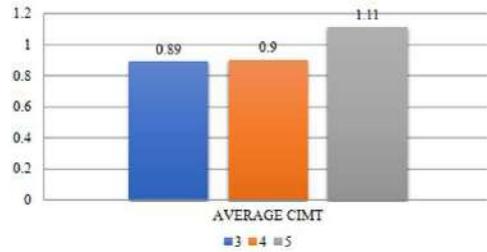




# National Board of Examination (NBE) Journal of Medical Sciences

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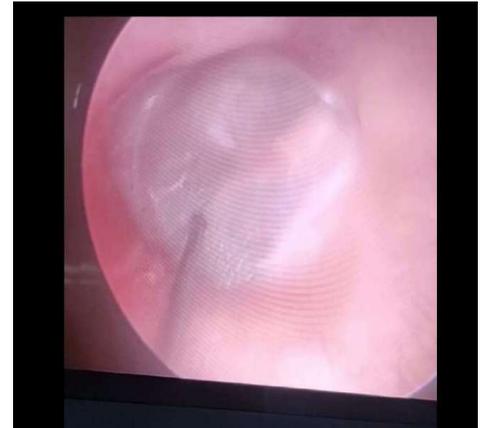
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B. Knee joint bruise and hemarthrosis



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EDITORIAL

**Strategic Planning for Clinical Services in Indian Health Care System**

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Providing affordable healthcare for all in a populous country like India is a complex and challenging task. The Ministry of Health & Family Welfare (MoHFW) in India plays a pivotal role in addressing this challenge by focusing on the formulation, coordination, and promotion of affordable healthcare facilities. The clinical services in Indian health care system are crucial in setting the direction for healthcare delivery in the country, with an emphasis on affordability, accessibility, and quality. The ministry works to coordinate healthcare services at the national and state levels. This coordination is essential to ensure that healthcare resources are effectively distributed and utilized to reach all segments of the population. A major focus should be promotion of affordable healthcare facilities. This includes initiatives to reduce the cost of medical treatment, medicines, and healthcare services, especially for vulnerable and economically disadvantaged groups. It also required the development and maintenance of public health infrastructure, including hospitals,

clinics, and healthcare centers. Expanding and strengthening this infrastructure is critical to making healthcare more accessible and affordable. The government has introduced various health insurance schemes, such as Ayushman Bharat, to provide financial protection to citizens and ensure that they can access healthcare services without being burdened by high costs. Our policies should emphasize more towards preventive healthcare measures, including vaccination programs and health education. Preventing diseases and promoting healthy lifestyles can help reduce the overall burden on the healthcare system. Collaborations between the government and private healthcare providers should be encourage to expand the reach of affordable healthcare services. These partnerships can bring in expertise and resources to complement public efforts. Ensuring that healthcare services are available in rural and remote areas is a significant challenge. We should focus to establish and support healthcare facilities in these underserved regions. Regular monitoring and evaluation of healthcare programs and initiatives are essential to assess their impact and make necessary improvements.

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### **The Importance of Strategic Planning in Indian health services**

Strategic planning is of paramount importance in Indian health services for several reasons. India's healthcare system is vast and complex, serving a population of over a billion people. Effective strategic planning helps address the unique challenges and opportunities within the Indian healthcare landscape. Areas which need focus are:

- Resource allocation
- Health equity
- Disease burden
- Infrastructure development
- Human resource development
- Public-private partnership
- Health information system
- Regulatory framework
- Technology integration
- International collaboration

India's healthcare system often faces resource constraints, including funding, infrastructure, and human resources. Strategic planning helps prioritize resource allocation to areas of greatest need, ensuring efficient utilization and equitable access to healthcare services. We have significant disparities in healthcare access and outcomes between urban and rural areas, as well as among different socioeconomic groups. A well-structured strategic plan can focus on reducing these disparities by targeting interventions in underserved regions and vulnerable populations. We are facing a high burden of communicable and non-communicable diseases. Effective strategic planning can identify prevailing health challenges, set priorities for disease prevention and management, and allocate resources for healthcare programs accordingly. We need substantial investments in healthcare infrastructure, including hospitals, clinics, and diagnostic facilities. Strategic planning guides the expansion and modernization of healthcare

infrastructure to meet current and future demands. The healthcare workforce in India needs to be adequately trained, motivated, and distributed to ensure the delivery of quality healthcare services. Strategic planning can address human resource gaps and develop strategies for recruitment, training, and retention of healthcare professionals. Our country's healthcare system comprises both public and private providers. Strategic planning can facilitate collaboration between the public and private sectors to leverage their strengths and ensure comprehensive healthcare coverage. Efficient data collection and analysis are critical for evidence-based decision-making in healthcare. Strategic planning can include the development and implementation of health information systems to monitor health trends, evaluate program effectiveness, and inform policy decisions. Our healthcare sector requires robust regulatory frameworks to ensure the quality and safety of healthcare services. Strategic planning can address regulatory gaps, enhance monitoring and enforcement, and promote accountability within the healthcare industry. The integration of technology, such as telemedicine and electronic health records, can improve healthcare delivery and access, especially in remote and underserved areas. Strategic planning can guide the adoption and implementation of health tech solutions. India can benefit from international collaborations and partnerships in healthcare research, innovation, and knowledge exchange. Strategic planning can identify opportunities for such collaborations and enhance the country's position in global health.

### **Levels of Health Care Strategy in India**

In India, healthcare strategies are typically implemented at various levels to address the diverse and complex healthcare needs of the population. These levels of healthcare strategy encompass different aspects of planning,

delivery, and management within the healthcare system. Some of the key levels of healthcare strategy in India are:

- National Healthcare Strategy
- State Healthcare Strategy
- District and Regional Healthcare Strategy
- Institutional Healthcare Strategy
- Disease-Specific Healthcare Strategy
- Primary, Secondary, and Tertiary Care Strategy
- Public-Private Partnership (PPP) Strategy
- Health Information Management Strategy
- Rural and Urban Healthcare Strategy

At the national level, India formulates healthcare policies and strategies that set the overarching direction for the entire healthcare system. This includes the development of national health plans and policies, such as the National Health Policy, which outlines the country's long-term healthcare goals and priorities. India is a federal country with a decentralized healthcare system, and each state has its own healthcare strategy. State governments develop their healthcare policies, plans, and budgets to align with the national health goals while addressing state-specific healthcare challenges. These strategies are critical in tailoring healthcare services to the unique needs of each state's population. At the district and regional levels, healthcare strategies are developed to cater to the healthcare needs of local communities. District health plans and strategies are often aligned with both national and state health policies, but they also account for district-specific factors, including population demographics, health infrastructure, and prevalent health issues. Healthcare institutions such as hospitals, medical colleges, and public

health centers develop their strategies to provide high-quality healthcare services. These strategies encompass aspects like facility expansion, staff training, technology adoption, and patient care protocols. They are essential for ensuring the efficient functioning of healthcare institutions. India faces a wide range of health challenges, from communicable diseases like tuberculosis and malaria to non-communicable diseases like diabetes and cardiovascular diseases. Disease-specific strategies are formulated to address the prevention, control, and management of these diseases. These strategies often involve partnerships with international organizations and NGOs. Healthcare strategies also differentiate between primary, secondary, and tertiary care levels. Primary care strategies focus on preventive care, health promotion, and basic healthcare services at the community level. Secondary and tertiary care strategies involve specialized medical services and advanced treatments, often coordinated through district hospitals and medical colleges. Public and private sector collaboration is crucial in India's healthcare system. Strategies for promoting PPPs are designed to leverage the strengths of both sectors to expand healthcare access, improve quality, and manage costs effectively. Effective healthcare planning and decision-making rely on accurate health data and information systems. Strategies for health information management include the development of electronic health records, health information exchanges, and data analytics for evidence-based policymaking. India's healthcare challenges vary significantly between rural and urban areas. Strategies are developed to address the specific needs of these regions, including healthcare infrastructure development, staffing, and healthcare delivery models.



Figure 1. Types of health care strategies in India.

## Strategy Types

There are several types of strategies that organizations, governments, and individuals can employ to achieve their goals and objectives. These strategies can be broadly categorized into various types based on their scope, focus, and application. Some common types of strategies are mentioned in the Figure 1.

- **Business Strategy**

- **Corporate Strategy**

This type of strategy is developed at the highest level of an organization and defines the overall direction and scope of the company. It includes decisions related to diversification, mergers and acquisitions, and market positioning.

- **Competitive Strategy**

Competitive strategies focus on how a business can gain a competitive advantage within its industry. Common approaches include cost, leadership,

differentiation, and niche market strategies.

- **Marketing Strategy**

Marketing strategies outline how a company plans to promote its products or services to target customers, including pricing, distribution, and advertising plans.

- **Organizational Strategy**

- **Organizational Development (OD) Strategy**

OD strategies aim to improve an organization's effectiveness and efficiency by focusing on its structure, culture, and processes.

- **Change Management Strategy**

Change management strategies are designed to guide an organization through significant changes, such as restructuring, technology implementation, or mergers, while minimizing disruption and resistance.

- **Government and Public Policy Strategies**

- **Public Policy Strategy**

Governments use public policy strategies to address societal issues, regulate industries, and achieve specific policy objectives, such as healthcare reform or environmental protection.

- **Economic Development Strategy**

These strategies focus on stimulating economic growth, often through infrastructure development, attracting investments, and creating jobs.

- **Personal Development Strategies**

- **Career Development Strategy**

Individuals may develop strategies for advancing their careers, which may involve acquiring new skills, networking, or seeking higher education.

- **Financial Planning Strategy**

Personal financial strategies include budgeting, investing, and saving for retirement or other financial goals.

- **Health and Wellness Strategies**

- **Wellness Strategy**

These strategies are aimed at improving an individual's overall well-being through lifestyle changes, such as exercise, diet, and stress management.

- **Healthcare Strategy**

Healthcare strategies involve planning for healthcare needs, including preventive care,

insurance, and access to medical services.

- **Technology and Innovation Strategies**

- **Technology Adoption Strategy**

Organizations may develop strategies for adopting and integrating new technologies into their operations.

- **Innovation Strategy**

These strategies focus on fostering creativity and innovation within an organization to drive product or process improvements.

- **Environmental and Sustainability Strategies**

- **Environmental Sustainability Strategy**

Organizations develop these strategies to reduce their environmental footprint, minimize waste, and promote sustainable practices.

- **Corporate Social Responsibility (CSR) Strategy**

CSR strategies encompass an organization's efforts to contribute positively to society and the environment, often through philanthropy and ethical business practices.

- **Risk Management Strategy**

- **Risk Mitigation Strategy**

Organizations and individuals develop strategies to identify, assess, and mitigate various types of risks, including financial, operational, and reputational risks.

- **Global Expansion and International Strategies:**

- **Global Expansion Strategy**

Organizations looking to expand internationally may develop strategies for entering new markets, managing cultural differences, and complying with international regulations.

- **International Trade Strategy**

These strategies pertain to the import and export of goods and services between countries and may involve trade agreements and partnerships.

- **Security and Defense Strategies**

- **National Security Strategy**

Governments develop these strategies to protect their countries from external threats, including military, cyber, and homeland security measures.

- **Cybersecurity Strategy**

Organizations and governments develop cybersecurity strategies to protect their digital assets and information from cyberattacks.

### **Demand in India's healthcare market**

Demand in India's healthcare market will keep growing out to 2035, driven by:

1. **Large and Growing Population:** India has a massive and continually growing population, which accounts for almost one-fifth of the global population. This demographic challenge places significant pressure on the healthcare system and resources.
2. **Double Burden of Diseases:** India faces a double burden of infectious diseases, such as tuberculosis, and rising non-communicable diseases (NCDs) like heart disease, diabetes, and obesity. NCDs are becoming a major health concern, and

urbanization and lifestyle changes are expected to fuel their growth.

3. **Diabetes Epidemic:** By 2035, it's projected that 109 million people in India will suffer from diabetes, reflecting the increasing prevalence of this NCD.
4. **Growing Consumer Class:** India's growing middle-class population has the ability to spend on healthcare, which can drive the demand for better healthcare services and technologies.
5. **Penetration of Insurance:** Increasing penetration of health insurance can support greater healthcare spending by providing financial security for medical expenses.
6. **Ageing Population:** The proportion of elderly individuals (over 65) in India is expected to increase from 6 percent to 13 percent by 2050. This demographic shift will lead to a higher demand for age-related healthcare and aged care services.
7. **Under-provision of Medical Goods:** India's medical device market is growing rapidly, but a significant portion of medical goods is still imported. This highlights opportunities for domestic production and innovation.
8. **Nutraceutical Market:** India is likely to become a major driver of growth in the global nutraceutical market due to rising incomes and increasing consumer awareness of health and wellness.
9. **Air Pollution:** Air pollution is a severe issue in India, causing more than one million premature deaths annually. Addressing this problem is crucial for public health, and it requires cleaner energy sources and conservation agriculture practices, for example, Delhi experiences extreme air pollution during its winter months due to a combination of factors, including weather conditions, vehicular and industrial emissions, and agricultural practices like burning chaff in neighboring states. This issue underscores the need for coordinated efforts to improve air quality.

India faces complex challenges in healthcare and environmental sustainability due to its large

and diverse population, changing disease patterns, and environmental issues like air pollution. Addressing these challenges will require a multi-pronged approach involving healthcare infrastructure development, public health campaigns, environmental conservation efforts, and policy initiatives.

### Indian Supply

India's health sector is also growing and modernizing & has to keep pace with rising demand.

India's healthcare sector and its challenges:

1. **Growth and Modernization:** India's healthcare sector is experiencing significant growth and modernization. The sector is growing at a Compound Annual Growth Rate (CAGR) of 16 percent, reflecting the increasing demand for healthcare services.
2. **Low Health Spending:** Despite this growth, India's spending on health remains relatively low. Total spending on health in India, which includes both public and private spending, is only 4 percent of GDP. This is significantly below the global average of 9.9 percent.
3. **Limited Government Spending:** Government spending on healthcare in India is particularly low, accounting for only 1.4 percent of GDP (combined central and state spending). This is well below the global average of 6 percent. This low government expenditure has persisted for a decade.
4. **Reliance on Private Healthcare:** The inadequacy of public healthcare facilities has led many individuals to rely on expensive private healthcare services. Low public expenditure shifts the financial burden of healthcare to out-of-pocket expenses, which account for 62 percent of total health spending. This lack of financial protection schemes can be financially burdensome for many.
5. **Need for Health Financing System:** There is a need for a comprehensive health financing system that includes a

workable coding framework for after-the-fact payment systems. This would help streamline and regulate healthcare billing and payment processes.

6. **Fragmented Private Sector:** While the private sector has fostered pockets of efficiency, it is fragmented, which can result in varying quality of care and accessibility across regions.
7. **Inadequate Medical Infrastructure:** Despite growth, the medical infrastructure in India still lags behind global standards. India has 1 hospital bed per 1,000 people, which is below the world median of 2.9. Similarly, the ratio of physicians to population is also below the global median, with only 0.7 physicians per 1,000 people compared to the world median of 2.5.

To address these challenges in India's healthcare sector will require significant investments, policy reforms, and efforts to improve the quality and accessibility of healthcare services. It will also involve finding ways to increase government healthcare spending, reduce the reliance on out-of-pocket expenses, and bridge the gaps in medical infrastructure and human resources.

### Comparative analysis of global health care services vs India

Comparing global healthcare services to those in India involves examining various aspects of healthcare systems, including access, quality, financing, and outcomes. It's important to note that healthcare systems can vary significantly from one country to another, and India's healthcare system faces unique challenges and opportunities. Here's a comparative analysis of global healthcare services versus those in India:

#### 1. Access to Healthcare:

Global Perspective: In many developed countries, access to healthcare is nearly

universal due to comprehensive public healthcare systems or universal health coverage. Wait times for non-emergency care are often shorter, and there is a broader network of healthcare facilities.

India Perspective: India's healthcare system faces challenges related to equitable access. While there have been efforts to expand access through initiatives like Ayushman Bharat, access to healthcare can still be limited, especially in rural areas. There is a wide disparity in healthcare infrastructure between urban and rural regions.

## 2. Quality of Care:

Global Perspective: Developed countries generally have well-established healthcare infrastructure and higher healthcare quality standards. There is often a focus on evidence-based medicine, patient safety, and quality assurance.

India Perspective: India has a wide range of healthcare facilities, from world-class hospitals in major cities to basic healthcare centers in rural areas. Quality can vary significantly between facilities. There have been efforts to improve quality and patient safety, but challenges remain.

## 3. Healthcare Financing:

Global Perspective: Many developed countries have publicly funded or heavily subsidized healthcare systems funded through taxation. This often results in lower out-of-pocket expenses for patients. Private health insurance is also common.

India Perspective: India's healthcare financing is characterized by a mix of public and private spending. Government spending is relatively low, leading to a significant reliance on out-of-pocket expenses. Health insurance penetration is increasing but remains limited for many.

## 4. Healthcare Outcomes:

Global Perspective: Developed countries generally have better healthcare outcomes, including higher life expectancy, lower infant mortality rates, and lower disease burden. This is often attributed to comprehensive healthcare services and preventive care.

India Perspective: India has made progress in improving healthcare outcomes, but challenges remain. Life expectancy has increased, but there are still high rates of maternal and child mortality. Non-communicable diseases are on the rise, contributing to the disease burden.

## 5. Infrastructure and Workforce:

Global Perspective: Developed countries typically have a higher density of healthcare infrastructure and healthcare workers per capita. This contributes to better access and shorter wait times.

India Perspective: India faces shortages of healthcare infrastructure, including hospital beds and healthcare professionals. There is a need for substantial investments in medical education and healthcare infrastructure to meet the growing demand.

## 6. Innovations and Technology:

Global Perspective: Developed countries often have access to cutting-edge medical technologies, research facilities, and clinical trials. They tend to be leaders in medical innovations.

India Perspective: India is emerging as a hub for medical tourism and has a growing pharmaceutical industry. It has the potential for healthcare innovations, but there is a need for more research and development investments.

Thus, while global healthcare services in many developed countries generally offer higher quality, better access, and more comprehensive coverage, India's healthcare system faces unique challenges due to its large and diverse

population. India has made progress in expanding access and improving healthcare outcomes, but addressing disparities, increasing healthcare financing, and enhancing healthcare quality are ongoing priorities for the Indian healthcare system.

Strengthen efforts to bring India into global and regional regimes on health security issues

Strengthening efforts to bring India into global and regional regimes on health security issues is crucial for several reasons. India's participation and collaboration in these regimes can enhance global health security, facilitate coordinated responses to health emergencies, and contribute to the well-being of its own population and the global community. Here's how this can be achieved:

#### **1. Disease Surveillance and Reporting:**

India can collaborate with international organizations and neighboring countries to strengthen disease surveillance and reporting mechanisms. Sharing real-time data on disease outbreaks and health threats is vital for early detection and response.

#### **2. Information Sharing and Capacity Building:**

India can participate in capacity-building programs and knowledge sharing initiatives offered by global health organizations, such as the World Health Organization (WHO). This would enhance India's preparedness to manage health emergencies.

#### **3. Bilateral and Multilateral Partnerships:**

India can establish and strengthen bilateral and multilateral partnerships with countries in its region and globally. These partnerships can involve joint research, resource sharing, and mutual support during health crises.

#### **4. Vaccine Diplomacy:**

India has a significant role to play in vaccine production and distribution. Expanding

its involvement in global vaccine initiatives, like COVAX, can ensure equitable access to vaccines during pandemics.

#### **5. Development of Regional Health Frameworks:**

India can work with neighboring countries to develop regional health security frameworks. These frameworks can outline collective responses to health crises and promote regional cooperation in areas such as healthcare infrastructure and resource sharing.

#### **6. Participation in Global Health Initiatives:**

India can actively participate in and support global health initiatives, including the Global Health Security Agenda (GHSA). GHSA encourages countries to enhance their health security capacities and collaborate on preparedness and response efforts.

#### **7. Research and Innovation:**

India has a strong pharmaceutical and biotechnology sector. Encouraging research and innovation in health security-related areas, such as vaccine development, diagnostics, and medical technologies, can contribute to global health preparedness.

#### **8. Capacity Strengthening:**

India can invest in strengthening its healthcare infrastructure, including hospital systems, laboratories, and public health agencies. This will enable the country to respond more effectively to health emergencies and provide support to neighboring countries when needed.

#### **9. Regional Health Workforce Development:**

Collaborative efforts can be made to develop a skilled healthcare workforce capable of

responding to regional health security threats. Training and exchange programs can facilitate the sharing of expertise.

#### 10. **Policy Advocacy and Diplomacy:**

India can advocate for global and regional health security issues on international platforms. Diplomatic efforts can include pushing for policies that promote health security and rallying support from other nations.

#### 11. **Emergency Response Coordination:**

India can establish mechanisms for effective coordination during health emergencies, both domestically and regionally. This includes the establishment of rapid response teams and stockpiling of essential medical supplies.

In conclusion, India's active engagement in global and regional regimes on health security issues is vital for fostering international cooperation, enhancing preparedness, and responding effectively to health crises. By working collaboratively with its neighbors and the global community, India can contribute to the overall improvement of global health security and ensure the safety and well-being of its own citizens and those in the region.

#### **India has policy ambitions to significantly improve its health sector**

India's policy ambitions to significantly improve its health sector are crucial for addressing the country's healthcare challenges, enhancing healthcare access, and improving the overall well-being of its population. Several policy initiatives and reforms have been launched to achieve these ambitions:

1. **National Health Policy (NHP):** India released its National Health Policy in 2017, which outlines a comprehensive roadmap for the transformation of the healthcare system. The policy emphasizes universal health coverage, strengthening

primary healthcare, and reducing the burden of non-communicable diseases.

2. **Ayushman Bharat:** Ayushman Bharat, often referred to as the world's largest health insurance program, consists of two components: Pradhan Mantri Jan Arogya Yojana (PM-JAY) and Health and Wellness Centers (HWCs). PM-JAY provides financial protection to vulnerable populations, while HWCs focus on preventive and primary care services.
3. **Digital Health Initiatives:** India has been actively promoting digital health initiatives, including the development of electronic health records, telemedicine services, and health information exchange platforms. These technologies aim to improve healthcare access and information sharing.
4. **National Rural Health Mission (NRHM):** NRHM has been instrumental in improving rural healthcare infrastructure, staffing, and access to maternal and child health services. It has now been subsumed under the National Health Mission (NHM), which continues to focus on strengthening healthcare delivery in underserved areas.
5. **National Medical Commission (NMC) Act:** The NMC Act, passed in 2019, aims to reform medical education and regulation in India. It seeks to enhance the quality of medical education, streamline the licensing process, and improve healthcare workforce standards.
6. **Mental Health Care Act:** India passed the Mental Health Care Act in 2017 to provide a legal framework for mental

health services and protect the rights of individuals with mental illnesses.

7. **Janani Suraksha Yojana (JSY):** JSY is a maternity benefit program that provides financial incentives to pregnant women for delivering in healthcare facilities. It has contributed to increasing institutional deliveries and reducing maternal mortality.
8. **Tuberculosis Control Programs:** India has launched various initiatives to control and eliminate tuberculosis, including the Revised National Tuberculosis Control Program (RNTCP) and the TB-Free India campaign.
9. **COVID-19 Response:** During the COVID-19 pandemic, India implemented several measures, including lockdowns, testing, contact tracing, and vaccination campaigns, to mitigate the spread of the virus and protect public health.
10. **Health Infrastructure Expansion:** India has been working to expand healthcare infrastructure, including the construction of new hospitals and primary health centers, to enhance access to healthcare services.
11. **Innovation and Research:** India's healthcare sector is increasingly focusing on innovation and research, with efforts to develop indigenous medical technologies, drugs, and vaccines.
12. **Private-Public Partnerships:** Collaborations between the public and private sectors have been encouraged to leverage resources, expertise, and innovations in healthcare delivery.

These policy ambitions demonstrate India's commitment to improving its healthcare system and addressing the unique healthcare challenges it faces. While significant progress has been made, there are ongoing efforts required to ensure that healthcare is accessible, affordable, and of high quality for all segments of the population. Additionally, continued investments in healthcare infrastructure, human resources, and health technologies will play a crucial role in achieving India's health sector goals.

### Global trends in healthcare

Global trends in healthcare are continuously evolving in response to demographic shifts, technological advancements, economic factors, and public health challenges. These trends shape the way healthcare is delivered, accessed, and managed worldwide. Some of the prominent global trends in healthcare:

1. **Telehealth and Telemedicine:** The COVID-19 pandemic accelerated the adoption of telehealth and telemedicine services. These technologies allow patients to access healthcare remotely, improving access to medical advice, consultations, and monitoring, particularly in remote or underserved areas.
2. **Digital Health and Health Tech:** The healthcare industry is increasingly leveraging digital technologies such as mobile health apps, wearable devices, remote patient monitoring, and electronic health records (EHRs) to enhance patient care, streamline operations, and collect health data for research and analysis.
3. **AI and Machine Learning:** Artificial intelligence (AI) and machine learning are being used to analyze large datasets, assist with diagnostics, predict disease

- outbreaks, personalize treatment plans, and improve healthcare decision-making.
4. **Personalized Medicine:** Advances in genomics and molecular biology have paved the way for personalized medicine. Tailoring treatments and therapies to an individual's genetic makeup and health characteristics can enhance treatment outcomes and minimize side effects.
  5. **Value-Based Care:** Many healthcare systems are shifting from fee-for-service models to value-based care. Value-based care focuses on improving patient outcomes while controlling costs, often through coordinated and preventative care.
  6. **Population Health Management:** Healthcare providers are increasingly adopting population health management strategies to improve the overall health of communities by addressing social determinants of health, preventive care, and chronic disease management.
  7. **Global Health Security:** The COVID-19 pandemic highlighted the importance of global health security. International collaboration on pandemic preparedness, early detection, and response is a growing focus.
  8. **Aging Population:** Many countries are experiencing an aging population, leading to a higher demand for healthcare services related to age-related conditions and long-term care.
  9. **Mental Health Awareness:** There is a growing awareness of mental health issues globally, leading to increased efforts to reduce stigma, expand access to mental health services, and integrate mental health into overall healthcare systems.
  10. **Environmental Health:** Climate change and environmental factors are impacting public health. Addressing environmental health issues is becoming a priority, including reducing air pollution, improving water quality, and promoting sustainable practices.
  11. **Health Equity and Access:** Achieving health equity and ensuring access to healthcare services for all populations, including vulnerable and underserved communities, is a persistent global challenge and goal.
  12. **Health Data Privacy and Security:** As healthcare systems digitize patient records and data, ensuring the privacy and security of health information has become a paramount concern. Regulatory frameworks like GDPR and HIPAA are guiding data protection efforts.
  13. **Biotechnology Advancements:** Biotechnological innovations, including gene editing, stem cell therapies, and regenerative medicine, are opening new possibilities for disease treatment and prevention.
  14. **Pharmaceutical Innovation:** Pharmaceutical research continues to advance, leading to the development of targeted therapies, immunotherapies, and vaccines for various diseases.
  15. **Healthcare Workforce Challenges:** Shortages of healthcare professionals, especially in certain specialties and regions, are driving discussions on

workforce training, retention, and telehealth support.

These global trends are reshaping healthcare systems and practices worldwide, with an emphasis on improving patient outcomes, enhancing healthcare access, and addressing emerging health challenges. Adapting to and leveraging these trends is essential for healthcare organizations, policymakers, and stakeholders to meet the evolving healthcare needs of populations around the world.

### **Opportunities in care services in India**

The healthcare sector in India presents several opportunities in various care services due to the country's large and diverse population, increasing healthcare awareness, and evolving healthcare needs. The key opportunities in care services in India are:

1. **Primary Healthcare Services:**

Establishing and operating primary healthcare centers (PHCs) and sub-centers in rural and underserved areas to provide essential healthcare services, preventive care, and health education.

2. **Telehealth and Telemedicine:**

Developing telehealth platforms and telemedicine services to expand access to healthcare in remote and rural regions, including virtual consultations, remote monitoring, and telehealth apps.

3. **Specialized Care Centers:**

Setting up specialized care centers, such as cancer treatment centers, cardiac care units, and neurology centers, to cater to the increasing demand for specialized medical services.

4. **Home Healthcare Services:**

Offering home healthcare services that include home nursing, physiotherapy, and medical equipment rental to support patients who prefer receiving care at home.

5. **Geriatric Care Services:**

Meeting the needs of the growing elderly population by providing geriatric care services, including assisted living facilities, senior day care centers, and home care for the elderly.

6. **Mental Health Services:**

Expanding mental health services by establishing mental health clinics, crisis helplines, and online counseling platforms to address the rising awareness of mental health issues.

7. **Maternal and Child Health Services:**

Focusing on maternal and child health services, including prenatal care, neonatal care, and pediatric care, to reduce maternal and infant mortality rates.

8. **Rehabilitation Services:**

Offering rehabilitation services, such as physical therapy, occupational therapy, and speech therapy, to address the needs of patients recovering from injuries or surgeries.

9. **Diagnostics and Pathology Services:**

Establishing diagnostic laboratories and pathology centers to provide accurate and timely diagnostic services, including radiology, imaging, and lab tests.

10. **Health and Wellness Centers:**

Creating health and wellness centers that offer preventive care, health check-ups, and lifestyle management programs to

promote a culture of wellness and disease prevention.

11. **Pharmaceutical and Medical Supplies:**  
Manufacturing and distributing pharmaceuticals, medical devices, and healthcare equipment to meet the growing demand for healthcare products.
12. **Healthcare IT and Digital Health Solutions:**  
Developing healthcare information technology solutions, including electronic health records (EHRs), healthcare management systems, and mobile health apps.
13. **Medical Tourism:**  
Catering to the needs of medical tourists by providing high-quality medical services, wellness retreats, and holistic health experiences.
14. **Health Education and Training:**  
Offering healthcare education and training programs for healthcare professionals, including doctors, nurses, technicians, and administrators.

15. **Community Health Services:**  
Collaborating with communities to implement health awareness campaigns,

preventive care initiatives, and health education programs.

16. **Alternative and Traditional Medicine:**  
Exploring opportunities in alternative and traditional medicine systems, such as Ayurveda, Yoga, Naturopathy, Unani, Siddha, and Homeopathy (AYUSH), and integrating them into healthcare services.
17. **Health Insurance and Health Financing:**  
Developing health insurance products and services to provide financial protection and improve healthcare access for individuals and families.

These opportunities in care services in India align with the country's healthcare needs and provide avenues for investment, innovation, and entrepreneurship. However, it's important to conduct thorough market research, consider regulatory requirements, and assess local healthcare demands when pursuing opportunities in the Indian healthcare sector. Additionally, collaborations with government health programs and public-private partnerships can play a significant role in expanding and scaling care services in India.



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ORIGINAL ARTICLE

**Correlation of serum phosphate levels and carotid intimal thickness in CKD patients**

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**Abstract**

**Background-** Chronic kidney disease is a significant global health issue characterized by notable morbidity and mortality rates. Among CKD patients, cardiovascular disease stands as the primary cause of death, often accompanied by accelerated atherosclerosis. Hyperphosphatemia, characterized by elevated serum phosphate levels in CKD patients and has been implicated in the progress of vascular calcification and cardiovascular events.

**Aim:** To observe relationship between serum phosphate and carotid intimal thickness in individuals with CKD.

**Discussion:** Existing studies have presented conflicting findings, with some demonstrating a positive correlation while others reporting no significant association. Consequently, a cross-sectional study was conducted on CKD patients representing various stages of renal impairment. Serum phosphate levels were measured, and carotid intimal thickness was assessed using ultrasound imaging.

**Conclusion:** This study demonstrates a significant association between serum phosphate levels and carotid intimal thickness in CKD patients. Elevated serum phosphate levels were found to be correlated with increased carotid intimal thickness, suggesting a potential role of phosphate in the progression of atherosclerosis in CKD.

**Keywords:** Carotid intimal medial thickness, CKD, diabetes, serum phosphate.

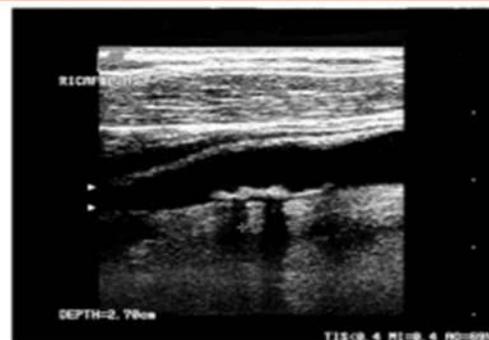
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**Abbreviations**

CKD	:	Chronic Kidney Disease
RAAS	:	Renin Angiotensin Aldosterone System
mTOR	:	Mammalian Target of Rapamycin
ESRD	:	End Stage Renal Disease
IL-6	:	Interleukin-6
AGEs	:	Advanced Glycation End Products
TNF- $\alpha$	:	Tumor Necrosis Factor Alpha
CIMT	:	Carotid Intimal Medial Thickness
TGF- $\beta$	:	Transforming Growth Factor Beta
eGFR	:	estimated Glomerular Filtration Rate

**Graphical Abstract**

**STUDY OF S.PHOSPHATE CORRELATION WITH CIMT IN CKD**



**Background & aim:**  
 •CKD is a well established risk factor for atherosclerosis but the role of phosphate has not been established  
 •In this study we aim to find out the role of s.phosphate in arterial wall thickness by using CIMT as measure

**Methodology:**  
 •In This hospital based observational cross-sectional study, we take 90 ckd patients(stages 3,4,5) and measure CIMT, S. Phosphate  
 •CIMT is measured by B mode ultrasound using 7-12 mhz linear transducer. Three measurements were taken at 0.5, 1, 2cm from carotid bifurcation

**Results:**  
 •mean average CIMT in study participants is 0.944±0.296.  
 •our study revealed statistically significant correlation between serum phosphorus and CIMT (correlation coefficient of 0.704)  
**Conclusion:**  
 Our study concludes that increased phosphate level is significant factor contributing to increased CIMT in CKD patients and improvement of hyperphosphatemia may be considered for avoidance of atherosclerosis progression in CKD

## Introduction

CKD is a significant global health issue characterized by notable morbidity and mortality rates. Diabetes mellitus, particularly type 2 diabetes, is a leading cause of CKD worldwide. Persistent hyperglycemia, the hallmark of diabetes, plays a central role in the development and progression of diabetic CKD [1].

Among CKD patients, cardiovascular disease stands as the primary cause of death, often accompanied by accelerated atherosclerosis. Hyperphosphatemia, characterized by elevated serum phosphate level in CKD patients and has been implicated in progress of vascular calcification and cardiovascular events [2].

However, the precise relationship between serum phosphate levels and carotid intimal thickness, a recognized indicator of subclinical atherosclerosis, in CKD patients remains unclear. Existing studies have presented conflicting findings, with some demonstrating a positive correlation between serum phosphate levels and carotid intimal thickness, while others reporting no significant association.

## CKD Pathophysiology

The pathophysiology of diabetic CKD is multifaceted and involves numerous interconnected mechanisms.

One of the primary mechanisms is the activation of the RAAS. Increased glucose levels promote the production of angiotensin II, a potent vasoconstrictor that causes renal arteriolar constriction and promotes inflammation and fibrosis. Angiotensin II also stimulates the release of aldosterone, which contributes to sodium and water

retention, further increasing intraglomerular pressure and renal damage [3]. Another imperative factor in pathophysiology of diabetic CKD is accumulation of AGEs. These toxic metabolites form as a result of prolonged exposure to high glucose levels and contribute to oxidative stress, inflammation, and endothelial dysfunction in the kidneys. AGEs also interact with specific receptors, such as the receptor for AGEs, leading to further inflammatory responses and tissue injury [4].

Hyperglycemia stimulates the release of pro-inflammatory cytokines, like IL-6 and TNF- $\alpha$ , promoting recruitment and activation of immune cells in the renal tissue [5]. TGF- $\beta$  is a key mediator that promotes the accumulation of extracellular matrix proteins, leading to glomerulosclerosis and tubulointerstitial fibrosis. Additionally, aberrant activation of intracellular signaling pathways, such as protein kinase C and mTOR, contributes to abnormal cell proliferation, apoptosis, and hypertrophy, further worsening renal damage [6].

## CKD and Cardiovascular effects

CKD is associated with a significantly increased risk of CVD, making it a major contributor to morbidity and mortality in CKD patients. The pathophysiology of CKD-related cardiovascular effects is multifactorial and involves a complex interplay of various mechanisms [7].

Hypertension, in particular, is commonly observed in CKD and plays a central role in promoting vascular remodeling, endothelial dysfunction, and atherosclerosis [8]. The dysregulation of

mineral and bone metabolism in CKD, characterized by elevated phosphate levels and deranged calcium-phosphate balance, also plays a significant role in cardiovascular complications. Hyperphosphatemia promotes vascular calcification, a process similar to atherosclerosis, leading to arterial stiffening and increased cardiovascular risk [9]. Elevated parathyroid hormone levels in CKD contribute to vascular calcification and left ventricular hypertrophy, further exacerbating cardiovascular effects [10].

### **Carotid Intimal Medial Thickness**

Carotid intimal-medial thickness is a valuable indicator of atherosclerotic vascular disease, providing a comprehensive representation of arterial wall alterations resulting from numerous cardiovascular risk factors over time [11]. Arteries and veins consist of three layers, with the middle layer being thicker in arteries compared to veins. CIMT specifically refers to the combined thickness of the intimal and medial layers of the vessel wall. It serves as a direct marker of atherosclerosis and has predictive value for cardiovascular mortality. The non-invasive nature, cost-effectiveness, and accessibility of CIMT measurement make it an attractive alternative to invasive methods like angiography for detecting atherosclerosis [12]. Ultrasound imaging using B-mode with a frequency range of 7-12 Hz can be performed on easily accessible large vessels such as the carotid, radial, brachial, and femoral arteries. Among these, the carotid artery is the preferred site for CIMT measurement. The procedure involves locating the best site for measurement using a transverse view while the patient is in a

supine position [13]. Calipers are used to measure CIMT, with readings taken on each side and an average value calculated. A CIMT measurement exceeding 1 mm is considered significant. The focus on studying the intimal layer of the artery stems from the fact that atherosclerosis primarily affects this region. The accessibility of the carotid arteries makes them suitable for measuring intimal-medial thickness due to their superficial location [14].

### **Serum Phosphate level in CKD**

Elevated serum phosphate levels are commonly observed in patients with CKD due to impaired kidney function. The kidneys play a vital role in regulating serum phosphate, and the loss of this regulatory function leads to a propensity for phosphate retention [15]. In early stages of CKD, the filtered phosphate load is reduced, leading to an imbalance in serum phosphorus levels. Normal serum phosphorus levels typically range from 2.5 mg/dl to 4.5 mg/dl [16]. However, as the eGFR falls below 25 to 40 mL/min/1.73 m<sup>2</sup>, overt hyperphosphatemia develops [17]. Serum phosphorus levels continue to rise as CKD progresses to ESRD [18]. Hyperphosphatemia has been linked to raised morbidity and death rate in CKD patients. Specifically, it has been independently linked to the calcification of large arteries e.g. aorta and small arteries e.g. coronary arteries, left ventricular hypertrophy in individuals with ESRD. These findings highlight the importance of managing serum phosphate levels in CKD patients to mitigate the adverse cardiovascular effects associated with hyperphosphatemia [19].

## **Material and Methods**

### **Biochemical assay**

A venous blood sample was collected to measure the levels of serum phosphate (inorganic). The samples were processed using a fully automated biochemistry analyzer (XL-1000). The test utilized the principle of U.V. Molybdate, where serum phosphate reacts with Ammonium molybdate to form reduced phosphomolybdate in presence of strong acids. The reduced phosphomolybdate level was measured, which is directly proportional to the concentration of inorganic phosphorus in the sample. Additional tests including serum albumin, serum creatinine, hemoglobin, C-reactive protein, serum calcium and serum lipid profile were measured using the XL-1000 analyzer.

### **Carotid intimal medial thickness**

CIMT was assessed using B-mode ultrasound with a Siemens Acuson x 300 machine equipped with a 7 to 12MHz linear transducer. CIMT is determined by measuring the distance between the leading edge of the first echogenic line (Lumen-Intima interface) and the second echogenic line (Media-Adventitia interface) on the far wall of the carotid artery. Measurements were taken at three locations i.e., 0.5 cm, 1 cm, and 2 cm below the common carotid bifurcation on each side, referred to as the upper, middle, and lower CIMT, respectively. The average of these measurements was calculated. The CIMT values from both left and right sides were obtained, and its average was used. A single radiologist performed the CIMT measurements in plaque-free arterial segments.

Plaques were identified as areas of localized enlargement compared to the neighboring segment, characterized by protrusion into the lumen.

### **Inclusion criteria**

- Age  $\geq$  18 years
- CKD stage  $\geq$  3

### **Exclusion criteria**

- History of carotid surgery
- AKI
- H/o IHD, MI, CVA
- Pregnancy

## **Observation and Results**

The relationship between CIMT average and different clinical parameters was examined in a study involving 90 patients. The mean age of the study participants was  $57.2 \pm 14.4$  years, with maximum participants of age between 51-60 years, followed by 41-50 years. Males constituted 57.8% of the study population, while females accounted for 42.2%. The mean body mass index was observed to be  $25.1 \pm 3.15$  kg/m<sup>2</sup>, indicating that most patients fell into the obese category. Hypertension was prevalent among the majority of patients, with a mean SBP of  $143.98 \pm 21.67$  mmHg and a mean DBP of  $84.44 \pm 14.85$  mmHg. Furthermore, the study revealed that a significant number of participants tested positive for C-reactive protein, indicating inflammation. Mean hemoglobin, GFR, and serum albumin levels were found to be low, while parameters such as creatinine, blood urea, random blood sugar, serum triglycerides, and urine albumin were high. Distribution of lab investigations are as shown in Table 1.

Table 1. Laboratory investigations statistics

Parameter	Mean	Median	Std. Dev.	Minimum	Maximum
Hb (g/dl)	8.54	8.1	2.37	5.7	16.1
S. Creat. (mg/dl)	5.22	4.28	3.35	1.4	16.1
B. Urea (mg/dl)	131.42	114	74.97	38.6	399
GFR (ml/min)	21.67	17	16.26	5	123
RBS (mg/dl)	232.88	201	157.01	83	793
S. Albumin (g/dl)	2.79	2.6	0.63	1.9	4.5
Urine Albumin	1.48	1	0.5	1	2
S. Calcium(mg/dl)	7.98	8.2	1.96	4	14.12
S. HDL (mg/dl)	35.92	28.2	16.28	6	106
S. LDL (mg/dl)	69.74	64	40.79	15	187
S. TC (mg/dl)	140.14	128	63.3	48	319
S. TG (mg/dl)	173.64	157	95.11	67	491

The mean right sided CIMT in upper, middle, and lower portion was measured 0.99 mm, 0.87 mm and 0.87 mm respectively as shown in Table 2 while mean left sided CIMT in

upper, middle and lower portion was measured 1.17mm, 0.91 mm, and 0.86 mm respectively as shown in Table 3. Mean average CIMT was  $0.944 \pm 0.296$ .

Table 2. Right CIMT statistics on carotid doppler

Right CIMT				
	Upper	Middle	Lower	AVERAGE RIGHT CIMT
Mean	.9889	.8711	.87333	.91111
Median	.9000	.9000	.80000	.90000
Std. Deviation	.50201	.21107	.295585	.293202
Minimum	.30	.60	.400	.467
Maximum	2.70	1.40	2.700	1.867

Table 3. Left CIMT statistics on carotid doppler

<b>Left CIMT</b>				
	Upper	Middle	Lower	AVERAGE LEFT CIMT
Mean	1.166	.909	.858	.977
Median	1.100	.800	.900	.967
Std. Deviation	.561	.286	.259	.330
Minimum	.500	.500	.400	.500
Maximum	3.000	2.000	2.000	1.933

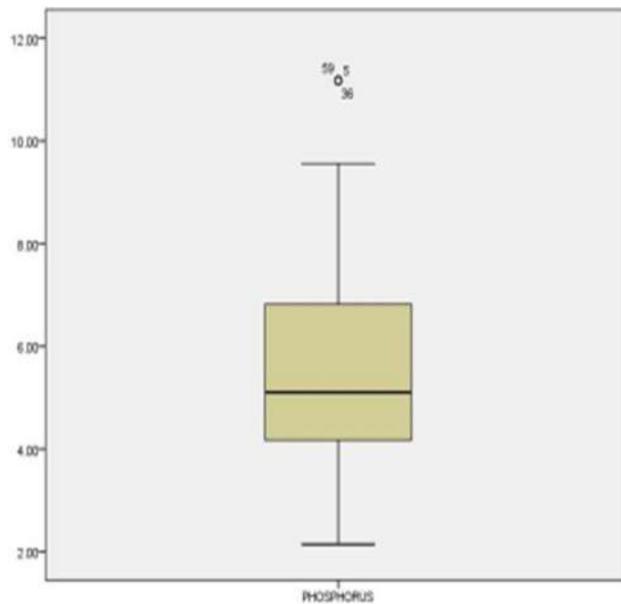


Figure 1. Box whisker plot and table of S. phosphate levels depicting its statistics.

Table 4. Statistics of S. phosphate levels

<b>Parameter</b>	<b>Mean</b>	<b>Median</b>	<b>Std. Dev.</b>	<b>Minimum</b>	<b>Maximum</b>
S. Phosphate (meq/L)	5.5290	5.1000	2.0062	2.14	11.18

Serum phosphate being the central core of the study was plotted on a box whisker plot as shown in Figure 1 with the help of its statistical values as shown in Table 4, to evaluate its distribution among the patients.

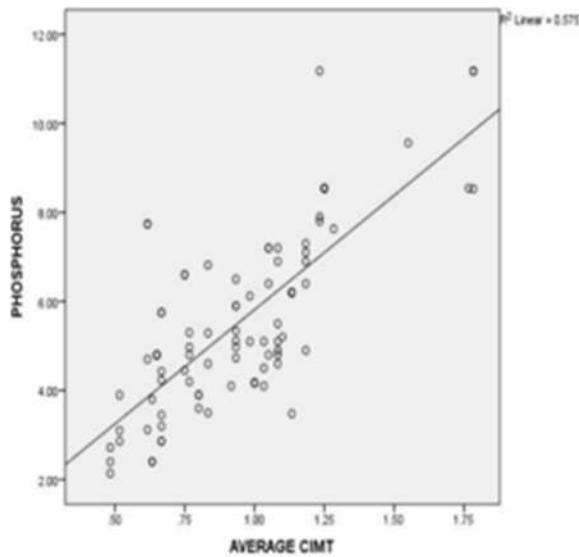


Figure 2. Correlation between average CIMT and S. phosphate levels

To assess the correlation between CIMT and various parameters, scatter plots were created, plotting the average CIMT value against serum phosphate, age, RBS, BMI, serum triglycerides and hemoglobin individually. In this study, a significant positive correlation was observed between serum phosphate levels and CIMT as shown in Figure 2, with a correlation coefficient ( $\rho$ ) of 0.704. Also, justifying the monitoring and management of S. phosphate levels to mitigate cardiovascular risk. Affirmative correlation is also seen with age as shown in Figure 3.

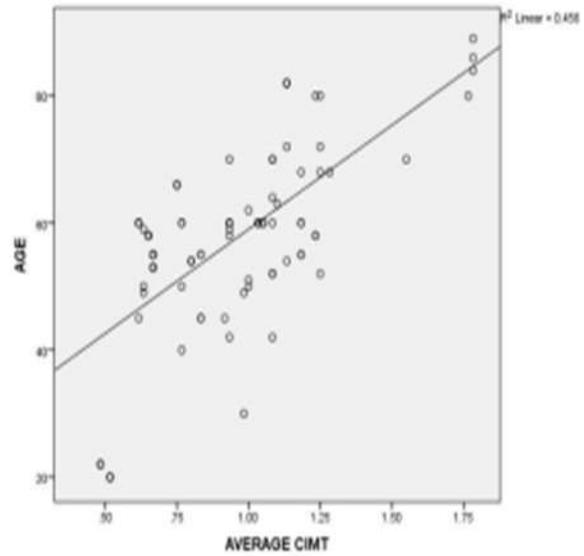


Figure 3. Correlation between average CIMT and Age

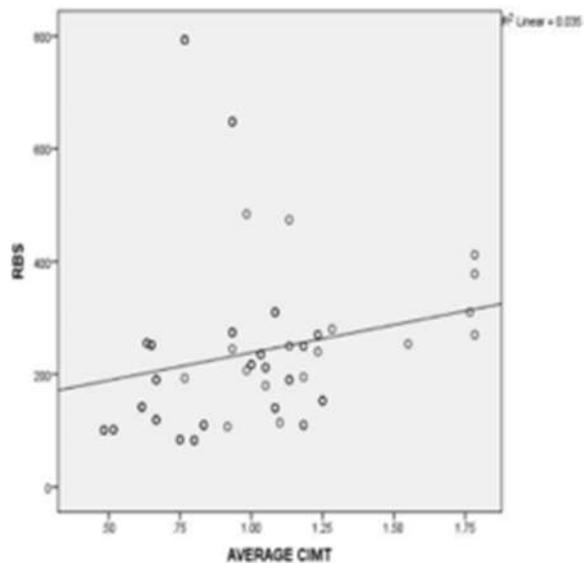


Figure 4. Correlation between average CIMT and Random blood sugar levels

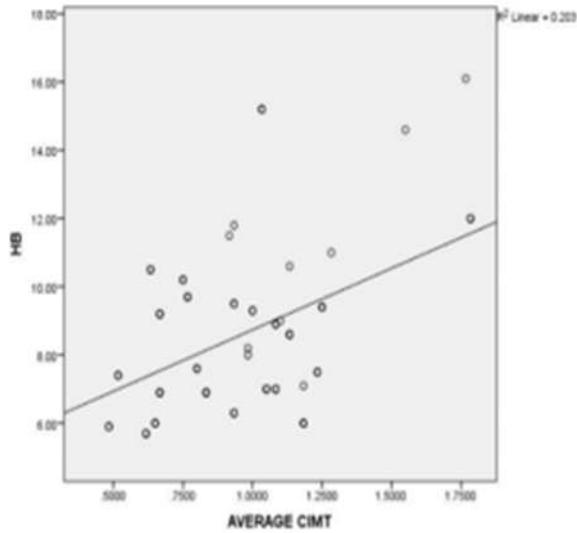


Figure 5: Correlation between average CIMT and BMI

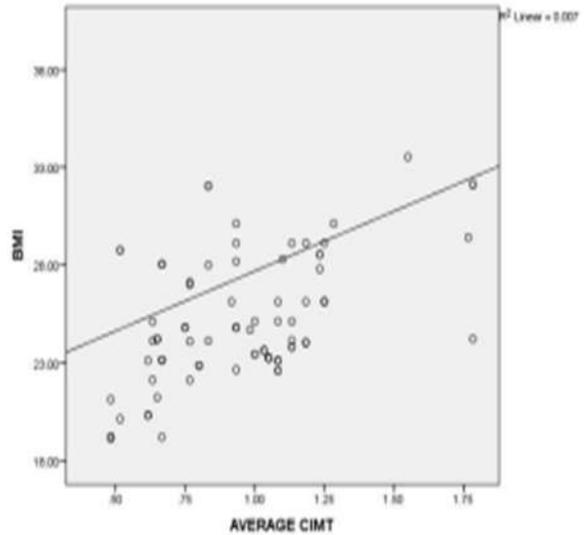


Figure 7: Correlation between average CIMT and Hemoglobin

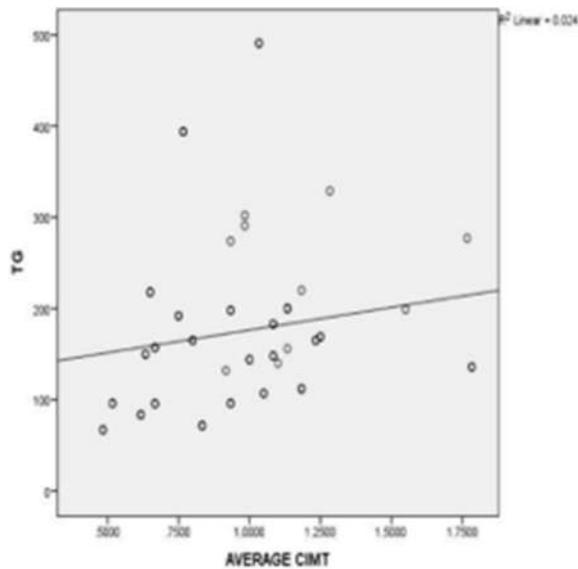


Figure 6: Correlation between average CIMT and S. Triglyceride levels

Positive scatter plot between RBS and CIMT average as well as BMI and CIMT average highlighting its correlation are depicted in Figure 4 and 5 respectively.

The scatter plots of CIMT vs Triglycerides and Hb are positively correlated but not strongly linked to each other as shown in Figures 6 and 7.

Figure 8 shows that CIMT has increased with worsening of CKD stages indicating that atherosclerosis intensifies with CKD.

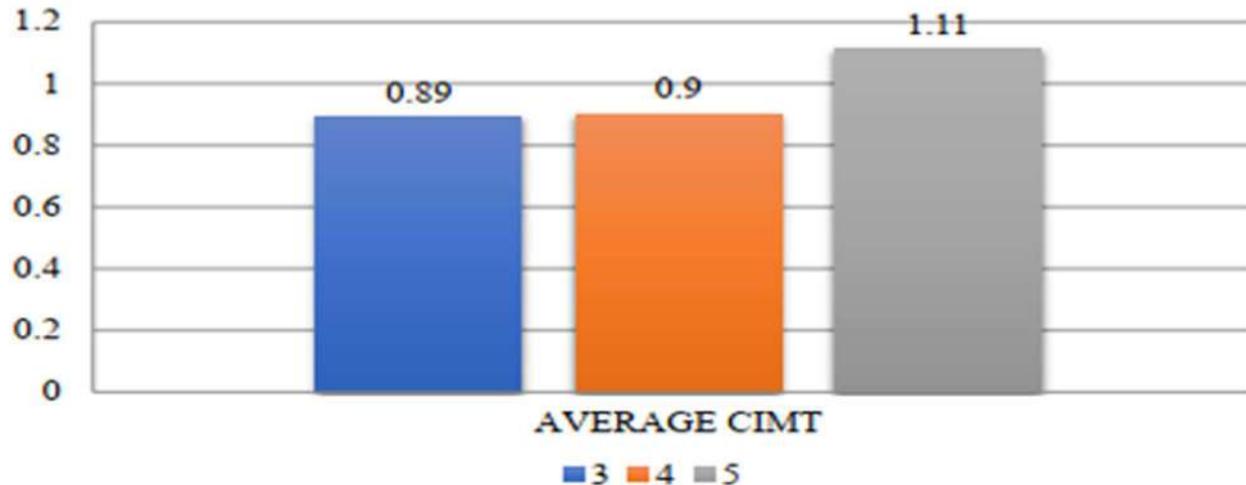


Figure 8. Variation of average CIMT with stages 3, 4 and 5 of CKD

**Conclusion**

The examination of CIMT in patients with CKD led to the observation that elevated serum phosphate levels were a notable factor associated with increased CIMT. Alongside this finding, other factors such as advanced age, higher levels of Hemoglobin (Hb), Body Mass Index (BMI), Serum Triglycerides (TG), and Random Blood Sugar (RBS), were also linked to increased CIMT. Addressing hyperphosphatemia could be considered as a potential measure to prevent the progression of arteriosclerosis in CKD patients.

**Future Scope**

The association between serum phosphate and average CIMT in CKD patients is a topic that holds promise for further exploration and research. Longitudinal studies can be conducted to establish a cause-and-effect relationship. Furthermore, it would be beneficial to investigate the impact of interventions targeting serum phosphate levels on carotid intimal thickness and cardiovascular outcomes in CKD patients. This could involve evaluating the effectiveness of

phosphate-lowering therapies, such as dietary modifications, phosphate binders, or novel pharmacological agents. Incorporating advanced imaging techniques and biomarkers related to vascular calcification and atherosclerosis could enhance the understanding of the underlying mechanisms. Exploring genetic and molecular factors that influence phosphate metabolism and vascular health may also provide valuable insights.

**Ethics declarations**

**Funding** This study did not receive any funding.

**Conflict of interest**

The authors declare that they have no competing interests.

**Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability**

Not applicable.

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**REVIEW ARTICLE**

**SARS COV-2 and its association with vertigo**

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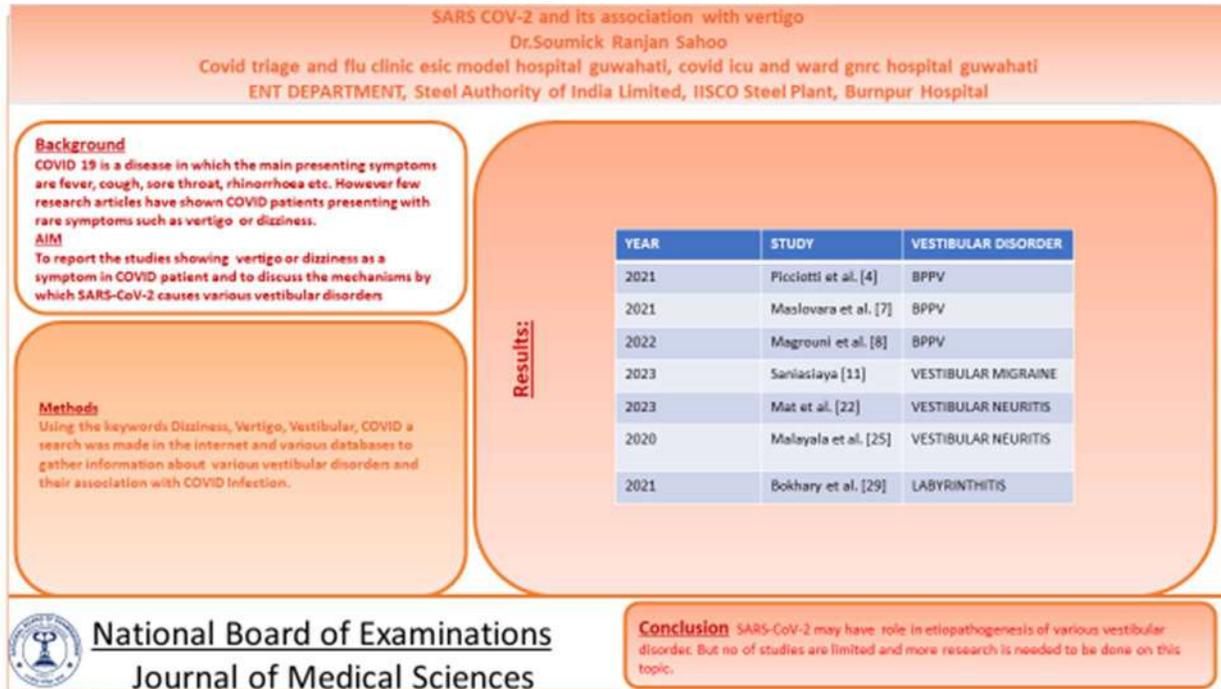
**Abstract**

COVID-19 is a disease which has affected many systems of the body such as respiratory, cardiovascular, gastrointestinal systems. New research has shown that the nervous system also gets affected by COVID. A small number of COVID patients have presented with dizziness as a primary chief complaint with few presenting with acute vertigo. Studies have found association between COVID and various important balance disorders such as BPPV, Vestibular Migraine Menieres Disease, Vestibular Neuritis, Labyrinthitis. In this article a brief discussion of the mechanism by which SARS-CoV-2 virus causes these various vestibular disorders is explained.

**Keywords:** Dizziness, Vertigo, Vestibular, COVID

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## Graphical Abstract



### Introduction

The COVID-19 Pandemic is one of the greatest challenging situation faced by mankind in modern times. The various complaints for which patients visited hospitals include sore throat, rhinorrhoea, cough, dyspnoea etc. From the otorhinolaryngology point of view in addition to these clinical features, anosmia was a chief complaint found in many patients. One of the rare complaints for which COVID patient visited the hospital was dizziness. The incidence of dizziness ranges from 7–12% in COVID patients [1]. As per a study conducted 18.4% of COVID patients had balance disorder, amongst them 94.1% reported dizziness and 5.9% reported severe vertigo attack [2]. In other study dizziness was reported in 31.8% and true vertigo in 6% of the patients [3,4]. In this article a brief discussion will be held on COVID and association with balance

disorders such as BPPV, Vestibular migraine, Menieres disease, Vestibular neuritis and Labyrinthitis.

### BPPV

BPPV is the most common of the peripheral vestibular disorders seen by otorhinolaryngologists. Most of the cases are idiopathic while there may be certain secondary causes like menieres disease, vestibular neuritis, otologic and nonotologic surgeries, herpes zoster oticus, inner ear ischaemia [4]. The clinical features consist of rotational vertigo lasting less than 1 minute, caused by head positional change [5]. The proposed mechanism are canalolithiasis and cupulolithiasis. Post canal BPPV accounts for 60-90% while horizontal canal BPPV accounts for 5-30% [6].

Some cases of BPPV have been reported among COVID patients. A study reported two cases of BPPV in COVID patient [7]. In the first case who had tested positive for SARS-CoV-2, patient developed acute attack of circular dizziness when changing position. The vertigo attack was preceded by occipital headaches and followed by nausea and vomiting. Dix Hallpike test was positive and confirmed the diagnosis of BPPV. The patient was managed by Epley procedure. The second patient experienced a mild COVID-19 course which started with a moderate frontal headache accompanied by musculoskeletal pain, vomiting, diarrhea, and general weakness. This was followed by acute attack of circular dizziness along with nausea on turning to right side and getting out of bed without any audiological or neurological symptoms. The case was diagnosed as BPPV and treated by epley procedure.

A retrospective study reported 8 cases of BPPV in COVID patients [4]. All of them had rotatory vertigo attacks triggered by position change along with associated symptoms like nausea, vomiting and unsteadiness. They were treated by Epley maneuver, Semont maneuver, Lempert maneuver, and Gufoni maneuver.

A case was also reported where a 30 year old female health worker developed attacks of positional vertigo, consistent with BPPV after 3 weeks of developing COVID Symptoms. Diagnosis of BPPV was made according to history and positive Dix-Hallpike maneuver [8].

The possible mechanism by which SARS- CoV-2 virus is implicated in the pathogenesis of BPPV are as follows:

1. Drugs and inflammation cause decalcification and damage the otoconia and cause BPPV [5].
2. Endothelial dysfunction involving cerebral venous hemodynamics [9].
3. Direct effect of the viral infection on the otolith membrane [10].
4. Direct cytopathic effect of virus, inflammatory response, cytokine storm, vascular event is also proposed [4].

Horizontal BPPV more than typical forms as patient placed in prone position to improve oxygenation modifies the course of positional vertigo [4].

### **Vestibular Migraine**

Numerous studies in vestibular migraine reported involving children, adolescent, adults [11,12]. It is defined as occurrence of migraine headache with either vertigo or non specific dizziness [13]. Risk factors include motion sickness or first degree relative with migraine [11].

Two cases of vestibular migraine were reported in COVID patients of paediatric age group. In the 1<sup>st</sup> case a previously healthy girl in middle childhood presented with intermittent dizziness, headache localized over the frontotemporal region, photophobia which precipitated following COVID infection. The case was diagnosed as vestibular migraine of childhood and was treated with Home-based vestibular rehabilitation [11].

The 2<sup>nd</sup> patient developed bilateral, throbbing temporal region headaches and imbalance following COVID-19 infection. The associated symptoms included photophobia and phonophobia. The case was

diagnosed as vestibular migraine of childhood. The patient was treated with flunarizine 5 mg daily, lifestyle modifications and home-based vestibular rehabilitation [11].

The possible mechanism by which SARS- CoV-2 virus is implicated in the pathogenesis of vestibular migraine are as follows:

1. Altered neural activity within the trigeminovascular system [14].
2. Substance P and calcitonin gene related peptide which are the main neuropeptides of trigeminovascular system cause vasodilatation and neurogenic inflammation leading to migraine headache are also expressed in vestibular system and thereby causing dizziness [14]. The substance P elevated in COVID [15].

Elevated neurotransmitter which triggered the trigeminovascular system may lead to vestibular migraine in children with COVID [11].

Stress found in COVID children could be a triggering factor for vestibular migraine [11].

### **Menieres Disease**

This disease affects people between 40-60 years and is characterized by stiffening of stereocilia that line the cochlea along with clinical features such as tinnitus, deafness, vertigo, dizziness and loss of balance leading to increase risk of falls [16–18]. Falls in case of menieres disease come without warning or loss of consciousness or neurologic symptoms and

are known as Tumarkin drop attacks or otolithic crisis [18].

COVID induced Menieres Disease causes impact on physical, social, psychological and financial dimensions of health [16].

The possible mechanism by which SARS- CoV-2 virus is implicated in the pathogenesis of Menieres disease are as follows:

1. Cochleitis can be caused by viral involvement of cochlea and perilymphatic tissues.
2. Embolus formation can cause disruption of microvascular structure in the inner ear and increase endolymph volume [19,20].
3. Damage to sensory cells of the cochlea may cause stiffening of stereocilia which line the cochlea [18,20]
4. Autoimmune dysfunction with viral antibodies attacking inner ear antigen [20].
5. Haemorrhage within the labyrinth [21].

### **Vestibular Neuritis**

Vestibular neuritis is a acute vestibular syndrome which is characterized by sudden onset of vertigo, nausea and vomiting, unsteady gait, head motion intolerance and spontaneous nystagmus lasting days to weeks [22,23]. This disorder is not associated with any auditory deficit [24].

Some of the cases of vestibular neuritis reported in COVID patients are as follows

A 13 year old girl with proven COVID-19 infection had severe sudden onset continuous rotatory vertigo, intractable vomiting, right spontaneous horizontal

nystagmus on physical examination, head impulse test positive for left side. Based on the findings a diagnosis of left side vestibular neuritis was made and vestibular rehabilitation was started [22].

Malayala et al. reported a case of vestibular neuritis in a COVID patient. The case was a female covid patient with intractable vertigo, nausea, vomiting diagnosed as vestibular neuritis [25].

The possible mechanism by which SARS- CoV-2 virus is implicated in the pathogenesis of Vestibular Neuritis are as follows:

1. SARS COV2 entry depends on ACE2 and TMPRSS2 receptors [26]. In mice these receptors found in mucosal epithelium in middle ear and also in inner ear [27]. These receptors act as a gate for virus to enter inner ear and cause vestibular neuritis.
2. Ischaemia of the vasa nervorum and demyelination caused by inflammatory process could cause vestibular neuritis [28].
3. Trigger reactivation of herpes simplex virus [24].

**Labyrinthitis**

This may be defined as inflammation of the membranous labyrinth of ear.

Peripheral vertigo is the hallmark symptom of labyrinthitis. The presence of hearing loss and tinnitus helps in differentiating it from vestibular neuritis and BPPV [29,30].

Common etiology are viral URTI, bacterial spread from infected middle ear meninges, autoimmunity, HIV, syphilis.

A labyrinthitis case was reported in which patient had a presentation of vertigo, hearing loss, tinnitus, and aural fullness. The patient was diagnosed as positive for COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR) nine days prior to developing these symptoms. Patient was symptomatically treated with prochlorperazine thrice a day for up to four weeks [29].

The possible mechanism by which SARS- CoV-2 virus is implicated in the pathogenesis of Labyrinthitis is as follows:

1. The virus has neurotrophic and neuroinvasive properties which can affect several areas of nervous system which includes inner ear and cause labyrinthitis. The important studies discussed in this review article have been summarized in Table 1.

Table 1. Summary of studies reporting vestibular disorders in Covid-19 Patients

YEAR	STUDY	VESTIBULAR DISORDER
2021	Picciotti et al. [4]	BPPV
2021	Maslovara et al. [7]	BPPV
2022	Magrouni et al. [8]	BPPV
2023	Saniasiaya [11]	VESTIBULAR MIGRAINE
2023	Mat et al. [22]	VESTIBULAR NEURITIS
2020	Malayala et al. [25]	VESTIBULAR NEURITIS
2021	Bokhary et al. [29]	LABYRINTHITIS

### Conclusion and Future Directions

From the above discussion it is clear that SARS-CoV-2 may have role in etiopathogenesis of various vestibular disorder. Although the number of studies is very scarce and future research is to be done on this aspect of otorhinolaryngology.

Research may be conducted on this topic under the guidance of ICMR and Department Of Health Research [Ministry Of Health And Family Welfare] by which a database of patients who had dizziness/vertigo as a symptom during COVID Infection or Long COVID/Post COVID Syndrome may be created.

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### Conflict of interest

The author declare that they have no competing interests.

### Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

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**REVIEW ARTICLE**

**Sinus Headache and Facial Pain: A Diagnostic Dilemma**

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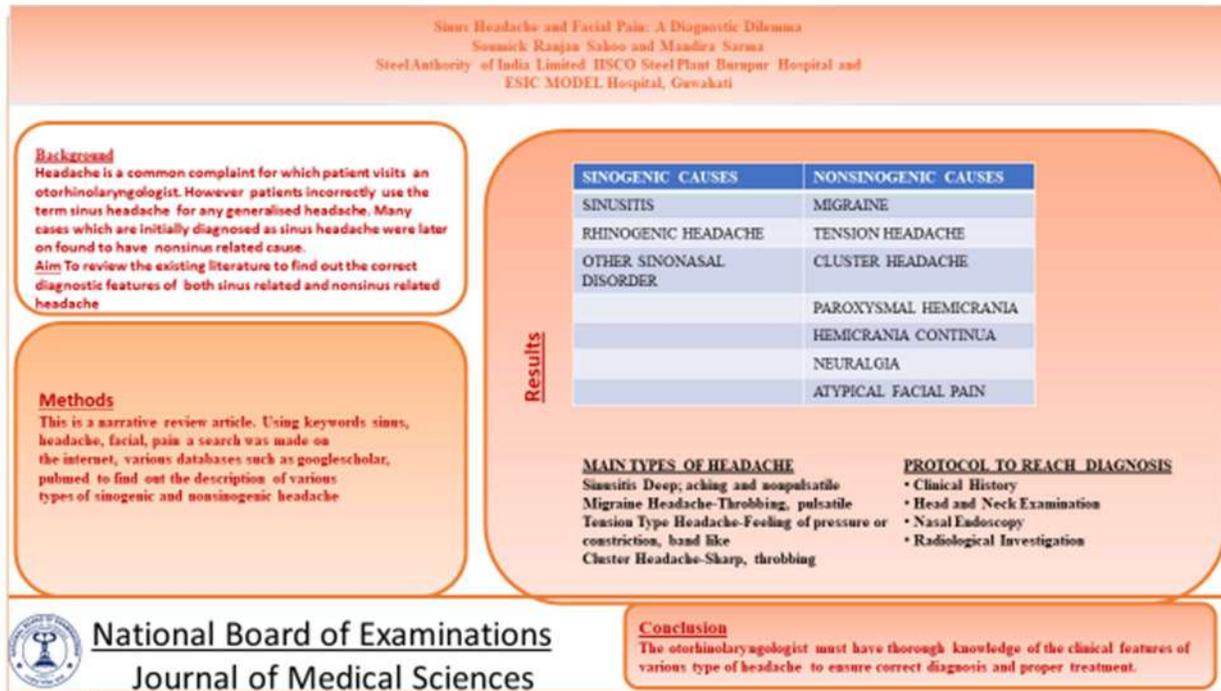
**Abstract**

Headache and facial pain are common complaints for which patient visits otorhinolaryngologist. Many patients have a misconception that all types of headache are sinus related and incorrectly refer it as sinus headache. It is the duty of an otorhinolaryngologist to correctly differentiate between sinogenic and nonsinogenic causes of headache/ facial pain through proper history taking, diagnostic nasal endoscopy, radiological investigation to reach at an appropriate diagnosis. In this article various sinogenic and non sinogenic causes of headache are briefly discussed. A proper knowledge of diagnostic criteria of different types of headache will ensure correct and timely treatment of the patient and improve patient satisfaction.

**Keywords:** Sinus, Headache, Facial, Pain

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## Graphical Abstract



### Introduction

Headache is one of the chief complaints of patients attending otorhinolaryngology clinic, the patients inappropriately use the term sinus headache instead of headache [1,2].

This incorrect use of the term sinus headache for any generalized headache is also being done by few primary care physicians [1,3,4].

It is important for an otorhinolaryngologist to properly frame a definition for sinogenic and non sinogenic headache and differentiate between them. This will ensure correct treatment and referral of non sinogenic causes to appropriate specialist. In this brief narrative review we will discuss about the different sinogenic and nonsinogenic causes of headache.

### Problem Statement

There are various studies which support the fact that a problem genuinely exists while evaluating patients of headache. In many cases initially incorrect diagnosis has led to wrong treatment.

From the literature data we got some studies where a proportion of the patients who were initially diagnosed as having sinus headache were later on discovered to have migraine [1,5–8].

Similarly in studies it has been found that a proportion of the patients initially diagnosed as migraine were later on discovered to have headache suggestive of sinogenic etiology after investigations [1,9].

There are also studies where both migraine and sinogenic causes may coexist as co morbidities [1,6,10].

## **Sinogenic Headache**

This headache refers to any headache in which a rhinologic pathology is the causative factor [1,11]. The explanation of this headache is the activation of trigeminovascular system by the trigeminal afferent in nose and sinus. Immunological activation from allergy and infection act as peripheral trigger [1,12].

The various causes are as follows:

### **1. Sinusitis**

Acute Rhinosinusitis is characterized by history of unilateral severe pain along with nasal obstruction. There is history of fever in 50% of the cases.

When there is facial pain along with dental pain it is suggestive of maxillary sinus infection [1,13].

Acute infection of the frontal sinus presents as frontal headache, fever, tiredness and may be accompanied by tenderness over the medial part of the infraorbital margin [14]. Nasal endoscopy findings include hyperemia of the sinonasal mucosa and purulent secretions.

Pain at the vertex is suggestive of acute sphenoid sinus infection which is very rare.

Chronic Rhinosinusitis is usually painless with pain occurring only during acute exacerbation [1,15]. The other clinical features include purulent nasal discharge and respiratory obstruction [1,5,16].

Features of headache or facial pain in sinusitis are [17-21]:

Clinical, nasal endoscopic and / or radiological evidence of acute or acute-on-chronic

rhinosinusitis. There should be no other features of a primary headache which could present simultaneously.

Facial pain must develop simultaneously with the onset or acute exacerbation of rhinosinusitis.

Facial pain must resolve within seven days of remission or successful treatment of acute or acute-on-chronic rhinosinusitis.

Sinonasal pain is usually deep, aching and non-pulsatile.

Acute viral rhinosinusitis is treated with analgesics and antipyretics, saline irrigations, intranasal glucocorticoids. In case of acute bacterial rhinosinusitis antibiotics are additionally prescribed along with symptomatic management which is same as for acute viral rhinosinusitis [22].

### **2. Rhinogenic Headache**

This type of headache affects the face and is caused by impingement of the mucosal surface with each other within the nose and sinuses and there is absence of inflammation, hyperplasia of the mucosal surfaces, pus filled discharge, nasal or sinus polyposis, mass [1,23].

The common sites of rhinogenic headache includes the area around the orbit, canthus medially and superiorly, zygomaticotemporal region and pain is usually unilateral.

A variation of normal anatomy may lead to impingement such as pneumatized middle turbinate.

Sometimes middle turbinate may impinge on the septum or the lateral wall of the nose causing headache. This condition is

known as middle turbinate headache syndrome [1,24]. Therapeutic option include excision of a portion of the middle turbinate to relieve the headache [1,25].

It has been proposed by Greenfield that cutaneous branches of the nasal afferent of cranial nerve V synapse in the cerebral cortex leading to perception of nasal stimulation as pain [1,26]. Because of failure of the cortex to localize these afferent impulses the nasal stimulation is perceived as facial pain [1,27].

It has been suggested by Stammberger and Wolf that mucosal pooling occurs as a consequence of anatomical aberration with infection occurring and causing facial pain. [1,28]. They hypothesize that neurotransmitter peptide substance P released due to mucosal impingement had a role in pain transmission.

### 3. Other Sinonasal Disorder

Among the other miscellaneous sinogenic causes of headache include pain in case of mucocele and neoplasm.

Impingement on the osteous wall of sinus by a enlarging mucocele causes facial pain. The most prominent among the various mucocele is the frontoethmoidal mucocele which causes frontal headache and pain in the orbit.

The sites of pain in Sphenoethmoidal mucocele are occipital region, vertex and deep nasal region [1,29,30].

A worsening of facial pain along with the presence of neural signs should raise suspicion of neoplasm. But neoplasm rarely present as facial pain. Nasal blockage and unilateral serosanguinous pus filled

nasal discharge are the common presentation of neoplasm. Advanced stage neoplasm present as facial pain. Radiological imaging required to confirm the diagnosis of neoplasm.

### Nonsinogenic Headache/Facial Pain

The various causes are as follows:

#### 1. Migraine

Worldwide 11% of the adult suffer from migraine [1,31]. Females are affected more compared to males, cause being attributed to hormonal change. The daily incidence in general population is 3000 in 1000000 [1,32].

Migraine headache is defined as headache lasting for 4 to 72 hours if untreated, along with features like pulsating pain on one side and affecting the face along with the head [1,33].

The orbit, cheek and nose are some of sites of migraine pain in few cases.

A small percentage of the patients also describe an aura affecting vision. The headache which follows aura may occur along with other symptoms such as photophobia, acoustic hyperresponsivity, nausea and vomiting.

The treatment of headache in migraine depends on whether it is an acute or chronic presentation and includes abortive or prophylactic therapy [17].

Abortive therapy comprises simple analgesics alone or in combination with other compounds which can provide relief for mild to moderately severe headaches. For severe headaches and facial pain, 5-HT<sub>1</sub> agonists and / or opioid analgesics alone or

in combination with dopamine antagonists can be used.

Prophylactic therapy is used when there is chronic migraine or the symptomatic treatment are ineffective or contraindicated. Prophylactic therapy includes nortriptyline and propranolol which have been found to be very effective for chronic facial migraine. In recent years, botulinum toxin has also shown good results as a prophylactic therapy

## 2. Tension Headache

This headache has a prevalence of 1 to 3% [1,31]. The headache is perceived by the patient as a feeling of pressure or constriction. The headache is bilateral and keeps on recurring. The duration of headache is minutes to weeks. There is absence of nausea and vomiting. However excessive sensitivity to lights and sounds may be present [1,34]. Mostly no worsening or relieving factors are identified. The soft tissues become very sensitive to touch and certain points when touched may be painful.

Notably pressing on one point for long time can cause referred pain in other areas.

Tension type headache is precipitated by psychological pressure, disturbed sleep, inadequate eating habits.

Management of TTH consists of pharmacotherapy, physical therapy and psychophysiologic therapy [17].

Pharmacotherapy consists of abortive therapy and long-term preventive therapy. These headaches generally respond to simple over-the-counter (OTC) analgesics. Preventive drugs are the main therapy for Chronic Tension Type Headache.

Preventive medications may be considered if headaches are frequent (>2 attacks per week), of long duration (>3-4 h), severe enough to cause significant disability. Nortriptyline in low dosage (10-100 mg) is the most frequently used tricyclic antidepressant for prophylaxis. A few minimally invasive techniques may also provide pain relief such as “trigger point” injections, greater or lesser occipital nerve blocks and auriculotemporal nerve block.

Physical therapy techniques include hot or cold applications, positioning, stretching exercises, traction, massage, ultrasound therapy, transcutaneous electrical nerve stimulation (TENS) and manipulations. Psychophysiologic therapy includes reassurance, counselling, relaxation therapy, stress management programmes and biofeedback techniques.

## 3. Cluster Headache

It is a primary one sided recurring headache affecting patients sleep. Usually the same side is affected again and again and sometimes the pain is very severe. The site of pain include behind the orbit or the midorbit. Each episode lasts for 15 minutes to 3 hours. There are associated clinical symptoms and signs such as nasal discharge, tearing, inability to sweat, tiny pupils and ptosis. Attacks occur periodically and they are present for 8 to 10 weeks in a year. Around 15 to 20 % of chronic cluster headache don't have asymptomatic interludes. These patients don't experience prodromal symptoms or aura [1,35].

Males are affected more than females. The common age group affected is 20 to 40 years [1,36].

Treatment of an acute cluster headache is with oxygen (8 L/min or 100% by mask for 10 min), which may abort the headache if used early. Subcutaneous injections of sumatriptan (6 mg) can be effective, in large part due to the rapidity of onset of action [17].

#### **4. Paroxysmal Hemicrania**

The pain in this disorder is usually present on one side around the eyes and forehead. The duration of pain may vary from 2 to 45 minutes. The age of presentation of the first episode of such type of headache is usually within the fourth decade of life.

There may be a remission period of 3 months to 3 years. The disorder must include at least one clinical feature which suggests autonomic dysfunction such as blocked nose, nasal discharge, tearing, bloodshot eyes, ptosis, swollen eyelid, altered cardiac rhythm, localized epiphora, saliva production and flushing of the face [1,37].

#### **5. Hemicrania Continua**

This headache has many features similar to paroxysmal hemicranias. The headache occurs on one side and shows good response to pharmacological management with drugs like indomethacin. The headache is of moderate severity, doesn't shift sides and the pain is unswerving. Although the intensity of the pain may vary and the intensity is maximum when there is autonomic dysfunction [1,38].

#### **6. Neuralgia**

Patients having Trigeminal Neuralgia describe electric shock like pain at the sites having trigeminal nerve

innervations. They are unilateral with sudden onset and recurring in nature [33,39]. Talking, eating, shaving, washing the face, teeth brushing etc trigger the pain of trigeminal neuralgia [1,39].

Carbamazepine or other antiepileptic drugs are initially used for treatment. Surgical microvascular decompression and gamma knife radiation have been shown to treat cases caused by compression of the trigeminal nerve from pontine vessels. Other less invasive techniques include balloon dilatation of the trigeminal ganglion and glycerol ganglion lysis [17].

The pain of glossopharyngeal neuralgia occurs in flare ups. The common sites include the pharynx, lingual base, velum and tonsillar fossa [1,40]. The lower jaw angle or external acoustic meatus can also be potential sites of pain [1,40].

The most common site of pain in cluster neuralgia include the medial ocular angle. The other common site of the pain may be superciliary, orbital, nasal and mandibular areas. The characteristic signs and symptoms include tearing, bloodshot eyes, blocked nose, sternutation and frontal erythema [1,41,42].

#### **7. Atypical Facial Pain**

The pain usually affects one side, is unremitting and deeply felt [1].

The symptoms of the patient are unclear and keeps on changing. There are multiple sites of pain in the face, head and neck.

The patients give a history of previous sinus operation and dental

treatment who are unsatisfied with the outcome.

Many patients with this condition have psychological problems.

**Learning Points**

A protocol must be followed to reach at an appropriate cause of the headache after which correct treatment can be given to the patient. The protocol consists of the following points.

- **Clinical History** - onset, site, character of pain, duration, laterality, aggravating and relieving factors along with associated symptoms
- **Head and neck examination** - should be performed including

testing of the cranial nerves, palpation for points of tenderness and trigger points [17].

- **Nasal endoscopy** - looking for purulence, oedema, inflammation if sinogenic cause is suspected.
- **Radiological Investigations** - CT scan of nose and paranasal sinuses if rhinosinusitis is suspected. MRI Brain may be done if intracranial pathology such as tumor is suspected.
- The main types of headache which are seen in the ENT clinic with the differentiating features are summarized in Table 1.

**Table 1. Important Types of Headache Seen In ENT Clinic**

	<b>Sinusitis Headache</b>	<b>Migraine Headache</b>	<b>Tension type Headache</b>	<b>Cluster Headache</b>
Type of pain	Deep; aching and nonpulsatile	Throbbing, pulsating pain	Feeling of pressure or constriction, band like.	Sharp, throbbing
Associated symptoms and signs	Fever, Nasal Obstruction, Rhinorrhoea	Nausea, Aura(+/-) and Photophobia	Absence of Nausea. Excessive Sensitivity to Lights or Sounds May be Present.	Nasal Discharge, Inability to Sweat, Tiny Pupils and Ptosis
Treatment	Analgesics and Antipyretics, Saline Irrigations, Intranasal Glucorticoids.	Abortive or Prophylactic Therapy	Pharmacotherapy, Physical Therapy and Psychophysiologic Therapy	Oxygen, Subcutaneous Injections of Sumatriptan

**Conclusion**

The otorhinolaryngologist must have a thorough knowledge of clinical features of various types of headache or facial pain so

that proper diagnosis can be made and correct treatment is provided for the relief of the headache.

### Conflicts of interest

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

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## REVIEW ARTICLE

### Newer Advances in Hearing Conservation Programme

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#### Abstract

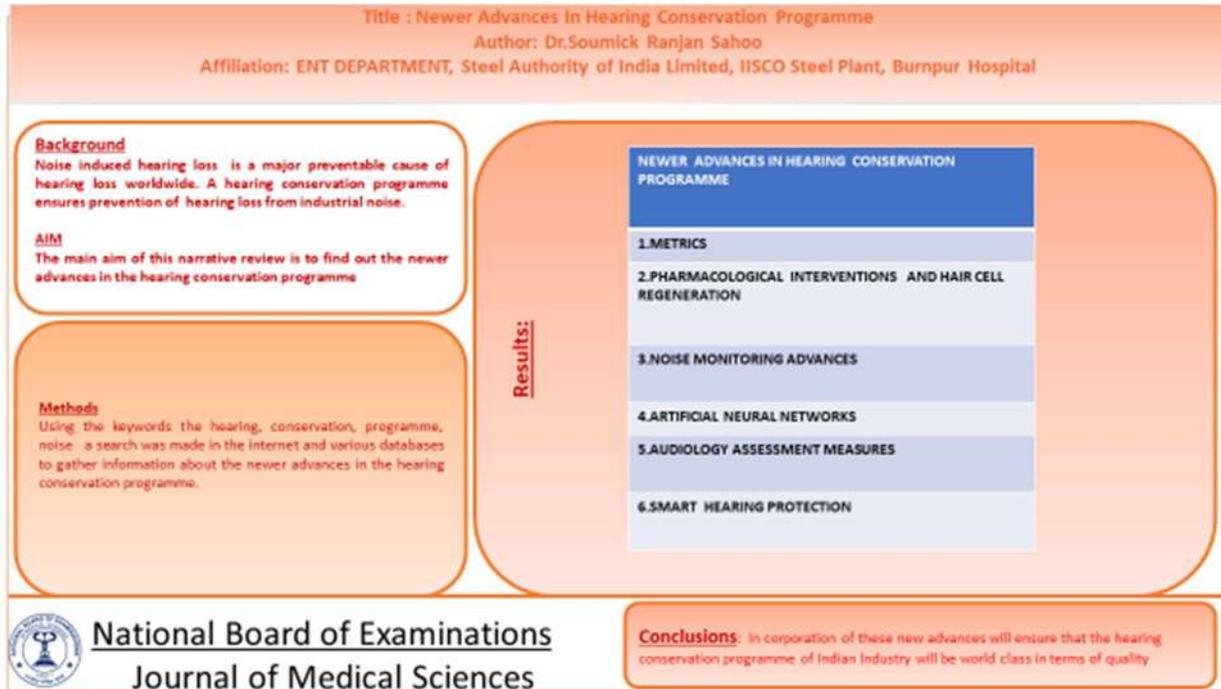
A Hearing Conservation Programme is an important component of the strategy to prevent Noise Induced Hearing Loss (NIHL) at workplace. Recently a lot of advancement has occurred in hearing conservation programme which includes new strategies being adopted to prevent NIHL at workplace. These consist of metrics, pharmacological interventions and hair cell regeneration, noise monitoring advances, artificial neural network, audiology assessment measures, smart hearing protection etc. These topics will be briefly discussed. These strategies if incorporated will strengthen the existing Hearing Conservation Programme to prevent NIHL.

**Keywords:** Hearing, Conservation, Programme, Noise

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## Graphical Abstract



### Introduction

Noise Induced Hearing loss is a major avoidable cause of hearing loss. Worldwide, 16% of the disabling hearing loss in adults is attributed to occupational noise, ranging from 7 to 21% in the various subregions [1]. Noise in addition to hearing loss also causes additional ill effects like lack of concentration, irritation, fatigue, headache, sleep disturbances.

To prevent NIHL a hearing conservation programme is followed in an industrial setup at the workplace. The hearing conservation programme consists of Engineering Control, Administrative Control, Hearing Surveillance and Hearing Protection Devices. A variety of measures have been implemented in Indian Industry setup to prevent NIHL. Some of these measures (Figure 1) include replacement of old machinery with new machinery which emit less noise and periodic maintenance

and check up of the machinery. In addition to that workers are provided with ear plugs or ear puffs for protection from noise, pure tone audiometry done periodically to monitor the hearing status of the worker, noise monitoring done at workplace to measure noise levels, health education imparted by doctors regarding importance of hearing and the proper use of hearing protection devices.

However sometimes compliance of workers in using hearing protection devices remains poor. So alternative strategies and advanced ear protection devices are required. A lot of newer advances in strategies to address noise induced hearing loss at workplace have taken place in the world. The aim of this narrative review is to briefly discuss these recent advances in hearing conservation programme. At the end a roadmap is provided for implementation of these advances.



Figure 1. Important Components of Hearing Conservation Programme Followed in Indian Industry Setup.

### Methods

A search on the above topic was done on the internet and various databases by using the keywords Hearing, Conservation, Programme, Noise. Information was gathered from various review articles and original articles written by researchers.

### Discussion

These new advances consist of metrics, pharmacological interventions and hair cell regeneration, noise monitoring advances, artificial neural network, audiology assessment measures, smart hearing protection etc. which are briefly discussed.

### Metrics

They may be defined as a set of quantitative tools which can be used for assessment, monitoring, improving or evaluating the programme's compliance and success so as to set and track goals of the implemented programme [2,3].

Examples include statistical metric kurtosis and energy metric [2,4].

A static feedback-based noise monitoring model is also proposed by some researchers [2,5].

Metrics have been proposed based on excitation patterns. [2,6]

The risk of exposure to noise can be assessed and monitored by using metrics [2,7].

Noise emissions can be measured and attenuated by using metrics [2,8].

They may also be used in administrative controls, audiometric evaluations, personal hearing protection, education and training, monitoring and record keeping [2,5].

### **Pharmacological Interventions and Hair Cell Regeneration**

They may be defined as approaches which are used for the prevention or treatment of NIHL using antioxidant drugs. Balance is restored between antioxidant defence and the formation of free radicals in the cochlea by using these drugs [2,9,10]. These approaches may be divided into approaches that aim at prevention of NIHL and those approaches which aim at treatment or reversing the problem.

Review has been conducted on the therapeutic benefit of antioxidant drugs for treating NIHL [2,10].

Zheng and Zuo in their study have commented on medications for reversing loss of hair cell and promoting regeneration of hair cells [2,11].

Some researchers have discussed NIHL pathophysiology, underlying molecular mechanisms and the therapies for improving the function of auditory system [2,12].

Santaolalla et al. have discussed the clinical application of inner ear hair cell regeneration [2,13].

### **Noise Monitoring Advances**

A wireless headset noise exposure dosimeter has been invented for noise monitoring [2,14].

A hearing protection device is now available which consists of two microphones for calculating the exposure dosage of periods [2,15].

A noise monitoring device is now available comprising of a dosimeter carried in a pocket or worn on a belt or helmet [2,16].

Some researchers have measured the noise exposure inside hearing protection device by fitting it with a dosimeter attached to a microphone [2,17,18]. The benefits are appropriate and timely intervention.

### **Artificial Neural Networks (ANN)**

They are defined as analytical techniques which are based on the learning processes of human cognitive system and the neurological functions of the brain.

Information is processed like biological neurons in the brain. [2,19].

Aliabadi et al. [2,20] and Badri [2,21] have described neural network models.

Artificial intelligence has also been used for determining the hearing loss thresholds [2,22].

In a workshop the main noise source has been found out using ANN [2,23].

There are many benefits of ANN. They may be used as an alternative method in engineering analysis. Large and complex systems can be handled effectively. Quicker and more practical predictions can be provided by using ANN. They are immune to noise [2,24].

### **Audiology Assessment Measures**

For people exposed to excessive noise cochlear neuropathology is diagnosed by using these measures [2,25-28].

People who are exposed to noise may have normal audiogram findings even after they have started developing early stage hearing loss. It helps in diagnosis of hearing loss in the early stage.

In rats researchers have studied how exposure to noise is related to production of large temporary threshold shift, significant auditory brain response wave-I reduction and hearing-in-noise deficits.

Cochlear hidden hearing loss may be detected early by using this approach.

### **Smart Hearing Protection**

They are novel strategies where integrated microphone and data transfer are utilized for monitoring and providing alerts in relation to wear rates and noise exposure. In this way action can be taken before permanent hearing loss develops [29].

Speakers and microphones are incorporated for accurate and safe reproduction of sound from the surrounding worksite.

The hearing protection wear rates can be tracked and improvised.

A guarantee is ensured of the effectiveness of the hearing protection provided. This is possible because the workers personal exposure to noise is tracked so that required intervention is done before permanent hearing loss occurs.

Improved situation awareness replaces the blindfold effect of traditional hearing protection thus improving safety at the site.

Data from smart hearing protection can be used to remove the hazards which helps in controlling unexpected noise hazards.

Complete and continuous data source is used to assess the noise risk.

### **Future Proposal**

A model has been proposed (Figure 2) which will ensure that this aspect of otorhinolaryngology is being discussed and implemented in India by a multidisciplinary coordinated approach involving the experts in Indian Industry, academicians in medical and engineering field, policy makers, researchers in field of occupational health.

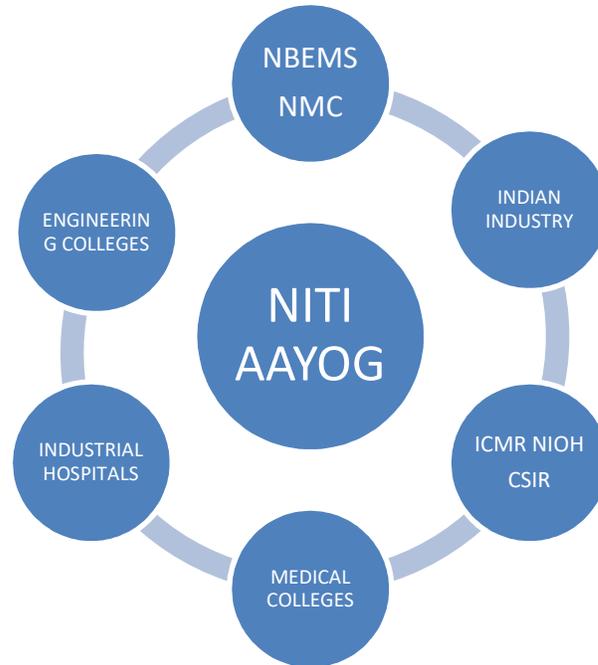


Figure 2. NBEMS Model.

### Objectives

- Convergence of medical and engineering field to innovate and invent new technologies for hearing protection under Make In India initiative.
- To ensure that newer advances in hearing conservation program are made applicable in Indian Industry setup.
- This model may also be used in other occupational diseases such as occupational asthma, occupational allergic rhinitis, occupational cancers etc.
- To raise awareness among the medical students about hearing conservation program and other occupational diseases and their management by including this topic in course curriculum after consultation with NMC and NBEMS.

### Conclusion

- Incorporation of these new strategies will increase the effectiveness of the

hearing conservation programme in the industrial sector of India.

An effective hearing conservation programme will ensure a healthy worker free from NIHL who will be more productive in his work and lead to an economically prosperous industrial sector of India.

### Ethics declarations

**Funding** This study did not receive any funding.

### Conflict of interest

The authors declare that they have no competing interests.

**Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability**

Not applicable.

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**REVIEW ARTICLE**

**Nanoparticles in Inner Ear Diseases**

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**Abstract**

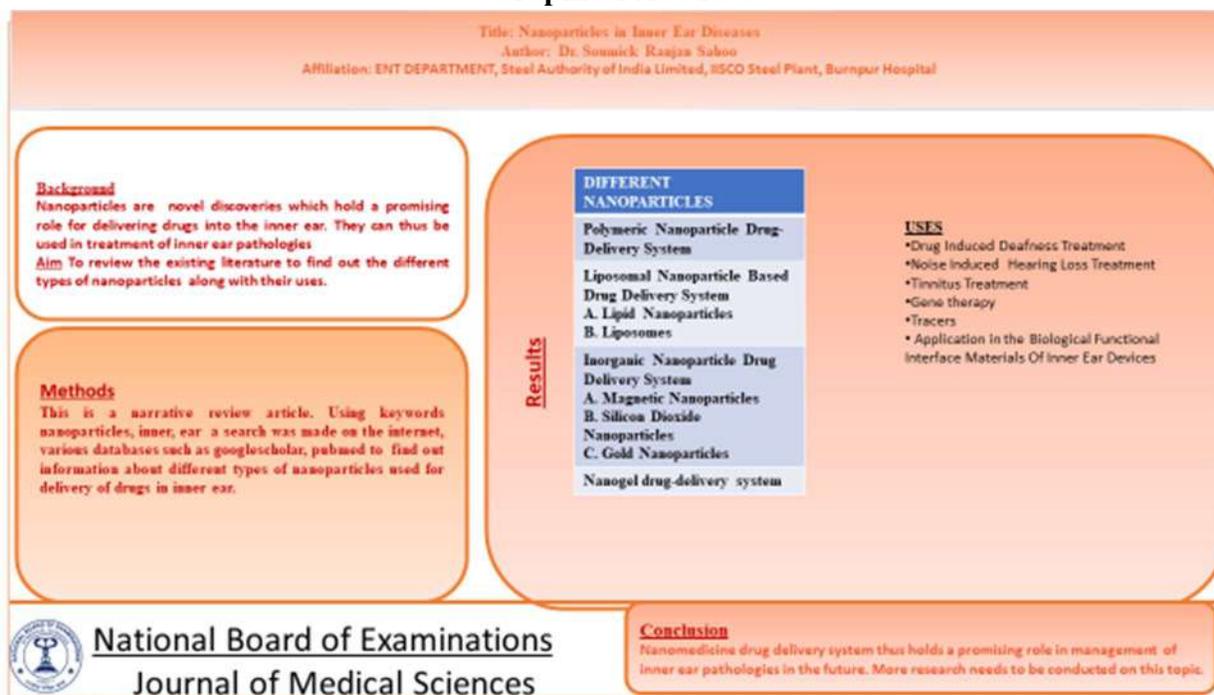
Nanoparticles are novel discoveries which hold a promising role for delivering medications into the inner ear in the future. Nanoparticles are formed by the preparation of different biomaterials. They are capable of encapsulating various types of medications. The various nanoparticle drug delivery systems include polymers, liposomal Nanoparticles, magnetic Nanoparticles, silicon dioxide Nanoparticles, gold Nanoparticles and nanogels which will be briefly discussed in this narrative review article.

**Keywords:** Nanoparticles, Inner, Ear

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## Graphical Abstract



### Introduction

Nanomedicine can be defined as a complex, multi-disciplinary branch of medicine, in which nano-bio-technologies, and other nano-sciences are applied at every step of disease management which includes diagnosis, treatment, prognosis, and monitoring of biological parameters and biomarkers [1,2]. The term “nanomedicine” was coined by the American engineer Eric Drexler (1955) and Robert Freitas Jr. (1952) in the nineties [3], with the publication of the multi-volume textbook entitled “Nanomedicine”, released in October 1999.

Moreover different super-specialties such as nano-surgery [4,5], nano-neurosurgery [6,7] nano-otorhinolaryngology [8], nano-dentistry [9], nano-ophthalmology [10], nano-neurology [11], nano-cardiology [12], nano-orthopedics [11], nano-infectiology [11],

and nano-oncology [13], among others [11], are emerging within nanomedicine.

The countries with the highest percentages of articles in the field of nanomedicine were North America (38.3%) and Europe (35.1%) [1].

In recent years, regions such as China, India, and South Korea have been productive in this field of nanomedicine [1]. In India ICMR is responsible for the promotion of biomedical research and has funded 154 projects on studies related to nanomedicine [14].

### Nanomedicine In Inner Ear Diseases

Hearing loss is an important health issue faced by mankind. Amongst the many pathologies causing hearing loss, inner ear pathologies have a significant contribution. The various types of inner ear disorders where the therapeutic interventions are

required include Menieres disease,ssnhl,acoustic shock etc. These therapeutic drugs such as steroids are delivered by systemic route and intratympanic injection (Figure 1).

Due to complexity of blood labyrinth barrier therapeutic drugs given by systemic route find it difficult to reach their site of action. In case of direct inner ear delivery drugs are delivered directly into the inner ear [15].

Nanoparticles are novel discoveries which hold a promising role for delivering medications into the inner ear in the future. Various types of biomaterials are used for forming nanoparticles. These biomaterials have the ability of encapsulating various types of drugs used for therapeutic purposes [15] Higher biocompatibility, better drug stability, high controlled drug release and targeting by surface modification are some of the advantages of nanoparticles.

The various types of nanoparticle drug delivery systems are as follows:

#### 1. Polymeric Nanoparticle Drug-Delivery System

This system includes poly(lactic-co-glycolic acid) (PLGA) which is a biodegradable polymer. Numerous advantages include good biocompatibility and hydrophilicity along with controlled degradation [15]. The target area of delivery of drugs is scala tympani through the *trans*-Round Window Membrane injection.

The route of diffusion of these nanoparticles after the intratympanic injections have been reported by researchers [16].

Using guinea pig cochlea a novel drug-delivery system has been developed by researchers. [17]

Other examples of polymeric nanoparticles include polylactic acid, polycaprolactone and PEG. They have been used for the treatment of inner ear diseases [18-20]

#### 2. Liposomal Nanoparticle Based Drug Delivery System

##### A. Lipid Nanoparticle

They are biodegradable and both hydrophilic and lipophilic drugs can be delivered through this type of nanoparticle. [15,21,22]. Various diseases have been treated by using solid lipid nanoparticles (SLNs) as novel drug-delivery systems [23-25].

There are numerous benefits like low cost, easy scale-up of SLNs production and proven production method [26].

Researchers have reported SLNs based on stearic acid as excellent nanocarriers for drug delivery.[26]

##### B. Liposomes

They have numerous benefits like improved stability, nontoxicity, high biocompatibility etc [15,27]. Recent advances in targeting ligand design have led to clinically promising and efficient drug-delivery systems with targeting ligands.Examples include peptides [28,29], antibodies [30,31], oligonucleotide aptamers [32,33] and folic acid [34].



Figure 1: Intratympanic injection of steroid.

It has been shown that drugs can be carried across the Round Window Membrane by liposomes leading to delivery of drugs into the inner ear cells. [35,36]

### 3. Inorganic Nanoparticle Drug Delivery System

#### A. Magnetic Nanoparticles

Various benefits of this type of nanoparticle drug delivery system includes less toxicity, greater biocompatibility and convenient manipulation [15]. The representative of this category is superparamagnetic iron oxide Nanoparticles (SPION). Specific advantages include:

Magnetic responsiveness [37]

Superparamagnetism [38]

Small particle size [39]

An *in vitro* Round Window Membrane model was designed through which SPION could be transported thus allowing the quantitative assessment of the

expected targeted drug or gene delivery [40].

Irreversible and bilateral sensorineural deafness is a side effect of cisplatin used for treating head and neck tumors [41,42]. To solve this side effect, a novel nanostructure was designed by Kayyali *et al* composed of SPION [43].

#### B. Silicon dioxide Nanoparticles

Numerous advantages include greater drug-loading capacity, greater yield and less production cost [15]. The commonest choice is silica and is being used in biomedical applications. Amongst them Mesoporous silica Nanoparticles preferred over other porous silica Nanoparticles. Mesoporous silica supraparticulate delivery systems have been used for evaluation of the pharmacokinetics and biodistribution of exogenous neurotrophin-3 delivered by this system in the inner ear [44].

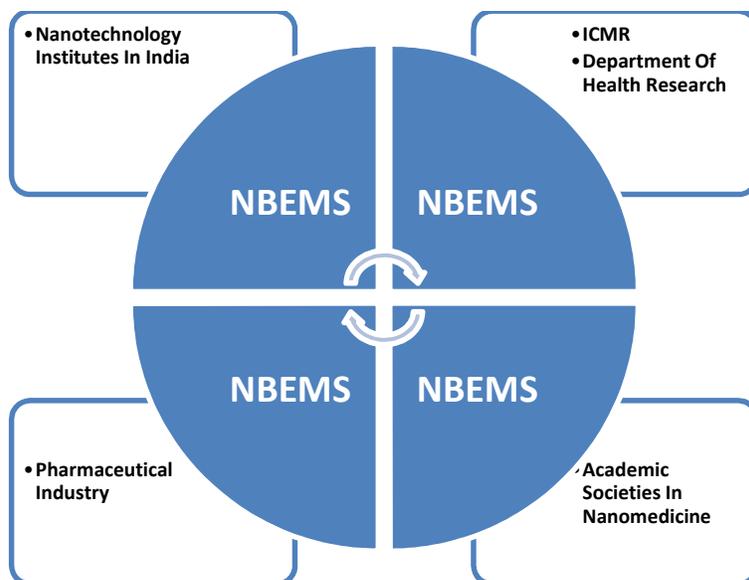


Figure 2: NBEMS Model of Nanomedicine Research.

### C. Gold Nanoparticles

These nanoparticles have been used in the treatment of tumors and in bioimaging [15]. The advantages include their distinctive optical properties and higher biocompatibility [45].

They have been used as an effective drug and gene delivery vehicle for treating inner ear pathology [46].

### 4. Nanogel drug-delivery system

This nanoparticle has distinctive hydrogel properties and nanoporous structure [15,47]. This makes this nanoparticle a potential drug-delivery carrier [15,47]. Numerous advantages of this system includes high biocompatibility, long circulation time, small size of the particle.

A minimally invasive nanohydrogel drug-delivery system was developed by researchers in 2015 [19].

Modifications were performed by researchers for introducing a targeting

peptide to specifically recognize prestin [48].

To address issue of cisplatin ototoxicity a dextran–PEG hydrogel delivery system was designed and investigated using mouse model [49].

### Applications [50]

- Drug Induced Deafness Treatment
- Noise Induced Hearing Loss Treatment
- Tinnitus Treatment
- Gene therapy
- Tracers
- Application in the Biological Functional Interface Materials of Inner Ear Devices

### Limitations

- The interaction between nanomedicine and various molecules, cells and organs of the body is based on a series of complex interactions between particles and biological media. [50]
- Sometimes nanoparticles can be toxic and damage the immune system. [50]

## Conclusion

Nanomedicine drug delivery system thus holds a promising role in management of inner ear pathologies in the future. More research needs to be conducted on this topic. A coordinated approach of various centres doing research in nanotechnology is required. A model is being proposed (Figure 2) which will help in manufacturing nanoparticles in India and their clinical application in patients.

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## Conflict of interest

The authors declare that they have no competing interests.

## Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable.

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## CASE REPORT

### **Acquired Hemophilia 'A' – An Uncommon Condition Presented with Common Manifestations**

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#### **Abstract**

Hemophilia A is usually a congenital bleeding disorder, which manifest in males due to its X linked recessive pattern of inheritance. It commonly presents with bruises, uncontrolled bleeding post minor trauma or post circumcision, knee swelling etc. Acquired hemophilia is a rare condition and could be associated with autoimmune diseases. We discuss this rare condition of acquired hemophilia in a female patient who presented with common manifestations but in unlikely host.

**Keywords:** Hemophilia A, Acquired haemophilia, Factor viii, Autoimmune disorder, AMA antibody

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## **ABBREVIATIONS**

AHA – ACQUIRED HEMOPHILIA A

SLE – SYSTEMIC LUPUS ERYTHMATOSUS

RA – RHEMATOID ARTHRITIS

APTT – ACTIVATED PARTIAL THROMBOPLASTIN TIME

PT – PROTHROMBIN TIME

TT – THROMBIN TIME

OPD – OUT PATIENT DEPARTMENT

CHD – CONGENITAL HEART DISEASES

VSD – VENTRICULAR SEPTAL DEFECT

TFT – THYROID FUNCTION TESTS

LFT – LIVER FUNCTION TESTS

KFT – KIDNEY FUNCTION TESTS

FFP – FRESH FROZEN PLASMA

PCV – PACKED RED CELL

## **Introduction**

One of the rare autoimmune diseases, acquired hemophilia A (AHA) is associated with a high morbidity and is often missed by physicians due to its rare presentation. While hemophilia usually is a congenital condition and affects only males due to its X linked recessive pattern of inheritance. Rarely, AHA can also affect females and is usually associated with other auto immune conditions like SLE, RA.

AHA patients present with subcutaneous ecchymoses, joint hematomas, muscle and gum bleeding. A few cases of intracranial bleeds were also reported [1]. The key features for diagnosis include the classical clinical presentation and family history. Investigations show increased APTT, near normal or mildly deranged PT and TT, low levels of factor

viii. Some cases even show decreased factor ix and VWF and Platelet count is usually normal [2].

Acquired Hemophilia differs from familial hemophilia with absence of family history of bleeding disorder and no specific age prevalence. High degree of suspicion and investigation into the cause of bleeding tendency is required to diagnose such cases.

## **Case presentation**

A 19-year Female presented to outpatient department with chief complaint of painful swelling of right knee joint for two weeks, with petechial haemorrhages over forearm, abdomen and left lower limb. Patient also complained of fatigue, decreased appetite, and joint pains in the last 2 weeks (Figures 1 to 3).



Figure 1. 7- 10 days old bruise on left fore arm.



Figure 2. Knee joint bruise and heamarthrosis.



Figure 3. Limbs showing old bruises and knee hemarthrosis.

Patient had repeated bruises all over the body in the last 2 years. Patient had increased bleeding even with minor trauma like brushing teeth or any abrasions while playing outdoor games. Patient had moderate to severe bleeding during menses usually lasting for 5 – 7 days. Patient had visited many physicians and gynaecologists over the last one year for her increased bruises and menorrhagia without any relief.

Patient did not have any comorbidities and was not on any medication. Dietary history was unremarkable. No bowel and bladder abnormality noted. There was no history of any bleeding disorders in the family.

On general examination, patient was pale with multiple bruises over the body. Normal vital signs. Systemic

examinations revealed no significant findings.

Lab reports revealed haemoglobin – 4.7g/dl, mcv – 72fl, platelet 1.4 lakh/ul. Prothrombin time – 23.6 sec, prothrombin index – 52.9%, INR – 1.88. APTT – 51.3 seconds. In suspicion of hemophilia, factor viii and xi has been paged which revealed factor viii < 0.70% and factor xi – 48.32%. An autoimmune panel showed AMA-M2 to be strongly positive. Other antibodies like Sm, SS – a/b, dsDNA, Jo1, scl 70 were negative.

TFT, RFT, LFT, serum electrolytes, urine routine were within normal limits. Ultrasonography abdomen was not contributory.

Patient had been treated with FFP and corticosteroids. Patient was given 4 PRC transfusions in view of severe anemia.

Patient was also given, calcium and vit d3 supplements, tranexamic acid 500mg, iv iron and b12 preparations. After the availability of factor VIII, 5 vials had been transfused. Intranasal desmopressin was started. Patient had been discharged on 10<sup>th</sup> day in stable condition. Decreased bruises and joint swelling seen although patient had pain in knee joint on weight bearing.

Repeated hemoglobin – 8.1 g/dl, prothrombin time is 18.2 seconds, and APTT is 40.3 seconds.

### **Discussion**

Acquired hemophilia A is condition carrying high mortality and morbidity. Disease is characterized by formation of auto antibodies against coagulation factors, mostly against factor VIII. It carries about 8 – 20% mortality if not diagnosed and treated promptly. It might be associated with many autoimmune disorders like RA, SLE, dermatomyositis although some cases found no underlying conditions [3]. Our patient had AMA-M2 positivity which shows possibility of underlying autoimmunity.

Though, common clinical features include skin ecchymoses (post trauma, injection sites), and gastrointestinal bleeds. Surprisingly joint arthrosis is not as common as congenital hemophilia A. Our patient showed classical features of congenital hemophilia including hemarthrosis but turned out to be acquired hemophilia. The absence of positive family history and presenting age well beyond the typical years of hemophilia makes it difficult to suspect.

Severe Anaemia in our patient underlines the importance of early diagnosis and treatment. Minor bleeds can be treated conservatively with avoidance of any invasive procedures, and desmopressin supplements (0.3 – 0.5mg/kg) are helpful if factor viii level > 5%. But major bleeds

need to be treated aggressively. If there are low titres of auto antibodies (<5BU), human factor VIII or desmopressin can be considered as first line treatment. But in cases where auto antibody titres are high, bypassing agents (activated prothrombin complex concentrates and recombinant activated factorVII) are preferred [4,5].

### **Conclusion**

Any patient with bleeding tendency should be investigated and treated aggressively. Possibility of acquired hemophilia should be considered when the family history is absent. Association with other autoimmune conditions should be explored.

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### **Conflict of interest**

The authors declare that they have no competing interests.

### **Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability**

Not applicable

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