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JIMSA
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2025 January - March

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JIMSA aims to promote interdisciplinary dialogue in the field of medical science. Manuscripts pertinent to health care, medical research, medical education and health policies will be considered for publication in this journal. Articles in various formats such as original articles, review articles, case reports, debates, clinical images, letters to editor, hypothesis, technical innovations, 'How I do it', viewpoints and grand rounds. Occasionally poetry related to Medicine, historical vignettes and obituaries of IMSA members as well as prominent scientists will be considered for publication. News items pertinent to IMSA as well as important medical news will also be published. Although Editorials are Editor's prerogative, concisely written thought provoking short essays submitted by readers will be considered under invited editorials.

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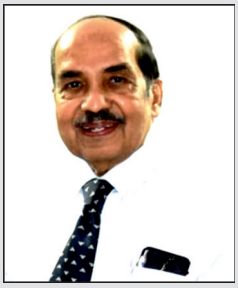

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IMSA publishes quarterly journal, JIMSA in which original articles, updates, symposia, special issues on topics of current interest are published.

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.

Thanking you in anticipation and warm regards,

K. Jagadeesan

Yours Sincerely,
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Dear Fellows, Members and Associates,

It is my pleasure to address you through this medium. This issue features a special focus on microplastics as a health hazard, a topic that I am confident will be of significant interest to our esteemed members and readers.

"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

Microplastics and Human Health: Confronting the Hidden Tsunami

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Introduction

Global plastic production has increased dramatically over the past two decades. Between 2000 and 2020, global plastic production rose from 234 million tons to 435 million tons, and may increase by nearly 70% by the year 2040, reflecting a rapid expansion in manufacturing and consumption. Plastics are synthetic materials of polymeric compounds such as polyester, polyethylene, polypropylene copolymers, and polyurethane which are frequently combined with different additives to enhance performance characteristics such as durability, flexibility, and resistance to heat or ultraviolet radiation [1].

Plastic materials comprise of a large number of chemical substances and approximately over 13,000 chemicals are involved in production and processing of plastic. Among these chemical substances, a few categories of chemicals have been identified as particularly attention due to their toxicity and their potential to leach or migrate from plastic products into the environment. These high-priority groups include certain flame retardants, UV stabilizers, per- and polyfluoroalkyl substances (PFAS), phthalates, bisphenols, alkylphenols and their ethoxylates, biocides, metals/metalloids, and polycyclic aromatic hydrocarbons. Many of these chemicals are known for their persistence in the environment and potential adverse effects on ecosystems and human healthcare system, which has raised growing global public health concern regarding the chronic impact of plastic production and usage [2].

Microplastics

Microplastics referred to plastic particles size of less than 5 mm in diameter. These particles originate from the breakdown of larger plastic debris in the environment and it can enter into the human body through inhalation or ingestion. Specifically, very small airborne particles of 2.5 ìm or less in diameter are capable of reaching the lung alveoli, entering the bloodstream, and subsequently distributing to different tissues in the body [3]. In addition to airborne exposure, microplastics have been detected in a variety of food items, beverages, and drinking water sources, allowing them to enter the body through dietary intake.

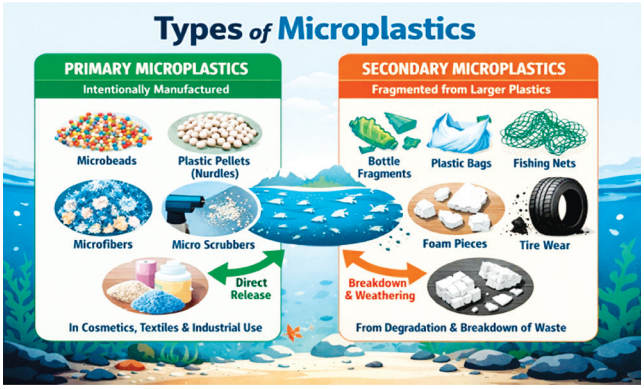
Evidence of microplastic contamination in beverages has also been documented. A study conducted in Mexico in 2020 examined 57 commonly consumed drinks, including soft drinks, beer, iced tea, and energy drinks. Detectable microplastics were found in 48 of these samples. Among them, 36 beverages contained fewer than five particles per liter, nine samples contained between five and ten particles per liter, and three samples contained between eleven and thirty particles per liter. The highest concentration was observed in a beer sample, with an average of 28 particles per liter [4].

Microplastics are also present in several everyday consumer products such as clothing, cosmetics, and personal care items. The use of these products may increase human exposure through accidental ingestion or inhalation of airborne particles. A systematic review published in 2024 analyzed 38 studies covering 2,379 cosmetic and personal care products and reported that approximately 16.4% of the products contained microplastics. Face scrubs were the most frequently examined products in the review, accounting for nearly half of the tested items, and about one-quarter of these scrubs were found to contain microplastic particles [5].

The structural characteristics of microplastics, including their irregular shapes and relatively large surface area, allow them to function as carriers for a wide range of environmental contaminants. These particles can adsorb or absorb pollutants through

hydrophobic interactions, electrostatic attraction, or pore-filling mechanisms. As a result, microplastics may accumulate and transport harmful substances such as microorganisms, polycyclic aromatic hydrocarbons, and heavy metals.

Experimental studies using human cell cultures, organoid models, and animal systems have demonstrated that exposure to microplastics can trigger several biological effects. These include increased oxidative stress, excessive generation of reactive oxygen species, damage to cellular membranes and organelles, activation of immune responses, and potential DNA damage. In laboratory studies using liver organoids, exposure to polystyrene microplastics produced signs of liver toxicity. This was indicated by increased levels of liver enzymes such as alanine aminotransferase and aspartate aminotransferase in the culture medium, along with disruption of antioxidant balance. Even at low concentrations, microplastic exposure was associated with oxidative stress and inflammatory responses, reflected by elevated levels of interleukin-6.



Analytical techniques used for measuring microplastics

Several analytical techniques are currently used to identify and measure microplastics in environmental and biological samples. Commonly applied approaches include microscopy, spectroscopic methods—which analyze the light absorbed or emitted by substances—and thermal analytical techniques [6]. A large proportion of existing studies have primarily focused on identifying polystyrene microplastic particles.

Although many of these analytical procedures have been developed, validated, and described in scientific literature, important challenges remain. One major limitation involves the difficulty of isolating microplastic particles from complex environmental or biological matrices, such as water, food, or tissue samples. In addition, accurately distinguishing between different types of plastic polymers can be technically demanding.

Because of these challenges, ongoing research is aimed at developing more reliable, standardized, and sensitive methods for detecting and quantifying microplastics. Improved analytical techniques are essential for ensuring accurate assessment of microplastic contamination and for facilitating comparisons across different scientific studies.

Microplastics in Human Tissues

Microplastics have been identified in several human organs and biological samples, including the lungs, brain, blood, liver, kidneys, heart, spleen, colon, testes, ovarian follicular fluid, placenta, breast milk, and even in newborns' first stool. Research over recent decades suggests that the concentration of microplastics in human tissues has gradually increased. For example, a comparison of post-mortem samples showed higher levels of microplastics in individuals studied in 2024 than in those examined in 2016, particularly in brain and liver tissues [7].

Health Effects Associated with Microplastics

Several observational studies have suggested a link between microplastic exposure and adverse health outcomes, although a direct causal relationship has not yet been firmly established. In one investigation involving 257 individuals with asymptomatic carotid artery disease, polyethylene microplastics were detected in carotid artery plaque samples in 58.4% of patients. Additionally, measurable amounts of polyvinyl chloride were identified in a smaller proportion of the samples. Individuals whose arterial plaques contained microplastics were found to have a substantially higher risk of major cardiovascular events—including myocardial infarction, stroke, or death—during a follow-up period of approximately 34 months compared with those in whom microplastics were not detected [8].

Evidence from post-mortem studies also suggests a possible association between microplastics and neurological conditions. Brain tissue samples from patients with dementia were reported to contain significantly higher concentrations of microplastics compared with samples from individuals without dementia. Although these findings highlight potential health concerns, further research is required to better understand the biological mechanisms through which microplastics may contribute to organ dysfunction and disease.

Experimental and observational evidence suggests that MPs disrupt metabolic pathways (causing insulin resistance and â-cell dysfunction), and may enhance carcinogenesis through genotoxicity, epigenetic alterations, and chronic inflammation [9].

Regulation to Reduce Plastic Pollution

Various local and national regulations have been introduced to address plastic pollution; however, comprehensive global agreements remain limited. Some international measures have been implemented to manage plastic waste and reduce its environmental impact. For example, the **2019 Basel Convention Plastic Waste Amendments** [10] regulate the cross-border movement of plastic waste, particularly preventing its transfer to countries that lack adequate recycling infrastructure or technical capacity to manage plastic waste safely.

Another important international regulation is **MARPOL Annex V [11]**, a legally binding agreement adopted by more than 150 countries. This convention prohibits ships from discharging plastic waste into the oceans, thereby aiming to reduce marine pollution caused

by maritime activities. In addition, global efforts are underway to develop stronger international frameworks.

On August 18, 2024, in New Delhi, the Food Safety and Standards Authority of India (FSSAI) initiated a project to address the rising concern of microplastic contamination in food. The initiative, titled **"Micro- and Nano-Plastics as Emerging Food Contaminants: Establishing Validated Methodologies and Understanding the Prevalence in Different Food Matrices,[12]"** began earlier in March 2024. Its objective is to develop and standardize reliable analytical techniques to detect micro- and nano-plastics in food items and to evaluate their occurrence and potential exposure levels within the Indian population.

Conclusion

The detection of microplastics in various human tissues has become increasingly common, reflecting the expanding presence of plastic contaminants in the environment. Emerging evidence suggests that exposure to these particles may be linked to potential health risks, although the full extent of their impact is still being investigated. The widespread contamination of air, water, and soil with plastic debris underscores the urgent need for coordinated global efforts. Strengthening international policies, improving waste management strategies, and developing safer, environmentally sustainable alternatives to conventional plastics are essential steps to reduce plastic pollution and protect both environmental and human health.

Conflict of Interest:	Author declare no COI
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ORIGINAL ARTICLE

Comparison of Quality Assurance using Six Sigma between Chemiluminescence and Electrochemiluminescence Techniques for Thyroid Function Test

Anisha Mathew[1], Sanjukta Naik[2], Preeti Chauhan[3], Seema Patel[3]

Abstract

Background: Thyroid function tests are critical for diagnosing and monitoring thyroid disorders. They are usually performed using Electrochemiluminescence Immunoassay (ECLIA) or Chemiluminescence Immunoassay (CLIA). However, variations in test results across different laboratories can impact patient management, particularly in subclinical thyroid dysfunction. To address this, evaluating the Six Sigma performance of both systems using quality control (QC) data can help assess their precision and reliability, ensuring more consistent and accurate results for diagnosis and treatment decisions. **Methods:** The present study was a retrospective study conducted in Hormone lab of Tertiary care Hospital, New Delhi for a period of five months. Thyroid Stimulating Hormone (TSH), free Triiodothyronine (fT3), free Thyroxine (fT4) assays were performed on Beckman Coulter DXI 800 (CLIA) and Elecsys TSH, fT3, Ft4 on Roche cobas e411 (ECLIA). BIAS% was taken from External Quality scheme of Randox and Total Allowable Error (TEa) value was taken from Westgard website. Mean and SD and CV was calculated using excel from Internal Quality Control data. **Results**: For TSH, it was seen for all 3 levels, maximum sigma for CLIA was 5 in the months of April and minimum was 3 in February and May while for ECLIA it was 6 in the month of March and minimum it is 4 in both months of May and June. For fT3, it was found that for all 3 levels, maximum sigma for CLIA was consistently 2 for all 5 months while in ECLIA, the score varied between 2 and 3. For fT4 for all 3 levels, for CLIA sigma was consistently between 1 and 2 for all 5 months while in ECLIA, the score varied between 1-3. **Conclusion:** The present study indicates that ECLIA offers better accuracy and precision for TSH testing compared to CLIA, though both methods need improved standardization and internal quality control for fT3 and free fT4 measurements. ECLIA seems to have better accuracy and precision in comparison to CLIA and it is imperative to follow Westgard's Rules to ensure consistent, high-quality results and minimize variability in thyroid function testing.

Keywords: Electrochemiluminescence Immunoassay (ECLIA), Chemiluminescence Immunoassay (CLIA), Thyroid Stimulating Hormone (TSH), free Triiodothyronine (fT3), free Thyroxine (fT4) assays

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Introduction

Quality or conformance to requirements of a user or customer is the embodiment of a well working medical laboratory. No report is processed or accepted if the analyte and machine do not conform to the quality it is supposed to provide. In a lab, good quality is often detected by reduced number of quality material runs, maintained turn around time, the values matching the diagnosis etc. While running quality control materials to assess the quality of test results is worldwide practise, many times we miss possible biases and errors despite stringent assessment of quality control every run. To over come this, in recent times, the inclusion of six sigma metrics has been a huge game changer [1-2].

Many times, relying on IQC practices and SD, many problems are masked. Six Sigma metrics helps the lab to see the reality and unmask these issues associated with analytical and preanalytical errors. Six sigma metrics also shows IQC rules that need to be followed to improve the sigma and also how we can maintain it and catch bias before it affects patient results. Thus, six sigma is like a microscope to assess quality. For this reason, like CV%, six sigma should also be used as an important attribute when doing intermachine comparison or when comparing two methodologies for starting or verifying the sensitivity and specificity of any analyte [2-3].

With an increase in thetesting of the thyroid function, it has been

important to get as precise and accurate result as possible as drug monitoring and treatment changes are heavily dependent on TSH levels and T3, T4 values to corroborate the diagnosis. Thyroid function test is generally performed on immunoassay with hospitals choosing either Electrochemiluminescence (ECLIA) or Chemiluminescence (CLIA). While the major school of thoughts remain that ECLIA is more sensitive than CLIA, the cost factor and maintenance gives more props to CLIA. This is because, ECLIA combines analytical advantages of chemiluminescent analysis with ease of reaction control by applying electrode potential [4-5].

Both ECLIA and CLIA are considered as 3rd generation testing for TSH. However, this often leads to variations in numerous labs which may impact the patient results. Thus, there is the need for an evaluation of thyroid function tests assay in order to distinguish between euthyroid, hyperthyroid and hypothyroid especially if patient is in subclinical stages. This is particularly important to ensure good quality of the results which corroborate with the diagnosis and treatment monitoring of patients having thyroid disorders [5]. While majority of method comparisons is done using patient sample and consequent comparison, in this study we compare the six sigma of our ECLIA and CLIA machine using their respective QC data.

Materials and Methods

Study was conducted in a tertiary care hospital from North India

Study Design

Retrospective Study

Study Period

Five months

Analytes Studied

Thyroid Stimulating Hormone (TSH), free Triiodothyronine (fT3), free Thyroxine (fT4)

Analyser

Access TSH, fT3, fT4 on Beckman Coulter DXI 800 (CLIA) and Elecsys TSH, fT3, Ft4 on Roche cobas e411 (ECLIA). Manufacturer directions were followed regarding maintenance of machine, reconstitution of Primer, Calibrator and Quality control materials, after which QC and Calibrator were stored according to said instructions.

Statistical Analysis

Three levels and two levels of internal quality controls (Provided by BioRad QC materials & Elecsys QC materials respectively) results over 5 months were compiled and mean was calculated to establish CV%. BIAS% was taken from External Quality scheme of Randox (RIQAS) and Total Allowable Error (TEa) value was taken from Westgard website [6]. Mean and SD was calculated using excel. CV, Coefficient of Variation was determined from calculated laboratory mean and calculated standard deviation, obtained from 5 months of IQC data

$$CV\% = \frac{Standard\ Deviation}{Laboratory\ mean} \times 100$$

Sigma metrics for each parameter was calculated using below formula

$$Sigma = \frac{TEa - Bias}{CV}$$

The minimum acceptable performance of process was 3 sigma and world class performance is 6 sigma or higher.

Using CV%, bias and SD, Method decision chart was plotted for each month to evaluate the imprecision and inaccuracy.

Results

Since our internal quality control was often within acceptable limits, present study it was decided to calculate the Bias from RIQAS values. Mean, SD and CV has been calculated for all parameters per month from the IQC data collected over 5 months. Sigma was calculated for internal QC level 1, 2, 3 of CLIA and Level 1 and 2 of ECLIA using TEa values from CLIA and Westgard website [6].

For TSH, it was seen for all 3 levels, maximum sigma for CLIA is 5 in the months of April and minimum is 3 in February and May while for ECLIA it is 6 in the month of March and minimum it is 4 in both months of May and June. This showed that ECLIA had a better sigma score as not even once the score had gone less than 3 while CLIA has had only once a score of 5 but otherwise maintained the score above 3. [Table 1]

For fT3, it was found that for all 3 levels, maximum sigma for CLIA was consistently 2 for all 5 months while in ECLIA, the score varied between 2 and 3, 3 majority in the months of February, march, and June. While both machines maintained the minimum sigma requirements of a medical testing laboratory, it indicates the need for improvement especially in comparison to TSH. [Table 2]

Table 1: Calculating Sigma for TSH IQC in Dxi 800 and Cobas e411

Chemiluminescence (CLIA)						**Electrochemiluminescence (ECLIA)**				
	Feb	**March**	**April**	**May**	**June**	**Feb**	**March**	**April**	**May**	**June**
Level 01						**Level 01**				
TEa	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7
Sigma	3	4	5	3	4	5	6	5	4	4
Level 02						**Level 02**				
TEa	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7	23.7
Sigma	3	4	5	3	4	5	6	5	4	4
Level 03										
TEa	23.7	23.7	23.7	23.7	23.7					
Sigma	3	4	5	3	4					

Table 2: Calculating Sigma for fT3 for IQC in Dxi 800 and Cobas e411

Beckman Coulter DXI 800						Electrochemiluminescence (ECLIA)				
	Feb	March	April	May	June	Feb	March	April	May	June
Level 01						**Level 01**				
TEa	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3
Sigma	2	2	2	2	2	3	3	2	2	3
Level 02						**Level 02**				
TEa	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3	11.3
Sigma	2	2	2	2	2	3	3	2	2	3
Level 03										
TEa	11.3	11.3	11.3	11.3	11.3					
Sigma	2	2	2	2	2					

Table 3: Calculating sigma for different fT4 IQC in DXI 800 and Cobas e411

Beckman Coulter DXI 800						Electrochemiluminescence (ECLIA)				
	Feb	March	April	May	June	Feb	March	April	May	June
Level 01						**Level 01**				
TEa	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33
Sigma	1	2	2	2	1	2	3	1	2	1
Level 02						**Level 02**				
TEa	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33	8.33
Sigma	1	2	2	2	1	2	3	1	2	1
Level 03										
TEa	8.33	8.33	8.33	8.33	8.33					
Sigma	1	2	2	2	1					

TSH: Thyroid stimulating Hormone; fT: Free Thyroxine; CLIA: Chemiluminescence Immunoassay; ECLIA: Electrochemiluminescence Immunoassay; Tea: Total allowable error

For fT4 for all 3 levels, for CLIA sigma was consistently between 1 and 2 for all 5 months while in ECLIA, the score varied between 1-3, 3 sigma majorities in the months of March. Both machines maintained the show lower than the minimum sigma requirements of a medical testing laboratory; it spectacles the need for improvement and standardization. [Table 3]

These values were plotted on a method decision chart to see how much of the sigma values fell within the acceptable limits [6]. The charts were plotted for all levels of IQC of both machines based on the calculated bias and CV from the TEa given for all three parameters. The sigmas for the graph were plotted based on the

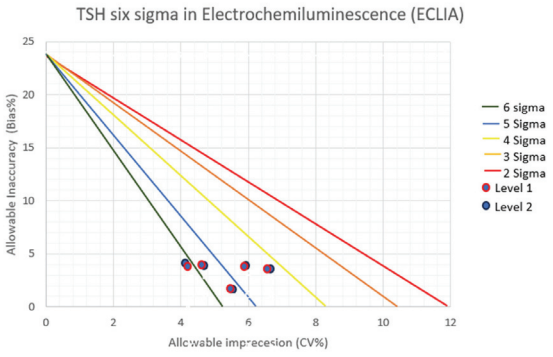

Figure 1: TSH six sigma for ECLIA in method decision chart (TEa-23.7)

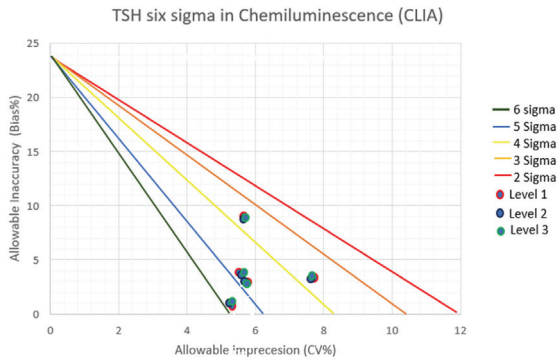

Figure 2: TSH Six Sigma for CLIA in method decision chart (TEa-23.7)

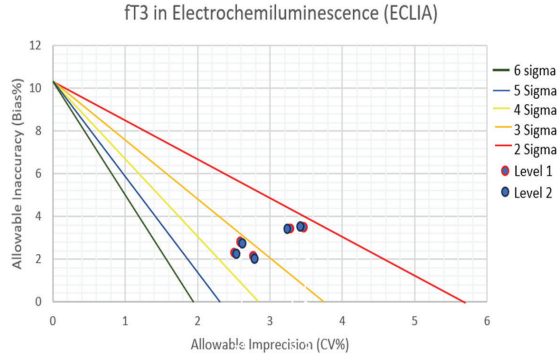

Figure 3: fT3 six sigma in ECLIA in method decision chart (TEa – 11.3)

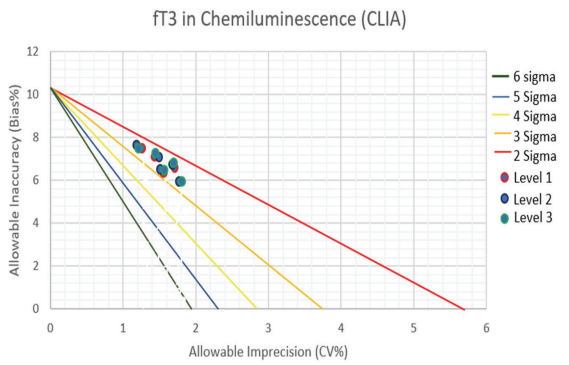

Figure 4: fT3 six sigma in CLIA in method decision chart (TEa – 11.3)

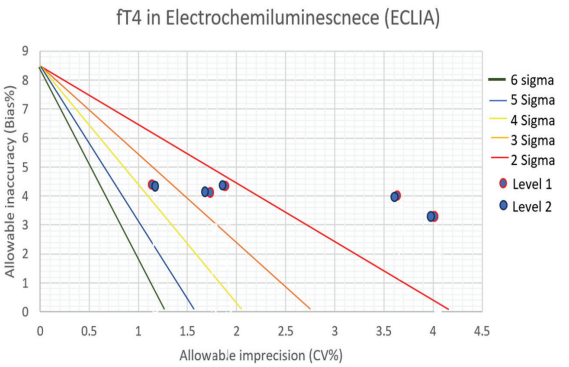

Figure 5: fT4 six sigma in ECLIA in method decision chart (TEa-8.33)

TEa and the CV. [Figure1-6]

Discussion

Six sigma metric analysis is used by many laboratories to assess their quality and results accuracy. It has been noted that six sigma metrics may be a better tool to use being a sensitive marker to a method's performance as six sigma utilizes Coefficient of variation (cv), bias and Standard Deviation (SD) in its calculated. As CV, bias and SD is an indicator of precision and accuracy, however we do not take the total allowable error (TEa) into consideration when looking into the three attributes. As six sigma takes all these into consideration into its calculation, it provides a better outlook to the quality of the lab [1-3].

As per six sigma rules, a sigma e" 6 shows world class performance while <3 sigma shows the need for improvement and is associated with accuracy and precision. Six sigma metrics takes into emphasis how the result of each parameter should be within the designated TEa that has been denoted by CLIA or in Westgard website. Over the years, comparison between methodology and machines, CV% is often taken into consideration to assess if the method or machine is sensitive. However this practise does not take into consideration the standard deviations of the results, nor does it consider the quality control practises being utilized in that lab. Six Sigma, takes all these into consideration and should thus be used when doing method and machine comparison [2-3].

In our study, TSH in Cobas e411, which uses electrochemiluminescence method, was found to have a much better sigma than TSH in Beckman coulter dxi 800 which uses Chemiluminescence. TSH sigma in Cobas e411 varied between 4-6

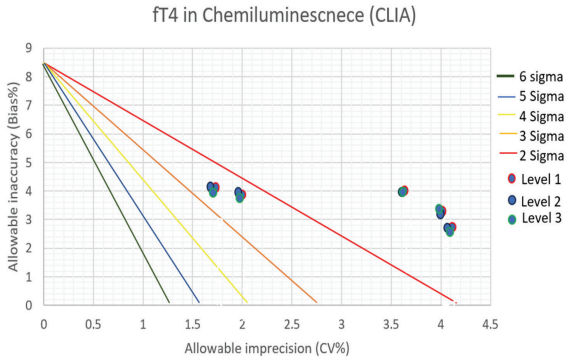

Figure 6: fT4 six sigma in CLIA in method decision chart (TEa - 8.33)

while in DXI 800 it varied between 3-5 over the 5 months it was analysed. It shows that both machines TSH is within acceptable sigma and have a good performance but also indicates that Cobas e411 is more sensitive and more accurate and precise. fT3 and fT4 have shown relatively poor performance in both machines, irrespective of methodology, however it can be noted that fT3 and fT4 had still better sigma in cobas e411 than that of DXI 800 [5-7].

It could be sought that, while the electrochemiluminescence methodology is found to be more sensitive, ECLIA machine uses 2 levels of QC while the chemiluminescence uses 3 levels. Since more QC levels tend to make the values more accurate, it can be noted that along side QC practises, the method through which the parameter is measured, plays an important role in its accuracy and precision as well. When CV of both methods was taken in consideration, the CV for Cobas e411 was lower compared to DXI 800. The six sigma metrics took into consideration both the CV and the QC practise and had established the result [5-9].

While TSH seems to be showing a better sigma for both machines in comparison in fT3 and fT4. fT3 and fT4 have been found to have a poor sensitivity and specificity in many other papers, who found their TSH having acceptable six sigma value but their fT3 and fT4 having just acceptable to poor sigma values. This could because fT3 and fT4 analysis is still to be properly standardized and assessed. However, despite this, in electrochemiluminescence, fT3 and fT4 maintained a minimum of 2 sigma which is accepted for medical laboratories, while in chemiluminescence often dipped down to 1 which is unacceptable [10—11].

Literature reviews have found that electrochemiluminescence techniques had better six sigma values and much better CV%. In chemiluminescence, while TSH is better maintained, there is a reduced sigma for fT3 and fT4 mostly at 1 which is consistent with present study [8-9]. Many labs either have chemiluminescence or electrochemiluminescence, and sometimes this variation in can cause a variation in laboratory results as well. By having both methods in our lab, we were able to compare and assess the quality, accuracy and precision of our results on both machines while taking both advantages to run the sample. There are studies which also show that Electrochemiluminescence methods fared better than Chemiluminescence method. The CV% of ECLIA for TSH was lower in comparison to CLIA, however in either method, fT3 and fT4 had higher in both ECLIA and CLIA methodologies [10-12].

With study, by comparing the sigmas of both machines, it may be established that the ECLIA is good, quite accurate for TSH in comparison to CLIA, however both methods require better standardization and IQC practices for fT3 and fT4. For this, six

sigma rules should be followed if sigma is less than 3, and maximum westgard rules are to be followed till the sigma score improves. As our TSH for both machines is more than 3, it is still imperative that we stick to the westgard rules to ensure accurate and precise TSH levels.

Conclusion

In conclusion, with a better sigma score, ECLIA seems to have better accuracy and precision in comparison to CLIA and it is imperative to follow Westgard rule according to the sigma score calculated to ensure improvement and consistent quality of results.

Conflict of Interest:	Author declare no COI
Ethics:	There is no ethical violation as it is a retrospective study with use of quality control material. no human sample were taken for this study.
Funding:	No external funding
Guarantor:	Dr Preeti Chauhan, will act as guarantor of this article.

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ORIGINAL ARTICLE

The Effectiveness and Quality of Life in Pediatric Population with Stage III Empyema Undergoing Open Decortication

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Abstract

Introduction: Empyema thoracis is a common medical condition in which children have a typical presentation of fever, cough and respiratory distress. There are three developmental stages of empyema thoracis. Treatment options include thoracentesis, chest tube placement, fibrinolytic therapy, video-assisted thoracoscopic surgery and open thoracotomy and decortication. This condition affects the quality of life of the patients. Aim of our study was to assess the effectiveness of open decortication and quality of life in patients with stage III empyema.

Method: Study was conducted in 18 Children with stage III empyema. Data were collected using a pre-designed and pretested questionnaire. The follow up assessment was done by PedsQL 4.0 instrument scale. Physical Function, Emotional Function, Social Function as well as School Function of the patients were assessed at 1, 2 & 3 months.

Result: The majority of the patients were in the age group of 8-12 years. Pus culture in 12 patients (66.7%) was sterile. One-third of patients required postoperative ventilation. None of the cases was reoperated or readmitted to the hospital. Mean duration of hospital stay of patients was 10.89±3.51 days. Physical Function, Emotional Function, Social Function as well as School Function of the patients in follow up at 1,2 & 3 months showed constant decline in all the domains of PedsQL.

Conclusion: Our study concluded that Open decortication is the standard treatment for stage III empyema. Functional results were also excellent, as all patients returned to the normal activities that they performed before surgery.

Key words: Empyema, Open decortication, Pediatric empyema thoracis

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Introduction

Empyema thoracis is a common medical condition in which children have a typical presentation of fever, cough and respiratory distress [1]. Children with poor nutritional status of deficient immunity are more commonly affected and follow a bout of pneumonia which may have been particularly virulent [2]. Other conditions associated with emphysema are, tuberculosis, penetrating chest trauma, infected hemothorax, after pulmonary resection or iatrogenic during thoracocentesis or intercostal tube insertion [3]. Emphysema thoracic is associated with high mortality (15%) in the absence of prompt management [2,4]. There are three developmental stages of empyema thoracis; **Stage I**, the acute or exudative stage, is characterized by a thin serous fluid with minimal debris. **Stage II**, the fibrinopurulent stage, is characterized by a thicker fluid and thick fibrin strands. **Stage III**, the organizing stage, is characterized by a thick fibrous peel and scar formation [5]. Singh M, Singh SK, Chowdhary SK. Management of empyema thoracic in children. Stage-1 may respond to antibiotic treatment (non-operative management) with or without chest tube drainage; Stage-2 and Stage-3 respond to the decortication (operative management) [6]. However, there is inconclusive evidence about the treatment modalities of empyema thoracis in children; [6] Options for treatment include antibiotic therapy, thoracentesis, chest tube placement, fibrinolytic therapy, video-assisted thoracoscopic surgery (VATS) and open thoracotomy and decortication. Open thoracotomy and decortication require general anesthesia, endotracheal tube (single or double lumen) insertion, and requirement of mechanical ventilation throughout the procedure. The lowest pneumothorax recurrence rate (approximately 0-1%) is the most important advantage of open thoracotomy and parietal pleurectomy [7].

This condition affects the quality of life of the patients which is assessed using Pediatric Quality of Life Inventory (PedsQL), a modular scoring system which is designed to integrate generic and disease specific measures, and includes both self- and proxy-reports.

It takes into account the biomedical endpoints, like response rate and survival, and also focuses on behavioral and emotional problems for capturing the daily health-related problems [8].

Despite recent advances, the appropriate management is controversial [2,6]. Presently, Cheng YJ et al. [7] advocates treatment of chronic empyema with minimally invasive techniques, such as video thoracoscopy. One school of thought is that thoracotomy and decortication involve an increased risk of morbidity and mortality [8]. Importantly, there are also reports which indicate that morbidity and mortality are low when using this procedure. To that end, thoracotomy and decortication is still considered to be the best treatment for chronic empyema [9].

Aim of the treatment is to increase the lung volume by freeing the trapped lung with surgical removal of the thickened pleura. Improvement of lung volume, perfusion and diffusion capacities are the benefits of lung decortication mentioned in several reports in the literature [10]. An improvement in quality of life after decortication has not been studied in detail. Insufficient data in the literature regarding the quality of life in stage III empyema in the pediatric population. So, the aim of this study was to determine the quality of life in stage III empyema after open decortication in the pediatric population and also to assess the effectiveness of open decortication in patients with stage III empyema.

Methodology

The present study was conducted in our department from 1st December 2019 - 31stAugust 2021. The sample size was calculated with help of Epi Info (TM) 7.2.2.2. Data were collected using a pre-designed and pretested questionnaire containing demographic variables, blood investigations, microbiological tests, radiological tests, and hospital course. Total 18 children with stage III empyema were included in the study. The follow up assessment was done by Peds QL 4.0 instrument scale after taking copyright permission. The study was conducted during global pandemic of COVID, so less number of cases were there.

Children with in the age group of 3-12years with stage III empyema i.e., organized empyema more than 3 weeks were included, whereas, those who had empyema that was associated with trauma, tuberculous empyema, hydatid disease, or foreign body presence were excluded from the study. During the course of study, we have assessed the improvement during the post operative phase by:

(a) Intravenous pain killers on postoperative day1, followed by diclofenac dermal patch from postoperative day 2 were given,

(b) Chest physiotherapy along with spirometry was done,

(c) Pain in follow-up period was assessed by WONG-BAKER'S FACES PAIN SCALE [11]. Postoperatively follow-up of patients was done on 4 weeks, 8weeks and 12weeks.

The data was analysed using SPSS version 24 software. Categorical variables were presented as frequency and percentages, continuous variables were presented as the mean and standard deviations. Chi-square (÷2) and Z-test was used to test the association of different categorical variables. The t-test was used to compare the means, $p<0.05$ will be taken to be statistically significant.

Observation and Results

The present cross-sectional study was conducted in the Department of Pediatric Surgery, at our institute among 18 children with stage III empyema under the age group of 3-12 years and either sex.

Table 1: Demographic details, disease distribution and postoperative characteristics (N=18).

Variables		N (%)
Demographic details		
Age Group (Years)	3-4	5 (27.8)
	5-7	3 (16.7)
	8-12	10 (55.6)
	Mean ± SD (Range)	7.94± 3.40 (3-12)
Sex	Male	8 (44.4)
	Female	10 (55.6)
Disease distribution		
Disease	Right Empyema Thoracis	10 (55.6)
	Left Empyema Thoracis	8 (44.4)
Pus Culture	Sterile	12 (66.7)
	S. Pneumoniae	4 (22.2)
	K. Pneumoniae	1 (5.6)
	MRSA	1 (5.6)
Duration of Disease (Days)	≤45	9 (50)
	>45	9(50)
	Mean ± SD (Range)	44.72 ±13.27 (20-70)
Post-operative characteristics		
Need of Post-Operative Ventilator (Days)	Yes	6 (33.3)
	No	12 (66.7)
Need of Postoperative Oxygen (Days)	Yes	16 (88.9)
	No	2 (11.1)
Readmission Required	Yes	0
	No	18 (100)
Reoperation Required	Yes	0
	No	18 (100)

The majority of the patients, 10 (55.6%), were in the age group of 8-12 years, the mean age of patients was 7.94±3.40 Years. Majority of them were females, 10 (55.6%). Ten (55.6%) of them had right empyema thoracic, 9 ailing for d"45 days and other 9 were suffering for >45 days, the mean duration of disease was (44.72±13.27days). While pus culture in 12 patients (66,7%) was sterile, in 4 patients (22.2%) culture was *S. Pneumoniae positive*, and culture *in* other 1 patient was *K. Pneumoniae* positive and in yet another it was *MRSA positive*. (Fig.: 1.1)

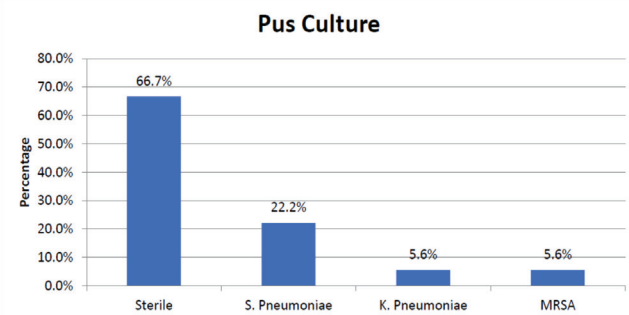

Fig.1: Pus Culture wise distribution of studied patients

One-third of patients, 6 (33.35) required postoperative ventilation, while 16 patients (88.9%) needed postoperative oxygen, two others did not need it. None of the cases was reoperated or readmitted to the hospital. [Table 1].

Majority of the sterile pus culture sample was from the age-group of 8-12 years (44.8%). Likewise, the need of postoperative ventilation was least required for the age group of 8-12 years (44.8%). However, postoperative oxygen therapy was mostly

required for the age-group of 8-12 years (44.8%). Although, p-values with respect to all the three age groups implies that age wise variation with respect to these parameters was not significant.

On perusal of the data, we observe that the mean duration of hospital stay of patients was 10.89±3.51 days, mean days of postoperative ventilation was 1.5±0.79 days, mean duration of postoperative oxygen support was 4.19±2.49 days and ICD removal was after 6.11±1.41 days.

The duration of disease, duration of hospital stays, need of oxygen days as well as ICD removal days were maximum in the patients of age group of 5-7 years and need for ventilator was maximum in the patients belonging to age group 8-12 years. The difference observed in the duration of hospital stay between the groups was statistically significant.

Table 2: Mean studied variables distributed in various age groups

Variables	Age Group (Years)				F value*	P value
	Total (n=18)	2-4 (n-5)	5-7 (n=3)	8- 12 (n=10)		
Disease Duration (days)	44.72±13.27	38.20±15.01	51.67±17.56	45.90±11.08	1.062	0.370
Duration of Hospital Stay (Days)	10.89±3.51	10.00±1.58	15.33±4.16	10.00±3.23	3.846	0.045
Need of Ventilator (Days)	1.50±.79	0.60±.89	1.00±1.00	30.00±0.67	0.968	0.402
Need of Oxygen (Days)	3.72±2.49	4.00±2.55	5.33±2.89	3.10±2.38	0.965	0.403
ICD Removal (Days)	6.11±1.41	5.60±1.14	8.00±1.00	5.80±1.23	4.679	0.26

Independent sample t test

Table 3: Age wise distribution of mean PedsQL score at various follow up

Variables		Total (n=18)	Age Group (Years)			F value	P value
			2-4 (n=5)	5-7 (n=3)	8- 12(n=10)		
1 Month Post-operative	Physical Function	23.17±4.98	21.00±6.59	26.00±1.73	23.40±4.65	0.964	0.404
	Emotional Function	12.78±4.76	8.60±3.29	14.00±0.00	14.50±4.95	3.453	0.058
	Social Function	10.50±4.46	6.00±2.83	10.00±0.00	12.90±4.04	6.691	**0.008**
	School Function	11.67±6.18	6.20±2.95	7.33±1.15	15.70±5.21	9.814	**0.002**
2 Month Post-operative	Physical Function	13.22±4.26	11.60±5.50	12.33±2.08	14.30±4.11	0.722	0.502
	Emotional Function	6.61±2.75	5.40±2.61	5.67±.58	7.50±3.03	1.217	0.324
	Social Function	5.94±3.28	3.60±1.52	5.33±1.15	7.30±3.71	2.591	0.108
	School Function	5.56±3.42	4.00±1.87	4.00±1.73	6.80±3.99	1.597	0.235
3 Month Post-operative	Physical Function	4.50±4.42	4.40±4.62	3.33±1.15	4.90±5.15	0.132	0.878
	Emotional Function	1.50±2.43	1.00±2.24	0.67±1.15	2.00±2.83	0.462	0.639
	Social Function	1.39±2.45	1.40±2.19	0.00±0.00	1.80±2.90	0.592	0.566
	School Function	1.44±3.26	1.20±1.64	0.00±0.00	2.00±4.22	0.423	0.662

One way ANOVA test

Table 3 lists out functions like Physical Function, Emotional Function, Social Function as well as School Function of the patients after recovery from ailment after a period of 1, 2 & 3 months respectively to see the change in the pediatric quality of life (PedsQL).

There was a constant decline in all the domains of PedsQL from 1-month to 3-month follow-up. Age wise distribution of mean PedsQL showing pediatric quality of life score at various follow. After 1-month Post-operative Physical Function was 26.00±1.73, being maximum in the age group 5-7 years. Emotional function was 14.50±4.95 maximum for the age group 8-12 years. Social Function was 12.90±4.04 maximum for the age group 8-12 years. School Function was maximum 15.70±5.2 for age group 8-12 years. The difference was statistically significant for social and school function. However, there was no significant difference in the mean PedsQL score between all the three age-groups at second and third month follow up. [Table 3]

On gender-wise comparison PedsQL score after treatment, we observe that the females have performed much better in respect of all the above parameters, thereby showing a better pediatric quality of life (PedsQL) as compared to male patients 3 Month Post-operative, however, the difference was not statistically significant.

Discussion

The mainstay of treatment of pyogenic pleural empyema is control of ongoing infection and the prevention of recurrent infection. Early drainage by chest tube drainage or through a thoracotomy and open decortication is the early management of complicated pleural effusion or empyema [12]. Early treatment of pleural empyema avoids complications, extensive operations, and lengthy hospital stays. In some patients due to delayed diagnosis and referral chronic empyema will develop. In such patients, open thoracotomy and decortication are the standard treatment. Open procedures in some reports have also shown higher morbidity and mortality [13]. So we decided to study the quality of life and clinical outcome of open decortication in the management of stage-III empyema in pediatric patients.

In our study there were 18 patients in the age range between 3 to 12 years; with Mean age of patients was 7.94±3.40 years. In a similar study, Sahina A et al. [12] reported the ages ranged from 1.25 to 15

years, with a median age of 4.3 years and Goyal V et al. [13] showed a mean age of 5.44 years in the study group.

Goyal V et al. [13] reported that 48.6% were male and 51.4% were females in their study. While Sahina A et al [12], Singh AP et al. [14] and Angurana SK et al. [15] reported a higher proportion of male patients in their respective studies. In this study, 44.4% were males and 55.6% were female patients.

Our study shows the duration of disease, 50.0% ailing for d"45 days and the other half were suffering for >45 days. The mean duration of the disease was 44.7 days. Jaiswal LS et. al. [16] and Angurana SK et. al. [15] reported a lower median duration of symptoms before thoracotomy, 24 days and 12.2 days, respectively. In our study duration of the disease is higher may be due to delayed referral from distant remote areas.

We found that 55.6% of patients were suffering from right empyema thoracic. Similarly, Goyal V et al. [13] and Singh AP et al. [14] in their study reported that there were 57% and 55% right empyema, respectively. Angurana SK et al. [15] also reported a higher incidence of right lung empyema (63.0%) which are similar to our findings.

This study shows the Pus Culture in 66.7% of patients was sterile, in 22.2% patients' culture was *S. Pneumoniae* positive, and Culture in other 5.6% patient was *K. Pneumoniae* positive andin yet another, it was *MRSA* positive. Angurana SK et al. [15] study showed *Staphylococcus aureus* as the most common isolate (66.7%). *MSSA* accounted for 56.3%, *MRSA* 10.3%, *Streptococcus pneumoniae* 14.3%, *Klebsiella pneumonia* 10.3% and *Pseudomonas aeruginosa* 8% of isolates. Goyal V et al., [13] Sahina A et al. [12] reported the most frequently identified micro-organism was *S. aureus,* 34.2 percent, and 14.6 percent, respectively. Pleural fluid is sterile due to wide spread early use of antibiotics as was also seen in our study as the patients due to late presentation and use of antibiotics before presentation to hospital.

In the present study, 33.3% of patients required postoperative ventilation with a mean postoperative ventilator duration of 1.5±0.79 days. Similarly, Reichert M et al. [17] reported the need for postoperative ventilation was 29.6%. In our study 88.9% of patients needed post operative oxygen with a mean duration of post-operative oxygen support was 4.19±2.49 days. Singh AP et al. [14] reported a similar mean duration of ICD removal of 4 days which is in concordance with our findings of removal after 6 days.

The mean duration of hospital stays of patients was 10.9 days in our study. Goyal V et al. [13] and Andrade-Alegre R et al. [18] reported similar post-procedure stays of 9.5 and 10 days, respectively. While Angurana SK et al. [15] reported a comparatively longer duration of hospital stay of 17.2 days.

The Pediatric Quality of Life Inventory (PedsQL) is a modular instrument that was designed to take into account not only the biomedical endpoints, such as response rate and survival but also to focus on behavioral and emotional problems in order to capture the daily health-related problems that pediatric patients with cancer have [12]. There was a constant decline in all the domains of PedsQL from 1-month to 3-month follow-up. After 1-month Post-operative Physical Function was maximum in the age group 5-7 years, emotional function, social function, and school function were maximum for the age group 8-12 years. There was a significant difference in the social and school function between the three age groups. However, there was no significant difference in the mean PedsQL score between all the three age groups at second and third month follow up. Mollberg NM et al. [19] reported at 1 month postoperatively, a non-significant decline in global health QoL, physical, role, cognitive and social function scores.

In our study we observed the gender wise PedsQL score showing the variation in the pediatric quality of life in respect of physical function, emotional function, social function as well as school function after treatment. We observed a non-significant improvement in the PedsQL score in females compared to male patients at the 3 Month Post-operative.

The instruments used to measure quality of life in different studies were also highly variable and often non-comparable with each other, thus making it difficult to quantify the effect of each surgical approach on quality of life. Another source of variability was that quality of life measurement was often performed at baseline and then after surgery at different time points, from 1 to 6 months, and occasionally at 1 year. The use of different quality of life measures at different times limited the number of studies included in comparisons. Patients included in the quality-of-life studies were very heterogeneous in age, stage, and comorbidities. Also, whenever the quality-of-life questionnaires are used, the ill (and lowest quality of life) may be excluded, who are unable to respond, or those with better performance status who prefer to continue with their daily activities rather than remain involved in clinical studies [20].

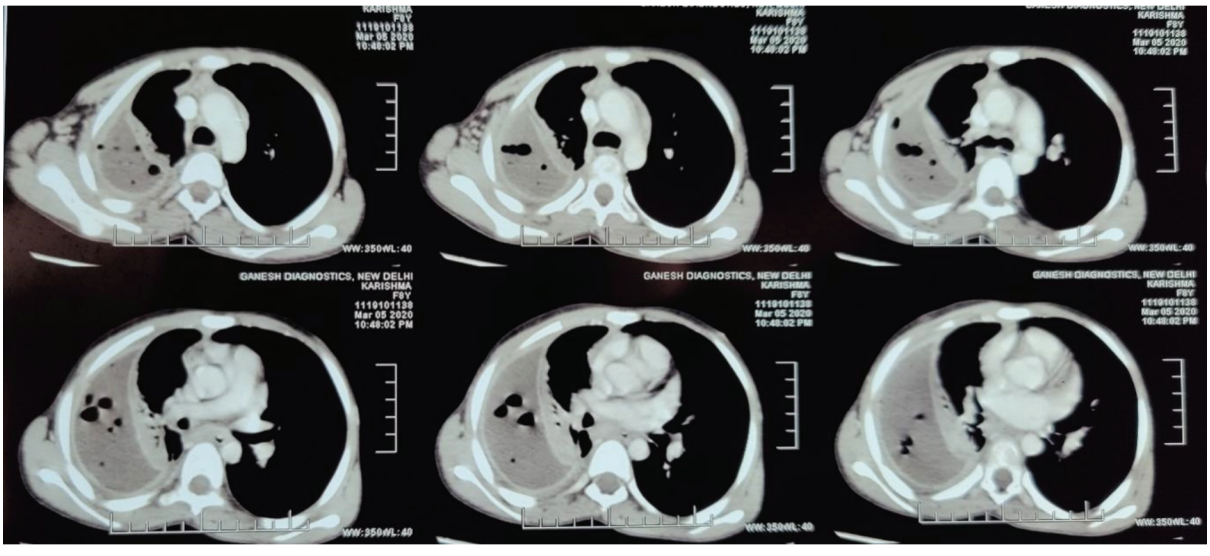

Figure 2: Axial Section of CT scan left side Empyema Thoracis

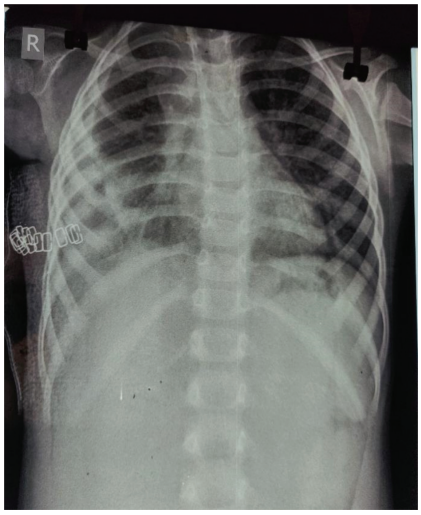

Figure 3 : Post operative X-Ray chest right side Empyema

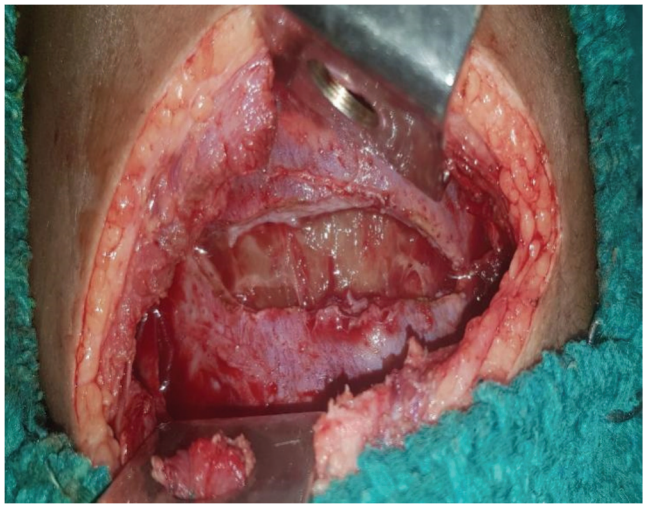

Figure 4: Intraoperative image

Limitations

The present study had several limitations; Major limitation to our study was that it was conducted during COVID crisis. Globally all hospital were closed for routine cases and only emergency cases were dealt on that time. Initial calculated sample size was 36 but due to COVID pandemic sample size curtailed and only 18 patients were enrolled during study period. Our study was single centered and limited time duration so the number of cases was relatively small, although all patients were operated on by a single surgeon using the same approach and technique. In our study, we opted the open decortication there was no other technique for comparing.

Conclusion

Our study concluded that the open decortication was found to be an excellent surgical procedure with low morbidity and mortality. Functional results were also excellent, as all patients returned to the normal activities that they performed before surgery. There was a significant improvement in the general condition of the patient and chest radiograph in the postoperative period. Open decortication is the standard treatment for stage III empyema. Very few studies regarding the quality of life in patients with empyema thoracis are mentioned in Indian literature, our study is one step closer to the assessment of the quality of life in patients with empyema thoracic.

Conflict of Interest:	Author declare no COI
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Funding:	No external funding
Guarantor:	Dr. Atul Kumar Meena, will act as guarantor of this article.

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ORIGINAL ARTICLE

Use of KJ Nano Cap Nanoscience Application in the Reversal of Autism

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Abstract

The broad syndrome is an impairment of neurological and environmental disorders which together develops into an incurable disease that stands as an autism spectrum disorder (ASD). It is characterised by repetitive behavioural patterns and a lack of cognition. It is caused due to chains of biological and psychosomatic aspects which occur in toddler life but realization or symptoms are delayed [1]. Hence, the abnormalities hamper the after-birth, especially during neuron development, brain growth, immune system, and inflammatory reactions. The universal incidence of autism is just lower than 1%, nevertheless, the estimations are sophisticated in economically advanced countries [2]. Currently, the evidence says that the biological factors of autism spectrum disorder are analysed from genetics, brain development, and other aspects. There has been a recent concern in finding therapies for autism [3]. We have attempted to reverse autism by applying nanoscience.

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Introduction

Autism Spectrum Disorder is regarded as by variances in communication and social interface. Individuals with autism spectrum disorder (ASD) repeatedly demonstrate constrained and tiresome interests or outlines of conduct. ASD is observed in folks around the world, irrespective of race and civilization, culture, economic background, caste, creed, or colour. The Centres for Disease Control and Prevention (CDC), fathomed that ASD is identified in boys than in girls in a ratio of 4:1 (Boys: Girls) and 77 % in identical twins [4].

The term autism was coined by Eugen Bleuer in 1908. A recent study analysed the DNA of more than 35584 people worldwide including 11986 autistic individuals, the researchers discovered variations in 102 genes associated with a higher risk of developing ASD. Additionally, 53 genes were shown to be largely linked to autism and not to other developmental disorders, according to researchers [5, 6].

Types

The following are the major classifications of autism [7]:

i. **Asperger's Syndrome:** In this type, the individuals can speak and talk freely but are socially non-cognitive.
ii. **Autistic Disorder:** Neither communicates socially nor plays actively which can be seen in children younger than 3 years.
iii. **Childhood disintegrative disorder:** Very distinctive growth for minimum 2 years and gradually mislays their presenting and social skills.
iv. **Pervasive developmental disorder:** Individuals can socialize and communicate easily but in a delayed manner.
v. **Rett Syndrome:** Psychomotor regression with loss of volitional hand use of spoken language, the development of repetitive hand, stereotypes and gait impairment.

Treatments

Play therapy is a pronounced treatment which can help patients with autism. It includes playing with them, joint attention symbolic play engagement and regulation (JASPER), and integrated play groups (IPGs). Occupational therapy helps patients perform daily tasks with ease and promote physical wellness. Other therapies such as speech therapy, and applied behavioural analysis (ABA)

are also reported to be effective and improve the quality of life in autism patients. Different types of ABA are useful for the treatment and management of autism. These all are aimed to improve behaviour and skills. Speech therapy is a type of therapy that aimed to improve overall communication skills. It can help autistic patients to articulate interaction and develop communication[8]. Therapeutic Horse Riding (hippotherapy) is a type of physical therapy which is reported to help children of 5 to 16 age to articulate and develop social skills. The alternative remedies available for autism include vitamins, chelation therapy, and hyperbaric oxygen therapy (HBOT)[9], where Vitamin D inhibits the synthesis and biological actions of pro-inflammatory prostaglandins, which are elevated in autism and in a recent study showed that daily intake of vitamin D supplements showed decreased in core symptoms associated with autism, and chelation therapy a method to remove excess heavy metals in the human body. The idea of using chelation as a tool for treating autism grew out of a belief that mercury-containing thimerosal (a preservative) in vaccines was the direct cause of a rapid increase in autism spectrum diagnoses. In one human study, 12 autistic children were treated with HBOT at 1.3 atm/24% oxygen, while another group of six children received HBOT at 1.5 atm/ 100% oxygen. The researchers measured biomarkers for inflammation in the brain before and after the therapy sessions. Results showed that in both groups, HBOT significantly reduced cerebral inflammation and improved behaviour[10]. Non-verbal autism patients can learn through technology-based augmentative communication systems for the development of social, behavioural, and speech skills. Compulsive behavioural therapy (CBT) is a type of therapy which is proven efficient in the management and control of anxiety in autism patients.

Autism therapy is one of the least evaluated areas in the case of treatment and management. A recent review identified that only less than 41 social studies on adults have been published so far from 1980 to 2017. Furthermore, a systematic review in 2012 noted also identified only 32 treatment studies published from 1980 to 2010. This provided evidence that considerable interest and attention should be given to the reinforcement and recalibration of autism therapies[11].

Xueqin He and his team performed and evaluated an innovative approach for autism that a nanoparticle system that encapsulated aspirin (an anti-inflammatory drug) enhanced social skill and behaviours in ASD mice. Their nanoparticle system successfully crossed the blood-brain barrier (BBB) and inhibited microglial cell activation. Overall, it resulted in a safe and enhanced anti-inflammatory effect of aspirin in neurons. This clearly shows that nanoparticle systems are a safe and efficacious strategy for the treatment of ASD and other neurodevelopmental disorders[12].

Materials and Methods

This is a novel approach to treat autism with the supply of nano energy through a skull cap impregnated with nanoparticles, emitting energy around a zeta potential of 28.8 mV. The energy distribution must be equal in all areas of the cap. Also, we found that, with increase in number of nanoparticles the biological effect drops, so study of surface profilometry and electron microscopy to determine the distribution curve as shown in figure 1, figure 2, and figure 3[13].

The material for KJ nano autism cap, in which the nanoparticles has to be incorporated is preferably cotton, which has an even surface area. Synthetic fabrics and metallic parts should be avoided. The energy of the coated nano particles declines at a non linear rate

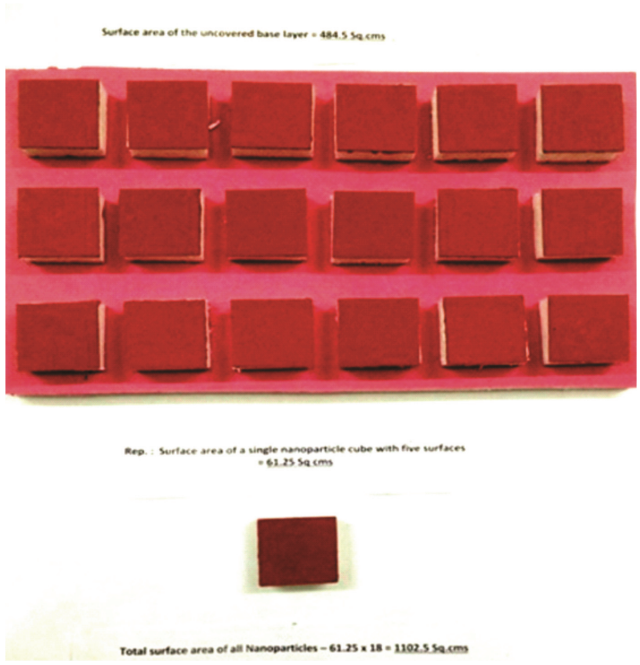

Figure 1: Physical model of Nanoparticles cubes deposited at intervals between each other on the uncovered base.

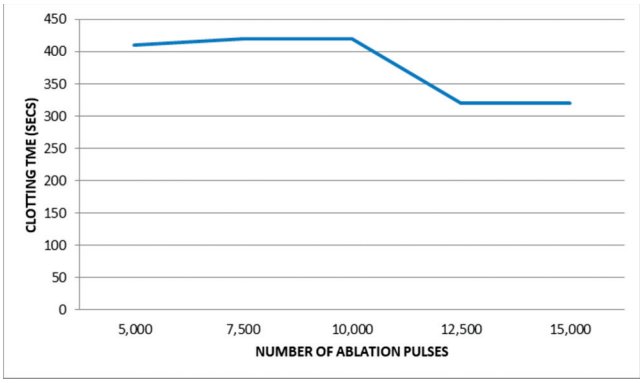

Figure 2: Representation of Anti-coagulation effect of Copper Nanoparticles deposited Pyrolytic carbon

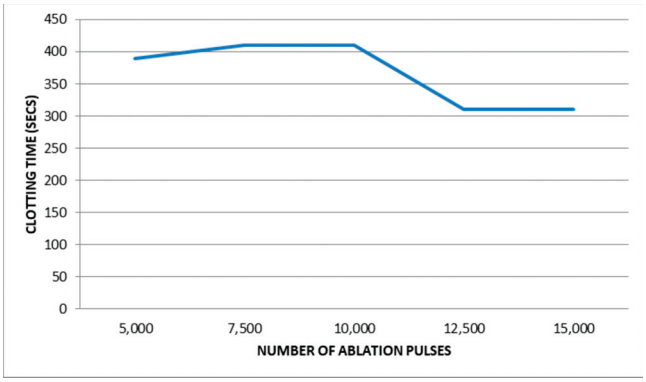

Figure 3. Representation of Anti-coagulation effect of Silver Nanoparticles deposited Pyrolytic carbon.

and to increase the longevity, the cap should be sealed in a wooden box when not in use. The Micro electricity charged in KJ nano cap has a life span of about three months, then it has to be replaced with fresh energy loaded caps or should be coated again with nanoparticles as shown in figure 4.

Figure 4. KJ Nano Cap

Figure 5: Patient with KJ Nano Cap

Result

From our speculations, we noticed, the Nano energy is effective and promising in reversing the conditions associated with Autism Spectrum Disorder. Currently, more number of individuals are being inducted in this program. The WHO president stated that 25% of world population could be autistic by 2050, so it could be grave problem similar to global environmental threats, everyone has to contribute to save humanity from extinction. Hope this study might help to remediate Autism Spectrum Disorder with application of Nano Particle.

Discussion

In our attempt to reverse autism, on the basis of, level of micro electricity in the brain of autistic children, we found that metallic nano-particle carries a certain amount of positive micro electricity. This observed from our previous work, where normal breast shows less energy output and less electricity when compared to malignant neo plastic breast lesions[14]. On assessing autistic individuals, we observed the nano potential of -27mV whereas normal brain has zeta potential of +38.6 So, we selected a suitable material to make the nano particle to makeup the deficit of autism zeta potential. We coated the nano particle on cotton skull cap, after assessing the distribution of nano particle in the KJ Nano Autism Cap with surface profilometry analysis, we have applied this cap to autistic individual preferably 24 hrs except during bath. Some of the individuals complained of excessive sweating, nobody complained headache or any associated symptoms.

Our first patient as shown in figure 5 in this trial has a history delayed speech, not maintaining eye contact, not communicating verbally with parents at the age of 4, necessary investigations were done and reported normal MRI of brain, normal gait but diagnosed as delayed speech with autism by paediatrician.

In this first case, we found, within three months of wearing the KJ nano cap, the autistic movements totally disappeared and the autistic individual showed interest in his environment. After recovery, he started washing clothes in household on his own, from this we found the individual is aware of his surrounding and environment. Since he showed reversal of symptoms, we have enrolled the individual in speech therapy and occupational therapy for further rehabilitation.

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. K Jagadeesan, will act as guarantor of this article.

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ORIGINAL ARTICLE

Prothrombotic State in Patients of Chronic Obstructive Pulmonary Disease with Acute Exacerbation

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Abstract

Background: Knowledge of COPD evolved towards growing recognition of a systemic component of the disease and the role of its comorbidities. Although chronic obstructive pulmonary disease (COPD) is not a high-risk factor for pulmonary embolism (PE), acute exacerbations of chronic obstructive pulmonary disease (AECOPD) complicated with PE occur in numerous patients. AECOPD is often complicated with respiratory failure. In the majority of patients, due to hypoxemia and carbon dioxide retention the blood is in a hypercoagulable or prothrombotic state. Venous thromboembolism (VTE) is also a common threat to hospitalized COPD patients. In a meta-analysis, pulmonary embolism prevalence was estimated to affect 20% of subjects with COPD exacerbation, whereas deep vein thrombosis was detected in 12.4% of those patients. In the present study, D-dimer, Fibrinogen, Mean Platelet Volume and Hematocrit were used as markers of the prothrombotic state in patients of COPD presenting with acute exacerbation. The evidence of thromboembolism was seen by imaging like CT-pulmonary angiography and ultrasound Doppler of lower limb. The study also analysed effect of Low Molecular Weight Heparin on preventing thromboembolism. **Methodology:** Forty-four (44) patients of acute exacerbation of COPD were prescribed a standardized treatment regimen. All patient's D dimer, fibrinogen, haematocrit and mean platelet volume were measured within 48 hours of admission. Every alternate patient was given LMWH, Enoxaparin for 6 days irrespective of their thrombotic state. All patients in the study were subjected to venous doppler bilateral lower limb on day 7 and after 3 months and CT pulmonary angiography at 3 months or during the time of development of symptoms of suspected Pulmonary Embolism. **Results:** The D Dimer level was elevated in 35 (79.5%) out of 44 patients with value above 250ng/ml. 10 patients (22.7%) had fibrinogen values greater than 500 mg/dL. The mean hematocrit value was 47% with 6 patients had haematocrit of >52%. The values of D-Dimer and fibrinogen decreased on the 7th day in both groups. The post-treatment means value of D-Dimer and fibrinogen decreased in both the groups; however, it was not significantly statistically. One patient was reported to have chronic PTE in CT pulmonary angiography done at 3rd month. He belonged to the control group, hence had not received LMWH as treatment. **Conclusions:** Among the prothrombotic markers, D-Dimer was significantly elevated in the majority. No significant change in prothrombotic markers was observed in patients of COPD with acute exacerbation receiving low molecular weight heparin in addition to conventional treatment. One patient witnessed a thromboembolic event in the form of pulmonary embolism and had elevated D-Dimer, Fibrinogen, and hematocrit levels and had received conventional treatment.

Key words: Acute exacerbations of chronic obstructive pulmonary disease, D-Dimer, Fibrinogen, Hematocrit, CT pulmonary angiography

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a disease of increasing public health importance around the world. COPD is currently the fourth leading cause of death in the world but is projected to be the 3rd leading cause of death by 2020 [1]. COPD is a leading cause of long-term illness and death globally, with numerous individuals enduring the disease for many years and ultimately dying prematurely due to the condition or its associated complications. Globally, the COPD burden is projected to increase in the coming decades because of continued exposure to COPD risk factors and aging of the population. It is well known that COPD is a syndrome of progressive airflow limitation caused by chronic inflammation of the airways and lung parenchyma, but it also produces significant systemic consequences. The role of systemic inflammation as evidenced by the rise in inflammatory markers is now being increasingly recognized to play an important role in systemic effects. The relationship between acute exacerbations of COPD (AECOPD) and pulmonary embolism (PE) has been an important subject of research. The pathophysiological changes in COPD are as follows: i) reconstruction of the pulmonary

vascular bed: extensive contraction and arterial hypertension caused by long-term hypoxia, vascular intimal hyperplasia, and vascular fibrosis and occlusion; and ii) blood hypercoagulability: blood stasis caused by increased erythrocyte formation due to long-term hypoxia, vascular endothelial cell dysfunction, pulmonary heart disease combined with right ventricular dysfunction, dependence on corticosteroids and increased concentrations of blood-clotting substances. These changes cause venous blood stasis, vein endothelial injury, and blood hypercoagulability (the three elements of Virchow's triad), leading to the formation of the prothrombotic state (PTS). AECOPD is often complicated with respiratory failure. In the majority of patients, due to hypoxemia and carbon dioxide retention [2-4] the blood is in a hypercoagulable or PTS state, with the formation of small pulmonary artery thrombi leading to a poor prognosis [5-6]. Fibrinogen is a glycoprotein synthesized by the liver. Agnelli et al [11] indicated that an increased fibrinogen level was an important risk factor for thrombosis and cardiovascular diseases. D dimer is the specific degradation product of cross linked fibrin and is used as a molecular marker of hypercoagulation and secondary increased fibrinolytic activity [7-8].

It is known that platelets play a major role in inflammation as in thrombosis. Mean platelet volume disturbances reflect changes in either the level of platelet stimulation or the rate of platelet production. Moreover, mean platelet volume has been used as an indicator of platelet function for inflammatory diseases, and because inflammation plays a crucial role in COPD, alterations in platelet activity and consequently in the mean platelet volume are expected [9-11].

Materials and Methods

Study Design

This was a randomized controlled study carried out over a period of one year in the Department of Medicine, Maulana Azad Medical College, and associated Lok Nayak Hospital, New Delhi, India, after obtaining clearance from the Institutional Ethics Committee.

Inclusion Criteria

Patients of COPD with acute exacerbation (as defined by GOLD criteria) (1), aged e" 35 years. Acute exacerbation of COPD is defined as an acute event characterized by worsening of the patient's respiratory symptoms that are beyond the normal day to day variations and requires a change in the medication of patients.

Exclusion Criteria

Known cases of hypercoagulable states, coronary artery disease, pregnant women, past history of myocardial infarction, a previously diagnosed case of other chronic respiratory diseases, chronic kidney disease, chronic liver disease.

Methodology

A total of 44 patients of COPD were enrolled in this study. Informed consent was obtained from all patients. These patients were subjected to complete history and physical examination and particulars of the patients such as name, age, sex, pack-years of smoking, pre-existing comorbidities, etc. were noted in a pre-structured proforma. Chest X-Ray and ECG were done. A series of hematological and biochemical investigations i.e. hemogram, liver function test, kidney function test, and arterial blood gas analysis were carried out. Also, D-Dimer, Fibrinogen, Mean Platelet Volume, and Haematocrit were observed in all 44 patients within 48 hours of admission.

Of the 44 patients, 22 patients were given low molecular weight heparin 0.4ml subcutaneous once a day for 6 days irrespective of the prothrombotic markers. Bilateral lower limb venous doppler for all patients was done on day 7 and at 3rd month and CT pulmonary angiography was done on 3rd month. Thus, the prothrombotic markers were studied for all 44 patients, and the role of anticoagulation in preventing any thromboembolic event was observed.

Statistical Analysis

The data was analyzed using IBM SPSS version 25.0 software. The analysis of quantitative variables was conducted using the mean, standard deviation (SD), median, and other relevant measures. The association between two qualitative variables was done using Chi-square test while that between two quantitative variables was done using the Pearson correlation test. A P- value of & lt; 0.05 was considered significant.

Observations and Results

Demographic Characteristics

The majority of the study population was in the age group of 50-70 years. The study population had an average age of 64.7 years. The mean of males was 65 years and that of females was 62 years. Approximately 84% of the patients in the study were males while 15% were females.

Smoking Habits

Out of 44 patients, 39 were either bidi or cigarette smoker's majority being bidi smokers. The remaining were exposed to chulha smoke, all of them being females.

Among bidi/cigarette smokers: Mean pack years 36.38 ± 4.95 years

Among chulha smoke exposure: Mean exposure 15.6 ± 3.7 years.

Comorbidities

14 Out of 44 patients had comorbidity. Out of 14, all of them either had Type2 DM or Hypertension and one among them had both.

Prothrombotic Markers

Since the values observed for D-dimer had a skewed distribution, the median value was also calculated which was 990ng/ml (Range:190-5340 ng/ml).

Thromboembolic Event

None of the study population had any evidence of DVT on the 7th day and 3rd month after admission. One patient had evidence of chronic PTE diagnosed at 3rd month by CT pulmonary angiography.

Discussion

This study was undertaken in the Department of Medicine of Lok Nayak hospital, Maulana Azad Medical College, New Delhi. A total of 44 patients of COPD in acute exacerbation were enrolled in the study after informed valid consent. Based on previous studies, the sample size was calculated to be 44 (22 in each group) using OpenEpi, Version 3.

Age Distribution

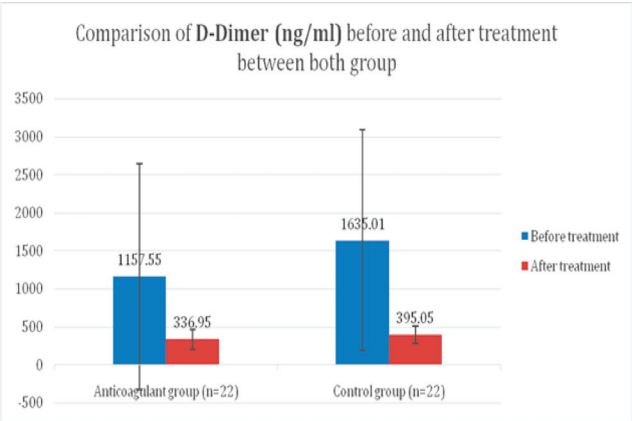
The mean age of males was 65.19 years with a standard deviation of 7.3 years. The mean age of females was 62.57 years with a standard deviation of 9.36 years. The age distribution found in this

Table 1: Blood coagulation profile of study subjects (44)

	D-DIMER (ng/ml)	FIBRINOGEN (mg/dl)	Haematocrit (%)	MPV (fL)
Mean	1396.27	422.93	47.002	8.56
SD	1469.656	126.839	4.2020	1.44

Table 2: Comparisons of blood coagulation state of the two groups of patients before and after treatment.

	Anticoagulant group (n=22)		Control group (n=22)		P-value between groups
	Mean	SD	Mean	SD	
MPV (fL)					
Before treatment	8.56	1.48	8.55	1.43	0.67
After treatment	8.31	0.93	8.54	0.94	0.57
P-value between before and after treatment within the group	0.07		0.97		
Haematocrit (%)					
Before treatment	46.09	3.37	47.91	4.80	0.27
After treatment	45.45	3.22	46.85	4.43	0.41
P value between before and after treatment	<0.001		<0.001		
	Anticoagulant group (n=22)		**Control group (n=22)**		**P-value between groups**
	Mean	**SD**	**Mean**	**SD**	
D-Dimer (ng/ml)					
Before treatment	1157.55	1484.97	1635.01	1448.46	0.12
After treatment	336.95	132.61	395.05	118.96	0.08
P value between before and after treatment within group	<0.001		<0.001		
Fibrinogen (mg/dl)					
Before treatment	413.64	146.27	432.23	106.60	0.48
After treatment	275.09	73.15	298.18	67.49	0.19
P value between before and after treatment	<0.001		<0.001		



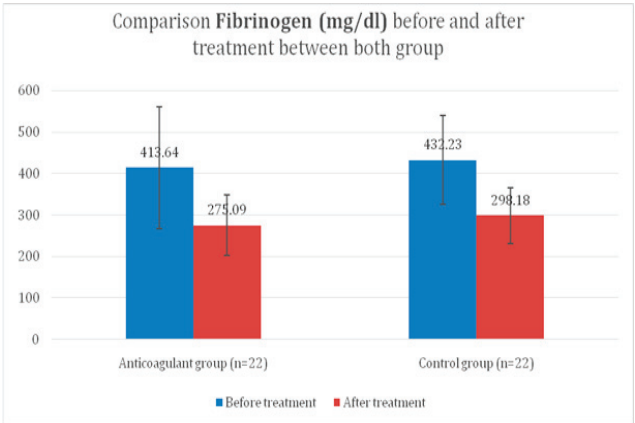


Table 3: Comparisons of arterial blood gas indicators of the two groups before and after treatment

	Anticoagulant group (n=22)		Control group (n=22)		P-value between groups
	Mean	SD	Mean	SD	
PaO_2					
Before treatment	64.42	29.75	65.05	19.85	0.61
After treatment	87.47	3.15	86.05	3.84	0.27
P value between before and after treatment	<0.01		<0.01		
$PaCO_2$					
Before treatment	59.68	15.51	68.80	19.79	0.10
After treatment	50.02	6.24	53.28	6.82	0.11
P value between before and after treatment	<0.001		<0.001		
$3SaO_2$					
Before treatment	88.73	11.57	87.73	7.47	0.24
After treatment	94.71	2.58	93.85	2.74	0.24
P value between before and after treatment	<0.001		<0.001		

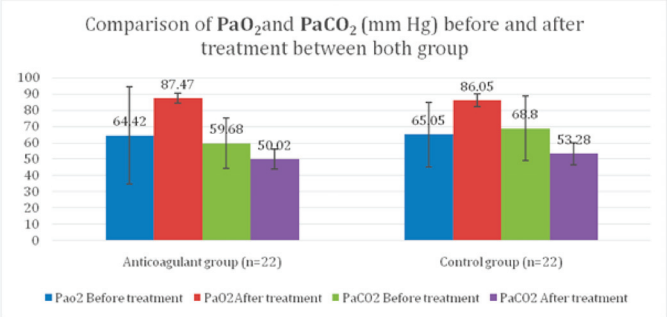


Table 4: Comparisons of blood coagulation state of the two groups of patients before and after treatment

	Intubated (n=9)	
	Mean	SD
D-Dimer (ng/ml)		
Before treatment	2751.22	1989.61
After treatment	455.56	121.13
Fibrinogen (mg/dl)		
Before treatment	467.56	116.47
After treatment	337.0	58.92
	Intubated (n=9)	
	Mean	**SD**
MPV (fL)		
Before treatment	8.48	1.29
After treatment	8.58	1.08
Haematocrit (%)		
Before treatment	49.36	5.80
After treatment	48.18	4.80

study group is similar to previous studies. A study conducted by Jain et al [12] among 702 patients of COPD, the mean age of the patients was 60.61 ± 10.36 years. Another study conducted by Ashitani et al [4] the mean age was found to be 72.6 ± 5.2 years. Mean age was found to be 68.3 ± 3.9 years and 62.3 ± 7.92 years in a study conducted by Cella et al [13] and Zhang et al [14]. Thus the age distribution observed in this study is unvarying with the previous studies.

Gender

The study population comprised predominantly of males. Around 84% were males and 15.9% were females in the study population. In a study conducted by Jain et al [12], 70.2% were males and 29.8% were females. As the smoking habit is more common in males, COPD is more prevalent among males. The prevalence of chronic obstructive pulmonary disease (COPD) in women is increasing, as is hospitalization for COPD. Increased tobacco use in women likely explains some of the increase in the prevalence of COPD in women, but evidence suggests that women might be more vulnerable to lung function impairment caused by smoking, experience more severe shortness of breath, and have a poorer overall health status compared to men with equivalent tobacco exposure. Non- smokers with COPD are also more likely to be female.

Smoking

Among 44 patients 88% were either bidi or cigarette smoker majority being males. Most of them were bidi smokers. The remaining 11.6% had chulha smoke exposure, all of them being female. Although smoking (tobacco consumption) is widely recognized as the most important risk factor for COPD, it is now also recognized that a substantial proportion of COPD cases (one quarter to one-third of all cases) cannot be explained only by smoking, and the disease also occurs in non-smokers. It has been suggested that the interaction of other risk factors, such as biomass exposure, with smoking, might further increase the risk of COPD. The PUMA study reported that individuals exposed to household biomass smoke are twice as likely to develop COPD than unexposed people [14]. In this study, among bidi/cigarette smokers, mean pack-years was found to be 36.38 ± 4.95 years and among chulha smoke exposure mean duration of exposure was 15.6 ± 3.7 years. In PUMA study, subjects with COPD had an average of 44 pack-years of tobacco smoking and 12 years of biomass exposure [15].

Comorbidities

Chronic obstructive pulmonary disease (COPD) is frequently associated with comorbid conditions such as cardiovascular diseases, diabetes, hypertension, osteoporosis, and mental health disorders. However, the prevalence of these comorbidities varies significantly across studies. In our study we excluded chronic kidney disease as inflammatory and prothrombotic markers are elevated in mild to moderate renal disease. We excluded chronic liver disease as they have baseline coagulation abnormalities hence giving false results. Patients with known coronary artery disease were excluded from the study due to their use of antiplatelet therapy, which could affect the results. Among the study group of 44 participants, approximately 68% did not have any comorbidities. Of the remaining individuals, the most common comorbid conditions were hypertension and Type 2 diabetes mellitus, observed in 15.9% and 13.6% of the group, respectively. Similarly, in a study involving 270 hospitalized COPD patients, Antonelli Incalzi and colleagues identified hypertension in 28%, diabetes in 14%, and ischemic heart disease in 10% [16].

Pulmonary embolism (PE) appears to be a more prevalent comorbidity in COPD than previously recognized, though current data remains limited and somewhat inconsistent. Diagnosing PE in COPD patients is challenging because the primary symptoms of PE often overlap with those of a COPD exacerbation. In one study of 211 consecutive patients admitted for severe COPD exacerbations of unknown origin, spiral CT or ultrasonography revealed PE in 25% of cases, as reported by Tillie-Leblond and colleagues [17]. Conversely, Rutschmann and collaborators found a low incidence of PE in a study of 123 consecutive patients admitted for acute COPD exacerbations. PE was identified in 6.2% of patients with clinical suspicion and only 1.3% of those with low suspicion [18].

ABG analysis:

The mean pO_2 in the study group was 64.73 mm Hg and mean pCO_2 was 64.24 mm Hg with a mean pH of 7.33 indicating type 2 respiratory failure with respiratory acidosis. Arterial blood gas findings in COPD are non-specific but are characterized by hypoxemia and hypercapnia, with elevated bicarbonate indicative of chronic metabolic correction of respiratory acidosis. In a case report of 3 patients with known COPD complicated by PE, Lipmann et al [19] suggested a drop in $PaCO_2$ of 10mmHg or more in otherwise previously hypercapnic COPD patients as indicative of thromboembolism. On the other hand, Lesser et al [20] reported 108 patients presenting with a history of COPD and newly diagnosed PE to have no difference in the reduction in $PaCO_2$, despite prior hypercapnia on arterial blood gas. But old ABG analysis of the study group could not be traced. The correction of hypoxemia with oxygen or positive pressure flow may support the diagnosis of COPD, while major pulmonary embolism with an intrapulmonary or intracardiac shunt may be resistant to correction. In our study group, post-treatment ABG revealed a correction of hypoxemia. Thus, ABG data alone or in combination with other clinical data are not useful in the assessment of suspected PE.

Prothrombotic State in COPD

Here we analyzed the blood coagulation profile of the patients which included D-Dimer, Fibrinogen, Haematocrit, and mean platelet volume.

D-Dimer

Out of 44 patients, 35 of them (79.5%) had a D-Dimer value above 250ng/ml which is the normal value. In our study group mean D-dimer value was 1396.27 ng/ml with a high standard deviation of 1469 ng/ml, due to a small sample size and skewed distribution. The median D-Dimer found in this group was 929ng/ml, with the lowest value being 190ng/ml and the highest being 5340ng/ml. In a similar study conducted by Song et al [21] on 30 patients presenting with acute exacerbation, the D-dimer mean value was 3600ng/ml. In another study conducted by Zhang et al [14], the median of D-dimer in the exacerbated COPD patients was 2839 ng/ml. Our study population had a large variation in D-Dimer values hence not consistent with similar studies. D-Dimer is a specific degradation product formed by the hydrolysis of cross-linked fibrin by plasmin and it is the smallest peptide generated by cross-linked fibrin degradation. Due to good stability, high sensitivity, and strong specificity in plasma, D-Dimer has been recognized as a mark of thrombosis. However, D-dimer is also an acute-phase reactant whose production stimulates high levels of cytokines, so D-dimer can be served as an inflammatory marker and COPD is a chronic inflammatory disease. Hence, the D-dimer levels in COPD patients are still conflicting.

Table 5: CT Pulmonary angiography finding in COPD subjects (n=44)

CT Pulmonary angiography finding	No. (%)
No PTE	43 (97.7)
Chronic PTE	1 (2.3)

Table 6: Parameters in patient with chronic PE

D-dimer (ng/ml)	Fibrinogen (mg/dL)	Haematocrit (%)	Mean Platelet Volume (fL)
3540	470	53.1	8.7

Fibrinogen

Out of 44, only 10 patients (22.7%) had values greater than 500 mg/dL. The mean of the observed fibrinogen values was 422.9 mg/dL with a standard deviation of 126 mg/dL. The median fibrinogen value was 446 mg/dL. This value was consistent with fibrinogen levels observed in a study conducted by Zhang et al [14] during the exacerbation phase of COPD, the mean value of fibrinogen was 352 ± 81.3 mg/dL. Elevation of the fibrinogen level is an important risk factor of thrombosis. It is an indicator of prothrombotic state, airway progressive inflammation, and lung tissue injury. Though the levels were not greater than 500mg/dL, the mean value is closer to the upper limit of the normal range and is consistent with similar studies.

Haematocrit

The mean hematocrit value was 47% in our study group, with 6 patients out of 44 who had a haematocrit of >52%. In a study conducted bySchwarcz et al [22] to evaluate thromboembolic events in smoker's polycythemia and non-smokers polycythemia, the mean hematocrit value was 59.0 ± 3.2 % in smokers polycythemia. Only 1 patient in smokers polycythemia had evidence of DVT/PTE as compared to 9 in the polycythemia group. In conclusion, it was found in that study that patients with smokers' polycythemia had significantly fewer thromboembolic events per patient and episodes of peripheral arterial thromboembolism than did individuals with Polycythemia vera, the results of this study demonstrated that smokers' polycythemia does not represent a hypercoagulable state equivalent to that of polycythemia vera. In another case-control study by Nadeem et al [22] compared the prevalence of VTE in age- and sex-matched patients with COPD with and without secondary polycythemia, which demonstrated that the frequency of VTE events was similar in patients with and without secondary polycythemia. These results indicate that secondary polycythemia itself is unlikely to be an independent risk factor for VTE. Hence hematocrit is not a useful parameter to assess the hypercoagulable state in COPD.

Mean Platelet Volume

The mean value of the mean platelet volume in the study group was 8.56±1.44 fL. In a study conducted by Agapakis et al [23], he studied different parameters in patients of COPD presenting in acute exacerbation and compared it with those of stable COPD. The mean platelet volume in the study population was 8.5±0.9 fL whereas in stable COPD it was 9.3±1.3 fL thus depicting a decrease in mean platelet volume during exacerbation. In a similar study done by Kocak et al [24], it was observed that mean MPV (fL) in COPD with acute exacerbation was 8.96 fL whereas in stable COPD it was 7.92 fL. Since we did not have a control group to study the difference, the mean platelet volume observed in this study does not convey if it is low or high. MPV is a simple and easy method of assessing platelet function and reûects the platelet production rate and stimulation. Larger platelets are both metabolically and enzymatically more active than smaller platelets and they have greater prothrombotic potential. Therefore, increased MPV can be accepted as a simple marker of platelet activation. In another study conducted by Talay et al [25] on patients presenting with pulmonary embolism, it was found that MPV in the PE group was significantly higher than in the control group (9.42±1.22 fl vs. 8.04±0.89 fl, p<0.0001). In another similar study conducted by Valor et al[26] to evaluate platelet indices in PE, MPV was signiûcantly higher among PE patients when compared with the control group (9.6 ± 1.0 vs. 8.1 ± 0.8 fL, respectively; p<0.001). Because MPV reflects thrombocyte activation and inflammation, it may also reflect the inflammatory burden of acute attack in COPD. However, the results of studies observed MPV in COPD are conflicting in literature.

Effect of Low Molecular Weight Heparin (enoxaparin)

Here we evaluated the role of LMWH in preventing any thromboembolic event. Every alternate patient was administered enoxaparin for 6 days irrespective of their prothrombotic state.

- The values of D-Dimer and fibrinogen decreased in both treatment and control groups on the 7th day. However, the post-treatment mean value of D-Dimer and fibrinogen was lower in the treatment group than the control group but it was not statistically significant.
- There was a fall in hematocrit in both the treatment and control group.
- There was no significant change in mean platelet volumes in both groups. However, the mean value of MPV was lower in the treatment group than the control group.
- In ABG analysis, pO2 in both the groups improved after treatment irrespective of whether they received enoxaparin or not. However, the mean pO2 value was higher in the anticoagulation group as compared to the control group. The pCO2 value also decreased in both group but the mean pCO2 was lower in the treatment group. However, the difference between the two groups was not statistically significant. No evidence of DVT in any of the patients.
- One patient was reported to have chronic PTE in CT pulmonary angiography done at 3rd month. He belonged to

the control group, hence not received enoxaparin as treatment.

No side effects of enoxaparin were observed in any of the patients.

In a similar study conducted by Shi et al [27] where 70 patients of COPD presenting with acute exacerbation were randomly divided into two groups (one receiving anticoagulation and the other group getting the routine treatment) and D-dimer and fibrinogen levels were observed in both the groups. Following the treatment, the D-Dimer level and blood coagulation indicators of the anticoagulation group were significantly improved compared with those before treatment, and the extents of the improvements were significantly greater than those in the control group. For the control group, there was no significant difference between the D-Dimer level and blood coagulation indicators before and following treatment.

In another study conducted by Song et al [21], the conditions of the patients in the LMWH and conventional treatment groups were noticeably improved following treatment. Compared with the conventional treatment group, the hematocrit, Fibrinogen, PaO2, and PaCO2 of the LMWH treatment group were improved. The differences were significant ($P<0.05$). The D dimer levels of the patients in the two groups were decreased following therapy. Compared with the conventional treatment group, the LMWH group was improved noticeably, but the difference between groups was not significant ($P>0.05$), similar to the results observed in our study. And in this study, in the conventional treatment group, one patient was complicated by cerebral infarction and another by lower limb vein embolism. In our study, one patient in the conventional treatment group developed chronic PTE. As we had evaluated the patients only for DVT and PE, no other thromboembolic events like cerebral infarction were studied. No obvious focal neurological deficit was observed in any of the patients, hence ruling out any major cerebrovascular events.

In our study, there was no significant difference in the changes in the prothrombotic markers in both the anticoagulation and conventional treatment group. D-dimer and fibrinogen. These are also markers of inflammation and COPD is a state of chronic inflammation. The drop in mean D-dimer and fibrinogen levels was seen in both the groups and the difference between the two groups was insignificant.

In a study conducted by Kampolis et al [28], 50 patients of COPD who presented with acute exacerbation were evaluated for PE despite low Well's score. PE was detected in 10 patients (20%). D-dimer levels of COPD patients with PE (median value: 7655 ng/ml) were significantly higher than those of the patients without PE (median value: 940 ng/ml) ($p<0.001$). The calculated area under the ROC curve for D-dimer was 0.89 with an optimal cut off value at 2190 ng/ml. It was observed that patients hospitalized for COPD exacerbation with low clinical probability for PE present D-dimer levels higher than normal, even without PE. The D-dimer cut off value used to exclude PE should be adjusted, thus reducing the unnecessary use of diagnostic procedures.

Thromboembolic Events

In our study, only one patient (i.e. 2.3%) out of 44 had evidence of chronic PTE. None of the patients had any evidence of DVT. In a study conducted by Akpinar et al [29] showed that PE was present in 29.1% of the patients who were hospitalized due to an exacerbation of COPD. The D-dimer value in this patient was 3540ng/ml which is above the cut off value of D-Dimer in COPD patients with pulmonary embolism observed in the study conducted by Kampolis et al [15]. Also fibrinogen level was 470mg/dL, hematocrit observed was 53.1% and mean platelet volume was 8.7 fL which were close to the observed mean values of the study group except for higher hematocrit. The precise prevalence of PE in patients experiencing an acute exacerbation of COPD, as well as the clinical characteristics of these patients, remains uncertain.

Conclusion and Recommendations

Chronic obstructive pulmonary disease was more prevalent in the age group of 50-70 years and more prevalent in males with smoking history. Among the prothrombotic markers, D-Dimer was significantly elevated in the majority. Most of them had mean platelet volume, fibrinogen, and hematocrit in the normal range. No significant change in prothrombotic markers was observed in patients of COPD with acute exacerbation who received low molecular weight heparin in addition to conventional treatment alone. One patient witnessed a thromboembolic event in the form of pulmonary embolism and had elevated D-Dimer, Fibrinogen, and hematocrit levels and had received conventional treatment. The prothrombotic markers D-Dimer and fibrinogen are also markers of inflammation and hence can be elevated in chronic inflammatory conditions like COPD who present in acute exacerbations. Smokers polycythemia can be considered as a risk for thromboembolism in patients of COPD. The role of mean platelet volume needs to be further studied. The benefits of anticoagulation treatment in patients of COPD with acute exacerbation in preventing thromboembolic events can be demonstrated by recruiting a larger study population.

Limitation of Study

The sample size was small therefore the statistical power of the study was low and the study duration was very short. We did not have baseline values of mean platelet volume of patients during a stable phase, availability of which would have helped in getting more elaborate results about mean platelet volume. We did not exclude patients with pneumonia where D-Dimer value could be raised due to sepsis as well. There was no uniformity in the severity of disease in the study population.

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
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ORIGINAL ARTICLE

Serum Albumin Level as a Prognostic Tool: A Clinico-Biochemical Study

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Abstract

Background: The correlation between hypoalbuminemia and Acute Febrile Medical Illness has not been extensively investigated in prospective controlled studies and only a few studies are available in the world literature. Seeing paucity of such a research in India, especially in North India, the present study was undertaken. **Methods**: In this study 60 patients suffering from Acute Febrile Medical Illness having fever of 38°C or higher and of less than seven days duration were taken. As per criteria, study patients who besides having Acute Febrile Medical Illness also had at least two organ dysfunctions while those with pre-existing co- morbidities were excluded. On admission, investigation for serum albumin and other markers of organ dysfunction were done and the results recorded. Patients were divided on the basis of baseline serum albumin level into group I (d" 2.4 g/dl) and Group II (e"2.5 g/dl). On recovery, serum albumin was again estimated at their first follow up. **Results:** Hypoalbuminemia (Serum albumin d"3.5 g//dl) was seen in 90% of the study population with 2.99± 0.52 g/dl of Mean S. Albumin on admission. All the survivors, on the first follow up showed an appreciable improvement in albumin levels with a mean serum albumin level of 3.73 ± 0.31g/dl with a statistically highly significant p-value ($p<0.001$). Group I patients compared to Group II showed significant differences in hypotension, renal dysfunction and mean Hemoglobin values. However, the difference between group I and II regarding the need for ventilatory support, mean duration of hospitalization and mortality was appreciable but not significant statistically. **Conclusions**: Hypoalbuminemia, invariably, is an accompaniment to Acute Febrile Medical Illness and the level of serum albumin is inversely proportional to the severity of this illness.

Key words: Hypoalbuminemia, Acute Febrile Medical Illness, Predictor, Prognostic Tool

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Introduction

It is observed that hypo-albuminemia, a decrease in serum albumin concentration, is consistently found to accompany severe diseased conditions. Review of literature shows that estimation of serum albumin alone in diseased conditions could act as predictor of mortality in many clinical conditions [1]. A link has been shown to exist between low serum albumin level and an increase in morbidity and mortality [2]. Serum albumin estimation in elderly patients could be an indicator of subclinical disease. Hypo-albuminemia is found to be associated with higher complication rates, increased length of hospital stays and higher mortality in studies of hospitalized patients [3]. Serum albumin estimation have prognostic value also in critically ill patients [4,5]. Hypo-albuminemia is associated with ventilator dependency, increased length of hospitalization and development of new infection [6].

The purpose of this study was to evaluate if serum albumin level could also serve as another marker of disease severity as well as a prognostic tool in patients suffering from Acute Febrile Medical Illness.

Materials and Methods

In this study 60 patients suffering Acute Febrile Medical Illness admitted from time to time in Medical Wards as well as ICU of SGT Medical college and Hospital, Gurugram were taken up for study**.** Only those patients who fulfilled the study criteria were chosen and admitted.

Selection of Patients

Selection of the patients was done as per the study criteria for inclusion and exclusion which was as follows:

Inclusion Criteria

1. Patients included were in the age group of 18-60 years
2. Patients with fever e" 38°C
3. Febrile duration < 7 days
4. Acute Febrile Medical Illness patients having at least two organ dysfunctions as well.

Criteria used to define organ system involvement were as follows:

Cardiovascular System

Systolic BP<90 mm Hg and Diastolic Pressure < 60 mm Hg despite requisite measures to maintain blood pressure.

Respiratory System

PaO2 < 70mm of Hg or oxygen saturation < 90% on pulse oximetry in room air or PaO2 / Fi O2 < 250.

Renal System

Urine output <0.5ml/kg or <30 ml / hour despite requisite measures or Serum Creatinine >2 mg dl.

Hepatobiliary System

Serum total bilirubin > 2mg/dl or AST > 80 U/L (>twice the upper limit of normal) and / or ALT > 112 U/L (> twice the upper limit of normal) or Prothrombin Time > 6 seconds

Hematological System

WBC < 4,000/cumm or >12,000/cumm or ESR >15mm / Ist hr. or Platelet count <1,00,000/cumm

Exclusion Criteria

Patients excluded were those who had any of the pre-existing co-morbidities like Chronic liver disease, Chronic kidney disease, Chronic infection, Malabsorption, Malnutrition, Burns and Pregnancy.

On admission written consent for the study was taken from the family, a detailed history of the patients taken, thorough clinical examination and laboratory investigations done and findings recorded on the Clinical Proforma.

Laboratory investigations included Hemoglobin estimation, Haematocrit values, Platelet and Leucocyte counts, Prothrombin time, Serum albumin, Serum total bilirubin, Blood urea, Serum creatinine, AST & ALT. Reports of the laboratory investigations were recorded on the proforma.

Monitoring was then done by watching the signs of disease-severity on the basis of the altered laboratory values as mentioned with the disease .We monitored Anaemia (Hemoglobin level < 13g/dl in men and < 12gdl in women), Leucocytosis (> 12000 /ml WBCs) , Thrombocytopenia (< 100,000 / ml platelets) , Prolonged Prothrombin time (> 6 seconds), Increased Total Bilirubin (> 2 mg/dl), Increased AST / ALT (AST > 80 U /L , ALT > 112 U/L), Hypotension (Systolic Pressure < 90 mmHg , Diastolic Pressure < 60mm Hg) , Renal Dysfunction (Urine output < 0.5ml/Kg or <30ml/hour &/or Serum creatinine > 2 mg / dl) , Need for Ventilatory Support , mean duration of Hospitalization and Mortality if any. For the purpose of evaluation, study population was divided into two severity groups based on their serum albumin levels at the time of admission:

Group I d” 2.4 g/dl

Group II e”2.5 g/dl

On recovery, serum albumin estimation was repeated on the first follow up within 21 days. On completion of the Clinico-Biochemical study, all the data so obtained were then compared among these two groups and statistically analyzed.

Statistical Analysis:

The results were initially assessed with mean, range and standard deviation measures. Suitable percentage and proportion expression were also recorded. The parametric variables were analyzed using Student “t” test (independent for different groups) and paired t test (for dependent variables) and the results were expressed as significant if p value was less than 0.05.

Study Outcome Measure

Outcome measure was assessed in terms of difference in serum albumin levels at the time of admission as well as at the time of discharge and between group I and group II.

Ethical Consideration

An informed written consent was taken from the attendants of the patients selected for this study after explaining them the purpose and procedure of the study. They were told that their participation was entirely voluntary and even if they choose not to participate, they will still get the same treatment. They were told that they were free to stop participating even if they change their mind later. They were apprised that the outcome of the study may be of benefit to them and other patients with alike disease. The participating subjects were ensured that their identity would not be shared and the information so collected about them during the study would be kept confidential. They were also informed that data so generated from the study would only be published without divulging their identity.

Results

Hypoalbuminemia (Serum albumin d”3.5 g /dl) was seen in 90% of the study population with 2.99± 0.52 g /dl of Mean S. Albumin on admission while only 6 patients had a serum albumin more than 3.5gm /dl. Only 25% of study population was found to have d” 2.4 g /dl serum albumin (Group I) while rest of the 75% study population had e” 2.5 g /dl serum albumin (Group II). Forty-two patients (70% of study population) were in the age group of 18-40 years and eighteen patients (30% of study population) were in the age group of 41-60 years. Sex distribution showed 73.4% males and 26.6% females. The causes of acute febrile medical illness in the study population were Systemic Viral Illness in 23.33 %, Dengue in 20%, Sepsis in 16.67%, Enteric fever and Malaria in 10% each, UTI in 8.33%, Pneumonia in 6.67% and Meningitis in 5%.

The study population showed mean values of age (in years) as 33.55 ± 12.32, Mean S. Albumin on admission (g /dl) as 2.99± 0.52 and on follow up as 3.73 ± 0.31, Hemoglobin (gm %) as 12.26 ± 2.66, TLC (/cumm) as 13251.67 ± 12, Platelet Count (/cumm) as 162350 ± 103807, ESR as 23.60 ± 15.44, S. Bilirubin (mg/dl) as 1.71 ± 3.02, AST (IU/L) as 275.88 ±613.46, ALT (IU/L) as 257.05 ± 655.11, Total Protein (g/dl) as 6.37 ± 0.83, Hypotension as 33.3%, Renal Dysfunction as 16.7%, Ventilatory Support as 15 %, Mean number of days in hospital as 7.18 ± 6.62and Mortality as 3.3 %.

All the survivors, on the first follow up showed an appreciable improvement in S. Albumin level which rose from Mean S. Albumin of 2.99 g /dl on admission to 3.67 g /dl on follow up with a statistically highly significant p-value (p<0.001). In Group I mean serum albumin rose from 2.22 g /dl to 3.65 g /dl and in Group II from 3.25 g /dl to 3.76g /dl. Here again p-value being (p<0.001) was highly significant statistically (Table1 and Figure 2).

On comparative analysis of the two groups with other parameters showing disease severity, Group I patients as compared to Group II showed statistically significant differences in Hypotension as 73.33% vs. 20%, p- 0.001(Figure 3) and renal dysfunction as 40% vs. 8.88 %, p- 0.005 (Figures 3 & 4). The difference between the

mean Hemoglobin values among group 1 and 2 was also found to be statistically significant with p value of <0.001. However, the difference in mean values of TLC, platelet count, S Bilirubin, AST/ ALT was not found to be significant statistically (Table 2 and Figure 5).

However, the difference between group I and II regarding the need for ventilatory support was 33.33% % vs.8.88 % p-0.022, for mean duration of hospitalization in days was 9.53 vs. 6.40, p-value 0.113 and for mortality was 6.66 % vs. 2.22% & p-value 0.406 was appreciable but not statistically significant.

Table 1: Graph showing Group wise Albumin Levels on Admission & Follow-up.

Group	Mean S. Albumin at admission (g/dl)	Mean S. Albumin at follow-up (g/dl)	P-value
I	2.22	3.65	
II	3.25	3.76	<0.001
Total	2.99	3.67	

Statistical Test applied: Student t test

Table 2: Relationship between serum albumin groups and Median values of Haematological and Biochemical parameters.

	Group I	Group II	p-value
Hemoglobin (gm%)	9.987	13.013	<0.001
TLC (/cumm)	16600.00	12135.56	0.211
Platelet Count (/cumm)	127600.00	173933.33	0.136
S. Bilirubin (mg/dl)	1.5533	1.7669	0.815
AST (IU/L)	207.00	298.84	0.620
ALT (IU/L)	106.67	307.18	0.309

Statistical Test applied: Student t test

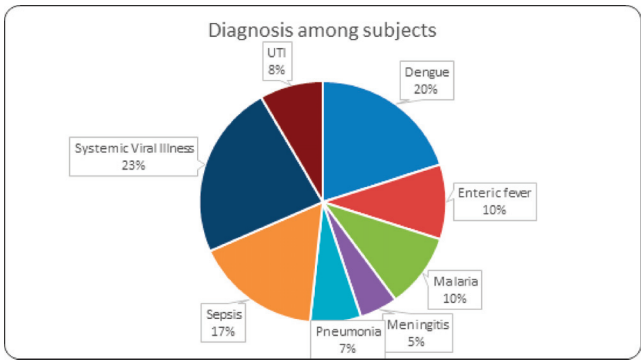

Fig.1: Pie graph showing diagnosis percentage in study population

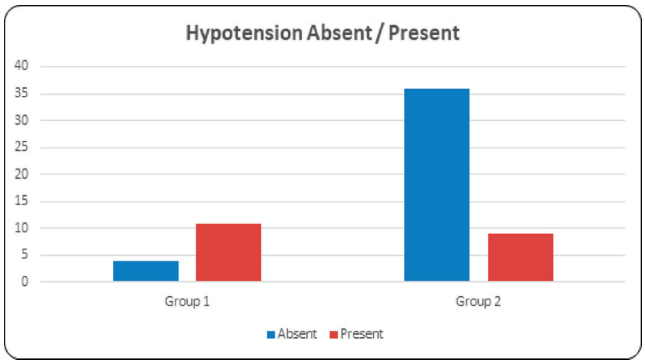

Figure 3: Relationship between serum albumin groups and Hypotension

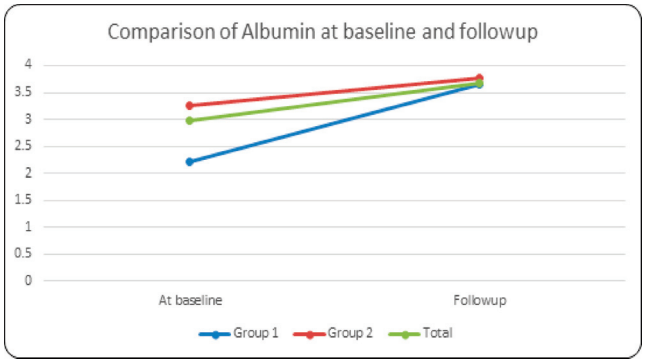

Fig. 2: Line graph showing group wise improvement in Albumin level on recovery in Group I, Group II and total study population

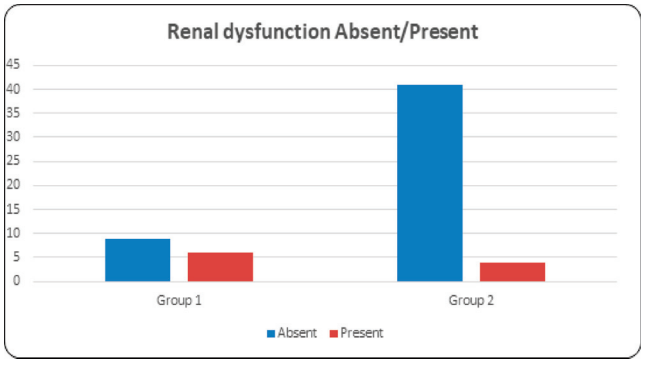

Fig. 4: Relationship between serum albumin groups and Renal Dysfunction

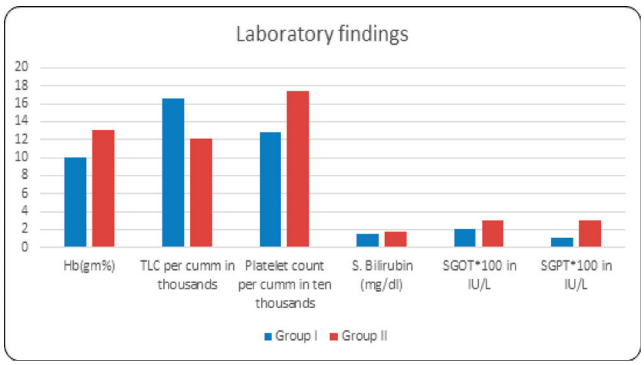

Fig. 5: Relationship between serum albumin groups and Median values of Hematologicaland Biochemical parameters

Discussion

Hypoalbuminemia is found to be related to complications and mortality in cases of acute infectious diseases [7]. Likewise, hypoalbuminemia was seen in about 25%-69.2 % of patients suffering from scrub typhus [8,9]. A similar study in scrub typhus patients by Chang-Seop Lee et al [10,11] showed a close relation between hypoalbuminemia and a higher rate of complications which required more efficient medical management and a longer hospital stay and thus raising the treatment cost. A study on cases of Hanta virus renal syndrome, revealed statistically significant correlation between hypoalbuminemia and parameters of morbidity like liver enzymes, length of hospital stays and mortality. However, in these cases kidneys were diseased and hence hypoalbuminemia could have been due to proteinurea and not because of the severity of systemic illness [12]. However, we excluded the patients having co-morbidities from our study population to evade the interference of factors which could affect the serum albumin levels.

Even though relation between hypoalbuminemia and many diseases has been studied but its correlation with fever, such a commonly presenting complaint, has not been extensively studied, more so in North India. Hence, the study was conducted on individuals suffering from fever and to be more precise on individuals suffering from Acute Febrile Medical Illness. It has been postulated that hypoalbuminemia occurs as a result of decreased synthesis of albumin due to hepatic dysfunction, increased catabolism of protein, decreased intestinal absorption of protein due to poor oral intake, extensive vascular leakage of serum protein due to increased capillary permeability and albuminuria [13]. Hypoalbuminemia is quite commonly seen in critically ill patients where it appears to be due to increased albumin losses through bleeding from the gastrointestinal tract [14], a redistribution of albumin from the intravascular to the interstitial space due to increased capillary permeability [15] and dilution owing to intravenous fluid administration. As we excluded co-morbidities and the factors that could influence the intake and metabolism of albumin, the mechanism that results hypoalbuminemia in Acute Febrile Medical Illness appears to be the result of vascular changes like increased vascular permeability and impaired vascular tone which is accomplished by inflammatory mediators and endotoxins as also reported by Moshage et al [11]. To evade the influence of variables like insufficient food intake which could impact the albumin levels, patients suffering from Acute Febrile Medical Illness of less than 7 days duration only were taken up for study. Another ground for choosing patients of short duration fever was the fact that half-life of albumin is 19 days [16-18]. To nullify the effect of age on serum albumin levels, study was carried out on patients between the age group of 18-60 years only because serum albumin levels decrease by 9.7 % for each decade after 60 years of age [19,20]. Seventy percent of patients in our study were in the age group of 18-40 years where we could anticipate good albumin levels. As per study criteria patients suffering from Acute Febrile Medical Illness with at least two organ dysfunctions were included and those with pre-existing co- morbidities were excluded from the study.

In our study 25% patients had serum albumin d" 2.4 g/dl, 65% had albumin 2.5-3.5 g/dl and 10% had albumin > 3.5 g/dl. Hypoalbuminemia (Serum albumin d"3.5 g//dl) was seen in 90% of our study population while only 6 patients had a serum albumin level more than 3.5gm/dl. Such a high prevalence of hypoalbuminemia in patients with short duration of Acute Febrile Medical Illness unaccompanied by any pre-existing co-morbidity was indicative of severe nature of the disease under study. Prevalence of hypoalbuminemia in as high as 90% of our study population suffering from Acute Febrile Medical Illness prompted us to investigate if hypoalbuminemia is an accompaniment to Acute Febrile Medical Illness. To prove our observation, serum albumin estimation was repeated in the recovered patients on their first post-hospitalization follow up within 21 days. It was quite surprising to find that serum albumin level had appreciably increased in all the recovered patients from their baseline levels irrespective whether they were hypo- albuminic or normo-albuminic. On recovery, the mean baseline serum albumin level of 2.22 g / dl rose to mean serum albumin level of 3.65 g /dl in group I study population and likewise in the group II study population it rose from 3.25 g /dl to 3.76 g /dl. Thus, all the patients showed a significant increase in albumin levels on recovery with a statistically highly significant p-value p<0.001). Prevalence of hypoalbuminemia in majority (90%) of patients of the study population which disappeared on recovery proves that hypoalbuminemia, invariably, is an integral accompaniment to Acute Febrile Medical Illness.

Further, to investigate if any correlation exists between levels of serum albumin and disease-severity , the study population was divided on the basis of baseline serum albumin levels, into two groups and both the groups were compared with disease severity parameters namely hypotension, renal dysfunction, liver dysfunction, need for ventilatory support, mean duration of hospitalization, haematological and biochemical investigations like haemoglobin, TLC , platelet count , serum bilirubin, AST, ALT and mortality.

In our study, Group I patients compared to Group II patients showed significant differences in hypotension (73.33% vs. 20%, p< 0.001) and renal dysfunction (40% vs. 8.88%, p- 0.005). The difference between the mean Haemoglobin values among group I and II (9.99 vs. 13.01, p<0.001) was also found to be highly significant statistically with p value of<0.001. However, the difference between group I and II regarding need for Ventilatory Support (33.33% % vs. 8.88% p- 0.022), mean duration of hospitalization (9.53 vs. 6.40, p- 0.113) and mortality (6.66 % vs. 2.22%, p-o.406) was appreciable but not statistically significant.

In our study hypotension, renal failure and hemoglobin level correlated statistically with the severity of hypoalbuminaemia. Though the relationship of serum albumin level with the need for ventilatory support, mean days of hospitalization and mortality was not statistically significant but grossly the incidence was higher in Group I which had the lowest serum albumin levels. Our study also did not show statistically significant correlation with other parameters of morbidity like raised liver enzymes and low platelet counts. This could possibly be due to the fact that our study

population was not debilitated enough to have baseline serum albumin level as low as which could have statistically significant influence on parameters like ventilatory support, mean duration of hospitalization, mortality and parameters of morbidity like raised liver enzymes and low platelet counts.

Our study differs in regard to need for ventilatory support which was lesser and the mean duration of hospitalization again was shorter than the results of a nearly similar study from South India by Vijapur and Varghese [21]. This difference seems to be due to comparatively lower baseline serum albumin levels of the patients of the above study reported which resulted in more severity of disease in them necessitating higher need for ventilatory support and longer hospitalization and this very well corroborates with our observations that level of serum albumin is inversely proportional to severity of illness. Our study also gets reinforced from another study done on indoor patients of medical and surgical ICUs wherein hypoalbuminemia showed a good outcome predictor at admission and the level of serum albumin correlated with other conventional markers of severity [12].

Limitation of our study is that it was conducted on a group of heterogeneous diseases presenting with Acute Febrile Medical Illness. Had the study been conducted separately on individual disease, there could have been better overall interpretations of these individual parameters. A similar study on individual diseases with Acute Febrile Medical Illness is recommended. However, authors have already started a retrospective study on individual diseases.

To sum up, hypoalbuminemia in our study significantly correlated with parameters of morbidity like hypotension, renal dysfunction and parameter of disease severity like Anaemia. Though not significant statistically, still the incidence of need for ventilatory support, mean duration of hospitalization and mortality was much higher in group I than in group II. We infer from our study that hypoalbuminemia, invariably, is an integral accompaniment to Acute Febrile Medical Illness and its level correlates with severity of disease and thus it can predict the severity of disease and can also serve as a prognostic tool to gauge the severity of disease in Acute Febrile Medical Illness and our observations are in consonance with many other studies [11,12,22-25].

Conclusion

From our observations of high prevalence of hypoalbuminemia in Acute Febrile Medical Illness at the start of illness and its disappearance on recovery, we conclude that hypoalbuminemia, invariably, is an integral accompaniment to Acute Febrile Medical Illness and there undoubtedly, exists a correlation between level of serum albumin and severity of disease. The level of serum albumin is inversely proportional to the severity of this illness The serum albumin level thus, can serve as another marker of disease severity as well as a prognostic predictor like conventional markers of disease severity in patients suffering from Acute Febrile Medical Illness. From our study we infer that a simple test like serum albumin estimation on the outset of the disease can serve as a predictor as well as a prognostic tool to anticipate the severity of disease.

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ORIGINAL ARTICLE

A study of Etiological evaluation of hearing loss in children

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Abstract

Background: Detecting hearing loss early in childhood is crucial for the optimal development of children. Identifying the causes of hearing impairment in the paediatric age group, up to 6 years old, along with understanding their sociodemographic background, provides an excellent opportunity to administer timely treatment and appropriate precautions. Therefore, exploring methods for early identification of hearing issues can greatly benefit these young children.**Methods**: This descriptive study was conducted at the ENT department over 18 months, involving 150 children aged between 0 and 6 years. During the study, data collection encompassed various demographic parameters and a comprehensive birth history, covering prenatal, perinatal, and postnatal details. Additionally, the children underwent thorough clinical and audiological assessments to identify risk factors and ascertain the type and severity of their hearing loss. **Results**: Mean age of study participants were 3.80±1.22 years with maximum 77 (51.5%) cases in the age group of 2.1-4 years. The gender distribution among the participants revealed that 56% were males, resulting in a male-to-female ratio of 1.3:1. Among the 150 patients with hearing loss, 87 (58%) were diagnosed with sensorineural hearing loss, while 63 (42%) were found to have conductive hearing loss. **Conclusion:** More than half of the patients had sensorineural hearing loss (58%) and revealed severe to profound (53.3%) degree of hearing impairment. The delayed diagnosis of hearing loss can be attributed to limited social awareness and the lack of active health surveillance.

Key-words: Hearing loss, etiology, sensorineural hearing impairment, conductive hearing impairment.

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Introduction

Hearing is crucial for language acquisition, speech development, and cognitive abilities. It enables a child to learn, differentiate sounds, recognize objects and events, and internalize various concepts. During critical periods of language development, even minor hearing impairment can hinder a child's natural progression. Hearing loss has a negative impact on a child's learning, communication, and socialization skills.

In 2014, the World Health Organization (WHO) reported more than 360 million individuals worldwide experienced varying degrees of hearing impairment. Out of this number, approximately 328 million were adults, and remaining 32 million were children [1]. Among the children affected, 7.5 million were under the age of 5 [2]. WHO also reported that approximately 42 million people over the age of 3 were dealing with some form of moderate to profound hearing impairment [3]. In children considered to be at high risk, more than 4% were diagnosed with moderate to profound hearing loss [3]. Notably, infants born in resource-rich countries were almost twice as likely to have hearing loss compared to those born in resource-poor countries (6 cases per 1000 children in resource-rich countries versus 2-4 cases per 1000 children in resource-poor countries) [4,5].

Types of hearing impairment involves conductive, sensorineural, and mixed hearing loss [6].

1. Conductive hearing loss: It refers to reduction in sound transmission through the external ear canal and middle ear, and affecting passage of sound into the inner ear.
2. Sensorineural hearing impairment results from damage to the inner ear (cochlea) or the nerve pathways connecting the inner ear to the brain.
3. Mixed hearing loss: It refers to both sensorineural and conductive hearing impairment. While conductive hearing loss is more prevalent, most cases of permanent childhood hearing loss are of the sensorineural type.

Hearing loss can be classified into two main categories: congenital and acquired [7]. Congenital deafness is primarily of the sensorineural type and is present from birth. It may be associated with chromosome disorders or inborn errors of development, typically manifesting before the development of language skills (prelingual presentation.

In young children, certain variables can increase the likelihood of hearing impairment, such as infectious diseases like measles, mumps, and meningitis, as well as chronic otitis media. It is common for more than three fourth of children to experience at least one episode of acute otitis media before the age of 3, and fluid in the middle ear often persists for weeks to months after its onset [8]. Moreover, maternal infections like rubella, jaundice after birth, birth anoxia, low birth weight, ototoxic drugs and exposure to loud noises can also elevate the risk of hearing impairment and deafness. The estimated incidence of hearing loss, whether congenital or acquired, in preschool children is generally around 1 to 2 cases per 1000 children [9].

Identifying hearing impairment in children at an early stage and providing appropriate interventions can positively impact their academic achievements and communication abilities. Developed countries commonly conduct routine screenings to detect hearing issues in children. However, in developing countries, access to advanced diagnostic technology, effective hearing aids, cochlear implants, specialized schools, and other rehabilitative measures is limited and unevenly distributed. As a result, the diagnosis of hearing loss in these regions is often delayed [10]

Children living in rural areas are more likely to experience hearing impairment at a higher rate, possibly due to insufficient hygiene, restricted access to medical services, and challenges in receiving timely treatment [11,12]. Moreover, certain studies indicate that children of parents with low literacy and household income levels are more susceptible to hearing loss. A higher risk of chronic otitis media, which is associated with hearing loss, is observed in children whose parents have low educational attainment [13].

The research aimed to determine the occurrence of hearing loss and identify related factors in children up to the age of 6. The purpose of this study is to implement timely and essential preventive measures to safeguard paediatric populations from experiencing hearing impairment.

Methodology

This descriptive study took place at the outpatient department (OPD) of the hospital. The research was conducted over a duration of eighteen months, spanning from January 2019 to June 2020. The study comprised 150 children between the ages of 0 and 6 years, whose parents provided consent for their participation. The selection of cases followed specific inclusion and exclusion criteria, outlined as follows.

Inclusion Criteria

- All children, regardless of gender, within the age range of 0-6 years, showing indications of unilateral or bilateral hearing impairment during the 18-month period.

Exclusion Criteria

- Children older than 6 years.
- Preterm children were not included in the study.
- Children displaying signs and symptoms of mental retardation and other neurological disorders were excluded from the study

To gather data from the sample, a comprehensive birth history encompassing prenatal, perinatal, and postnatal details was recorded to identify various risk factors associated with deafness. Additionally, information regarding previous illnesses, treatments, immunization, and accidents was obtained. Demographic parameters such as religion, occupation, income, and education were also collected. Thorough clinical examinations were conducted, and children with earwax or fungal issues were treated before further evaluation. Audiometry tests were performed to precisely determine the type and degree of hearing loss in the children, including the following procedures:

- Brainstem evoked response audiometry (BERA)
- Impedance audiometry
- Pure tone audiometry
- Visual reinforcement audiometry (VRA) Behavioural observation audiometry (BOA)/Play audiometry.

The children were informed about the necessity of hearing aids and, based on the cause of their hearing impairment, were recommended either conservative or surgical treatment as needed. The appropriate treatment was then administered to address their hearing issues effectively.

The study followed ethical guidelines by obtaining approval from the ethical committee. Informed and written assent was obtained from the participants, ensuring their understanding and agreement to participate. The confidentiality of all collected data was upheld throughout the study**.**

Microsoft Excel was used to enter and compile the data, and SPSS v21.0 (IBM SPSS statistics for windows, Armonk, NY: IBM Corp, USA,). The qualitative data were presented as numbers and percentages, while continuous quantitative data were illustrated as mean±standard deviation (SD).

Results

In this study involving 150 cases, the majority of subjects fell within the age group of 2.1-4 years, constituting 51.5% of the sample. Among the affected children, 56% were males, resulting in a male-to-female ratio of 1.3:1 (Table 1).

Regarding the demographic profile, the socioeconomic status was evaluated using the modified Kuppuswamy scale. Among the participants, 52% belonged to the lower middle class, followed by 28% in the upper lower class. A smaller proportion of cases, 12%, were from the lower class, and 8% were from the upper middle class (Table 2).

Furthermore, the study revealed that 67.8% of the cases had a rural background, while 32.7% came from an urban background.

To investigate the causes of hearing loss, the study found that 58% of the patients had sensorineural hearing loss, while 42% had conductive hearing loss (Table 3). Among those with conductive hearing loss, the most prevalent etiology was otitis media with effusion (OME), accounting for 47.5% of cases, followed by acute suppurative otitis media (ASOM) in 32.8% of cases. Chronic suppurative otitis media (CSOM) was observed in 12.7% of cases, while otitis externa was found in 4.8% of cases. The least common cause of conductive hearing loss was traumatic tympanic membrane (TM) perforation, seen in only 1.6% of cases (Table 4).

TABLE 1: Distribution of cases based on both age and gender

AGE	MALE	FEMALE	TOTAL NO. OF CHILDREN
0 to ≤2 YEARS	8	10	18
>2 to ≤4 YEARS	44	33	77
>4 to 6 YEARS	32	23	55
TOTAL	84	66	150

In this present study, 8 males and 10 females were in age group of 0 to d”2 years, 44 males and 33 females in age group of >2 to d”4 years. 32 males and 23 females were in age group of >4 to 6 years.

Table 2: Distribution of cases based on socioeconomic class

SOCIOECONOMIC CLASS	CHILDREN N(%)
UPPER	0 (0)
UPPER MIDDLE	12 (8)
LOWER MIDDLE	78 (52)
UPPER LOWER	42 (28)
LOWER	18 (12)
TOTAL	150 (100)

In the present study according to the modified Kuppuswamy scale, 78 (52%) cases were of lower middle class followed by upper lower class with 42 (28%) cases. However, 18 (12%) cases belonged to lower class followed by upper middle class with 12 (8%) cases.

Table 3: Distribution of cases based on type of hearing loss

TYPE OF HEARING LOSS	CHILDREN N(%)
CONDUCTIVE	63 (42)
SENSORINEURAL	87 (58)
TOTAL	150 (100)

In the present study, 87 (58%) children had sensorineural hearing loss and 63 (42%) children had conductive hearing loss.

Table 4: Etiological distribution of conductive hearing loss

RISK FACTORS	FREQUENCY N(%)
OME (OTITIS MEDIA WITH EFFUSION)	31 (49.2%)
ASOM (ACUTE SUPPURATIVE OTITIS MEDIA)	20 (31.7)
CSOM (CHRONIC SUPPURATIVE OTITIS MEDIA)	8 (12.7)
OTITIS EXTERNA	3 (4.8)
TRAUMATIC TYMPANIC MEMBRANE (TM) PERFORATION	1 (1.6)
TOTAL	63 (100)

In the present study, OME was observed as the most common etiology for conductive hearing loss in children with 31 (49.2%) cases followed by ASOM in 20 (31.7%) cases. CSOM was observed in 8 (12.7%) cases followed by otitis externa in 3 (4.8%) cases. While the least common etiology observed was traumatic TM perforation observed in 1 (1.6%) cases.

Among the 87 cases (58%) of sensorineural hearing loss, 10.3% of children had a history of neonatal meningitis, 9.2% had a history of fever, 8% had a history of hyperbilirubinemia, and 6.8% were born with low birth weight for gestational age (LBW for GA). However, the largest group, consisting of 37.9% of children, had sensorineural hearing loss with unknown causes (Table 5).

The child's hearing sensitivity was assessed according to World Health Organisation (WHO) degree of hearing impairment as follows: [14]

Normal	-	d+25	dBHL
Slight/Mild	-	26-40	dBHL
Moderate	-	41-60	dBHL
Severe	-	61-80	dBHL
Profound	-	e"81	dBHL

The study result revealed that among the cases, 36% had a mild degree of hearing loss, 10.7% had a moderate degree, 11.3% had a severe degree, and the highest proportion of 42% had a profound degree of hearing loss (Table 6).

Discussion

Hearing plays a crucial role in the initial stages of spoken language, reading, and learning. For young children, consistent exposure to listening experiences is vital for the development of speech and language skills, establishing a strong foundation for successful reading. Early intervention in children with hearing challenges can significantly reduce developmental setbacks. Therefore, it is essential to conduct hearing screenings for all children at birth to enable early detection and prompt intervention.

The average age of the children presenting with symptoms was found to be 3.80±1.22 years. The largest proportion of cases, 51.5%, belonged to the age group of >2 to d"4 years, followed by 36.7% in the >4 to 6 years age group, and the smallest number of

Table 5: Etiological distribution of sensorineural hearing loss

RISK FACTORS		CHILDREN N(%)
ANTENATAL	H/O INFECTION TO MOTHER	2 (2.3)
	H/O USE OF OTOTOXIC DRUGS BY THE MOTHER DURING PREGNANCY	4 (5)
	BIRTH ASPHYXIA	2 (2.3)
PERINATAL/INTRANATAL	PROLONGED/ OBSTRUCTED LABOUR	5 (5.7)
	LBW FOR GA	6 (6.8)
	NEONATAL SEPTICEMIA	3 (3.4)
POSTNATAL	NEONATAL MENINGITIS	9 (10.3)
	HYPERBILIRUBINEMIA	7 (8)
	OTOTOXIC MEDICATIONS	2 (2.3)
	HISTORY OF FEVER	8 (9.2)
	HEAD INJURY	5 (5.7)
SOCIAL HISTORY	FAMILY HISTORY	1 (1.1)
NO IDENTIFIABLE RISK FACTOR		33 (37.9)
TOTAL		87 (100)

Out of 87 cases of sensorineural hearing loss, 9 (10.3%) children had history of neonatal meningitis, 8 (9.2%) children had history of fever, 7 (8%) had history of hyperbilirubinemia while, 6 (6.8%) children presented as low birth weight for gestational age. However, majority of 33 (37.9%) children were reported to have unknown causes of sensorineural hearing loss

Table 6: Distribution of cases according to the degree of hearing loss

GRADES	FREQUENCY N(%)
MILD	54 (36)
MODERATE	16 (10.7)
SEVERE	17 (11.3)
PROFOUND	63 (42)
TOTAL	150 (100)

In our analysis, mild degree was observed in 54 (36%) cases, moderate degree in 16 (10.7%) cases, severe degree in 17 (11.3%) cases and profound degree was observed in maximum of 63 (42%) cases.

cases, 12%, were in the 0 to d”2 years age group. Detecting hearing loss at an early age is crucial for the management and rehabilitation of deaf children. Early detection can significantly prevent deaf mutism and improve outcomes for the affected children.

In our study involving 150 children, 56% were males, and 44% were females. The male-to-female ratio among children with hearing loss was found to be 1.3:1, which aligns with a similar study conducted by Dippen et al on 60 infants, where the male-to-female ratio was also 1.3:1 [15]. It was observed that there was a slightly higher number of male patients than female patients in our study. This difference could be attributed to increased attention given by parents to male children. However, as the patients were randomly selected, this variation is likely due to chance. The prevalence of male predominance in hearing loss cases is commonly reported in the literature by various other authors as well, including Doifode PV et al, Bhadauria et al, Aiyer RG et al, and Singh M et al [16-19].

The sociodemographic profile of the cases in our study revealed that 67.8% of the children belonged to a rural background, while 32.7% came from an urban background. This difference in distribution can be attributed to factors such as illiteracy, poor sanitary conditions, inadequate personal hygiene, and overcrowding in rural areas, which contribute to a higher incidence of diseases among rural populations. The variation may also result from a lack of awareness about the disease among rural communities, limited healthcare facilities, restricted access to medical services, and a lack of proper referral services to specialized centres.

In another study conducted by Parvez A et al at Aligarh, it was found that 13.5% of cases in the urban group had hearing loss, whereas 18.8% of cases in the rural group were affected [20]. This observation is consistent with our study, where the occurrence of hearing loss was higher among rural children compared to those in urban areas.

In our study, the majority of cases, 52%, belonged to the lower middle class, followed by 28% in the upper lower class, based on the modified Kuppuswamy scale. Among the parents of the children included in the study, skilled workers constituted the largest group with 31.3%, followed by clerical/farmer/shop owner with 30%. Additionally, 18.7% of parents were unskilled workers, 14.7% were semi-skilled workers, and 3.3% were unemployed. In terms of education, most parents of the children, 38.7%, had completed high school, while 28.7% had middle school education, and 10.7% were illiterate.

This observed pattern might be due to a lack of awareness among parents regarding hearing loss in their children. It highlights the need to study the sociodemographic profile of preschool children to plan and deliver appropriate facilities effectively. Early diagnosis of hearing impairment is crucial, especially since people from lower socioeconomic classes and rural areas are often unaware of available rehabilitative measures in society. Poverty can also contribute significantly to their lack of knowledge.

Similarly, Parvez A et al conducted a study where they found that 30% of the children came from families belonging to the lower socioeconomic class, 25% from the lower middle class, 20% from the upper middle class, 13.33% from the middle class, and 11.67% from the upper class. [20].

In our study, sensorineural hearing loss was found to be more prevalent, accounting for 58% of cases, while conductive hearing loss constituted 42% of cases. The majority of subjects came from economically disadvantaged families and were involved in manual occupations. Many of them sought handicap certificates or were referred from primary health care centres, indicating a low level of awareness among parents regarding available support for their children.

Similarly, Adegbiji WA et al also reported that sensorineural hearing loss was the most common type, with 61.4% of cases, followed by conductive hearing loss (27%) and mixed hearing loss (12%) [21].

In our study, OME was the most common cause of conductive hearing loss in children (49.2%), followed by acute suppurative otitis media (ASOM) in 31.7% of cases. Traumatic tympanic membrane (TM) perforation was the least common cause (1.6%). Among children with sensorineural hearing loss, neonatal meningitis was the most common etiological factor (10.3%), followed by fever (9.2%), hyperbilirubinemia (8%), and low birth weight for gestational age (6.8%). A significant proportion of cases (37.9%) had unknown causes of sensorineural hearing loss.

Other studies have also reported similar findings regarding the etiological causes of hearing impairment in children, with otitis media, neonatal jaundice, febrile illness, birth trauma, and maternal infections being identified as potential risk factors [22].

Gutierrez-Farfan et al found that risk factors such as hypoxia, prematurity, low birth weight, ototoxic drugs, jaundice with exsanguineous-transfusion, meningitis, jaundice treated with phototherapy, and maternal infections were related severe to profound sensorineural hearing impairment in children under 3 years of age [23]. Samdi MT et al also reported that 73.20% of children had predisposing risk factors, with febrile illness being the most common risk factor, followed by middle ear infections [24]. The presence of risk factors significantly affects the auditory system and can lead to hearing impairment, but it can also occur in the absence of identifiable risk factors, emphasizing the importance of universal hearing screening programs.

Regarding the degree of hearing loss, our study observed a distribution of 36% mild, 10.7% moderate, 11.3% severe, and 42% profound degrees of hearing loss. Archbold et al noted that children with mild to moderate hearing loss are less likely to be diagnosed at early ages due to their developing speech and language skills being intelligible to teachers [25]. Consequently, they may go unnoticed and receive less support from school or health professionals compared to children with severe or profound hearing impairments.

The presence of risk factors significantly affects the auditory system and can lead to hearing impairment, but not all cases of hearing impairment are associated with identifiable risk factors. Therefore, there is a need for universal hearing screening programs to ensure early detection and intervention.

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CASE REPORT

Fatal Barium Aspiration Pneumonitis: A Case Report

Yatin Gupta[1], N. P. Singh[2], Anoop Chhabra[1]

Abstract

Barium Aspiration Pneumonitis is an infrequent complication which may occur inadvertently during examination of the upper gastrointestinal system with barium study using contrast media. Owing to relatively non-irritant nature of barium sulphate, its aspiration is unlikely to cause severe lung injury. However, though rarely, large amounts of barium sulphate are aspirated accidently which may result in inflammation or rarely even death.

Here we present the case of a patient who had fever and difficulty in swallowing. For dysphagia, a radiographic contrast study with barium sulphate was done. Accidently the patient aspirated a large amount of the radiographic medium and became dyspneic. Chest X-rays showed multiple patchy and confluent radio opacities in bilateral lung fields and linear radio opacities along the tracheal and bronchial line. X-ray findings were suggestive of post procedural aspiration of barium contrast. Patient was shifted to MICU and was intubated but the next day evening patient developed hypotension. He was put on vasoconstrictors but developed cardiac arrest and could not be revived.

Key words: Barium swallow, barium sulphate, aspiration pneumonitis

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Introduction

Barium sulphate, a radiographic contrast medium, is a relatively insoluble salt of barium. Barium swallow is a common routine procedure adopted for examination of the oropharynx and esophagus [1]. During upper-gastrointestinal radiographic contrast procedure, rarely large amounts of barium sulphate are inadvertently aspirated into the lung which may result into complications like airway obstruction, chemical pneumonitis, lung injury and even death.

We report a rare case of fatal barium aspiration pneumonitis in a 75-year-old female who initially presented to the otolaryngology department with complaints of fever and difficulty in swallowing. A barium swallow study was performed to evaluate dysphagia, during which the patient accidentally aspirated a large amount of contrast medium and developed acute dyspnea. She was immediately transferred to the emergency ward, where detailed clinical evaluation and investigations were carried out, and supportive therapy was initiated. Despite treatment, her condition progressively worsened, necessitating transfer to the medical intensive care unit (MICU) and endotracheal intubation. However, her respiratory distress and hemodynamic instability continued to deteriorate and by the following evening, she suffered cardiac arrest and could not be revived despite resuscitative efforts.

Case Report

We present the case of a 75-year-old female patient who initially presented in the outpatient department of Otolaryngology with the complaints of fever and difficulty in swallowing. The patient was evaluated for dysphagia. Her laryngoscopic examination showed everything within normal limits. Thereafter, a radiographic contrast study by way of barium swallow test was done to assess the condition of oesophagus but unfortunately a large amount of the barium contrast accidently got aspirated into the airways and lungs and the patient became dyspnoeic.

The patient was immediately shifted to the casualty ward where the patient was attended by a team of General Physicians. Patient gave the history of low-grade intermittent fever, cough with expectoration and difficulty in swallowing for the last five days. There was no history of orthopnea or hemoptysis. There was no past history of tuberculosis, diabetes mellitus, bronchial asthma, hypertension or any other chronic illness. However, she gave the history of use of chullah (Wood fueled stove) for cooking.

On Examination the patient was found to have B.P. 90/76 mm Hg, Pulse Rate 118/mt., SPO_2 86% on room air and 94% with 3L of oxygen, Resp rate 22/mt. On auscultation crepitations were heard in both lungs while heart appeared normal. She was conscious and well oriented.

Investigations

Sputum Exam.	AFB -ve, CBNAAT -ve
CBC	Within Normal Limits
ABG Analysis	PH 7.268, PCo_2 44.6 mm Hg, Spo_2 80%
Kidney Function Test	Blood Urea 120.0 H mg/dl, Creatinine1.6 H mg/dl
Liver function Test	Bilirubin 1.4H mg/dl, AST 64 U/L , ALT 27 U/L
Serum Electrolytes	Within Normal Limits
ESR	06 mm Ist Hr
X-Ray PA view	Showed multiple patchy and confluent radio opacities in bilateral lung fields, predominantly in right upper and right middle zones with subpleural sparing. Linear radio opacities were seen along the tracheal and bronchial line. Findings were suggestive of post procedural aspiration of barium contrast (Fig.1). **However, CT Chest was not in view of the precarious condition of the patient.**
Barium Swallow	A thick bolus given and serial films taken after deglutition but during the test, the patient inhaled barium contrast medium into the bronchial tree. Both lungs, valleculae and pyriform fossae appeared normal. No evidence of irregularity or filling defect seen in thoracic oesophagus. Gastro-oesophageal function appeared normal. No evidence of reflux or hiatus hernia seen. Radio-opacification seen along the trachea, bronchi and its lobar branches, likely to be due to barium aspiration. No significant oesophageal abnormality seen in barium study.

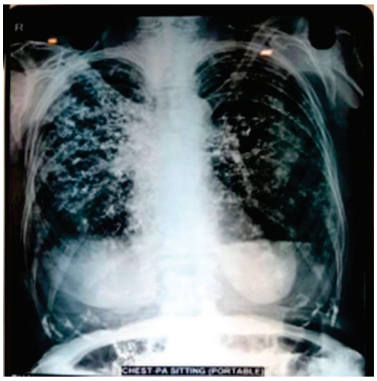

Figure 1: Fatal Barium Aspiration Pneumonitis: A Case Report

Treatment

Patient was immediately put on IV fluids, IV antibiotics, oxygen support and other supportive measurements but the measures proved inefficacious. In the evening patient's condition deteriorated further and she developed increasing respiratory distress and ABG was suggestive of Type 2 respiratory failure and the Patient was shifted to MICU and was put on non- invasive mechanical ventilation but the patient was unable to maintain saturation on Bipap support. She had altered sensorium and her respiratory rate was persistently more than 40/mt. Later in view of increasing respiratory distress, patient was intubated and put on ventilator but the next day evening patient developed hypotension for which inotropic support was started but patient developed cardiac arrest but could not be revived. Patient was managed as per ACLS protocol.

Discussion

Barium swallow is a commonly practiced investigation for upper gastrointestinal examination. Barium sulphate is an inert material and is widely used to visualize anatomy and to reveal abnormalities in the gastrointestinal tract. Oral intake of Barium sulphate is usually harmless unless it is aspirated in large amounts. This investigation - technique is considered to be a safe procedure. However, during contrast studies of upper gastrointestinal tract, barium sulphate may accidentally be aspirated into the lungs and this is a well-established complication during such studies [2]. However, rarely barium may be aspirated during upper gastrointestinal examination which may lead to complications and even death [3,4]. If aspirated it may give rise to anaphylactic shock, airway obstruction, chemical pneumonitis, long term lung injury, clinical decompensation and even death [5,6]. In the hospital population, the overall incidence of aspiration pneumonia is estimated to be nearly 8 in 1000, but 40% of such cases remain asymptomatic and are detected incidentally [7]. The mortality rate in cases of massive barium aspiration is around 30% and it may exceed to 50% in patients having initial shock or apnoea, adult respiratory distress syndrome or secondary pneumonia [8]. However, the exact incidence is not known. Depending on the severity of the reported cases, incidence has been reported in the world literature either as rare [9,10] or frequent [11].

The gravity of complications is proportional to concentration and amount of barium aspirated. Severity of complications also depends upon anatomy of upper gastrointestinal tract and predisposing factors [6]. So, we should calculate the dose and volume of barium very precisely before administration and we should avoid this study in patients having predisposing risk factors like head and neck cancer, frequent aspirations etc. Here we should resort to alternative study measures [6,12]. We don't have appropriate treatment for Aspiration pneumonitis and we have to keep the patient on supportive therapy like oxygen supplementation, intravenous fluids and antibiotics to avoid superimposed infections [6,12].

The predisposing factors for the occurrence of aspiration might be alcoholism [10], the extremes of age [11] disordered swallowing, neuromuscular dysfunction, broncho-esophageal fistula [13], head and neck cancer and psychological illness. Psychological illness is usually associated with functional gastrointestinal disorders [14]. We should focus on early recognition of the predisposing factors, pre-treatment with antireflux medications, such as domperidone or omeprazole, and correct choice of contrast media. Unlike barium sulphate, iopydol (Hytrast®), normally used for bronchography, demonstrates no pulmonary harm [15].

For prevention of accidental barium aspiration, a check list of preventive measures is recommended:

1. To recognise the predisposing factors and to manage the

underlying risk factors

2. To give pre-treatment with antireflux medications if needed
3. To choose the correct type of contrast medium
4. To maintain proper positioning of the patient while undertaking barium swallow study. Make the patient sit upright or elevate the head end of the bed between 30 to 45 degrees during and after the procedure
5. **To avoid distractions like talking, watching on mobile etc. during the procedure. 6. To keep ready to handle unexpected events This check list is a takeaway message for the clinicians to reduce such a rare but fatal complication.** Fatal Barium Aspiration Pneumonitis is usually seen when barium swallow investigation is done in patients having predisposing risk factors. Contrast study in our patient showed no evidence of irregularity or filling defect in thoracic oesophagus, reflux or hiatus hernia and the study showed Gastro-oesophageal function also to be normal. Our case is rare and unique as barium aspiration occurred despite being having no predisposing factors and becomes still rarer as barium swallow proved fatal.

Conclusion

Barium swallow tests are done in patients with symptoms of dysphagia, swallowing disorders and the like. Before performing the test, we should review the general physical condition of the patient and rule out any predisposing factors. In case there is any predisposing factor, we should avoid barium swallow and resort to alternative study measures.

Complications of barium sulphate aspiration occurs due to use of inaccurate density and quantity of barium sulphate solution, the extent of tracheobronchial distribution and the general physical condition of the patient. So, we should use correct concentration and correct quantity of barium sulphate for this investigation.

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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

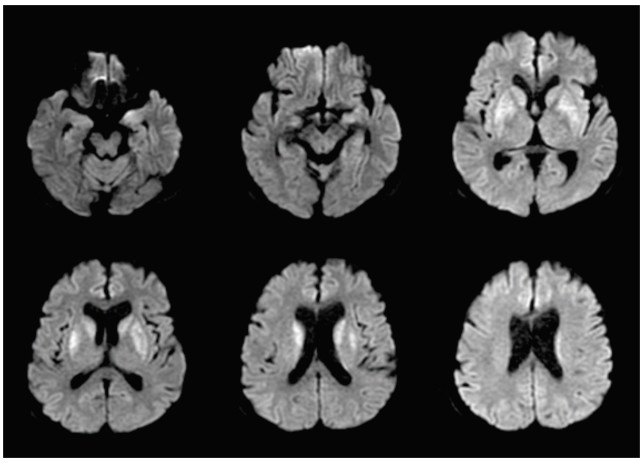

Fig. 1: MRI image of west nile encephalitis showing diffusion restriction in bilateral caudate and putamen

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.

Conflict of Interest:	Author declare no COI
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