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2025 April - June

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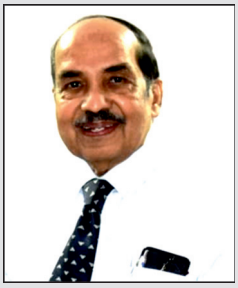

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IMSA has been in the service of medical profession and has been encouraging development of medical sciences by bringing information technology into the profession thus improving the health of people in nations.

Our organization is committed to the medical profession for promoting Continuing Medical Education and also holds educational programmes on topics of National and public health importance. We need to conduct more seminars, organize lectures by National and International experts and hold regular workshops and group discussions. For arranging such activities we are in the process to establish adequate infrastructure and facilities like an Auditorium, projection room, library, committee rooms for interactive sessions etc.

Friends, we have been fortunate to get a piece of land about 500 sq.mtrs allotted to us by the Lt. Governor of Delhi for developing the IMSA World Head Quarters at Delhi. I am approaching all Fellows and Members to donate at least Rs. 5000/- each to meet the cost of the land as well as for construction of our own building. The donations are exempted from tax under 80G; the cheque may please be made in the name of "**IMSA – Building Fund**" payable at New Delhi, and sent to the Headquarters.

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K. Jagadeesan

Yours Sincerely,
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Message From The President

Dear Fellows, Members and Associates,

It is my pleasure to address you once again through this issue of the journal. This edition brings together a range of articles of relevance to our clinical and academic community, and I would like to draw your attention to one contribution in particular.

This issue carries an editorial titled "Pegylated Interferon Lambda and Ramatroban as Host-Directed Countermeasures for Future Respiratory Viral Pandemics: A Position Paper." The piece explores host-directed therapeutic strategies that could serve as important tools in our collective preparedness against future respiratory viral outbreaks. Given the lessons learned from recent global health challenges, I believe this discussion is both timely and thought-provoking, and I encourage all members to engage with it closely.

I would like to take this opportunity to convey my best wishes to all of you.

K. Jagadeesan

Dr. K. Jagadeesan,
President, IMSA,WHQ

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EDITORIAL

Pegylated Interferon Lambda and Ramatroban as Host-Directed Countermeasures for Future Respiratory Viral Pandemics: A Position Paper

Ajay Gupta[1], Narinder Pal Singh[2], Dinesh Khullar[2], Anish Kumar Gupta[2]

Abstract

Future respiratory viral pandemics will require deployable countermeasures before pathogen-specific vaccines and direct antivirals become available. Host-directed therapies may offer broader activity across respiratory viruses and greater resilience to viral evolution. Pegylated interferon lambda (pegIFN-ë), a type III interferon with epithelial-predominant antiviral activity, and ramatroban, an antagonist of thromboxane A2/prostaglandin D2 signaling, have both been proposed as pandemic-agnostic interventions. Current evidence supports a stronger case for pegIFN-ë than for ramatroban. PegIFN-ë has randomized outpatient efficacy data in COVID-19 and a biologic rationale aligned with early respiratory epithelial infection [1,2]. Ramatroban has mechanistic plausibility and repurposing appeal but lacks robust clinical efficacy data in viral respiratory disease [3,4]. Neither agent can currently be expected to terminate outbreaks or prevent pandemics as a standalone intervention [5,6]. A rational preparedness strategy would prioritize pegIFN-ë for protocolized early-use evaluation and stockpiling assessment, while positioning ramatroban within adaptive repurposing trials [7,8].

Keywords:

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Introduction

Pandemic preparedness has historically depended too heavily on pathogen-specific countermeasures that arrive after widespread transmission is already established [8-10]. The COVID-19 pandemic illustrated this vulnerability: effective vaccines required approximately one year of development, and direct-acting antivirals such as nirmatrelvir/ritonavir reached clinical use even later. During the intervening period, the global community relied on non-pharmaceutical interventions, repurposed drugs of uncertain efficacy, and supportive care.

This recurring gap has renewed interest in broad-acting and host-directed antivirals that could be deployed early, before a new respiratory pathogen is fully characterized [7,11,12]. Host-directed therapies target conserved cellular pathways exploited by diverse viruses, potentially offering activity that is less vulnerable to viral mutation and more readily transferable across pathogen families.

This position paper evaluates two host-directed candidates — pegylated interferon lambda and ramatroban — and proposes a tiered preparedness framework based on the current strength of evidence for each.

Pegylated Interferon Lambda

Biologic rationale

Type III interferons (IFN-ë1–4) signal through a heterodimeric receptor complex (IFNLR1/IL-10Râ) whose expression is largely restricted to epithelial cells at barrier surfaces, including the respiratory, gastrointestinal, and hepatic epithelia [2,13,14]. This restricted receptor distribution enables IFN-ë to induce potent antiviral gene programs at the site of initial respiratory viral infection while producing less systemic immune activation than type I interferons. The kinetics of IFN-ë signaling are also distinct, with a slower onset but more sustained antiviral state that may be particularly suited to early intervention [13-14].

This biology is directly relevant to pandemic preparedness because most respiratory viruses — including influenza, coronaviruses, respiratory syncytial virus, and parainfluenza viruses — establish

initial infection in the airway epithelium, precisely where IFN-ë exerts its dominant effects.

Clinical evidence in COVID-19

PegIFN-ë is among the few host-targeted agents to have demonstrated efficacy in a randomized phase 3 trial during a respiratory pandemic. In the TOGETHER trial, 1,951 high-risk outpatients with COVID-19 were randomized to a single 180 ìg subcutaneous injection of pegIFN-ë or placebo within 7 days of symptom onset. The primary composite outcome of hospitalization or prolonged emergency department observation (>6 hours) occurred in 2.7% of the pegIFN-ë group versus 5.6% of the placebo group (relative risk 0.49; 95% Bayesian credible interval 0.30–0.76) [1].

Subgroup analyses suggested that benefit was greatest among patients treated within 3 days of symptom onset and among those with higher baseline viral loads, consistent with the mechanistic expectation that early intervention at the epithelial level would be most effective before systemic disease is established [1,2]. Effects were broadly consistent across SARS-CoV-2 variants and vaccination strata [1].

Earlier phase 2 data from Feld et al. demonstrated accelerated viral clearance with pegIFN-ë, particularly among patients with baseline viral loads above 10v copies/mL [2]. A separate phase 2 trial by Jagannathan et al. did not meet its primary endpoint, though differences in patient population and timing of treatment may account for the discrepancy [15]. Santer et al. reported that pegIFN-ë accelerated SARS-CoV-2 clearance even in older adults with delayed adaptive immune responses [16].

Preclinical breadth

Evidence from preclinical investigations indicates that IFN-ë exerts antiviral activity against MERS-CoV in animal models and demonstrates inhibitory effects against multiple RNA viruses, including influenza, under laboratory conditions [17-18]. While these observations support its potential as a broad-spectrum respiratory antiviral therapy, further clinical studies are required to confirm its efficacy across diverse viral infections in humans.

Safety profile

Clinical development programs evaluating pegIFN-ë for hepatitis B, C, and D have generally demonstrated a more favorable tolerability profile compared with pegIFN-á, with lower incidences of flu-like symptoms, hematological toxicities, and neuropsychiatric adverse effects [19-22]. Nevertheless, abnormalities in liver function tests have been reported consistently across studies. Elevations in serum transaminases and bilirubin levels, the latter potentially related to the inhibition of organic anion-transporting polypeptides, have been documented and, in some cases, necessitated discontinuation of therapy [20,23,24]. Although the single-dose regimen used in the TOGETHER trial was reported to be well tolerated, wider clinical implementation would warrant careful monitoring of hepatic function to ensure patient safety [1].

Ramatroban

Biologic rationale

Ramatroban is a dual antagonist of the thromboxane A, (TP) and prostaglandin D, (DP2/CRTH2) receptors, both of which are involved in the pathogenesis of severe viral respiratory infections [3,4,25,26]. By inhibiting these pathways, it may reduce thrombotic, inflammatory, and immune-mediated complications associated with severe disease [25,26]. The drug is orally active and has been used in Japan for allergic rhinitis since 2000, with a well-established safety profile [4,27].

Evidence limitations

Despite its strong mechanistic rationale, current clinical evidence supporting the use of ramatroban in viral respiratory infections remains limited. Human data are restricted to a small uncontrolled case series involving four patients with COVID-19 pneumonia, and no randomized controlled trials have assessed its efficacy for prevention, treatment, or reduction of transmission in respiratory viral diseases [3,4]. Furthermore, the complex nature of prostanoid signaling necessitates careful interpretation, as modulation of these pathways may produce variable effects depending on the biological context, with some studies suggesting the potential for enhanced immunopathology [28,29]. Consequently, although ramatroban shows therapeutic promise, robust clinical trials are required before its widespread use can be recommended.

Can These Therapies Terminate Outbreaks or Prevent Pandemics?

The potential of host-directed therapies to control outbreaks or prevent pandemics is a key consideration in pandemic preparedness. However, current evidence is insufficient to support such a role for either pegIFN-ë or ramatroban. Effective outbreak control through therapeutic interventions requires early administration, large-scale accessibility, an acceptable safety profile, and the ability to significantly reduce transmission.[5,6] Experience with influenza antivirals has shown that although early treatment may decrease transmission within households and communities, its impact is highly dependent on timing, coverage, and epidemiological circumstances [5,6,30–32]. Moreover, antiviral therapy alone has generally been inadequate to halt widespread transmission once an epidemic becomes established [6,9,10]. For pegIFN-ë, evidence regarding reduction of viral transmission is lacking, as clinical studies have primarily focused on patient outcomes rather than transmission dynamics [1]. In the case of ramatroban, conclusions regarding outbreak control remain speculative due to the absence of robust efficacy data [3,4]. Therefore, while these agents may help lessen disease severity, lower viral burden, and potentially contribute to transmission reduction, they should be viewed as complementary measures rather than substitutes for established public health strategies such as surveillance, diagnostic testing, isolation measures, and vaccination programs [5,8,9]. Based on the current evidence, a rational preparedness strategy should position these agents in distinct tiers.

Operational integration

Effective use of these therapies during future outbreaks requires integration into a coordinated preparedness framework. Key components include predefined emergency activation criteria, rapid diagnostic testing for early case detection, continuous pharmacovigilance for safety monitoring, alignment with emerging virus-specific interventions, and clear communication regarding their investigational status, benefits, and limitations.

Preparedness Tier	Therapeutic Candidate	Strategic Objective	Key Preparedness Actions
Tier 1	**Pegylated Interferon Lambda (pegIFN-λ)**	**Priority investigational countermeasure with potential for early outbreak mitigation**	• Establish regulatory readiness through early engagement with health authorities to avail emergency-use pathways. • Assessment of manufacturing capacity, supply-chain resilience, and feasibility of stockpiling. • Development of adaptive clinical trial platforms that can be rapidly implemented during the emerging outbreaks. • Pre-define treatment path emphasizing administration during the early symptomatic phase (preferably within 72 hours of symptom onset). • Design protocols for hepatic function evaluation and ongoing safety monitoring parameters. • Prioritize research areas assessing post-exposure prophylaxis, transmission reduction, and effectiveness in high-risk or closed-population settings.
Tier 2	**Ramatroban**	**Repurposing candidate requiring rapid clinical evaluation**	• Include ramatroban within pre-established adaptive platform trial networks for rapid evaluation during outbreaks. • Focus initial assessments on patients exhibiting early respiratory compromise, hypoxemia, or evidence of thrombo-inflammatory activation. • Restrict its role to investigational use only until availability of robust randomized clinical trial evidence. • Support translational and mechanistic studies to identify optimal patient populations and disease stages most likely to benefit.

Conclusion

Host-directed therapies may play an important supportive role in future respiratory pandemic preparedness, but their present evidence base warrants cautious interpretation. PegIFN-ë has emerged as the more advanced agent, supported by a plausible biological mechanism and encouraging clinical data, whereas ramatroban remains an investigational option requiring further evaluation. At present, neither therapy can be considered a standalone solution for outbreak control or pandemic prevention. Future outbreak preparedness efforts should focus on strengthening clinical trial readiness, regulatory planning, manufacturing capacity, and integration of these agents with established public health measures. With continued research and validation, these therapies could become valuable components of a comprehensive early-response strategy against emerging respiratory viral threats.

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Reference

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Evaluating the Lung Function Parameters of the Residents of Delhi: A Cohort Study

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Abstract

Background: Chronic lung diseases contribute significantly to the global disease burden, with air pollution being a major risk factor. This study aimed to assess changes in lung function parameters among permanent residents of Delhi, one of the world's most polluted capital cities. **Methods**: A cohort study was conducted with 190 participants. Lung function parameters were evaluated using spirometry during October-November 2019 (baseline) and October-November 2021 (follow-up). Forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC ratio were measured, and subgroup analysis was done based on the participant's age, gender, and smoking status. **Results**: The study found an overall decline in lung function parameters between 2019 and 2021. The reduction in FVC was statistically significant across both genders, regardless of smoking history and particularly notable in the 41-60 years age group. **Conclusions**: The study demonstrated a significant decline in lung function parameters, particularly FVC, among Delhi residents over two years. These findings highlight the need for air quality monitoring, screening programs in highly polluted urban environments, and targeted interventions for vulnerable populations. **Categories**: Public Health, Pulmonology, Environmental Health.

Keywords: Air pollution, lung function tests, spirometry, Delhi, India

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Introduction

Chronic lung diseases accounted for 10.6% of the global disease burden, with smoking and air pollution being major risk factors [1]. Air pollution, both indoor and outdoor, can harm our lungs. Air pollution from particulate matter, ozone, and nitrogen oxides exacerbate pulmonary diseases with a higher impact on vulnerable populations. Together, these pollutants lead to serious health issues, including asthma, lung infections, chronic diseases like Chronic Obstructive Pulmonary Disease (COPD), and even lung cancer [2,3].

Lung function tests are useful for assessing an individual's respiratory health. These tests can detect compromised lung health long before any signs or symptoms of chronic respiratory diseases appear [4]. Correlating lung function parameters directly with air pollution is difficult, and information regarding the direct impact of air pollution on the health of the respiratory system in the Indian population is lacking. The period from October to November specifically is known for high pollution levels, attributed to factors such as stubble burning, firecracker use due to Diwali, and thermal inversion, in addition to vehicular pollution, burning of fossil fuels, and emissions from thermal power plants [5].

Materials And Methods

A cohort study was conducted to assess lung function parameters of permanent residents of Delhi. Participants were selected using convenient sampling.

Inclusion Criteria were:

(1) Permanent resident of Delhi;
(2) Age 18 years or older;
(3) Ability to perform spirometry;
(4) Willingness to participate in follow-up assessments;

Exclusion Criteria included:

(1) Known respiratory conditions;
(2) Active respiratory infection;

Baseline lung function evaluation was tested from October to November 2019 and subsequent evaluations were done for the same

population between October and November 2021. Spirometry was chosen to assess the lung function of the study population, and a MIR Spirolab spirometer was used [6]. Forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) were measured and the FEV1/FVC ratio was calculated. Looking at FEV1, FVC and FEV1/FVC ratio together gives a better assessment and helps to classify the pathologies as obstructive or restrictive patterns. Ethics approval was obtained from the Institutional Ethics Committee. A total of 190 apparently normal adults were enrolled after obtaining written informed consent and were followed up. Participants with any identified severe disease were excluded from the study and referred to the linked hospital for further management.

Results

Our study population comprised 190 participants with a mean age of 43.15 ± 15.73 years. There were 91 (47.9%) participants who were aged less than 40 years, 70 (36.8%) who were in the age group 41-60 years, and 29 (15.3%) who were over 60 years, with an age range of 18 to 82 years. The demographic distribution showed 103 females (54.2%) and 87 males (45.8%). Among the participants, 156 (82.1%) were non-smokers and 34 (17.9%) were current or former smokers. Participants reported spending a median of 5 hours (Inter quartile range (IQR): 2.5, 8.9) outdoors daily.

From the baseline assessment in 2019, a drop in FEV1, FVC, and FEV1/FVC was noticed in 2021 in the study population (Table 1). However, only the reduction in FVC was found to be statistically significant. The lung function parameters of the participants were evaluated and analysed after segregating the data according to age, gender, and smoking status (Table 1).

A declining trend for FEV1 and FVC was noticed even when segregating for age, gender, and smoking status. The decline in FVC was statistically significant across both genders, irrespective of their smoking history. The decline in FVC was also found to be significant in the age group 41 to 60 years. The declining trend in FEV1 was statistically significant overall, but sub-group analysis across gender, age groups, and smoking history did not give statistically significant results.

Discussion

In this study, we found a general trend of declining lung function parameters. On subgroup analysis, a significant decline in FVC was detected in the 41 to 60 years age group, and gender-wise analysis revealed both males and females showing significant FVC decline. The declining trend in lung function parameters observed in our study can be attributed to several factors. In their study, Arora S et.al. reported that women were particularly vulnerable to indoor air pollution. Their study also found that decreased lung function was associated with both tobacco smoking and vehicular pollution exposure [7].

Studies from across the world have linked air pollution to deranged lung function parameters. A study from Sweden found that exposure to traffic-related air pollution, especially in males, is associated with reduced lung function [8]. Among children, higher levels of air pollution were linked to significant retardation in lung growth rates, which was more among boys compared to girls [9]. Studies among school children from China found that prolonged exposure to ambient air pollution had an association with wheezing and cough. PM10 had a notable association with these disease conditions and with deranged pulmonary function [10,11].

The significant decline in FVC across various subgroups is particularly noteworthy. FVC tends to decrease with age due to various anatomical and physiological changes in the respiratory system [12]. A systematic review by Thomas et.al. (2019) consistently showed that lung function measured by FEV1 and FVC declines with age. Men showed a faster decline in absolute values compared to women, and an age-specific analysis revealed that the rate of decline increased every decade [13].

Kelkar et.al. (2019) found that people who lived in Delhi for more years had poorer lung function parameters. Those who used closed transportation like cars and air-conditioned buses had better lung function than those who used open transportation like non-air-conditioned buses and scooters. People living near factories that produce smoke also leads to lower lung function. Additionally, both active smokers and people exposed to second hand smoke from family members had significantly poorer lung function compared to non-smokers [4].

The meta-analysis of multi-centric cohort data by Adam et.al. (2015) revealed that higher exposures to nitrogen oxides and PM10 were linked to significantly lower cross-sectional levels of FEV1 and FVC, with traffic density near residences also associated with decreased FEV1. Meanwhile, no association was detected between air pollution and a longitudinal decline in lung function from the analysis. The authors points out that this lack of longitudinal association may be due to several methodological issues, including the differences of measuring changes in lung function over time and potential limitations in the ability to accurately assess air pollution exposure throughout the study period. Also, external influences like seasonal and diurnal variations, changing the spirometer used as technology advanced, and other individual-level confounding factors may have affected any real effects of chronic pollution exposure on the decline in lung function over time. [14].

As per the World Air Quality Report 2023, India ranked as the third most polluted country, and Delhi as the most polluted capital city with an average Air Quality Index (AQI) ranging from 234 to 312 between October and November 2019 and an AQI of 173 to 377 during the same period in 2021. These consistently high pollution levels likely play a significant role in the declining lung health of the population [15,16]. A recent study by Chen Y (2025) highlights that particulate matter pollution in Delhi, particularly PM1, may be significantly underestimated. This underestimation stems from the hygroscopic growth of PM1 particles, which is affected by environmental humidity and chloride content. This leads to notable fluctuations based on season, time of day and surrounding conditions. The author comments that such bias is considerably much smaller on PM2.5 and PM10 as compared to PM1 [17].

The study by Feng et.al. (2022) in China followed college students from 2019 to 2020, including the COVID-19 lockdown period, to examine how changes in air pollution affected lung function. It was found that lung function parameters improved over time and were associated with a decrease in average values of PM 2.5 and PM 10. The results remained consistent after accounting for indoor air pollution. Also, no significant difference was found between male and female population [18].

Study Limitations and Future Directions

Despite relevant findings, this study had a few limitations. Firstly, the sample size of the cohort was small, and the follow-up period was short due to limited resources. However, being the first cohort study assessing change in lung function tests in highly polluted areas in India, this study generates crucial evidence to guide future studies. Secondly, the change in lung function can only be attributed to air pollution in Delhi and not directly correlated to it, as the

Table 1: Changes in Lung Function Parameters (2019-2021) by Demographic Characteristics

Variable (N = 190)(100%)	Mean ± SD 2019	Mean ± SD 2021	p-value
FEV1	2.2497 ± 0.6535	2.1675 ± 0.6699	0.028
FVC	2.7318 ± 0.7580	2.5829 ± 0.7519	<0.001
FEV1/FVC	81.0288 ± 10.0647	81.3816 ± 8.0495	0.633
Males (n = 87) (45.8%)			
FEV1	2.5144 ± 0.6289	2.4269 ± 0.7019	0.129
FVC	3.0986 ± 0.6920	2.9314 ± 0.7295	0.015
FEV1/FVC	79.0675 ± 11.7040	79.9575 ± 8.1450	0.474
Females (n = 103) (54.2%)			
FEV1	2.0261 ± 0.5896	1.9483 ± 0.5569	0.115
FVC	2.4220 ± 0.6702	2.2885 ± 0.6386	0.018
FEV1/FVC	82.6854 ± 8.1335	82.5845 ± 7.8062	0.908
Smokers (n = 34) (17.9%)			
FEV1	2.4297 ± 0.5911	2.3374 ± 0.6109	0.144
FVC	3.0626 ± 0.7310	2.8553 ± 0.6970	0.023
FEV1/FVC	77.2079 ± 14.6979	80.3971 ± 5.0022	0.204
Non-smokers (n = 156) (82.1%)			
FEV1	2.2104 ± 0.6616	2.1304 ± 0.6782	0.066
FVC	2.6597 ± 0.7467	2.5235 ± 0.7524	0.006
FEV1/FVC	81.8615 ± 8.5806	81.5962 ± 8.5687	0.712
Age ≤ 40 years (n = 91) (47.9%)			
FEV1	2.5100 ± 0.5319	2.4193 ± 0.5553	0.102
FVC	2.9526 ± 0.6624	2.8724 ± 0.6046	0.225
FEV1/FVC	84.2495 ± 7.0471	83.2495 ± 7.1063	0.199
Age 41 to 60 years (n = 70) (36.8%)			
FEV1	2.1417 ± 0.6309	2.0557 ± 0.68103	0.119
FVC	2.6857 ± 0.7164	2.4457 ± 0.7809	<0.001
FEV1/FVC	77.7896 ± 12.0639	80.2243 ± 7.8630	0.125
Age > 60 years (n = 29)(15.3%)			
FEV1	1.6934 ± 0.6498	1.6469 ± 0.6138	0.685
FVC	2.1503 ± 0.8303	2.0055 ± 0.6886	0.162
FEV1/FVC	78.7414 ± 10.0069	78.3138 ± 9.9125	0.803

study's primary objective was to assess only the change in lung function. Lastly, information related to COVID-19 infection was not collected, which could have been a confounder of our study.

The findings of this study highlight the need to undertake measures to protect the health of the people. Better control measures to mitigate harmful exposures, especially in heavily polluted cities like Delhi. Conducting screening camps for early detection of declining lung functions and implementing interventions, especially for vulnerable groups like children and the elderly, will help improve the health outcomes of the people. The study may shed evidence on air pollution induced health effects in a broader aspect.

Conclusions

Our study showed an overall decline in lung function parameters measured using spirometry, and the decline in FVC has been found to be statistically significant. This can be attributed to many factors, and air pollution is expected to play a significant role. Future studies should correlate the impact of air pollution - with a continuously monitored Air Quality Index (AQI) on lung function tests.

Declaration of patient consent

The all authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Data Access Statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request. The datasets shall be made available from the corresponding author on request.

Conflict of Interest:	Author declare no COI
Ethics:	There is no ethical violation as it is based on voluntary anonymous interviews
Funding:	No external funding
Guarantor:	Dr.Akshithanand Kuzhikkat Jayaprakasan will act as guarantor of this article.

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Evaluation of the occipital condyles through morphometric and morphological analysis: An examination of bony landmark in the transcondylar approach

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Abstract

Background: On the inferior surface of the occipital bone two bony projections present in the skull are known as occipital condyles. During the surgical approaches like transcondylar, for the harmless occipital condylar resection the anatomical landmarks should be well known. Hence the morpho-logical and the morpho-metric examination of the occipital condyles and their facet become important clinically. **Methods:** 60 human adult dry skulls of unidentified sex were studied for shape, width, length and height of the occipital condyles. Anterior inter-condylar distance, the posterior inter-condylar distance and the distance between the anterior tip and posterior tip of the occipital condyles from basion and the opisthion were recorded. **Results:** Most frequent shape of occipital condyles seen was oval (21.6%) followed by reniform (17.5%), biconvex (15%), S shaped (14.6%), 8 shaped (13%), irregular (9.16%), condyle in two parts (4.2%), quadrangular (2.5%) and triangular (2.5%). All parameters were found to be more on right side except width of the occipital condyles. There was no significant difference observed between right side and left side except distance between the anterior tip of occipital condyles and basion was statistically highly significant. **Conclusion:** For safe occipital condyle resection in various surgeries the morpho-logical and the morpho-metric analysis of occipital condyles becomes utmost important.

Keywords: Morpho-metric, Morpho-logical evaluation, Occipital condyles, Transcondylar approach

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Introduction

Occipital bone largely forms posterior part of the human skull. Two bony projections found on inferior aspect of occipital bone recognized as occipital condyles (OC). These condyles situated lying on each region of foramen magnum at base of skull. Superior articular facade of atlas connects by means of occipital condyles to compose atlanto-occipital joint. Oval in shape, occipital condyles positioned obliquely, with anterior end nearer to the midline than the posterior ending. These structures play a crucial role in maintaining the head in a vertical position and are essential for the steadiness of the craniovertebral junction [1].

It is crucial to have a comprehensive understanding of anatomical foundation of the craniovertebral anomalies while performing surgeries in this specific section. The lateral techniques utilized in craniovertebral surgery necessitate the removal of occipital condyles, while transcondylar approach emphasizes significance of morphometry of these condyles [2-4]. Flexion, extension, and lateral bending movements do not present any challenges in terms of the symmetry of occipital condyles. However, the presence of asymmetrical facets in condyles will result in modified kinematics within the atlantooccipital joint [5]. Numerous individuals who experience closed head injuries face the potential danger of occipital condylar fractures. In order to safely remove the occipital condyle during the transcondylar approach, it is imperative to possess a thorough understanding of the anatomical landmarks [4]. Consequently, the clinical importance is underscored by the morpho-logical and the morpho-metrical assessment of occipital condyles in addition to their facet.

Given aforementioned clinical significance, it is imperative to investigate the typical and altered structure of the occipital condyles. Therefore, this research was conducted to furnish data regarding the occipital condyles and their distances from established anatomical reference points in the dry skulls of adult individuals.

Material and Methods

The current cross-sectional study utilized a sample of 60 human adult dry skulls of unidentified sex. Skulls were obtained from Anatomy Department of two Medical Colleges. Only dry, macerated skulls that were free from physical deformities or abrasions were incorporated in the study. Linear dimensions were taken by means of a digital Vernier caliper with a least count of 0.01 mm. In cases where the Vernier caliper couldn't be used, a steel needle, ruler, silk thread, and divider were employed to measure curved distances and other distances. All measurements

were conducted with careful consideration of any potential zero error in the instruments. The data was compiled on Excel spreadsheet, statistical assessment performed by means of the SPSS software version 25.0. Statistical assessment was done using chi-square test. Values $p<0.05$ were taken as statistically significant.

Shape, width (transverse maximum distance between medial and lateral borders of OC), length (greatest anteroposterior space between anterior and posterior tips of OC, measured with external jaws of Vernier caliper) and height (vertical maximum distance between superior border and inferior border of medial margin of OC, measured with internal jaws of Vernier caliper) were noted (Fig. 1A).

Anterior inter-condylar distance (AICD) (distance among anterior tip of left and right occipital condyle in horizontal plane, measured with internal jaws of Vernier caliper), posterior inter-condylar distance (PICD) (distance among posterior tip of left and right occipital condyle in horizontal plane, measured with internal jaws of Vernier caliper) were recorded (Fig. 1A).

Distances among anterior tip of OC and basion (AOCB), the anterior tip of OC and opisthion (AOCO), posterior tip of OC and basion (POCB) and the posterior tip of OC and opisthion (POCO) were noted (Fig. 1B).

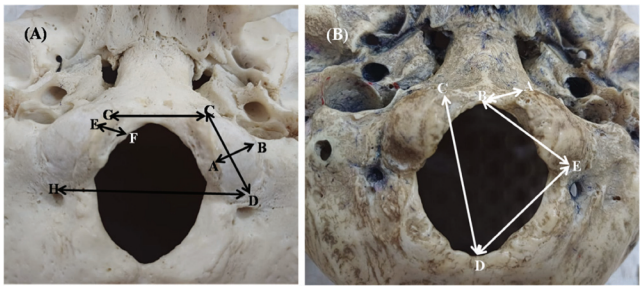

Fig. 1: Morpho-metric parameters of the occipital condyles (A): Width (AB), length (CD), height (EF), anterior inter-condylar distance (CG), posterior inter-condylar distance (DH); (B): Distance between anterior tip of occipital condyle to basion (AB), anterior tip of occipital condyle to opisthion (CD), posterior tip of occipital condyle to basion (EB), posterior tip of occipital condyle to opisthion (ED)

Ethical Consideration

Since the study was based on human dry skulls already present in the departments of anatomy of two Medical Colleges, Ethical consideration was not required for the study.

Results

Most frequent shape of occipital condyles seen be oval (21.6%) followed by reniform (17.5%), biconvex (15%), S shaped (14.6%), 8 shaped (13%), irregular (9.16%), condyle in two parts (4.2%), quadrangular (2.5%) and triangular (2.5%) (Fig. 2). **(Table 1)**

All parameters were found to be more on right side except width of OC, distance AOCB and distance POCB. Between right side and left side no significant difference was observed except distance among anterior tip of OC and basion was calculated to be statistically highly significant.

Mean breadth and length of occipital condyle were 12.10±1.66mm and 23.71±2.95mm respectively, at the same time mean height was found to be 7.52±1.33mm.

Distance among anterior tip of OC and basion was 11.14±2.90mm while the distance among opisthion and anterior tip of OC was 38.25±4.98mm. Mean value of distance among posterior tip of OC and basion was calculated to be 27.44±2.35mm, whereas the distance among posterior tip of OC and opisthion was 28.25±2.28mm. Anterior inter-condylar distance and posterior inter-condylar distance were 18.75±3.09 mm and 42.63±3.21 mm respectively.

All the parameters were found to be more on right side except width of OC, distance between AOCB and distance POCB which were slightly greater on left side and no statistically significant disparity in relation to these parameters on both sides was there. However, the distance among anterior tip of OC and basion was statistically highly significant. **(Table 2)**

Discussion

Previous studies have reported various morpho-logical shapes of the OC in the literature. **(Table 3)** In Egyptian population most common shape reported was reniform shape,[6] in Turkish population it was oval shape,[7] in Greek population it was "S" shaped,[8] while in Brazilian population "8" shape be most common [9].

In the current study, mean value of width of OC were more on left side than right side while other studies reported the reverse [10-12]. This difference could be attributed to the race and the genetic the factors in the different regions of the population. Similarly in current study, mean value of length of occipital condyle reported to be greater on right side which corroborates with the findings of study made by Saluja et al. [10] and Ramkrishna et al. [12] whereas Cheruiyot et al. [11] reported the reverse. In another study on dry skulls, mean value of length of occipital condyle reported to be 23.1 mm [4] which was also comparable to the current study. On comparing mean height of occipital condyle Saluja et al. [10] and Ramkrishna et al. [12] reported values to be greater on right side whereas in another study the values reported were same on both sides [11]. The differences observed could potentially be attributed to distinct approaches in gathering data and the genetic foundation of diverse populations. **(Table 4)**

Mean value of distance from anterior tip of occipital condyle till basion and opisthion were higher in the current study in comparison to that reported by Saluja et al. [10]**.** This difference could be attributed to race and genetic factors in different region of population. Similarly, mean value of distance from posterior end of occipital condyle till basion and opisthion were comparable to study done by Saluja et al. [10]**.** Knowledge of these findings can help avoid harm to the surrounding neurovascular components. **(Table 4)**

Table 1. Shapes of Occipital condyles

No.	Shape of OC	Right N(%)	Left N(%)	Total N(%)
1.	Oval	12 (20)	14 (23.3)	26 (21.6)
2.	Reniform	12 (20)	9(15)	21(17.5)
3.	Biconvex	9 (15)	9(15)	18(15)
4	S Shaped	10 (16.6)	7(11.6)	17(14.6)
5.	8 Shaped	8 (13.3)	8(13.3)	16(13)
6.	Irregular	4 (6.7)	7(11.6)	11(9.2)
7.	Condyle in two part	2(3.3)	3(5)	5(4.2)
8.	Quadrangular	1(1.7)	2(3.3)	3(2.5)
9.	Triangular	2 (3.3)	1(1.6)	3(2.5)

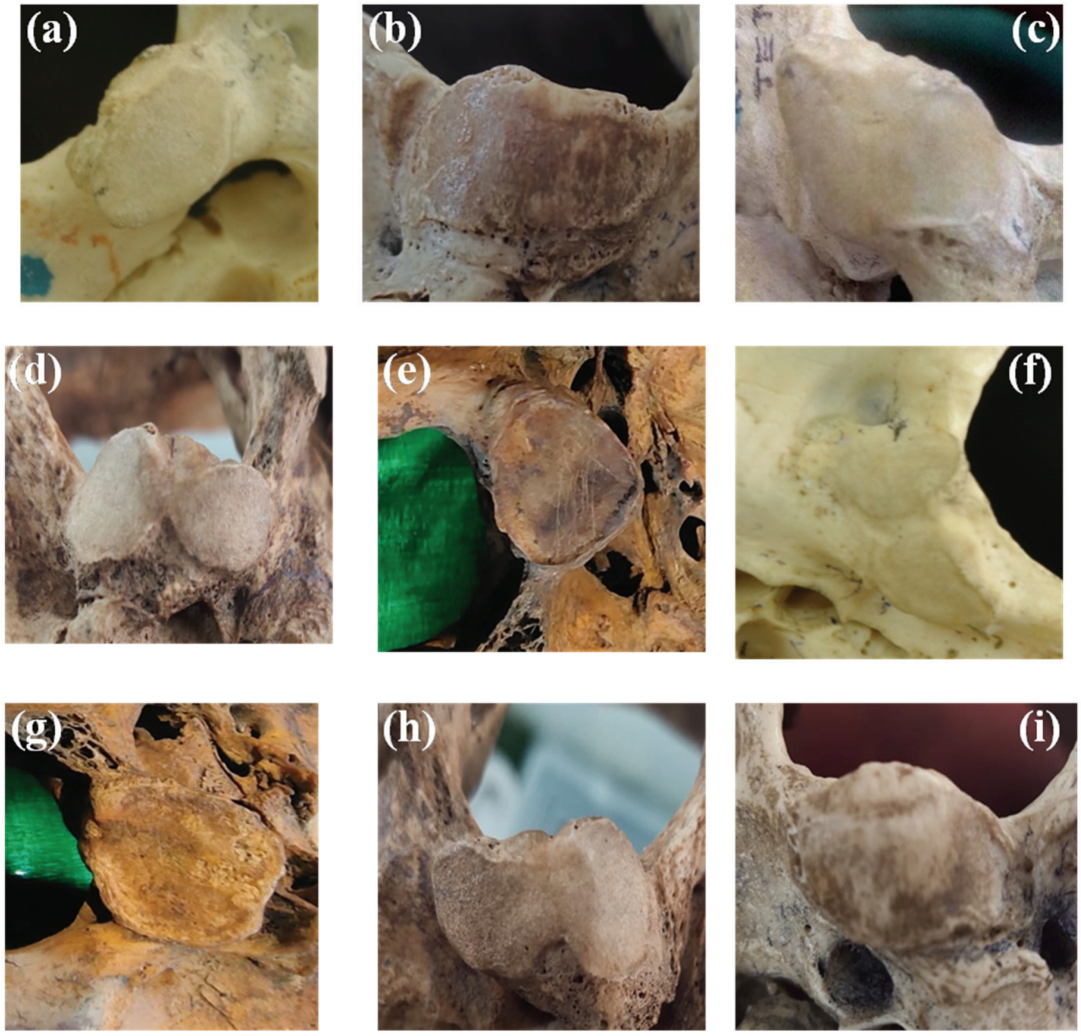

Fig. 2: Various shapes of occipital condyle (a) Oval, (b) Reniform, (c) S shape, (d) 8 shape, (e) Triangular, (f) Condyle in two parts, (g) Quadrangular, (h) Irregular, (i) Biconvex

Table 2: Morpho-metric measurement of the occipital condyles

Parameters	Mean ± SD (mm)			Range Minimum-Maximum (mm)			p-value
	Right	Left	Total	Right	Left	Total	
Width OC	12.02±1.499	12.17±1.8	12.10±1.66	8.42-16.71	9.05-17.24	8.42-17.24	0.42979
Length OC	23.99±2.997	23.43±2.88	23.71±2.95	14.66-29.82	11.08-8.65	14.66-29.82	0.07228
Height OC	7.53±1.42	7.52±1.2	7.52±1.33	4.3-10.82	5.02-9.7	4.3-10.82	0.90114
Dist. AOCB	11±2.91	11.28±2.88	11.14±2.90	4.15-29.65	4.15-29.65	4.15-29.65	**0.04516***
Dist. AOCO	38.28±5.07	38.22±4.88	38.25±4.98	8.53-44.95	10.43-45.46	8.53-45.46	0.66658
Dist. POCB	27.36±2.43	27.52±2.29	27.44±2.35	20.8-32.7	20.8-32	20.8-32.7	0.39907
Dist. POCO	28.4±2.307	28.1±2.47	28.25±2.28	23.66-34.26	22.05-32.7	22.05-34.26	0.21495
Dist. AICD	-		18.75±3.09	-		7.1-51.29	-
Dist. PICD	-		42.63±3.21	-		22.8-51.29	-

Statistical analysis done using chi-square test. Values p< 0.05 were considered Staistically significant. (OC- occipital condyle; AOCB -Distance between the anterior tip of OC and basion; AOCO- Distance between the anterior tip of OC and opisthion; POCB- Distance between the posterior tip of OC and basion; POCO- Distance between the posterior tip of OC and opisthion; AICD- Anterior inter-condylar distance; PICD- Posterior inter-condylar distance)

Table 3: Comparison of the percentage distribution of morpho-logical types of the occipital condyle with prior research findings.

Shape of occipital condyles	Fetouh et al. [6]	Ozer et al. [7]	Natsis et al. [8]	Aragao et al. [9]	Present study
1. Oval	16	59.7	7.6	6.1	21.6
2. Reniform	22	23	6.2	7.9	17.5
3. "S" shaped	19	4	30.7	18.2	14.6
4. "8" shaped	12	4.5	10.6	19.2	13
5. Triangular	6	4.2	16.2	9.3	2.5
6. Ring	7	2.3	4.4	14.5	
7. Condyle in two parts	13	0.3	1.6	4.7	4.2
8. Deformed	-	1.7	5.8	-	-
9. Quadrilateral	5	-	-	8.4	2.5
10. Irregular	-	-	-	3.7	9.16
11.Biconvex	-	-	-	7.9	15

Table 4: Comparison of the morpho-metric measurements of the occipital condyle with prior research findings.

Authors		Saluja et al. [10]	Cheruiyot et al. [11]	Ramkrishna et al. [12]	Present study
Width OC (mm)	Right	12.98±1.62	12.27±1.25	11.03±2.22	12.02±1.49
	Left	12.97±1.46	12.20±1.33	11.01±2.34	12.17±1.8
Length OC (mm)	Right	22.90±3.11	20.51±2.02	21.79±0.09	23.99±2.99
	Left	22.60±2.72	20.59±2.09	21.48±0.87	23.43±2.88
Height OC (mm)	Right	9.32±1.23	8.64±1.10	6.18±1.31	7.53±1.42
	Left	9.12±1.23	8.64±1.07	6.09±1.36	7.52±1.2
AOCB (mm)	Right	9.74±1.78	-	-	11±2.91
	Left	9.56±1.33	-	-	11.28±2.88
AOCO (mm)	Right	37.53±2.26	-	-	38.28±5.07
	Left	37.88±2.5	-	-	38.22±4.88
POCB (mm)	Right	28.16±3.26	-	-	27.36±2.43
	Left	26.93±2.16	-	-	27.52±2.29
POCO (mm)	Right	26.78±1.92	-	-	28.4±2.307
	Left	26.17±2.51	-	-	28.1±2.47
AICD (mm)		17.81±2.93	19.71±2.47	19.41±3.99	18.75±3.09
PICD (mm)		38.91±4.16	39.41±2.73	37.36±4.03	42.63±3.21

(OC- occipital condyle; AOCB -Distance between the anterior tip of OC and basion; AOCO- Distance between the anterior tip of OC and opisthion; POCB- Distance between the posterior tip of OC and basion; POCO- Distance between the posterior tip of OC and opisthion; AICD- Anterior inter-condylar distance; PICD- Posterior inter-condylar distance).

In the current study, mean anterior inter-condylar distance was reported was slightly more than that reported by Saluja et al. [10] and less than Cheruiyot et al. [11] study and Ramkrishna et al. [12]. However in current study**,** mean posterior inter-condylar distance was higher in comparison to other studies [10-12]. The inter-condylar distances, whether anterior or posterior, indicate the alignment and convergence of the OC. This alignment plays a vital role in the precise placement of screws in occipitocervical fixation surgeries. **(Table 4)**

Treatment of craniovertebral region lesions is currently carried out through lateral approaches, such as the transfacetal, partial transcondylar, and complete transcondylar, along with extreme-lateral transjugular and transtubercular. The widely used out of these methods involve the partial or the complete removal of occipital condyle. Size and alignment of OC can affect the selection of surgical approach for various craniovertebral junction lesions [13, 14].

Limitations

Limitations of the study can be considered as the study sample did not include skulls with asymmetries and infant skulls.

Conclussion

In the current study, all parameters were more on right side except width of OC, distance AOCB and distance POCB. No significant statistical difference was observed between two sides except

distance from anterior tip of OC till basion which was statistically highly significant. The assessment of the morphology and the morphometry of occipital condyles play a crucial role in the surgical planning techniques for the skull base, as well as in the excision of occipital condyles in various approaches to the skull base.

Conflict of Interest:	Author declare no COI
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ORIGINAL

Application of Interstitial High Dose Rate (HDR) Brachytherapy with Microselectron HDR for early Breast Cancers

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Abstract

Background: Breast cancer forms a commonest cancer in women, and due to earlier detection and awareness, more patients come to hospital at early stages. Treatments for early breast cancers have evolved from radical mastectomy towards breast conserving surgery (BCS) and radiotherapy. In high-risk patients, a boost dose to tumor bed, 15-20 Gy is required, by high energy electrons or by interstitial brachytherapy (IBT). As our centre did not have high energy electron linear accelerator, we resorted to interstitial brachytherapy for boost dose to tumor bed. The pattern of care followed at our center in early breast cancers and biologically effective doses (BED), efficacy of treatment, needs documentation. **Methods:** From the year 2017, interstitial BT for BCS patients are carried out at our center with microSelectron (M/s Nucletron). A 2-plane template is used to implant needles with treating 'distance' 1.2 cm. 10mm on either side of the catheter was kept cold to avoid excess skin/subcutaneous excess dose, maintain cosmoses and prevent skin spots. Two regimens, 1) HDR BT and External Beam Radiotherapy (EBRT) and 2) Accelerated Partial Breast Irradiation (APBI) with only BT as mono-therapy are followed. 78 patients were treated in 6 years. In 73 patients, doses to 100% covering line was delivered with 6h inter-fraction BT as 8 Gy x 2 fractions(n=1), 4 Gy x 4fr (n=27), 3.65 Gyx4fr (n=24), 3 Gyx4fr (n=19), 3 Gyx3fr (n=2) along with EBRT by Tele-cobalt tangential fields, 5fr/week, breast cone, 40Gy/15 fr equivalent of 46.7 Gy in 2Gy/fr. Second group (mono-therapy) had 5 patients, 3.65 Gy x 10fr (n=1), 3.40 Gy x 10fr (n=3) and 5.88 Gy x 10fr, completing treatment in 5 days. **Results :** BED_{10} for BT = 19.93 Gy for 3.65Gy x 4Fr; This BT dose equal to EBRT dose In 2Gy/fr 8.3 = 16.61 Gy. 40Gy/15Fr @ 2.67Gy/Fr is equal to dose of 42.3Gy at 2Gy/fr. Total dose of whole regimen is 58.9Gy (<1.5% to 60Gy). BED_{10} for BT of 3.65Gy x 10Fr is 49.83G, which is equivalent of 41.5Gy EBRT total dose at 2Gy/fr, 5 fr/week. There was no toxicity recorded on short term follow up. **Conclusion:** As more cancer patients are treated with breast conservation, HDR BT can be practiced, with available brachytherapy machines. Treatment times are very short in breast interstitial BT, and patients tolerate these treatments well. In centres with low energy linacs without electron facility, still this method could help in treatments of early breast cancers.

Key Words: Breast conservation, Breast implants, High dose rate brachytherapy, Early breast cancers

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Introduction

Treatments for early breast cancers have evolved from radical mastectomy towards breast conserving surgery (BCS) and radiotherapy, for more than 40 years. In high risk patients, a localized boost dose to tumor bed, about 15-20 Gy is required. This is achieved by high energy electrons or by interstitial brachytherapy (BT). The EORTC trial investigated the role of boost dose in breast conserving therapy and demonstrated significant better local control rate with higher radiotherapy dose in women of around 50 years age group [1]. They analysed 2661 randomised patients who received a boost dose of 16 Gy to the primary tumor bed after complete tumorectomy and 50 Gy dose by External Beam Radiation Therapy (EBRT). In the above analysis, 63% received boost dose by high energy electrons, 28% with photons and 9% with interstitial brachytherapy. Local recurrences (LR) were compared in these three groups. LR were 4.8% in electron group, photon boost group 4.0%, and interstititial boost 2.5%. Based on the outcome of the above study, they highlighted that interstitital boost has given similar local control and same extent of local fibrosis.

In another report[2], pulsed doserate (PDR) brachytherapy was delivered as boost in 113 patients who received median dose of 50 Gy EBRT(range 46 to 52Gy). 20-25Gy boost dose was based on the pathologic grading, or 15Gy in T2-G3 stage. At median follow up of 61 months, they reported 4.4% local failure, and actuarial 5 and 8 year local recurrence free survival rates 95% and 93% respectively. Cosmesis was 90%, and 14 out of 113 patients experienced Grade III (planar telangiectasia) and none of the

patients had Grade IV late toxicity of the skin. 25 Gy boost dose resulted in significantly higher rate of toxicity. The American Brachytherapy Society (ABS) recommends a dose fractionation scheme that yields early and late effects are approximately equivalent to those of 10 Gy to 20 Gy followed by 45 to 50 Gy of EBRT [3]. In our hospital, linear accelerator with high energy electron facility is commissioned in the year 2023 only. We resorted to boost dose with high dose rate (HDR) in breast conserving treatments during 2017-2023. Our experience is highlighted.

Materials and Methods

Implantation Procedure

We have an High Dose Rate(HDR) brachytherapy, 6 Channel MicroSelectron HDR (M/s Nucletron, Netherlands) with Iridium-192, capacity of 10Ci commissioned during 2013. From July 2017 we started interstitial BT for BCS patients and now completed >5 years. A 2 plane template supplied from along with the machine is used, along with flexible plastic catheters (Flexicath Single Leader, Trichy, India). Implantation done with length and number of catheters decided by surgeons based on the extent of primary disease. Dwell points were selected continuous, and the treated length of each catheter determined by the Nucletron Ruler. 10mm on either side of the catheter is left cold, to avoid excess dose to the skin, avoid excess skin/subcutaneous excess dose and to preserve cosmesis. All were two plane implants with treating distance 1.2cm. Sometimes, the treatment distance was altered to avoid increase of hot zones and better uniformity of dose. Dose was prescribed to 100% covering line as per Paris Technique (85% delivering basal dose). For IBT, inter-fraction interval was kept minimum 6 hours, a gap between two successive HDR, IBT fractions

External Beam Radiotherapy (EBRT)

In our center, cobalt bunker houses HDR, BT machine also. EBRT was delivered by Theratron 780E Telecobalt machine, pair of tangential fields with breast cone. Following interstitial brachytherapy (IBT), they received 40 Gy in 15 Fractions, at 5Fr/ week, without treatments on Saturdays, Sundays.

Details of treatments

Two types of regimens were followed, based on the decision by clinical board. As the clinic wanted to evolve an optimal dose prescription, various fraction sizes were prescribed in these patients.

1. In the first group, 73 patients completed HDR BT was followed by External Beam Radiotherapy (EBRT). Following are the details of doses delivered. 8Gy x 2 fr (n=1), 4Gyx 4fr (n=27), 3.65 Gy x 4fr (n=24), 3 Gy x 4fr (n=19), 3Gy x 3fr (n=2)
2. In second group, Accelerated Partial Breast Irradiation (APBI) (only IBT) as mono-therapy was carried out in 5 patients. The doses prescribed in these patients were
3. In these patients were 3.65Gyx10fr(n=1), 3.40Gyx10fr(n=3) and 5.88Gy x 10fr (n=1),. They completed their full course of IBT in 5 days.

The geometry of implanted catheters and the covering isodose pattern are shown in Fig.1. It can be seen that the treatment planning and prescription of dose to 100% covering volume with adequate basal dose of 85% isodose line.

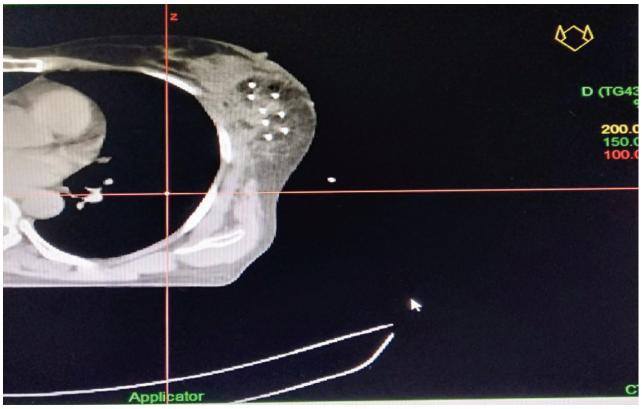

Fig.1 Implant geometry in CT image

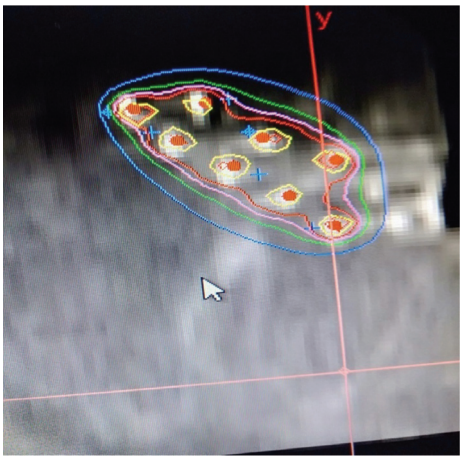

Fig.2 Resultant isodose pattern

Table 1: BED values for all the regimens IBT+EBRT or IBT alone in CCHRC

Group	IBT Dose Schedule Dose /Fr and Number of fractions	EBRT Equiv. BED Gy_{10}	EBRT Dose Gy in total fractions	EBRT Eq. Dose Gy @2Gy/fr	EBRT + IBT Eq. Gy	Pattern of care in our center
1	3.00Gy x 3fr (n=2)	9.75	40 in 15	42.3	52.05	
	3.00Gy x 4fr (n=19)	13.00	40 in 15	42.3	55.30	*Opti-
	3.65Gy x 4fr (n=24) *	16.60	40 in 15	42.3	58.90	mized
	4.00Gy x 4fr (n=27)	18.67	40 in 15	42.3	60.97	
	8.00Gy x 2fr (n=1)	24.00	40 in 15	42.3	66.30	
2	3.40Gy x10fr	45.56		37.97	37.97	*Opti-
	3.65Gy x10fr *	49.82	No EBRT	41.50	41.50	mized
	5.88Gy x10fr**	93.37		77.87	77.87	**Hot

Biologically Effective Doses (BED)

BED values were estimated to see the effectiveness of treatments, using the Linear Quadratic Model (LQ) model (Refer Equations 1,2,3). Table-1 shows the BED values for all the regimens.

$$\mathbf{BED}_{\mathbf{EBRT}} = n.d[\ 1+ d/(\alpha/\beta)] \quad \text{——} \quad (1)$$

$$\mathbf{BED}_{\mathbf{HDR\ BT}} = d[1+d(\alpha/\beta)] \quad \text{——} \quad (2)$$

$$\mathbf{BED}_{\mathbf{EBRT\ Eq\ HDR\ BT}} = \mathbf{BED}_{\mathbf{HDR\ BT}}/[n.2(1+2/10)] \quad \text{——} \quad (3)$$

Results

Table-1 highlighted the dose prescriptions and calculated EBRT equivalent total dose to the selected target volume of the breast. 40Gy/15Fr @ 2.67Gy/Fr is equal to dose of 42.3Gy at 2Gy/fr. Total dose of whole regimen (1) is 58.9Gy (which is just <1.5% to 60Gy). For monotherapy, regimen (2), the standardized prescription is 3.65Gy x 10Fr followed at our center. BED_{10} for BT of 3.65Gy x 10Fr is 49.83Gy, which is equivalent of 41.5Gy EBRT total dose at 2Gy/fr, 5 fr/week. There was no short term toxicity recorded on till their last follow up. Patients' compliance was satisfactory.

Discussion

As more patients are seen fit for breast conservation, HDR BT can be practiced for delivering boost dose to high risk group, substituting linear accelerator treatments. Based on our experience on 78 patients highlighted in this study 3.65 Gy/fraction has been standardized for future patients. An earlier study in India, in a non-randomized pilot group of 10 patients [4] reported 100% local control in treated patients. Dose rate effect on total fraction dose delivered with HDR, had not been outlined in literature. It is common that as the Ir-192 high intensity source decays, in a useful span of 4 to 6 months, the BCS patients are treated at different dose rate, with total fraction size remains constant. There was a report based on experience with low dose rate manual Ir-192 implants [5]. They treated with linear activities ranging from 1.3 to 1.8 mCi/cm. In this report, they highlighted that in the patient groups with mean dose rates less than 0.53 Gy/hr local recurrence were encountered, whereas dose rates 0.56 Gy/hr have shown recurrence free. Local failure was more with implant dose rates < 0.3Gy/hr. Incidence of normal tissue complications and poor cosmetic outcome were correlated to high dose rates > 1Gy/hr. In another study [6], the radiation electron boost dose was 16 Gy, and dose by fractionated HDR brachytherapy were 12 to 14.5 Gy in their group of 207 patients. 5 year local control was 91.4% and they reported good cosmetic results in 88.5% of total HDR BT boost groups, which gives confidence to obtain explained consent in favour of interstitial boost brachytherapy in breast conservation. The role of HDR brachytherapy in breast conservation is explained by Polgar et al [7] based on long term results. 100 early breast cancers underwent conservative surgery, with whole breast irradiation and boost implantations. Multi-fractionated HDR boost was delivered with different doses 4Gy x 3 fr (n=19); 4.75 Gy x 3 fr (n=70); 6.4 Gy x 2 fr (n=1). They reported only 7% ipsilateral breast failures 8 year survivals 'disease free' 76.1%; 'cancer specific' 82.8%; and 'overall survival' 80.4%. Cosmetic outcome were, 'excellent' 17%; 'good' 39%; 'fair' 33% and 'poor' in 11%. Late radiation effects in 91% of patients were, Grade 3 Fibrosis in 6.6% and Grade 3 Telangiectasia 2.2%. They concluded good long term tumor control with acceptable cosmetic outcome and low rate of Grade 3 radiation effects. Unlike external radiotherapy boost with electrons, brachytherapy dose pattern is well localized with least peripheral doses to proximal critical structures like heart or contra-lateral breast. Accelerated Partial Breast Irradiation (APBI) (only IBT), 34 Gy delivered in 10 fractions either 2 fractions/day in one week, or once daily fractions for 2 weeks, reported by an image guided clinical protocol in 40 patients [8]. They used paired applicators, and patient-specific 3 dimensional dosimetry to deliver prescribed dose to 100% isodose line. Same researchers reported their results from their further clinical trials [9,10]. In this present study, we also used same total dose of 34 Gy in 10 fractions for APBI group.

From our experience we recommend that implant catheters used for HDR IBT shall be of correct specifications. Otherwise there will be bending of catheters leading to source stuck problems, and probability for incorrect dose delivery. Treatment times are very short even with low activity HDR source also. In some centres where HDR machine is housed inside Cobalt Bunker like ours, EBRT dose could be delivered in succession to HDR fractions. The above treatments were held at our hospital, when linear accelerator facility was not available, therefore no conflicts of interests faced by surgical oncologists, to practice this IBT boost in all breast conservation patients. Also, as the procedure of placement of treatment plastic catheters in situ is intra-operatively carried out, the boost tumor volume could be accurately selected. A preliminary communication on our experience was outlined earlier [11]. The interstitial HDR boost in BCS appears to be easy to practice and could be implemented in all the brachytherapy centres in India. In hospitals who do not have linear accelerators, boost dose can be delivered using HDR brachytherapy machine. In countries with earlier diagnosed breast cancers large in number (such as Middle East Countries), HDR BT can be practiced, as more cancer patients are treated with breast conservation.

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ORIGINAL

Evaluation of Dexmedetomidine as an Adjuvant to Ropivacaine in Epidural Anaesthesia for Gynaecological Surgery

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Abstract

Background: Epidural anesthesia, particularly when combined with an adjuvant, offers superior pain relief and promotes early mobilization compared to using a local anesthetic alone. This study aimed to evaluate the effectiveness and safety of administering a lower dose of dexmedetomidine as an adjuvant for gynecological surgery. **Methods:** Total of 100 patients were equally randomized to two groups i.e. Group R and Group RD. Group RD was prescribed 20 ml of 0.75% ropivacaine with 0.6 µg/kg of dexmedetomidine, while patients in group R administered 20 ml of 0.75% ropivacaine with 1 ml of 0.9% normal saline. Regular monitoring was conducted for hemodynamic variables such as heart rate, non-invasive blood pressure, oxygen saturation, and respiratory rate. Additionally, parameters include sensory block, analgesia duration, quality of intraoperative analgesia, motor block, and recorded sedation score. **Results:** Group RD experienced a shorter average onset time of analgesia at the T6 level compared to Group R. The time required to reach maximum motor block was significantly shorter in Group RD ($p < 0.001$). Sedation scores of 2, 3, and 4 were observed in 46%, 38%, and 8% of patients in Group RD, respectively, while no patients in Group R achieved these scores ($p<0.001$). Excellent analgesia quality was reported by 94% of patients in Group RD, compared to 16% in Group R ($p< 0.001$). In Group RD, the duration of sensory analgesia was significantly prolonged ($p < 0.001$), whereas in Group R, the duration of motor block was notably shorter ($p < 0.001$). All side effects were statistically non-significant, except for dry mouth, which was highly significant ($p<0.001$). **Conclusion:** A lower dose of dexmedetomidine can be used safely and effectively as an adjunct to ropivacaine in epidural anesthesia for lower abdominal gynecological procedures.

Keywords: Analgesia, Epidural anaesthesia, Gynaecological surgery, Dexmedetomidine, Ropivacaine.

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Introduction

Epidural anesthesia is widely utilized for both peri-operative surgical anesthesia and post-operative pain management in lower abdominal and limb surgeries [1]. It is especially effective when a local anesthetic is paired with an adjuvant, as this combination enhances pain relief and promotes early mobilization more effectively than using a local anesthetic by itself [2]. Adjuvant drugs alter the effects of local anesthetics and help mitigate side effects. During surgery, these drugs influence the latency, or the onset time of the local anesthetic block, and the duration of analgesia. Postoperatively, they impact the analgesic gap, which is the interval between subsequent doses, as well as the quality of analgesia, reflected in patient satisfaction and perceived pain relief, while also reducing adverse effects of local anesthetics [3]. Key desirable attributes of an adjuvant in neuraxial anesthesia include the ability to provide smooth and prolonged post-operative analgesia with sedation and stable hemodynamics [4]. Various additives to local anesthetics have been studied to extend the duration of the block and enhance postoperative pain relief. Among these, alpha-2 adrenergic agonists are notable for their analgesic and sedative properties when used as adjuvants in regional anesthesia [5]. Particularly, epidural dexmedetomidine has demonstrated a synergistic effect with local anesthetics, prolonging the duration of both sensory and motor block, enhancing postoperative analgesia, and creating a strong motor block without causing additional morbidity. Studies in both humans and animals have reported no neurological deficits with its epidural use [6].

While many studies have emphasized the analgesic and sedative advantages of using dexmedetomidine as an adjuvant in epidural anesthesia, the ideal dosage is still unclear. Therefore, this study aims to assess the efficacy and safety of a lower dose of dexmedetomidine for gynecological surgery.

Material and Methods

This study was conducted as a randomized controlled trial with 100 female patients undergoing elective gynecological surgeries under epidural anesthesia at MMIMSR, Mullana, after receiving approval from the Hospital Ethics Committee. Female patients aged 35 to 65 years with ASA I or II status were included, while those who refused epidural anesthesia, had known sensitivities to the

study drugs, coagulation abnormalities, or local site infections were excluded.

A pre-anesthetic evaluation was conducted one day before surgery, including a thorough medical history, physical examination, and standard laboratory tests. The epidural analgesia technique and pain assessment using the Visual Analog Scale (VAS) were described to all participants. All participants were randomly assigned to two groups of 50 each using the chit method. Patients on Group RD were administered 20 ml of 0.75% ropivacaine combined with 0.6 µg/kg dexmedetomidine (solution completed to 1 ml with 0.9% normal saline), while Group R received 20 ml of 0.75% ropivacaine with 1 ml of 0.9% normal saline, maintaining a total volume of 21 ml for both groups.

All patients fasted overnight and were given 0.25 mg of alprazolam and 150 mg of ranitidine the night before surgery, with an additional dose taken early in the morning with a sip of water. On the day of surgery, baseline parameters (HR, BP, RR, and SpO2) were recorded, and an 18-gauge IV line was established. Patients were preloaded with Ringer Lactate at a rate of 10 ml/kg/hr and received no premedication before being moved to the operating theater. Routine monitoring was initiated, and after recording baseline vitals, the patient was positioned laterally for epidural catheter insertion at the L3-L4 level using an 18G Tuohy needle by the loss of resistance technique. An 18-gauge epidural catheter (Portex epidural minipack) was introduced and secured. To rule out intravascular or intrathecal placement, a test dose of 3 ml of 2% lidocaine with 1:200,000 epinephrine was administered, and monitor the heart rate response and sensory feedback. Subsequently, patients were positioned supine and received the 21 ml study solution as specified.

Hemodynamic parameters (HR, NIBP, SpO2, RR) were monitored initially every 2 minutes for the first 10 minutes, then every 5 minutes up to 30 minutes, every 10 minutes until 90 minutes, and subsequently every 30 minutes throughout the surgery. Parameters such as sensory block onset, duration of analgesia, intraoperative analgesia quality, motor block degree and duration, and sedation score were recorded. Side effects like bradycardia, hypotension, shivering, dry mouth, respiratory depression, dizziness, headache, nausea, and vomiting were monitored throughout the perioperative period. Postoperative block characteristics were observed for 8 hours, including time to regression to Bromage 0 and time to first rescue analgesia. All data were recorded in a proforma for statistical analysis.

Statistical Analysis

Data analysis was conducted using SPSS® Version 21.0 (Chicago, IL). Continuous data were presented as either mean (SD) or median with inter-quartile range (IQR). The Kolmogorov-Smirnov test was employed to assess the normality of quantitative data. For skewed continuous variables, the Mann-Whitney U-test was applied, while the t-test was used for comparing normally distributed variables between groups. Categorical data were expressed as frequencies or proportions, and comparisons were made using the Chi-square test or Fisher's exact test, as appropriate. Statistical significance was set at a p-value of <0.05 with a 95% confidence interval.

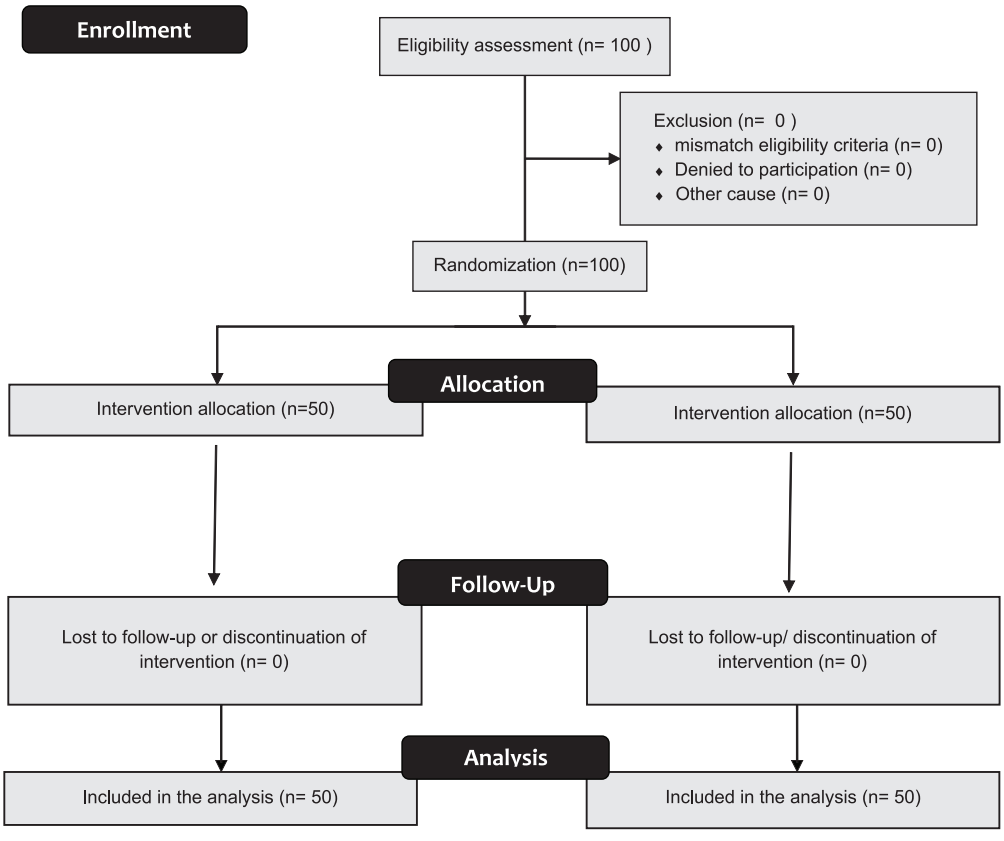

Figure 1. Consort flow diagram showing distribution of patients

Table 2: Demographics characterstics between two groups.

Parameter	Group R Mean ± SD	Group RD Mean ± SD	p value
Age [$](Yrs)	46.62±6.11	47.28±7.69	0.636
Weight[$](Kgs)	66.10±6.10	66.10±7.87	1.00
Height[$](Cms)	157.66±3.00	157.44±2.85	0.71
There was no significant difference in demographic characteristics between both groups (p>0.05).			

[$]Unpaired t-test.

Table 3: Preoperative vitals in both groups.

VITALS	Group R Mean ± SD	Group RD Mean ± SD	t value	p-value
PreOp HR (bpm)	77.40±5.10	77.44±8.06	-.030	.976
PreOpSBP (mmHg)	124.10±6.35	126.64±7.30	-1.857	.066
PreOpDBP (mmHg)	80.84±6.51	79.64±7.13	.878	.382
PreOp SPO2(%)	98.70±.46	98.60±.61	.927	.356
PreOp RR (per min)	14.34±.82	15.82±6.90	-1.506	.135
*Unpaired t-test				

Table 3 shows the comparison of preoperative vitals between the two groups. Both the groups were comparable concerning pre-operative vitals. On statistical analysis the difference was non-significant. (P value>0.05).

Table 4 shows the mean onset time of sensory analgesia up to T6 level in both groups. The time taken was 16.18±3.85minutes with a range of 10 -25 min in group R while 11.16±2.06 min with a range of 8-16 minutes in group RD. On statistical analysis, the difference was highly significant (P value <0.001).

Table 5 shows the distribution of patients according to the maximum sensory level achieved. 8(16%) patients in group R while 19(38%) in group RD achieved T4 level. 42 (84%) patients in group R while 30(60%) patients in group RD achieved sensory level T6. On statistical analysis the difference was significant (P value<0.05).

Table 6 shows the onset time of maximum motor block in both groups.In group R the mean time taken to achieve maximum motor block was 27.70±5.10 minutes with the range of 15-40 while in group RD it was to 22.40±5.17 with range of 15-35 min. On statistical analysis highly significant difference (P value <0.001) was found.

Table 7 shows the distribution of patients according to the grades of motor block. In group R 8(16%) patients achieved grade 1, 15 (30%) patients achieved grade 2 and 27(54%) patients achieved grade 3 motor block. In group RD no patient remained at grade 1, 11(22%) achieved grade 2 and 39(78%) patients achieved grade 3 motor block. Maximum patients in group R (54%) and in group RD (78%) achieved grade 3 motor block. On statistical analysis, the difference was significant (P value <0.05).

Table 8 shows that in group R 18(36%) patients achieved sedation score 0 as compared to only 1(2%) in group RD. In group R score 1 is achieved by 32 (64%) patients as compared to 3(6%)in group RD. In group RD sedation score 2,3 and 4 were achieved by 23(46%),19(38%) and 4(8%) patients respectively while none of the patient achieved these scores in group R. The difference was highly significant on statistical analysis. (P value <0.001).

Table 9 shows that on statistical analysis the decrease in mean heart rate between 6 minutes to 60 minutes from baseline was statistically significant (P value <0.05).

Table 10 shows statistically significant difference in SBP was noted in two groups from 6 – 30 minutes (P value<0.05).

Table 11 shows that during 6 minutes to 50 minutes, difference in DBP found between two groups was statistically highly significant (P<0.001) and during 60 minutes to 80 minutes, Difference found was statistically significant (p<0.05).

Table 4: Onset time of analgesia upto T6 level.

GROUP	RANGE (in min)	Mean (in min)	t VALUE	PVALUE
R	10-25	16.18±3.85	8.130	<.001
RD	8-16	11.16±2.06		
Unpaired t-test				

Table 5: Level of Sensory block achieved in both groups

SENSORY BLOCK LEVEL	GROUP R N (%)	GROUP RD N (%)	*P*
T4	8(16.0%)	20(40%)	.034
T6	42(84.0%)	30(60.0%)	.157

Table 6: Onset time for maximum motor block in both groups.

GROUP	RANGE (In mins)	MEAN (In mins)	t Value	P value
R	15-40	27.70±5.10	-4.210	<.001
RD	15-35	22.40±5.17		

Table 7: Degree of motor block achieved

Motor grade	GROUP R N (%)	GROUP RD N (%)	P value
G1	8(16.0%)	0(0%)	.006
G2	15(30.0%)	11(22.0%)	.433
G3	27(54.0%)	39(78.0%)	.140

Table 8: Sedation scores in both groups

SEDATION SCORE	GROUP R N (%)	GROUP RD N (%)	*P*
0	18(36.0%)	1(2.0%)	<.001
1	32(64.0%)	3(6.0%)	<.001
2	0(.0%)	23(46.0%)	<.001
3	0(.0%)	19(38.0%)	<.001
4	0(0%)	4(8.0%)	.117

Table 9: Mean heart rate at different time intervals between two groups during intraoperative period.

TIME INERVALS	GROUP R MEAN ±SD	GROUP RD MEAN ±SD	t Value	p Value
0 Min	78.84 ± 5.38	80.16 ±10.19	-.810	.420
2 Min	79 ± 6.14	80.62 ± 9.56	-1.009	.316
4 Min	79.26 ± 5.34	77.82 ± 9.76	.916	.362
6 Min	79.84 ± 5.70	75.80 ±10.29	2.428	.017
8 Min	78.88 ± 6.65	73.66 ±10.35	3.000	.003
10 Min	77.66 ± 7.00	72.92 ±10.39	2.675	.009
15 Min	76.68 ±7.37	71.16 ±10.26	3.089	.003
20 Min	75.48 ± 8.10	71.08 ±10.35	2.367	.020
25 Min	73.30 ± 9.53	69.22 ± 8.68	2.238	.028
30 Min	71.80 ± 8.50	68.64 ± 8.70	1.837	.049
40 min	71.18 ± 7.67	67.20 ± 9.23	2.346	.021
50 Min	70.66 ± 7.05	66.84 ± 8.19	2.500	.014
60 Min	69.90 ± 6.95	65.50 ± 7.93	2.951	.004
7o min	69.22 ± 6.45	66.16 ± 8.99	1.956	.053
80min	68.88 ± 6.63	66.24 ± 7.43	1.876	.064
90 Min	68.26 ± 7.23	65.60 ± 8.06	1.738	.085
120 Min	69.88 ± 6.72	65.11 ± 7.13	2.477	.071
150 Min	72.00 ± 4.95	66.33 ±15.31	.798	.455

Table 12 shows the comparison of quality of analgesia in both groups.In group R 8(16%) patients had excellent quality of analgesia while in group RD 47(94%) had excellent analgesia.In group R 39(78%) patients had good quality of analgesia as compared to only 3(6%)in group RD. In group R 3(6%) patients had fair quality of analgesia while no patient had fair quality in group RD .On statistical analysis the difference was highly significant.(p value <0.001).

Table 13 shows the comparison of duration of analgesia in both the groups. The mean duration in group R was 305.30±43.52 minutes with a range of 210 -380 minutes while in group RD was to 428.90±39.52 minutes with a range of 340-500 minutes. On statistical analysis the difference was highly significant (p value<0.001).

Table 14 shows the duration of motor block in two groups. The mean duration of motor block in group R was 211.60±42.41minutes with a range of 100-300 minutes while in group RD was337.04±39.14minutes with a range of 250-430 minutes. On statistical analysis the difference was highly significant(p value <0.001).

Table 10: Comparison of mean SBP between two groups during intraoperative period.

INTERVALS	GROUP R Mean ±SD	GROUP RD Mean ±SD	t value	p value
0 Min	123.66 ± 7.44	126.46 ± 8.21	-1.787	.077
2 Min	123.36 ± 8.67	124.60 ± 7.95	-.746	.458
4 Min	122.52 ± 15.51	121.52 ± 8.12	.404	.687
6 Min	122 ± 9.18	118 ± 9.26	2.170	.032
8 Min	120.44 ± 9.04	114.90 ± 9.03	3.065	.003
10 Min	118.16 ± 9.80	112.28 ± 9.35	3.070	.003
15 Min	115.84 ± 10.22	109.54 ±7.84	3.458	.001
20 Min	115.48 ± 9.31	108.88 ± 8.37	3.728	.001
25 Min	113.10 ± 10.07	108.24 ± 8.10	2.659	.009
30 Min	111.82 ± 9.07	108.14 ± 8.49	2.094	.039
40 min	111.78 ± 11.35	107.96 ± 9.26	1.843	.068
50 Min	110.38 ± 7.57	108.06 ± 8.06	1.483	.141
60 Min	107.58 ± 15.46	107.24 ±8.05	.138	.891
70 min	108.10 ± 7.98	107.74 ± 9.15	.210	.834
80 min	107.88 ± 6.87	107.06 ± 9.34	.500	.618
90 Min	106.74 ± 8.20	108.04 ± 8.95	-.757	.451
120 Min	110.08 ± 8.86	109 ± 7.25	.482	.632
150 Min	115.80 ± 5.21	105 ± 7.07	2.291	.071

Table 11: Comparison Of mean DBP between two Groups during Intraoperative Period.

DBP	GROUP R Mean DBP±SD	GROUP RD Mean DBP±SD	t value	P value
0 Min	80.48 ± 6.37	81.20 ± 8.19	-.491	.625
2 Min	82.06 ± 6.37	79.70 ± 8.42	1.580	.117
4 Min	81.32 ± 6.56	79.46 ± 8.24	1.248	.215
6 Min	80.78 ± 6.31	75.14 ± 8.27	3.831	<.001
8 Min	79.32 ± 6.04	72.32 ± 8.15	4.879	<.001
10 Min	78 ± 6.09	69 ± 7.85	6.403	<.001
15 Min	77.78 ± 5.74	68.76 ± 7.85	6.560	<.001
20 Min	75.94 ± 6.06	67.66 ± 7.50	6.065	<.001
25 Min	75.46 ± 6.24	67.30 ± 7.30	6.002	<.001
30 Min	74.96 ± 4.73	66.82 ± 7.56	6.454	<.001
40 min	73.32 ± 6.26	66.68 ± 7.45	4.824	<.001
50 Min	71.72 ± 5.76	65.42 ± 8.57	4.313	<.001
60 Min	70.66 ± 6.42	66.80 ± 7.49	2.765	.007
70 min	69.64 ± 6.39	66.76 ± 7.79	2.022	.046
80 min	69.64 ± 5.71	66.64 ± 7.20	2.308	.023
90 Min	69.06 ± 5.65	68.24 ± 6.83	.654	.515
120 Min	69.72 ± 6.24	70.44 ±6.89	-.396	.694
150 Min	75 ± 3.46	72.32 ± 6.81	2.074	.083

Table 12: Quality of analgesia in both groups

QUALITY OF ANALGESIA	GROUP R N (%)	GROUP RD N (%)	P value
Excellent	8(16.0%)	47(94.0%)	<.001
Fair	3(6.0%)	0(0%)	<.001
Good	39(78.0%)	3(6.0%)	0.242

Table 13: Duration Of Analgesia in both groups

GROUP	RANGE (in minutes)	MEAN (in minutes)	t Value	P value
R	210-380	305.30±43.52	-	<.001
RD	340-500	428.90±39.52	14.867	

Table 14: Duration of Motor Block in both groups

GROUP	RANGE (In minutes)	MEAN (In minutes)	t Value	P value
R	100-300	211.60±42.41	-15.370	<.001
RD	250-430	337.04±39.14		

Table 15: Side effects in both groups

SIDE EFFECTS	R	RD	p value
Nausea	10(20%)	8(16%)	.795
V0miting	6(12%)	5(10%)	1.00
Bradycardia	5(10%)	7(14%)	.538
Hypotension	10(20%)	15(30%)	.356
Headache	9(18%)	4(8%)	.137
Dry Mouth	2(4%)	15(30%)	.001
Shivering	10(20%)	7(14%)	.424
Dizziness	1(2%)	2(4%)	1.000

Table 15 shows the comparison between side effects observed during intraoperative and post operative period in two groups. On statistical analysis all the side effects were non-significant except for dry mouth which was highly significant (p value< 0.001).

Discussion

In this study, there was no significant difference between the two groups regarding demographic factors such as age, weight, and height. The average onset time of analgesia at the T6 level was significantly shorter in Group RD compared to Group R, with a highly significant p-value ($p < 0.001$). These findings align with studies by Bajwa et al. [4,7], Babu et al. [8], Manal et al. [9], Gupta K et al. [10], Kaur S et al. [11], and Chiruvella S et al. [12]. However, the results contrast with the study by P.F. Salgado et al. [6], possibly due to differing techniques of administering dexmedetomidine and the selection of different levels for noting onset time.

The mean time to achieve maximum motor block was 22.40 ± 5.17 minutes in Group RD compared to 27.70 ± 5.10 minutes in Group R, with the difference being highly significant ($P < 0.001$). Similar results were observed by Bajwa et al. [4] and Gupta K et al. [10], although Kaur S et al. [11] found no statistically significant difference in their study.

Our study indicates that dexmedetomidine enhances the motor block of local anesthetics ($P < 0.05$), corroborating the findings of Gupta K et al. [10] and Kaur S et al. [11]. With the addition of dexmedetomidine, sedation scores of 2, 3, and 4 were achieved by 46%, 38%, and 8% of patients, respectively, whereas none of the patients receiving ropivacaine alone reached these scores. This difference was highly significant ($P < 0.001$), consistent with the results of P.F. Saravia et al. [6], Lopez SAO et al. [13], Bajwa et al. [7], Jain D et al. [14], Gupta K et al. [10], Kaur S et al. [11], and Chiruvella S et al. [12].

There was a notable difference in mean heart rate between the groups from 6 to 60 minutes ($P < 0.05$). Significant differences in SBP were observed between 6 and 60 minutes ($P < 0.05$), while DBP showed highly significant differences from 6 to 50 minutes ($P < 0.001$). Similar results were reported by Gupta K et al. [10], Babu et al. [8], and Jain D et al. [14]. However, Bajwa et al. [7] found that dexmedetomidine decreased heart rate approximately 30-35 minutes after epidural injection, with mean arterial pressure (MAP) also decreasing from baseline at 30-50 minutes post-injection. The use of a lower dose of ropivacaine in their study might explain the variations in statistical significance, and our study separately evaluated SBP and DBP rather than MAP.

In the study, the quality of analgesia was rated as excellent in 94% of patients in Group-RD in comparison to 16% in Group-R ($P < 0.001$), which is consistent with findings by Kaur S et al [11]. The mean duration of sensory analgesia was 123.60 ± 4 minutes longer

in Group RD, which was highly significant (P <0.001), indicating that dexmedetomidine prolongs sensory analgesia. Similar results were obtained by Fukushima et al. [15], P.F. Salgado et al. [16], P.F. Saravia et al. [6], Bajwa et al. [7], Xiang et al. [17], Babu et al. [8], Kaur S et al. [11], and Chiruvella S et al. [12].

The mean duration of motor block in Group R was 211.60 ± 42.41 minutes compared to 337.04 ± 39.14 minutes in Group RD, with the difference being highly significant (P < 0.001). Similar findings were reported by Bajwa et al. [7], Kaur S et al. [11], P.F. Saravia et al. [6], and Li F et al. [18].

Postoperative hemodynamic parameters showed no significant differences between the two groups, supported by studies from Bajwa et al. [7], Jain D et al. [14], Gupta K et al. [10], and Kaur S et al. [6]. Statistical analysis indicated that all side effects were non-significant except for dry mouth, which was highly significant (P < 0.001).

Conclusion

Based on the above observations it is concluded that dexmedetomidine given epidurally along with ropivicaine potentiates the effect of ropivacaine causing rapid onset of analgesia and motor blockade. Sedation, anxiolysis and prolonged postoperative analgesia are other beneficial effects providing immense patient and surgeon satisfaction. So, it is recommended that dexmedetomidine can be safely and effectively used as an adjuvant to ropivacaine in epidural anaesthesia in lower dose for major lower abdominal surgery.

Conflict of Interest:	Author declare no COI
Ethics:	There is no ethical violation as it is based on voluntary anonymous interviews
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ORIGINAL

Inculcating Hand Hygiene Practices Among Budding Dentists: A Multidisciplinary Requirement

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Abstract

Introduction: Hands are the major source of transmission of harmful germs in health care settings. Cross-transmission of microorganisms can be prevented by hand hygiene decreasing the incidence of Healthcare Associated Infections (HAI). Hand hygiene (HH) in dental practice is a crucial part of the infection control strategy. Dental participants are at a greater risk of transmission of germs and must comply with scientifically accepted and evidence-based principles of infection control. There is a requirement to explore the concept of hand hygiene among the dental participants. Aim of the study was to determine knowledge on internationally recommended hand hygiene practices among dental undergraduate students and to analyze impact of training on hand hygiene practices among dental undergraduate students. **Methods**: This interventional study was conducted in two phases. Phase 1 for evaluating Baseline knowledge, Phase 2 for awareness sessions on internationally recommended hand hygiene guidelines followed by observation on compliance to hand hygiene guidelines. The analysis was performed using descriptive statistics, ANOVA test and correlation analysis. **Results**: Overall knowledge on hand hygiene in phase I was 46.8%. Statistically significant difference (p=0.000) was in knowledge about hand hygiene among participants after training. DPMO (Defects Per Million Opportunities) was found to be 2.67 lakhs corresponding to six sigma level 2.12. **Conclusion**: Study identifies various causes of improper and inadequate Hand hygiene practices. Educational institutes need to strive to build work culture achieving sig sigma and internalization of Hand hygiene practices for a long lasting impact on the society. Organizations need to adopt multiple scientifically proven strategies like quality improvement tools, curricular amendment, infrastructure changes and leadership based motivation to achieve higher levels.

Keywords: hand hygiene, hand wash, dental infections, healthcare associated infections, training, curriculum, quality tools, Six Sigma, infection control, motivation, hospital, healthcare.

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Introduction

For centuries hand washing with soap and water has been considered a significant measure of personal hygiene. It was identified in the mid-1800s that transmission of hospital-acquired diseases occurred through the hands of health care workers. In 1847, Semmelweiss hypothesized that "cadaverous particles" were transmitted via hands of students and doctors from the autopsy room to the delivery room resulting in puerperal fever [1].

In 1995-1996, the Centre for Disease Control and Prevention (CDC); Healthcare Infection Control Practices Advisory Committee (HICPAC), USA recommended the use of either antimicrobial soap or a waterless antiseptic agent for cleansing hands after leaving the patient rooms [2,3]. In 2000, Pittet et al. reported remarkable improvement in hand hygiene compliance and reduction in Healthcare Associated Infections (HAI) [4]. The CDC/ HICPAC guidelines issued in 2002 defined alcohol-based handrubbing as the standard of care for hand hygiene practices in health-care settings. However, in many other countries, handwashing is still considered the standard of care and alcohol-based handrub is reserved for particular situations only (i.e. emergency, no sinks available) [5,6].

In year 2009, Hand hygiene originated as a global effort with the 'Save Lives: Clean Your Hands' campaign - an extension programme of WHO 'Clean Care is Safer Care' strategy for infection control [7-9]. World Health Organization (WHO) designed the 'My five moments of hand hygiene' – including two before care and three after care moments. These five moments of hand

hygiene include washing and cleaning of hand :

1. Before touching a patient,
2. Before clean/aseptic procedures,
3. After body fluid exposure/risk,
4. After touching a patient and
5. After touching patient surroundings [10].

Hands are the major source of transmission of harmful germs in health care settings [11,12]. Hand Hygiene (HH) in dental practice is a crucial part of the infection control strategy [13]. Dentists are at a higher risk of getting infected themselves since the risk of cross infection is high due to characteristics of dental settings [14]. This enhances danger of exposure to pathogens [15]. Hand hygiene got highlighted as crucial COVID-19 preventive measure [11,12]. COVID-19 pandemic emerged as a major setback for unaware dental practitioners and generated an innate need to adopt safe practices for infection prevention.

Need for Study

Several studies have reported lower knowledge, attitude and observance of hand hygiene by the undergraduate students [16-20] and lower compliance among healthcare workers [21]. Some of them addressed hand hygiene practice on college campuses primarily as observation cross sectional studies [22]. Neither of study was conducted to assess the impact of in-house training on hand hygiene practices. This study aims to determine the level of knowledge regarding internationally recommended hand hygiene practices among dental undergraduate students and to analyze the impact of training on their hand hygiene practices.

Material and methods

Study design

This study was conducted at a leading private dental college in northern India. This interventional study was conducted in two phases.

Phase 1: Baseline knowledge evaluation.

Phase 2: Awareness sessions on internationally recommended hand hygiene guidelines followed by observation on compliance guidelines.

Study Population

Study population comprised of 1st, 2nd, 3rd, 4th yr students and interns. List of all students and interns was obtained from the college. They were approached during their free time and explained about the nature and content of the study. They were informed that participation in study was voluntary and confidentially of responses was assured. A written consent was obtained from each participant before filling questionnaire.

Inclusion/Exclusion Criteria

Those willing to participate and provide consent were included. Those who were not willing to participate and provide consent were not included.

Out of 351 eligible participants, 308 participated in study (few were absent or did not submit distributed questionnaire). Incomplete questionnaires (n =19) were excluded from analysis and final analysis was done on 289 respondents.

Ethical statement /IEC approval

Ethical approval for the conduct of study was obtained from institutional ethical committee with ref no. DC/2019.

Study procedure and interventions

Phase 1: Baseline knowledge evaluation was conducted between December 2018 and April 2019. During this phase knowledge on internationally recommended hand hygiene guidelines among dental undergraduate students was assessed. Self-assessment based multiple choice questionnaire (12 questions) was prepared after due consultation with senior professors and subject experts.

Phase 2: Awareness sessions were conducted for participants (students and interns) on WHO hand hygiene guidelines. Guidelines on hand wash steps as per WHO were displayed at various prominent places. This phase was conducted at one of the eight departments selected by choice for having higher risk of HAI.

Interns during their rotational clinical posting were observed for compliance to WHO hand Hygiene requirements between July 2019 and February 2020 against the predefined criterion of HH being performed for each of the 5 moments. Everyday half an hour was randomly selected to observe hand hygiene being performed as per guideline. Term 'Opportunity' was defined as each of the 5 moments when participant was supposed to perform hand hygiene. Participants were observed for hands wash/hand rub being performed for all the applicable 5 moments of hand hygiene. A predefined checklist was prepared in tabulated format. Every time hand hygiene was performed (when applicable), '1' unit score was assigned for such moment and each time candidate missed to perform hand hygiene '0' score was assigned against that moment. Sum of scores of all observations was taken as numerator and count of all observations was taken a denominator.

Percentage compliance was calculated as below.

$$\textbf{Percentage compliance}_{\text{(Hand hygiene)}} = \frac{\text{Sum of scores}}{\text{Count of scores}} \times 100$$

Reliability and validity

Reliability and validity of the study questionnaire was assessed. Cronbach's alpha **(alfa coefficient)** was calculated as a measure of internal consistency. It was found to be 0.830.

Statistical analysis

The information obtained from the questionnaires was fed in spread sheet and analyzed using SPSS 20 (IBM, NY, USA). Each correct response was assigned 1 point and incorrect response was assigned 0 point. The analysis was performed using descriptive statistics, correlation between variables were tested using Pearson's correlation and ANOVA test followed by post hoc test was used for multiple comparisons among various groups. The p-value of 0.05 was considered to be statistically significant.

Results

Study groups comprised of all the students (1st, 2nd, 3rd, 4th year students) and interns. Out of 351 participants 289 participated in study with a response rate of 82%. Participants included 1st year students 26% (n=75), 2nd year students 22% (n=64), 3rd year students 11% (n=30), 4th year 1 students 9% (n=56) and interns 22% (n=64) as per proportions shown in Figure 1. Gender wise distribution included 89% (n=256) female participants and 11% (n=33) male participants (Figure 2).

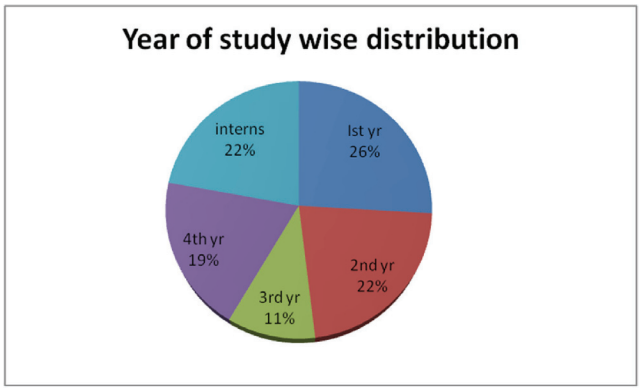


Figure 1: Year of study wise distribution

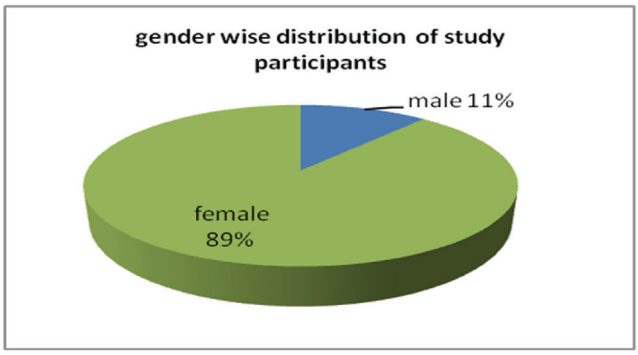


Figure 2: Gender wise distribution of study participants

WHO guidelines recommend that minimum contact time for hand rub is 20 sec and maximum is 30 sec time [5]. In our study only (62/289) 21.4% participants responded correctly as 20 sec. Knowledge regarding proper technique proposed by WHO for hand wash was found in (201/289) 70% participants. There was significant variation p=0.024 and p=0.000 among study participants regarding knowledge of correct time and right technique for hand wash.

About (167/289) 57.7% participants responded that hands should be dry before care, (107/289) 37% responded that hands can be dried with a towel after using hand rub and (13/289) 4.5% responded that hands should be dripped with alcohol. Only 17% preferred to use gloves depending on the case and 83% participants preferred to use gloves during each patient examination shown in Table1.

Regarding awareness of five moments of hand hygiene, (220/289) 76% was observed for moments like hand hygiene before touching a patient and (246/289) 85%. Immediately after a risk of body fluid exposure After exposure to immediate surroundings of a patient, (127/289) 43%. Immediately before a clear/ aseptic procedure, (190/289) 65%. After touching a patient (107/289) 37% (Figure 3).

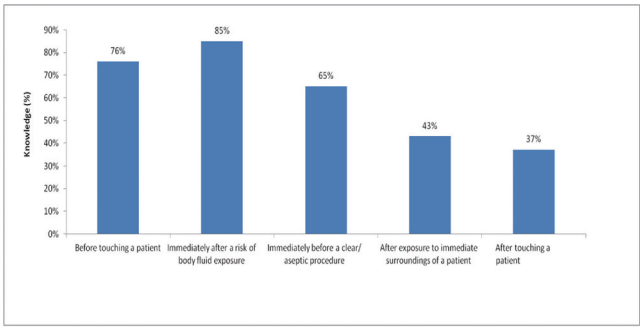


Figure 3: Awareness of five moments of hand hygiene

Awareness/knowledge about hand washing with soap and water versus hand rubbing with an alcohol-based hand rub was tested. Only (34/289) 11.7% participants correctly responded that hand rubbing is more rapid than hand washing, whereas, (27/289) 9.3% responded that hand rubbing cause more skin dryness than hand washing and , (62/289) 21.4% responded that hand rubbing is more effective against protection from germs than hand washing and (177/289) 61.2% responded that hand washing and hand rubbing are recommended to be performed in sequence shown in figure 4. In phase I overall knowledge among participants was 46.8%.

Half of the study participants, (149/289) 51% had received formal training in hand hygiene in the past. Statistically significant

Table 1: Knowledge of hand hygiene among participants (n=289)

1.	**What is the minimal time needed for alcohol- based hand rub to kill most germs on your hands?**	**%**
a.	3 s	3.8%
b.	10 s	47%
c.	1 min	27%
d.	20 s	21.4%
2.	Knowledge regarding proper technique proposed by WHO for hand wash	
a.	yes	70%
b.	no	30%
3.	Which of following statements are true?	
a.	hands should be dry before care,	57.7%
b.	hands can be dried with a towel after using hand rub	37%
c.	hands should be dripped with alcohol	4.5%
4.	How do you prefer to touch/examine the patient?	
a.	Depends on the Case	17%
b.	Gloves	83%

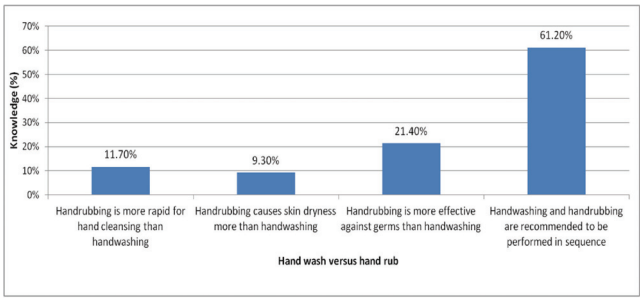


Figure 4: knowledge of hand was versus hand rub among study participants

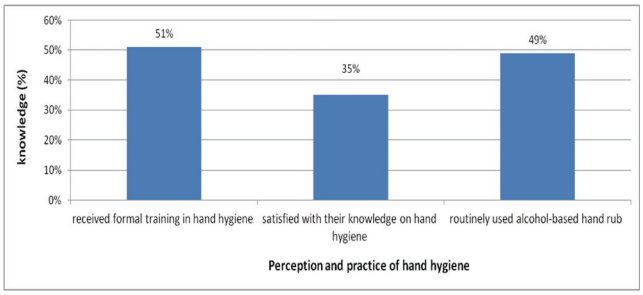


Figure 5: Practice of hand hygiene among study participants

correlation 0.000 (Pearson's). 492** was found between formal training and knowledge levels at 0.01 level of confidence. However smaller proportion of participants, (102/289) 35% were satisfied with their knowledge on hand hygiene. Half of study (144/289) 49% participants expressed that they routinely used alcohol based hand rub in their clinical rotations and during patient care (Figure 5).

Statistically significant difference (p=0.000) was found in overall knowledge among participants and year of education (Table 1).

Multiple comparison analysis of overall knowledge of various parameters showed a statistically significant difference (p value < 0.005) among students in different years of study (Table 2).

Overall knowledge on hand hygiene in phase 1 was 46.8%. Phase 2 was planned to provide training followed by observations feeding in spread sheet and analysis. Table 3 shows percentage compliance on monthly basis displayed as line graph (Fig.5) providing pictorial representation of gap and monthly variation. It is to be noted that

Table1: Analysis of variance (ANOVA) of knowledge among participants and year of education

Variable	Sum of Squares	df	Mean Square	F	P value
Between Groups	124.342	4	31.086	11.401	0.000
Within Groups	774.371	284	2.727		
Total	898.713	288			

Table 2: Multiple comparisons of knowledge among participants depending on year of dental education, using analysis of variance (ANOVA)

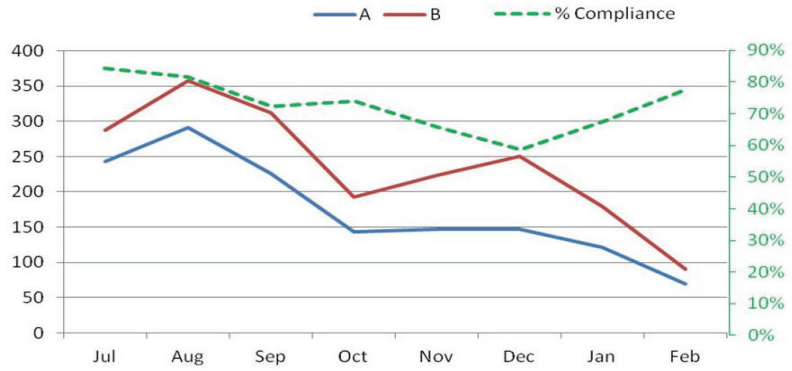
Multiple Comparisons					
Dependent Variable: overall					
	(I) year	**(J) year**	**Mean Difference (I-J)**	**Std. Error**	**P value**
Tukey HSD	First	Second	-0.066	0.281	0.999
		Third	0.067	0.357	1.0
		Fourth	-0.568	0.292	0.295
		Interns	-1.644*	0.281	0.0
	Second	First	0.066	0.281	0.999
		Third	0.132	0.365	0.996
		Fourth	-0.502	0.302	0.459
		Interns	-1.578*	0.292	0.0
	Third	First	-0.067	0.357	1.0
		Second	-0.132	0.365	0.996
		Fourth	-0.635	0.374	0.437
		Interns	-1.710*	0.365	0.0
	Fourth	First	0.568	0.292	0.295
		Second	0.502	0.302	0.459
		Third	0.635	0.374	0.437
		Interns	-1.076*	0.302	0.004
	Interns	First	1.644*	0.281	0.0
		Second	1.578*	0.292	0.0
		Third	1.710*	0.365	0.0
		Fourth	1.076*	0.302	0.004

*p value ≤ 0.005

Table 3: Percentage compliance with respect to hand hygiene based on 5 moments of hand hygiene as defined by WHO.

Month/year	HH actually performed #	HH opportunities *	Percentage compliance
Jul-19	243	288	84%
Aug-19	291	357	82%
Sep-19	226	312	72%
Oct-19	143	193	74%
Nov-19	147	223	66%
Dec-19	147	251	59%
Jan-20	121	179	68%
Feb-20	70	90	78%
Total	**1388**	**1893**	**73%**

* Based on WHO defines 5 moments of WHO
# based on applicable 5 moments



A= Total: HH actually performed, B= Total: HH opportunities

Figure 5: line graph showing percentage improvement in hand hygiene knowledge

the set of participants changed every month as per the participant's rotation schedule.

Defects per Million Opportunities 'DPMO' (or nonconformities per million opportunities) is a measure of performance. In terms of hand-washing non-compliance, it is defined as:

DPMO= No of times HH being not performed *1000000/Total of opportunities for HH.

In the current study DPMO was found to be 2.67 lakhs corresponding to six sigma level 2.12.

Discussion

In our study 51% participants received formal training in hand wash in contrast to 85.4% by Kamble VS et al [23] and 79% by Sreejith Nair et al [17] but higher than findings (26.3% and 43%) by Glad Mahesh et al [24] and Modi PD et al [11]. These findings showed institutional variation to compliance. Overall knowledge on hand hygiene in phase 1 was 46.8%. Similar findings on knowledge (40%) were observed in other study conducted in Raichur, India [17] but in contrast to 12.2% of study carried in Bombay, India [11].

Regarding Five moments of hand hygiene higher awareness i.e. 76% was found with respect to moment (before touching a patient) similar to the findings (70.9 %) by Kamble VS et al [23] but less than findings (91.6%) by Sreejith Nair et al. [17] higher awareness (60%) was found for hand hygiene actions which prevent transmission of germs immediately before a clean/aseptic procedure than 20% of Kamble et al [25] and 80.3% by Sreejith Nair et al [17]. Awareness for hand hygiene actions which prevent transmission of germs after risk of body fluid exposure was 55% in present study participants in comparison to 69.1% of study by Kamble [42] and 22.9% by Mohesh [24]. In present study 45% responded correctly for knowledge of hand hygiene actions which prevent transmission of germs after the exposure to immediate surroundings of a patient in contrast to findings (58.1%) of a study carried in India [23].

Hand hygiene can be achieved by hand washing and hand rub, in our study 50% participants preferred alcohol-based hand rub, similar to the findings (58.1%) of another study [23] carried in Gulbarga, India and in contrast to findings (9%) of study [26] carried in west Bengal, India. In our study 21% participants responded that hand rubbing is more effective than hand washing as compared to findings (50.9% and 69.6%) [23-24] of studies in India. In one study by Kamble VS et al [23] 50.9% participants responded that Hand rubbing is less effective than washing and 21.8% responded that both hand washing and hand rubbing should not be performed in a sequence which are similar to present study findings i.e. 51% and 17%. in one study [24]. In present study 61% participants responded correctly that minimal time needed for alcohol-based hand rub to kill germs on hands is 20s and these are in contrast to results i.e. 38.1%, 38.3% of two studies [23,24]. In a study carried among dental participants in western India [27]

more than 76.8% participants used soap and water for maintenance of hand hygiene in contrast to 50% in present study. During patient care use of gloves protects hand from direct acquisition of pathogens [7].

Training during graduation and internship needs to be adequate for sensitization among students [28,29]. Organizations need to define a training team and empower trainers with information material so that they can educate students and staff through induction program regularly [30]. Education is most crucial interventional tool and faculty plays an imperative role educating and revamping unskilled to skilled professionals. Theoretical knowledge is achieved at the time of graduation is partly practiced clinically [31]. Lower knowledge can be attributed to the inadequacy in curriculum inadequate facilities, lack of training [31].

Hand hygiene compliance in phase 2 was analyzed. Episodic/single training and educational efforts lagged to achieve 100% compliance. Noncompliance observed could be attributed to organizational culture, lesser awareness on scientifically proven hand hygiene guidelines, insensitivity to HAI, inability to recognize hand hygiene opportunities, insensitivity to burden of HAI on patients [16-20].

Six sigma value of 2.12 showed gross deviation from expected compliance. RCA was attempted by brainstorming session. At the place of study, July to September are the summer months, winter starts from October and subsides by the month of March. Non-compliance was discussed with candidates and college authorities to explore the possible causes. At the time of study, only hand wash facility was provided by college and available for candidates. Alcohol rub was optional for them at their own expense. Decrease in compliance during colder months could be attributed to hand rub being not freely available and cold water for hand wash become a limiting factor.

In March 2020, COVID-19 pandemic changed the scenario and hand hygiene was identified the most important infection control measure. Layman to a professional and from child to elderly everyone started performing HH. Handrub started appearing in hospitals and homes in abundance. Situation forced authorities to make alcohol rub frequently available. It is pertinent to note that such rigorous Hand Hygiene practices adopted (identified regulation) were probably in response to threat of spread of infection from patient/third party to self. The alternative to improve the compliance is building of organization culture and to enhance the motivational levels of the employees. Motivation of healthcare providers plays an important role in adoption of new practices and needs to be focused upon by organizational leaders.[32] On probable explanation of adoption of HH practices during COVID times was threat to self and family rather than with the intent to prevent cross transmission from one patient to another.

Conclusion

Training during early stages of education is crucial to inculcate scientific practices into building habits. Hand hygiene practices need to be entrenched in the system and organizational culture. Such practices need to be included and focused upon by institutional infection control committee toward achievement of patient safety goals. The question that remains to be explored is how to make care provider equally responsive and compliant on HH practices for prevention of HAI to patients and achieving higher six sigma. Such compliance would thus require a multifaceted approach.

Organizations need to adopt scientifically proven quality tools for systematic focus with focus on following:

*Infrastructure/ facility component***:** Access hand wash facilities, liberal hand rub material, ambient hand wash water temperature during extreme weather.

*Information, Education and Communication***:** Posters as education material for students, faculty, hospital staff, Placard based reminder, create awareness among patients by education material such as videos, posters, patient's awareness activities.

Reinforcement: regular reinforcement sessions, audits and recognition for compliers. *Quality Control:* developing QC department, active monitoring of HAI, use of quality tools, root cause analysis, issues of advisory to respective practices.

Management focus: to build and support organizational culture which adopts and promotes HH practices to reduce HAI. Educational institutes additionally must strive to build work culture achieving higher sig sigma level and thus making student internalize the HH practices for a long-lasting impact on the budding professional and consequently on society.

To conclude organizations, need to adopt multiple scientifically proven strategies like quality improvement tools, curricular amendment, infrastructure changes and leadership-based motivation to achieve higher levels.

Scope and Limitations of the study

As the study was conducted in one dental institute results may not be generalizable to other dental education institutes.

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CASE REPORT

Complex Encephalitis in a Middle-Aged Male with Systemic Hypertension and West Nile Fever: A Diagnostic and Therapeutic Challenge

Ummer Karadan[1], Priyanka Shridharan[1], Thabsheer[2], Anuja[3]

Abstract

This case report details the clinical presentation, diagnostic evaluation, and treatment of a 52-year-old male water authority superintendent with systemic hypertension who developed severe neurological symptoms following a febrile illness. The patient's history of travel to remote areas, night duty shifts, and exposure to a colleague with febrile illness complicated the diagnostic process. The CSF showed characteristics neutrophilic leukocytosis and MRI abnormalities. Despite comprehensive medical intervention, including antimicrobial, antiviral, and supportive therapies, the patient's condition deteriorated, highlighting the challenges in managing complex cases of encephalitis with potential viral etiologies.

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Introduction

Encephalitis, an inflammation of the brain parenchyma, can be caused by various infectious agents, autoimmune processes, and other inflammatory conditions. This report describes a challenging case of encephalitis in a middle-aged male with a background of systemic hypertension, emphasizing the diagnostic and therapeutic complexities encountered [1,2,5].

Case Presentation

A 52-year-old male water authority superintendent, with a known history of systemic hypertension, presented with a three-day history of low-grade fever, rhinitis, and dry cough. His condition escalated to high-grade fever, severe dysphagia, dysarthria, and tremors over the past 24 hours. He had recently traveled to remote areas such as Chokli and Monthal (regions near Mahi) and had night duty shifts over the past two weeks. A colleague had a recent history of fever, vomiting, and diarrhea, initially treated as food poisoning, with residual fatigue.

Clinical Findings

On arrival at the hospital:

- **Glasgow Coma Scale (GCS):** E4V5M6
- **Respiration:** Tachypneic
- **Tremors:** Resting tremors observed
- **Vital Signs:** Stable
- **Neurological Examination:**
  - Facial deviation to the right
  - Pooling of saliva in the mouth
  - Bilaterally absent palatal movement
  - No limb weakness
  - Preserved deep tendon reflexes
- **Other Systems:** Within normal limits

The patient was admitted to the Neuro ICU. Shortly after admission, he developed paradoxical respiration and desaturation, necessitating intubation and mechanical ventilation.

Diagnostic Investigations

- **MRI Brain (with contrast):** Subtle increase in leptomeningeal enhancement in bilateral frontoparietal regions and early bilateral basal ganglia hyperintensities, no exudates.

Repeat MRI - west nile encephalitis showing diffusion restriction in bilateral caudate and putamen

- **MRA and MRV:** Normal
- **CSF Analysis (Day of Admission):**
  - Protein: 94.1 mg/dL
  - Glucose: 149 mg/dL (corresponding RBS: 255 mg/dL)
  - WBC: Elevated with neutrophilic predominance
- **Echocardiogram (ECHO):** New onset regional wall motion abnormalities (RWMA) and severe left ventricular (LV) dysfunction

- **Troponin I:** 4297 ng/L
- **Other Blood Tests:** CBC, LFT, RFT, serum electrolytes, CPK and blood sugars within normal limits.
- **Tropical Fever Workup:** Negative for Dengue, Scrub typhus, Leptospirosis, and malarial parasites
- **Viral Markers:** Negative for HBsAg, HCV, and HIV

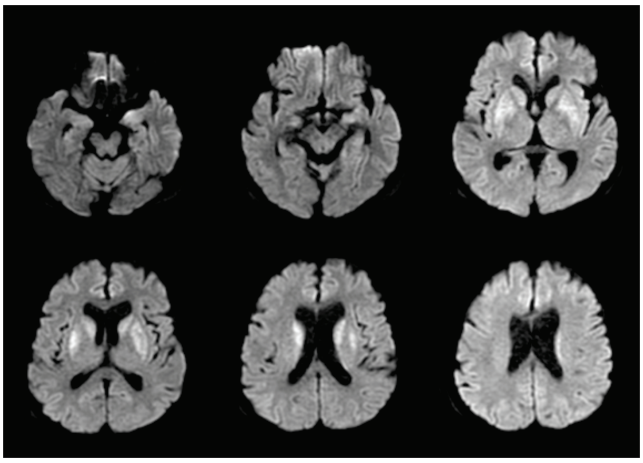

Fig. 1: MRI image of west nile encephalitis showing diffusion restriction in bilateral caudate and putamen

Clinical Course and Management

The patient was initiated on IV antibiotics, IV Acyclovir, and Inj. Methylprednisolone, alongside other supportive measures. Despite treatment, his condition worsened, and he developed generalized tonic-clonic seizures, necessitating the addition of antiepileptic drugs. An EEG revealed evidence of diffuse cerebral dysfunction [3,4].

Further Diagnostic Findings

- **CSF Meningoencephalitis Panel:** Negative (including E. coli, H. influenzae, Listeria, Neisseria, Streptococcus, CMV, Enterovirus, HSV 1 & 2, HHV 6, Varicella Zoster Virus)
- **CSF Autoimmune Encephalitis Panel:** Negative
- **CSF, Blood, and Urine Cultures:** Sterile
- **Serum IgM:** Positive for West Nile fever, mildly positive for Japanese Encephalitis

Treatment Adjustments

Due to the declining GCS (E1VTM1 by day 3 of admission), the patient was started on IVIG infusion. Repeat CSF analysis showed:

- Protein: 48.4 mg/dL
- WBC: Elevated (100 cells/mm³, 100% neutrophils)

The patient received Inj. Minocycline and Ribavirin without improvement in neurological status. Repeat MRI showed hyperintensities in bilateral basal ganglia and thalamus.

Complications

During the ICU stay, the patient developed acute kidney injury, flaccid quadriplegia and bulbar involvement progressing to deep coma, likely due to Ribavirin-induced hemolysis, and was started on hemodialysis following nephrology consultation.

Discussion

This case underscores the diagnostic and therapeutic challenges in managing encephalitis with potential viral etiologies, particularly in patients with complex clinical presentations and pre-existing conditions such as systemic hypertension. The patient's travel history and exposure to remote areas posed additional challenges in identifying the causative pathogen. Despite extensive diagnostic efforts and aggressive treatment, the patient's condition deteriorated, reflecting the severe impact of these infections on the central nervous system.

Conclusion

This report highlights the complexity of diagnosing and treating encephalitis in patients with multifactorial etiologies and pre-existing conditions. Early recognition and comprehensive management are crucial, although outcomes may remain unfavorable despite best efforts. Further research into more effective therapeutic strategies and preventive measures for encephalitis is warranted.

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