



INTERNATIONAL JOURNAL FOR GYNECOLOGY AND PEDIATRICS RESEARCH

● VOLUME 1, ISSUE 1, 2025

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Telemedicine for Chronic Disease Management in Rural India: An Observational Study on Glycemic Control and Patient Adherence Among Diabetic Patients.

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Abstract:

Rural India faces persistent healthcare access barriers due to infrastructure deficits and geographic isolation. This observational study investigates the impact of online doctor consultations (telemedicine) on healthcare access and utilization from 2019 to 2024, analyzing data from national telehealth initiatives like eSanjeevani and published research. Results indicate a substantial increase in consultation volumes, particularly among women and elderly patients, and improved care continuity. However, challenges including technological limitations, low digital literacy, and system integration hurdles were identified. The study recommends enhanced infrastructure, targeted training programs, seamless healthcare system integration, and supportive policy frameworks to maximize telemedicine's effectiveness in improving rural healthcare delivery.

Keywords: Telemedicine, Rural India, eSanjeevani, Healthcare Access, Digital Health.

Introduction:

India, a nation of over 1.4 billion people, presents a complex tapestry of healthcare access, marked by stark disparities between its urban and rural populations. While urban centers boast advanced medical facilities and a concentration of healthcare professionals, rural and underserved communities face formidable challenges in accessing even basic healthcare services. This divide, deeply rooted in geographical isolation, infrastructural deficiencies, and socioeconomic inequalities, has historically resulted in compromised health outcomes and a significant burden of preventable diseases. The urgency to bridge this healthcare gap has become increasingly evident, particularly in light of the evolving healthcare landscape and the transformative potential of digital technologies. The persistent challenges facing rural healthcare in India are multifaceted. Firstly, the shortage of qualified healthcare professionals in rural areas remains a critical concern. The reluctance of doctors and specialists to practice in remote regions, coupled with inadequate infrastructure and limited career opportunities,

contributes to this scarcity. This translates into long wait times, limited access to specialist care, and a reliance on unqualified or untrained practitioners, often leading to misdiagnosis and delayed treatment. Secondly, infrastructural limitations, including poorly equipped healthcare facilities, unreliable electricity supply, and inadequate transportation networks, further exacerbate the challenges. The vast distances separating rural communities from healthcare centers, combined with the lack of reliable transport, often deter individuals from seeking timely medical attention. This is particularly critical in emergency situations, where delays can have life-threatening consequences. Thirdly, socioeconomic factors, such as poverty, illiteracy, and cultural barriers, play a significant role in shaping healthcare access and utilization. Financial constraints often prevent individuals from seeking medical care, while low levels of health literacy and cultural beliefs can hinder the adoption of modern medical practices. The advent of digital technologies, particularly the internet and mobile telephony, has opened new avenues for addressing these disparities. Telemedicine, specifically online doctor consultations, has emerged as a promising strategy to overcome geographical barriers and deliver quality healthcare services to remote populations. By leveraging digital platforms, patients can connect with doctors remotely, receive consultations, obtain prescriptions, and access specialist care without the need for physical travel. This approach holds immense potential for improving healthcare access, enhancing patient outcomes, and reducing the burden on the already strained healthcare system. In India, the government has recognized the transformative potential of telemedicine and has launched several initiatives to promote its adoption. The eSanjeevani platform, a national telemedicine service, stands as a testament to this commitment. This initiative has facilitated millions of online consultations, particularly during the COVID-19 pandemic, demonstrating its efficacy in delivering healthcare services to remote areas. However, despite these advancements, the widespread adoption of telemedicine in rural India faces several challenges. Firstly, the digital divide, characterized by limited internet connectivity and low digital literacy, poses a significant obstacle. Many rural communities lack access to reliable internet services, and a significant portion of the population lacks the necessary digital skills to utilize telemedicine platforms effectively. Secondly, infrastructural limitations, such as the lack of computers, smartphones, and reliable power supply, further restrict the accessibility of telemedicine services. Thirdly, the integration of telemedicine into the existing healthcare system presents a complex challenge. Ensuring seamless communication and data exchange between online and offline healthcare providers is crucial for providing comprehensive and coordinated care. Moreover, addressing concerns related to data privacy, security, and ethical considerations is essential for building trust and ensuring the long-term sustainability of telemedicine initiatives.

Materials and Methods

This observational study employed a retrospective, synthetic analysis of secondary data to assess the impact of online doctor consultations on healthcare access and utilization among rural and underserved populations in India. The study period spanned from 2009 to 2010, allowing for the examination of trends and changes in telemedicine adoption over time, including the significant impact of the COVID-19 pandemic.

Data Sources: The study utilized a comprehensive approach to data collection, drawing from multiple sources to ensure a robust and multifaceted analysis. These sources included:

1. **Official Government Records:** Data from the eSanjeevani platform, a national telemedicine initiative, provided detailed information on the volume of teleconsultations, patient demographics (age, gender, location), and the types of medical services provided. These records offered a direct measure of telemedicine utilization within the government-led program.
2. **Government Reports:** Reports published by the Ministry of Health and Family Welfare (MoHFW, 2025) were analyzed to gather data on national healthcare policies, infrastructure development related to telemedicine, and overall healthcare access trends in rural areas.
3. **Telecom Surveys:** Surveys conducted by the Ministry of Communications (MoC, 2024) provided insights into internet and mobile phone penetration rates in rural India, crucial for understanding the digital infrastructure supporting telemedicine adoption.
4. **Peer-Reviewed Academic Literature:** A comprehensive review of peer-reviewed research articles (e.g., Mohan et al., 2012; Verma et al., 2023) was conducted to identify relevant studies on telemedicine in India, including its impact on healthcare access, utilization, and patient outcomes. These studies contributed to a broader understanding of the context and challenges associated with telemedicine implementation.

Data Extraction and Analysis: Data were extracted from the identified sources, focusing on key metrics relevant to the study's objectives. These metrics included:

- **Volume of Teleconsultations:** The total number of online doctor consultations provided through eSanjeevani and other telemedicine platforms, analyzed to assess the overall utilization of telemedicine services.
- **Demographic Trends:** Analysis of patient demographics, including age, gender, and geographical location, to identify patterns in telemedicine utilization among different population subgroups.
- **Reported Health Outcomes:** Data on patient health outcomes, such as changes in disease management, adherence to treatment plans, and satisfaction with telemedicine services, were extracted from available sources.
- **Internet and Mobile Phone Penetration:** Data on internet and mobile phone access in rural areas, to assess the digital infrastructure available for telemedicine implementation.
- **Infrastructure Development:** Data regarding governmental investment in infrastructure for telemedicine.
- **Policy changes:** Data regarding policy changes related to telemedicine.

Analytical Methods: The study employed a combination of descriptive and comparative analysis methods to examine the collected data.

- **Descriptive Analysis:** Descriptive statistics, including frequencies, percentages, and means, were used to summarize and describe the key metrics related to telemedicine utilization, demographics, and health outcomes.

- **Comparative Analysis:** Comparative analysis was conducted to examine trends in telemedicine utilization over time and to compare healthcare access and utilization between different rural regions and demographic groups. This involved looking at changes in consultation rates, patient demographics, and reported health outcomes.
- **Trend Analysis:** Trend analysis was conducted to identify patterns and changes in telemedicine utilization over the study period, helping to assess the impact of specific interventions or policy changes.
- **Qualitative Synthesis:** A qualitative synthesis of the peer-reviewed literature was conducted to provide contextual understanding and supplement the quantitative data.

Evaluation of Effectiveness: The effectiveness of telemedicine interventions in improving healthcare access for rural populations was evaluated by examining changes in the volume of teleconsultations, the demographics of patients utilizing telemedicine services, and reported improvements in health outcomes. The study also considered the challenges and barriers to telemedicine adoption, such as digital literacy gaps and infrastructural limitations, to provide a comprehensive assessment of its effectiveness.

Results;

The analysis of secondary data revealed a substantial increase in telemedicine utilization in rural India, particularly following the launch of the eSanjeevani platform in 2019. By early 2020, the platform had facilitated over 338 million consultations (Ministry of Health and Family Welfare, 2025), demonstrating a significant uptake of telemedicine services.

Demographic Trends:

- A detailed examination of user demographics indicated that women constituted a significant majority of teleconsultation participants, accounting for 56% of all consultations.
- Senior citizens represented 13% of the user base, highlighting the role of telemedicine in enhancing healthcare access for the elderly population.
- These results demonstrate a positive impact on reducing access barriers for traditionally underserved demographics.

Clinical Applications:

- The primary focus of teleconsultations was on the management of chronic illnesses, including hypertension, diabetes, and dermatological conditions, as well as paediatric care (Vaidya et al., 2024; Singh et al., 2024).
- The Chunampet Rural Diabetes Prevention Project, as documented by Mohan et al. (2012), provided evidence of improved glycaemic control and a reduction in referrals to higher healthcare centers through telemedicine interventions.

Satisfaction and Effectiveness:

- Patient and healthcare provider satisfaction rates were consistently high, exceeding 80% (centresya & Rai, 2016). This indicates a positive perception of telemedicine's effectiveness in rural settings.
- The high consultation numbers indicate high usage of the services provided.
- The data indicates that telemedicine is being used for chronic care, which is very important for rural populations.

Conclusion

This study demonstrates that online doctor consultations, particularly through platforms like eSanjeevani, have significantly transformed healthcare access and utilization in rural India. By bridging the geographical divide and connecting rural patients with healthcare professionals, telemedicine has effectively reduced the burden of long-distance travel, facilitated timely access to medical care, and enhanced participation among marginalized groups, including women and the elderly. The results presented herein underscore the efficacy of digital health solutions in addressing the unique healthcare challenges faced by rural populations, especially in the management of chronic diseases. The substantial volume of teleconsultations, coupled with high patient and provider satisfaction rates, provides compelling evidence of telemedicine's positive impact. Furthermore, the observed improvements in glycaemic control and reduced referrals in the Chunampet Rural Diabetes Prevention Project highlight the clinical benefits of this approach.

However, to fully realize the transformative potential of telemedicine and ensure its long-term sustainability, strategic investments and targeted interventions are crucial. This includes:

- **Infrastructure Development:** Strengthening digital infrastructure in rural areas by improving internet connectivity and ensuring reliable access to digital devices.
- **Digital Literacy Enhancement:** Implementing programs to enhance digital literacy among rural populations, enabling them to effectively utilize telemedicine services.
- **System Integration:** Ensuring seamless integration of telemedicine platforms with existing local healthcare systems to facilitate coordinated and comprehensive care.
- **Policy Support:** Developing and implementing supportive policies that promote the adoption and scaling of telemedicine initiatives.

As India progresses towards achieving universal health coverage, telemedicine emerges as a scalable and replicable solution that can significantly enhance healthcare delivery for underserved populations. By addressing the identified challenges and leveraging the demonstrated benefits, India can harness the power of digital health to bridge the healthcare divide and improve the health outcomes of its rural citizens.

Discussion

The findings of this observational study highlight the significant impact of online doctor consultations, particularly through the eSanjeevani platform, on healthcare access and utilization in rural India. The substantial increase in teleconsultations, reaching over 338 million by early 2025, underscores the growing acceptance and reliance on telemedicine as a viable healthcare delivery model in underserved areas. This surge in utilization can be attributed to several factors, including the reduction of geographical barriers, the convenience of remote consultations, and the increasing availability of digital infrastructure. The demographic analysis revealed a notable trend of increased participation among women and the elderly. The fact that women accounted for 56% of teleconsultations suggests that telemedicine addresses specific barriers they face in accessing traditional healthcare, such as mobility constraints and socio-cultural restrictions. Similarly, the 13% representation of senior citizens highlights telemedicine's potential to improve access for a population often burdened by chronic illnesses and limited mobility. This underscores the potential of telemedicine to address health equity. The focus of teleconsultations on managing chronic illnesses, such as hypertension, diabetes, and dermatological conditions, aligns with the growing burden of non-communicable diseases in rural India. The observed improvements in glycaemic control in the Chunampet Rural Diabetes Prevention Project demonstrate the clinical effectiveness of telemedicine in chronic disease management. Furthermore, the high patient and provider satisfaction rates indicate that telemedicine services are perceived as valuable and effective. However, despite these positive outcomes, several challenges remain. The need for improved infrastructure, expanded digital literacy, and seamless integration with existing healthcare systems is crucial for the long-term sustainability of telemedicine initiatives. The digital divide, characterized by limited internet connectivity and low digital literacy, continues to be a significant barrier. Addressing this requires targeted interventions, such as investing in broadband infrastructure, providing digital literacy training, and developing user-friendly telemedicine platforms. Integrating telemedicine into the existing healthcare system is another critical challenge. Ensuring seamless communication and data exchange between online and offline healthcare providers is essential for providing coordinated and comprehensive care. This requires the development of interoperable electronic health records (EHRs) and the establishment of clear protocols for referrals and follow-up care. The study's limitations, primarily stemming from its reliance on secondary data, should be acknowledged. Potential biases in data collection and reporting from different sources could affect the accuracy and generalizability of the findings. Future research should consider conducting primary data collection through surveys and interviews to gain a deeper understanding of patient and provider experiences. Furthermore, future studies should investigate the cost-effectiveness of telemedicine interventions in rural India. While this study demonstrates the positive impact on access and utilization, a comprehensive economic evaluation is needed to inform policy decisions regarding resource allocation and investment. The results of this study have significant implications for policymakers and healthcare providers. As India strives to achieve universal health coverage, telemedicine offers a promising avenue for improving healthcare access and equity. By addressing the identified challenges and leveraging the demonstrated benefits, India can harness the power of digital health to bridge the healthcare divide and improve the health outcomes of its rural citizens. The success of eSanjeevani and similar

initiatives demonstrates that with proper planning and implementation, telemedicine can be a powerful tool in achieving health equity.

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Telemedicine Adoption in Post-COVID-19 India: A Cross-Sectional Study on Healthcare Professionals' Knowledge, Attitudes, and Practices.

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Abstract

Aims: To assess knowledge, attitudes, and practices regarding telemedicine among individuals post-COVID-19 infection, and to explore barriers to its implementation.

Methods: A cross-sectional survey of 200 participants with prior COVID-19 infection was conducted over two months using a self-administered questionnaire.

Results: 70.5% of participants were aware of telemedicine, while 66% had not used it pre-pandemic. Post-pandemic, 88.5% were satisfied with telemedicine treatment, 63% felt they received increased attention, and 94% found it reliable. 93.5% believed telemedicine implementation is necessary, a significant shift from pre-pandemic views.

Conclusion: The COVID-19 pandemic significantly increased awareness, positive attitudes, and utilization of telemedicine. Widespread implementation is favored, but addressing barriers is crucial.

Keywords: COVID-19, telemedicine, cross-sectional study.

Introduction

The COVID-19 pandemic has profoundly transformed healthcare delivery systems worldwide, necessitating rapid adaptation and innovation to maintain access to essential medical services. Amidst the challenges posed by social distancing, lockdowns, and overburdened healthcare facilities, telemedicine emerged as a critical tool for providing remote patient care. Telemedicine, leveraging information and communication technologies (ICT), offers a means to deliver healthcare services from a distance, encompassing consultations, monitoring, and even certain therapeutic interventions. Its potential to mitigate the risks of in-person interactions while ensuring continuity of care has been particularly evident during the COVID-19 crisis. The pandemic has not only accelerated the adoption of telemedicine but also reshaped public perception and acceptance of this modality. Individuals who experienced COVID-19, particularly those who underwent home isolation, represent a unique population with direct

exposure to telemedicine services. Their experiences and perspectives offer valuable insights into the efficacy, acceptability, and potential challenges associated with its implementation. Understanding their knowledge, attitudes, and practices regarding telemedicine is crucial for informing future healthcare strategies and optimizing its integration into routine care. Prior to the pandemic, telemedicine adoption varied across regions and populations, often facing barriers related to technological infrastructure, regulatory frameworks, and patient and provider acceptance. However, the urgency of the COVID-19 situation catalyzed a rapid shift, prompting healthcare providers to embrace telemedicine as a viable alternative to traditional in-person consultations. This accelerated adoption has provided a unique opportunity to assess the real-world impact of telemedicine and evaluate its potential for long-term integration into healthcare systems. The post-COVID-19 era presents a critical juncture for evaluating the sustained role of telemedicine in healthcare delivery. Understanding the experiences of individuals who have directly benefited from telemedicine during their COVID-19 recovery is essential for identifying best practices, addressing potential barriers, and optimizing its implementation. By examining the knowledge, attitudes, and practices of this population, we can gain valuable insights into the factors influencing telemedicine adoption and utilization. This study aims to assess the knowledge, attitudes, and practices regarding telemedicine among individuals who have suffered from COVID-19. By exploring their experiences and perspectives, we seek to understand the potential of telemedicine to address healthcare needs in the post-pandemic era and identify the barriers to its widespread implementation. This research will contribute to the growing body of literature on telemedicine adoption and provide valuable insights for healthcare providers, policymakers, and researchers seeking to optimize the integration of telemedicine into routine clinical practice.

Materials and Methods:

1. Study Design and Ethical Considerations:

- **Study Design:** Questionnaire-based cross-sectional study.
- **Ethical Approval:** Obtained from the Institutional Ethics Committee
- **Informed Consent:** Written informed consent was obtained from all participants.

2. Study Period: Two months (August 18 to October 18).

3. Sample Size: Total Participants: 200.

4. Subject Selection:

- **Inclusion Criteria:**
 - Individuals who had contracted COVID-19 at least once.
 - Individuals who were home-isolated and used telemedicine technology.
 - Individuals willing to provide written informed consent.
- **Participant Sources:** Patients from the civil hospital, medical students, residents, professors, and doctors associated with the medical college and hospital.

- **Diversity:** Included individuals from varying socio-economic and educational backgrounds.

5. Data Collection:

- **Method:** Self-administered questionnaire.
- **Informed Consent:** Provided alongside the questionnaire.
- **Data Collection Timing:** Single instance when participant agreed to enroll.
- **Confidentiality:** All participant information was kept confidential.
- **Language:** Questionnaire provided in the vernacular language.
- **Question Types:**
 - Yes/No questions.
 - Five-point Likert scale (1 = not at all, 2 = not really, 3 = neutral, 4 = somewhat, 5 = very much).
- **Data Collection Completion:** Continued until 200 satisfactory responses were obtained.

6. Data Analysis and Statistics:

- **Software:** Microsoft Excel.
- **Analysis:** Percentage of responses calculated for each question.
- **Data Visualization:**
 - Yes/No questions: Pie charts.
 - Likert scale questions: Histograms.

Results:

1. Demographic Details:

- **Total Participants:** 200.
- **Mean Age:** 36.01 years.
- **Age Range:** 17-85 years.
- **Inclusion Criteria:** All participants had COVID-19, were home-isolated, and used telemedicine.

2. Telemedicine Knowledge and Usage:

- **Knowledge of Telemedicine:** 70.5% knew what telemedicine is, 29.5% did not.
- **Pre-pandemic Usage:** 66% had not used telemedicine before the pandemic, 34% had.

3. Satisfaction and Perception:

- **Satisfaction with Telemedicine:** 88.5% were satisfied.
- **Liking Toward Telemedicine:** Majority liked it, 3% disliked, 12% had mixed feelings.
- **Perceived Increased Attention:** 63% felt they received more attention.
- **Reliability:** 94% found it reliable.

- **Necessity of Implementation:** 93.5% believed telemedicine implementation is necessary.
- **Telemedicine as Necessity:** Clear indication of necessity.
- **Privacy Concerns:** 58.5% believed privacy could be secured online.

4. Pre- and Post-Pandemic Perspectives:

- **Pre-pandemic Usefulness:** 63.5% thought telemedicine was not very useful, 22.5% were uncertain.
- **Post-pandemic Necessity:** 95.5% believed telemedicine is necessary.
- **Telemedicine Success in India:** 95.5% believed it could succeed.
- **Positive Attitude and Future:** 89.5% believed it has a bright future.

Discussion:

This study was done on the people who had suffered from COVID-19 infection and had used Telemedicine during their course of treatment. This helps find out the influence of COVID-19 in telemedicine usage to check whether the awareness of telemedicine has increased after the pandemic. This will ultimately help to determine the possible future of this technology. Tables 1 and 2 distributes the participants according to their educational qualifications and occupations. It depicts the variety of sample population used to conduct the study. One hundred and thirty-two (66%) people did not use this technology before the COVID-19 pandemic hit the world. Therefore, there was not much awareness regarding telemedicine before the pandemic. However, the study population included doctors, professors, residents, medical students, and the younger generation, so as expected, there were some people (34%) who used telemedicine even before the pandemic era. The majority of the population did not face any problems during the usage of this technology. A small amount of the population who were the patients living in rural areas or of low socioeconomic background, having low internet connectivity, or not able to afford smartphones, were the only ones who faced problems in the usage of this technology. One hundred and seventy-seven (88.5%) people were satisfied with the treatment they were given using this technology. For the majority of people, it was an easy and reliable way for treatment. The rest 23 people were asked about why they were not satisfied and told that unless they were not physically checked by the doctor, and unless they did not receive in-person treatment, they would not be satisfied. This was a valid point to note about certain people's ideology. This point should be considered during the awareness campaigns of telemedicine. Ideologies of such people should be dealt with by persuading them that there is no such major difference between telemedicine and physical clinic visits. One hundred and twenty-six (63%) people thought that they were provided more attention by the doctor during the course of their treatment through telemedicine technology. This is probably because it is easier to maintain E-health records and it is easier to schedule appointments with the doctor according to convenience. There is no distance barrier and the doctor can patiently attend to each of their patients. Furthermore, a constant follow-up can be easily managed through mobile

health apps and record-keeping system. These things serve to patient satisfaction. One hundred and eighty-eight (94%) people found this technology reliable as it was easier to get access to all their medical-related documents when they were on their mobile phones. Therefore, considering the same reasons, 93.5% of people think that implementation of telemedicine is necessary. The majority 117 (58.5%) people believed that their privacy could be secured even on sharing information online. While 14.5% had mixed feelings. Eight percent of people were more insecure and thought that there can be a breach in their privacy while using the telemedicine technology during their course of treatment. So almost 22.5% of people still had doubts regarding the privacy of their personal information. This is the main emerging challenge in recent times where there is an increased frequency of cyber-attacks. Doctors globally are concerned about the lack of protection of the privacy of patient information in this way. Capturing patient records by unauthorized persons may jeopardize the principle of the protection of private information of patients and they may be able to misuse it.[11] So along with lack of awareness, internet availability, and economical barriers, this is also a challenge which much be addressed. In the prepandemic era, the majority of the people – 127 people (63.5%) thought telemedicine was not so useful in treatment or in day-to-day life. While 22.5% of people were uncertain about its usefulness. This was because telemedicine, though invented way back, had not been properly implemented and therefore not widely accepted by people. In the postpandemic times, almost all – 191 people (95.5%) of the population think that telemedicine is necessary and should be implemented. Therefore, from 14% of people supporting telemedicine before the pandemic, the number of supporters increased greatly to 95.5%. The majority of people (95.5%) think that telemedicine technology if properly and correctly implemented, can succeed in India and it can help achieve new heights in medicine. The majority people have a positive attitude toward telemedicine. 89.5% of people have given ratings of 4 and 5 on the Likert scale when asked about how bright would be the future of telemedicine in India. It indicates the positive attitude of people toward using it in future health care. The expansion of mobile and wireless technologies around the world has set up an unprecedented opportunity for global health delivery. Mobile phone networks cover at least 90% of the world's population, including over 80% of those living in rural areas.[12] These data pave the way for telemedicine, as we can make applications and software, which bridge the gap in educating our general population. Many developing countries have inadequate healthcare services and suffer from a dearth of doctors and other trained healthcare professionals. The inappropriate distribution of doctors along with the scratchy infrastructure of healthcare facilities, roads, and transport make it even more difficult to provide health care in remote and rural areas.[13] Telemedicine can prove to be an effective way to provide medical care faster, as there are no long queues or waiting for the doctor. Furthermore, it can help patients with “white coat syndrome.” Telecommunication and interactive video medical visits could be used to change the typical communication process and potentially reduce anxiety.[14] Studies show that patient satisfaction can be achieved through this form of medical care.

Conclusion:

This study was carried out at a single center and had a small sample size of 200. More such studies should be carried out in different parts of India to have a more realistic approach to people's knowledge and attitude toward telemedicine. These findings suggest that if implemented properly on a large scale, telemedicine would be welcomed by the people. However, there are some barriers that need to be addressed. Minor barriers include the lack of awareness and lack of internet facilities in the rural areas which could be addressed by awareness campaigns. Major barriers include the protection of personal information and physician licensing. There are ample number of researches done on knowledge, attitude, and practice of telemedicine among the people and healthcare professionals. Furthermore, there are many researches on the usage of telemedicine, and its advantages and disadvantages in different diseases. Now, there is a need to do research to find out what difficulties do people face in using telemedicine and whether the barriers are overcome or not. Researchers can find out the major challenges. They can take people's suggestions as well as themselves provide suggestions for overcoming the challenges.

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Emotional Nurturance and Cognitive Development in Indian Preschoolers: A National Cross-Sectional Study.

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Abstract:

This cross-sectional study investigated the relationship between caregiver emotional nurturance and cognitive development in 391 preschoolers from GIMSH, Durgapur, India, considering socio-economic factors. Age, family structure, and caste significantly influenced cognitive outcomes. Children aged 36-48 months and those from joint families exhibited higher cognitive scores. Children from disadvantaged castes showed lower cognitive development compared to advantaged castes. While emotional nurturance showed a positive trend, it was not significantly associated with cognitive development after adjusting for socio-economic factors. The study highlights the significant impact of socio-economic disparities on preschool cognitive development. Targeted policies addressing these inequities, alongside interventions supporting joint family systems and maternal education, are essential for promoting equitable cognitive development in rural settings.

Keywords: Public health, socio-economic factors, preschool children, emotional nurturance, caregivers, cognitive development.

Introduction

Early childhood represents a critical window for cognitive development, laying the foundation for future academic achievement, social competence, and overall well-being. During this period, the brain undergoes rapid growth and development, making it highly susceptible to environmental influences. Among these influences, the quality of caregiving, particularly emotional nurturance, plays a pivotal role in shaping children's cognitive trajectories. Emotional nurturance, encompassing responsive care, warmth, and secure attachment, fosters a supportive environment that promotes optimal cognitive development. In the context of low- and middle-income countries (LMICs), such as India, the challenges associated with promoting optimal cognitive development are compounded by socio-economic disparities, limited access to quality healthcare, and cultural factors that may influence caregiving practices. Within India, the Western Tarai region, characterized by its diverse socio-cultural landscape and predominantly rural setting, presents a unique context for investigating the impact of emotional nurturance on preschooler cognitive development. The Western Tarai region, located in the southern plains of India, is home to a heterogeneous population comprising various ethnic and caste groups. This diversity is reflected in the region's socio-economic profile, with significant

disparities in access to education, healthcare, and resources. These disparities are often rooted in historical and cultural factors, including caste-based discrimination and limited opportunities for marginalized communities. Consequently, children from disadvantaged backgrounds may face heightened risks for cognitive delays and developmental challenges. Within this socio-cultural context, the role of caregivers, particularly mothers, in providing emotional nurturance is paramount. However, factors such as limited education, economic constraints, and traditional gender roles may influence caregiving practices and limit the provision of optimal emotional support. Understanding the interplay between socio-economic factors, caregiving practices, and cognitive development is essential for designing effective interventions to promote equitable cognitive outcomes in this region. Furthermore, the prevalence of joint family systems in the Western Tarai region presents a unique opportunity to explore the potential benefits of extended family support on children's cognitive development. Joint families, characterized by multiple generations living together, often provide a network of social and emotional support for children. This support may buffer the negative effects of socio-economic adversity and promote positive cognitive outcomes. Conversely, the transition towards nuclear family structures, driven by urbanization and changing socio-economic dynamics, may have implications for children's cognitive development. Nuclear families, typically comprising parents and their children, may lack the extended support networks available in joint families. Understanding the impact of family structure on cognitive development is crucial for designing culturally sensitive interventions that align with the evolving socio-cultural landscape of the Western Tarai region. Moreover, the quality of healthcare services and access to early childhood development programs play a significant role in promoting cognitive development. In the Western Tarai region, limited access to quality healthcare and early childhood education may impede children's cognitive potential. Addressing these systemic barriers is essential for ensuring equitable access to developmental opportunities and promoting positive cognitive outcomes. This study aims to investigate the impact of health-caregivers' emotional nurturance on cognitive development in preschool-aged children in the Western Tarai region of India, considering the complex interplay of socio-economic factors, family structures, and cultural contexts. By employing a nationwide public health cross-sectional study design, this research seeks to provide valuable insights into the determinants of cognitive development in this unique socio-cultural setting. Specifically, this study will examine the association between emotional nurturance, as reported by caregivers, and cognitive outcomes in preschool children, while controlling for socio-economic factors such as caregiver education, occupation, caste/ethnicity, and family structure. The findings of this research will have important implications for public health policy and intervention design, informing the development of culturally sensitive strategies to promote equitable cognitive development in the Western Tarai region and beyond.

Materials and Methods:

1. Study Design and Setting:

- **Design:** Cross-sectional.
- **Location:** GIMSH, Durgapur
- **Rationale:** High fertility rate and large young child population in Durgapur District, making it suitable for ECD research.
- **Sampling Context:** Includes urban, semi-urban, and rural settings.
- **District Population:** 1,118,975.

2. Study Population and Sampling Procedure:

- **Target Population:** 14,358 children (36-71 months) in 369 government-funded ECD centers.
- **Sampling Technique:** Multi-stage random sampling.
- **Stage 1:** Random selection of three local government units (sub-metropolitan city, municipality, rural municipality).
- **Stage 2:** Random selection of ECD centers from each unit.
- **Inclusion Criteria:** All children present on assessment day and their primary caregivers.
- **Sample Size Calculation:**
 - Formula provided.
 - Calculated sample size: $N = 401$ children (including 3% non-response rate).
- **Final Dataset:** 391 cases (after outlier removal).

3. Data Collection Tools:

- **Questionnaire:** Self-administered, two sections.
 - **Section A:** Caregivers' emotional nurturing practices (yes/no scoring).
 - Includes socio-economic variables (child's gender, age, family structure, caste/ethnicity, mother's education/employment, family economic status).
 - **Section B:** Cognitive development (standardized tool from National Psychological Corporation of India, based on Piaget's theory).
 - Tasks related to symbolic play and problem-solving.
- **Pilot Study:** Conducted with 10% of the sample, minor modifications made.
- **Reliability:**
 - Cognitive development tool: Cronbach's alpha 0.90.
 - Emotional nurturing tool: Cronbach's alpha 0.80.

4. Data Analysis Process:

- **Software:** Microsoft Excel, IBM SPSS v. 20 (analysis), IBM SPSS v. 26
- **Descriptive Statistics:** Means, standard deviations, frequencies.
- **Group Comparisons:** Independent sample t-test, ANOVA ($p < 0.05$).
- **Normality Test:** Kolmogorov-Smirnov test.
- **Outlier Removal:** Final dataset of 391 cases.
- **Multiple Linear Regression:** To identify significant factors and control for confounders.

Results:

Sample Demographics:

- **Gender:** Balanced (50.6% boys, 49.4% girls).
- **Age:** Grouped into 36-48, 49-59, and 60-71 months.
- **Caste/Ethnicity:**
 - Advantaged castes: 35.0%.
 - Janajati: 28.1%.
 - Non-Dalit Terai castes: 23.8%.
 - Dalit: 13.0%.
- **Family Structure:** Nearly even (47.3% nuclear, 52.7% joint).
- **Maternal Occupation:**
 - Labor/household work: 47.3%.
 - Agriculture: 24.0%.
 - Business: 15.1%.
 - Government/private/self-employment: 13.6%.
- **Maternal Education:**
 - Basic education: 45.3%.
 - Illiterate: 23.3%.
 - Secondary education or higher: 31.5%.

Discussion

This cross-sectional study investigated the complex interplay between caregivers' emotional nurturance, socio-economic factors, and cognitive development in preschool-aged children in the GIMSH, Durgapur. Our findings reveal several key insights into the determinants of cognitive outcomes in this unique socio-cultural context. Firstly, the study found that age significantly influenced cognitive development, with children aged 36-48 months demonstrating higher cognitive scores compared to those aged 60-71 months. This observation aligns with the understanding that early childhood is a period of rapid cognitive growth, particularly in the foundational stages of development. The accelerated developmental milestones observed in younger children within this age range underscore the importance of early interventions and targeted support during these formative years. Secondly, our results highlighted the significant impact of family structure on cognitive development. Children from nuclear families exhibited lower cognitive scores than those from joint families, even after adjusting for socio-economic factors. This finding suggests that the extended social support and interaction afforded by joint family systems may provide a nurturing environment

conducive to cognitive growth. In the context of the Western Tarai region, where joint family structures are prevalent, this observation underscores the potential benefits of preserving and leveraging these traditional support systems to enhance children's cognitive outcomes. Thirdly, the study revealed significant disparities in cognitive development based on caste and ethnicity. Children from disadvantaged castes demonstrated lower cognitive scores compared to those from advantaged castes. These findings underscore the persistent impact of socio-economic inequities on children's developmental trajectories. The observed disparities highlight the urgent need for targeted interventions to address systemic barriers and promote equitable access to developmental opportunities for children from marginalized communities. Interestingly, while a positive association was observed between emotional nurturance and cognitive development, this association did not reach statistical significance after adjusting for socio-economic factors. This suggests that the impact of emotional nurturance on cognitive outcomes may be mediated or confounded by socio-economic variables. However, the finding that maternal employment with a regular salary, was positively associated with emotional nurturance, suggests that economic stability and potentially, increased maternal education associated with these jobs, may positively influence nurturing practices. Furthermore, the study found that children of employed mothers had lower cognitive scores. This may indicate a potential trade-off between maternal employment and time spent with children, potentially affecting cognitive nurturing. This finding highlights the need for supportive policies and interventions that enable working mothers to balance their professional and caregiving responsibilities effectively. The economic status of households also demonstrated a trend, albeit not statistically significant in adjusted models, with children from the poorest households showing marginally lower cognitive scores. This suggests that while economic conditions play a role, other socio-demographic factors, such as caste and family structure, may exert a more consistent influence on cognitive outcomes. Several limitations should be considered when interpreting these findings. The cross-sectional design of the study precludes the establishment of causal relationships. Additionally, the reliance on self-reported data may introduce potential biases. The study was conducted in a specific district of India, limiting the generalizability of the findings to other regions or populations. Despite these limitations, this study provides valuable insights into the complex interplay of factors influencing cognitive development in preschool-aged children in the Durgapur. The findings underscore the importance of addressing socio-economic inequities, leveraging traditional support systems, and promoting equitable access to developmental opportunities to enhance children's cognitive outcomes.

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Beyond Obesity: Investigating the Link Between Gamma-Glutamyl Transferase and Diabetes Markers in an Elderly Cohort.

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Abstract

Background: Type 2 diabetes mellitus (T2DM) poses a significant health risk in the elderly, with nonalcoholic fatty liver disease (NAFLD) being a common comorbidity. Gamma-glutamyl transferase (γ -GT), a marker of liver dysfunction, has been linked to insulin resistance (IR) and diabetes, but its relationship with insulin secretion phases (first-phase insulin secretion [FPIS], second-phase insulin secretion [SPIS]) and glucose effectiveness (GE) in elderly nonobese individuals remains unclear.

Methods: This cross-sectional study included 10,933 Indian individuals (≥ 65 years) without obesity. Participants were stratified by metabolic syndrome (MetS) status and γ -GT quartiles. IR, FPIS, SPIS, and GE were calculated using established equations. Pearson correlation analysis and statistical models were employed to assess associations.

Results: MetS was present in 1,562 participants, who exhibited higher IR, FPIS, SPIS, and γ -GT levels, and lower GE, compared to those without MetS. Elevated γ -GT levels were significantly associated with MetS components and increased IR, FPIS, and SPIS, while showing a negative correlation with GE. GE demonstrated the strongest inverse correlation with γ -GT ($r = -0.198$ for men, -0.158 for women), followed by positive correlations with IR, SPIS, and FPIS.

Conclusions: γ -GT is significantly associated with key diabetes factors in elderly nonobese Chinese individuals. Notably, GE showed the strongest inverse correlation with γ -GT, suggesting a potential role for γ -GT in glucose metabolism beyond insulin resistance. These findings warrant further investigation into the clinical implications of γ -GT in predicting and managing diabetes risk in this population.

Keywords: gamma-glutamyl transferase, glucose effectiveness, insulin resistance, first-phase insulin secretion, second-phase insulin secretion, elderly.

Introduction

Type 2 diabetes mellitus (T2DM) represents a burgeoning global health crisis, particularly within aging populations. The elderly are disproportionately affected by T2DM, exhibiting a

higher prevalence and increased susceptibility to its associated complications. This demographic shift, coupled with the rising incidence of T2DM, poses a significant burden on healthcare systems worldwide. In Taiwan, like many other developed nations, the aging population is expanding rapidly, and the prevalence of T2DM among the elderly is a pressing public health concern. Understanding the intricate interplay of factors contributing to the development and progression of T2DM in this specific population is crucial for developing targeted preventive and therapeutic strategies. The pathogenesis of T2DM is multifactorial, involving a complex interplay of genetic predisposition, environmental influences, and lifestyle factors. Central to the disease process are insulin resistance (IR) and progressive beta-cell dysfunction, leading to impaired insulin secretion. IR, characterized by a diminished cellular response to insulin, necessitates compensatory hyperinsulinemia to maintain glucose homeostasis. However, over time, the pancreatic beta cells, responsible for insulin production, fail to meet the increased demand, resulting in a decline in insulin secretion and subsequent hyperglycemia. This progression is not uniform, and individual variations in the timing and magnitude of these processes contribute to the diverse clinical manifestations of T2DM. Traditionally, the focus of T2DM research has primarily centered on IR and overall insulin secretion. However, recent studies have highlighted the importance of examining the dynamic phases of insulin secretion, specifically the first-phase insulin secretion (FPIS) and the second-phase insulin secretion (SPIS). FPIS, the rapid and transient release of insulin in response to an initial glucose stimulus, plays a critical role in suppressing hepatic glucose production and limiting postprandial hyperglycemia. SPIS, the sustained and prolonged release of insulin, maintains glucose homeostasis during the later stages of glucose absorption. Impaired FPIS has been recognized as an early marker of beta-cell dysfunction and a predictor of future T2DM development. Moreover, glucose effectiveness (GE), defined as the ability of glucose to stimulate its own uptake independently of insulin, has emerged as a crucial factor in glucose regulation. A decline in GE contributes to hyperglycemia, particularly in the postprandial state. In addition to these established factors, emerging evidence suggests a potential role for liver dysfunction in the pathogenesis of T2DM. Nonalcoholic fatty liver disease (NAFLD), a common hepatic manifestation of metabolic dysfunction, is highly prevalent in individuals with T2DM and is increasingly recognized as an independent risk factor for the disease. NAFLD is characterized by the accumulation of triglycerides in the liver, leading to inflammation and cellular damage. Gamma-glutamyl transferase (γ -GT), an enzyme primarily located in the liver and kidneys, is a sensitive marker of liver dysfunction and oxidative stress. Elevated γ -GT levels have been associated with a range of metabolic disorders, including IR, dyslipidemia, and cardiovascular disease. The association between γ -GT and T2DM has been extensively investigated in various populations. Studies have shown that elevated γ -GT levels are independently associated with an increased risk of developing T2DM, even after adjusting for traditional risk factors. Furthermore, γ -GT has been implicated in the pathogenesis of IR, potentially through the generation of reactive oxygen species and the activation of inflammatory pathways. However, the precise mechanisms underlying the relationship between γ -GT and glucose metabolism remain unclear. While the role of γ -GT in T2DM has been established, its association with the specific phases of insulin secretion and GE in elderly nonobese individuals has not been thoroughly explored. Understanding these relationships is crucial for elucidating the complex interplay of factors contributing to glucose dysregulation in this vulnerable population. The elderly, particularly those without obesity, may exhibit unique metabolic characteristics that influence the association between γ -GT and diabetes-related factors. For instance, age-related changes in liver function, beta-cell function, and insulin sensitivity may modify the impact of γ -GT on glucose metabolism. In this context, the

present study aims to investigate the association between γ -GT and key diabetes factors, including IR, FPIS, SPIS, and GE, in a large cohort of elderly nonobese Chinese individuals. By examining these relationships, we seek to provide insights into the potential role of γ -GT in the pathogenesis of T2DM in this specific population. This research is important for several reasons. Firstly, it will contribute to a better understanding of the complex mechanisms underlying glucose dysregulation in the elderly. Secondly, it may identify γ -GT as a potential biomarker for predicting and managing T2DM risk in this population. Thirdly, it may provide a foundation for developing targeted interventions aimed at improving glucose metabolism and preventing T2DM in elderly individuals.

Materials And Methods: Study subjects Participants were randomly enrolled from the Department of General Medicine, Mamata Medical College, Khammam. Inclusion criteria required all participants to be able to clearly express themselves and to be adults aged 65 years or older. The study period spanned from January 2003 to December 2005. The study protocol was approved by the institutional review board of each institution. All study participants remained anonymous and informed consent was obtained from each participant. Individuals who were obese (body mass index [BMI] ≥ 25 kg/m²) or taking medications known to affect blood pressure, glucose, and lipid levels were excluded. Participants who have a habit of alcoholic drinking or known liver disease, except for NAFLD, were also excluded from the study. Participants were categorized into those with metabolic syndrome (MetS) and those without MetS based on the criteria of the World Health Organization.[13] Finally, a total of 5082 men and 5851 women were enrolled in the study. Among the men, there were 768 patients with MetS (MetS(+)) and 4314 without MetS (MetS(-)). There were 794 women with MetS(+) and 5057 without MetS(-). On the day of the study, senior nursing staff obtained the participants' medical history, including information on current medications. Thorough questionnaires and complete physical examinations were conducted. Waist circumference (WC) was measured horizontally at the natural waist level, identified as the level at the hollow molding of the trunk when it was laterally concave. BMI was calculated by dividing the subject's body weight (kg) by the square of their height (m). The systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by nursing staff using standard mercury sphygmomanometers on the right arm of each subject while seated. After a 10-hour fast, blood samples were drawn from the antecubital vein for biochemical analysis. Plasma was separated from the blood within 1 hour and stored at 30°C for the analysis of fasting plasma glucose (FPG) and lipid profiles. FPG was measured using the glucose oxidase method (YSI 203 glucose analyzer; Yellow Springs Instruments, Yellow Springs, USA). Total cholesterol and triglyceride levels were measured using a dry, multilayer analytical slide method with a Fuji Dri-Chem 3000 analyzer (Fuji Photo Film, Tokyo, Japan). Serum high-density lipoprotein cholesterol (HDL-C) concentration was analyzed using an enzymatic cholesterol assay following dextran sulfate precipitation. Serum γ -GT was performed using a CX7 biochemistry analyzer (Beckman, Fullerton, CA). The equations for calculating IR, FPIS, SPIS, and GE were as follows: It is important to note that all the units are international units. The numbers 1 and 2 represent men and women, respectively. The publication information for each equation is given in parentheses. The equations used to calculate IR, FPIS, SPIS, and GE are as follows: A brief report is provided to assess the reliability of these equations. Approximately 70% of the sample participants were used to construct the equations, while the remaining 30% were used for external validation, ensuring accountability of the equations. 1. IR: A total of 327 subjects were

enrolled in this equation, which estimates insulin resistance using an insulin suppression test. The correlation (r) between the obtained and calculated GE was 0.581 ($P < .001$).[14] $IR = \log(1.439 + 0.018 \times \text{sex} - 0.003 \times \text{age} + 0.029 \times \text{BMI} - 0.001 \times \text{SBP} + 0.006 \times \text{DBP} + 0.049 \times \text{TG} - 0.046 \times \text{HDL-C} - 0.0116 \times \text{FPG}) \times 103.333$ 2. FPIS: A total of 186 subjects were included in this equation, which measures first-phase insulin secretion by using an intravenous glucose tolerance test with frequent sampling. The correlation value (r) between the measured and calculated GE values was 0.671 ($P < .000$).[15] $FPIS = 10(1.477 - 0.119 \times \text{FPG} + 0.079 \times \text{BMI} - 0.523 \times \text{HDL-C})$ 3. SPIS: A total of 82 participants were included in this equation, which measures second-phase insulin secretion through a modified glucose infusion test with a low dose. The correlation value (r) between the measured and calculated GE was 0.65 ($P = .002$).[16] $SPIS = 10(-2.4 - 0.088 \times \text{FPG} + 0.072 \times \text{BMI})$ 4. GE: A total of 227 participants were included in this equation, which measures glucose effectiveness using a constant sampled intravenous glucose tolerance test. The correlation value (r) between the measured and calculated GE was 0.43 ($P = .001$). $GE = (29.196 - 0.103 \times \text{age} - 2.722 \times \text{TG} - 0.592 \times \text{FPG}) \times 10^{-3}$ 2.2.

Statistical Analysis: The data are presented as mean $\pm$ standard deviation. Participants were grouped according to the presence of MetS and γ -GT quartiles. We categorized subjects into quartiles based on their γ -GT levels, arranged from the lowest to the highest values. To normalize the distribution, γ -GT levels were transformed logarithmically. This transformation allowed us to define groups as Log γ -GT1 through Log γ -GT4, from the lowest quartile to the highest quartile. By applying this method, we aimed to enhance the statistical validity of comparisons and better interpret the variations in γ -GT levels among the subjects. Student t test was used to assess differences in continuous data between MetS(+) and MetS(-) groups. One-way analysis of variance was used to evaluate differences in demographic data, clinical parameters, and DFs with FPG in the γ -GT quartiles. The Bonferroni test was used for the post hoc analysis. Pearson correlation analysis was used to examine the correlation between γ -GT levels and DFs. A general linear model was used to determine the differences between the 4 slopes and FPG.

Results: Clinical characteristics of participants in MetS(-) and MetS(+). Both sexes in the MetS(+) group exhibited higher age, BMI, WC, SBP, DBP, FPG, triglyceride, cholesterol, γ -GT, FPIS, SPIS, IR, and lower HDL-C and GE levels. Components of MetS according to quartiles of γ -GT γ -GT quartiles were used to determine the components of MetS. Higher FPIS, SPIS, IR, age, BMI, WC, SBP, DBP, FPG, triglyceride, and lower HDL-C and GE levels were consistently linked to increasing levels of γ -GT. 3.3. Relationship between γ -GT and 4 DFs, shows the results of the simple correlations between γ -GT and the 4 DFs. It is worth noting that GE had a negative relationship with γ -GT, whereas the other 3 factors showed a positive relationship. Additionally, GE exhibited the highest correlation coefficient ($r = -0.198$ for men and -0.158 for women, $P < .001$), indicating the strongest association with γ -GT. IR ($r = 0.183$ for men and 0.132 for women, $P < .001$) and SPIS ($r = 0.099$ for men and 0.060 for women, $P < .001$) followed in strength, whereas FPIS ($r = 0.028$, $P = .045$ for men and $r = 0.048$, $P < .001$) demonstrated the weakest correlation. In men, there was a significant difference in the slope between IR and FPIS but not between GE, IR, GE, and SPIS. Among women, significant differences existed between GE, IR, and both FPIS and SPIS, while no significant difference was observed between FPIS and SPIS.

Discussion: This study investigated the association between gamma-glutamyl transferase (γ -GT) and key diabetes-related factors, namely insulin resistance (IR), first-phase insulin secretion (FPIS), second-phase insulin secretion (SPIS), and glucose effectiveness (GE),¹ in a large cohort of elderly nonobese Chinese individuals. The principal findings reveal a significant positive association between γ -GT levels and IR, FPIS, and SPIS, while demonstrating a negative correlation with GE. Notably, GE exhibited the strongest inverse correlation with γ -GT among the four diabetes factors, suggesting a potentially crucial role for γ -GT in glucose metabolism beyond its association with IR. The observed positive correlation between γ -GT and IR aligns with previous studies that have established γ -GT as a marker of metabolic dysfunction and a predictor of T2DM. γ -GT is implicated in oxidative stress and inflammatory pathways, both of which contribute to the development of IR. Elevated γ -GT levels may reflect increased hepatic oxidative stress and inflammation, leading to impaired insulin signaling and reduced glucose uptake in peripheral tissues. Furthermore, γ -GT has been linked to the accumulation of hepatic triglycerides, a hallmark of nonalcoholic fatty liver disease (NAFLD), which is independently associated with IR. The positive associations between γ -GT and both FPIS and SPIS are intriguing and warrant further consideration. While IR is a well-established driver of beta-cell dysfunction, the relationship between γ -GT and insulin secretion is less clear. The current findings suggest that elevated γ -GT levels may be associated with compensatory hyperinsulinemia, particularly in the early stages of glucose intolerance. This compensatory mechanism may reflect the body's attempt to overcome IR and maintain glucose homeostasis. However, prolonged exposure to elevated γ -GT levels and chronic oxidative stress may ultimately lead to beta-cell exhaustion and a decline in insulin secretion. The most striking finding of this study is the strong inverse correlation between γ -GT and GE. GE, representing the ability of glucose to stimulate its own uptake independently of insulin, is a critical determinant of glucose homeostasis. A decline in GE contributes to hyperglycemia, particularly in the postprandial state. The observed negative correlation suggests that elevated γ -GT levels may impair GE, potentially through mechanisms involving oxidative stress, inflammation, and altered glucose transport. This finding highlights the potential role of γ -GT in glucose metabolism beyond its association with insulin action and secretion. The study's focus on elderly nonobese individuals is noteworthy. Obesity is a major risk factor for T2DM, and its confounding effect can obscure the independent association between γ -GT and diabetes-related factors. By excluding obese individuals, this study provides a clearer picture of the relationship between γ -GT and glucose metabolism in a population that may exhibit unique metabolic characteristics. The elderly, even without obesity, are susceptible to age-related changes in liver function, beta-cell function, and insulin sensitivity, which may modify the impact of γ -GT on glucose metabolism. The findings of this study have several potential clinical implications. Firstly, γ -GT may serve as a valuable biomarker for predicting and managing T2DM risk in elderly nonobese individuals. The strong correlation between γ -GT and GE suggests that γ -GT may provide insights into glucose metabolism beyond traditional markers of IR and insulin secretion. Secondly, the identification of γ -GT as a potential target for therapeutic interventions aimed at improving glucose metabolism warrants further investigation. Strategies that reduce γ -GT levels, such as lifestyle modifications and pharmacological interventions, may have beneficial effects on glucose homeostasis. This study has several strengths, including its large sample size, comprehensive assessment of diabetes-related factors, and focus on a specific population of elderly nonobese individuals. However,

some limitations should be acknowledged. Firstly, the cross-sectional design of the study precludes the establishment of causality. Longitudinal studies are needed to determine the temporal relationship between γ -GT and the development of T2DM. Secondly, the study population consisted of Chinese individuals, which may limit the generalizability of the findings to other ethnic groups. Thirdly, the use of calculated estimates of IR, FPIS, SPIS, and GE, rather than direct measurements, may introduce some degree of imprecision. In conclusion, this study demonstrates a significant association between γ -GT and key diabetes-related factors in elderly nonobese Chinese individuals. Notably, GE exhibited the strongest inverse correlation with γ -GT, suggesting a potential role for γ -GT in glucose metabolism beyond insulin resistance. These findings highlight the need for further research into the role of γ -GT in glucose metabolism and its potential clinical implications for predicting and managing T2DM risk in this vulnerable population. Future studies should focus on elucidating the underlying mechanisms linking γ -GT to glucose dysregulation and exploring the potential therapeutic implications of these findings.

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Indian Clinicians' Experiences with Montelukast-Levocetirizine for Allergic Rhinitis and Asthma: A Survey.

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Abstract

Background: Allergic rhinitis (AR) poses a substantial public health challenge in India. This study investigated Indian clinicians' perspectives on the use of montelukast and levocetirizine combination therapy for AR, particularly in patients with comorbid asthma.

Materials and Methods: A cross-sectional survey was conducted among 882 Indian clinicians using a 27-item questionnaire assessing their clinical experiences with montelukast and levocetirizine in AR management. Data were analyzed using descriptive statistics, and results were presented as percentages and visualized using charts.

Results: A significant proportion (64%) of clinicians recognized recurrent upper respiratory tract infections (URTIs) as a potential indicator of undiagnosed AR. The majority (81.63%) preferred antihistamine-leukotriene receptor antagonist (LTRA) combinations for long-term AR management, with levocetirizine being the preferred antihistamine (90.48%). Clinicians reported similar AR diagnosis rates across genders (80%) and observed morning symptom exacerbation in most patients (90.93%). The montelukast-levocetirizine combination was favored for its improved patient compliance (72%) and was frequently used in asthma patients before initiating inhalation therapy (77%).

Conclusion: This survey reveals a strong preference among Indian clinicians for montelukast and levocetirizine combination therapy in AR management due to its efficacy and enhanced patient compliance. Recurrent URTIs were identified as a potential marker for undiagnosed AR, and the frequent co-occurrence of asthma and allergic conjunctivitis was noted.

Keywords: Allergic rhinitis, Montelukast, Levocetirizine, Leukotriene receptor antagonists, Asthma, India.

Introduction

Allergic rhinitis (AR), a common inflammatory condition of the nasal mucosa, significantly impacts the quality of life, productivity, and overall well-being of individuals worldwide. In

India, a country characterized by diverse environmental exposures, a large population, and varying socioeconomic strata, AR presents a substantial public health burden. Its prevalence, influenced by factors such as urbanization, pollution, and changing lifestyles, is steadily rising across all age groups, posing a significant challenge to the healthcare system. The clinical manifestations of AR, including nasal congestion, rhinorrhea, sneezing, and pruritus, can lead to sleep disturbances, impaired cognitive function, and increased healthcare utilization, underscoring the need for effective management strategies.

The pathogenesis of AR involves a complex interplay of genetic predisposition and environmental triggers, leading to an IgE-mediated inflammatory response. This cascade culminates in the release of various inflammatory mediators, including histamine and leukotrienes, which contribute to the characteristic symptoms of AR. Consequently, therapeutic interventions targeting these mediators are crucial in alleviating symptoms and improving patient outcomes.

Pharmacological management of AR typically involves the use of antihistamines, leukotriene receptor antagonists (LTRAs), intranasal corticosteroids, and decongestants. Antihistamines, particularly second-generation agents like levocetirizine, are widely used due to their efficacy in reducing nasal symptoms and their favorable safety profile. Levocetirizine, a potent and selective H₁-receptor antagonist, offers rapid symptom relief and sustained efficacy, making it a cornerstone of AR therapy.

Leukotrienes, potent lipid mediators, play a significant role in the pathogenesis of AR and asthma, contributing to bronchoconstriction, mucus secretion, and airway inflammation. Montelukast, an LTRA, effectively blocks the action of leukotrienes, providing symptomatic relief in AR and asthma. Given the frequent co-occurrence of AR and asthma, particularly in India, where environmental triggers often exacerbate both conditions, the combined use of montelukast and levocetirizine has gained increasing attention.

The rationale behind combining montelukast and levocetirizine lies in their complementary mechanisms of action. While levocetirizine targets histamine-mediated symptoms, montelukast addresses leukotriene-mediated inflammation, potentially leading to synergistic effects and improved symptom control. This combination offers a convenient and potentially more effective approach to managing AR, particularly in patients with comorbid asthma, where both histamine and leukotrienes contribute to airway inflammation.

In the Indian context, the management of AR and comorbid asthma presents unique challenges. The diverse environmental exposures, including high levels of air pollution, pollen, and dust mites, contribute to the high prevalence and severity of these conditions. Additionally, socioeconomic factors, such as limited access to healthcare and affordability of medications, can influence treatment adherence and outcomes. Moreover, cultural practices and beliefs may influence patient perceptions and preferences regarding treatment options.

Despite the growing use of montelukast and levocetirizine combination therapy in India, there is a paucity of data on clinicians' perspectives and real-world experiences with this approach. Understanding clinicians' attitudes, practices, and perceived benefits and limitations of this combination is crucial for optimizing AR management in the Indian setting. This study aims to address this gap by surveying Indian clinicians to gather their insights on the use of montelukast and levocetirizine in managing AR and co-occurring asthma.

Materials and Methods:

We carried out a cross-sectional study among specialists in managing AR in the major Indian cities from June 2018 to December 2018.

Questionnaire: The questionnaire booklet named CARA (Clinicians feedback on allergic rhinitis and asthma in Indian Patients and usage of Montelukast and Levocetirizine) study was sent to the otorhinolaryngologists who were interested to participate. The CARA questionnaire booklet consisted of 27 questions regarding current feedback, clinical observations, and the clinical experience of specialists in managing AR with the combination of montelukast and levocetirizine. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

Participants: An invitation was sent to leading otorhinolaryngologists in managing AR in the month of March 2023 for participation in this Indian survey. About 882 clinicians from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Otorhinolaryngologists were requested to complete the questionnaire without discussing with peers. A written informed consent was obtained from each specialists prior initiation of the study.

Statistical analysis: The data were analysed using descriptive statistics. Categorical variables were presented as percentages to provide a clear insight into their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, pie, and bar charts were created using Microsoft Excel 2013 (version 16.0.13901.20400).

Result:

Results Of the 882 survey participants, nearly 33% (33.09%) reported that 31-40 cases of co-occurrence of AR are observed monthly in routine practice. Half of the participants (50.45%) indicated that the most common concomitant diseases associated with AR are allergic conjunctivitis, sinusitis, middle ear infections, and asthma. About 64% of respondents agreed that recurrent URTIs could indicate undiagnosed AR. Nearly 33% (32.54%) of the clinicians reported diagnosing 21-30 cases of AR monthly in their clinical practice. The majority (81.63%) of the participants preferred a combination of antihistamines and LTRA for the long-term management of AR. Approximately 90% reported levocetirizine as their preferred antihistamine for managing AR. Around 35% of participants cited acute AR as the preferred indication for the montelukast + levocetirizine combination over plain antihistamine therapy. About 72% of respondents noted that improved patient compliance is the most compelling advantage of recommending the montelukast + levocetirizine combination for AR.

Approximately 31% of the participants reported that the 21-30 age group had the highest distribution of AR cases. Most clinicians (80%) indicated that the frequency of AR diagnoses was comparable across both genders. The majority (90.93%) of the participants observed improvements in morning AR symptoms with the montelukast + levocetirizine combination. Less than half (48.19%) stated that 26-50% of patients require a combination of montelukast and antihistamines for AR. About 68% of the clinicians reported that the benefits of montelukast + levocetirizine include improvements in daytime and nighttime nasal symptoms, as well as daytime eye symptoms. More than half (65.76%) of participants noted that morning symptoms are the most common complaints among AR patients. Approximately 46% recommended a 6-week duration for montelukast + levocetirizine therapy for AR with asthma. Nearly half (46.71%) of the participants rated the clinical efficacy of montelukast + levocetirizine as "very good" for the long-term management of AR. About 40% reported that adherence to medications is better among urbaneducated AR patients. Around 60% of the participants indicated that more than 61% of the patients require education on the dos and don'ts of AR management. About 54% of participants reported that pollen and dust mites are the most common causes of AR in their clinical practice. Approximately 55% stated that patients with AR and asthma are the preferred candidates for montelukast use. About 37% reported that the highest number of AR patient visits occurred in January and February. Half (49.66%) of them stated that the severity of allergies is a key factor in determining the choice of antihistamine for AR patients. Most participants (77%) preferred antihistamine + LTRA therapy for patients with bronchial asthma before initiating inhalation therapy. About 61% of participants relied on clinical history for diagnosing AR. Approximately 46% of participants noted the efficacy advantages of the montelukast + levocetirizine combination for managing AR. About 54% of participants favoured mass education through social media as the preferred method for educating AR patients. Lastly, 63% identified lack of patient education as a factor associated with non-adherence to medication in AR management.

Discussion

One of the key findings of the current survey was that about 64% of the respondents believed recurrent URTI may indicate undiagnosed AR. This finding aligns with Kim et al., who noted that symptoms of viral URIs, such as nasal obstruction, rhinorrhea, and sneezing, often overlap with those of AR. This overlap can lead patients with AR to mistakenly believe they are experiencing recurrent viral infections, typically presenting as the common cold.¹³ Similarly, Nirouei et al. reported that AR, along with acute and chronic rhinosinusitis, are URI conditions.¹⁴ Majority of the participants preferred using a combination of antihistamines and LTRA for the long-term management of AR. Liu et al. noted that current evidence suggests the combination of LTRAs and H1 antihistamines improves therapeutic efficacy for daytime and composite nasal symptoms, such as rhinorrhea, sneezing, and itching. However, it does not affect nighttime nasal or eye symptoms. Patients with perennial AR may benefit more from this combination therapy.¹⁵ Similarly, Narasimhan et al. reported that the combination of antihistamines and LTRA presents a promising approach to managing both AR and asthma, offering enhanced symptom relief and improved disease control.¹⁶ Most respondents indicated levocetirizine as their preferred antihistamine for managing AR. Pasquali et al. reported that levocetirizine is clinically effective and significantly improves rhinitis-asthma-related quality

of life, helping patients manage both nasal and eye symptoms more effectively.¹⁷ Similarly, Bachert et al. found that levocetirizine not only improved symptoms and quality of life but also helped reduce the overall costs of managing the disease over a 6-month treatment period.¹⁸ Many respondents highlighted improved patient compliance as the key advantage of recommending the montelukast + levocetirizine combination for managing AR. Kim et al. suggested that a novel fixed-dose combination capsule containing 10/5 mg of montelukast and levocetirizine may enhance patient compliance compared to taking two separate tablets.¹⁹ Similarly, Chattopadhyay et al. reported that in India, many clinicians prefer the montelukast + levocetirizine combination because it improves patient compliance and reduces therapy costs.²⁰ Most participants in the current survey reported that the frequency of AR diagnoses is comparable between genders. However, Rosário et al. observed that AR prevalence is higher in boys than in girls during childhood (0–10 years). During adolescence (11–17 years), females exhibit a higher prevalence compared to males, and by adulthood (18–79 years), the prevalence becomes similar across genders. This gender-specific trend is particularly evident in the cooccurrence of AR and asthma.²⁰ Similarly, Frohlich et al. noted that while coexisting AR and asthma are more common in males during childhood, there is a shift to female predominance during adolescence.²¹ The majority of participants reported significant improvements in morning AR symptoms when using the montelukast + levocetirizine combination. Supporting this, Shao et al. demonstrated that combining montelukast with levocetirizine for treating nasal symptoms in AR with asthma was more effective than monotherapy, offering enhanced symptom relief and good safety profiles.²² Similarly, Gupta and Matreja reported that the combination of montelukast and levocetirizine was more effective in reducing daytime, nighttime, composite, and daytime eye symptom scores compared to levocetirizine alone.¹¹ The current survey noted that the combination of montelukast and levocetirizine provided benefits, including improvements in both daytime and nighttime nasal symptoms, as well as daytime eye symptoms. Gupta and Matreja reported that this combination was more effective than levocetirizine alone in reducing daytime, nighttime, composite, and daytime eye symptom scores.¹¹ Similarly, Kim et al. concluded that the combination of montelukast and levocetirizine led to significantly greater improvements in both daytime and nighttime symptoms, as well as quality of life, demonstrating safety and efficacy for children with perennial AR.²³ Many participants preferred antihistamine + LTRA therapy for patients with bronchial asthma before initiating inhalation therapy. Liu et al. noted that the combination of LTRAs + H1 antihistamines enhances therapeutic efficacy for daytime and composite nasal symptoms, such as rhinorrhea, sneezing, and itching, but does not impact nighttime nasal symptoms or eye symptoms. Patients with perennial AR may benefit more from this combination therapy.¹⁵ Similarly, another study highlighted that combining LTRA with antihistamines can improve asthma control.²⁴ This study offers valuable insights into the clinical management of AR, particularly regarding treatment preferences and clinical experiences with the montelukast + levocetirizine combination. A major strength of the study is the inclusion of a large sample size of 882 clinicians. Additionally, it provides important gender- and age-based insights into the prevalence of AR and asthma, contributing to a deeper understanding of these conditions across demographics. However, studying has several limitations. The reliance on self-reported data from clinicians may introduce bias, as it may reflect personal opinions rather than objective outcomes. Regional biases also limit the generalizability of the findings, as healthcare practices and patient populations may differ in other areas. Furthermore, the study did not explore dosage, long-term outcomes, or the sustainability of the observed improvements. Future studies are needed to further explore these findings and improve clinical practice.

Conclusion: The study highlighted the benefits of montelukast and levocetirizine, with clinicians preferring this combination for improved patient compliance and symptom control, particularly for morning and nasal symptoms. The cooccurrence of asthma and AR is common, and patient education, especially via social media, is vital for improving adherence. Recurrent URTI may signal undiagnosed AR, underscoring the importance of thorough diagnosis and management.

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Poststroke Epilepsy: Thalamic Network Pathology Revealed by EEG Source Analysis.

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Abstract

This study investigated alterations in the intrinsic thalamic network in poststroke epilepsy (PSE) using electroencephalography (EEG) source-level analysis. A retrospective observational study, following STROBE guidelines, enrolled 39 PSE patients and 34 stroke patients without epilepsy. Resting-state EEG data underwent source localization using minimum norm imaging and standardized low-resolution brain electromagnetic tomography (sLORETA). Thalamic network functional connectivity was assessed using coherence, with nodes defined by the Talairach atlas. Graph theory analysis compared network properties between groups. EEG source-level analysis revealed significant differences in thalamic network connectivity between PSE and non-PSE patients. Specifically, modularity, a measure of network segregation, was significantly lower in PSE patients (0.038 vs. 0.106, $p = 0.024$) in the undirected weighted connectivity matrix. Similar differences were observed using binary undirected graphs across a fixed density range. This study demonstrates altered intrinsic thalamic network organization in PSE patients compared to stroke patients without epilepsy, as revealed by EEG source-level analysis. These network changes may contribute to PSE development.

Keywords: electroencephalography, epilepsy, stroke, thalamus, poststroke epilepsy.

Introduction

Poststroke epilepsy (PSE) is a significant neurological complication that develops after a stroke, affecting a considerable proportion of stroke survivors. It is characterized by recurrent seizures occurring beyond the acute phase of stroke, typically after one week. The incidence of PSE varies depending on the study population and the definition used, but it is generally accepted that stroke survivors have a significantly higher risk of developing epilepsy compared to the general population. The occurrence of PSE not only impairs the quality of life of affected individuals but also poses a substantial burden on healthcare systems. The pathophysiology of PSE is complex and multifactorial, involving a cascade of events triggered by the initial

ischemic or hemorrhagic insult. These events include neuronal death, gliosis, inflammation, and alterations in neurotransmitter systems, all of which contribute to the development of epileptogenic foci within the brain. While the cortical involvement in the pathophysiology of PSE has been relatively well studied, the role of subcortical structures, particularly the thalamus, remains less understood. The thalamus, a central relay station for sensory and motor information, plays a critical role in regulating cortical excitability and synchrony. It has been implicated in the generation and propagation of seizures in various epilepsy syndromes. Recent neuroimaging studies have demonstrated structural and functional alterations in the thalamus of patients with epilepsy, suggesting its involvement in the epileptogenic network. In the context of PSE, stroke-induced damage to thalamic nuclei or their connections with cortical regions may disrupt the delicate balance of excitatory and inhibitory neurotransmission, leading to increased neuronal excitability and seizure susceptibility. Electroencephalography (EEG) is a non-invasive neurophysiological technique that measures electrical activity in the brain. It is widely used in the diagnosis and management of epilepsy, providing valuable information about seizure onset, propagation, and interictal epileptiform discharges. Traditional scalp EEG, however, has limitations in localizing deep brain structures like the thalamus due to volume conduction and spatial blurring. Advances in EEG source localization techniques, such as minimum norm imaging and standardized low-resolution brain electromagnetic tomography (sLORETA), have enabled the estimation of brain electrical activity at the source level, offering improved spatial resolution and the ability to investigate deep brain structures. Graph theory analysis provides a powerful framework for studying brain network organization by quantifying the topological properties of functional connectivity networks. Functional connectivity, measured using EEG coherence or other synchronization measures, reflects the statistical dependencies between brain regions. Graph theory metrics, such as modularity, clustering coefficient, and path length, can reveal alterations in network segregation and integration, providing insights into the pathophysiology of neurological disorders. In this study, we aimed to investigate the alterations in the intrinsic thalamic network in patients with PSE compared to stroke patients without epilepsy using EEG source-level analysis and graph theory. We hypothesized that PSE patients would exhibit significant changes in thalamic network connectivity and topological properties, reflecting the involvement of the thalamus in the epileptogenic network. By utilizing EEG source localization and graph theory, this study seeks to provide a more comprehensive understanding of the pathophysiology of PSE and potentially identify novel biomarkers for diagnosis and prognosis. The findings of this research may contribute to the development of targeted therapeutic strategies for PSE, ultimately improving the clinical management of stroke survivors at risk for developing epilepsy.

Material and Methods:

Participants This study received approval from the Institutional Review Board. All participants provided written informed consent before enrollment. A total of 39 patients with stroke and PSE and 34 patients with stroke without PSE were enrolled in this study. PSE was defined as the occurrence of at least 1 unprovoked seizure in the late poststroke period. Late poststroke seizures were defined as those occurring within the timeframe of 1 week to 2 years after stroke onset.[8,20] All patients were newly diagnosed with PSE at our institution and had no history of seizures before their stroke. Patients in the non-PSE group had no prior diagnosis of epilepsy

or seizures before stroke onset. Additionally, none of the patients in either group had a history of psychiatric disorders, developmental conditions, or other severe debilitating diseases. Clinical data were collected for all participants, including sex and age at the time of EEG, and stroke etiology based on the Trial of ORG 10172 in Acute Stroke Treatment classification (large-artery atherosclerosis, cardioembolism, smallartery occlusion, other causes, or undetermined origin).[21] Other recorded variables included the affected stroke hemisphere and location, initial National Institutes of Health Stroke Scale (NIHSS) score,[22,23] presence of hemorrhagic transformation, comorbid conditions (atrial fibrillation, hypertension, diabetes mellitus, dyslipidemia, or others), time interval between stroke onset and EEG acquisition, and occurrence of seizures. Electroencephalography acquisition EEG recordings were obtained from all stroke patients while they were awake and in a resting state with their eyes closed. The recordings were obtained using a standardized EEG system (TWin® EEG software system) with consistent methodologies across all participants. Trained technical staff performed the EEG acquisition using gold electrodes applied with electrode paste. A total of 23 electrodes (Fp1, Fp2, F7, F8, T1, T2, T3, T4, T5, T6, O1, O2, F3, F4, C3, C4, P3, P4, Cz, Pz, Oz, A1, and A2) were positioned in accordance with the international 10 to 20 system. Electrode impedance was maintained below 5 k Ω throughout the recordings. The EEG signals were sampled at a frequency of 250 Hz, and each recording session lasted a minimum of 30 minutes. EEG acquisition followed the same methodology as described in our previous article. Electroencephalography preprocessing and source modeling The analysis of EEG was conducted using Curry software (version 8). During data processing, EEG signals were referenced to an average. A band-pass filter was applied, with a low cutoff at 1.0 Hz and a high cutoff at 30.0 Hz. The EEG recordings were manually examined, and 3-second epochs were selected, ensuring the presence of alpha activity with maximal voltage in posterior regions while excluding artifacts or epileptiform discharges. The selection of epochs was carried out by DA Lee. Sources were subsequently computed based on their scalp electrical potentials using a minimum norm imaging method, which estimated the amplitude of brain sources distributed across the brain, and the standardized LOw-REsolution brain Electromagnetic TomogrAphy (sLORETA) approach. To construct a functional connectivity matrix, the Talairach atlas was utilized to define nodes, while the coherence method was applied to assess brain synchronization, represented as edges. Among various nodes, only 14 nodes corresponding to the thalamus were selected to analyze the intrinsic thalamic network (Supplementary File 1, Supplemental Digital Content, <http://links.lww.com/MD/O581>). 2.4. Graph theoretical analysis Graph theoretical analysis was conducted using the BRAPH software.[25] Functional connectivity metrics were computed from the undirected weighted connectivity matrix, including average degree, average strength, radius, diameter, characteristic path length, global efficiency, local efficiency, mean clustering coefficient, transitivity, modularity, and the small-worldness index.[26] These measures were analyzed and compared between patients with and without PSE. Additionally, binary undirected graphs were employed for further analysis at a fixed connection density (ranging from 15% to 95% in 5% increments) when statistically significant differences were identified in the weighted connectivity analysis. 2.5. Statistical analyses The clinical characteristics of patients with and without PSE were analyzed using the chi-squared test or an independent Student t test, as appropriate. All statistical analyses were performed using MedCalc® Statistical Software (version 20.014, MedCalc Software Ltd., Ostend, Belgium; <https://www.medcalc.org>; 2021).

Results:

Patient demographics and clinical features No significant differences were observed between patients with and without PSE in terms of age, sex, etiology of stroke, side and location of stroke, NIHSS score, presence of hemorrhagic transformation, or comorbidities. However, the time interval between stroke onset and EEG acquisition differed significantly, with a longer interval in patients with PSE compared to those without PSE (61.0 vs 5.0 months, $P < .001$). Intrinsic thalamic network presents the differences in the intrinsic thalamic network between patients with and without PSE, as analyzed using EEG source-level data. Among the functional connectivity metrics, modularity was the only measure that significantly differed between the groups, with patients with PSE exhibiting lower modularity compared to those without PSE (0.038 vs 0.106, $P = .024$). Additionally, graph theoretical analysis using binary undirected graphs at fixed density connections confirmed significant differences in modularity between the groups. However, the other functional connectivity measures, including the average degree, average strength, radius, diameter, characteristic path length, global efficiency, local efficiency, mean clustering coefficient, transitivity, and small-worldness index, did not differ between the groups.

Discussion

This study investigated the alterations in the intrinsic thalamic network in patients with poststroke epilepsy (PSE) compared to stroke patients without epilepsy, using EEG source-level analysis and graph theory. The key finding was a significant reduction in modularity within the thalamic network of PSE patients, suggesting a disruption in the segregated organization of this critical brain region. This alteration was observed in both weighted and binary undirected network analyses, reinforcing its robustness. The observed decrease in modularity in PSE patients indicates a less distinct segregation of thalamic subregions. Modularity reflects the extent to which a network can be divided into distinct modules or communities. A reduction in this metric suggests that the thalamic network in PSE patients is less compartmentalized, potentially leading to increased cross-talk and abnormal synchronization between thalamic nuclei. This disruption could contribute to the increased neuronal excitability and seizure susceptibility observed in PSE. The thalamus plays a pivotal role in regulating cortical excitability and synchrony through its extensive connections with cortical regions. Stroke-induced damage to thalamic nuclei or their connections may disrupt the delicate balance of excitatory and inhibitory neurotransmission, leading to abnormal thalamocortical interactions. The observed decrease in thalamic modularity in PSE patients may reflect this disruption, potentially contributing to the generation and propagation of seizures. It is noteworthy that the time interval between stroke onset and EEG acquisition was significantly longer in PSE patients compared to those without epilepsy. This difference may reflect the evolving nature of poststroke epileptogenesis. The delayed onset of seizures in PSE suggests that the epileptogenic process unfolds over time, involving progressive changes in neuronal circuitry and synaptic plasticity. The observed thalamic network alterations may represent a consequence of these long-term pathological changes. While this study demonstrated significant differences in thalamic modularity between the groups, other graph theory metrics, such as global and local efficiency, clustering coefficient, and path length, did not show significant differences. This suggests that the primary alteration in the thalamic

network of PSE patients is related to modular organization rather than overall network efficiency or clustering. This finding may reflect the specific role of the thalamus in regulating network segregation and its vulnerability to stroke-induced damage. This study has several strengths. Firstly, it utilized EEG source-level analysis, which offers improved spatial resolution compared to traditional scalp EEG, allowing for a more accurate assessment of thalamic network connectivity. Secondly, it employed graph theory analysis, a powerful tool for quantifying network properties and revealing subtle alterations in brain organization. Thirdly, it included a well-defined cohort of PSE patients and stroke patients without epilepsy, minimizing confounding factors. However, several limitations should be acknowledged. Firstly, the retrospective design of the study limits the ability to establish causality. Longitudinal studies are needed to examine the temporal relationship between thalamic network alterations and the development of PSE. Secondly, the sample size, while adequate for detecting significant differences in modularity, may have limited the power to detect subtle changes in other network metrics. Thirdly, the study focused on the thalamic network; future studies should explore the interactions between the thalamus and cortical regions in PSE. Finally, the exact mechanisms through which stroke leads to alterations in thalamic modularity need to be further investigated.

In conclusion, this study provides evidence for altered intrinsic thalamic network organization, specifically reduced modularity, in PSE patients compared to stroke patients without epilepsy. These findings suggest that the thalamus plays a crucial role in the pathophysiology of PSE and that disruptions in its modular organization may contribute to increased seizure susceptibility. Future research should focus on elucidating the underlying mechanisms of these alterations and exploring their potential as biomarkers for PSE diagnosis and prognosis.

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Xiphisternum Fusion Patterns and Their Utility in Age Estimation: A Cross-Sectional Radiological Analysis.

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Abstract: Age estimation is crucial in forensic and medico-legal contexts. This cross-sectional study evaluated the utility of radiological assessment of xiphisternum fusion for age estimation in individuals aged 31-45 years. Radiographs were analyzed to determine the presence or absence of complete fusion of the xiphisternum joint. The study found that 63% of participants exhibited fusion, with a slightly higher occurrence in females (33%) than males (30%). The mean age of fusion was 40.05 ± 4.89 years in males and 40.95 ± 3.87 years in females, while non-fusion occurred at a mean age of 35.83 ± 3.38 years in males and 33.30 ± 3.09 years in females. Statistical analysis revealed no significant difference in fusion rates between genders (Chi-Square = 0.287, $p = 0.592$). The findings indicate that xiphisternum fusion can be a supplementary tool for age estimation, though its reliability requires further investigation.

Introduction

Age estimation stands as a cornerstone of forensic science, playing a pivotal role in various medico-legal investigations. The ability to accurately determine an individual's age is crucial in scenarios ranging from criminal investigations and mass disaster victim identification to civil cases involving undocumented individuals. In essence, age estimation bridges critical gaps in personal identification, significantly impacting legal proceedings and humanitarian efforts. The human skeletal system undergoes predictable developmental changes throughout life, providing valuable clues for age estimation. These changes, particularly the ossification and fusion of skeletal elements, are widely utilized in forensic anthropology and radiology. Among these, the study of sternal ossification, and specifically the fusion of the xiphoid process to the sternal body, has garnered increasing interest. The sternum, comprising the manubrium, body, and xiphoid process, exhibits a complex pattern of ossification. The xiphisternum joint, where the xiphoid process articulates with the sternal body, undergoes progressive fusion with advancing age. This process, observable through radiological examinations, presents a potential avenue for age estimation, particularly in adult populations where other developmental markers may be less reliable. Traditional age estimation methods often rely on dental development, skeletal maturation of the hand and wrist, and pubic symphysis changes. However, these methods may exhibit limitations, especially in adult age ranges. Dental changes, for instance, can be influenced by environmental factors and individual habits. Similarly, the reliability of pubic symphysis assessment may decrease with age. Therefore, the exploration of alternative skeletal markers, such as xiphisternum fusion, is warranted.

Radiological imaging, including conventional radiography and computed tomography (CT), provides a non-invasive means of visualizing the sternal skeleton and assessing the degree of xiphisternum fusion. The objective evaluation of fusion stages through these imaging modalities offers a potential advantage over subjective assessments. However, the application of xiphisternum fusion in age estimation necessitates a thorough understanding of its variability across different populations and age groups. Factors such as sex, ethnicity, and nutritional status may influence the timing and pattern of fusion. Therefore, population-specific studies are essential to establish reliable age estimation norms. Furthermore, the accuracy and reliability of radiological assessment of xiphisternum fusion require rigorous validation. Establishing standardized criteria for fusion staging and evaluating the inter-observer and intra-observer variability of radiological assessments are crucial steps in ensuring the method's applicability in forensic practice. This research aims to contribute to the existing body of knowledge by investigating the relationship between radiological findings of xiphisternum fusion and chronological age in a cross-sectional study. By analyzing radiographs from a defined population, this study seeks to establish age-related patterns of xiphisternum fusion and assess its potential as a supplementary tool for age estimation. The findings of this research may have implications for forensic investigations, particularly in cases where other age estimation methods are limited. By providing greater insight into the value of radiological assessment of the xiphisternum, it is hoped that this will contribute to the general advancement of forensic science.

Material and Methods:

We have carried out our study in the Department of Forensic Medicine and Toxicology, of a tertiary care center situated in GIMSH, Durgapur, India. Sample size calculation was done by using online web based software OpenEpi. Version 3 developed by CDC. According to the study conducted by Wadhwan et al⁸ In their study, mean age for complete fusion in males and in females was 65.81 ± 10.68 years and 58.36 ± 5 years respectively. Two-sided significance was taken at 95% and power of the study was fixed at 80, minimum sample size obtained was 20 in each group. A total of 60 individuals from this region comprising both sexes in equal proportion between the age group of 31 to 45 years were taken. Samples were recruited by a simple random sampling method. Only cases whose exact age is available from birth records (date of birth certificate or Aadhar card) and who gave consent, were included in this study. Persons with any visible deformity to the anterior chest wall were not included in the study. Over-exposed or underexposed X-ray films were excluded from the study. People on hormonal therapy, having medical conditions impairing growth were also be excluded from the study. Radiological examination Cases those, written consent was obtained, were radiologically examined for the lateral view of the sternum with the exposure factors 20-25 mAs and 75-85 kVp for the fusion of the xiphi-sternal joint for determination of age. Fusion Status Fusion: Only the complete fusion of the Xiphoid process Statistical analysis Microsoft Excel (Windows 11; Version 365, Microsoft Corporation, New York, USA), was used to enter the data. Statistical Package for Social Sciences version 23.0 (SPSS

RESULTS

A Total of 30 consented individuals from each sex, in the age range of 31 to 45 years were included in the present study. The age range is further sub-classified into the age groups of 31-35 years, 36 - 40 years, and 41 - 45 years with 20 individuals from both sexes included in each group. The mean age for the males and females was 38.36 years and 38.4 years respectively. The status of xiphisternum fusion was determined as explained in the method. Cases were placed according to age group, separately for each sex, and the mean age for both fusion and non-fusion was calculated for each sex. To observe the proportion of fusion status in each sex cases were classified according to age groups. To observe the total number of fused and unfused cases against the age, a scatter plot was drawn. Cases with non-fusion of xiphisternum were clustered at early age group (31-35 years) and in later age group (41-45 years) cluster of fused cases were seen. The results of the status of xiphisternum fusion were cross tabulated with sex to obtain a p-value. All the cases showing fusion and non-fusion of the xiphisternum joint were analysed and the mean age for fusion and non-fusion of all the cases was calculated. In the present study, the earliest fusion of the xiphoid process with the body of sternum was observed at 31 years in male and at 32 years for female. Fusion of xiphoid process with body of the sternum seen latest at 44 years in males & at 40 years in females which are the latest fusion in our study.

DISCUSSION

Determining age holds significant importance in forensic settings in the deceased and also in the living. In cases involving the deceased, it primarily aids in identification by establishing a biological profile, which can then be compared to records of missing persons. For living individuals, the objective is to address legal or civil matters related to age.⁹ In the present study, 30 cases from each sex were included. A higher incidence of fusion was noted in females (66.6%) as compared to males (60%) in their group (n=30). A slightly lower mean age of fusion (40.05 ± 4.89 years) was noted in males as compared to females (40.95 ± 3.87 years). The observed mean age of non-fusion was less (33.30 ± 3.09 years) in females as compared to male (35.83 ± 3.38 years). The above findings suggest that the process of fusion took longer time in males as compared to females. Comparing the fusion status between sexes in all the age groups (Table 4), out of total cases (60), 5% of male showed fusion as compared to 3.3% of females in the 31-35 years age group. In the later age group fusion was observed more in females as compared to males. Fusion was observed in all the cases except one case of males, in the age group of 41-45 years. Of the total cases fusion was observed in 63.3% of cases, comprising 30% male and 33.3% female. The Chi-Square test did not reveal any statistically significant difference ($p > 0.005$) in the fusion of xiphisternum in males and females. A radiological study conducted by Reddy et al¹⁰ on 420 healthy individuals, comprising equally of males and females, in the age range of 25-60 years. They observed a lateral view of the sternum on X-ray. In their study mean age at which the fusion of the xiphoid process with the body of the sternum occurred was 40 years in males and 42 years in females. The findings of our study are also comparable to their study. An autopsy study was conducted by Kumar et al¹¹ on 100 cases (70 males and 30 females). The mean age of the complete fusion of the xiphoid process with the body of the sternum was observed as $50.83 \text{ years} \pm 1.641$ in males. The mean age range was higher ($58.58 \text{ years} \pm 2.831$) in the case of females in their study. The higher mean age of fusion compared to the present study could be explained by the fact that they have included 68 samples aged more than 40 years. The results of the present study were

inconsonance with their study where we also did not find any statistically significant difference in the age of fusion of the xiphoid process with the body of the sternum between males and females. A radiological study conducted in Delhi¹², observed complete fusion of the xiphoid process with the body of the sternum occurs after the mean age of 49.74 years in the case of males and 50.39 years in the case of females. A postmortem study on 100 cases conducted by Manoharan et al¹³ in Tamil Nadu observed an “absence of fusion between the xiphoid process and the body of the sternum below 32 years in males and, below 40 years in case of females.” They concluded that fusion of the xiphoid with the body occurs between 32 – 60 years regardless of sex. The present study also found similar observation where fusion was noted as early as 31 years for males and 32 years for females. The maximum age range in our study was up to 45 years thereby, the mean age of fusion of the xiphoid process was less in the present study as compared to other studies

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Unraveling Thalamic Network Dysfunction in Poststroke Epilepsy Through EEG Source Analysis.

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Abstract

This study investigated alterations in the intrinsic thalamic network in poststroke epilepsy (PSE) using electroencephalography (EEG) source-level analysis. A retrospective observational study, following STROBE guidelines, enrolled 39 PSE patients and 34 stroke patients without epilepsy. Resting-state EEG data underwent source localization using minimum norm imaging and standardized low-resolution brain electromagnetic tomography (sLORETA). Thalamic network functional connectivity was assessed using coherence, with nodes defined by the Talairach atlas. Graph theory analysis compared network properties between groups.

EEG source-level analysis revealed significant differences in thalamic network connectivity between PSE and non-PSE patients. Specifically, modularity, a measure of network segregation, was significantly lower in PSE patients (0.038 vs. 0.106, $p = 0.024$) in the undirected weighted connectivity matrix. Similar differences were observed using binary undirected graphs across a fixed density range.

This study demonstrates altered intrinsic thalamic network organization in PSE patients compared to stroke patients without epilepsy, as revealed by EEG source-level analysis. These network changes may contribute to PSE development.

Keywords: electroencephalography, epilepsy, stroke, thalamus, poststroke epilepsy.

Introduction

Poststroke epilepsy (PSE) is a significant neurological complication that develops after a stroke, affecting a considerable proportion of stroke survivors. It is characterized by recurrent seizures occurring beyond the acute phase of stroke, typically after one week. The incidence of PSE varies depending on the study population and the definition used, but it is generally accepted that stroke survivors have a significantly higher risk of developing epilepsy compared to the general population. The occurrence of PSE not only impairs the quality of life of affected individuals but also poses a substantial burden on healthcare systems. The pathophysiology of PSE is complex and multifactorial, involving a cascade of events triggered by the initial ischemic or hemorrhagic insult. These events include neuronal death, gliosis, inflammation,

and alterations in neurotransmitter systems, all of which contribute to the development of epileptogenic foci within the brain. While the cortical involvement in the pathophysiology of PSE has been relatively well studied, the role of subcortical structures, particularly the thalamus, remains less understood. The thalamus, a central relay station for sensory and motor information, plays a critical role in regulating cortical excitability and synchrony. It has been implicated in the generation and propagation of seizures in various epilepsy syndromes. Recent neuroimaging studies have demonstrated structural and functional alterations in the thalamus of patients with epilepsy, suggesting its involvement in the epileptogenic network. In the context of PSE, stroke-induced damage to thalamic nuclei or their connections with cortical regions may disrupt the delicate balance of excitatory and inhibitory neurotransmission, leading to increased neuronal excitability and seizure susceptibility. Electroencephalography (EEG) is a non-invasive neurophysiological technique that measures electrical activity in the brain. It is widely used in the diagnosis and management of epilepsy, providing valuable information about seizure onset, propagation, and interictal epileptiform discharges. Traditional scalp EEG, however, has limitations in localizing deep brain structures like the thalamus due to volume conduction and spatial blurring. Advances in EEG source localization techniques, such as minimum norm imaging and standardized low-resolution brain electromagnetic tomography (sLORETA), have enabled the estimation of brain electrical activity at the source level, offering improved spatial resolution and the ability to investigate deep brain structures. Graph theory analysis provides a powerful framework for studying brain network organization by quantifying the topological properties of functional connectivity networks. Functional connectivity, measured using EEG coherence or other synchronization measures, reflects the statistical dependencies between brain regions. Graph theory metrics, such as modularity, clustering coefficient, and path length, can reveal alterations in network segregation and integration, providing insights into the pathophysiology of neurological disorders. In this study, we aimed to investigate the alterations in the intrinsic thalamic network in patients with PSE compared to stroke patients without epilepsy using EEG source-level analysis and graph theory. We hypothesized that PSE patients would exhibit significant changes in thalamic network connectivity and topological properties, reflecting the involvement of the thalamus in the epileptogenic network. By utilizing EEG source localization and graph theory, this study seeks to provide a more comprehensive understanding of the pathophysiology of PSE and potentially identify novel biomarkers for diagnosis and prognosis. The findings of this research may contribute to the development of targeted therapeutic strategies for PSE, ultimately improving the clinical management of stroke survivors at risk for developing epilepsy.

Material and Methods:

Participants This study received approval from the Institutional Review Board. All participants provided written informed consent before enrollment. A total of 39 patients with stroke and PSE and 34 patients with stroke without PSE were enrolled in this study. PSE was defined as the occurrence of at least 1 unprovoked seizure in the late poststroke period. Late poststroke seizures were defined as those occurring within the timeframe of 1 week to 2 years after stroke onset.[8,20] All patients were newly diagnosed with PSE at our institution and had no history of seizures before their stroke. Patients in the non-PSE group had no prior diagnosis of epilepsy

or seizures before stroke onset. Additionally, none of the patients in either group had a history of psychiatric disorders, developmental conditions, or other severe debilitating diseases. Clinical data were collected for all participants, including sex and age at the time of EEG, and stroke etiology based on the Trial of ORG 10172 in Acute Stroke Treatment classification (large-artery atherosclerosis, cardioembolism, smallartery occlusion, other causes, or undetermined origin).[21] Other recorded variables included the affected stroke hemisphere and location, initial National Institutes of Health Stroke Scale (NIHSS) score,[22,23] presence of hemorrhagic transformation, comorbid conditions (atrial fibrillation, hypertension, diabetes mellitus, dyslipidemia, or others), time interval between stroke onset and EEG acquisition, and occurrence of seizures. Electroencephalography acquisition EEG recordings were obtained from all stroke patients while they were awake and in a resting state with their eyes closed. The recordings were obtained using a standardized EEG system (TWin® EEG software system) with consistent methodologies across all participants. Trained technical staff performed the EEG acquisition using gold electrodes applied with electrode paste. A total of 23 electrodes (Fp1, Fp2, F7, F8, T1, T2, T3, T4, T5, T6, O1, O2, F3, F4, C3, C4, P3, P4, Cz, Pz, Oz, A1, and A2) were positioned in accordance with the international 10 to 20 system. Electrode impedance was maintained below 5 k Ω throughout the recordings. The EEG signals were sampled at a frequency of 250 Hz, and each recording session lasted a minimum of 30 minutes. EEG acquisition followed the same methodology as described in our previous article. Electroencephalography preprocessing and source modeling The analysis of EEG was conducted using Curry software (version 8). During data processing, EEG signals were referenced to an average. A band-pass filter was applied, with a low cutoff at 1.0 Hz and a high cutoff at 30.0 Hz. The EEG recordings were manually examined, and 3-second epochs were selected, ensuring the presence of alpha activity with maximal voltage in posterior regions while excluding artifacts or epileptiform discharges. The selection of epochs was carried out by DA Lee. Sources were subsequently computed based on their scalp electrical potentials using a minimum norm imaging method, which estimated the amplitude of brain sources distributed across the brain, and the standardized LOw-REsolution brain Electromagnetic TomogrAphy (sLORETA) approach. To construct a functional connectivity matrix, the Talairach atlas was utilized to define nodes, while the coherence method was applied to assess brain synchronization, represented as edges. Among various nodes, only 14 nodes corresponding to the thalamus were selected to analyze the intrinsic thalamic network (Supplementary File 1, Supplemental Digital Content, <http://links.lww.com/MD/O581>). 2.4. Graph theoretical analysis Graph theoretical analysis was conducted using the BRAPH software.[25] Functional connectivity metrics were computed from the undirected weighted connectivity matrix, including average degree, average strength, radius, diameter, characteristic path length, global efficiency, local efficiency, mean clustering coefficient, transitivity, modularity, and the small-worldness index.[26] These measures were analyzed and compared between patients with and without PSE. Additionally, binary undirected graphs were employed for further analysis at a fixed connection density (ranging from 15% to 95% in 5% increments) when statistically significant differences were identified in the weighted connectivity analysis. 2.5. Statistical analyses The clinical characteristics of patients with and without PSE were analyzed using the chi-squared test or an independent Student t test, as appropriate. All statistical analyses were performed using MedCalc® Statistical Software (version 20.014, MedCalc Software Ltd., Ostend, Belgium; <https://www.medcalc.org>; 2021).

Results:

Patient demographics and clinical features No significant differences were observed between patients with and without PSE in terms of age, sex, etiology of stroke, side and location of stroke, NIHSS score, presence of hemorrhagic transformation, or comorbidities. However, the time interval between stroke onset and EEG acquisition differed significantly, with a longer interval in patients with PSE compared to those without PSE (61.0 vs 5.0 months, $P < .001$). Intrinsic thalamic network presents the differences in the intrinsic thalamic network between patients with and without PSE, as analyzed using EEG source-level data. Among the functional connectivity metrics, modularity was the only measure that significantly differed between the groups, with patients with PSE exhibiting lower modularity compared to those without PSE (0.038 vs 0.106, $P = .024$). Additionally, graph theoretical analysis using binary undirected graphs at fixed density connections confirmed significant differences in modularity between the groups. However, the other functional connectivity measures, including the average degree, average strength, radius, diameter, characteristic path length, global efficiency, local efficiency, mean clustering coefficient, transitivity, and small-worldness index, did not differ between the groups.

Discussion

This study investigated the alterations in the intrinsic thalamic network in patients with poststroke epilepsy (PSE) compared to stroke patients without epilepsy, using EEG source-level analysis and graph theory. The key finding was a significant reduction in modularity within the thalamic network of PSE patients, suggesting a disruption in the segregated organization of this critical brain region. This alteration was observed in both weighted and binary undirected network analyses, reinforcing its robustness. The observed decrease in modularity in PSE patients indicates a less distinct segregation of thalamic subregions. Modularity reflects the extent to which a network can be divided into distinct modules or communities. A reduction in this metric suggests that the thalamic network in PSE patients is less compartmentalized, potentially leading to increased cross-talk and abnormal synchronization between thalamic nuclei. This disruption could contribute to the increased neuronal excitability and seizure susceptibility observed in PSE. The thalamus plays a pivotal role in regulating cortical excitability and synchrony through its extensive connections with cortical regions. Stroke-induced damage to thalamic nuclei or their connections may disrupt the delicate balance of excitatory and inhibitory neurotransmission, leading to abnormal thalamocortical interactions. The observed decrease in thalamic modularity in PSE patients may reflect this disruption, potentially contributing to the generation and propagation of seizures. It is noteworthy that the time interval between stroke onset and EEG acquisition was significantly longer in PSE patients compared to those without epilepsy. This difference may reflect the evolving nature of poststroke epileptogenesis. The delayed onset of seizures in PSE suggests that the epileptogenic process unfolds over time, involving progressive changes in neuronal circuitry and synaptic plasticity. The observed thalamic network alterations may represent a consequence of these long-term pathological changes. While this study demonstrated significant differences in thalamic modularity between the groups, other graph theory metrics, such as global and local efficiency, clustering coefficient, and path length, did not show significant differences. This suggests that the primary alteration in the thalamic network of PSE patients is related to modular organization rather than overall network efficiency or clustering. This finding may reflect the specific role of the thalamus in regulating network segregation and its vulnerability to stroke-induced damage. This study has several strengths. Firstly, it utilized EEG source-level analysis, which offers improved spatial

resolution compared to traditional scalp EEG, allowing for a more accurate assessment of thalamic network connectivity. Secondly, it employed graph theory analysis, a powerful tool for quantifying network properties and revealing subtle alterations in brain organization. Thirdly, it included a well-defined cohort of PSE patients and stroke patients without epilepsy, minimizing confounding factors. However, several limitations should be acknowledged. Firstly, the retrospective design of the study limits the ability to establish causality. Longitudinal studies are needed to examine the temporal relationship between thalamic network alterations and the development of PSE. Secondly, the sample size, while adequate for detecting significant differences in modularity, may have limited the power to detect subtle changes in other network metrics. Thirdly, the study focused on the thalamic network; future studies should explore the interactions between the thalamus and cortical regions in PSE. Finally, the exact mechanisms through which stroke leads to alterations in thalamic modularity need to be further investigated.

In conclusion, this study provides evidence for altered intrinsic thalamic network organization, specifically reduced modularity, in PSE patients compared to stroke patients without epilepsy. These findings suggest that the thalamus plays a crucial role in the pathophysiology of PSE and that disruptions in its modular organization may contribute to increased seizure susceptibility. Future research should focus on elucidating the underlying mechanisms of these alterations and exploring their potential as biomarkers for PSE diagnosis and prognosis.

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Advancements in Cochlear Implant Technology: Signal Processing to Wireless Connectivity.

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Abstract

Cochlear implants (CIs) are surgically implanted devices that restore hearing in individuals with severe to profound sensorineural hearing loss. By converting sound into electrical signals that stimulate the auditory nerve, CIs have dramatically improved hearing rehabilitation. Over the past two decades, CI implantation rates have surged, driven by advancements in device design, minimally invasive surgical techniques, and refined programming strategies, all contributing to enhanced safety and efficacy. These technological developments have also broadened CI candidacy, now including individuals with greater residual hearing and infants under one year old. This overview examines current CI designs, their historical evolution, and future prospects. It highlights key figures in otology and CI design who have shaped this technology's progress. Recognizing the pivotal role of clinical and surgical anatomy, physiology, and treatment methodologies, this article underscores the significant technological advancements that have benefited CI recipients, paving the way for future innovations.

Keywords: Cochlear implant, Future designs, Deafness, Hearing Rehabilitation.

Introduction:

Hearing, a fundamental sense, intricately weaves us into the fabric of social interaction, communication, and environmental awareness. Its impairment, particularly severe to profound sensorineural hearing loss (SNHL), profoundly impacts an individual's quality of life, hindering language acquisition, social development, and overall well-being. The advent of the cochlear implant (CI) has revolutionized the management of SNHL, offering a pathway to auditory rehabilitation for individuals who derive limited benefit from conventional hearing aids. This sophisticated electronic device, surgically implanted, bypasses damaged hair cells in the cochlea and directly stimulates the auditory nerve, transforming sound into electrical signals that the brain can interpret. The journey of CI technology is a testament to the relentless pursuit of scientific innovation and clinical excellence. From its rudimentary beginnings in the mid-20th century to the sophisticated systems of today, the CI has undergone a remarkable transformation. Early pioneers, driven by a vision to restore hearing, laid the groundwork for a technology that would profoundly impact millions of lives. Initial devices, while groundbreaking, were limited in their ability to provide clear and natural sound perception. However, through decades of dedicated research and development, CI technology has evolved into a sophisticated system capable of delivering increasingly refined auditory experiences. This review paper delves into the technological innovations that have propelled CI technology forward, focusing primarily on two critical domains: signal processing and wireless

connectivity. These areas represent the vanguard of CI advancement, driving improvements in speech perception, sound localization, and overall user experience. Signal processing, the heart of CI functionality, has witnessed significant strides in sound coding strategies, electrode design, and personalized algorithms. Wireless connectivity, a more recent but equally impactful development, has transformed CI usage by enabling seamless integration with everyday devices and facilitating remote programming and telehealth. The evolution of signal processing within CIs is a narrative of continuous refinement. Early CI systems relied on simplistic sound coding strategies, often resulting in distorted and unnatural sound perception. However, the development of advanced sound coding algorithms, such as SPEAK, CIS, and HiRes, has dramatically improved speech understanding, particularly in noisy environments. These strategies, by more accurately representing the temporal and spectral features of sound, enable CI recipients to perceive speech with greater clarity and naturalness. Concurrently, advancements in electrode design have played a crucial role in enhancing CI performance. The evolution from single-channel to multi-channel electrodes, coupled with improvements in current steering and focused stimulation, has significantly improved frequency resolution and reduced channel interaction. This has translated to a more nuanced and detailed representation of sound, allowing CI users to better discriminate between different auditory stimuli. Furthermore, the advent of flexible electrode arrays has minimized cochlear trauma during implantation, leading to improved long-term outcomes. Recognizing the heterogeneity of hearing loss and individual patient needs, researchers have increasingly focused on personalized signal processing. The development of algorithms tailored to individual auditory profiles, based on objective measures such as auditory brainstem response (ABR), has optimized CI settings for each recipient. Moreover, the application of machine learning and artificial intelligence holds immense promise for further refining personalized sound processing, potentially leading to even greater improvements in speech perception and sound localization. Beyond signal processing, the integration of wireless connectivity has ushered in a new era of CI usage. The incorporation of Bluetooth technology has enabled direct audio streaming from smartphones, tablets, and other devices, enhancing user convenience and accessibility. This has transformed the CI from a standalone medical device to a seamlessly integrated component of the user's digital ecosystem. Moreover, wireless connectivity has facilitated the development of remote programming and telehealth solutions. Remote CI adjustments, enabled by secure wireless communication, have significantly reduced the need for frequent clinic visits, particularly for individuals living in remote areas or with mobility limitations. Telehealth platforms have further expanded access to CI care, allowing for remote monitoring, counseling, and troubleshooting. The integration of CIs with assistive listening devices (ALDs), such as FM systems and induction loops, has also enhanced auditory performance in challenging listening environments. These combined systems provide a more robust and versatile hearing solution, allowing CI users to participate fully in various social and professional settings. The development of user-friendly mobile applications has further simplified CI control and monitoring. These apps, often featuring intuitive interfaces and customizable settings, empower CI users to take an active role in their hearing rehabilitation. As we look towards the future, the CI landscape is poised for even greater technological advancements. Artificial intelligence and machine learning hold immense potential for optimizing CI signal processing, predicting individual hearing outcomes, and developing personalized hearing solutions. Gene therapy and biological approaches, while still in their early stages, offer the prospect of regenerating damaged auditory structures, potentially leading to even more natural and effective hearing restoration. The development of advanced biomaterials will enhance biocompatibility and long-term device performance. Optical cochlear implants, utilizing light to stimulate auditory neurons, represent a promising avenue

for improving frequency selectivity and reducing channel interaction. Brain-computer interfaces (BCIs) may eventually enable direct communication between the CI and the brain, potentially leading to even more sophisticated and personalized hearing experiences. This review paper aims to provide a comprehensive overview of these technological innovations, tracing the evolution of CI technology from its early days to the cutting-edge systems of today. By examining the advancements in signal processing and wireless connectivity, we seek to illuminate the remarkable progress that has been made in CI technology and to provide a glimpse into the exciting possibilities that lie ahead. The ultimate goal of these technological advancements is to improve the lives of individuals with severe to profound hearing loss, enabling them to fully participate in the rich tapestry of auditory experiences that surround us.

1.1. Incidence of hearing impairment in world: Worldwide perspective According to the WHO (2017) reported untreated HL costs nations between \$750 and \$790 billion a year in direct medical expenses and lost productivity³ According to the World Burden of Disease survey, HL prevalence increased from 1.2 billion people (17.2%) in 2008 to 1.4 billion people (18.7%) in 2017. ⁶Hearing impairment, which contributed more than 39.5 million years of healthy life lost since 2000, has been ranked by the World Health Organization as the third most common cause of loss of time due to disability, with an increase from 27 million in 2000. WHO projected that Disabled Hearing Loss affected 466 million people worldwide in 2018 (or 6.12% of the world's population). This estimate is projected to rise to 630 million by 2030 and to over 900 million by 2050.

1.2. Incidence of the hearing impairment in Indian context: According to the Census of India (2011), 1.98 million people in the population have various of speech impairments, while 5.07 million people have hearing impairment. ⁴ In underdeveloped nations, there are more than 10 newborns born alive with bilateral severe to profound hearing loss for every 1000 live births, according to Pasolini and Smith (2009). ¹¹ As per NSSO survey, currently there are 291 persons per one lakh population who are suffering from severe to profound hearing loss (NSSO, 2001). Of these, a large percentage is children between the ages of 0 to 14 years. With such a large number of hearing-impaired young Indians, it amounts to a severe loss of productivity, both physical and economic. An even larger percentage of our population suffers from milder degrees of hearing loss and unilateral (one sided) hearing loss. In a hospital-based survey, Niskar et al. in 1998 discovered 14.9% of kids had either low-frequency or high-frequency hearing loss. ¹² According to Norman et al., (2016) 30.9% of schoolchildren (aged 8 to 14) in the villages of Vadamavanthal, Tamil Nadu, have hearing impairment. According to the Census of India (2011), one out of every 100 children between the ages of 0 and 6 have a disability. There are 2.42 million (20.42 lakh) impaired children in this age group, and 23% of them have hearing impairment¹³ Moreover, 20% of the 7.87 million disabled people in the 0–19 age range have hearing impairments. The age range 10 to 19 years has the biggest number of impaired people (4.62 million)¹⁴ Just 61% of impaired children aged 5 to 19 are observed to be enrolled in educational institutions. Children aged 0 to 14 made up 25.9% of the population in 2018, according to data from India's sample registration survey (Sample Registration Survey of India, 2018). ¹⁵ India has the highest school-age child population with hearing impairments given the prevalence rate of hearing impairment in this age group. These kids can be easily located in schools for hearing tests, as well as for the proper rehabilitation, speech therapy, and educational facilities for their best development. The Right to Person with Disabilities Act of 2016 and the Right to Education Act of 2009 both guarantee rehabilitative and educational

assistance for children who have hearing impairments. 15 Hence for the treatment and management of the hearing impairment who do not benefit from other medical treatments, various devices like Cochlear Implants were introduced.

1.3. History of cochlear implant development: Allesandro Volta in the year 1800 did an experiment on himself and discovered that electrical stimulation of the auditory system could produce sound. After initiating a w50- V circuit, he felt "une recousse dans la tete" ("a boom within the brain") and heard a sound like boiling thick paste. In the early 1900s, researchers discovered that electrical current directly stimulates the cochlear nerve to create auditory perceptions.¹⁶ French otologist Djournio and physicist Eyrie described the consequences of directly stimulating the auditory nerve in a deaf patient in (1957).¹⁸ Radical excision for severe bilateral cholesteatomas sacrificed the right cochlear and facial nerves. The proximal auditory nerve stump was electroded before grafting the facial nerve. After applying a current, the patient was able to distinguish intensity and frequency, appreciate environmental sounds, and recognize many short words. 19 Volta's first report of auditory percepts elicited with electrical stimulation, although it is not certain if the experiment was produced with direct electrical activation of auditory neurons or via electromechanical effects, such as those underlying electrophonic hearing. While his experiment was the first, Volta's observation sparked sporadic attempts to investigate the phenomenon over the next 50 years in Paris, Amsterdam, London, and Berlin. Wilson & Dorman (2008) present that the sensation described by patients was always momentary and lacked tonal quality. Since sound is an alternating disturbance in an elastic medium, it was soon realized that stimulating the auditory system with a direct current could not reproduce a satisfactory hearing sensation. Several US groups implanted prototype CIs in the early 1960s. Blair Simmons from Stanford University implanted 6 stainless-steel electrodes into the auditory nerve through the modiolus in 1964. 19 One of his patients gave William House in Los Angeles an article on Djournio and Eyrie's earlier work. Motivated by this narrative, House implanted numerous gold electrodes in 1961 and worked with engineer Jack Urban to build long-term devices in 1965. House began clinical testing in 1973 with a commercial implant containing a wearable signal processor, platinum electrodes, and an induction coil system. Despite these early successes, other specialists in the area were skeptical, and electrical stimulation for meaningful audiologic rehabilitation in deaf individuals was denounced by the scientific community.²⁰ A National Institutes of Health-commissioned investigatory team reviewed the first thirteen single-channel electrode implantees in 1977, legitimizing cochlear implantation. Robert Bilger reported that CI technology could increase hearing, lipreading, environmental sound detection, and voice modulation with minimal patient risk. 22 In 1978, Graeme Clark in Sydney, Australia implanted his first patient with a multichannel banded electrode for limited open-set speech recognition. The University of Melbourne, the Australian government, and Nucleus Ltd., a medical equipment company, founded Cochlear Ltd. after early success. 21 Computer microcircuit and implanted pacemaker technologies aided early CI commercial device development. The FDA approved the first single-channel CI (House/3 M) for adult profound post lingual deafness patients on November 26, 1984. 3M/Vienna single channel cochlear implant provided sufficient information both in intracochlear and extracochlear stimulation to result in open-set word recognition without lipreading. These results corroborated the previous findings of Hochmair-Desoyer et al. 40 In the last 10 years, speech recognition performance in quiet has plateaued, thus our focus has switched to more demanding listening tasks including background noise, sound localization, and music enjoyment to better simulate normal hearing.

1.4. Cochlear implant function and design: Separate external and internal components make up the behind the ear Cochlear Implant system (Figure 1). The transmitter antenna, external magnet, speech processor, battery, and microphone are among the external components. The electrode array, antenna, receiver-stimulator, and internal magnet are among the internal components. An earworn microphone picks up sound, which is then transformed into an electrical signal. The external sound processor receives this signal and converts it into digital electrical code using one of its numerous processing schemes. Via the skin, a transmitting coil that is held externally above the receiver-stimulator by a magnet transmits this digital signal through radiofrequency. The receiver-stimulator ultimately decodes this signal into quick electrical impulses that are sent to a number of electrodes specific for particular frequency on an array implanted within the cochlea (specifically, the Scala tympani). The auditory nerve axons and spiral ganglion cells are then electrically stimulated by the electrodes and proceed to the brain for additional processing with digital signal. You may communicate the frequency, and intensity of sound by using these signals to carefully control the firing of intracochlear electrodes not in the continuous time domain. Currently, there are four CI manufacturers: Advanced Bionics Company (Valencia, CA, USA), Cochlear Corporation (Lane Cove, Australia), MED-EL GmbH. (Innsbruck, Austria) & Nurotron (Zhejiang Hangzhou, China). All four implant manufacturers' devices are largely comparable in terms of performance and dependability. Electrode arrays have been developed over the past ten years to be thinner, softer, and more flexible in order to reduce trauma during insertion and protect the fragile neuroepithelial structures within the cochlea.

1.5. Minimizing trauma: Early Cochlear Implant systems were thought to cause considerable intracochlear trauma during electrode insertion, which would then irreversibly lose any remaining hearing. The adoption of altered surgical methods and electrode design, however, has resulted in increased rates of hearing preservation following implantation during the past 20 years. In the past ten years, there has been a paradigm change toward the creation of soft surgical procedures and less invasive electrode designs in order to enhance performance. When electrodes are inserted, there are at least three primary processes that might cause an acute mechanical inner ear injury. The electrode can also be implanted through the membrane of the round window or by a cochleostomy established anterior to the round window. It is possible to fracture the osseous spiral lamina or spiral ligament during electrode insertion since the round window membrane is situated close to the vertically oriented osseous spiral lamina. Traumatic abutment of the lateral scalar structures at the first basal turn of the cochlea and beyond is a second frequent cause of harm. The majority of electrodes show a very straight mid-scalar route along the cochlea's basal turn. The majority of electrodes, on the other hand, are compelled to go toward the basilar membrane once they reach their first turn. If enough force is exerted, the electrode may fracture the interscalar partition or dislodge the basilar membrane, which would allow the electrode to extend into the Scala media or perhaps the Scala vestibuli. Finally, there seems to be a limit to how deep an electrode can go without causing significant harm with today's designs. During implantation, reducing electrode-related trauma has a number of positive effects, including: Limiting damage can preserve natural hearing in patients with residual low-frequency hearing, enabling concurrent electric-acoustic stimulation (EAS) strategies. 2. Revision surgery may be less difficult if intracochlear damage is reduced as this may reduce the amount of intracochlear fibrosis and ossification. A smaller cochleostomy can be achieved with a thinner, shorter electrode since it is less likely to harm the sensitive scalar structures. On the other hand, a deeper insertion in case of bipolar stimulation would potentially allow for better frequency coverage as the electric field is created in a smaller region limits the stimulation of frequencies. Therefore, it is necessary to stimulate more populations of surviving

nerve fibres or spiral ganglion cells to activate in that case. Length of insertion depends on the type and size of electric field generated by ground and active electrode. The subject of the appropriate depth of insertion is therefore brought up by this factor, which is one of the most significant in terms of current CI electrode design when stimulation is bipolar electric field. Canfarotta et.al, reported in his article, cochlear implant recipients implanted with a 31.5-mm array experienced better speech recognition than those with a 28- mm array at 12 months post activation. Deeper insertion of a lateral wall array appears to confer speech recognition. What is too deep, considering the other end of the spectrum? Contrastively Van de Marel et al. found no correlation between angular insertion depth and postoperative CVC word scores, while correcting for age at implantation, duration of deafness, preoperative phoneme score, and preoperative word score ($p=0.89$). In their analysis, Van de Marel et al. did not correct for electrode scalar location and electrode-to-modiolus proximity. All participants were implanted with the same type of electrode (HiFocus I/II) and with the same surgical technique (extended round window approach). This homogeneity in implantation characteristics prevented bias of results caused by differences in CI systems and by differences in electrode designs which is a strength of this study. Spiral ganglion frequency mapping indicates that an electrode must be placed deeper to stimulate low tone frequencies (1000 Hz); according to place theory. The place theory for normal hearing suggests that neurons closer to the base of the basilar membrane are optimized for encoding high frequency signals (up to 20kHz), while neurons near the apex encode low frequency signals (down to 20hz). Nevertheless, it appears that with the current electrode models, such as depth of insertion would result in unacceptable harm. The place theory fails to account for human frequency discrimination below 1000hz (Mannell, Robert Theories of Hearing Macquarie University, 2008). This relatively low electrode count compared to the estimated 32,000 sensory hairs. The sound processing unit typically groups, compresses, and delivers frequencies to localized electrodes in trains of pulses limiting the frequency range and sample rate which is less than ideal for tonal languages. (Plack, Chris earring Pitch Right Place, Wrong time He Psychologist, Vol. 25, NO, 12, PG. 892, December 2012). Longer implant stems are needed to accommodate more electrodes increasing risk of surgical trauma. (MD et al., 2016 in his article importance of electrode location in cochlear Implantation Laryngoscope Investigation Otolaryngology.

Summary:

Today's CIs use 9 to 22 electrodes to stimulate fewer spiral ganglion cell populations than the healthy cochlea's 3000 inner hair cells and 30,000 auditory neurons. We cannot recover normal hearing after sensorineural deafness. Difficulty understanding speech in noise, perception of music and most delicate the perception of tonal languages is still a major issue in cochlear implants. This is because the coding strategies are speech focused. There is an interleaved 'radio' silence' in between to avoid current flow on other electrodes leading to channel interactions in digital signals. Therefore, the speed at which digital signal stimulate each electrode should be very fast. However, it doesn't correspond the input sound signal speed which leads to robotic perception, raises all the major problems related to music perception, speech in noise & tonal languages. We must be heartened that even with gross stimulation tactics, a majority of patients are experiencing remarkable hearing recovery, and we continue to witness consistent development with each implant design and processing strategy. Implant users had improved speech recognition in noise, musical appreciation, and sound localization thanks to bilateral cochlear implantation. Spatial and temporal resolution and user performance

variations will likely be addressed in future versions. Innovation is accelerating, and cochlear implantation's future looks bright. 5.

Conclusion:

In order to advance medical science, it is crucial to have a deep understanding of the developments in clinical and surgical anatomy, physiology, treatment techniques, and the influential individuals involved. The history of Cochlear Implants is marked by pioneering figures and collaborative efforts in their design. In recent years, Cochlear Implants have seen notable progress, integrating technological advancements to improve patient outcomes.

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A Digital Lifeline: Telemedicine's Contribution to Healthcare Access in India.

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Abstract:

Rural India faces persistent healthcare access barriers due to infrastructure deficits and geographic isolation. This observational study investigates the impact of online doctor consultations (telemedicine) on healthcare access and utilization from 2019 to 2024, analyzing data from national telehealth initiatives like eSanjeevani and published research. Results indicate a substantial increase in consultation volumes, particularly among women and elderly patients, and improved care continuity. However, challenges including technological limitations, low digital literacy, and system integration hurdles were identified. The study recommends enhanced infrastructure, targeted training programs, seamless healthcare system integration, and supportive policy frameworks to maximize telemedicine's effectiveness in improving rural healthcare delivery.

Keywords: Telemedicine, Rural India, eSanjeevani, Healthcare Access, Digital Health.

Introduction:

India, a nation of over 1.4 billion people, presents a complex tapestry of healthcare access, marked by stark disparities between its urban and rural populations. While urban centers boast advanced medical facilities and a concentration of healthcare professionals, rural and underserved communities face formidable challenges in accessing even basic healthcare services. This divide, deeply rooted in geographical isolation, infrastructural deficiencies, and socioeconomic inequalities, has historically resulted in compromised health outcomes and a significant burden of preventable diseases. The urgency to bridge this healthcare gap has become increasingly evident, particularly in light of the evolving healthcare landscape and the transformative potential of digital technologies. The persistent challenges facing rural healthcare in India are multifaceted. Firstly, the shortage of qualified healthcare professionals in rural areas remains a critical concern. The reluctance of doctors and specialists to practice in remote regions, coupled with inadequate infrastructure and limited career opportunities, contributes to this scarcity. This translates into long wait times, limited access to specialist care, and a reliance on unqualified or untrained practitioners, often leading to misdiagnosis and delayed treatment. Secondly, infrastructural limitations, including poorly equipped healthcare facilities, unreliable electricity supply, and inadequate transportation networks, further exacerbate the challenges. The vast distances separating rural communities from healthcare centers, combined with the lack of reliable transport, often deter individuals from seeking timely medical attention. This is particularly critical in emergency situations, where delays can

have life-threatening consequences. Thirdly, socioeconomic factors, such as poverty, illiteracy, and cultural barriers, play a significant role in shaping healthcare access and utilization. Financial constraints often prevent individuals from seeking medical care, while low levels of health literacy and cultural beliefs can hinder the adoption of modern medical practices. The advent of digital technologies, particularly the internet and mobile telephony, has opened new avenues for addressing these disparities. Telemedicine, specifically online doctor consultations, has emerged as a promising strategy to overcome geographical barriers and deliver quality healthcare services to remote populations. By leveraging digital platforms, patients can connect with doctors remotely, receive consultations, obtain prescriptions, and access specialist care without the need for physical travel. This approach holds immense potential for improving healthcare access, enhancing patient outcomes, and reducing the burden on the already strained healthcare system. In India, the government has recognized the transformative potential of telemedicine and has launched several initiatives to promote its adoption. The eSanjeevani platform, a national telemedicine service, stands as a testament to this commitment. This initiative has facilitated millions of online consultations, particularly during the COVID-19 pandemic, demonstrating its efficacy in delivering healthcare services to remote areas. However, despite these advancements, the widespread adoption of telemedicine in rural India faces several challenges. Firstly, the digital divide, characterized by limited internet connectivity and low digital literacy, poses a significant obstacle. Many rural communities lack access to reliable internet services, and a significant portion of the population lacks the necessary digital skills to utilize telemedicine platforms effectively. Secondly, infrastructural limitations, such as the lack of computers, smartphones, and reliable power supply, further restrict the accessibility of telemedicine services. Thirdly, the integration of telemedicine into the existing healthcare system presents a complex challenge. Ensuring seamless communication and data exchange between online and offline healthcare providers is crucial for providing comprehensive and coordinated care. Moreover, addressing concerns related to data privacy, security, and ethical considerations is essential for building trust and ensuring the long-term sustainability of telemedicine initiatives.

Materials and Methods

This observational study employed a retrospective, synthetic analysis of secondary data to assess the impact of online doctor consultations on healthcare access and utilization among rural and underserved populations in India. The study period spanned from 2009 to 2010, allowing for the examination of trends and changes in telemedicine adoption over time, including the significant impact of the COVID-19 pandemic.

Data Sources: The study utilized a comprehensive approach to data collection, drawing from multiple sources to ensure a robust and multifaceted analysis. These sources included:

1. **Official Government Records:** Data from the eSanjeevani platform, a national telemedicine initiative, provided detailed information on the volume of teleconsultations, patient demographics (age, gender, location), and the types of medical services provided. These records offered a direct measure of telemedicine utilization within the government-led program.

2. **Government Reports:** Reports published by the Ministry of Health and Family Welfare (MoHFW, 2025) were analyzed to gather data on national healthcare policies, infrastructure development related to telemedicine, and overall healthcare access trends in rural areas.
3. **Telecom Surveys:** Surveys conducted by the Ministry of Communications (MoC, 2024) provided insights into internet and mobile phone penetration rates in rural India, crucial for understanding the digital infrastructure supporting telemedicine adoption.
4. **Peer-Reviewed Academic Literature:** A comprehensive review of peer-reviewed research articles (e.g., Mohan et al., 2012; Verma et al., 2023) was conducted to identify relevant studies on telemedicine in India, including its impact on healthcare access, utilization, and patient outcomes. These studies contributed to a broader understanding of the context and challenges associated with telemedicine implementation.

Data Extraction and Analysis: Data were extracted from the identified sources, focusing on key metrics relevant to the study's objectives. These metrics included:

- **Volume of Teleconsultations:** The total number of online doctor consultations provided through eSanjeevani and other telemedicine platforms, analyzed to assess the overall utilization of telemedicine services.
- **Demographic Trends:** Analysis of patient demographics, including age, gender, and geographical location, to identify patterns in telemedicine utilization among different population subgroups.
- **Reported Health Outcomes:** Data on patient health outcomes, such as changes in disease management, adherence to treatment plans, and satisfaction with telemedicine services, were extracted from available sources.
- **Internet and Mobile Phone Penetration:** Data on internet and mobile phone access in rural areas, to assess the digital infrastructure available for telemedicine implementation.
- **Infrastructure Development:** Data regarding governmental investment in infrastructure for telemedicine.
- **Policy changes:** Data regarding policy changes related to telemedicine.

Analytical Methods: The study employed a combination of descriptive and comparative analysis methods to examine the collected data.

- **Descriptive Analysis:** Descriptive statistics, including frequencies, percentages, and means, were used to summarize and describe the key metrics related to telemedicine utilization, demographics, and health outcomes.
- **Comparative Analysis:** Comparative analysis was conducted to examine trends in telemedicine utilization over time and to compare healthcare access and utilization between different rural regions and demographic groups. This involved looking at changes in consultation rates, patient demographics, and reported health outcomes.
- **Trend Analysis:** Trend analysis was conducted to identify patterns and changes in telemedicine utilization over the study period, helping to assess the impact of specific interventions or policy changes.
- **Qualitative Synthesis:** A qualitative synthesis of the peer-reviewed literature was conducted to provide contextual understanding and supplement the quantitative data.

Evaluation of Effectiveness: The effectiveness of telemedicine interventions in improving healthcare access for rural populations was evaluated by examining changes in the volume of teleconsultations, the demographics of patients utilizing telemedicine services, and reported improvements in health outcomes. The study also considered the challenges and barriers to telemedicine adoption, such as digital literacy gaps and infrastructural limitations, to provide a comprehensive assessment of its effectiveness.

Results;

The analysis of secondary data revealed a substantial increase in telemedicine utilization in rural India, particularly following the launch of the eSanjeevani platform in 2019. By early 2020, the platform had facilitated over 338 million consultations (Ministry of Health and Family Welfare, 2025), demonstrating a significant uptake of telemedicine services.

Demographic Trends:

- A detailed examination of user demographics indicated that women constituted a significant majority of teleconsultation participants, accounting for 56% of all consultations.
- Senior citizens represented 13% of the user base, highlighting the role of telemedicine in enhancing healthcare access for the elderly population.
- These results demonstrate a positive impact on reducing access barriers for traditionally underserved demographics.

Clinical Applications:

- The primary focus of teleconsultations was on the management of chronic illnesses, including hypertension, diabetes, and dermatological conditions, as well as paediatric care (Vaidya et al., 2024; Singh et al., 2024).
- The Chunampet Rural Diabetes Prevention Project, as documented by Mohan et al. (2012), provided evidence of improved glycaemic control and a reduction in referrals to higher healthcare centers through telemedicine interventions.

Satisfaction and Effectiveness:

- Patient and healthcare provider satisfaction rates were consistently high, exceeding 80% (centresya & Rai, 2016). This indicates a positive perception of telemedicine's effectiveness in rural settings.
- The high consultation numbers indicate high usage of the services provided.
- The data indicates that telemedicine is being used for chronic care, which is very important for rural populations.

Conclusion

This study demonstrates that online doctor consultations, particularly through platforms like eSanjeevani, have significantly transformed healthcare access and utilization in rural India. By bridging the geographical divide and connecting rural patients with healthcare professionals, telemedicine has effectively reduced the burden of long-distance travel, facilitated timely access to medical care, and enhanced participation among marginalized groups, including women and the elderly. The results presented herein underscore the efficacy of digital health solutions in addressing the unique healthcare challenges faced by rural populations, especially in the management of chronic diseases. The substantial volume of teleconsultations, coupled with high patient and provider satisfaction rates, provides compelling evidence of telemedicine's positive impact. Furthermore, the observed improvements in glycaemic control and reduced referrals in the Chunampet Rural Diabetes Prevention Project highlight the clinical benefits of this approach.

However, to fully realize the transformative potential of telemedicine and ensure its long-term sustainability, strategic investments and targeted interventions are crucial. This includes:

- **Infrastructure Development:** Strengthening digital infrastructure in rural areas by improving internet connectivity and ensuring reliable access to digital devices.
- **Digital Literacy Enhancement:** Implementing programs to enhance digital literacy among rural populations, enabling them to effectively utilize telemedicine services.
- **System Integration:** Ensuring seamless integration of telemedicine platforms with existing local healthcare systems to facilitate coordinated and comprehensive care.
- **Policy Support:** Developing and implementing supportive policies that promote the adoption and scaling of telemedicine initiatives.

As India progresses towards achieving universal health coverage, telemedicine emerges as a scalable and replicable solution that can significantly enhance healthcare delivery for underserved populations. By addressing the identified challenges and leveraging the demonstrated benefits, India can harness the power of digital health to bridge the healthcare divide and improve the health outcomes of its rural citizens.

Discussion

The findings of this observational study highlight the significant impact of online doctor consultations, particularly through the eSanjeevani platform, on healthcare access and utilization in rural India. The substantial increase in teleconsultations, reaching over 338 million by early 2025, underscores the growing acceptance and reliance on telemedicine as a viable healthcare delivery model in underserved areas. This surge in utilization can be attributed to several factors, including the reduction of geographical barriers, the convenience of remote consultations, and the increasing availability of digital infrastructure. The demographic analysis revealed a notable trend of increased participation among women and the elderly. The fact that women accounted for 56% of teleconsultations suggests that telemedicine addresses specific barriers they face in accessing traditional healthcare, such as mobility constraints and socio-cultural restrictions. Similarly, the 13% representation of senior

citizens highlights telemedicine's potential to improve access for a population often burdened by chronic illnesses and limited mobility. This underscores the potential of telemedicine to address health equity. The focus of teleconsultations on managing chronic illnesses, such as hypertension, diabetes, and dermatological conditions, aligns with the growing burden of non-communicable diseases in rural India. The observed improvements in glycaemic control in the Chunampet Rural Diabetes Prevention Project demonstrate the clinical effectiveness of telemedicine in chronic disease management. Furthermore, the high patient and provider satisfaction rates indicate that telemedicine services are perceived as valuable and effective. However, despite these positive outcomes, several challenges remain. The need for improved infrastructure, expanded digital literacy, and seamless integration with existing healthcare systems is crucial for the long-term sustainability of telemedicine initiatives. The digital divide, characterized by limited internet connectivity and low digital literacy, continues to be a significant barrier. Addressing this requires targeted interventions, such as investing in broadband infrastructure, providing digital literacy training, and developing user-friendly telemedicine platforms. Integrating telemedicine into the existing healthcare system is another critical challenge. Ensuring seamless communication and data exchange between online and offline healthcare providers is essential for providing coordinated and comprehensive care. This requires the development of interoperable electronic health records (EHRs) and the establishment of clear protocols for referrals and follow-up care. The study's limitations, primarily stemming from its reliance on secondary data, should be acknowledged. Potential biases in data collection and reporting from different sources could affect the accuracy and generalizability of the findings. Future research should consider conducting primary data collection through surveys and interviews to gain a deeper understanding of patient and provider experiences. Furthermore, future studies should investigate the cost-effectiveness of telemedicine interventions in rural India. While this study demonstrates the positive impact on access and utilization, a comprehensive economic evaluation is needed to inform policy decisions regarding resource allocation and investment. The results of this study have significant implications for policymakers and healthcare providers. As India strives to achieve universal health coverage, telemedicine offers a promising avenue for improving healthcare access and equity. By addressing the identified challenges and leveraging the demonstrated benefits, India can harness the power of digital health to bridge the healthcare divide and improve the health outcomes of its rural citizens. The success of eSanjeevani and similar initiatives demonstrates that with proper planning and implementation, telemedicine can be a powerful tool in achieving health equity.

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