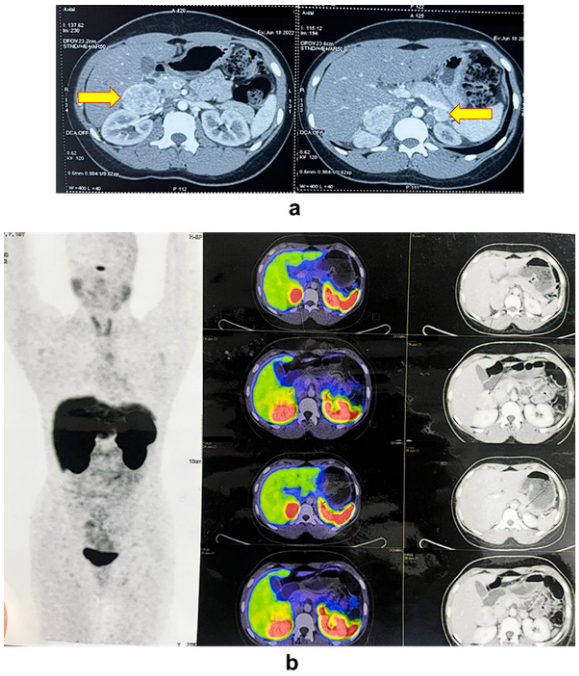

Figure 1. **a) CECT findings: Well circumscribed enhancing lesions in the right and left suprarenal regions. b) GA DOTATATE scan shows multiple somatostatin receptor expressing lesions in bilateral suprarenal regions**

showed two well-circumscribed lesions showing significant arterial phase enhancement in the suprarenal regions on both sides. On right side, lesions measured 4x3.9x3.9 cm and 4.2x4x2.9cm. On the left side, the lesions measured 2.4x2.5x1.7cm and 2.2x1.9x1.4cm. With the strong clinical suspicion of Pheochromocytoma, plasma metanephrine, normetanephrine, and 3 methoxy tyramine levels were assessed. She was found to have elevated plasma normetanephrine - 3720 ng/dl (normal-20-135 ng/dl) and 3 methoxy tyramine-272ng/dl (normal <18.4ng/dl), and normal metanephrine level. So further, a GA DOTATATE scan was done, which showed the Somatostatin receptor expressing multiple intensely enhancing lesions involving bilateral adrenal glands (R>L), see **Figure 4**. No similar foci were detected elsewhere in the body.

Considering bilateral Pheochromocytoma of adrenal location, producing normetanephrine, VHL mutation was the most likely possibility. Clinical exome sequencing was hence done, which confirmed VHL gene mutation. Our patient was also screened for other lesions coming under the spectrum of VHL mutation, all of which turned out to be negative. Any additional gene mutations was ruled out.

Our patient was planned for bilateral adrenalectomy. Preoperatively, she was started on alpha-blocker Prazosin and was also advised liberal salt intake.

Figure 2. **Adrenalectomy specimen: a) Right and b) Left.**

Metoprolol was added after 5 days. Preoperatively, pulse rate was 70/min and blood pressure was 120/80mm of Hg. Though laparoscopic adrenalectomy was planned since the patient had intraoperative bleeding and hypotension, right open adrenalectomy was done on 22/10/2022. Following adrenalectomy, she had intraoperative hypertension, which was managed with NTG (Nitroglycerin) injection. Blood pressure was controlled and left adrenalectomy was planned a few months later. On post-operative day 1, the patient had hypotension which was managed with IV fluids. The rest of the post-operative period was uneventful and she had partial remission of symptoms. A left adrenalectomy was done on 13/2/2023, following which the patient recovered nearly well.

Bilateral adrenalectomy specimens were received in the Department of Pathology at an interval of 3 and half months. We received two brown nodular masses from each side, lesions on the right side measuring 4x4x2.5 cm and 4x4x3 cm, and on the left side measuring 3.2x2.5x1.5cm and 2x1x1.5cm see **Figure 2.**

Microscopy from right side showed **(Figure 3)** a compressed adrenal cortex with a circumscribed

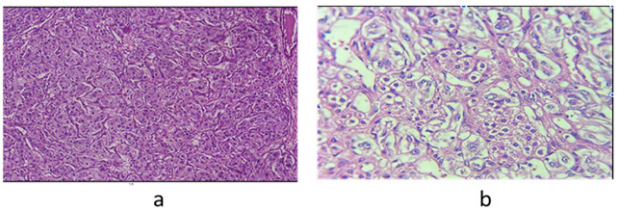

Figure 3. **a) Right adrenalectomy shows neoplasm arranged in zellballen pattern (100X) and b) Cells are round to oval with moderate amount of clear cytoplasm and vesicular nuclei (400X).**

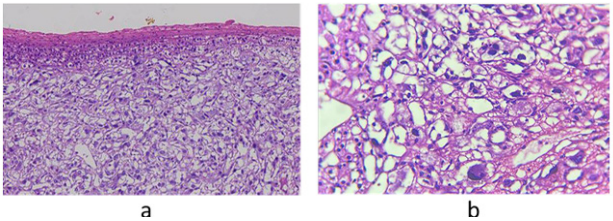

Figure 4. **a) Left adrenalectomy shows neoplasm arranged in diffuse sheets and b) Cells are pleomorphic with moderate to abundant clear cytoplasm and hyperchromatic nuclei, with occasional bizarre forms.**

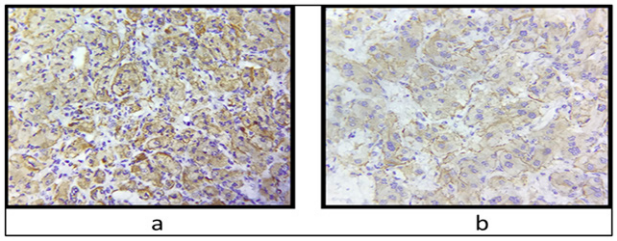

Figure 5. **Immunohistochemistry Synaptophysin : a) right and b) left**

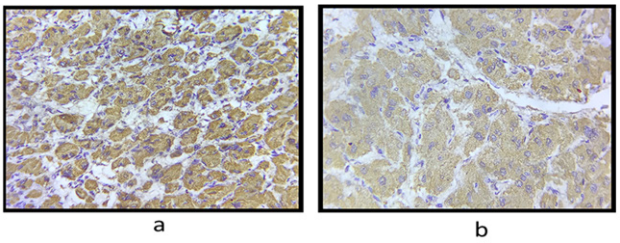

Figure 6. **Immunohistochemistry chromogranin: a) right and b) left.**

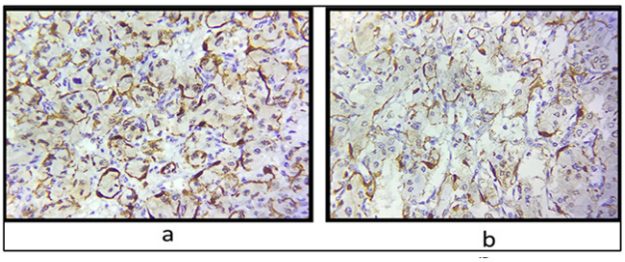

Figure 7. **Immunohistochemistry S100: a) right and b) left.**

neoplasm underneath, predominantly arranged in zellballen pattern. Individual cells were round to oval with a moderate amount of clear cytoplasm, and round vesicular nuclei. Microscopy from the left side showed **(Figure 4)** an encapsulated neoplasm arranged predominantly in sheets, with individual cells showing pleomorphism with moderate to abundant clear cytoplasm and pleomorphic hyperchromatic nuclei. Bizarre cells were also seen.

Immunohistochemistry was done in both lesions, which showed positivity for Synaptophysin and Chromogranin, and S100 highlighted the sustentacular cells. Ki67 was 5% on both sides **(Figures 5, 6 and 7)**. Diagnosis of bilateral Pheochromocytoma was hence confirmed.

DISCUSSION

Pheochromocytoma and Paraganglioma (PPGL) have the highest degree of heritability among all human tumors[11] and genetic susceptibility is the only known risk factor development of PPGL.[1] Nearly 70% of these have underlying genetic alterations and most frequent genes involved are RET, VHL, SDHB, SDHC, SDHD. Number of genetic syndromes have

Table 1. Tumors associated with subtypes of VHL (Von Hippel Lindau).

VHL subtypes	Tumors
TYPE 1	Hemangioblastoma, Renal cell Carcinoma
TYPE 2A	Hemangioblastoma, Pheochromocytoma
TYPE 2B	Hemangioblastoma, Renal Cell Carcinoma, Pheochromocytoma
TYPE 2C	Pheochromocytoma

Pheochromocytoma as its component, like MEN2, VHL, Neurofibromatosis-1 etc. Pheochromocytoma in the setting of VHL syndrome is normetanephrine producing and rarely dopamine producing.

VHL (Von Hippel Lindau) syndrome is an autosomal dominant cancer syndrome with many components, one of which is pheochromocytoma. It is divided into subtypes based on components present **(Table 1)**.[1] Our patient had only bilateral pheochromocytoma, so she falls to Type 2C. She neither had any other lesions nor a positive family history. In a study conducted by Kittah et al.,[12] out of the 1161 patients with Pheochromocytoma considered, 94 (8%) patients had bilateral disease. Family history was reported in 37% patients, and 18% patients had history of bilateral disease. Of the 75 patients with genetic disease, most had MEN2A (40.53%), followed by VHL (18.24%), MEN2B (9.12%) and NF1(8.11%).

As far as pathology of Pheochromocytoma is considered, a morphological diagnosis is not challenging and is often easily made. Pheochromocytoma in the setting of VHL mutation shows histopathological features like thick capsule, myxoid and hyalinized stroma, rich vascular network and clear cell change. They don't show medullary hyperplasia.[1]

Identification of specific underlying gene mutation becomes of utmost importance in current era because of the advent of precision medicine. An interesting advancement in this field is the characterization of the genetics of Pheochromocytoma and Paraganglioma (PPGL), which puts forward a potential molecular classification of PPGL based on the underlying gene mutations.[2–11] PPGL falls into 3 specific gene clusters, based on the gene mutations present. Cluster 1 involves genes of hypoxia signaling pathway and includes genes of Krebs citric acid cycle- mainly SDHB, SDHC, and SDHC in Cluster 1A and VHL and related genes in Cluster 1B. Cluster 2 involves genes of kinase signaling pathway like RET, MET, NF1. Cluster 3 involves genes of WNT signaling pathway. These three clusters have different clinical, biochemical and imaging signatures

Table 2. Gene clusters of Pheochromocytoma and Paraganglioma (PPGL)

	Cluster 1A	Cluster 1B	Cluster 2	Cluster 3
Gene	SDH x (SDHA, B, C, D, F2) FH, MDH2	VHL, EPAS1 (HIF2A), Sporadic noradrenergic	RET, NF1, MAX, TMEM127, HRAS, Sporadic noradrenergic	CSDE1, MAML3
Signalling pathways	Pseudo hypoxia (HIF-1a) & aberrant VEGF signaling		Kinase signaling: PI3 kinase/AKT, RAS/RAF/ERK, & mTorC1/p70S6K	Wnt signaling
Catecholamine type	Dopamine (DA), mixed DA & Noradrenaline	Noradrenaline	Adrenaline	Unknown
Tumour location	Extra-adrenal	Adrenal & Extra-adrenal	Adrenal	Adrenal
Age of presentation	Early (under 30 year-old)	Early	Late	Unknown
Imaging	[^{68}Ga]-DOTA-SSA PET/CT	[^{18}F]FDOPA PET/CT	[^{18}F]FDOPA PET/CT	Unknown
Metastatic risk by GAPP	Intermediate - High	Low - Intermediate	Low	High – intermediate

and also have different long-term prognosis. Features of three clusters are summarized in **Table 2.**

Clinical diagnosis in this case was not very challenging because of the classic spells and hypertension. Early age of onset in this case was as expected according to the cluster type. Further, Pheochromocytoma in this case was normetanephrine secreting which is in concordance with VHL mutation. GA DOTATATE scan was the imaging modality used, however, recent studies based on cluster identification advocates use of [^{18}F] FDOPA PET/CT scan superior to GA DOATATE scan. Cluster 1B shows both adrenal and extra adrenal locations of tumor, but in our case the patient had only bilateral adrenal tumor. Extra adrenal locations are associated most often with SDHB mutations. The patient needs long term close follow up as per the present consensus.[2]

Till date, she is symptomatically fine, except in stressful conditions like fever, where she takes more than normal time to recover to normalcy. Follow up MRI of brain and whole body showed no other lesions elsewhere. Considering the patient side, on comparing the advantages and disadvantages of partial against complete adrenalectomy, partial adrenalectomy was associated with higher risk of recurrence than total adrenalectomy. However, patients undergoing partial adrenalectomy had lower odds ratio of developing acute adrenal crisis as compared to the ones undergoing total adrenalectomy.[13] In a study that assessed the long-term outcome of surgical excision in children with pheochromocytoma, 26.7% patients recurred after the first operation. According to them, early diagnosis, surgical excision, and long term follow up are key to appropriate management of childhood Pheochromocytoma.[14]

However, considering the newer insights into the molecular signatures of morphologically similar Pheochromocytomas, development and availability of targeted drugs, which act at different levels of the genetic pathways involved in their tumorigenesis are much awaited, for a better and tailored patient management plan.

CONCLUSION

Our case was that of ya oung female who presented with hypertension and was found to have bilateral Pheochromocytoma. She was detected to have a VHL gene mutation (subtype 2C) and hence falls under Cluster 1B according to the new consensus of molecular classification based on underlying gene mutations. These molecular clusters are proven to have definite implications on the age of presentation, tumour location, catecholamine type, cell differentiation, malignant potential and genetic anticipation. Although targeted drugs are not yet available in our hospital settings, early identification, proper screening and molecular classification remain the cornerstone of future management strategy for Pheochromocytoma, which is precisely personalized.

END NOTE

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CASE REPORT KERALA MEDICAL JOURNAL

Malignant Melanoma of the Anal Canal - A Rare Case Report from a Tertiary Care Center in South India

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ABSTRACT

Anorectal melanoma is a rare entity that accounts for less than 1% of all anorectal malignancies. It is often mistaken for benign anorectal conditions since the symptoms resemble each other. The predominant symptoms of anorectal melanoma are per rectal bleeding, anorectal pain, mass per rectum, tenesmus and altered bowel habits. All suspected cases of anorectal malignancy should be subjected to sigmoido-colonoscopy and biopsy. Management of anorectal melanoma remains controversial including surgery, chemotherapy, radiotherapy and target therapy as treatment options. Surgical treatment is considered as the primary treatment modality for anorectal melanoma. Anorectal melanoma must be kept in mind as differential diagnosis for patients pesenting with per rectal bleeding and pain.

Keywords: Melanoma, Anorectum, Carcinoma, Abdominal perineal resection

*See End Note for complete author details

INTRODUCTION

Anorectal melanoma is a rare entity that accounts for less than 1% of all anorectal malignancies.[1,2] It is often mistaken for benign anorectal conditions since the symptoms resemble each other.[3] The predominant symptoms of anorectal melanoma are per rectal bleeding, mass per rectum, and altered bowel habits.[4] All suspected cases of anorectal malignancy should undergo sigmoido-colonoscopy and biopsy. Management of anorectal melanoma remains controversial including surgery, chemotherapy, radiotherapy and target therapy as treatment options. Surgical treatment is considered as the primary treatment modality for anorectal melanoma. We present the case of a patient who presented to the outpatient department of a tertiary care centre in south India.

CASE REPORT

61 year old lady presented with complaints of progressive constipation for the past 8 months. She gave history of passage of blood and mucus in stools and intermittent lower abdominal pain of 1 year duration. She complained of fatigue and significant weight loss in the past 6 months. On admission pulse rate was 80 beats per minute, blood pressure 130/80mm Hg. On examination pallor was present. Abdomen was soft and non distended without any palpable mass. Per rectal examination revealed a large, fleshy, firm mass along the six o clock to twelve o clock position in the distal rectum and anal canal. The lower limit of the mass was less than 1 cm from the anal verge and the proximal limit nearly 5cm from the anal verge. There was no blood staining. The anal sphincter was intact. There were no palpable inguinal lymph nodes. She was suspected to have malignancy involving the rectum and anal canal and evaluated with USG abdomen and CEMRI pelvis. CEMRI pelvis revealed a polypoidal lobulated mass measuring 4.6cm X 4.0cm X 7.4cm (AP X TR X CC) within the lumen of the rectum with the stalk being 4.6cm from the anal verge. Effacement of the rectal walls was noted. Significant invasion of the submucosa and muscularis propia at 9 o clock position was noted. Two lymph nodes measuring 0.5cm X 0.cm were seen in the right pararectal fossa with normal enhancement. Visceral pelvic fat, anal sphincters and pararectal fat was normal. USG abdomen was done to rule out liver

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Figure 1. **Colonoscopy images showing tumor at anorectal region**

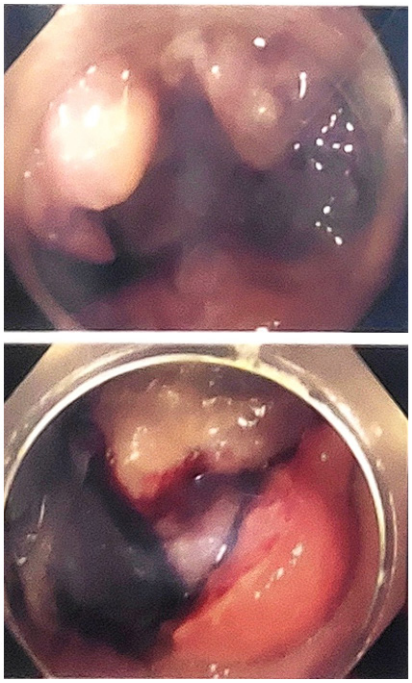

Figure 2. **Abdominoperineal resection specimen showing tumor at inferior end**

metastasis and ascites and it was reported as normal. She underwent colonoscopy **(Figure 1)** which revealed an ulceroproliferative mass extending from the anal canal into the rectum, likely to be malignant. Colonoscopic/colonoscopy guided biopsy was also taken. The biopsy was reported as spindle cell tumor/ gastrointestinal tumor (GIST) of the anal canal. IHC was strongly positive for CD117, suggestive of GIST. She was managed in consultation with Medical oncology team and planned for abdominal perineal resection. She underwent abdominal perineal resection **(Figure 2)** under general anesthesia. Intraoperatively the rectosigmoid was mobilised and descending colon divided midway via midline laparotomy approach. The rectum and anal canal were dissected via perineal approach. A highly friable fleshy growth arising from just above the posterior anal margin and extending cranially for a length of 7cm in contact with the right lateral wall was noted. The posterior vaginal wall was found in close contact with tumour. The descending colon, rectum and anal canal was delivered via the perineal wound. End colostomy was fashioned in the left iliac fossa. Postoperatively she was managed in the surgical ICU and subsequently in the high dependency unit with intravenous antibiotics, analgesics, and other supportive measures. She was started on oral diet on postoperative day 2 and colostomy was functional within 48 hours of surgery. Her condition gradually improved and she was discharged on post operative day ten after suture removal. Histopathology of the resected specimen showed 5cm X 4.5cm X 4cm lesion with spindle cells, coarse chromatin, irregular nuclear membrane and moderate cytoplasm. Brownish coarse pigment consistent with melanin was noted in occasional tumour cells. Surgical margins were uninvolved. 2 lymph nodes identified were uninvolved. Perineural and angiolymphatic invasion were absent. Immunohistochemistry was positive for CD 117 and S100 suggestive of spindle cell type of malignant melanoma of the anal canal. She was followed up on outpatient basis and surgical wounds had healed well. She has been advised PET scan to rule out metastases and follow up after 3 months.

DISCUSSION

The hindgut develops into the distal part of the transverse colon, descending colon, rectum and anal canal. The dentate line divides the anal canal into an upper and lower part and marks the junction between endoderm and ectoderm. At the dentate line the columnar epithelium of the upper anal canal changes into stratified squamous epithelium. Melanocytes are located in the squamous zone. Melanocytes originate from the neural crest and migrate towards the skin and other regions.[5,6]

The first case of malignant melanoma of the anorectum was reported by Moore in 1857.Since then nearly 500 cases have been reported till date.[7]

Cutaneous melanomas account for nearly 90% of all melanomas followed by retinal melanomas (5%), melanomas of unknown origin (2%) and mucosal melanomas(1%).[8] Mucosal melanomas occur in the

regions of head and neck(55%), anorectum (24%) and vulvovaginal areas (18%).[9] Anorectal melanomas are extremely rare and usually arise near the dentate line and can rarely be found in the distal ileum. They account for 0.5%-4% of all anorectal malignancies. It is the third most common primary melanoma after skin and retina.

The mean age of presentation is in the sixth decade of life.[10] It is more common in females than males.[11]

The predominant symptoms of anorectal melanoma are per rectal bleeding, anorectal pain, mass per rectum, tenesmus and altered bowel habits.[4] Pain occurs since most of the melanomas are located at or near the anal verge which is rich in nerve fibres. The most common presentation is per rectal bleeding. Most patients are asymptomatic in the early stages and especially more so in cases of amelanotic melanoma. Anorectal melanomas are frequently mistaken for hemorrhoids and other benign anorectal diseases due to its rarity.[3] Amelanotic melanomas maybe mistaken for lymphoma or sarcoma.[12] This leads to diagnostic dilemma and delay in the diagnosis.

All suspected cases of anorectal malignancy should undergo sigmoido-colonoscopy and biopsy to confirm the diagnosis and rule out any synchronous or metachronous lesions in the colon or anorectum.[13] Majority of the lesions are polypoid. They maybe ulcerated as well.[14] One third of anorectal melanomas are amelanotic.[12] CECT and MRI scan of the abdomen & pelvis help in staging the disease particularly if chemotherapy or radiation therapy are considered in the treatment.[15] Staging of anorectal melanomas differs from that of cutaneous melanomas (TNM STAGING).

PET scan has been used for staging cutaneous melanoma and maybe useful for staging anorectal melanomas as well.[16]

Immunohistochemistry plays a significant role in the diagnosis of anorectal melanomas. S-100 protein, HMB -45, Melan-A and tyrosinase are the commonly used stains positive for melanomas. Among these, melan A and HMB-45 are highly specific.[17-21]

Management of anorectal melanoma remains controversial including surgery, chemotherapy, radiotherapy and target therapy as treatment options. Surgical treatment is the primary treatment modality. However, standard operative procedures have not been established. Abdominoperineal resection was thought to be the standard treatment[22,23] with wide local excision gaining more attention.[23-25] Abdominoperineal resection offers the benefit of safe resection margins and lymphatic control. Wide local excision has advantages like less invasive procedure, faster recovery and absence of colostomy.

A study by Brady et al[22] in 1995 suggested that aggressive treatment with abdominoperineal resection had favourable outcomes. In recent years there has been a shift towards less radical procedures. According to the Yeh et al[26] study, there is no significant difference between patients treated with abdominoperineal resection and wide local excision.

Endoscopic mucosal resection has been performed by some surgeons with long term survival (>6years) achieved in several cases.[27]

Ramakrishnan et al showed that survival rates were better in patients who received wide local excision with radiotherapy when compared to patients who underwent surgery alone.

There has been no proven benefit of inguinal lymphadenectomy. Lymph node dissection maybe indicated in clinically apparent disease or for occult disease identified with sentinel lymph node.

Patients are often diagnosed at the late stages and require abdominoperineal resection as definitive or palliative procedure as in our case.

Anorectal melanoma has a very dismal prognosis with a 10-19 months survival after diagnosis.[22] One year survival rate is 21% and five year survival rate is 37%.

CONCLUSION

Malignant melanoma of the anorectum is extremely rare and accounts for less than 1% of all anorectal malignancies. It is often diagnosed in the late stages as it is easily mistaken for benign conditions of the anorectum. Anorectal melanoma should be kept in mind as differential diagnosis for patients presenting with per rectal bleeding and pain. Surgery is the mainstay of treatment with abdominoperoneal resection and wide local excision being commonly performed procedures for anorectal melanoma. Early diagnosis and radical surgery are key factors in prompt management of anorectal melanoma.

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Stereoscopic Visualization: A Novel Approach to Anatomy Teaching and Procedural Planning

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ABSTRACT

Traditional anatomy teaching in medical curricula, particularly in India, relies heavily on cadaveric dissection and two-dimensional diagrams. While these methods provide foundational knowledge, they fail to convey the intricate three-dimensional complexities necessary for understanding anatomical structures in the context of surgical and interventional procedures. Stereoscopic visualisation, which leverages binocular vision to simulate depth perception when adapted for medical education, offers a promising alternative by enhancing spatial understanding of anatomical structures.

The stereoscopic visualisation system, developed collaboratively by the Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) and Government Engineering College Barton Hill (GECBH), successfully provided 3D visualisations of patient anatomy, enhancing spatial understanding. Key features included real-time processing of CT and MRI data, the ability to visualise large groups simultaneously, and cost-effectiveness. The system allowed for direct visualisation of DICOM files without preprocessing and included customisable features such as windowing techniques and arbitrary plane sectioning. Users reported significant improvements in understanding complex anatomical relationships and planning surgical interventions. Additionally, the system was superior to cadaveric learning for certain visceral anatomies due to its ability to maintain anatomical orientation and spatial relationships. All this makes it a valuable tool in medical education and practice. Despite challenges such as the need for specific software, hardware, and a dark room setup, the system's benefits outweigh these limitations. Future improvements could enhance its capabilities and applicability in medical education and surgical precision. The system thus represents a significant advancement in leveraging stereoscopic technology to bridge the gap between traditional anatomy education and modern clinical requirements.

Keywords: Stereoscopic Visualisation, Anatomy Teaching, Surgical Planning, 3D Virtual Reality, Medical Education, Spatial Understanding

*See End Note for complete author details

INTRODUCTION

Traditionally anatomy has been taught during preclinical years of medical curriculum in India using cadaveric dissection and 2D diagrams. However, understanding anatomy's relevance in surgery and interventional procedures requires a deeper, three-dimensional comprehension. Each procedure (surgical or interventional) needs a unique plan due to the variability in patient anatomy. In a semi poetic statement it is often stated

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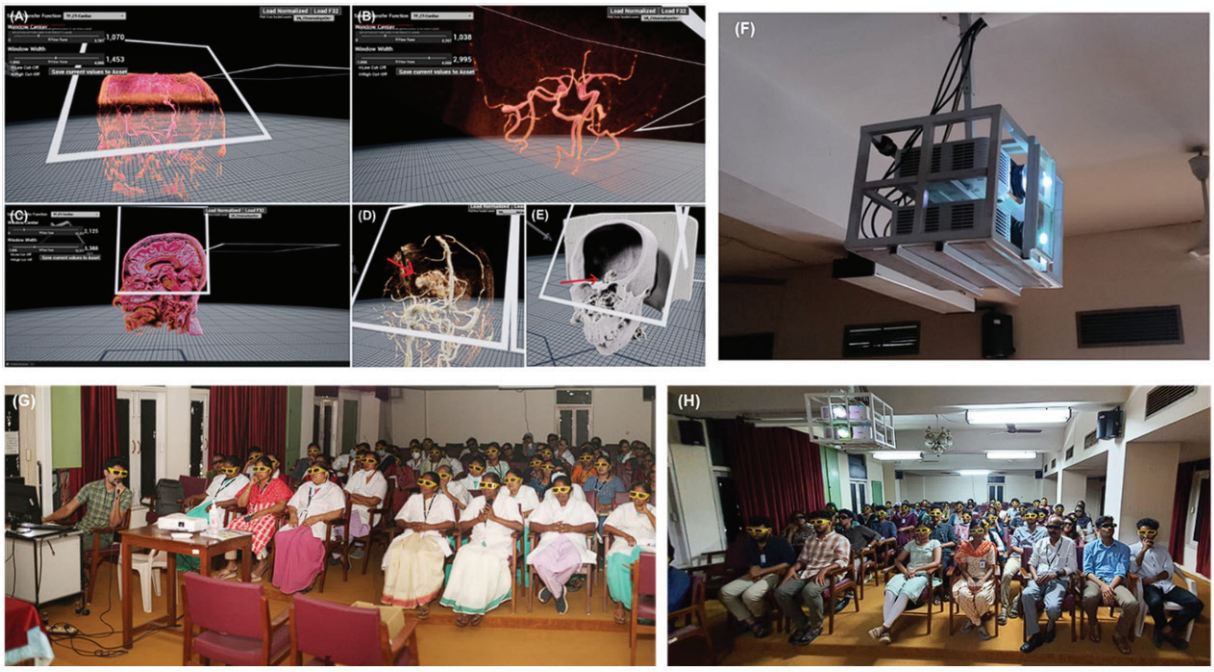

Figure 1. **Surgical planning system at SCTIMST: (A-E) Images of the renderings of different anatomical regions using the developed tool, (F) Photograph of 3D dual projector setup, and (G-H) clinicians and students viewing images using 3D glasses.**

that 'Anatomy is the war map for the operations of a physician".[1] Current imaging techniques often lack depth perception, which is crucial for spatial anatomical concepts, limiting effective procedural planning and cross communication among various disciplines of medicine (Physician, Radiologist and surgeon).

STEREOPSIS AND STEREOSCOPY

Stereopsis is the ability to perceive depth due to binocular vision, where each eye captures a slightly different image because of the location of the eye balls (interpupillary distance - 6 cm), so that the images falling on each of the retinae are slightly different (retinal/binocular disparity) and the brain merges these images in to a single three dimensional image with an illusion of depth.[2]

Stereoscopy replicates this by using two images with slight differences to create a 3D effect, enhancing the understanding of spatial relationships in anatomy. The term Stereoscopy is derived from Greek, where 'stereo' means solid and 'scopy' means to see. This technique which was widely used in the entertainment industry for making 3D movies, is now being used in medical education and procedural planning to provide detailed anatomical visualisation.

THE STEREOSCOPIC VISUALISATION SYSTEM

The system developed by SCTIMST and GECBH, a cost-effective, indigenous, student-built, 3D virtual reality system to aid anatomy teaching and surgical planning. The software part of the system is developed using a high-performance 3D game development tool. The entire software **(Figure 1A-1E)** is controlled using a customised handheld device. The system uses a dual projector setup (developed as part of an earlier project in collaboration with IIIT Hyderabad and SCTIMST[3,4] with two polarising lenses in front of each projector **(Figure 1B)**, each projecting an image of a slightly different perspective. The viewer wears a simple pair of polarised glasses **(Figure 1C)** to ultimately "cheat the brain" into perceiving a 3-dimensional image.

Unique features of include:

1. Stereoscopic Vision and 3D visualisation of patient data from CT or MRI
2. A larger group of audience can visualise at the same time
3. Direct visualization of DICOM files without pre-processing
4. Cost effective

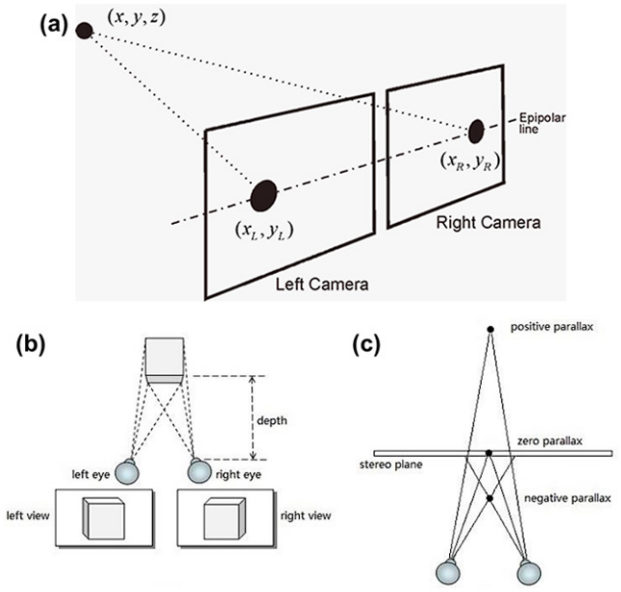

Figure 2. **Two cameras, acquiring images of the same scene, have two different 2D representations of a common 3D point. With proper processing, the position and depth of the 3D point can be extracted from the images.[5] B) Principles of stereoscopic 3D. (a) Binocular views. (b) Three types of horizontal parallax.[6]**

CAPABILITIES OF THE SYSTEM

The system processes CT data (plain or contrast) in the DICOM format (Digital Imaging and Communications in Medicine - A file format used in radiology for images) in no time generating 3D images visible through stereoscopy (which we call models) (See **Figure 2**) These models thus produced, can be tilted or rotated in any direction to change the view. They can also be sectioned through any arbitrary plane. This approach is distinct from the currently available graphic models in the market for anatomy teaching. Windowing techniques allow the visualisation of specific structures by adjusting the intensity values. Structures can be distinctly coloured based on intensity values for better differentiation.

POTENTIAL USES AND IMPLICATIONS

Teaching Anatomy:

Though traditional teaching methods in anatomy are time-tested, studies have shown that students often fail to translate their anatomical understanding in clinical practice.[7] This may be more relevant in the current era where use of clinical imaging has advanced exponentially. Stereoscopic visualisation tool could be an effective teaching aid for medical students due to its capability to provide an effective spatial understanding of anatomy and the correlation with radiological and surgical anatomy.[8] The 3D model in this technology is derived from actual patient data, which creates an "early clinical exposure" (ECE) to the preclinical phase students, which is what NMC currently recommends. Traditional anatomy teaching can be complemented with 3D visualisation thus training medical students in the early years itself. This will avoid unnecessary 'unlearning' and 'relearning' of anatomy that can occur in the future years of medical training; but rather students can "build upon" what they learn in preclinical years.

Alternative to Cadaver Scarcity:

Since cadaver/ specimen availability is poor in various medical colleges (especially in private medical institutes) 3D virtual models seen here can be used. This is also a more ethical alternative and cadavers can be channelled to more practical training like surgical approach, procedures and skill training.

Superior to Cadaveric Learning:

Certain visceral anatomy (eg. cardiac chambers), its orientation and relations can be better learned through this method than in a cadaver. The reason for this is that once the heart is removed from its in-situ position the "attitude" of the heart can never be recreated. Also once dissected, repositioning the tissues is also not possible in cadaveric anatomy learning. These advantages of 3D visualisation makes it a superior choice for learning the spatial anatomy of certain structures.

Paramedical and Allied Health Science Training:

Paramedical courses like nursing, medical lab technologists, cardiac perfusionists, occupational therapists etc. who do not require dissection in their curriculum, can make use of this tool for making the students understand the proper orientation as per their learning requirement.

E-learning Modules:

Though stereoscopy is not practical in e-learning modules, photographs and videos of the 3D model can be taken in a non-stereoscopic mode and learning modules can be created in the setting of a digital classroom. As Indian medical education is reviving its e-learning capabilities, this tool can have a significant impact.

Procedural Planning (surgical and interventional) and Management:

Adult/ Paediatric cardiac intervention and surgery: Three dimensional visualisation enhances the cardiologist/cardiac surgeon to understand complex anatomical substrates such as congenital heart disease

and structural heart disease. This is essential because most of the procedures are done using 2D fluoroscopic images by the cardiologist and 2D CT images will not give complete information regarding the morphology in complex congenital heart disease for corrective surgeries.

Vascular surgery and intervention: The technology allows the surgeons to visualise the abnormality in the vasculature such as congenital abnormalities, the origin and extent of stenosis, dissection, aneurysm etc in aortic and other great vessels and allows for planning of the types and size of stents, flow diverters etc. without additional imaging such as DSA.

Neurosurgery requires precise trajectory to the lesions to avoid injury to eloquent areas of the brain. This technology can allow for planning of the surgery in areas involving eloquent areas and also to avoid injury to vessels and preservation of cranial nerve function in complex neurovascular and skull based surgeries.

Postgraduate Training: The system has immense application in the teaching and training of postgraduate students from various discipline. Application of this system to their curriculum will help them to have better appreciation of the anatomy thereby improving their procedural skills also.

CHALLENGES

- Requires specific software and hardware.
- Needs skills to operate (which can be acquired by some training)
- May cause eye strain and discomfort for spectacle users.
- Requires a dark room setup.
- Initial setup cost can be high.
- Additional improvements needed for rendering certain tissues like brain.

FUTURE DIRECTIONS

This tool has immense potential in anatomy education and surgical planning, offering realistic and immersive environments. Further development can improve its efficacy and contribute significantly to medical education and practice.

CONCLUSION

Stereoscopic visualization, leveraging binocular vision to create 3D images, enhances anatomy teaching and surgical training. The SCTIMST system, with its dual projector setup and polarizing lenses, offers numerous advantages despite some challenges, with potential for further improvements to advance medical education and procedural precision.

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Breast Cancer in Kerala: Addressing the Concerns and Improving Outcomes

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ABSTRACT

Breast cancer is on the rise among women in Kerala, with a significant number of cases being diagnosed at a younger age compared to Western populations. This article discusses the challenges faced in early detection and management of breast cancer in Kerala, the limitations of relying on mammography for screening in younger women with dense breast tissue, and the potential benefits of clinical breast examinations as a cost-effective alternative. It also highlights the importance of proper management practices and the adoption of more intensive early detection methods to improve patient outcomes, reduce mortality, and enhance the quality of life for breast cancer patients.

Keywords: Breast Cancer, Kerala, Early Detection, Clinical Breast Examination, Breast Conservation, Sentinel Lymph Node Biopsy, Snehita Risk Calculator, Risk Stratification

*See End Note for complete author details

INTRODUCTION

Breast cancer is becoming an increasing concern in Kerala, with a significant number of patients being diagnosed at a younger age. Data from the Regional Cancer Centre (RCC) in Thiruvananthapuram indicates that around 50% of breast cancer patients in Kerala are under 50 years old, and 20% are diagnosed before the age of 40. This is in contrast to high-income countries, where the majority of breast cancer cases are found in women over 60 years old. This younger age profile of breast cancer patients in Kerala presents unique challenges in both the detection and management of the disease, highlighting the need for a tailored approach to breast cancer care in the region.[1-3]

Early Detection: Challenges and Strategies

The cure rate for breast cancer when detected early exceeds 90%, with outcomes in Kerala comparable to or even better than those in high-income countries. However, the majority of women in Kerala present with advanced-stage disease, leading to a high mortality rate, with nearly 50% of patients succumbing to the disease. This tragic situation often results in the loss of young mothers in the prime of their lives, leaving behind orphaned children. The absence of an effective system for early detection and management is a key contributor to this unfortunate scenario.[4,5]

In Western countries, screening mammograms are an integral part of early detection strategies. However, the effectiveness of mammography in younger women, particularly those with dense breast tissue, is limited. In Kerala, where a significant proportion of breast cancer patients are younger, mammograms are likely to miss early lesions, making them a less reliable screening tool.

A more appropriate approach to early detection in Kerala would be the implementation of routine clinical breast examinations (CBE) by trained healthcare providers. A simple, cost-effective method, CBE can detect breast lumps at an early stage, significantly improving the chances of cure. An expert clinician can detect lumps as small as 1 cm, with a cure rate exceeding 90%. Regular CBE for all women over 30 years of age, every 6 to 12 months, by trained volunteers could detect lesions below 2 cm, potentially

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saving up to 80% of patients and dramatically reducing the current mortality rate.[6]

Moreover, it is crucial to ensure that at least female general practitioners and gynecologists are trained in performing proper CBE. These healthcare providers should consider opportunistic CBE for all women 30 years and above, and particularly for high-risk women starting at 25 years of age. This proactive approach can significantly enhance early detection efforts, especially in a population where the risk of breast cancer manifests at a younger age.[7,8]

In addition to CBE, more intensive early detection methods should be adopted, particularly for high-risk groups. This includes beginning CBE at an earlier age and increasing the frequency of examinations. For those with a family history of breast, ovarian, pancreatic, or prostate cancer, appropriate imaging methods such as MRI breast may be utilized. The Snehita risk calculator (available at snehita.in) can also be employed to identify individuals who may require more intensive early detection strategies, ensuring that those at high risk receive the attention they need.[9,10]

Proper Management: Key to Improved Outcomes

Early detection alone is insufficient to improve breast cancer outcomes. Patients must also receive appropriate and effective management to ensure the best possible outcomes. Several practices in the management of breast cancer can be optimized to avoid unnecessary procedures and ensure that patients receive the most effective treatment:

- **Avoidance of Unnecessary Investigations:** Unnecessary investigations, such as PET, should be avoided in early-stage cases, and MRI shouldn't be used except for specific indications. Patients often spend significant amounts on these investigations, leaving insufficient funds for essential treatments like surgery.
- **Core Biopsy Over Excision Biopsy:** Breast cancer should be diagnosed using a core biopsy prior to surgery, which is feasible in over 95% of cases. This approach avoids unnecessary excision biopsies and ensures accurate diagnosis before surgical intervention.
- **Sentinel Lymph Node Biopsy (SLNB):** SLNB should be preferred over complete axillary clearance in appropriate cases. This practice reduces the risk of lymphedema and improves the patient's quality of life.
- **Breast Conservation Surgery:** Total mastectomy should be avoided in cases where breast conservation surgery would suffice. Breast conservation, when combined with margin-negative surgery and oncoplasty, offers equivalent oncological outcomes with better cosmetic results.[11]
- **Judicious Use of Adjuvant Therapy:** Adjuvant therapies should be used judiciously. The decision to use such therapies should be based on individual patient factors and the biology of the disease.

Additionally, surgery remains the cornerstone of breast cancer treatment and is the primary determinant of cure. Ensuring that surgeons are trained in performing margin-free excision of breast lumps with minimal margins, sentinel lymph node biopsy, and breast oncoplasty is imperative. These skills are critical for achieving oncologically safe surgeries while also optimizing cosmetic outcomes, thereby significantly enhancing the patient's quality of life.[12]

To assist in clinical decision-making and to educate patients about their treatment options, tools like Predict UK (accessible at predict.nhs.uk) can be invaluable. Predict UK is a prognostic model that helps clinicians and patients understand the likely benefits of different treatment options based on individual patient characteristics and tumour biology, allowing for more informed and personalized treatment decisions.[13]

CONCLUSION

The public needs to be better informed about the importance of early detection and proper management of breast cancer. This can only be achieved if general practitioners and non-oncology specialists are aware about the benefits of clinical breast examinations for early detection and the principles of proper initial surgery. Moreover, the adoption of more intensive early detection methods, such as CBE at an earlier age and more frequent intervals, along with appropriate imaging for high-risk individuals, can further reduce mortality rates. The Snehita risk calculator (https://snehita.in/risk) offers a valuable tool to identify those who may require these intensified strategies, while Predict UK (predict.nhs.uk) serves as an important resource for both clinicians and patients in making informed treatment decisions. The three major factors determining the cure in early breast cancer are early detection, the biology of the disease, and the quality of the initial curative surgery. Proper adjuvant therapy and appropriate follow-up are also crucial in ensuring

long-term survival and quality of life for breast cancer patients in Kerala. By addressing these concerns, we can significantly reduce breast cancer mortality and improve the lives of women in Kerala.

END NOTE

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MEDICAL PHILATELY-32

Diabetes Mellitus: Tasting to Testing and Treatment - Part 2

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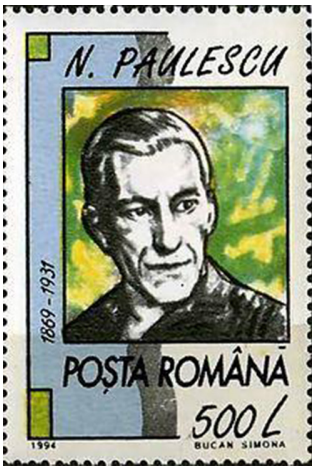
The discovery of insulin stands as a remarkable milestone, not only in medicine but also in the history of humanity. For children with type 1 diabetes, who are unable to produce insulin, survival was once limited to mere weeks or months. For them, insulin is far more than just a medication—it is a lifeline.

Anniversaries of the discovery of insulin are celebrated on postage stamps around the world. To commemorate the 50th year, a stamp issued by Canada in 1971 depicts the laboratory materials used by Banting and Best.

One hundred years of discovery of insulin by Banting and Best was commemorated by their native country Canada with a stamp, displaying the image of a vial of Insulin-Toronto, produced by Connaught Lab in 1924; and of an excerpt of Banting's handwritten memoir. The newspaper report of the momentous day can be seen on the Pakistani stamp along with the picture of Banting and Best.



Unfortunatley, the work of Romanian scientist **Nicolae Paulescu** (1869-1931) in the discovery of insulin is not well recognised. In 1921 Paulescu (1869-1931) isolated a substance from pancreatic islets which he called 'pancreine' and discovered that its injection induced hypoglycaemia in dogs. Despite the fact that Paulescu published his findings, he failed to get adequate recognition.

MAS PRODUCTION OF INSULIN

In the next year itself Lilly's Pharmaceuticals started its industrial production and marketing of insulin. Lilly's insulin was made from pork pancreas and was called

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iletin. For many years slaughterhouse pigs were the only source of insulin.

Nobel laureate, **August Krogh** (1874-1949), who had met with Banting and Macleod in Toronto, became actively involved in the ongoing development of insulin. August Krogh and his wife Marie brought insulin to Denmark. Together with Hans Hagedorn the Kroghs founded Nordisk Insulin laboratorium in 1923. Hans Hagedorn later developed the long acting NPH insulin.

THE STRUCTURE OF INSULIN

The primary structure of insulin, which consisted of two amino acid chains linked by two disulfide bonds, was only established in the early 1950's by the British biochemist **Frederick Sanger.** His work on insulin enabled chemists to synthesize insulin artificially.

British chemist, **Dorothy Hodgkin** (1910-1994) developed X-ray crystallography at Oxford, the technique she then used in 1969 for defining the complete three-dimensional structure of insulin. American **Rosalyn Yalow**(1921-2011) developed the radioimmunoassay method, using insulin, which, at that time, was the only purified and adequately characterized protein available. She also found that patients treated with insulin developed insulin antibodies.

Insulin crystals are depicted on stamps issued by Denmark as part of the 50th anniversary of the Danish Diabetic Association and on Japanese stamp as part of the 15th International Diabetic Congress.

Gerty Radnitz Cori (1896-1957) and her husband **Carl Cori** (1896-1984) clarified the biochemical reactions involved in the glucose-glycogen inter conversion now known as the Cori cycle. The treatment of diabetes is based partly on understanding the disposition of stored liver glycogen the source of glucose.

GLUCOMETERS

A blood glucose meter is a small, portable machine that's used to measure the blood glucose level. People

with diabetes often use a blood glucose meter to help them manage their condition.

PREVENTION OF COMPLICATIONS

Diabetes is a growing threat to human health, affecting around 463 million people worldwide. A normal life expectancy is possible for any diabetic if diagnosed early and treated properly. But if diagnosed too late or not treated properly, it can lead to serious complications. Dominican Republic 1974 Anti Diabetes stamps depict an eye, a heart and a kidney which are the organs commonly affected in diabetes.

Diabetes is one of the leading causes of heart attack and stroke. Diabetes affects the blood vessels in the eyes and causes loss of vision. Austria 1979 stamp on World Congress of Diabetes Federation features diabetic retinopathy and the Aruba stamp has a patient having stroke.

Diabetes complications can include nerve damage and poor blood circulation. These problems make the feet vulnerable to skin ulcers that can worsen quickly. Good diabetes management and regular foot care help prevent severe foot sores that are difficult to treat and may require amputation.

Bernado Houssay was an Argentinean physiologist who showed that pituitary ablation in dog normalized its blood glucose. He won a Nobel Prize for this finding. Before the advent of laser, pituitary ablation was used in selected patients to treat proliferative diabetic retinopathy.

WORLD DIABETES DAY

World Diabetes Day is the primary global awareness campaign focusing on diabetes mellitus and is held on 14 November each year.. the day itself marks the birthday of Frederick Banting.

World Diabetes Day provides an opportunity to raise awareness of diabetes as a global public health issue and what needs to be done, collectively and individually, for better prevention, diagnosis and management of the condition. The World Diabetes Day logo is the blue circle – the global symbol for diabetes as seen in the Uruguay stamp.

Brazil marked World Diabetes Day in 1992 with a stamp displaying a stylized hummingbird, with a tail that represents Clinistix.

Keeping weight in check, being active, eating a healthy diet and taking the right treatment can help prevent most of the complications of diabetes. All these steps are depicted in the two stamps issued by Cabo Verde.

END NOTE

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To be continued…

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4. Does the work appear to be original or does it appear like a copy of some existing literature. Provide relevant references.
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8. Was the study ethical, irrespective of ethics committee/IRB clearance?
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15. Is the abstract and keywords in agreement with the full text of the study?
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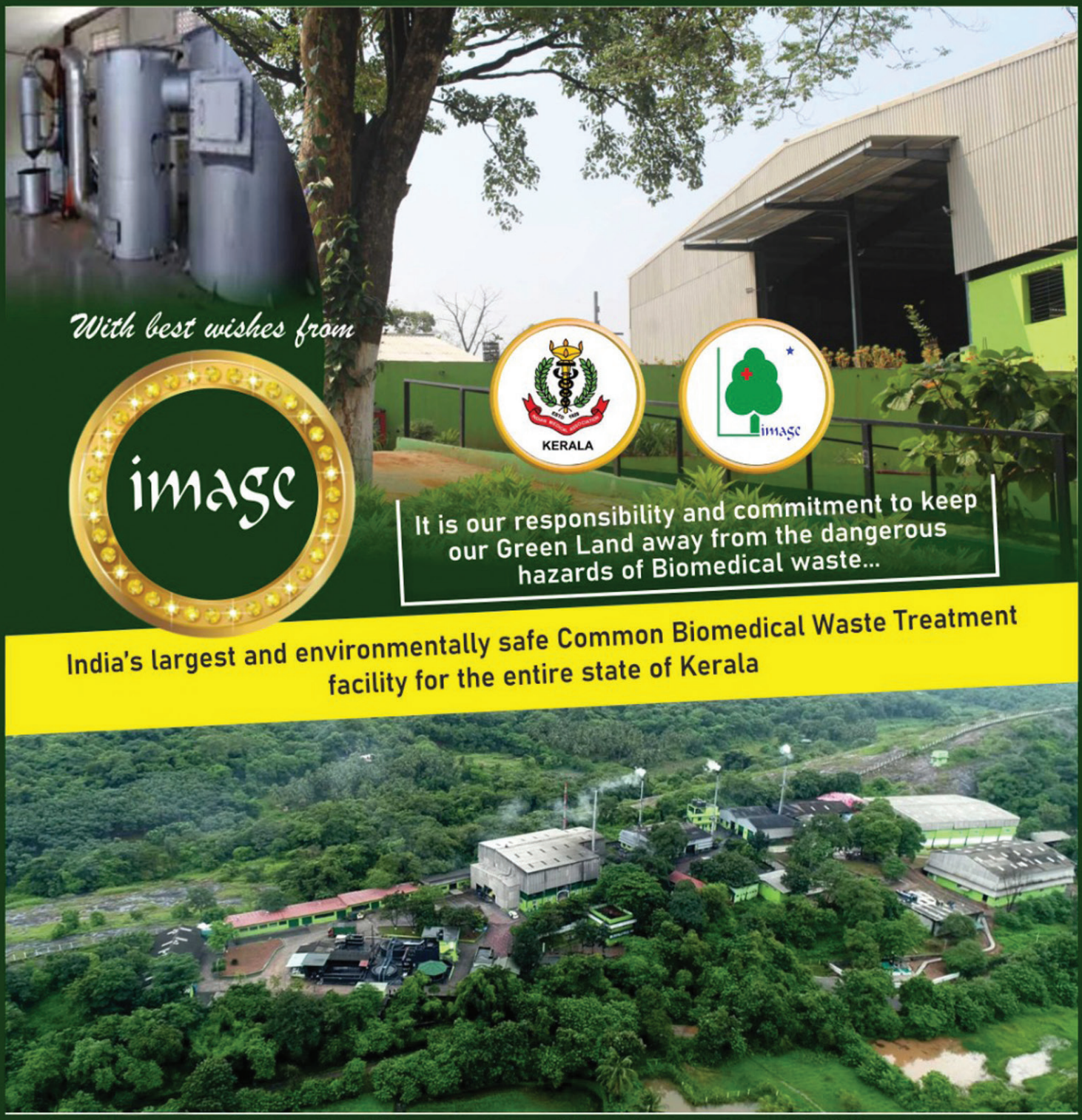

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