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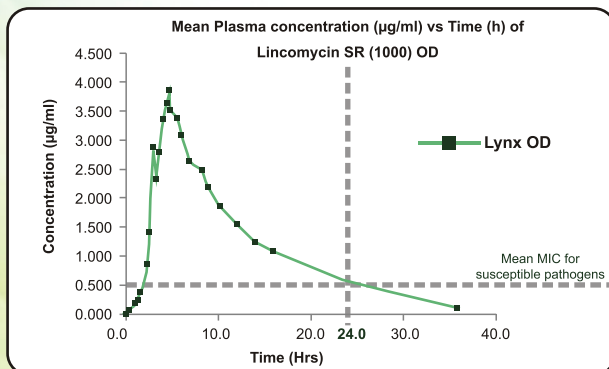
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We are really grateful to **Dr. R. V. Asokan**, our beloved National President and **Dr. Anilkumar J. Nayek**, our Hony. Secretary General for round the year support to JIMA Committee.

I express my heartfelt gratitude to all the JIMA Committee members, the Reviewers and Staffs of JIMA for this historical achievement of JIMA.

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5527	Journal of the History of Medicine and Allied Sciences	J. Hist. Med. Allied Sci.	00225045	14684373
5528	Journal of the History of the Behavioral Sciences	J. Hist. Behav. Sci.	00225061	15206696
5529	Journal of the History of the Neurosciences	J. Hist. Neurosci.	0964704X	17445213
5530	Journal of the Hong Kong College of Cardiology	J. Hong Kong Coll. Cardiol.	10277811	
5531	Journal of the Indian Chemical Society	J. Indian Chem. Soc.	00194522	
5532	Journal of the Indian Medical Association	J. Indian Med. Assoc.	00195847	
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CONTENTS

## Artificial Intelligence In Medical Sciences

Artificial Intelligence (AI) is defined as ‘a field of science and engineering concerned with the computational understanding of what is commonly called intelligent behaviour, and with the creation of artefacts that exhibit such behaviour’<sup>1</sup>. In today’s world, Artificial Intelligence (AI) is playing a crucial role in revolutionizing various industries, including healthcare. A recent study revealed that AI can perform medical interviews and provide diagnoses based on a patient’s medical history, potentially transforming the healthcare industry. This development can help doctors make more accurate diagnoses and provide better treatment options to patients.

AI can analyze vast amounts of data and identify patterns humans might miss. This ability of AI can help healthcare professionals detect diseases at an early stage, which can save lives. Moreover, AI can help create personalized patient treatment plans by considering their medical history, genetics, lifestyle, and other factors.

Alongside diagnostic capabilities, AI makes headway in unexpected areas such as human interaction. AI-powered assistants can provide emotional support to patients, which can help improve their mental health and well-being. Additionally, AI-powered technologies can help improve communication between healthcare professionals and patients, enhancing the overall quality of care (Fig 1).

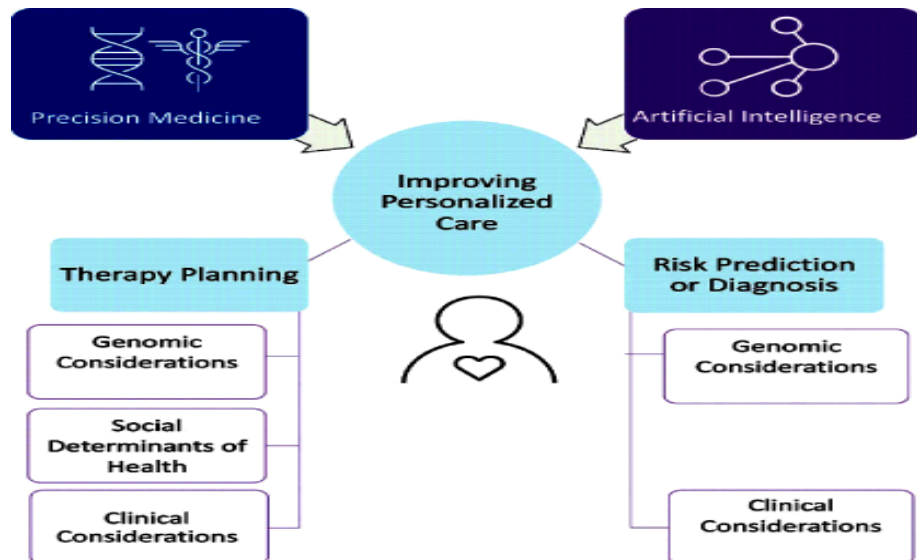


Fig 1 — AI and precision medicine collaborate to enhance personalized care by Leveraging Clinical, Genomic, Social and Behavioral Health Factors

### A Better Bedside Manner ?

Articulate Medical Intelligence Explorer (AMIE) is a chatbot designed to communicate with patients and provide them with medical advice. In a recent study, AMIE was tested against human doctors to assess its empathy and conversation quality performance. The study found that AMIE outperformed physicians in 24 out of 26 criteria for conversation quality. This means that the chatbot could provide patients with a similar level of empathy and support as human doctors, and in some cases, even better.

This is a significant development in the healthcare field, as it suggests that AI-powered chatbots like AMIE can support patients in ways that human doctors may be unable to. For example, AI chatbots can provide patients with 24/7 medical advice, which is not always possible for human doctors who have limited availability. Additionally, AI chatbots can analyze vast amounts of patient data to provide personalized medical advice, which can be difficult for human doctors to do promptly.

Overall, the results of this study are promising and suggest that AI-powered chatbots like AMIE have the potential to revolutionize the healthcare industry by providing patients with more accessible and personalized medical advice.

### AI for better Accessibility :

AI has the potential to improve healthcare access in remote or underserved areas. AI-powered telemedicine enables patients receive medical advice from doctors and specialists without needing physical visits or travel at any time and from anywhere. This can significantly benefit patients who might not otherwise have access to medical care due to distance or other barriers.

AI can also help streamline the healthcare process by automating routine tasks, simplifying administrative procedures, and reducing waiting times. For instance, AI-powered chatbots can help patients book

appointments, manage prescriptions, and ask medical questions without human intervention. This can save time and resources for healthcare providers and improve the patient experience.

Moreover, AI can aid healthcare professionals in diagnosing and treating diseases accurately and efficiently. AI algorithms can analyze medical images, detect patterns, and provide insights that might be difficult for human experts to see. This can help doctors make more informed decisions and improve patient outcomes.

### Diagnostics and drug discovery with AI :

AI has become an increasingly valuable tool in the healthcare industry. One of its most notable applications is diagnosing complex diseases like skin cancer. In recent years, AI-powered deep-learning models have been developed to assist dermatologists and doctors in identifying skin lesions. These models have been trained on tens of thousands of images, allowing them to improve diagnostic accuracy.

AI algorithms can analyze vast amounts of genetic information, clinical trial results, and patient history. This allows them to detect patterns and relationships that may not be immediately apparent to humans. Using this approach, researchers have discovered new medications and treatments for various conditions, including cancer and multiple myeloma.

Thanks to AI, researchers have identified new drug targets and designed more effective drugs targeting the underlying mechanisms of different diseases. This breakthrough may lead to better outcomes and quality of life for patients.

AI-powered systems can assist healthcare professionals in creating personalized treatments and therapies for patients based on their genetic makeup and medical history. This customized approach to treatment can result in improved patient outcomes as they receive treatments tailored to their specific needs and characteristics (Fig 2).

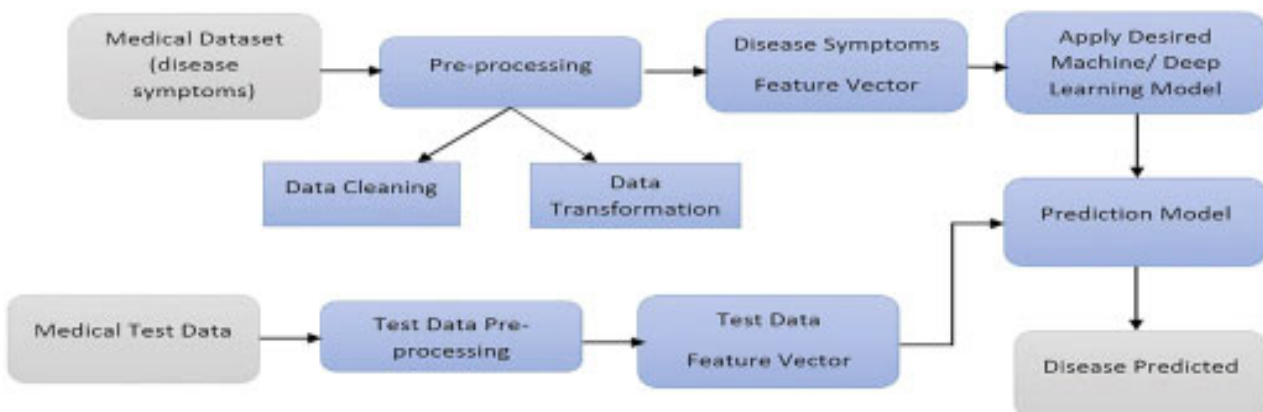


Fig 2 — Framework for an AI disease detection system

## DIAGNOSIS

ANNs have been used in the clinical diagnosis, image analysis in radiology and histopathology, data interpretation in intensive care setting and waveform analysis.

Stamey, *et al*<sup>2</sup> developed a neural network derived classification algorithm called Prostate Index which can classify prostates as benign or malignant. This model which was subsequently validated in prospective studies had a diagnostic accuracy of 90%, with a sensitivity of 81% and specificity of 92%. Some of the other surgically relevant diagnostic applications of ANNs include abdominal pain and appendicitis<sup>3</sup>, retained common bile duct stones, 4 glaucoma, 5 and back pain<sup>6</sup>.

ANNs have also been used in diagnosing cytological and histological specimens. PAPNET, a computerised automated screening system based on neural networks, has been developed to assist the cytologist in cervical screening and is one of the few ANN models which was promoted commercially.<sup>7</sup> Breast,<sup>8</sup> gastric, 9 thyroid,<sup>10</sup> oral epithelial cells,<sup>11</sup> urothelial cells,<sup>12</sup> pleural and peritoneal effusion cytology<sup>13</sup> have all been subjected to analysis by neural networks with varying degree of success. In radiology, it is possible to use both human observations and direct digitised images as inputs to the networks. ANNs have been used to interpret plain radiographs,<sup>14</sup> ultrasound,<sup>15</sup> CT,<sup>16</sup> MRI,<sup>17</sup> and radioisotope scans<sup>18</sup>.

ANNs pattern recognition ability has been used to analyse various wave forms including the interpretation

of ECGs to diagnose myocardial infarction,<sup>19</sup> atrial fibrillation,<sup>20</sup> and ventricular arrhythmias.<sup>21</sup> Analysis of Electro-encephalograms (EEG) by neural networks has led to its application in the diagnosis of epilepsy<sup>22</sup> and sleep disorders.<sup>23</sup> They have also been trained to analyse Electromyographic (EMG)<sup>24</sup> and Doppler ultrasound<sup>25</sup> wave forms as well as haemodynamic patterns in intensive care patients.<sup>26</sup>

### Drawbacks of Medical AI :

When considering the use of AI in healthcare, it is crucial to remember that although it may provide more accurate diagnoses than some doctors, it cannot replace the personal connection that patients can experience from face-to-face interactions. Patients often require more than accurate diagnoses and effective treatments; they also need emotional support and understanding from their healthcare providers. Without the human touch, patients may feel isolated,

anxious, and even depressed. Therefore, it is essential to balance the use of AI with the importance of human relationships in healthcare.

With the increasing use of AI technology in healthcare, there is a growing concern about the possibility of conveying misinformation to patients through these tools. This can happen for various reasons, such as incorrect data input or flawed algorithms. Patients may receive inaccurate information from AI tools, which can sow confusion, mistrust, and frustration, ultimately damaging the relationship between patients and physicians.

Continuous monitoring and evaluation of the AI tools' performance can help identify and rectify errors or biases, enhancing the effectiveness and reliability of the tools. It is essential to conduct comprehensive testing and validation to ensure these systems are safe and effective before implementing them in clinical care. Regulatory bodies such as the World Health Organization have issued guidelines for developing and evaluating AI in healthcare to ensure that AI algorithms remain transparent, explainable, and impartial.

However, despite these guidelines, the results of studies with AI systems have not yet been peer-reviewed, which means there is still uncertainty about their safety and efficacy. Therefore, it is crucial to proceed with caution and continue to monitor the use of AI in healthcare. This will help ensure that the technology is not only accurate, but also safe, effective, and ethical.

### A Future Fueled by Technological Innovations :

As research in the field of healthcare advances, the potential benefits of AI in the healthcare industry are becoming increasingly evident. AI can revolutionize healthcare in several ways, such as improving diagnoses and drug recommendations, which can save lives and reduce healthcare costs. With further research and development, AI systems could be designed to detect early signs of diseases and monitor patients' health in real-time, providing patients with better health outcomes and greater peace of mind.

Although the use of AI in healthcare is associated with specific challenges like ethical considerations and privacy concerns, the potential benefits are too significant to be ignored. As AI technology evolves, it will likely become a standard healthcare tool. This would enhance diagnostic accuracy, provide timely and cost-effective care to patients, and offer greater peace of mind to everyone involved.

Looking towards the future of healthcare, we have



## Original Article

# Comparison of Effect of Exercise on Lipid Profiles of Overweight Normoglycemic Offspring of T2DM Parents and Non-diabetic Parents

Emmanuel Olagboye Taiwo<sup>1</sup>

**Background :** The primary causes of Type 2 Diabetes Mellitus (T2DM) are largely unknown but abnormal lipid profile has been reported to be a risk factor for the T2DM through the alteration of lipid profile pattern.

**Aims and Objectives :** This study was designed to assess the effect of exercise on Lipid Profile (LP) on offspring of T2DM parents compared with offspring of Non-diabetic parents.

**Discussion :** This study involved 60 Offspring of T2DM parents (OODP) attending University College Hospital, Ibadan and 60 offspring of Non-diabetic parents (OONDP) who are undergraduate students of the University of Ibadan, Nigeria. Participants were randomly assigned into the two groups. Each participant followed a protocol of graded exercise using "tummy trimmer" everyday spending 45 minutes daily for 24 weeks. Blood samples were obtained after an overnight fasting for determination of lipid level using standard methods at baseline and at 24 weeks. Data were analyzed using descriptive statistics and student t test with significance at  $p < 0.05$ .

**Results :** The most populated aged group was 26 to 35 years of which 47.3% ( $n=26$ ) were OODP and 52.7% ( $n=29$ ) were OONDP. However, all subjects were overweight with mean BMI of OODP and OONDP ( $29.30\text{kg/m}^2 \pm 0.71$  versus  $26.37\text{kg/m}^2 \pm 0.88$ )  $p=0.035$  In OODP, the mean Total Cholesterol (TC) reduced significantly from  $131.29\text{mg/dl} \pm 1.29$  to  $123.90\text{ mg/dl} \pm 6.65$   $p < 0.001$  after 24 weeks of exercise. In OONDP, the mean TC also reduced significantly from  $156.12\text{ mg/dl} \pm 6.38$  to  $147.73\text{ mg/dl} \pm 5.93$   $p < 0.001$  after six months of exercise.

**Conclusions :** Serum Lipid improved after 24 weeks of exercise in the two groups. There was reduction of triglyceride and LDL- cholesterol while HDL-cholesterol increased.

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**Key words :** Exercise, Body Mass Index, Lipid Profile, Offspring of Diabetics, Offspring of Non-diabetics.

Diabetes mellitus, commonly known as diabetes, is a disorder of intermediary carbohydrate, protein and lipid metabolism. It is characterized by hyperglycemia, glucosuria, polydipsia, polyuria, polyphagia and weight loss. It is usually associated with secondary alterations in glucose, fat and protein metabolism, leading to many biochemical disorders. It is characterized by peripheral insulin resistance, impaired regulation of hepatic glucose production with declining  $\beta$ -cell function and eventually leading to  $\beta$ -cell failure<sup>1</sup>. Type 2 Diabetes Mellitus (Type 2DM) is characterized by a combination of peripheral insulin resistance and inadequate insulin secretion by pancreatic beta cells. Insulin resistance has been attributed to elevated levels of free fatty acids and pro-inflammatory cytokines in plasma, leading to reduced glucose transport into muscle cells, elevated hepatic glucose production, and pronounced break down of fat<sup>1</sup>.

Obesity at younger age, significantly increased

<sup>1</sup>MBBS, MSc, MD (Ibadan), Lecturer, Department of Physiology, Olabisi Onabanjo University, Sagamu, Osun, Nigeria and Corresponding Author

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### Editor's Comment :

- The primary causes of Type 2 Diabetes Mellitus (T2DM) are largely unknown but abnormal lipid profile has been reported to be a risk factor for the T2DM through the alteration of lipid profile pattern.
- This study was designed to assess the effect of exercise on Lipid Profile (LP) on offspring of T2DM parents compared with offspring of non-diabetic parents.
- This study involved 60 Offspring of T2DM parents (OODP) attending University College Hospital, Ibadan and 60 offspring of Non-diabetic parents (OONDP) who are undergraduate students of the University of Ibadan, Serum Lipid improved after 24 weeks of exercise in the two groups. There was reduction of triglyceride and LDL- cholesterol while HDL-cholesterol increased.

lifetime risk of Type 2 Diabetes Mellitus (T2DM)<sup>1</sup>. Family history of T2DM is associated with higher Body Mass Index (BMI), Dyslipidemia and Impaired Glucose Tolerance (IGT) in offspring<sup>2,3</sup>. There seems to be a vicious cycle, where obesity increases risk for T2DM and a family history of T2DM increasing the risk for obesity<sup>1,4</sup>. Parental history of T2DM is one of the dominant risk factors for development of T2DM<sup>5</sup>. The phenotype varies depending on which parent is affected and if the child was exposed to hyperglycemia in utero<sup>5,6</sup>.  $\beta$ -cell dysfunction has been

observed even in non-diabetic offspring of T2DM, more accentuated among those with maternal T2DM compared to paternal inheritance<sup>7</sup>. Here we report the effect of exercise on lipid profile in normoglycemic subjects.

In diabetes many factors may affect blood lipid levels, because of interrelationship between carbohydrates and lipid metabolism. Therefore, any disorder in carbohydrate metabolism leads to disorder in lipid metabolism and vice versa. Insulin resistance is a primary defect in the majority of patients with T2DM. In non-diabetic individuals insulin resistance in combination with hyperinsulinemia has a strong predictive value for future development for type 2 diabetes<sup>8</sup>. Several studies showed that insulin affects the liver apolipoprotein production and regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein, which causes dyslipidemia in diabetes mellitus. Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active lipoprotein lipase<sup>9,10</sup>. Hypertriglyceridaemia usually accompanies decreased HDL cholesterol, which is also a prominent feature of plasma lipid abnormalities seen in individuals with diabetes<sup>11,12</sup>. The cluster of lipid abnormalities associated with T2DM is defined by a high concentration of TG and small dense LDL and a low concentration of HDL cholesterol. The association between reduced HDL cholesterol levels and increased risk of heart disease is, on the other hand, well established, independently of TG levels and other risk factors<sup>13,14</sup>. The possible mechanism responsible for hypertriglyceridaemia may be due to increased hepatic secretion of Very Low Density Lipoprotein (VLDL) and delayed clearance of triglyceride rich lipoproteins, which is predominantly due to increased levels of substrates for triglyceride production, free fatty acids and glucose<sup>15</sup>.

Individuals who are obese are at high risk of developing T2DM, particular if a close family member is affected with T2DM. Researchers have not yet discovered a specific gene that causes obesity although, several genes are considered to play a role. There seems to be a connection between abdominal fat and diabetes, hence anything that will reduce abdominal fat will likely reduce diabetes<sup>2</sup>. Exercise has been known to ameliorate the effect of diabetes by improving insulin sensitivity and lipid profile. It is the aim of this to work to compare the effect of exercise on lipid profile of overweight normoglycemic offspring of patients with type 2 DM and non-diabetic parents.

## MATERIALS AND METHODS

This is a prospective study of a cross-section of 120 randomly selected subjects. All subjects are from South-west, Nigeria. The parents of the test group (normoglycemic offspring of Diabetic Parents) were attending the Medical Out-patient clinic (MOP) of the University College Hospital (UCH), Ibadan and Catholic Hospital Oluyoro, Oke-Ofa, Ibadan, South Western, Nigeria. The control group, normoglycemic offspring of non-diabetic parents were randomly selected from the general population of Ibadan Community, Ibadan and undergraduate students of University of Ibadan.

Hypertensive and diabetic subjects were exempted from this study. The weight of subjects was recorded in kilograms (to the nearest 1.0 kg) without wearing any heavy clothing like a coat, jacket, shoes, or Agbada (a flowing wide-sleeved robe), using a calibrated bathroom scale (Soehnle Waagen GmbH and Co. KG, D 71540 Murrhardt/Germany) positioned on a firm horizontal surface. Height of subjects was measured in meters (to the nearest 0.1m) using a stadiometer. Subjects stood erect, without shoes and headgears, on a flat surface with the heels and occiput in contact with the stadiometer (Prestige HM0016D) (India). The bathroom weighing machine and stadiometer had the reliability test using Rasch modeling approach and Samuel Messick's method to test their validity. The Body Mass Index (BMI) was subsequently calculated using the formula: weight (kg)/ height<sup>2</sup> (m<sup>2</sup>). There were two groups of subjects [control OONDP and test group (OODP)]. Estimation of blood lipid levels was conducted in each of the subjects as described below. Blood samples were obtained after overnight fasting for determination of LP levels using standard methods, at baseline start of week 1 and after 24 weeks of exercise. The LP determined from the fasting blood was measured spectrophotometrically utilizing standard laboratory kits supplied by BIOLABO, France. Data were analyzed using descriptive statistics. Continuous variables were compared with student t test and level of significance set at P<0.05.

*The following definitions were utilized:* Underweight – BMI <18.5 kg/m<sup>2</sup>. Normal weight – BMI 18.5-24.9 kg/m<sup>2</sup>, Overweight – BMI 25.0-29.9 kg/m<sup>2</sup>, Obesity – BMI ≥30 kg/m<sup>2</sup>.

Tummy trimmer, a portable, aerobic exercise, lightweight equipment (European Home Choice Company, Lagos, Nigeria) was used for exercise in this study. It is an in-door aerobic equipment. It is compact and can fit right in the subject's hand-bag.



During each phase of exercise the Tummy trimmer, a portable lightweight equipment, is held at the two handles and the sole of the two feet are put inside the pedal rest while the subject assume different positions. The subject will then pull the tummy trimmer's spring towards himself or herself either while lying flat or sitting up on the floor or carpeted hard surface. Subject sits up with leg straight, leans his or her body backwards until completely lying back with head on floor. He/she returns to sitting position in harmonic fashion. The subjects were trained to start slowly and work up with repetition as she/he feels comfortable with harmoniously. The subject was trained to lie flat on floor, extend his/her legs straight up in the air. He will be keeping his/her back on the floor and raise lower legs without bending them. The subjects would later sit erect with legs straight horizontally, he/she raises handle to tummy height using arms only. Then finally, subject would lie flat on the floor while he/she bends knees up to his/her chest. He/she makes circular motion push feet up and then round towards the floor again. The different positions were observed for exercise period of 45 minutes (a video clip of the exercise procedure was shown to the subject before the commencement of the exercise). Each subject was instructed as follows: (1) He/she to undergo the 4 phases of exercise for 45minutes daily (in the evenings). (2) He/she to contact the researcher on cell phone anytime when he/she has any problems with the unit. (3) There were regular weekly cell phone calls made to each of the subjects by the research assistant to ensure compliance with exercise schedule.

Experimental interventional study was carried out in which blood sample was collected from subjects in the test group and the control group after an overnight fasting.

10ml of venous blood specimen was obtained from each subject into plain bottles. Separation of serum at centrifugal force of 3,000 rpm was carried out at IMRAT (Institute of Medical Research and Training) of the College of Medicine, University of Ibadan. The serum so obtained was stored at temperature not exceeding -20°C in a refrigerator at IMRAT until used for the determination of lipid profile.

#### Determination of Total Cholesterol (TC):

TC level was measured spectrophotometrically using standard laboratory chemical supplied by BIOLABO, France. The cholesterol formed reacts with oxygen in the presence of cholesterol oxidase to form 4-cholesten-3-one and hydrogen peroxide. The hydrogen peroxide formed reacts with phenol and 4-

amino-antipyrine in the presence of peroxidase to give aminoneimine (pinkish in colour) and water. The intensity of the pink/red colour formed is proportional to the cholesterol concentration. It was performed according to standard protocols.

#### Determination of HDL Cholesterol HDL-C:

HDL-C level was measured spectrophotometrically using standard lab kits supplied by BIOLABO, France. LDL contained in serum are precipitated by the addition of phosphotungstic acid and magnesium chloride. High-density Lipoproteins (HDL) which remain in the supernatant (obtained after centrifugation) react with the cholesterol reagent and proportionally with the cholesterol standard. It was conducted according to standard protocols. Determination of TG and LDL levels were also carried out according to standard protocols.

#### Sample size estimation :

This was performed using formula  $(Z_{1-\alpha}/2)^2 \times SD^2/d^2$  where Z= normal variant, d= 5.0%, Type 1 error was used with SD of 25 mg/dl of fasting blood glucose from previous study. Attrition was 25%. This is equal to

$$\frac{1.96^2(25)^2}{5.0^2} = 96$$

If we add 25% attrition (24) making a total of 120 subjects. Cochran's formula (1977).

#### Statistical Analysis :

Statistical analysis was done using SPSS version 15 software (Lead Technologies, Chicago, USA). The data were expressed as mean  $\pm$  SD for various continuous parameters studied.

The study was approved by the Teaching Hospital Ethics Committee (UI/UCH joint IRB) and Catholic Hospital Ethics Committee prior to its implementation.

#### RESULTS

There were 120 participants in the study. Each of the 2 group had 60 subjects each with equal number of males and females. The most populated aged group was 26 to 35 years of which 47.3% (n=26) were OODP and 52.7% (n=29) were OONDP. However, all subjects were overweight with mean BMI of OODP and OONDP (29.30kg/m<sup>2</sup>  $\pm$  0.71 versus 26.37kg/m<sup>2</sup> $\pm$ 0.88), p=0.035 significantly (Table 1).

In OODP, the mean TC reduced significantly from 131.29 mg/dl  $\pm$  1.29 to 123.90 mg/dl  $\pm$  6.65, p<0.001 at the end of exercise period (after the exercise). In OONDP, the mean TC reduced significantly from 156.12  $\pm$  6.38 to 147.73 mg/dl  $\pm$  5.93, p<0.001 after the exercise. In OODP male subjects, the mean TC reduced significantly from 120.90  $\pm$  7.71 to 117.20

mg/dl  $\pm$  7.07  $p$ <0.001 after the exercise. In female OODP, the mean TC reduced significantly from 140.73 mg/dl  $\pm$  13.97 to 130.00 mg/dl  $\pm$  10.95,  $p$ <0.001 after the exercise (Table 2).

In OODP, the mean HDL increased significantly from 32.95 mg/dl  $\pm$  3.57 to 42.57 mg/dl  $\pm$  3.82,  $p$ <0.001 after the exercise. In OONDP, the mean HDL increased significantly from 43.27 mg/dl  $\pm$  2.86 to 50.35 mg/dl  $\pm$  2.46,  $p$ <0.001 after the exercise. In OODP male subjects, the mean HDL increased significantly from 31.90 mg/dl  $\pm$  4.38 to 38.30 mg/dl  $\pm$  5.65  $p$ <0.001 after the exercise. In female OODP, the mean TC increased significantly from 33.91  $\pm$  5.72 to 46.45 mg/dl  $\pm$  5.15,  $p$ <0.001 after the exercise (Table 3).

In OODP, the mean LDL-C reduced significantly from 71.14 mg/dl  $\pm$  7.29 to 66.05 mg/dl  $\pm$  7.17,  $p$ <0.001 after the exercise. In OONDP, the mean LDL-C reduced significantly from 86.62 mg/dl  $\pm$  6.13 to 78.92 mg/dl  $\pm$  5.67,  $p$ <0.001 after the exercise. In OODP male subjects, the mean LDL-C reduced from 66.60 mg/dl  $\pm$  8.05 to 62.00 mg/dl  $\pm$  7.44,  $p$ >0.001 after the exercise. In female OODP, the mean LDL-C reduced significantly from 85.90 mg/dl  $\pm$  9.35 to 75.10  $\pm$  7.87,  $p$ <0.001 after the exercise (Table 4).

## DISCUSSION

There was reduction in the lipid profile in the two groups. The present study assessed the lipid profile among normoglycemic offspring of T2DM subjects and controls without family members with T2DM. We observed lower mean lipid profile in the subjects studied after six months of exercise in normoglycemic offspring of individuals with T2DM compared to controls. Pimenta *et al*,<sup>16</sup> observed similar reduction in lipid profile in subjects with family history of DM compared to BMI-matched controls<sup>17</sup>. They advised that lowering total cholesterol prevented coronary heart disease in 33 out of 66 hypercholesterolaemic subjects that they studied. This is an important index when a physician is assessing the heart of a patient who has hypertension concurrently with diabetes mellitus.

Table 1 — Anthropometric Parameters of 120 Study Subjects

Variable	Category	Total	OODP	OONDP	P
Gender	Male	60 (50.0)	30 (50.0)	30 (50.0)	
	Female	60 (50.0)	30 (50.0)	30 (50.0)	
Age (years)	16-25	43 (35.8)	22 (36.7)	21 (35.0)	
	26-35	55 (45.8)	26 (47.3)	29 (52.7)	
	36-45	19 (15.8)	9 (15.0)	10 (16.7)	
	46-55	3 (2.5)	3 (5.0)	0 (0.0)	
Mean Weight (Kg)		69.80 $\pm$ 1.59	73.28 $\pm$ 2.38	67.00 $\pm$ 2.01	0.185
Mean BMI (Kg/m <sup>2</sup> )		27.70 $\pm$ 0.61	29.30 $\pm$ 0.71	26.37 $\pm$ 0.88	0.035*
P value significant at $P$ <0.05.					

Table 2 — Variability of Total Cholesterol (TC) in the Study Groups

Variable	Category	Before Ex	After Ex	T	P
TC/mg/dl	Total	145.02 $\pm$ 5.37	137.09 $\pm$ 4.71	4.048	0.001*
	OODP	131.29 $\pm$ 8.29	123.90 $\pm$ 6.65	3.015	0.007*
	OONDP	156.12 $\pm$ 6.38	147.73 $\pm$ 5.93	2.812	0.009*
	OODP-Male	120.90 $\pm$ 7.71	117.20 $\pm$ 7.07	2.924	0.017*
	OODP-Female	140.73 $\pm$ 13.97	130.00 $\pm$ 10.95	2.447	0.034*
	OONDP-Male	158.40 $\pm$ 10.79	144.10 $\pm$ 8.08	1.908	0.089
	OONDP-Female	154.69 $\pm$ 8.13	150.00 $\pm$ 8.36	5.825	0.001*

Table 3 — Variability of High Density Lipoprotein (HDL) in the Study Groups

Variable	Category	Before Ex	After Ex	T	P
HDL-C/mg/dl	Total	38.66 $\pm$ 2.35	46.87 $\pm$ 2.23	-6.574	0.001*
	OODP	32.95 $\pm$ 3.57	42.57 $\pm$ 3.82	-4.033	0.001*
	OONDP	43.27 $\pm$ 2.86	50.35 $\pm$ 2.46	-5.982	0.001*
	OODP-Male	31.90 $\pm$ 4.38	38.30 $\pm$ 5.64	-3.081	0.013*
	OODP-Female	33.91 $\pm$ 5.72	46.45 $\pm$ 5.15	-3.099	0.011*
	OONDP-Male	44.50 $\pm$ 4.91	53.90 $\pm$ 3.81	-4.572	0.001*
	OONDP-Female	42.50 $\pm$ 3.60	48.13 $\pm$ 3.18	-4.146	0.001*

Table 4 — Variability of Low density Lipoprotein (LDL) in the Study Groups

Variable	Category	Before Ex	After Ex	T	P
LDL-C/mg/dl	Total	79.70 $\pm$ 4.79	73.17 $\pm$ 4.50	5.679	0.001*
	OODP	71.14 $\pm$ 7.29	66.05 $\pm$ 7.07	4.329	0.001*
	OONDP	86.62 $\pm$ 6.13	78.92 $\pm$ 5.67	4.182	0.001*
	OODP-Male	66.60 $\pm$ 8.05	62.00 $\pm$ 7.44	1.884	0.092
	OODP-Female	75.27 $\pm$ 12.10	69.73 $\pm$ 11.95	9.114	0.001*
	OONDP-Male	85.90 $\pm$ 9.35	75.10 $\pm$ 7.87	2.381	0.041*
	OONDP-Female	87.06 $\pm$ 8.30	81.31 $\pm$ 7.92	6.446	0.001*

This signified that exercise can prevent or delay the onset of these twin diseases: (Hypertension and diabetes). In patients with T2DM, abnormal lipid profile continues to gain support as an important risk factor for premature coronary disease particularly concomitant hypertension, hyperinsulinemia, central obesity and the overlap of metabolic abnormalities of hypertriglyceridemia, low HDL and elevated FFA<sup>18</sup>. It is therefore likely that many of the beneficial effects of physical activity on cardiovascular risk are related to improvements in insulin sensitivity<sup>18</sup>. The study was carried out on normoglycemic type 2 diabetics and non-diabetics controls to assess the role of individual parameters of lipid profile in the dyslipidaemia of type 2 diabetes mellitus. Diabetes mellitus type 2 is typically associated with dyslipidaemia<sup>19</sup>. This is characterized

by hypertriglyceridaemia and low HDL-C levels, while the levels of total cholesterol and LDL-cholesterol may not differ significantly from those in the non-diabetics. However, patients with diabetes often have an abnormally high number of small dense LDL particles<sup>20</sup>. Many studies have also indicated an important predictive role of increased serum TG levels contributing to the risk for CHD, especially in type 2 diabetics<sup>21</sup>. In type 2 diabetics, high TG levels and low HDL-C levels frequently co-exist, which are important factors for CHD. HDL has been assigned a protective role against the development of atherosclerosis because of its role in reverse cholesterol transport. HDL is also associated with the metabolism of the TG rich lipoproteins, since it is the reservoir of apoprotein C-2,<sup>22</sup> which is the activator of lipoprotein lipase – the enzyme responsible for the metabolism of chylomicrons and VLDL in the peripheral tissues. During the postprandial metabolism of chylomicrons and VLDL in the peripheral tissues. During the postprandial metabolism of these lipoproteins, there is an active exchange of lipids and apolipoproteins with HDL.

### CONCLUSION

Regular exercise appear to significantly reduced serum lipid in overweight non diabetic individuals irrespective of diabetic status of their parents. People with family history of T2DM should engage in regular exercise to reduce their tendency to obesity and blood lipids.

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**Conflict of interest :** No conflict of interest.

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## Original Article

# Impact of Allergen Immunotherapy on Medication Score and Medicine Usage in Patients with Nasobronchial Allergy : A Single Centre, Prospective Observational Study in a Specialty Clinic in Eastern India

Shambo Samrat Samajdar<sup>1</sup>, Shatavisa Mukherjee<sup>2</sup>, Saibal Moitra<sup>3</sup>, Santanu Kumar Tripathi<sup>4</sup>

**Background** : Allergic diseases constitute a considerable burden on healthcare system in terms of increased cost of care and impaired Quality of Life in affected. To the rescue, Allergen Immunotherapy (AIT) is reported to be an available treatment modality for altering the natural course of allergic disorders. This study tried to assess the impact of medication usage on medication scoring in patients on Allergen Immunotherapy.

**Materials and Methods** : All consecutive asthma and allergic rhinitis patients prescribed allergen immunotherapy and consenting to join the study were included and interviewed for demographic details and all relevant information, including treatment history. Indication, pattern of prescribing in candidates of allergen immunotherapy, medication score and adherence to therapy were captured in a pre-structured data collection form.

**Results** : Over 50% patients in both asthma and allergic rhinitis group presented with more than 2 years of symptoms during initiation of AIT. As per reports from Skin Prick Test and specific allergen exposure triggering history, Subcutaneous Allergen Immunotherapy (SCIT) was selected for each patient. Apart from allergen species, drug usage pattern suggested use of antimicrobial, systemic/ inhaled/ intranasal corticosteroids, antihistamines/LTRAs, bronchodilators and beta 2 agonists. AIT causes Th2 mediated reaction conversion to Th1 mediated reaction. In our studied patients, we found that there is decrease in the need of intranasal and inhaled corticosteroids dose with subsequent days.

**Conclusion** : It is imperative to note that immunotherapy is not competitive with the conventional use of pharmacotherapy and should be administered in the context of general advice regarding overall disease management.

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**Key words** : Allergen Immunotherapy, Prescribing Pattern, Allergic Rhinitis, Asthma, Medication Scoring.

Allergic disorders like asthma are often under-diagnosed and undertreated, creating a considerable burden on individuals and families. It is responsible for approximately 1% of all disability-adjusted life years lost Worldwide<sup>1</sup>. Allergic disorders and its complications have also been reported to increase health care costs of the individual. Therefore, even though mostly a non-life-threatening condition, they can impair the person's ability to function. It thus has a huge socio-economic impact and can adversely influence psychological wellbeing and Quality of Life<sup>2</sup>.

Allergen Immunotherapy (AIT) is the available

### Editor's Comment :

- The study found that patients receiving Allergen Immunotherapy (AIT) experienced a reduction in the need for intranasal and inhaled corticosteroids over time, indicating AIT's potential to alter medication dependency in managing allergic diseases.
- More than half of the patients in the study had been experiencing symptoms for over two years before starting AIT, highlighting the chronic nature of allergic disorders and the need for effective long-term treatment strategies.
- While Allergen Immunotherapy can help modify the course of allergic diseases, it should be viewed as a complement to traditional pharmacotherapy rather than a replacement, emphasizing the importance of comprehensive disease management.

<sup>1</sup>MBBS, MD, DM, Assistant Professor, Department of Pharmacology, JMN Medical College and Hospital, Nadia, West Bengal 741222

<sup>2</sup>M Pharm (Pharmacology), MBA (Hospital & Health System Administration), PGDM (Epidemiology & Biostatistics), Department of Clinical & Experimental Pharmacology, School of Tropical Medicine, Kolkata 700073 and Corresponding Author

<sup>3</sup>MD (Respiratory Medicine), PhD, FCCP (USA), DAA (CMC) MNAMS, Professor, Department of Allergy and Immunology, Apollo Gleneagles Hospitals, Kolkata, West Bengal 700054

<sup>4</sup>MBBS, MD, DM, Professor, Department of Pharmacology, Jagannath Gupta Institute of Medical Science and Hospital, Budge Budge, Kolkata 700137

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treatment serving the purpose of altering the natural course of allergic disorders. Currently, it has an established role in the therapy of allergic rhinitis, allergic conjunctivitis, allergic asthma, and insect sting hypersensitivity, based on evidence obtained through randomized controlled trials<sup>3</sup>. Other than conventional Subcutaneous Immunotherapy (SCIT), the role of non-injection routes of immunotherapy such as Sublingual Immunotherapy (SLIT) and oral immunotherapy is not yet established, although there are several observations available showing

therapeutic trend. Newer modalities like anti-IgE therapy (omalizumab) used in combination with immunotherapy have significantly reduced the risk of systemic reactions. Novel immunotherapy approaches through recombinant technology and development of T-cell epitope-based allergy vaccines leading to the production of low-allergenicity extracts are the future goals of improving the outcome of allergic disorders. Allergen specific immunotherapy is a controversial topic in the field of asthma and allergic rhinitis treatment. Various randomized controlled trials demonstrated beneficial effects with some risks of severe and sometimes fatal anaphylaxis<sup>4</sup>. As per GINA 2017, SLIT can be considered as a treatment option in case of house dust mite sensitive adult patients suffering from allergic rhinitis or bronchial asthma who have exacerbation of despite inhalation of corticosteroids (provided FEV1 is >70%). Besides, SCIT is a unique therapy for allergic disease because it provides symptomatic relief while modifying the allergic disease by targeting the underlying immunological mechanism<sup>5</sup>. The present study tried to assess the impact of medication usage on medication scoring in patients on allergen immunotherapy.

#### MATERIALS AND METHODS

A prospective, observational, single center study was carried out in a Specialty clinic in Eastern India, where all consecutive asthma and allergic rhinitis patients prescribed allergen immunotherapy and consenting to join the study were included. Permission from Institutional Ethics Committee was obtained prior initiation of the study (CREC-STM/422). Written informed consent was obtained from all participants willing to be a part of the study. Sampling method for this study was convenient sampling, a non-probability sampling method. All consenting patients were interviewed for demographic details and all relevant information, including treatment history. Indication and pattern of prescribing in candidates of allergen immunotherapy were captured in a pre-structured data collection form.

Patients were assessed for their medication score. For medication score, total number of drugs consumed per day for allergic rhinitis and/or asthma was computed for each patient over various time intervals. Assuming one patient is taking Fixed Dose Combination (FDC) of montelukast 10 mg + fexofenadine 120 mg once daily and FDC inhaler of budesonide 200 mcg + formoterol 6 mcg 2 puffs twice daily in initial visit (baseline) and after 6 months he is

put on FDC inhaler of budesonide 200 mcg + formoterol 6 mcg 1 puff twice daily and he is taking montelukast 10 mg + fexofenadine 120 mg alternate day as per his own symptoms control requirement.

In this case,

Baseline medication score =  $\frac{\{(1+1) \times 30\} + \{(2+2) \times 30\}}{30} = 2+4+6$ ; while

Medication Score (6 months) =  $\frac{\{(1+1) \times 15\} + \{(1+1) \times 30\}}{30} = \frac{(30+60)}{30} = 3$

Patients were followed up to one year of allergen immunotherapy initiation. Adherence was checked by using Morisky Medication Adherence Scale (MMAS-8). Data collected was checked for completeness and then statistically analyzed. Descriptive data were represented as mean or percentages. Where possible, demographic and categorical data were analyzed with parametric or non-parametric tests whichever found applicable.

#### RESULTS

The study included a total of 186 patients with presentations of allergic rhinitis, asthma or both, who were prescribed allergen immunotherapy. Of the total patient population, 57% were males with mean age of the patient population being  $37.56 \pm 12.09$  years. Majority of the study participants belonged to the age group of 40-50 years (40.9%) followed by those in 20-30 years band (26.9%) (Table 1). Patients presented with symptoms like dry cough or cough with mucoid expectoration/ scanty expectoration, running nose, sneezing, breathlessness, wheeze, chest tightness, itchy eyes/ nose/ skin or rash. Most of the patients (over 50%) in both asthma and allergic rhinitis group presented with more than 2 years of symptoms during initiation of AIT. Of total 186 study participants, 47.3% presented with allergic rhinitis, 30.1% were asthma and 22.6% had presentations of both allergic rhinitis and asthma. Subcutaneous allergen Immunotherapy (SCIT) is selected for each patient of asthma and allergic rhinitis with skin prick test positivity, having predominant indoor symptoms,

Table 1 — Basic Demographics

Gender Distribution		Frequency (%)
Male		106 (57%)
Female		80 (43%)
Age Distribution		Frequency (%)
Age in Years		
<20		11 (5.9%)
20 – 30		50 (26.9%)
31 – 40		33 (17.7%)
41 – 50		76 (40.9%)
51 – 60		13 (7%)
>60		3 (1.6%)

having symptoms triggered by house dust exposure and suffering from perennial allergic rhinitis patients. SCIT for House Dust Mites - (*Dermatophagoides pteronyssinus* 50% + *Dermatophagoides farinae* 50%) was selected for all patients.

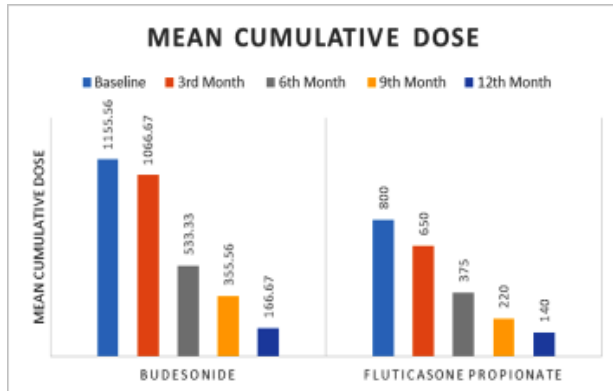
Drug usage pattern over the study time period was analyzed in asthma and allergic rhinitis patients (Table 2). In asthma patients, mostly prescribed antimicrobial was cefixime at baseline, which decreased in 6<sup>th</sup> month. Among systemic corticosteroid, deflazacort was majorly prescribed. Montelukast combined with either fexofenadine or levocetirizine were majorly prescribed. In these patients, mean cumulative dosage of inhaled corticosteroids like budesonide and fluticasone propionate significantly decreased from baseline in subsequent follow ups. Mean cumulative dose of budesonide was 1155.56 mcg at baseline, which decreased gradually to 166.67mcg at 12<sup>th</sup> month. Similarly for fluticasone propionate, mean cumulative dose was 800 mcg at baseline, which significantly decreased gradually to 140 mcg at 12<sup>th</sup> month. For allergic rhinitis patients, mostly prescribed antimicrobial was azithromycin at baseline to control flaring up of symptoms assumed to be due to infectious etiology which decreased in 3<sup>rd</sup> month. Among intranasal corticosteroid, fluticasone furoate (27.5 mcg/actuation) was majorly prescribed, followed by mometasone (50mcg/actuation) and FDC of fluticasone furoate (27.5 mcg/actuation) + azelastine (50 mcg/actuation). Montelukast 10 mg combined with either fexofenadine 120 mg or levocetirizine 5 mg were majorly prescribed. Mean cumulative dosage of intranasal corticosteroids like fluticasone furoate and mometasone significantly decreased from baseline in subsequent follow ups. Mean cumulative dose of fluticasone furoate was 95 mcg at baseline, which decreased gradually to 7.5 mcg at 12<sup>th</sup> month. Similarly, for mometasone, mean cumulative dose was 172.73 mcg at baseline, which significantly decreased

Table 2 — Drug Usage Pattern

Asthma					
Drugs	Percentage (%)				
	Baseline	3 <sup>rd</sup> Month	6 <sup>th</sup> Month	9 <sup>th</sup> Month	12 Month
<b>Antimicrobials :</b>					
Azithromycin	8.9	-	1.7	1.7	3.6
Moxifloxacin	8.9	-	0.0	3.6	0.0
Ceftriaxone	1.7	-	5.4	0.0	0.0
Cefixime	19.6	-	0.0	0.0	0.0
Cefpodoxime Proxetil	14.3	-	3.6	3.6	3.6
Levofloxacin	10.7	-	0.0	0.0	0.0
Amoxicillin + Clavulanic acid	12.5	-	3.6	5.4	1.7
Clarithromycin	1.7	-	7.1	0.0	1.7
<b>Systemic Corticosteroid :</b>					
Methylprednisolone	19.6	0.0	0.0	0.0	0.0
Deflazacort	82.1	10.7	3.6	0.0	0.0
<b>Inhaled Corticosteroids and Beta 2 Agonist :</b>					
Budesonide	57.1	58.9	71.4	82.1	82.1
Fluticasone	44.6	42.9	30.4	30.4	30.4
Salmeterol	37.5	23.2	12.5	12.5	12.5
Formoterol	46.4	76.8	89.8	89.8	89.8
Salbutamol	14.3	12.5	0.0	0.0	0.0
Levosalmamol	14.3	19.6	10.7	7.1	5.3
Ipratropium Bromide	16.1	7.1	5.3	3.6	3.6
Tiotropium	8.9	8.9	5.3	3.6	3.6
Beclomethasone	1.7	7.1	0.0	0.0	0.0
<b>Antihistamines, LTRAs and Oral Bronchodilators :</b>					
Montelukast + Fexofenadine	46.4	57.1	37.5	19.6	16.1
Montelukast + Levocetirizine	37.5	30.4	23.2	7.1	5.3
Montelukast	0.0	0.0	46.4	30.4	19.6
Montelukast + Theophylline	14.3	10.7	1.7	1.7	1.7
Montelukast +Acebrophylline	7.1	5.3	5.3	3.6	1.7
Fexofenadine	16.1	7.1	10.7	5.3	5.3
Levocetirizine	7.1	5.3	5.3	3.6	1.7
<b>Allergic Rhinitis</b>					
<b>Antimicrobials :</b>					
Azithromycin	11.4	2.3	0	0	0
Moxifloxacin	6.8	0	0	0	0
Amoxicillin + Clavulinic acid	4.54	2.3	0	0	0
<b>Intranasal Corticosteroid :</b>					
Fluticasone furoate	68.18	71.6	56.81	32.95	18.18
Mometasone	25	27.27	21.59	17.04	9.09
Azelastine + Fluticasone	6.8	2.3	0	0	0
<b>Antihistamines and LTRAs :</b>					
Montelukast + Fexofenadine	50	50	50	18.18	11.4
Montelukast + Levocetirizine	44.31	45.45	39.77	21.59	18.18
Montelukast	0	0	21.59	18.18	10.22
Bepotastine	4.54	5.68	4.54	0	0
Fexofenadine	3.4	2.3	4.54	4.54	18.18
Levocetirizine	3.4	5.68	9.09	4.54	10.22
<b>Others</b>					
Hydroxypropyl methylcellulose nasal powder	21.59	32.95	18.18	9.09	4.54

gradually to 13.64 mcg at 12<sup>th</sup> month. Azelastine + Fluticasone Propionate was prescribed in baseline and 3<sup>rd</sup> month only, mean cumulative dose being 646 mcg at baseline and 532 mcg at 3<sup>rd</sup> month respectively (Fig 1).

**(A) Asthma**



**(B) Allergic Rhinitis**

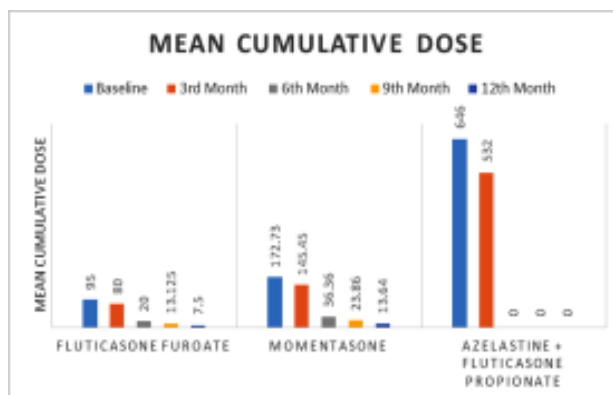


Fig 1 — Mean cumulative dosage of inhaled corticosteroid in Asthma and Allergic Rhinitis patients

Total Medication Score decreased over the study period. In cases of allergic rhinitis, mean medication score was  $5.99 \pm 0.97$  at baseline which gradually decreased to  $0.83 \pm 0.55$  by the end of the study period. In cases of asthma, mean score decreased from  $11.89 \pm 1.49$  at baseline to  $0.84 \pm 0.65$  at 12th month visit. In cases of both allergic rhinitis and asthma, mean medication score was  $10.69 \pm 1.44$  at baseline which gradually decreased to  $0.99 \pm 0.64$

by the end of the study period. Decrease in scores were found statistically highly significant at  $p < 0.001$ . (Table 3) Cumulative medication scoring significantly decreased over the time period ( $p < 0.001$ ) (Fig 2).

Medication adherence of the subjects was assessed using MMAS-8 scale. Total MMAS-8 scores can range from 0 to 8 and have been categorized into three levels of adherence: high adherence (score = 8), medium adherence (score of 6 to <8), and low adherence (score <6). In the present study, majority of the patients were observed to be in medium adherence group for all time points. Adherence levels showed non-significant graded change from low to medium level over the study time frame. ( $p = 0.13$ ) (Table 4)

**DISCUSSION**

Allergic diseases are among the commonest chronic diseases and encompass atopic eczema/dermatitis, asthma, allergic rhinitis and allergic rhinoconjunctivitis, food allergy and venom allergy. They frequently start in early childhood and continue throughout adulthood. Allergies can cause a considerable burden to individuals leading to impaired quality of life. On a societal level, they cause additional

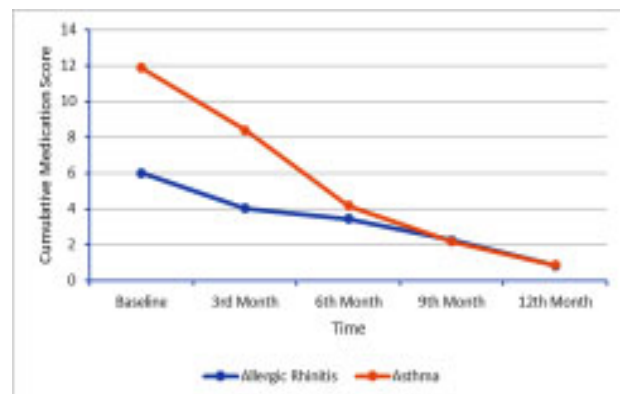


Fig 2 — Cumulative Medication Scoring for patients on AIT

Table 3 — Medication Score

	Baseline	3 <sup>rd</sup> Month	6 <sup>th</sup> Month	9 <sup>th</sup> Month	12 <sup>th</sup> Month
Allergic Rhinitis (N=88)	5.99 ± 0.97(4-8)	4.02 ± 0.69**(3-5)	3.43 ± 0.49**(3-4)	2.25 ± 0.81**(1-3)	0.83 ± 0.55**(0-2)
Asthma (N=56)	11.89 ± 1.49(9-14)	8.39 ± 1.33**(6-12)	4.18 ± 0.83**(3-6)	2.16 ± 0.8**(1-3)	0.84 ± 0.65**(0-2)
Allergic Rhinitis+Asthma (N=42)	10.69 ± 1.44(8-13)	8.24 ± 0.93**(7-10)	5.24 ± 0.85**(4-6)	2.17 ± 0.85**(1-3)	0.99 ± 0.64**(0-2)

Note : Values expressed as Mean ± Standard Deviation (Range) Significance tested considering  $p < 0.05$  (using 't-test'); NS- Not Significant, \*significant at  $p < 0.05$ , \*\*significant at  $p < 0.01$ , \*\*\*significant at  $p < 0.001$

Table 4 — Medication Adherence in Study Subjects

Adherence Level	Baseline	3 Months	6 Months	9 Months	12 Months	$\chi^2$ Statistics
Low (<6)	32 (17.20)	23 (12.36)	19 (10.21)	20 (10.75)	24 (12.9)	$\chi^2 = 12.55$ ; $p = 0.13^{NS}$
Medium (6-7)	130 (69.89)	145 (77.95)	147 (79.03)	152 (81.72)	151 (81.18)	
High (8)	24 (12.9)	18 (9.67)	20 (10.75)	14 (7.52)	11 (5.91)	

Note : Values expressed as N (%) ; NS= Non-Significant ; p value ( $p < 0.05$  considered significant)

costs, particularly in terms of health care utilization, reduction in economic productivity and impacting on activities of daily living. The latter may include loss of school days, work absence, presenteeism and early retirement. For allergic asthma and allergic rhinitis, many patients respond well to pharmacotherapy, whereas others do not or need treatment with more than one product<sup>6</sup>. However, there is good evidence for the clinical efficacy of AIT for allergic rhinitis, allergic asthma and moderate to severe venom allergy with many patients responding to therapeutic AIT, leading to a sustained reduction in symptoms and requirement for symptomatic treatment. AIT is considered a disease-modifying intervention in IgE-mediated allergic disease, with both a therapeutic, even beyond cessation of AIT and the potential for a preventive effect. It has been shown that children with allergic rhinitis have a 3-fold increased risk of developing asthma and that childhood AD and allergic rhinitis are strongly associated with the incidence and persistence of adult atopic asthma and with allergic asthma persisting into adulthood<sup>7</sup>. Studies assessing the long-term effectiveness of AIT in children with allergic rhinitis indicate that AIT might reduce the risk of developing asthma. AIT has the potential to induce immunological changes that result in immune modification. Immunotherapy is effective against hypersensitivity to pollens, animal allergens, dust mites, molds/fungi and insect stings. The present study aimed to assess the prescribing pattern in candidates for allergen immunotherapy in asthma and allergic rhinitis in a specialty clinic in Eastern India.

The present study included patients with asthma, allergic rhinitis and those with mixed presentation. Over 50% patients in both asthma and allergic rhinitis group presented with more than 2 years of symptoms during initiation of AIT. As per reports from skin prick test and focused history Subcutaneous Allergen Immunotherapy (SCIT) for house dust mites - (*Dermatophagoides pteronyssinus* 50% + *Dermatophagoides farinae* 50%) was selected for each patient. The commercially available extracts are relatively low in potency. If immunotherapy is prescribed, only glycerinated extracts should be used, and regionally relevant species should be included in the extracts. However, SCIT should only be performed by trained staff in an allergy clinic facility with an appropriate observation area, facilities for vaccine storage at 4°C, and access to resuscitation facilities, following proper immunotherapy protocols.

Apart from allergen species, drug usage pattern suggested use of antimicrobial, systemic/ inhaled/

intranasal corticosteroids, antihistamines/LTRAs, bronchodilators and beta 2 agonists. In addition, drug usage pattern was assessed for both asthma and allergic rhinitis patients. As in for asthma patients, mostly prescribed antimicrobial was cefixime. Other antimicrobials included azithromycin, moxifloxacin, ceftriaxone, cefixime, cefpodoxime proxetil, levofloxacin, amoxicillin + clavulanic acid, clarithromycin. Systemic corticosteroid prescribing included deflazacort and methylprednisolone. Montelukast combined with either fexofenadine or levocetirizine were majorly prescribed in antihistamines and LTRA group. Other bronchodilators including beta 2 agonists used were salmeterol, formoterol, salbutamol, levosalbutamol, ipratropium bromide, tiotropium, beclomethasone. For allergic rhinitis patients, azithromycin, moxifloxacin, amoxicillin + clavulanic acid were prescribed antimicrobials. Fluticasone, mometasone and fluticasone+azelastine combination were majorly prescribed intranasal corticosteroid. Montelukast combined with either fexofenadine or levocetirizine were majorly prescribed in LTRA and antihistamines group, with hydroxypropyl methylcellulose nasal powder being prescribed throughout the study period. AIT causes Th2 mediated reaction to Th1 mediated reaction. In our studied patients, we found that there is decrease in the need of intranasal and inhaled corticosteroids dose with subsequent days.

The spectra of medication usage have a direct impact on the total medication scoring. Total Medication Score is a prime effectiveness measure in patients of allergic disorders. Medication load signifies the presence of symptoms and need to alleviate it. A true decrease in medication load and eventually medication score is a significant determinant of treatment efficacy. The lower the medication score, the better the therapy. In our study, the cumulative medication score significantly decreased over the study period. Clinical effectiveness of SCIT in management of allergic rhinitis, including 759 patients (546 adults, 53 children, 160 all ages) from 16 studies had suggested that SCIT had produced improvement in medication scores significantly<sup>8</sup>. A Cochrane review including meta-analysis of 51 randomized double-blind placebo controlled trials (2871 subjects with seasonal allergic rhinitis or controls), had indicated that allergen immunotherapy significantly improved overall medication use, and humanistic outcomes<sup>9</sup>. To evaluate the efficacy and safety of SCIT in mite-sensitized subjects with asthma a meta-analysis was



done including a total of 796 subjects from 19 different randomized controlled trials. SCIT had reduced the asthma medication scores compared with the control group significantly<sup>10</sup>. Finding of our study corroborates with these findings. Antihistamine usage was decreased with progression of allergen immunotherapy. Taking a hint from decreased medication score, allergen immunotherapy may be an important option to manage allergic disease. However, we may need further studies specifically double blind randomized clinical trials to test these hypotheses. In the present study, adherence was assessed using MMAS and all subjects were found well adherent throughout all time points of their therapy. In this study, a reduction in medication score was observed after three months of therapy, though different guidelines suggest minimum 3 years of therapy to achieve the same. So, our study sparks the need to further explore whether short duration therapy provides more benefit or not.

An extensive literature search has shown that there exists a dearth of studies assessing the drug prescribing pattern in these AIT candidates. The study may be the first of its kind, however the study being unicentric in nature with a limited sample size, may not be a reflection of the true picture of AIT, but obviously opens up new avenue for further research addressing the limitations.

### CONCLUSION

Unlike anti-allergic drugs, immunotherapy has been shown to modify the underlying cause of the disease, with proven long-term benefits. However, AIT may be combined with appropriate allergen avoidance

strategies. It is imperative to note that immunotherapy is not competitive with the conventional use of pharmacotherapy and should be administered in the context of general advice regarding overall disease management.

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**Conflict of Interest :** None Declared

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— Hony Editor

## Original Article

# Tobacco use among Auto-rickshaw Drivers in Belagavi City, Karnataka

Amaresh P Patil<sup>1</sup>, S Yogeshkumar<sup>2</sup>

**Background :** Auto-rickshaws are still most commonly used mode of transportation in Tier II & III cities where metros or application-based cab aggregators are non-existent / not available. Auto Rickshaw Drivers (ARD's) are under constant physical and mental pressure due to various socio-economic and occupational factors which lead to various habits majority being tobacco use. Based on very few similar studies it has been found that overall prevalence of tobacco use among ARD's is very high compared to general population. Study was conducted to know prevalence of tobacco use among ARD's in Belagavi, North Karnataka.

**Materials and Methods :** It was a cross sectional study conducted among 600 regular ARD's operating within Belagavi city between January, 2017 to September, 2017. Sample size was estimated to be 600. Two ARD's who were last in queue were selected from 300 major Auto-rickshaw stands. Participants were interviewed personally after obtaining informed consent and data was collected using the questionnaire customized from Global Adult Tobacco Survey (GATS). Data was analyzed through descriptive statistics, Chi-square test and Fisher's exact test. Study was provided approval by Institutional Ethics Committee.

**Results :** Mean age of participants was  $39.71 \pm 11.07$  years. Prevalence of tobacco use in any form was found to be 62.17%. Smokeless form was predominant. Tobacco use was significantly associated with age, literacy, type of family, years in present occupation, length of working hours and night shifts.

**Conclusion :** Prevalence of tobacco use in ARD's is very high compared to general population which calls for immediate focused interventions.

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**Key words :** Auto-rickshaw Drivers (ARDs), Tobacco, Karnataka.

The three-wheel motored vehicles, commonly termed as Auto-rickshaws, are a pillar to urban transportation. Auto-rickshaws continue to be the most commonly commuted mode of transportation in Tier II & III cities where metros or Application-based cab Aggregators (ABCA) have not yet established their foothold. Passengers in Indian cities are served by around 5 million Auto rickshaws and the drivers have to manage through traffic-tangled streets all day for a living. They work for over 10-12 hours per day and form an important part of the urban informal sector in India. These drivers are self-employed and lack any kind of employment benefits and social security. Income insecurity is an important concern for the drivers as they earn on a daily basis with no fixed income. Health expenses are a major challenge for majority of them. They suffer from serious respiratory ailments as they are continuously exposed to vehicular pollution. They are also prone to road accidents given poor road infrastructure and badly

### Editor's Comment :

- Tobacco still continues to be a major public health menace.
- Occupational groups, specially the unorganized sectors bear the brunt of the tobacco use and its health hazard.
- The impact of occupational factors on tobacco use needs to be closely monitored in the community level.

maintained vehicles. Traversing on the road for majority of the day, the drivers suffer due to poor quality and lack of access to hygienic water and sanitation facilities further augmenting their health issues.

Auto-rickshaw Drivers (ARDs) are constantly under physical and mental pressure owing to multiple risk factors like lack of regular working hours, frequent up's and down's in fuel cost, unpredictable waiting hours, illiteracy, poverty, lack of proper knowledge about harms of tobacco and other socio-economic factors which lead to various habits majority being tobacco use<sup>1-4</sup>.

Tobacco use poses a great burden of disease in India and is a leading public health problem. The tobacco epidemic is one of the largest public health threats the World has ever faced, killing more than 8 million people a year. More than 7 million of these deaths are the results of direct tobacco use while around 1.2 million are the result of non-smokers being exposed to second-hand smoke<sup>5</sup>.

Jawaharlal Nehru Medical College, Belagavi, Karnataka 590010

<sup>1</sup>MBBS, MD, DNB, MNAMS, Project Co-ordinator, Department of Women's and Children's Health Research Unit and Corresponding Author

<sup>2</sup>MD, Fellowship Preventive Oncology, Professor, Department of Community Medicine

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In India, tobacco is used in a varied range of chewing and smoking forms available at varied cost, reflecting the diverse Socio-economic and demographic patterns of tobacco use<sup>6</sup>.

Cigarette smoking in any form damages nearly every organ of the body, causes many diseases and deteriorates the health in general<sup>7-8</sup>. It is known to diminish the overall health, increase sickness absenteeism and increased utilization of health care and also increase in the cost<sup>7</sup>. There are many diseases that are caused, increased or exacerbated by tobacco ranging from predisposition to Hypertension, Acute Gastritis, Diabetes Mellitus, Coronary Artery Disease, Stroke, Bronchial Asthma and Cancers to premature death<sup>9</sup>.

Author intends to find the prevalence of tobacco consumption among Auto-rickshaw Drivers in Belagavi, a northern district of Karnataka.

#### MATERIALS AND METHODS

##### Study Design :

This study is a descriptive, cross-sectional research conducted on registered Auto-rickshaw Drivers operating in Belagavi city which is a major city in the Northern part of Karnataka, in the period of January to September, 2017. Sample size was calculated to 597 & rounded off to 600 based on the estimated prevalence of 84%<sup>10</sup> with an absolute error of 3%. The inclusion criteria were as follows :

(a) Registered, regular Auto-rickshaw Drivers above 18 years of age in the study area.

(b) Those who were permanent residents of Belagavi city from the past one year.

Auto-rickshaw Drivers driving on a part time basis and those who were not willing to participate were excluded from the study.

##### Sampling Procedure :

As per the information from the Regional transport office, the city had around 300 major Auto-rickshaw Stands and among each stand two auto rickshaw drivers were selected for the study to meet the sample size. We purposively selected two Auto-rickshaw Drivers who were last in the queue. This was to have ample amount of time for the participant to be interviewed and examined for the study, which could not have been done if someone else from the queue were selected as they may had to discontinue the interview if their Auto-rickshaw was hired during that period.

##### Study tools :

The questionnaire for the study was customized from the questionnaire of the Global Adult Tobacco Survey (GATS)<sup>11</sup>. This was done to fit the needs of the

present study. Some questions related to the occupation and tobacco consumption were added to the original GATS questionnaire to meet the study objectives. Similarly, some other questions from GATS which were not relevant to the study were left out.

##### Methodology :

Personal interview of eligible participants was conducted by the investigator, using pre-designed and pre-tested questionnaire adopted from GATS questionnaire<sup>11</sup>. Data regarding Socio-demographic variables like age, address, educational status, years in present occupation, Socio-economic status and etc. were collected.

Visits were made by the investigator to all the 300 major Auto-rickshaw Stands within the limits of Belagavi City Corporation and Auto-rickshaw Drivers were identified according to the sampling procedure. These Auto-rickshaw Drivers were explained about the purpose of the study and after getting their written informed consent, they were interviewed and examined in the auto rickshaw stands or any convenient place nearby.

The participants were given free chance to discontinue from the study at any given point of time for any privacy or confidential issues or work related issues. It was ensured that the study participants did not face any kind hindrance in their work.

##### Data Analysis :

The data was analyzed through descriptive statistics, Chi-square test and Fisher's exact test using the SPSS software. A value of  $P < 0.05$  was considered statistically significant in the study.

##### Ethical Considerations :

This research project was provided approval by the Institutional Ethics Committee of J N Medical College, KLE University, Belagavi. Users of any form of tobacco were counselled regarding benefits of tobacco cessation after completion of the study and those willing to quit were offered help either by counselling or by attending tobacco cessation clinics. Those who had lack of awareness or were misinformed about the hazards of tobacco were given the correct information by inter-personal communication by the investigator.

#### RESULTS

Table 1 shows that all participants were male, age ranging between 18 to 70 years of age with an average age of  $39.71 \pm 11.07$  years. Mean number of years in the present occupation was  $15.80 \pm 10.11$  years. Study participants worked over a mean length of  $9.43 \pm 1.82$  hours per day.

Majority of the participants (89.83%) were married, 371 (61.83%) stayed in nuclear families and 346 (57.67%) resided in pucca house.

Fig 1 shows that among the participants, 373 (62.17%) were using tobacco in one or the other form.

Cigarettes (87.05%) were the most commonly smoked form followed only by beedis while gutkha (54.93%) was the commonest smokeless form followed by chewing tobacco (30.99%), lime with tobacco (12.32%) and other chewable forms. Majority of the tobacco users had initiated their habit before 20 years of age (46.38%) highlighting the need for interventions at an early age. Mean age at initiation was  $23.22 \pm 8$  years for smoke form and  $23.36 \pm 7.99$  years for smokeless form. Mean duration of use of tobacco was  $15.31 \pm 10.29$  years. More than half of the participants (54.96%) used tobacco within an hour of waking up. Close to three fourths of tobacco users never used in front of their children (74.8%).

Most of the users (54.69%) were advised to quit by a Health Care Professional in the last one year. Among the tobacco users, 227 (60.86%) tried to quit use in the previous year and more than half of them (54.63%) could sustain their efforts for few months before resuming the use. Self-motivation / own will

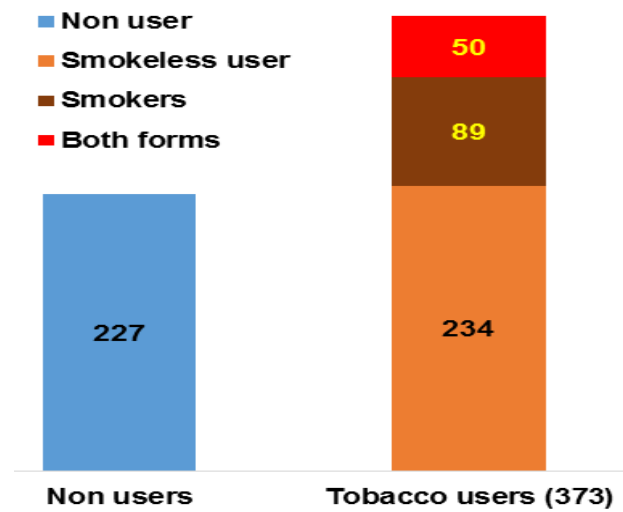


Fig 1 — Distribution of study participants according to use of tobacco

(90.75%) was the strongest driving force to quit. Majority of the tobacco users planned to quit within next one month (28.69%).

Table 2 shows that among the Socio-demographic factors considered, age and educational status were significantly associated with tobacco usage whereas religion and Socio-economic status had no significant association.

While type of family was significantly associated (Fisher's Exact Test, P value = 0.0456), marital status had no association (Chi-square value = 3.7173, df = 1, P value = 0.053).

Table 3 shows there was a significant association of tobacco use with all the three occupational factors considered ie, length of the work hours, number of years in current occupation and number of night shifts in an usual week.

### DISCUSSION

Auto-rickshaw Drivers spend a considerable amount of time in an environment full of pollutant gases, noise, continuous stress, accelerations and decelerations, lateral swaying from side to side and whole-body up and down vibrations when the vehicle is in motion. Further poor lifestyle practices like irregularity of meals, no proper rest rooms, awful quality of sanitary toilets, bad posture while driving and stressful occupational conditions during their working hours augment their health problems. Such working parameters may be associated with various gastro-intestinal disturbances, musculo-skeletal, cardio-vascular, respiratory, hearing and other problems<sup>2,4,12-13</sup>.

The present study was done to find the prevalence

Table 1 — Socio-demographic and occupational profile of participants (N=600)

Characteristics	N (%)	
Age (years)	< 30	159 (26.5)
	31 – 40	175 (29.17)
	41 – 50	164 (27.33)
	51 – 60	90 (15)
	> 60	12 (2)
Religion	Hindu	143 (23.83)
	Muslim	457 (76.17)
Educational qualification	Illiterate	49 (8.17)
	Primary School	141 (23.5)
	High School	327 (54.5)
	Pre university college	59 (9.83)
	Diploma / Graduate	24 (4)
Socioeconomic status (Modified BG Prasad SES Scale)	Class I	17 (2.83)
	Class II	65 (10.83)
	Class III	196 (32.67)
	Class IV	265 (44.17)
	Class V	57 (9.5)
Number of years in the present occupation	< 10	235 (39.17)
	11 – 20	189 (31.5)
	> 20	176 (29.33)
Length of working hours on an usual day	6 - 8 hours	51 (8.5)
	8 - 10 hours	218 (36.33)
	10 - 12 hours	191 (31.83)
	≥ 12 hours	140 (23.34)
Usual number of night shifts per week	0	582 (97)
	≥ 1	18 (3)

of tobacco among Auto-rickshaw Drivers. All the 600 study participants were male, consistent with other studies conducted among similar sub groups<sup>10,14</sup>. Most of the participants in this study had high school education (54.50%), followed by primary education (23.50%) whereas some were illiterate (08.17%). Study participants had a higher educational level when compared with similar studies<sup>10</sup>. This increase in education level in the present study may be attributed to better literacy level among south India as compared to the north.

Most of the study participants stayed in pucca houses (57.67%) and remaining in kuccha houses (42.33%). This was noteworthy as substantial number of participants stayed in kuccha houses which are known to be a risk factor for a range of health problems and the burden will only increase among those also using tobacco.

Mean years in present occupation was 15.80 years ± 10.11. This is because most of the participants started the present occupation in their early twenties (and as the mean age was in late thirties). Study conducted among Auto-rickshaw Drivers in Nagpur had participants with a mean length of occupation of 17.70 ± 7.62 years<sup>14</sup>. Mean length of working hours per day was 9.43 ± 1.82 hours in the present study whereas in the study done in Nagpur it was 11.52 ± 2.29 hours<sup>14</sup>.

Hardly 3.0% of participants did one or more than one night shifts per week. On the other hand, study done in Gwalior had 26.0% participants working till late night<sup>10</sup>. This may be because the data collection for the present study was done during day times due to which a good number of drivers driving exclusively in night shifts would have been missed.

Prevalence of tobacco use in the present study in any form was found to be 62.17%. The study among Auto-rickshaw Drivers in Gwalior showed prevalence of tobacco to be 84.26%<sup>10</sup> whereas 64.44% of the Auto-rickshaw Drivers surveyed in a study done in Bareilly, Uttar Pradesh consumed tobacco in any form<sup>15</sup> while 69% of auto rickshaw drivers surveyed in another study done in South Delhi were using tobacco in or the other form<sup>16</sup>. The difference in prevalence of tobacco use with Gwalior study can be attributed to the fact that the educational levels of the

Table 2 — Association of tobacco use with socio-demographic profile

Characteristics	Tobacco users	Non users	Total	χ <sup>2</sup>	
Association of tobacco use with age	< 30 years	104 (65.41)	55 (34.59)	159 (100)	34.39, df = 3, P value < 0.00001
	31 – 40 years	133 (76.00)	42 (24.00)	175 (100)	
	41 – 50 years	93 (56.71)	71 (43.29)	164 (100)	
	> 50 years	43 (42.16)	59 (57.84)	102 (100)	
	Total	373 (62.17)	227 (37.83)	600 (100)	
Association of tobacco use with religion	Hindu	88 (61.54)	55 (38.46)	143 (100)	0.032, df = 1, P value = 0.858
	Muslim	285 (62.36)	172 (37.64)	457 (100)	
	Total	373 (62.17)	227 (37.83)	600 (100)	
Association of tobacco use with educational status	Illiterate	37 (75.51)	12 (24.49)	49 (100)	27.901, df = 4, P value = 0.00001
	Primary	80 (56.74)	61 (43.26)	141 (100)	
	High school	221 (67.56)	106 (32.42)	327 (100)	
	PUC	29 (49.15)	30 (50.85)	59 (100)	
	Diploma & graduate	06 (25.00)	18 (75.00)	24 (100)	
	Total	373 (62.17)	227 (37.83)	600 (100)	
Association of tobacco use with Socio-economic status	Class I	12 (70.59)	05 (29.41)	17 (100)	4.535, df = 4, P value = 0.3384
	Class II	45 (69.23)	20 (30.77)	65 (100)	
	Class III	125 (63.78)	71 (36.22)	196 (100)	
	Class IV	161 (60.75)	104 (39.25)	265 (100)	
	Class V	30 (63.83)	27 (47.37)	57 (100)	
	Total	373 (62.17)	227 (37.83)	600 (100)	

participants in the present study was high in comparison to the study conducted in Gwalior and both the studies have revealed negative associations between educational level and tobacco use. A study done in Jaipur, Rajasthan concluded that the prevalence of tobacco use was 87.2% among Auto-rickshaw Drivers which was comparatively higher<sup>17</sup>. But a comparison with this study was less valid as

Table 3 — Association of tobacco use with occupational profile

Characteristics	Tobacco users	Non users	Total	χ <sup>2</sup>	
Association between tobacco use and years in present occupation	< 10 years	160 (68.09)	75 (31.91)	235 (100)	8.524, df = 2, P value = 0.0140
	11 to 20 years	118 (62.43)	71 (37.57)	189 (100)	
	> 20 years	95 (53.95)	81 (46.02)	176 (100)	
	Total	373 (62.17)	227 (37.83)	600 (100)	
Association between tobacco use and length of working hours	6 - 8 hours	22 (43.14)	29 (56.86)	51 (100)	27.901, df = 4, P value = 0.00001
	8 - 10 hours	175 (80.28)	43 (19.72)	218 (100)	
	10 - 12 hours	83 (43.46)	108 (56.54)	191 (100)	
	> 12 hours	95 (66.43)	47 (33.57)	140 (100)	
	Total	373 (62.17)	227 (37.83)	600 (100)	
Association between tobacco use and number of night shifts per week	No night shifts	355 (61)	227 (38)	582 (100)	Fisher's Exact Test, p = 0.0456
	≥ 1 night shifts	18 (100)	0	18 (100)	
	Total	373 (62.17)	227 (37.83)	600 (100)	

this study had a very small sample size of only 94 participants. The prevalence of tobacco use in Auto-rickshaw Drivers revealed by these studies was comparatively very high with respect to the prevalence in Indian adults aged 15 years and above which was just 28.6% according to GATS 16 -17<sup>18</sup>. It was also noted that the prevalence of tobacco use in present study was very high compared to the adults among general population in Belgaum city. A community based study done among adults in Belgaum revealed the prevalence of ever use of tobacco to be only 29.41%<sup>19</sup>.

The comparatively higher prevalence of tobacco among Auto-rickshaw Drivers can be attributed to various occupational factors like constant physical and mental pressure due to irregular shifts, continuous variation in fuel prices, long waiting hours coupled with low levels of education, poverty, lack of knowledge about hazards of tobacco, other Socio-economic factors and many unknown factors.

Smokeless form was the predominant form of tobacco use. Similar findings have been observed in several studies conducted among same subgroups<sup>10,20-21</sup>. These findings are consistent with the GATS survey done among adult Indian male<sup>18</sup>. This is also particularly true in Auto-rickshaw Drivers as their hands are pre-occupied in driving and hence smoking while driving would be cumbersome whereas chewing can be continued even while driving.

Mean age at initiation in present study for any form of tobacco was in mid-twenties ( $23.22 \pm 8.00$  years for smoke and  $23.36 \pm 7.99$  years for smokeless form). Many other studies also showed initiation of most of the participants at an early age<sup>17&22</sup>. These observations indicate towards initiation of tobacco at a very tender age at which their minds are very much inquisitive, outwardly try for new experiments, amenable to the peer pressures and deeply impacted by use of tobacco in close contacts, media and mass advertisements. In the present study, mean duration of tobacco use was  $15.31 \pm 10.29$  years. Similarly, the average duration of tobacco smoking was  $19.04 \pm 7.27$  years in the Nagpur study<sup>14</sup>. It is a known fact that tobacco is an addictive substance and this duration of tobacco use will only increase in the coming years unless some effective intervention measures are undertaken immediately.

Dependence on tobacco for physiological processes like bowel evacuation was observed in the present study by the fact that more than half of those using tobacco used it within an hour of waking up and other similar studies showed same results and this has to be curtailed off with various de-addiction measures at the earliest. More than 1/4<sup>th</sup> of the study

participants were using tobacco in front of their children & this has to be curtailed off as parents are one of the most important influencers for their children.

Majority (54.69%) of the tobacco users were advised to quit tobacco by any health care provider in last one year. There is still a lot of potential to counsel each & every tobacco user every time they encounter a health care professional which can have a deeper impact in reducing the use.

Around 61% of the study participants had tried to quit the use of tobacco in last one year. In the study done in Nepal, 75.8% of long route bus drivers had tried quitting the use of tobacco<sup>23</sup> whereas in the Gwalior study, only 28.47% had tried to quit the use of tobacco<sup>10</sup>. This difference in quit attempts can be attributed to the difference in various Socio-economic factors, educational level, knowledge regarding hazards of tobacco and the personality traits of the tobacco users as all of these play an important role to quit tobacco. Majority of those who attempted a quit could hardly sustain it for few months before resuming the use. This can be attributed to various religious events (like Ramadan, Diwali), strong peer pressure, addiction and physical dependence to tobacco along with ignorance. Self-motivation or strong will was found to be the most common approach (90.75%) by the participants to even attempt quitting. This own will can be augmented by providing education and raising the level of knowledge about tobacco and its hazards, providing emotional and mental support to those willing to quit. A Canadian study concluded that many smokers may be unaware of effective cessation methods and most also underestimate their benefit. Further, this lack of knowledge about effective cessation methods may represent a significant barrier to treatment adoption<sup>24</sup>.

Age of the participants was significantly associated with tobacco use, ie, tobacco use was highly prevalent in younger age group compared to older age. This could be due to reasons like curiosity, increased tendency for experimentation, considering tobacco as a sign of manhood, impact of mass media and movies, friends and fellow Auto-rickshaw Drivers.

There was a statistically significant association between educational status and tobacco use (ie, the tobacco use decreased with increase in educational status). This was consistent with Gwalior study ( $P=0.0014$ ) and secondary analysis of GATS 09-10<sup>25</sup>. This could be because of the reason that illiterates hardly have any knowledge regarding tobacco and its adverse effects and adding to it is their ignorant attitude about the same.

The study demonstrated a statistically significant

inverse association between years in present occupation and tobacco use ie, tobacco use decreased with increase in present occupation. This could be because younger age group had higher prevalence of tobacco.

Tobacco use was significantly associated with length of working hours per day and night shifts. Similar findings were seen in Gwalior study<sup>10</sup>. This reiterates a well-known fact that long working hours and night shifts lead to increased tobacco consumption which is usually because of longer waiting hours and boredom during waiting hours.

### CONCLUSION

Prevalence of tobacco use among Auto-rickshaw Drivers was 62.17% which is very high compared to general adult Indian population (28.6%)<sup>18</sup>.

### Limitations and Recommendations :

Apart from recall bias, those auto rickshaw drivers plying exclusively during night might have been missed from the study. Based on the study, we recommend that work place tobacco cessation model should be established for this group and tobacco cessation activities should be targeted at younger Auto-rickshaw Drivers to address the early initiators to prevent future addictions & health hazards. Periodic examination of the Auto-rickshaw Drivers should be conducted to identify risk factors and complications of long term exposure to initiate early preventive and control measures.

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## Original Article

# Perception and Constraints of Telemedicine Services among the Health Care Providers and Beneficiaries in Purba Bardhaman District, West Bengal : A Qualitative Study

Suman Sannigrahi<sup>1</sup>, Sanjib Bandyopadhyay<sup>2</sup>, Rupali P Thakur<sup>2</sup>, Pranita Taraphdar<sup>3</sup>,  
Aprajita Jha<sup>1</sup>, Anupam Mallick<sup>1</sup>

**Background :** Telemedicine has emerged as a potential solution to the country's expanding healthcare needs, particularly in rural and isolated locations. This study tries to pinpoint challenges and offer suggestions for improving Telemedicine services in India.

**Aims and Objectives :** To explore perception and constraints of Telemedicine services among the health care providers and beneficiaries

**Materials and Methods :** A qualitative study with phenomenological approach was conducted in Purba-Bardhaman District, West Bengal from March, 2023-June, 2023. All tiers of health-care delivery system (from HWC to tertiary-care facility) with provision of Telemedicine services were selected by SRS. From selected facilities, beneficiaries (those attended  $\geq 2$  Telemedicine consultations) were chosen purposively for focused group discussion. Similarly, doctors and Community Health Officers (providing Telemedicine service for  $\geq 3$  months) were selected for In-Depth Interviews. Data analysis done by inductive thematic approach. Ethical clearance obtained from Institutional Ethics Committee.

**Results :** Lack of access to technology and infrastructure, resource constraints, limited training and support, resistance to change and adoption of new technology, challenges in maintaining patient privacy and confidentiality, administrative and managerial issue emerged as significant challenges from service-provider's perspective. Beneficiaries faced various constraints, which includes accessibility and availability of Telemedicine services, resource constraints, acceptability and trust issue, quality and effectiveness related issues.

**Conclusion :** Acceptance of Telemedicine service in India is hampering due to lack of infrastructure and essential medicine, inadequate manpower and unrealistic target from higher authorities. However increasing adoption of technology and Government initiatives will help to promote growth and development of Telemedicine.

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**Key words :** Beneficiary, Constraints, Health Care Provider, Health and Wellness Centre, Perception, Qualitative, Telemedicine.

Telemedicine, also known as "healing at a distance," was coined in the 1970s by the Thomas Bird<sup>1</sup>. One of the first recorded instances of telemedicine occurred in the early 20th century when Willem Einthoven<sup>2</sup> transmitted electro-cardiograph data over telephone wires to a hospital 1½ km away.

Newer applications of "Telemedicine" are found as time goes on and older applications take hold and find a larger reach. WHO defined telemedicine as 'the delivery of health care services, where distance is a critical factor, by all healthcare professionals using information and communication technologies for the exchange of valid information for diagnosis, treatment and prevention of disease and injuries, research and

Department of Community Medicine, Burdwan Medical College and Hospital, Bardhaman, West Bengal 713104

<sup>1</sup>MBBS, MD, Postgraduate Trainee

<sup>2</sup>MBBS, MD, Associate Professor

<sup>3</sup>MBBS, MD, Professor and Head and Corresponding Author

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### Editor's Comment :

- Telemedicine services if properly implemented can be a gamechanger in healthcare delivery system.

evaluation and for the continuing education of health care providers, all in the interest of advancing the health of individuals and their communities<sup>3</sup>.

Though telemedicine is still a nascent field in India, our country is making efforts to catch up with the developed world. In 2001, the Indian Space Research Organisation (ISRO) launched a test project that connected Chennai's Apollo Hospital with its rural counterpart in Aragonda village<sup>4</sup>.

However, these measures did not gain widespread adoption in India due to inadequate resources, slow policymaking at the national and state levels and the perplexing status of Indian laws pertaining to Telemedicine, which control both the medical profession and information technology. In response to the epidemic, the Board of Governors, revised the



Medical Council Act, 1956 (102 of 1956) and released the Telemedicine Practice Guidelines<sup>5</sup>.

As per Telemedicine Practice Guidelines<sup>5</sup> there are three primary modes of Telemedicine:

- Video
- Audio
- Text (chat, messaging, email, fax etc)

The Government of India's leading Telemedicine system, eSanjeevani, is being implemented nationally for the Ministry of Health & Family Welfare at 1,55,000 Health and Wellness Centers<sup>6</sup>. The National Health Authority (NHA) announces the successful integration of eSanjeevani with its flagship scheme – Ayushman Bharat Digital Mission (ABDM)<sup>7</sup>. Until December 6, 2022 e-Sanjeevani had registered over 8 crore Teleconsultations<sup>8</sup>.

Based on eSanjeevani platform, Government of West Bengal has launched "Swasthya Ingit" to provide affordable, accessible, sustainable and high quality healthcare service delivery up to grass root level. The idea is to provide inclusive & accessible healthcare in rural bengal, so that it reduces out-of-pocket expenditure of villagers; facilitate early diagnosis of the disease, timely intervention and easy follow ups.

Health and Wellness Centers (HWC) act as spokes where patients visit and consult with the Community Health Officer (CHO). The CHO initiates a telemedicine consultation with a Medical Officer at the HUB via computer using the Swasthya Ingit portal. Doctors at the HUB provide consultations, e-prescribe drugs from the approved list and maintain electronic health records. Following this, the CHOs at the spokes dispense the prescribed drugs based on the received prescription through Swasthya Ingit and also print the prescription.

The relationship of trust between patients and doctors has evolved over thousands of years of face-to-face communication. Some patients may feel that their doctor does not genuinely understand their illness or care about their well-being without the personal interaction and visual clues that are crucial in medical care. Furthermore, the application of technology in Telemedicine may present fresh difficulties, such as security risks and technological difficulties, which may further erode trust. Even while telemedicine has advantages, it's necessary to think about how it can affect the doctor-patient relationship. However, it cannot be denied that remote areas like rural, tribal areas can greatly benefit from Telemedicine. Therefore, it is critical to understand people's perceptions of this new method of health care, which will have an impact on everyone's lives.

With this backdrop, a study will be undertaken by the researcher to explore perception and constraints of Telemedicine services among the health care providers and beneficiaries in Purba Bardhaman District, West Bengal.

#### AIMS AND OBJECTIVES

- To explore the perception and constraints faced by the health care providers to provide Telemedicine services in Purba Bardhaman district, West Bengal.

- To explore the perception and constraints faced by beneficiaries to avail Telemedicine services in the study area.

#### MATERIALS AND METHODS

**Type and Design of Study :** Qualitative study with phenomenological approach.

**Study Setting :** The study was conducted in the different level of health facilities providing Telemedicine services in Purba Bardhaman district, West Bengal. Different levels of Telemedicine services are as follows:

- 214 HWC (HWC currently conducting Telemedicine).

- 108 other health facilities including Primary Health Centers (PHC), Block Primary Health Centers (BPHC), Urban Primary Health Centers (UPHC) and Rural Hospitals (RH).

- Sub Divisional Hospital (SDH) and Burdwan Medical College and Hospital (BMCH)

**Study Duration :** Four months (March, 2023-June, 2023).

#### Study Population :

Beneficiaries were selected from different age groups (adolescents, adults, elderly) among those who were visiting HWC for Telemedicine consultation.

#### Service providers were :

- HWC level(Spoke) – Community Health Officer
- PHC level(Hub)–MOIC/GDMO (Medical Officer)

- BPHC/CHC level(Hub)–BMOH/GDMO

- SDH & Medical College level(Hub)–Specialist doctor.

#### Inclusion Criteria :

##### (1) For beneficiaries :

Study subjects who attended at least two Telemedicine consultations (excluding consultation on the day of interview).

##### (2) For service providers :

Service providers working in Telemedicine clinic for at least the last three months.

### Exclusion Criteria for beneficiaries :

Patients who are referred to nearby hospital.

**Sample Size and Sampling Technique :** The study being qualitative in nature, the size of the sample was determined by data saturation and data exhaustion.

10% HWC (that is 21) was selected by simple random sampling from a sampling frame of total 214 HWC (HWC currently conducting Telemedicine). In each HWC, one Focused Group Discussion (FGD) was conducted among six-eight beneficiaries (selected purposively) with the help of FGD guide. Data saturation achieved after five FGDs.

For service providers perspective, from each HWC, one CHO was interviewed with the help of In-depth Interview (IDI) guide. Data saturation achieved after twelve IDIs.

As the number of HWCs is almost twice of other health facilities (namely PHC, BPHC, UPHC, RH), we took 20% (two times of 10%) of 108 of other health facilities, that is 22 by simple random sampling. From each sampling unit one general physician was interviewed. Data saturation achieved after eight IDIs.

SDH and BMCH were visited and specialists were interviewed purposively. Minimum two specialists were interviewed from each hospital. It was also taken care of so that different specialities are represented. Data saturation achieved after ten IDIs.

**Tools and Techniques :** IDI & FGD guide was prepared in consultation with subject experts. It was translated into bengali from english and back translated by another expert keeping semantic and linguistic equivalence.

**Data Collection :** Data was collected after ethical approval by Ethics committee(Memo-BMC/I.E.C/027, Dated-9th Feb'23). Prior to data collection, district and block level health authorities were informed & co-operation was sought. IDI of purposively selected service providers conducted using IDI guide. Informed consent was taken for participation and recording of the interview. They were assured about confidentiality and anonymity. A careful approach was adopted not to give away too much detail to prevent bias. Clear, simple, open-ended questions were asked and the participants were given adequate time to fully express their views. For FGDs participants were briefed about the study and its purpose and written consent were sought. FGD was conducted using the FGD guide in the presence of a moderator. Sociograms were drawn and notes were taken during the sessions. It was taken care of that the notes contain all relevant information including the nonverbal cues. Sessions

were audio recorded while keeping anonymity for the purpose of creating a verbatim. The points raised throughout the session were reviewed with the participants at the conclusion, if required additions or modifications were made.

**Data Management and Analysis :** At first, the entire audiotape (both of the IDIs and FGDs) were transcribed. The verbal cues were also incorporated in the transcript to facilitate the capturing of the entire essence of the interviews and discussions. Then, the important and salient phrases that match the research question were identified from the transcript after which Inductive analysis of the verbatim were undertaken to generate specific codes, subthemes and themes. These themes are representing the collective understanding of the data as per perceived experiences and constraints. Thematic analysis were done to understand the opinion, behaviour and beliefs of the study participants. The data were entered and analysed by using Atlas-Ti Software. The report was prepared following the reporting guidelines of COREQ<sup>9</sup>.

### RESULTS

The results have been presented by tables of generated themes, subthemes, supportive codes and sample verbatims, as well as a hierarchical cluster analysis of themes and sub-themes by a sunburst chart and a tree map. The hierarchical cluster analysis explains how these factors (themes) relate to each other and shows the relative importance of the different facets of the challenges as per the study subjects' perspectives. Direct quotations from the respondent are in Italics. "Consolidated Criteria for Reporting Qualitative Research" (COREQ) guidelines<sup>9</sup> were followed during reporting the present qualitative work (Table 1 & Fig 1).

From the analysis of service providers IDI, six major themes emerged under which sub-themes are discussed.

- (1) Lack of access to infrastructure and equipment
- (2) Training and support related concern
- (3) Resistance to change and adoption of new technology
- (4) Challenge in maintaining patient privacy and confidentiality
- (5) Resource constraints
- (6) Administrative and managerial issue

From the analysis of beneficiaries FGD, four major themes emerged under which sub-themes are discussed (Table 2 & Fig 2).

- (1) Access and availability of Telemedicine services

Table 1 — Thematic representation of perception and constraints in providing the Telemedicine services from healthcare provider's perspective

Theme	Subtheme	Code	Sample Verbatims
Lack of access to infrastructure and equipment	A: Infrastructure challenges	1. Unreliable electricity 2. Limited availability of high speed internet in rural areas 3. Poor cellular service in rural areas	.... Electricity goes out frequently.....The speed of the internet is very bad.....Sometimes the website does not open, it fails for a day or two. Then there is a problem to handle the patient....
	B: Equipment challenges	1. Limited availability 2. Used equipment supply 3. Lack of maintenance and technical support	....Inverters are not yet operational in our center..... Gave me old laptop, earlier it was in another center. Very slow, battery is also bad.....
Training and support related concern	A: Training challenges	1. Limited access to telemedicine training program 2. Insufficient training on how to use specific telemedicine platform	.....we are not trained very well, but the CHOs are.....many CHOs don't know BP, RBS have separate places to write, write them together with commas. Can't understand anything.....Many doctors don't know that medicine can be selected, they write everything in place of OTHER.....
	B: Support challenges	1.limited support	.....My LAPTOP was damaged, in the shop I fixed it. Had to stop telemedicine for 2-3 days.....
Resistance to change and adoption of new technology	A: Attitudinal challenges	1. Concern about malpractice 2. Lack of trust on online mode of diagnosis 3. Strong preference for in person consultation 4. Difficulty in establishing trust with patients	The prescription is not (hand)written by me. If someone edits and writes something below my writing, it will be my responsibility.....(CHO) write down some numbers. It is often difficult to determine which is BP and which is weight. How to trust.....Is it like this? Can the treatment be done right without seeing the patient? ..... Is trust created without seeing the patient's face? .....If you don't hear it from the doctor's mouth, people never trust on some written words.....How serious the disease is can be understood a lot by looking at the patient's face.....
Challenge in maintaining patient privacy and confidentiality	A: Privacy related issues	1. Insufficient guidance on how to maintain patient privacy during telemedicine consultation	....If a patient (female) has any problem in the chest or genital area, we cannot show the doctor properly. The patient also does not want to show. If someone takes a picture or video and leaves it on the net(social media), we will be guilty. It is good if there are any proper guidelines.....
Resource constraints	A: Incentive challenges	1. No incentive for doctors	....We are doing extra telemedicine with normal duty, no extra incentive is given for that.....
	B: Inadequate availability of medicine	1. Lack of essential medicine	.....Many drugs are not available.....Suppose two drugs for high blood pressure, amlo and losar, many patients get both. Sometimes we have supply of one medicine, sometimes the other. The patient who gets both, how to give him? Medicine(lack of medicine) is our main problem.....
	C: Inadequate manpower	1. Unavailability of doctors 2. Long waiting period 3. Managing a large volume of patients	....Many times doctor is not available (online)..... (if)after 40-45 minutes line is available, that too gets denied.....many patients get stuck in opd. making trouble. It is better to increase the number of doctors.....
Administrative and managerial issue	A: Lack of coordination with doctors	1. Doctor unaware about medicine availability 2. Call denial by doctors	....Many times it happens, the medicine that the doctor prescribed has run out for me. Then the patient has to buy from outside.....Many doctors deny call, then there is a lot of problem. The data that I wrote, all gets deleted. Do not receive if they are busy. Then at least the data does not have to be written twice.....
	B: Unrealistic target	1. Quality compromised by quantity	....Now target is given from CMOH office. Same amount of patient does not come every day, how can I fulfill the target? Quality is being compromised while meeting targets.....

- (2) Acceptability and trust
- (3) Quality and effectiveness
- (4) Perception

**DISCUSSION**

The present study aimed to explore the perceptions and constraints of Telemedicine services among healthcare providers and beneficiaries of West Bengal. The study found that the service providers faced several challenges related to lack of access to technology infrastructure and equipment, limited

training and support, resistance to change and adoption of new technology, challenge in maintaining patient privacy and confidentiality, resource constraints and administrative and managerial issues. On the other hand, beneficiaries reported issues related to access and availability of Telemedicine services, acceptability and trust, quality and effectiveness of Teleconsultation, and perception.

The findings of this study are consistent with previous research conducted in different parts of the world. Powell, *et al*<sup>10</sup> identified lack of reimbursement,

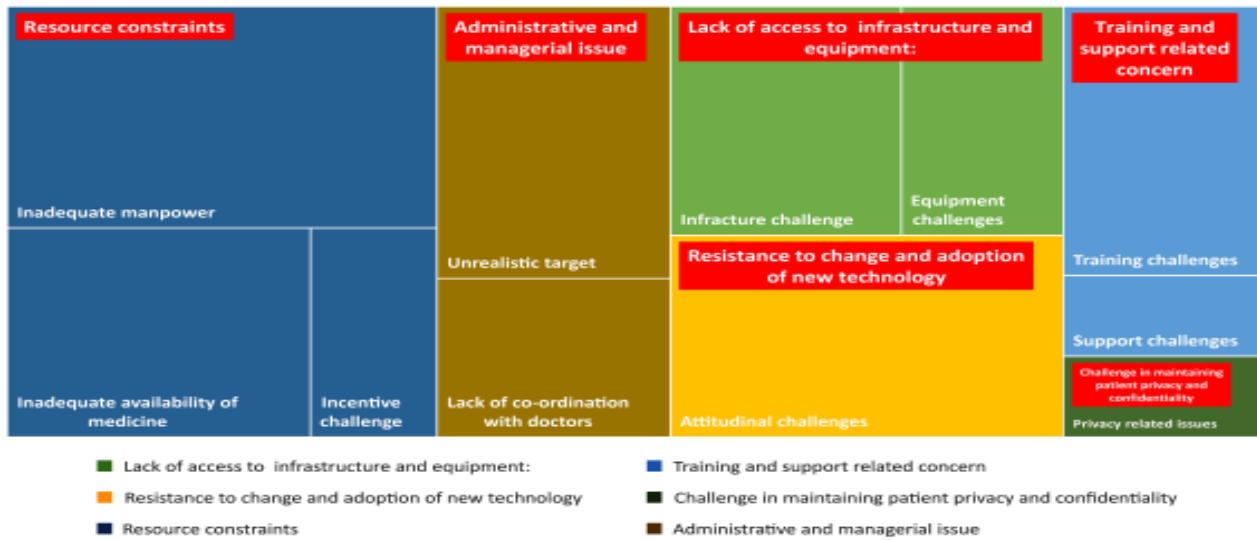


Fig 1 — A treemap diagram that shows a hierarchy chart of different themes and subthemes. It represents the identified themes and their relative importance. The different themes and the subthemes under each theme are nested into rectangles of different size and colour shade and the rectangular areas are proportional to the specified dimension of the coded data

Table 2 — Thematic representation of perception and constraints in availing the Telemedicine services from the beneficiaries' perspective

Theme	Subthemes	Codes	Sample Verbatims
Access and availability of telemedicine services	Internet connectivity	1.Poor signal strength	...sometimes the server is down....
	Staff availability	1. Long waiting period 2. Lack of CHO availability	.....You have to wait for one - one and a half hours to see the doctor. We have work too. (If)Doctor Babu is not available for a long duration, then CHO didi wrote down our problem, then sent medicine through ASHA's hand.....Sometimes the center is closed. Closed unless CHO is there.....
	Unavailability of medicine	1. Lack of variation of medicine 2. Shortage of medicine	.....Not all medications are available. We can't always buy from outside, then the medicine is discontinued.....I am fine with sugar medicine, many times it is not available. Then didi change the medicine. But that's always good to have.....
Acceptability and trust	A. Trust and confidence	1. Skepticism 2. Concern about privacy	....I don't know if it works or not. Not fully believed.....It is not possible to tell everything to the doctor on TV. Many people are standing here too.....
	B. Lack of physical examination	1.Difficulty in diagnosis 2.Concern about treatment efficacy	.....Can't see with hands (by doctor's own hand) . Everything is on Didi's word.....
Quality and effectiveness	A. Quality and effectiveness of teleconsultation	1. Limitation of examination by CHO 2. Potential of misdiagnosis 3. Need for in person consultation in complex cases	....It is a different matter if it is an old disease. If something new, who knows whether the doctor understands correctly!.....It seems that sometimes a doctor needs to come to see serious patients.....
	B. Concern about follow-up	1. Follow-up to same doctor	.....It would have been better if the checkup could have been done by the same doctor after being seen.....
Perception	A. Benefit of telemedicine	1. Increased access to healthcare services 2. Time and cost saving 3. Patient satisfaction 4. Anxiety relief	.....Before going to a big hospital, there was a lot of worry. I could not go alone. People used to complain in the hospital. No problem here. I can come alone.....Telemedicine has brought many benefits to people. Earlier, going to the hospital used to take a day, and travel costs were high....



Fig 2 — A Sunburst chart that depicts relative contribution of various themes and subthemes that emerged from analysis of FGD. The inner circle of the chart consists of themes and the surrounded outer circle contains the deeper hierarchy level, ie, subthemes. The angle of each segment is proportional to the representative data weightage. Each theme and the subthemes under it are different colour coded

regulatory barriers and technical issues as the major challenges faced by health care providers in implementing Telemedicine services in the United States. Another study<sup>11</sup> in United States showed that some disadvantages of telehealth include limitations with performing comprehensive physical examinations, possibilities for technical difficulties, security breaches and regulatory barriers.

In terms of beneficiaries' perspectives, previous researches has also identified similar themes. A systematic literature review conducted by Assefa, *et al*<sup>12</sup> in Ethiopia reported that lack of awareness, accessibility and affordability were some of the major barriers to the adoption of Telemedicine services among beneficiaries. Additionally, a study conducted by Bakshi, *et al*<sup>13</sup> in India reported that the quality of Teleconsultation, trust in the provider and convenience were important factors affecting the adoption of Telemedicine services among beneficiaries.

#### Limitations :

Data is collected from a rural district of Bengal thus lacking generalisability and so the findings are more applicable to different rural districts of Bengal.

#### CONCLUSIONS

In conclusion, this study provides valuable insights

into the perceptions and constraints of telemedicine services among healthcare providers and beneficiaries in India. The findings highlight the need for more investment in technology infrastructure, training and support for healthcare providers and resource allocation to overcome the barriers to the provision of Telemedicine services. Furthermore, the study findings emphasize the need to address the concerns of beneficiaries, such as trustability, quality, and effectiveness of Teleconsultation services and improve the perception of Telemedicine services to increase its adoption among beneficiaries.

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## Original Article

# Comparative Study of the Impact of Lifestyle Factors on the Health Among Students from Different Professional Backgrounds

Akhil R<sup>1</sup>, Vishakha Jayaram<sup>2</sup>, Kajal Srivastava<sup>3</sup>, Johnson S<sup>4</sup>, Mangala B<sup>5</sup>, Sai Mahesh Vajjala<sup>4</sup>

Healthy lifestyle is a choice. Those who wish to have a better life chose a lifestyle with a healthy diet, adequate physical activity, good mental health and abstain from addictions. Different professions have an impact on one lifestyle. Bad lifestyle choices lead to risk factors for non-communicable diseases. Early detection of these risk factors through blood tests helps in prevention of morbidity and mortality due to non-communicable diseases. A cross sectional analytical study was done among management, commerce and medical students using WHO STEPS questionnaire to assess physical activity and screening of risk factors done with blood investigations. Study revealed that physical activity was relatively high (81.33%) among the study population but addictions like smoking and alcohol intake was prevalent among a significant proportion of students. Risk factors like deranged HDL, LDL and BMI was observed among the study population. This urges individuals to inculcate change in their habits and daily routine for an improved life expectancy and productivity.

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**Key words :** Physical Activity, Lifestyle Diseases, Non-communicable Disease, Blood Parameters, Risk Factors.

Life is a gift, it gives you the Opportunity, Privilege and Responsibility to give something back. The joy of living a 'complete life' isn't a privilege given to all, rather a conscious choice.

A healthy lifestyle is one which helps to keep and improve people's health and well-being. Many Governments and Non-governmental organizations work at promoting healthy lifestyles. They measure the benefits with critical health numbers, including Weight, Blood Sugar, Blood Pressure and Blood Cholesterol<sup>1</sup>. A healthy lifestyle is mostly associated with adequate diet, appropriate physical activity, good sleep etc. Maintaining good Personal hygiene, absence of addictions, health education, safe environment, social support and healthy relationships are also required for good health<sup>2</sup>.

Life expectancy can be considered as a surrogate measure or tool to estimate health. The WHO estimates that life expectancy at birth reflects the overall mortality level of a population. It summarizes the mortality pattern that prevails across all age groups

### Editor's Comment :

- This study underscores the value of multidisciplinary approaches in student health promotion, encouraging both students and institutions to recognize and address the unique lifestyle challenges associated with different professional training environments.

in a given year – children, adolescent, adults and the elderly<sup>3</sup>.

- Two places come to mind when you hear the word Life expectancy; Sardinia, Italy and Okinawa, Japan. The life expectancy in these countries is 82.6 and 84.4 years respectively, the highest in the World<sup>4,5</sup>.
- The 'Okinawa Diet' is the main factor responsible for producing more than 400 centenarians because it is nutritionally dense yet low in calories<sup>5</sup>. Sardinia on the other hand credit its rich culture and homegrown produce for more longevity.
- Latest studies have shown that by inculcating 5 habits your life expectancy can be increased. A study found that the following 5 habits maintained during adulthood can add more than 10 years to your life expectancy:
  - (1) Eating a healthy diet.
  - (2) Exercising regularly.
  - (3) Keeping a healthy body weight.
  - (4) Not drinking too much alcohol.
  - (5) Not smoking<sup>6</sup>.

This study aims at comparative analysis of students of a fixed age group (19-21 years) from

Department of Community Medicine, Dr D Y Patil Medical College and Research Center, Pune, Maharashtra 411018

<sup>1</sup>MBBS, Junior Resident

<sup>2</sup>MBBS, Intern

<sup>3</sup>MD, Professor and Corresponding Author

<sup>4</sup>MBBS, Postgraduate Trainee

<sup>5</sup>MD, Assistant Professor

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different professional backgrounds to understand their lifestyle patterns and associated lifestyle disorders based on a questionnaire highlighting the above stated habits and by physically measuring the blood pressure, lipid profile, random blood sugar. Based on study outcome, we aim to provide recommendations in order to bring about the changes in their lifestyle factors which enable them to live a long and prosperous life.

The inspiration which led to this study is the fact that when students enter college, this is the period when habits are formed based on choices due to their different careers, demographic, relationships and apart from their already existing rigorous academic routine, the students face challenges such as changes in diet, decreased physical activity, susceptibility to smoking and alcohol consumption<sup>7</sup>. At the end of the study a definite pattern will be observed among the subjects and this will be helpful in raising awareness about the day-to-day changes that can be implemented among our youth since they are the future and the backbone of our economy and the well-being of their health is the priority of every nation in order to gain more economic productivity<sup>8</sup>.

#### MATERIALS AND METHODS

An Analytical-cross sectional study was conducted from 2019 to 2020 for a period of one year in three places namely a Medical College Hospital and Research Centre, Pune, College of Commerce and Science, Pune, Institute of Management Studies, Pune. Considering the proportion of adults in India with physical inactivity from the study "Physical activity and inactivity patterns in India - results from the ICMR-INDIAB study (Phase-1) [ICMR-INDIAB-5]"<sup>10</sup> by Anjana RM, *et al*, as 54.4%, with a confidence interval of 95% CI and an acceptable difference of 8%, sample size calculated was 149. Software used is winPepi version 11.65. Due to COVID-19 pandemic the sample size was reduced from 150 to 75.

By purposive sampling 35 students from the medical background, 25 from the management background and 15 from the commerce background who were of 19-21 years of age and who had given consent after being informed about the type of study and mode of data collection were included in the study based on their regularity to the college (including the ONLINE mode of teaching, Attendance >75%). Students who were suffering from any chronic conditions (eg: Type 1 diabetes, Hypertension etc.) or any type of genetic or metabolic disorders were excluded from the study.

**Methodology** — Data was collected based on an extensive questionnaire following the WHO STEPS criteria for the relevant factors that help understand the type of lifestyle maintained by the study population. The questionnaire was of 25 questions which highlight not just the health factors but also the socio demographic pattern, behavioral, environment and social life<sup>9</sup>.

The questionnaire consisted of three parts the first one being the socio demographic factors which include age, sex, professional background, any history of non-communicable diseases in self or family etc, followed by the 5 relevant lifestyle factors which determine the lifestyle pattern and in turn the life expectancy rate namely (1) Type of diet, personal hygiene, sleep pattern. (2) Frequency of exercise and type of exercise. (3) Consumption of Alcohol & Tobacco. (4) History of smoking and third one being the effects of the lifestyle patterns maintained on health which were assessed by measuring parameters like Height, weight, Blood pressure, Pulse, Waist-hip ratio, Waist circumference, Body mass index using standard techniques and by doing blood investigation such as lipid profile and random blood sugar analysis after obtaining the informed written consent from the study population. The instruments utilized for this comparative study included digital weighing scale, stadiometer, measuring tape, sphygmomanometer, vacutainers & calculator etc. Data was entered in MS-excel and then analysis was done using Epi-info 7 Appropriate test of significance was applied wherever required. Categorical variable was expressed in terms of frequency and percentage. Association between two categorical variables was analyzed using Chi square test with  $p < 0.05$  as statistically significant value at 95% confidence interval.

#### RESULTS

The type of study is a comparative study among students of the same age group but different professional backgrounds. The study was aimed at comparing not only the different professional backgrounds but also the lifestyle factors in an extensive manner, hence all modes of representing data is a comparison of different professional backgrounds and their respective lifestyle parameter.

Out of all the study participants from 3 different professional backgrounds, 15 (20%) were from commerce background, 25 (33.33%) from management background and 35 (46.67%) were from medical background and around 55 (73.33%) were >20 years of age (Figs 1 & 2).

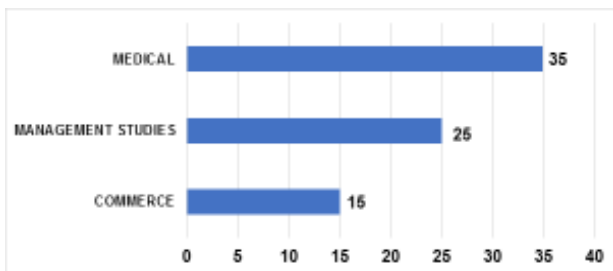


Fig 1 — Distribution of the Study Population according to Professional Category

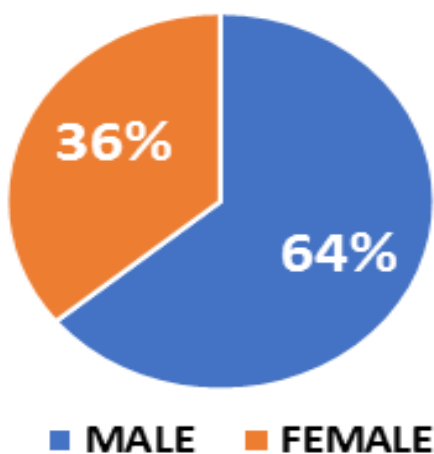


Fig 2 — Gender wise Distribution of the Study Population

Around 48 (64%) of the total study population were males and 27 (36%) were females.

The age category among the study population showed that commerce students, management students and medical college students with age less than 20 years were 9 (45%), 9 (45%) and 2(10%) respectively. Similarly, the composition of commerce students, management students and medical college students with age more than 20 were 6(10.91%), 16(29.09%) and 33(60%) respectively (Table 1).

In our study male participants were the majority ie, 17(68%), 9 (60%) and 22(62.86%) from management, commerce and medical college respectively (Table 2).

We observed that 8.57% students from medical students have high blood pressure followed by students of management (6.67%) and commerce college (4%). But there is no statistically significant association between blood pressure level and different professional education (p=0.849)(Table 3).

The study shows a single deranged value among the management professional background based on conducting random blood sugar test (Normal value for random blood sugar level was considered less than 140 mg/dl). Similar to blood pressure level, blood sugar

Table 1 — Age and Professional wise distribution of the Study Population

Age Category	Professional Category (N=75)			Total
	Commerce College (n=15)	Management College (n=25)	Medical College (n=35)	
<20 years	9(45%)	9(45%)	2(10 %)	20(100%)
>20 years	6(10.91%)	16(29.09%)	33(60%)	55(100%)

Table 2 — Gender and Professional wise distribution of the Study Population

Gender	Professional Category (N=75)		
	Commerce College (n=15)	Management College (n=25)	Medical College (n=35)
Female	6(40%)	8(32%)	13(37.14%)
Male	9(60%)	17(68%)	22(62.86%)
Total	15	25	35

level among different professional education groups do not show any association (p=0.533)(Table 3).

In our study, a deranged Total Cholesterol level was observed among 6(24%) medical students, 6(24%) management students and 4(26.67%) commerce students, based on a lipid profile test conducted (The normal range for Total Cholesterol varies according to the age category: The normal range for <20 years is <170mg/dl and the normal range for >20 category is 125-200mg/dl and any values below or above is considered as deranged). The study excluded any individuals having any metabolic disorders. There was no association between Total Cholesterol and professional background (p=1)(Table 3).

Proportion of deranged triglyceride levels were found high among students from commerce background followed by medical students (normal range for triglyceride values is <150mg/dl). Any value > or < 150mg/dl was classified as deranged. There was no association between the triglycerides level among different professional backgrounds. (p=0.0612)(Table 3).

It was noticed that the most number of deranged values were found in medical students (68.57%) followed by commerce college (66.67%) and then the management students (48%). The table also represents that almost 50% of the study population had elevated LDL levels (normal range for LDL values is <100mg/dl, any value >100mg/dl is considered as deranged). There was no significant association between serum LDL level and different professional backgrounds (p=0.2433)(Table 3).

The greatest number of deranged values of HDL were found in commerce students (46.67%) followed by the management students (44%) and then the



Variable		Professional Category			Total (N=75)	Test of Significance
		Commerce College (n=15)	Management College (n=25)	Medical College (n=35)		
Blood Pressure	Normal	14(93.33%)	24(96%)	32(91.43%)	70(93.33%)	Fisher's exact test=0.4898, p=0.849
	Hypertensive	1(6.67%)	1(4%)	3(8.57%)	5(6.67%)	
Random Blood sugar levels	Normal	15(100%)	24(96%)	35(100%)	74(98.67%)	Fisher's exact test=2.027, p= 0.533
	Deranged	0(0%)	1(4%)	0(0%)	1(1.33%)	
Total Cholesterol	Normal	11(73.33%)	19(76%)	27(77.14%)	57(76%)	$\chi^2=0.083$ , p=0.959
	Deranged	4(26.67%)	6(24%)	8(22.86%)	18(24%)	
Triglycerides	Normal	9(60%)	23(92%)	28(80%)	60(80%)	Fisher's exact test=6p=0.0612
	Deranged	6(40%)	2(8%)	7(20%)	15(20%)	
Low Density Lipoprotein (LDL)	<100	5(33.33%)	13(52%)	11(31.43%)	29(38.67%)	$\chi^2=2.8272$ , p=0.2433
	>100	10(66.67%)	12(48%)	24(68.57%)	46(61.33%)	
High Density Lipoprotein (HDL)	Normal	8(53.33%)	14(56%)	20(57.14%)	42(56%)	$\chi^2=0.0618$ , p=0.9696
	Deranged	7(46.67%)	11(44%)	15(42.86%)	33(44%)	
Body Mass Index (BMI)	Normal	5(33.33%)	9(36%)	18(5.43%)	32(42.67%)	Fisher's exact test=7.3903 p=0.5472
	Obese	2(13.33%)	3(12%)	2(5.71%)	7(9.33%)	
	Overweight	2(13.33%)	7(28%)	5(14.29%)	14(18.67%)	
	Pre-obese	3(20%)	5(20%)	8(22.86%)	16(21.33%)	
	Under weight	3(20%)	1(4%)	2(5.71%)	6(8%)	

medical college (42.86%). The table also represents that almost 50% of the study population had deranged HDL levels (The normal range for 0-19 years is >45mg/dl and any value <45mg/dl is classified as deranged. Similarly, the normal range for >20 category is further different for both males and females. For males a value >40mg/dl is considered normal and <40mg/dl is considered deranged. For females a value of >50mg/dl is considered normal and <50mg/dl deranged). We couldn't find out any association between serum HDL level and professional background (p=0.9696)(Table 3).

Based on BMI calculated, most medical students are in the pre-obese category followed by the normal category. Most management students are in the normal category followed by the overweight category. Commerce college also consists of a normal majority followed by the pre-obese category. The data for BMI was calculated by measuring the height and weight followed by utilizing the formula for BMI ie, BMI=

Weight (in Kg)/ (Height (in Mt))<sup>2</sup>. There was no statistically significant association between BMI distribution and different professions (p=0.5472) (Table 3).

It was found that physical activity was more among the students from commerce background, 14 students (93.33%) compared to other two groups. But there was no statistically significant association between physical activity and professional categories (P=0.4642)(Table 4).

In our study we observed that sleep of 33 (94.29%) medical students was affected because of workload followed by 13(86.67%) students from commerce background and 20 (80%) student from management background. There was no association between effect of workload on sleep and professional backgrounds (P=0.2163)(Table 4).

About 24% of study population were having history of smoking and smoking was predominant in medical students (40%), least was among

Variable		Professional Category			Total (N=75)	Test of Significance
		Commerce College (n=15)	Management College (n=25)	Medical College (n=35)		
Physical Activity	Present	14(93.33%)	20(80%)	27(77.14%)	61(81.33%)	Fisher's exact test=1.8568, p=0.4642
	Absent	1(6.67%)	5(20%)	8(22.86%)	14(18.67%)	
Effect of Workload on Sleep	Affected	13(86.67%)	20(80%)	33(94.29%)	66(88%)	Fisher's exact test=2.8499, p=0.2163
	Not affected	2(13.33%)	5(20%)	2(5.71%)	9(12%)	
Smoking	Present	2(13.33%)	2(8%)	14(40%)	18(24%)	Fisher's exact test=9.3567, p=0.0101
	Absent	13(86.67%)	23(92%)	21(60%)	57(76%)	
Alcohol Consumption	Consumed	2(13.33%)	9(36%)	22(62.86%)	33(44%)	$\chi^2=11.4255$ , p=0.0033
	Not consumed	13(86.67%)	16(64%)	13(37.14%)	42(56%)	

management students (8%). There was a statistically significant association between the history of smoking and different educational background. ( $P=0.0101$ )(Table 4).

It was noticed that alcohol consumption was predominant among the medical background (62.86%) followed by the management background (36%) and then commerce background (13.33%). (Any amount of alcohol consumption ie, low/moderate were considered as alcohol consumption and absolute zero consumption of alcohol is considered as not consumed in the study) There was a statistically significant association between alcohol consumption and professional backgrounds ( $P=0.0033$ )(Table 4).

### DISCUSSION

Lifestyle factors are the backbone of prolonging our life expectancy rate. The different study population selected gives an understanding of the health impacts of different professional backgrounds. This is a comparative study with the study population of college students from 19-21 years of age. Study describes the various lifestyle changes that have been brought about upon entering college which helps in becoming more innovative to form new ways which will help prolong our life expectancy rate as these young adults are the backbone of our nation.

Study carried out by Hee Jung Jang, *et al*<sup>11</sup> on the topic health promoting lifestyle and its subjective happiness among nursing and non-nursing students concluded that health promoting lifestyle like good interpersonal relations, health responsibility, stress management, and spiritual growth showed a significant difference between the groups but had no impact on the subjective happiness. Our study aimed at identifying the different types of lifestyle factors and inculcating only the lifestyle factors which have an impact on prolonging our life expectancy rate. Hence from the study referenced it is clear that based on our study the health promoting lifestyle factors for example, daily physical activity which was identified among different backgrounds can be selected as a health promoting parameter especially in this study where students from certain professional backgrounds need more emphasis on physical activity than others.

Study carried out by Seipone BM Mphole, *et al*<sup>12</sup> regarding stress and alcohol among students found evidence that most students engage in social drinking upon entering college itself ie, from 18 years onwards. Our study consisted of a study population of 19-21 years amongst which 33(44%) students were having

drinking habits and it has been observed that with different professional backgrounds the extent of drinking is more based on the workload and stress.

Study carried out by Ivane Chkhaideze, *et al*<sup>13</sup> regarding the prevalence of factors affecting smoking among medical and non-medical students presented with a greater number of smokers amongst medical students. A similar pattern is seen here to the extent that smoking among medical students is much greatly prevalent than non-medical students due to the social engagement upon entering college and due to excessive amounts of stress and workload.

In a study carried out by Kirti Deshpande, *et al*<sup>14</sup> regarding the lifestyle and obesity among college students, the categorization of BMI was based on lack of physical activity, disturbed sleep pattern due to workload, onset of habits such as smoking and alcohol and an overall habit of binge eating especially fast food. All these parameters have been compared in our study as well which notes a lack of physical activity amongst some backgrounds due to their busy schedules, disturbed sleep especially during exam time, indulgence in habits such as smoking and alcohol excessively and an overall lack of time which leads to an increase in the consumption of fast foods.

Study conducted by Pranita Ashok, *et al*<sup>15</sup> concluded that students among the obese and pre-obese category of obesity are at more risk of developing Type-2 Diabetes along with a sedentary lifestyle. Our study did not show any significant outcome in the random blood sugar test but the BMI measured categorized a large group of students into the pre-obese and obese category. Based on the professional backgrounds these students are at risk of developing Type-2 diabetes especially those professions which have a sedentary lifestyle for example the commerce and management background in our study.

Study conducted by Purushottam Pramanik<sup>16</sup> found a correlation between obesity and increased blood pressure. Our study focused on the students from different professional backgrounds and its impact on blood pressure whether they range from normal to hypertensive. It was observed that a very small group of students were categorized as hypertensive and that the medical students had an increased prevalence of hypertensive cases. Based on past studies which correlate BMI classification of obesity and hypertension many students are at risk of developing hypertension in the future which can also lead to the development of cardiovascular disease.

Study by Jalal SM, *et al*<sup>17</sup> compared the BMI of college going students during the COVID-19 pandemic and found an increase in the BMI values among college students due to a sedentary lifestyle and lack of physical activities. A similar range of students were seen in the pre-obese and obese category in our study and a correlation was seen amongst students as most of the academic period during COVID-19 pandemic, was conducted in the online mode i.e., a sedentary lifestyle.

In a recent study done by Chusak, *et al* in Bangkok to assess the lifestyle behavior and quality of life during COVID-19 pandemic among undergraduate students, it was found that only 47.2% of students had BMI in normal range, remaining are either underweight or overweight. Majority of students (53.7%) were not doing any exercise. Prevalence of smoking among the study population was 1.1%. There was an increased consumption of unhealthy food by participants<sup>18</sup>.

In another study done by Ali, *et al* among Palestinian male university student to look for the risk of tobacco smoking and energy drink consumption on obesity revealed that prevalence of obesity was high (42%) among participants, which was less in our study. In the same study they found out that prevalence of smoking and waterpipe smoking was 39.6% and 43.2% respectively. They concluded that waterpipe smoking is a risk factor for central obesity and smoking is a risk factor for underweight<sup>19</sup>.

Another important cross-sectional study done in China by Li, *et al* in 2022 detected that prevalence of hypertension among undergraduate students is 10.59% which was high compared to our study outcomes. Among the subjects, 13.33% were overweight and 3.33% were obese which was comparatively less than present study. They concluded that hypertension is correlated with increased neck circumference and BMI and a weak correlation between blood sugar level and hypertension<sup>20</sup>.

Another study done in Indian settings by Rao, *et al*, using similar methodology detected that prevalence of DM was 2.36% compared to 1.33% deranged random blood sugar level in current study. Prevalence of inadequate physical activity were 8.57% compared to 8.67% in our study. Proportion of participant with High Total cholesterol, high triglyceride, high LDL, abnormal HDL were 4.43%, 17.24%, 5.71%, 43.57% respectively in this study compared to 24%, 20%, 61.33%, 44% respectively in our study which must be considered as an alarming fact<sup>21</sup>. Reason may be more

outside eating and less knowledge of cooking oil may be associated with such levels.

### CONCLUSION

Lifestyle factors are one of the important modifiable risk factors for non-communicable diseases like Type 2 diabetes mellitus, Hypertension, Cardiovascular Diseases. Different professions have a different impact on one's lifestyle. College students, our study population, are at the risk of adapting to wrong lifestyle, which if detected earlier can be reversed back by implementation of lifestyle modifications like simple physical activity, diet control and restriction of use of alcohol and tobacco products. Deranged blood sugar levels, lipid profile with sedentary lifestyle depending on profession increases the risk of developing non-communicable diseases. This urges individuals to inculcate change in their habits and daily routine for an improved life expectancy and productivity. Further researches must be done among various spectrum of professional backgrounds for a better understanding and the impact of COVID-19 appropriate behavior on physical activity and other risk factors.

### Recommendations :

This study revealed that the lifestyle patterns are having a major impact on our life expectancy rate and the problems start between the age group of 19-21 years.

To overcome this, we start off by raising awareness about the day-to-day changes that can be implemented among our youth since they are the future and the backbone of our economy and the well-being of their health is the priority of every nation. Simple yet highly effective changes are required to be implemented like:

- (1) Introducing 1 hour of exercise in the form of Yoga/ any form of physical activity which helps physical as well as mental fitness.
- (2) Participation in an outdoor activity for at least 1 hour is also rejuvenating to the mind and body.
- (3) Conducting sessions regarding the health hazards of alcohol and smoking over a period of time.
- (4) Educating about diet patterns and management of stress levels in college lifestyle through simple techniques which are highly effective.
- (5) Need to understand the socio-demographic factors impacting our lifestyle and implementing changes which include careful expenditure on food, alcohol, cigarettes etc. and also bringing about a more disciplined and healthier lifestyle to increase our life expectancy rate.

- (6) Explore the effect of increased life expectancy rate on the economy of our country.

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## Review Article

# Burden of Metabolic Dysfunction-associated Steatotic Liver Disease in India and the way forward

**Sanjay Bandyopadhyay<sup>1</sup>**

Liver disease is a significant public health issue in India and the burden of the disease is rapidly growing. Liver-related deaths in India account for 3.17% of all deaths and 18.3% of global liver-related deaths. Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) accounts for 8 to 20% of all Chronic Liver Disease (CLD). Progressive adoption of western diet and sedentary lifestyle, along with increasing prevalence of Obesity, Type 2 diabetes and other components of metabolic syndrome will further increase the prevalence of MASLD and corresponding health care expenditure in near future. Unfortunately, there are limitations in the quality of the available epidemiological data resources in India. Better screening strategies, more effective linkage to care for early-stage liver disease and improved awareness on preventive steps in an integrated way could be useful interventions.

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**Key words :** Metabolic Dysfunction-associated Steatotic Liver Disease, Type 2 Diabetes, Prevalence, Screening.

The burden of Liver Disease in India is high, since it accounted for 18.3% of the two million fatalities Worldwide attributable to liver disease in 2015<sup>1</sup>. Cirrhosis and its consequences, commonly known as Chronic Liver Diseases (CLDs), have been growing as a cause of death in India since 1980. However, the quality of the available epidemiological data on liver disease is limited in this country. There has been a recent rise in the cases of Metabolic Dysfunction-associated Steatotic Liver Disease (MASLD) as cause of liver disease in addition to viral factors and alcoholic etiology. Adoption of sedentary lifestyle, lack of exercise, unhealthy dietary habits, increasing prevalence of obesity and metabolic syndrome, rising life expectancy are significant demographic factors influencing this development. MASLD is rapidly becoming recognised as an important public health issue. In accordance with this, India has established encouraging health system response methods. A nationwide MASLD control programme including actions that incorporate liver disease control into other non-communicable disease control measures was established in 2021<sup>2,3</sup>.

### The Burden of MASLD :

Complications of MASLD and its associated metabolic syndrome are important cause of mortality in India. The Global Health Estimates (GHE) 2018

#### Editor's Comment :

■ In India, MASLD is progressively becoming an issue that is given emphasis in terms of public health. In order to battle the burden of MASLD, the magnitude of the problem and the obstacles in implementing effective care need to be identified. In a strategic shift, the Government of India has incorporated non-communicable diseases into its comprehensive primary healthcare approach for universal health coverage.

dataset documented that MASLD accounted for 10.9% of all deaths due to Cirrhosis and 9.6% of all deaths due to liver cancer<sup>4</sup>. MASLD is intricately related to several metabolic (like obesity, type 2 diabetes) and environmental factors (such as physical inactivity). These are common in the Indian population<sup>5</sup>. According to community-based studies, the prevalence of MASLD on ultrasonography in urban areas varied between 18.9% to 32%, and in rural areas between 8.7% to 30.7%<sup>6-9</sup>. In hospital-based studies, this prevalence was between 25.3% to 32.2%<sup>10,11</sup>. Indian studies have also shown high prevalence of fatty liver disease in patients with type 2 diabetes (10-5-88%) or amongst obese people (50-80%)<sup>12,13</sup>. Overall, 11-32% of patients with MASLD had a normal Body-mass Index (BMI)<sup>14</sup>. Table 1 shows the epidemiological studies on MASLD done in India over last two decades.

Over the years, India has witnesses a disproportionate increase in the number of overweight and obese adults and it nearly doubled to 18.6% in 2015-16 from 9.3% in 2005-06 in men, and to 20.7% from 12.6% in women<sup>15</sup>. Additionally, there are currently more than 70 million adults with type 2

<sup>1</sup>MD, DM, MNAMS, FACP, FRCP, Consultant, Department of Gastroenterology, Kolkata Gastro Care, Kolkata, West Bengal 700028 and Corresponding Author

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Table 1 — Epidemiological study on prevalence and risk factors of MASLD (NAFLD) in India

Study, year, reference	Setting	Total population screened	Prevalence of MASLD	Main findings	Risk factors
Amrapurkar, <i>et al.</i> 2007 [6]	Community-based, urban	1168	16.6%	Mean age 39.08 ± 12.3 years, 4% had diabetes, 57% had central obesity	Age > 40 years, male gender, central obesity, high BMR > 25, elevated FPG, raised AST, ALT
Mohan, <i>et al.</i> 2009 [7]	Community-based, urban	541	32%	Mean age: 42 ± 13 BMI 22.9 ± 3.6 years, AST 21.9, ALT 22.2	Type 2 diabetes (OR:2.9) and metabolic syndrome (OR:2.0)
Das, <i>et al.</i> 2010 [8]	Community-based, rural	1911	11%	75% had BMI <25 kg/m <sup>2</sup> , 54% neither over weight nor had abdominal obesity	BMI > 25, Abdominal obesity, dysglycemia, elevated HOMA
Majumdar, <i>et al.</i> 2016 [9]	Community-based, rural	216	30.7%	No significant difference in the calorie intake and average total physical activity in population with and without NAFLD	Hypertension (OR: 2.3), increased waist circumference (OR: 4.9)
Siraj, <i>et al.</i> 2012 [10]	Hospital-based	300	25.3%	Most subjects were males, between 36-45 years of age, from urban areas	High energy, protein and fat intake
Bajaj, <i>et al.</i> 2009 [11]	Hospital-based	121	32.2%	Subjects with NAFLD have significantly higher values of BMI, waist circumference, hip circumference, FBG, fasting insulin, total cholesterol and serum triglycerides	High BMI (OR 4.3), FPG (OR 5.4), and fasting insulin (OR 2.4)
Jali, <i>et al.</i> 2015 [12]	Hospital-based, patients with T2DM	1750	10.51%	Prevalence of obesity (65% vs 41%), hypertension (86% vs 58%), dyslipidemia higher	Increasing age (>60 years) increasing duration (>9 years) of DM
Kalra, <i>et al.</i> 2015 [13]	Hospital-based, patients with T2DM	924	56.5%	Prevalence higher in females, in northern states, highest (61.8%) in 61-70 years' age group. mean AST 54.8 ± 36.1 IU/L and mean ALT 55.6 ± 39.8 IU/L	Dyslipidemia, hypertension, obesity (had 38%, 17% and 14% higher risk of NAFLD respectively)

diabetes aged 20-79 years, and this population is likely to increase to 123.5 million by 2040, which would probably lead to an increase in the burden of MASLD<sup>16</sup>. One hospital-based study had shown that nearly half of patients with MASLD with increased aminotransferase concentrations had histologically confirmed Metabolic Dysfunction-associated Steatohepatitis (MASH) on liver biopsy, although majority (80-98%) had only stage 1 or stage 2 changes<sup>17</sup>. There is scarcity of prospective follow up data on the natural history of MASLD and MASH in India. In hospital-based studies between 2003 and 2011, cryptogenic cirrhosis, believed to be largely due to MASLD progression, accounted for 15.8-48.8% of patients with Cirrhosis<sup>18</sup>. Moreover, 4.6-19% of patients with liver cancer had no risk factor for liver disease (like HBV, HCV or Alcohol)<sup>19,20</sup>.

### Current Challenges :

India's epidemiological statistics are insufficient, making it challenging to estimate liver disease burden. Limitations of resources, hepatologists and healthcare facilities; cultural beliefs; dependence on untested and unproven traditional medicines and herbal supplements; lack of awareness of diseases and their modes of transmission – all contribute to making

management of these conditions difficult<sup>21</sup>. Moreover, due to rapid urbanization, industrialization and upwards movement of society in terms of affordability, the prevalence of diabetes, obesity and metabolic syndrome are increasing all over the country.

The number of health care personnel like doctors, nurses, technicians trained to manage liver disease and its complication at secondary/ tertiary care level is grossly insufficient in India. We also lack adequate number of health care personnel at primary level who are appropriately trained for detection and initial management of liver diseases and referral of those at risk of progressive disease to specialised centres. There are very few dedicated liver institutes, and the facilities for management of paediatric liver diseases are available in only a few centres.

The number of liver transplantation in India is much less compared to the large number of patients of decompensated chronic liver disease who die on waiting list. The facilities for transplantation are available only in a limited number of institutes. Most such institutes are private hospitals, situated in the metropolitan cities and beyond the reach of common people. Cadaveric transplantation has not yet gained momentum in this country.

### Screening for MASLD in Primary Care :

Although the gold standard for diagnosing MASLD and MASH with and without fibrosis is liver biopsy, this method is often impractical, expensive and not without risk. Because laboratory values alone are not a reliable indicator of MASLD, a three-pronged approach is suggested to screen for MASLD in high-risk patients.

First, patients should be screened for MASLD with abdominal ultrasound. Second, if fatty liver is present on ultrasound, patients should be assessed for the severity of liver fibrosis using clinical prediction rule(s). A commonly used system is FIB-4 score (a composite of age, alanine transaminase, aspartate transaminase and platelet count) as it has been shown to have the best diagnostic accuracy of the non-invasive scores in detecting advanced fibrosis and are simple to calculate in the clinic. Further, patients showing indeterminate values should be referred for transient elastography (Fibroscan of liver). Finally, patients who are at high risk for advanced fibrosis or who are found to have this condition should be referred to a hepatologist for further evaluation (Fig 1).

### Therapeutic Considerations for MASLD in India:

Lifestyle interventions including dietary calorie restriction and exercise constitute the central pillar of MASLD management. There is a dose-response relationship with weight loss of (3-5)%, 7% and 10% being associated with improvement in steatosis, steatohepatitis and fibrosis, respectively<sup>22</sup>. Even in lean individuals, exercise helps in improving hepatic triglycerides and insulin resistance. In India, INASL recommends daily calorie restriction by 30% or (500-1000) kcal to achieve the target weight loss<sup>5</sup>. It also recommends moderate intensity aerobic or resistance exercises 30-45 min/day at least 5 days in a week (at least 200 min per week) in all patients with MASLD irrespective of body weight. In the absence of randomized clinical trials, bariatric surgery cannot be recommended as a primary treatment for MASLD in India.

The choice of drugs for MASH pharmacotherapy should be individualized on the basis of age, gender and the presence/absence of diabetes/dyslipidemia, cost and availability.

Vitamin E is recommended as pharmacotherapy for MASH with or without hepatic fibrosis (F1-F3) in nondiabetic adult and pediatric patients; pioglitazone and saroglitazar in those with or without hepatic fibrosis (F1-F3) (in both diabetic and nondiabetic adult patients). In patients in whom liver biopsy is not available, NASH specific pharmacotherapy can be used in those having significant fibrosis on noninvasive assessment (like Fibroscan of liver). Obeticholic acid as pharmacotherapy is not recommended in India. Two recent meta-analyses by Indian authors have established the role of saroglitazar and injectable semaglutide in improving hepatocellular inflammation and to a smaller extent liver fibrosis, in MASLD patients<sup>23,24</sup>. Studies on oral semaglutide are underway. The use of pharmacotherapy in MASH-related cirrhosis is not recommended<sup>5</sup>.

### Government's Initiatives to Curb MASLD :

With an aim to curtail the burden of non-communicable diseases including MASLD, the Government of India has taken many initiatives. The Indian Ministry of Health and Family Welfare has reduced the diagnostic threshold of overweight to a

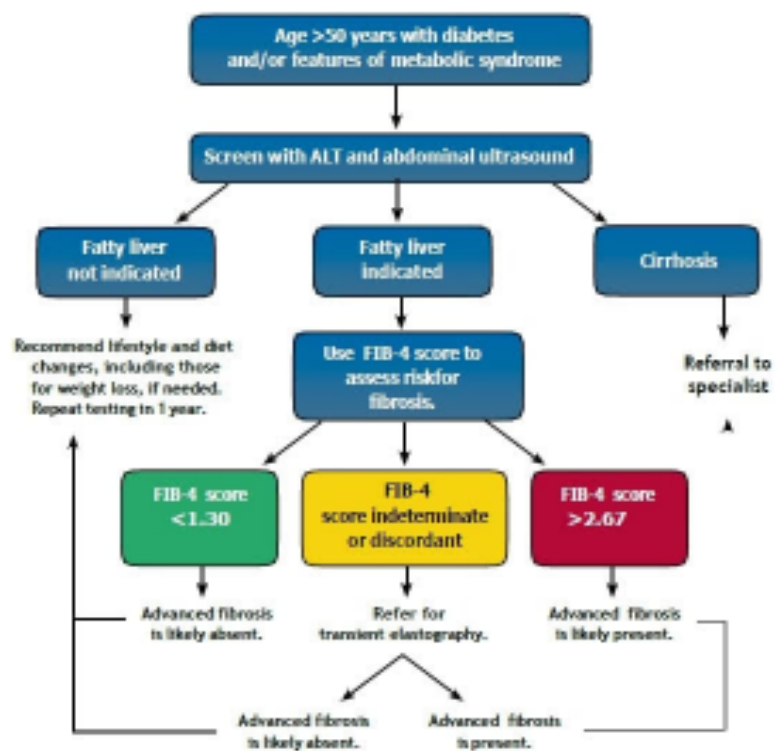


Fig 1 — Clinical care pathway for screening and evaluation of MASLD

BMI of 23 kg/m<sup>2</sup> (from 25), and the standard waist circumference diagnostic of abdominal obesity to 90 cm in men and 80 cm in women (internationally accepted values are 102 cm in men and 88 cm in women). This is a timely response to ameliorate the risk of death and burden of disability due to non-communicable diseases, as projected by Global Disease Burden (GBD) statistics in 2015. These standards have been published in the ministry's Consensus Guidelines for the Prevention and Management of Obesity and Metabolic Syndrome<sup>25</sup>.

The Government of India also initiated the integrated National Programme for Prevention and Control of Diabetes, Cardiovascular Disease and Stroke (NPCDCS) in 2017 and since 2021, MASLD is also included in it<sup>26</sup>. This is the recognition of the shared risk factors between these lifestyle-related diseases. The major objectives of NPCDCS are: (i) health promotion, awareness generation and promotion of healthy lifestyle, (ii) self-testing, screening and early detection, (iii) affordable point-of-care diagnosis, (iv) access to affordable treatment, and finally, (v) rehabilitation.

In India, there are no specific laws that regulate the marketing and advertising of fast foods. However, the State Governments of Delhi and Uttar Pradesh had taken small initiatives and instructed schools not to allow the sale of junk foods in their canteens. Local food vendors are also prevented from selling such items in the vicinity of educational institutions. The Food Safety and Standards Authority of India (FSSAI) had also produced guidelines to control the objectivity and accuracy of food advertisements. However, all of these measures are recommendations rather than mandatory and hardly any punishment is meted out for failure in compliance<sup>27</sup>. Amendments regarding packaging and labelling of food under part VII of the Prevention of Food Adulteration Rules of 1955 mandate the disclosure of health claims alongside nutritional labelling. However, stricter policies are required to prevent misleading information. In 2010, the FSSAI expert group formulated guidelines that recommend less than 10% trans fats in food products<sup>28</sup>. The state of Kerala has already imposed 14.5% fat tax on the consumption of certain foods<sup>29</sup>.

### The Way Forward :

We need dedicated public awareness campaigns to increase knowledge about MASLD, its risk factors, and preventive measures. Community health programmes may be arranged or digital media may be utilized to disseminate information.

Another way to prevent the menace of MASLD is to provide nutritional counselling services to individuals with MASLD on every consultation to promote healthy eating habits and weight management. Nutritionists can offer support groups or online resources for individuals to share experiences and seek guidance.

In the past decade, India has developed liver transplantation, largely from donors, with results comparable to Western countries. The newly established Indian Liver Transplant Registry (ILTR) may soon provide prospective and transparent countrywide statistics. As there is gross mismatch in the demand and supply of organs, liver transplantation from deceased brain-dead donors needs to be encouraged. Even in deceased donors, the organ-sharing policies should change from current rotational policy to a more pragmatic severity-based system.

To address the challenges of MASLD collectively, we need to foster collaborations between healthcare institutions, research organizations and community groups. Engaging with international experts and organizations to share best practices may be an innovative idea. Research priorities in India need to focus on the quality of data collection regarding the incidence and prevalence of MASLD and associated risk factors, as well as morbidity and mortality related to Cirrhosis and Liver Cancer in this condition. The effectiveness of potential interventions to prevent and treat MASLD needs to be investigated in longitudinal studies.

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## Review Article

# Clinical Profile, Laboratory Parameters, Radiological Findings of COVID-19 Patients and its Association with Outcome — A Retrospective Observational Study

P B Meenakumari<sup>1</sup>, Anitha Bhaskar<sup>2</sup>, Indu R M<sup>3</sup>, Clint Jose<sup>4</sup>

**Background :** To study the clinical and epidemiological profile, laboratory parameters, radiological findings of patients admitted in Covid ICU of General Hospital, Thiruvananthapuram and its association with outcome.

**Materials and Methods :** The study was a hospital based retrospective study among patients admitted with COVID-19, in ICU of General Hospital, Thiruvananthapuram, Kerala which is a tertiary care centre, between 1<sup>st</sup> May and 31<sup>st</sup> of July, 2021. Diagnosis of COVID was confirmed either by Rapid Antigen test or RT-PCR. The features analyzed were demographic profile, co-morbidities, symptoms, clinical characteristics, laboratory parameters, radiological findings and outcome.

**Results :** Mean age of the population was 55.46 years, maximum patients were in 50-60-year age group. Highest mortality was seen in above 60 age group. (68.5%). Male gender were affected more (59%), but mortality was high in females (62.2%). Breathlessness was the commonest symptom and ARDS the commonest complication noted. Hypertension, Diabetes Mellitus, Chronic Kidney Disease, Cardiovascular, Cerebrovascular Diseases, Cancer were associated with significant mortality. Lymphocytopenia, raised blood Urea, SGOT, SGPT, CRP, D dimer was increased significantly in the non-survivor group.

**Conclusion :** Advanced age and presence of co morbidities were associated with increased mortality. Hypertension, Diabetes Mellitus, Chronic Kidney Disease was associated with increased mortality. These group of patients need early recognition and prompt intervention which will help in bringing down the mortality.

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**Key words :** Lymphocytopenia, ARDS.

COVID-19 was declared as pandemic on 11th March, 2020. India has reported highest number of COVID cases second only to USA, but the case fatality rate was 1.2%. This was the lowest among the countries which had very high burden of Covid cases. The second wave in India was from April, 2021 and it spread across the country since the causative strain was highly transmissible. The number of cases started decreasing in other regions of India by May, 2021, but it took long for the cases to come down in Kerala, Maharashtra and North Eastern states<sup>1</sup>. In Kerala we had huge burden of COVID cases till end of July, 2021. Studies across the world proved that advanced age and co morbidities, certain specific clinical features, laboratory parameters, and radiological findings are associated with severe form of COVID-19 with adverse outcome. The present

### Editor's Comment :

- Early screening of COVID and appropriate management in elderly patients and in those with co morbidities help in better outcome.
- Proper control of Diabetes Mellitus, Hypertension, Chronic kidney disease help in reducing complications and mortality of COVID.

study was done to analyze these features and its association with outcome in our population<sup>2</sup>. The study was conducted at General Hospital Thiruvananthapuram which is a Tertiary Care Centre under Kerala State Health Services Department.

### MATERIALS AND METHODS

After getting institutional ethics committee approval, retrospectively collected data of patients admitted in ICU from 1<sup>st</sup> April to 31<sup>st</sup> July. All patients above 18 years of age and positive for either RT PCR or RAT were included. The decision for ICU admission and treatment protocols practiced were as per guidelines of Ministry of Health and Family Welfare Government of India. Severe category patients were admitted in ICU. Those with respiratory rate >30 per minute and /or oxygen saturation <90%.

Department of General Medicine, General Hospital, Thiruvananthapuram, Kerala 695035

<sup>1</sup>MBBS, Chief Consultant & Head and Corresponding Author

<sup>2</sup>MBBS, Professor and Head, Department of Community Medicine, Government Medical College, Thrissur, Kerala 680596

<sup>3</sup>MBBS, Assistant Surgeon, Department of Community Medicine

<sup>4</sup>MBBS, Junior Resident

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Details of age, gender, co-morbidities, symptoms and complications were collected. Co-morbidities included were Diabetes mellitus, Hypertension, Chronic Kidney Disease, Chronic Liver Disease, Cerebro Vascular Accident, Coronary Artery Disease, Chronic lung disease, Dyslipidemia, Malignancy and Hypothyroidism. Symptoms analyzed were fever, cough, breathlessness, sore throat, chest pain, hemoptysis, diarrhea, altered sensorium, anosmia, myalgia and fatigue. Complications considered were ARDS, Pneumonia, CAD, AKI, DKA, CHF, Transaminitis and outcome.

### Statistical Analysis :

Data were entered in MS Excel and analyzed using SPSS software version 20

### RESULTS

The present study included 205 patients; mean age of the population was 55.46 years (55.459±13.9840). Youngest patient was 24 years and oldest patient 85 years. Maximum patients were in the 50-60 years group (57 patients), followed by 60-70 years (44 patients) and 40-50 years (40 patient) respectively. (Figs 1&2).

Out of 205 patients 10 patients were referred to Government Medical College Hospital, Thiruvananthapuram. From the rest 195 patients 118 (57.6%) died and 77 (37.6%) patients survived the non-survivor group was divided into three (Fig 2).

As age advances mortality increases, highest mortality was seen in age group above 60 years (68.5%) and association of age with mortality was statistically significant ( $p=0.0001$ ). Mortality was lowest in less than 40 years age group (21.7%)(Fig 3).

Males were more affected in our study (59%) than females (40.9%) (Fig 3) mortality was higher among female patients (62.2%) than male patients (59.3%).

Breathlessness was the commonest symptom (69.3%), followed by cough in (60%). Saturation level at the time of admission was better in the survived group (mean  $SPO_2$  88.234), than in non-survivor group (mean  $SPO_2$  82.847). Fever was the next commonest symptom 38%, followed by myalgia (24.9%), fatigue (23.9%), diarrhea (10.7%). chest pain (9.8%), sore throat (6.3%)(Table 1).

Among the total 195 patients, 172(88.2%) had co morbidities, mortality was 64.5% in this group, whereas in the group who did not have any co morbidities, mortality was 30.4% and this difference in mortality was statistically significant ( $p=0.002$ ), (Table 2). Diabetes Mellitus was the commonest co morbidity with a prevalence of 59%. Mortality was

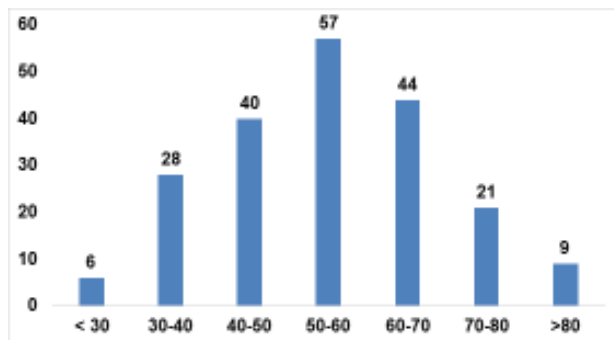


Fig 1 — Age Distribution of Study Population

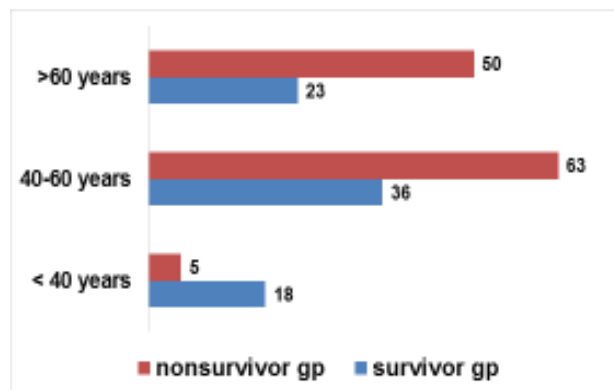


Fig 2 — Age Group Distribution in Survivor & Non-survivor Group

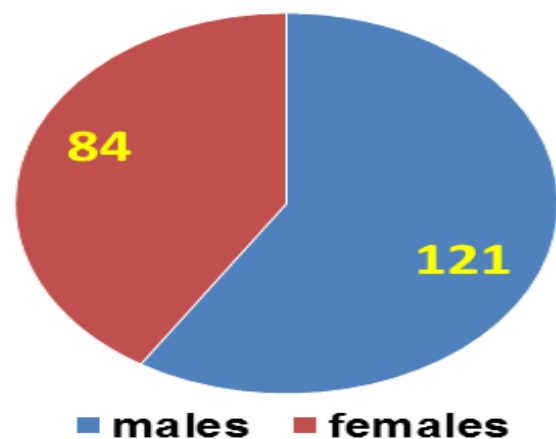


Fig 3 — Gender distribution

higher among the diabetic group (62.7%), compared to the non-diabetic group (57.1%). Hypertension was present in 50.2% of patients. Mortality among hypertensive group was 68% and in normotensive group 52.6%, this difference was statistically significant ( $p=0.028$ )<sup>1</sup>. Other co morbidities present were Dyslipidemia (20%), Hypothyroidism (17.43%), Chronic Kidney Disease (16.41%), Coronary Artery Disease (15.89%), Chronic Lung Disease (13.84%).

Symptoms	Number of patients	Survived	Died	P value
<b>Breathlessness :</b>				
Present	136	57(41.9%)	79(58.1%)	0.293
Absent	59	20(33.9%)	39(66.1%)	
<b>Myalgia :</b>				
Present	49	19(38.8%)	30(61.2%)	0.96
Absent	146	58(39.7%)	88(60.3%)	
<b>Fatigue :</b>				
Present	47	21(44.7%)	26(55.3%)	0.699
Absent	148	56(37.8%)	92(62.2%)	
<b>Chest pain :</b>				
Present	18	7(38.9%)	11(61.1%)	0.957
Absent	177	70(39.5%)	107(60.5%)	
<b>Sore throat :</b>				
Present	11	7(63.6%)	4(36.45)	0.09
Absent	184	70(38%)	114(62%)	
<b>Hemoptysis :</b>				
Present	6	6(100%)	0(0)	0.044
Absent	189	112(59.3%)	70 (39.5%)	
<b>Cough :</b>				
Present	118	70(59.3%)	48(40.7%)	0.674
Absent	77	48(62.35)	39(37.7%)	
<b>Fever :</b>				
Present	74	46(62.2%)	78(37.8%)	0.713
Absent	121	72(59.55)	49(40.5%)	

Coronary Artery Disease was present in 31 patients. Mortality was higher in patients with CAD (71%) than in the group who did not have CAD (29%). CKD was present in 32 patients and mortality was higher in patients with CKD (68.8%) than in those patients in whom CKD was absent (58.9%), but it was not statistically significant (p=0.297). Patients with hypothyroidism had higher mortality (67.6%). Malignancy was present in 10 patients, out of them 9 died (mortality 90%) and among patients without malignancy only 58.9% had mortality and the difference was significant statistically (p=0.05). Stroke was present in 7 patients (3.4%) with a mortality of 60.1%. Chronic Lung Disease was present in 27 patients, the mortality (51.9%), when compared with patients who did not have Chronic Lung Disease (48.1%) (Tables 2&3).

ARDS was the commonest complication present in (46.3%) patients. Mortality in the group whom developed ARDS was higher 75.8% compared to group who did not develop ARDS (47.1%) the difference was statistically significant (p=0.0001)(Table 3). Pneumonia was the next commonest complication (35.6%). Mortality was more among with pneumonia (74.6%) compared to without pneumonia (52.4%) which was statistically significant (p=0.002). Acute kidney injury developed in 32 patients; among them the mortality (75.9%) was higher than those who did not develop AKI (57.8%).

This association was not significant statistically (p=0.067). Transaminitis was present in 15 patients, mortality was higher in these patients 73.3% whereas in patients without transaminitis mortality was 59.4%. Coronary artery disease developed in 22 (11.7%) patients while in ICU, which included STEMI,

Comorbidity	Number of Patients	Outcome No(%)		p value
		Survived	Died	
<b>Diabetes Mellitus :</b>				
Present	118	44 (37.3%)	74(62.7%)	0.605
Absent	77	33 (42.9%)	44 (57.1%)	
<b>Hypertension :</b>				
Present	100	32(32%)	68(68%)	0.028
Absent	95	45(47.4%)	50 (52.6%)	
<b>Chronic Lung Disease :</b>				
Present	27	13(48.1%)	14(51.9%)	0.321
Absent	168	68(38.1%)	104 (61.9%)	
<b>Dyslipidemia :</b>				
Present	39	18(46.2%)	21(53.8%)	0.34
Absent	156	59(37.8%)	97(62.2%)	
<b>Coronary Artery Disease :</b>				
Present	31	9(29%)	22(71%)	0.194
Absent	164	68(41.5%)	96(58.5%)	
<b>Cerebrovascular Accident :</b>				
Present	7	2(28.6%)	5(71.4%)	0.547
Absent	188	75(39.9%)	113(60.1%)	
<b>Chronic Kidney Disease :</b>				
Present	32	10(31.3%)	22(68.8%)	0.297
Absent	163	67(41.1%)	96(58.9%)	
<b>Hypothyroidism :</b>				
Present	34	11(32.4%)	23(67.6%)	0.349
Absent	161	66(41.1%)	23(67.6%)	
<b>Malignancy :</b>				
Present	10	1(10%)	9(90%)	0.05
Absent	185	76(41.1%)	109(58.9%)	

Complication	Number of patients	Mortality		p value
		Survived	Died	
<b>ARDS :</b>				
Present	91	22(24.2%)	69 (75.8%)	0.0001
Absent	104	55(52.9%)	49(47.1%)	
<b>Pneumonia :</b>				
Present	71	18(25.4%)	53(74.6%)	0.002
Absent	124	59(47.6%)	65(52.4%)	
<b>CAD :</b>				
Present	22	5(22.7%)	17 (77.3%)	0.088
Absent	173	72(41.6%)	101 (58.4%)	
<b>CHF :</b>				
Present	4	1(25%)	3(75%)	0.549
Absent	191	76(39.8%)	115(60.2%)	
<b>DKA :</b>				
Present	13	5(38.5%)	8(61.5%)	0.938
Absent	182	72(39.6%)	110(60.4%)	
<b>AKI :</b>				
Present	29	7(24.1%)	22(75.9%)	0.067
Absent	166	70(42.2%)	96(57.8%)	
<b>CVA :</b>				
Present	3	0(0%)	3(100%)	0.159
Absent	192	77(39.6%)	115(59.9%)	

NSTEMI, LBBB with a mortality of (77.3%) and Cardiac failure developed in 4 (2.0%) patients, three of them succumbed. Cerebrovascular accident developed in 3 (1.5%) while in ICU. All of them died. Diabetic keto acidosis developed in 13 patients (7.3%) and the mortality was higher in patients with DKA (61.5%)(Table 4).

X-ray was taken in 114 patients. Consolidation was the most common finding seen in 71 patients with a mortality of 70.6%, followed by ground glass opacities in 44 patients with a mortality of (61.9%). Six patients had pneumothorax and all of them succumbed, one patient developed pneumomediastinum.

CT chest taken in 37 patients, out of them 25 had a score more than 15. While the group with CT score more than 15 had mortality of 50% the group with a CT severity score of less than 15 had mortality of 40%. Out of ECG taken in 195 patients 72 (35.1%) were abnormal. Among the laboratory parameters lymphocytopenia, hyperbilirubinemia and increased blood urea, was high in non-survivor group. Increased level of random blood sugar, serum creatinine, SGOT/

SGPT and low platelet count was present in non-survivor group.

Lymphocytopenia a characteristic feature in Covid 19 was present in 142 patients out of which 87 died (61.3 %) this is high when compared with normal lymphocyte group of 50 patients with a mortality of 58%. Raised values CRP, D dimer, were associated with high mortality.

Troponin T was done in 43 patients and was high in non-survivor group (87.5%).

All patients were given O<sub>2</sub> support, among them 104 patients received Noninvasive Ventilation. Five patients received invasive mechanical ventilation, others received O<sub>2</sub> support through simple face mask and non rebreathable mask.

Out of 205 patients 10 patients were referred to Medical College Hospital (4.9%), 118 patients died (57.6%), 58 patients shifted to ward (28.3%), 19 patients discharged from ICU (9.3%).

## DISCUSSION

In the present study of 195 patients 57.6% died and 37.6% survived. This observation of mortality is different from the studies conducted in other states of India<sup>3,4</sup>.

Mean age of the present study population was 55.46 years with highest mortality in age group above 60 years (68.5%). The association of age with mortality has statistical significance ( $p=0.0001$ )<sup>4,6</sup>.

This is comparable with studies across Globe which shows increased mortality as age advances.

Most studies showed that male patients are affected more with increased mortality. In the present study also, male patients were more affected than female patients. But mortality was higher in female group (62.25%) when compared with male group (59.3%)<sup>3</sup>. However, this association was statistically insignificant. Increased prevalence of co-morbidities like Diabetes Mellitus, Hypertension obesity and Social factors could be the reason for this observation of high mortality in female group.

In the present study mortality was higher (64.5%) in patients who had co morbidities and among the co-morbidities Diabetes Mellitus was the commonest. This could be attributed to the high prevalence of Diabetes Mellitus in Kerala. Studies across Globe showed association of Diabetes Mellitus and Covid having a poor outcome<sup>4,5,12</sup>. Diabetic patients have defective phagocytic and immune mechanism, there is increased chance of secondary infections, hyperglycemia due to drugs used in treatment of COVID like steroids all play a role. Our study showed increased mortality in patients with Diabetes Mellitus

Table 4 — Showing Laboratory Parameters

Laboratory parameters	No of patients	Mortality number	Mortality %	P value
<b>Random Blood Sugar :</b>				
<200	102	58	56.9	0.275
>200	93	60	64.5	
<b>B Urea :</b>				
Normal	77	38	49.4	0.036
Raised	115	78	67.8	
<b>S Bilirubin :</b>				
Normal	149	84	56.4	0.033
Raised	46	34	73.9	
<b>S Creatinine :</b>				
Normal	148	89	60.1	0.947
Raised	40	25	62.5	
<b>Lymphocyte :</b>				
Normal	50	29	58.0	0.899
Decreased	142	87	61.3	
<b>Platelet :</b>				
Normal	94	51	54.3	0.158
Decreased	95	64	67.4	
<b>SGOT :</b>				
Normal	84	45	53.6	0.176
Raised	110	72	65.5	
<b>SGPT :</b>				
Normal	97	60	61.9	0.654
Raised	97	57	58.8	
<b>D Dimer :</b>				
Normal	20	7	35	0.014
Raised	175	111	63.4	
<b>CRP :</b>				
Normal	75	39	52.0	0.05
Raised	120	79	65.8	
<b>Troponin :</b>				
Normal	24	11	45.8	0.008
Raised	16	14	87.5	

(62.7%), but without any statistical significance. Along with poor glycemic control.

Diabetic Keto Acidosis also had adverse outcome with a mortality of (61.5%).

Second commonest co-morbidity was hypertension with 68% mortality ( $p=0.028$ )<sup>4,5,8</sup>. The mortality among hypertensive patients was higher than in patients with Diabetes Mellitus<sup>5</sup>.

Chronic Kidney Disease patients are at increased risk of mortality which is evident from previous studies<sup>1</sup> in the present study CKD patients had 68.8% mortality<sup>14,15</sup>. Already existing renal dysfunction and electrolyte abnormalities added to the Mortality. The CKD patients definitely need early recognition of illness and appropriate treatment. In patients who developed Acute Kidney Injury mortality was 75.9%. Patients admitted in ICU are more to develop AKI. Various mechanisms like Direct Renal Injury, Acute Tubular Necrosis, Hypotension, Electrolyte Imbalance, Tissue Hypoxia, Nephrotoxicity of drugs play a role in development of AKI<sup>13</sup>.

A mortality of 77.3% was seen with Coronary Artery Disease and 75% mortality for those who developed cardiac failure<sup>16</sup>. Affinity of SARS-Cov-2 virus for ACE-2 receptors which are present in both heart and brain could be the reason. Vasculitis, hypoxic injury, microvascular dysfunction also plays a role in increased cardiovascular and cerebrovascular mortality. All three patients who developed stroke succumbed. All of them had ischemic stroke. Chronic Lung Disease is considered as risk factor for disease severity and mortality in COVID-19. But our study group did not show high mortality, Low prevalence of Chronic Lung Disease in the study population could be the reason.

Breathlessness was the most frequently reported symptom because study population included patients of Cat B and Cat C (ref). Decreased oxygen saturation level at the time of admission was associated with poor outcome indicating severe lung involvement. All 6 patients presented with hemoptysis died which could be due to the severe ARDS present in them. ARDS was the most frequent complication in our study, with mortality of 75.8% All patients in ICU were given O<sub>2</sub> support 5 patients required mechanical ventilation, Other advanced modes of oxygen support used were noninvasive ventilation, high flow nasal oxygen, Bains circuit, non-rebreathable mask. Patients in non-survivor group required advanced modes of oxygen support, whereas majority patients in survivor group received simple face mask and non rebreathable mask. Non-invasive mechanical ventilation was

commonest mode of support which was well accepted world over as the treatment of ARDS due to COVID-19. In our study those patients received NIV had a better outcome.

Among the co-morbidities malignancy had a significant impact (90% mortality)<sup>5</sup>. Immunosuppression defective phagocytosis, prothrombotic effect due to primary malignancy or treatment related might be the cause for high mortality. Patients with cancer have an increased risk of acquiring infection and rapid deterioration. So, early identification of illness in these patients and active intervention warranted.

Lymphocytopenia which is a characteristic feature of COVID-19 was present in 142 patients out of which 87 died (61.3%)  $p=0.899$ . In our study raised S bilirubin, raised B. Urea, Lymphocytopenia was observed in non-survivor group. Raised levels of blood sugar, S Creatinine, SGOT/SGPT, and Thrombocytopenia were also observed in non-survivor group (Table 4).

Acute phase reactant CRP was associated with disease severity and was raised in non-survivor group with a mortality of 65.8%. Elevated Troponin levels has a strong association with disease severity, it indicates both ischemic and non-ischemic myocardial injury<sup>16</sup>. Present study showed high Troponin levels in non-survivor group. High D dimer levels are associated with increased risk of thrombotic complications and poor outcome. In our study the mortality of group with raised D dimer was 63.4%<sup>17,18</sup>.

CT scan of Chest was taken in 37 patients only, since most of the patients were admitted with respiratory failure, they could not be mobilized for CT scan and radiological findings did not correlate with outcome.

## CONCLUSION

Highest mortality was seen in age group above 60 years. Presence Co-morbidities like Hypertension, Diabetes Mellitus, Chronic Kidney Disease, Cardiovascular and Cerebro Vascular Diseases, Cancer had increased Mortality. Complications like Acute Kidney Injury, ARDS, raised levels of CRP, D Dimer, Lymphocytopenia, Transaminitis were observed in non-survivor group.

## Limitations :

Since most patients were in respiratory failure, weight could not be recorded. CT scan of Chest could not be done in all patients.

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## Case Series

# A Case Series of Endometrial Stromal Sarcomas : A Relook at a rare kind of Uterine Malignancy

Payel Bandyopadhyay<sup>1</sup>, Gargi Ray Chaudhuri<sup>2</sup>, Abhishek Bandyopadhyay<sup>3</sup>, Soumita Ghosh Sengupta<sup>4</sup>

Endometrial Stromal Sarcomas (ESS) exhibits a very rare breed of uterine malignancy which comprises 10% of all uterine sarcomas but only around 0.2% of all uterine cancers. Depending on mitotic activity, vascular invasion or clinical outcome, broadly there are three varieties of Endometrial Stromal Tumours : Endometrial Stromal Nodule, Low-grade Endometrial Stromal Sarcoma, High-grade Endometrial Stromal Sarcoma. Our small series consists of five cases of ages ranging from 28 to 48, all of whom have been histologically and immunohistochemically diagnosed with low grade endometrial stromal sarcoma. The most common symptom out of all cases that warranted patient's attention was Abnormal Uterine Bleeding (AUB) bringing them to clinician and all underwent total hysterectomy and their specimen was finally diagnosed with low grade endometrial stromal sarcoma. Data from prospective or large randomized studies are still lacking due to the rarity of these tumours. Surgery represents the standard treatment for this disease. For uterus-limited disease (early stage), the en bloc resection of the tumour is strongly recommended which more or less necessitates total hysterectomy which is curative for early diseases. While all cases had nonspecific symptoms, underwent total hysterectomy as for presumed benign diseases and the eventual diagnosis in favour of stromal sarcoma were incidental, the principal purpose of this presentation is to evoke a sense of high degree suspicion of such rarity in the arena of uterine malignancy and an interest towards making an algorithm of diagnosing such malignancy known to have varied spectrum and outcome.

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**Key words :** Uterus, Endometrial Stromal Tumour, Endometrial Stromal Sarcoma, Diagnosis.

**E**ndometrial Stromal Sarcoma (ESS) is a rare mesenchymal neoplasm of uterus with occurrence of 10% of all uterine sarcomas and approximately 0.2% of all uterine malignancies<sup>1</sup>. Thanks to this rarity, sources of most of the relevant information are small series or case reports as available in online literature. With most clinical symptoms and other presentations being nonspecific, proper pre-operative diagnosis is unlikely and most cases are diagnosed in pathological laboratory after Histopathological Examination (HPE) and Immunohistochemistry (IHC)<sup>2</sup>.

For uterus-limited disease, en bloc removal of the tumour without morcellation is strongly recommended. Total hysterectomy with bilateral salpingo-oophorectomy (TAH & BSO) is the main line of management and complete cure is a reality for early cases. For advanced-stage disease, the standard surgical treatment is adequate cytoreduction with metastectomy. Although endometrial sampling, ultrasound and magnetic resonance imaging can provide diagnostic clues but in most cases final diagnosis is made over hysterectomy specimen done for a presumed benign disease.

The WHO has broadly classified endometrial stromal tumour into benign Endometrial Stromal Nodule (ESN) and

### Editor's Comment :

■ While the symptoms of per vaginal bleeding or uterine mass, points towards uterine fibroid or adenocarcinoma in most of the cases, endometrial stromal sarcoma is rarely suspected, specially when it is confined to the uterus. So, to avoid misdiagnosis and delay in treatment, importance of high degree suspicion, total hysterectomy with staging of the tumour and confirmation by IHC is paramount. Thus, despite the rarity or infrequent occurrence, case reporting or case series publication should be encouraged to avoid under-reporting of such cases.

malignant Endometrial Stromal Sarcoma . Again malignant ESS can be Low-grade and High-grade. Here, we present a small yet significant series of 5 cases of low grade endometrial stromal sarcoma as diagnosed in our institution in last three years (2018-2021).

### CASE SERIES

All five cases in our series fell in the age group of 28-48 years and they presented themselves to the gynaecology Outpatient Department (OPD) with cardinal complaint of Abnormal Uterine Bleeding (AUB) mostly. Suprapubic mass was often the presentation. Clinico-radiologically, all cases were diagnosed as fibroid, none of them had any features of extra uterine or metastatic disease and total abdominal hysterectomy with bilateral salpingo-oophorectomy had been successfully done in all cases. Surgical Specimens of them were sent to our pathology department for histopathological examination.

On first vision, tumour location, size, and gross appearance were noted and corroborated with operative notes. After conventional haematoxylin and eosin-based

Department of Pathology, College of Medicine and Sagore Dutta Hospital, Kolkata, West Bengal 700058

<sup>1</sup>MD (Pathology), Senior Resident

<sup>2</sup>MD (Pathology), Associate Professor

<sup>3</sup>MD (Pathology), Assistant Professor

<sup>4</sup>MD (Pathology), Associate Professor and Corresponding Author

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staining and fixing, we applied the proposed 2003 World Health Organization Classification criteria for the diagnosis of primary uterine ESS: oval or round, uniform cells resembling those of proliferative-phase endometrial stroma accompanied by a distinct vascular pattern (ie, small vessels resembling spiral arterioles of the endometrium), with an infiltrative border (finger-like projections extending >3 mm from the border of the mass into surrounding tissue) and/or vascular invasion. The following histopathologic characteristics were recorded: tumour contour (mostly well circumscribed vs. mostly infiltrative), presence of typical ESS vascular pattern and its extent (focal *versus* diffuse), presence or absence of pleomorphism (variation of nuclear shape and size that could be detected at intermediate magnification), fibroma-like stroma (absent, focal, or diffuse), presence or absence of vascular invasion, Mitotic Index (MI) obtained in the most mitotically active area by counting 10 consecutive High-power Fields (HPF), sex cord elements (absent *versus* present and extent), smooth muscle differentiation (absent *versus* present and extent) and the presence or absence of nuclear grooves, prominent myxoid change, edema, necrosis, hyaline plaques, endometriosis, foamy cells, cytoplasmic clearing, epithelioid features, calcifications, glandular differentiation and other unusual features<sup>3</sup>.

All specimen were staged pathologically according to FIGO classification, IHC were done to all cases for ER receptor and CD 10 & vimentin. Apart from active participation and supervision by two senior pathologists, we collected relevant information from clinicians, medical records and attending oncologists.

#### CASE 1

A 28 years old P(2+1) female attended Gynaecology OPD with complaint of gradual distension of abdomen for 6 months and her radiological investigations (CECT and

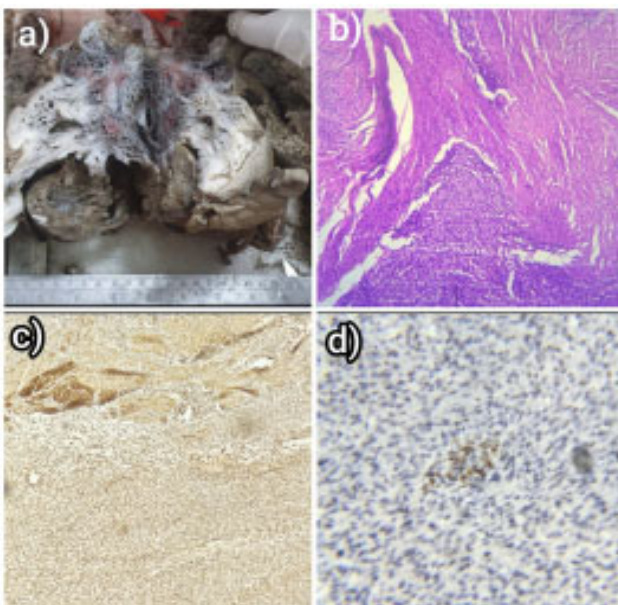


Fig 1 — (a) Cut section of tumor mass showing solid, cystic and haemorrhagic areas. (b) Tumor cells permeating into myometrium (H&E stain, 100x). (c) Diffuse Cytoplasmic CD10 positivity of tumor cells (100x). (d) Patchy nuclear ER positivity of tumor cells (100x).

USG) revealed a large predominantly solid abdomino-pelvic mass measuring (21.7×17.4×11.3) cm. Uterus and ovaries were not seen separately. After TAH & BSO, the received specimen revealed on gross examination, a tumour mass in the right side of uterine fundus measuring (25×23×12) cm. Cut section of tumour mass showed solid, cystic and haemorrhagic areas. Cervix and bilateral adnexa appeared free on gross (Fig 1a).

On microscopic examination, endo-myometrium showed histopathological features of proliferative stroma with tumour arising from it and invading myometrium (>50%). Irregular, densely cellular Islands of tumour cells with diffuse growth were seen permeating the myometrium in a classical tongue like pattern (Fig 1b). No lympho-vascular invasion was seen. Tumour cells had uniform, oval to fusiform nuclei with mild atypia with scanty cytoplasm with low mitotic activity. Tumour cells were seen whorled around the spiral arterioles.

According to the new 2009 FIGO Staging, it was stage IB disease and AJCC 8th edition PT1bNx. Immunohistochemistry (IHC) for CD10 showed diffuse cytoplasmic positivity (Fig 1c) while oestrogen receptor showed patchy nuclear positivity (Fig 1d) Postoperative period was uneventful. Patient was discharged after 5 days. On follow-up patient, patient was on tamoxifen therapy and there was no evidence recurrence on further follow-up.

#### CASE 2

The USG of this 45years old female patient revealed a large intramural fibroid. Gross examination of her TAH BSO specimen showed one large intramural fibroid projecting into the endometrial cavity and extending up to cervical canal measuring (11x10x5) cm. Cut section revealed solid whitish whorling pattern. On microscopy, endometrium showed features of non-secretory

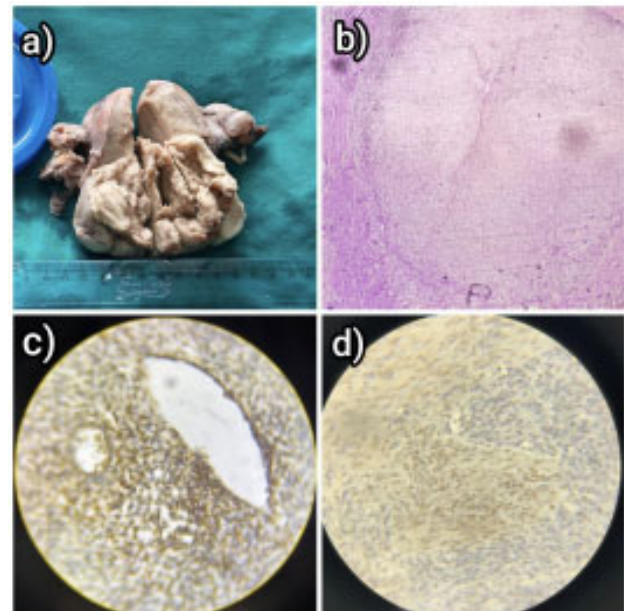


Fig 2 — (a) Fibroid like mass arising from lower endometrium extending upto cervix. (b) "Tongue" like extension of tumor cells into myometrium (H&E stain, 100x). (c) Strong CD10 positive tumor cells around blood vessels (100x). (d) ER positivity of tumor cells (100x).

endometrium with cystic changes and tumour arising from its stroma. Oval to spindle shaped tumour cells with fusiform nuclei and scanty cytoplasm were seen invading more than 50% myometrium. Lympho-vascular space invasion was absent. Cervix, bilateral adnexa were free from any tumour process.

According to the new 2009 FIGO Staging, it was stage IB disease and AJCC 8th edition stage was PT1bNx and IHC was confirmatory (Fig 2).

### CASE 3

There was one heterogeneous irregular friable area identified in the operated surgical specimen at uterine fundus measuring (2.5 x 2 x 1.5) cm. Multiple intramural fibroids are also discovered on cut section. On microscopic examination, endometrium again showed features of non-secretory endometrial glands and stroma. Tumour arising from endometrial stroma invades less than 50% of myometrium (Fig 3a). Tumour cells are spindle shaped with scanty cytoplasm with oval to fusiform nuclei and inconspicuous nucleoli. There is focal whorling of tumour cells around the small arterioles (Fig 3b). Focal smooth muscle differentiation, fibrosis, glandular elements and focal sex cord elements also noted. No lympho-vascular space invasion noted.

Sections from fibroids showed histopathological features of atypical epithelioid leiomyoma. Histopathological examination and immuno-histochemical study confirmed the diagnosis of low grade endometrial stromal sarcoma with focal muscle differentiation and focal sex cord elements.

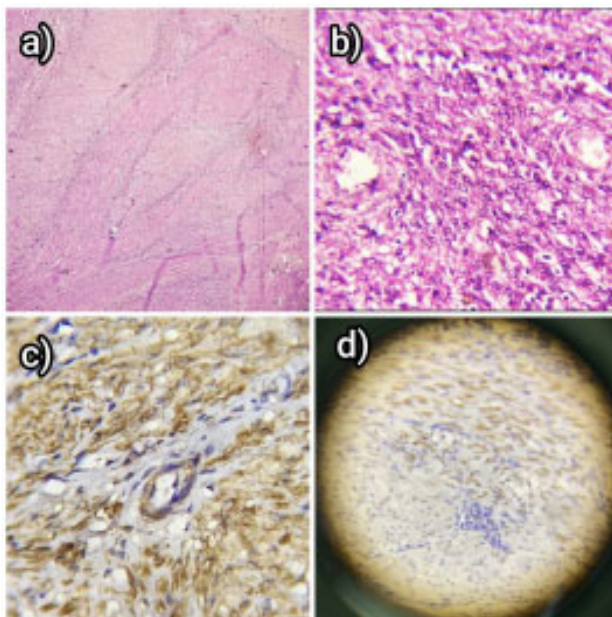


Fig 3 — (a) Tumor cells invading myometrium (H&E stain, 100x). (b) Whorling of tumor cells around arterioles (H&E stain, 100x). (c) Strong CD10 positive tumor cells (100x). (d) Patchy nuclear ER positivity of tumor cells (100x).

### CASE 4

In this case of 35 years old female, USG of the abdomen revealed a proliferative growth in uterus and her post operative surgical specimen showed on grossing an irregular proliferative growth measuring (7.5 x 2 x 2) cm.

almost obliterating the uterine lumen. Cut section revealed solid, soft, whitish multiple polypoidal growth (Fig 4a).

On microscopic examination, sections from the growth showed tumour cells infiltrating myometrium up to serosa (>50% of myometrium). Spindle tumour cells have fusiform nuclei with scanty cytoplasm with minimal atypia. Sections from left fallopian tube and left ovary and left parametrium showed infiltration by tumour process. Lymphovascular space invasion is noted. Staging was PT2aNxMx. Histopathological examination and immuno-histochemical study confirmed diagnosis of low grade endometrial stromal sarcoma.

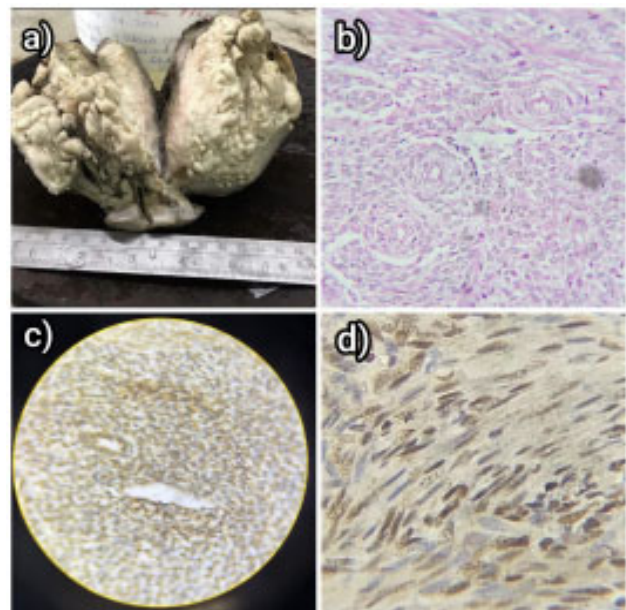


Fig 4 — (a) Solid and irregular, multiple polypoidal uterine growth on gross examination. (b) Tumor cells whorling around arterioles (H&E stain, 100x). (c) CD10 positive tumor cells around arterioles (100x). (d) Strong ER positivity (400x).

### CASE 5

On gross examination of this 48 years old patient's surgical specimen, a tumour mass was noted in the uterine fundus measuring (12cm x 7cm x 5cm). Cut section of tumour mass was heterogeneous with solid, cystic and hemorrhagic elements. Cervix and bilateral adnexa appeared free on grossing.

On microscopic examination, endo-myometrium showed histopathological features of non-secretory endometrial glands and stroma. Tumour arising from endometrial stroma invades more than 50% of myometrium in tongue like fashion. Tumour cells are oval cells with scanty cytoplasm with oval to fusiform nuclei and inconspicuous nucleoli. There is focal whorling of tumour cells around the small arterioles. Mitotic count was <3/10 high power fields. Patchy areas with high mitotic count, focal necrosis and focal xanthogranulomatous changes were also noted. Lymphovascular spaces were seen uninvaded ( staging PT1bNxMx). IHC again stamped diagnosis of ESS of low grade (Fig 5).

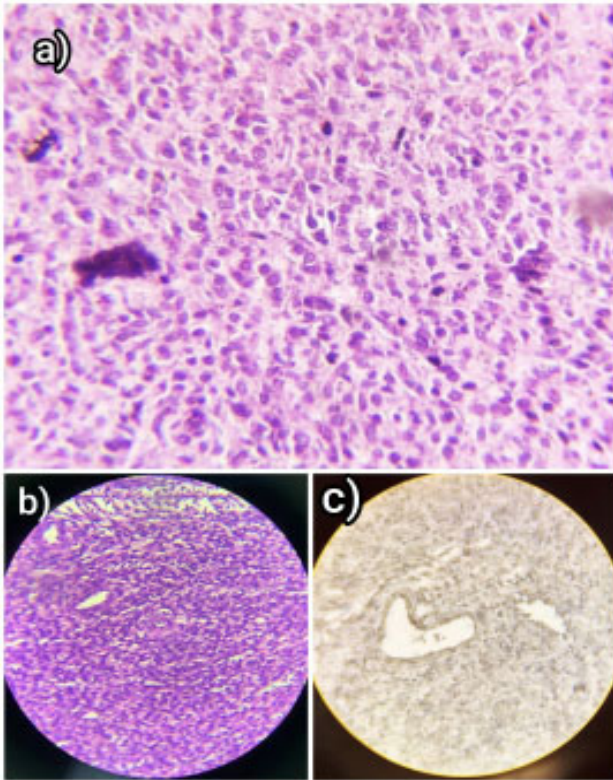


Fig 5 — (a) & (b) Diffuse sheet of tumor cells (H&E Stain, 400x & 100x). (c) Weak CD10 positivity of tumor cells around arterioles (100x).

### DISCUSSION

The clinical behaviour and pathological features of uterine stromal cancers were studied in details for the first time in 1966<sup>4</sup>. This new kind of neoplasms were then divided morphologically into two groups: one with pushing margins (stromal nodules) and one with infiltrating margins (endolymphatic stromal myosis or stromal sarcoma). Stromal nodule was considered benign while tumours with infiltrating margins were further divided by their mitotic activity: tumours containing fewer than 10 mitotic figures in 10 High-power Field (endolymphatic stromal myosis-low grade), and those containing 10 or more mitotic figures in 10 HPF (stromal sarcoma-high grade). Over the time, different authors have expanded or curtailed to integrate the description and classification of this type of neoplasm on the basis of their experiences in terms of clinic-pathological characteristics and patient survival.

The few scattered experiences from pathologists hinted existence of intermediary or continuum between two aforesaid types or further expansion of the spectrum but nothing was well supported by sufficient empirical data (Evans, *et al*) till WHO committee stepped in.

Initially, WHO 2003 classification recognized only two categories of stromal sarcomas simply on the basis of cytologic atypia, namely, Low-grade Endometrial Stromal Sarcoma (LG-ESS) and Undifferentiated Endometrial Sarcomas (UES)<sup>5</sup>. The 'UES' category was then too broad, meant to include a wide range of heterogeneous tumours with different clinical behaviour and outcome, morphology and genetic features. In 2012, the improvement of

cytogenetics and molecular biology further opened up the horizon which allowed the recognition another kind of ESS with more aggressive clinical picture and higher mitotic activity what led to their reinstatement in WHO classification (2014) as a distinct group of ESS, ie, High Grade ESS (HG-ESS), as defined as a malignant tumour of endometrial stromal derivation with high grade, round-cell morphology often associated with a low-grade spindle cell component and characterized by a t(10;17) leading to the YWHAЕ-NUTM2 rearrangement<sup>6</sup>.

Later in 2018, the recognition of HG-ESS was further strengthened and hence re-instated in WHO classification as definite intermediate between LG ESS and UES was on basis of unique features of cells with uniform but definite nuclear atypia, permeative myometrial invasion and mixed clinical behaviour<sup>7</sup>.

So the current WHO classification acknowledges four categories within the endometrial stromal family of tumours: Endometrial Stromal Nodule (ESN), Low Grade Endometrial Stromal Sarcoma (LG-ESS), High-grade Endometrial Stromal Sarcoma (HG-LSS) and undifferentiated uterine sarcoma (UES)<sup>8</sup>.

After leiomyosarcomas, LG-ESS represents the most common stromal tumour by frequency. It usually affects perimenopausal women, but occasionally arises in young women and adolescents as we had one such of 28 years (Case 1). Risk factors for this neoplasm include obesity and diabetes, younger age at menarche, tamoxifen intake or oestrogen use and pelvic radiation<sup>9</sup>. Abnormal uterine bleeding, pelvic pain and dysmenorrhea are the most frequent symptoms of the patients. About one-third of patients present symptoms suggestive of extrauterine spread, while one fourth are asymptomatic<sup>3</sup>. This neoplasm principally arises from uterine corpus while ovary is the commonest organ involved in extra uterine variety<sup>10</sup>. Besides ovary, abdominal cavity, vulva and vagina are the rare sites of extra uterine ESS. Extrauterine pelvic extension of LG-ESS is frequently associated with endometriosis<sup>11</sup>.

### PATHOLOGY

Both ESN & ESS can be submucosal or often growing into lumen (polypoidal form) or intramural. While ESN can exhibit expansile features but the absence of myometrial and lympho-vascular invasion is obligatory for diagnosis. In comparison, in ESS, the borders are defined and it usually presents specific pattern of permeation into the myometrium and parametrial tissue called 'worm like'<sup>13,11</sup>. Its polypoidal variety often gives positive yield in endometrial biopsy but not a single case in our small series had any such outcome. Macroscopically there might be areas of haemorrhage with necrosis and cystic degeneration (eg, Case 1) but pure cystic mass is unlikely. Often soft nodules can be recognized between the endometrium and the myometrium. Microscopically, the myometrial and lympho-vascular invasion in 'tongue like' fashion is classical (as in Figs 1b, 2b & 3a) and is a key point for the distinction between LG-ESS and ESN<sup>12</sup>.

Microscopically, LG-ESS resembles the proliferative phase of endometrial stroma featuring small cells with oval to spindle shaped nuclei arranged in sheet surrounded by spiral arterioles like vessels (Figs 3b & 4b). The mitotic index is usually low: about 5/10 per high power fields, but

in some cases it can be higher.

Although there is no single specific marker for ESS, the immune-stain panel should include CD10 and smooth muscle markers like desmin, vimentin as the latter two are important for the distinction between ESS and other tumours with overlapping immuno-phenotype<sup>13</sup>. LG-ESS cells express oestrogen and progesterone receptors and the tumours were seen to respond to administration of progestins.

Genetically, about 50% cases of Low grade Endometrial Stromal Sarcoma show translocation of t (7;17) with polycomb family genes fusion of JAZF1–SUZ12 (JJAZ1)<sup>14</sup>. These genetic findings can be utilized in aid of the diagnosis of Low Grade Endometrial Stromal Sarcoma by using FISH or RT-PCR, the facility our institution is unfortunately not equipped with<sup>4,14</sup>.

The natural history of Low-grade Endometrial Stromal Sarcoma is characterized by indolent clinical course and occasional local recurrences and metastases. All available literatures are in support of favourable prognosis when surgery, which is essentially hysterectomy and bilateral salpingo-oophorectomy is done early<sup>15</sup>. Cytoreduction is recommended in advanced tumours with extrauterine manifestations, however, in a study conducted by Leah, *et al*, the cytoreductive surgery did not seem to ensure any added benefit in survival<sup>16,17</sup>. The optimal adjuvant therapy remains unclear with options including observation without therapy, hormonal therapy, chemotherapy and radiation therapy, either alone or in varying combinations. Hormonal therapy with medroxyprogesterone, tamoxifen, Gonadotropin Releasing Hormone (GnRH) analogues and aromatase inhibitors are suggested for LG-ESS stage 3-4 and for recurrent disease.

Although, we have not encountered any recurrences during this study period of three years or less, the risk of recurrence is considered as high as 50% and often they can be very late<sup>18</sup>. In one large series, the interval before recurrence varied from three months to 23 years, with a median interval of three years<sup>19</sup>. In the largest clinicopathologic study to date on ESS, the median time between hysterectomy and relapse was 5.4 years and nine months for stages 1 and 3-4, respectively<sup>20</sup>.

High grade endometrial stromal sarcoma are more aggressive, often shows extrauterine extensions and necrosis as reflected histopathologically with extensive myometrial invasion with mitotic figure >10/10hpf. Higher chances of recurrences are seen in successive follow ups<sup>3</sup>.

Given the rarity of the pathology with few studies and Case Reports being available in electronic media, this presentation of 5 cases, however small, surely can help clinicians maintain an high degree of suspicion for such infrequent pathology, make a relook at its prospect of early diagnosis and management and improve its clinical outcome.

#### CONCLUSION

Low Grade Endometrial Stromal Sarcoma is an uncommon malignant stromal tumour of uterus, which occurs usually in perimenopausal women but can also occurs in young women. The clinical features or even gross pathology of endometrial stromal nodule, High Grade and Low Grade Endometrial Stromal Sarcoma often are

nonspecific & overlapping and extra uterine element of latter two can make the diagnostic field more confusing, but knowledge of their existence, careful histopathological examination, immunohistochemistry and if possible genetic study can surely diagnose it with more surety.

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## Case Report

### Atypical Presentation in a Lady with Acromegaly : A Case Report

Arnab Purkayastha<sup>1</sup>, Prithwiraj Bhattacharjee<sup>2</sup>, Madhusmita Khakholar<sup>3</sup>

**Background :** The blood IGF-1 level is a suitable marker for assessing the integrated secretion of GH and is advised for acromegaly diagnosis, monitoring and screening. Systemic diseases like Catabolic Disorders, Liver or Kidney Failure, Malnutrition and Diabetes Mellitus can lower IGF-1 levels and cause acromegaly screening to give false-negative results.

**Case Report :** A 49-year-old female presented with dysphagia, vomiting, abdominal distention with no associated pain but Grade 3 edema of both lower limbs, with frontal bossing, prominent jawline, and acral thickening. The abdomen was distended with fluid thrill otherwise unremarkable. Ascitic fluid showed predominantly mononuclear cells with an elevated protein (4.56 mg/dL) and normal ADA. Ascitic culture was negative with no evidence of malignant cells found. Lower levels of IGF-1, LH, FSH were observed with elevated TSH and Prolactin. Ultrasonography of the abdomen suggested Chronic Liver Parenchymal Disease with massive ascites. Doppler study of lower limbs showed DVT. Heel pad thickness of 30.7 mm and 26.4 mm on the left and right sides respectively. MRI of the Brain showed Pituitary Macroadenoma (13 mm).

**Discussion :** IGF-I concentrations correlated with heel pad thickness, fasting blood sugar concentrations and response to an OGTT in patients with acromegaly. Low IGF-1 in the context of clinical acromegaly may also indicate a later stage of a disease process that was once linked to high IGF-1 and caused the clinical signs of acromegaly but has now "burned out". Recent research has shown that acromegaly patients may have coagulation abnormalities causing hypercoagulable states and, therefore, increasing the risk of Thrombosis.

**Conclusion :** Renal or hepatic disease or impaired nutritional status should be viewed as confounding conditions and may cause alterations in IGF-I production and/or bioactivity, such that the IGF-I concentration may no longer accurately reflect disease activity.

[J Indian Med Assoc 2024; 122(11): 61-5]

**Key words :** Acromegaly, IGF-1, VTE.

**A** cromegaly is an endocrine disorder characterised by progressive facial and extremity deformities. It results from abnormally increased levels of serum Growth Hormone (GH) in adulthood and is most commonly caused by a pituitary adenoma. Many of the actions of Growth Hormone (GH) on somatic growth and tissue maintenance are mediated by insulin-like growth factor-1 (IGF-1), which is produced in response to GH by the liver. Biochemical confirmation of the diagnosis is substantiated by elevated IGF-1 levels and elevated blood GH levels that persist during Oral Glucose Tolerance Testing (OGTT). The blood IGF-1 level is a suitable marker for assessing the integrated secretion of GH and is advised for diagnosis, monitoring and screening of acromegaly. Systemic diseases like catabolic disorders, liver or kidney failure, malnutrition, and diabetes mellitus can lower IGF-1 levels and might give false-negative results while screening for acromegaly<sup>1</sup>.

The prevalence of endocrine and liver problems is rising in the general population. The most common

Department of Medicine, Silchar Medical College and Hospital, Silchar, Assam 788014

<sup>1</sup>MBBS, MD, Junior Resident and Corresponding Author

<sup>2</sup>MD, Professor and Head

<sup>3</sup>MBBS, MD, Junior Resident

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#### Editor's Comment :

- Serum IGF-1 may not be an accurate indicator of disease activity in patients with acromegaly, if the patient also presents with liver dysfunction concurrently.
- It may also indicate the later part of the disease process (previously linked with high IGF-1) suggesting "burnt-out acromegaly".

endocrine disorders are diabetes, thyroid and gonadal disorders. The most common liver disorders are chronic hepatitis and cirrhosis of the liver. In modern medicine, it is not unusual for illnesses that affect these two important systems to happen at the same time. The liver is an important organ for metabolism. It is also where proteins and different hormones are synthesised. In addition to the liver being a detoxifying site, systemic toxins build up when an individual develops chronic liver disease. Most proteins that bind to hormones, like Sex Hormone Binding Globulin (SHBG) and Thyroid Binding Globulin (TBG), are synthesised in the liver. Endocrinopathies are often linked to chronic liver conditions such as chronic hepatitis, primary biliary cirrhosis and autoimmune hepatitis. When the liver doesn't function properly, there may be dysfunction of endocrine glands. This happens through direct toxic effects and indirect changes to the production of carrier protein<sup>2</sup>.

Chronic Liver Disease (CLD) may lead to the

dysfunction of most endocrine organs, including the pituitary, thyroid and other glands. A few endocrine disorders linked to CLD may improve following liver transplantation. There are few reports from India on liver dysfunction in people with acromegaly.<sup>2</sup> Hence, we report a case of a patient with acromegaly who presented with low IGF-1 and Chronic Liver Disease.

### CASE REPORT

A 49-year-old female presented with difficulty in food intake, both solid and liquid, for the last 3 months with associated vomiting after every intake; abdominal distention for the last 2 months with no associated pain but with abdominal discomfort followed by reduced appetite and constipation. The patient also had swelling of both lower limbs, which was gradually progressive in onset and reduced urine output for the last 20 days, which improved after intake of medications during the hospital stay. The patient had a history of blurred vision for the past 10 years. The patient had no history of fever, cough, shortness of breath, jaundice, bleeding from the mouth or loose stools. The patient did not have any history of chronic illnesses like diabetes mellitus, hypertension, heart disease, thyroid disease, or tuberculosis. There was no history of a similar condition in any of her family members. The patient had no history of any trauma, headaches, convulsions, disturbed sleep or utterance of irrelevant words. The patient predominantly took a non-vegetarian diet. The patient had no history of intake of any herbal substance and no history of intake of alcohol. The patient is in post-menopausal status for last 8 years with history of normal menstrual cycles and no history of galactorrhoea. The patient had 2 sons.

**Examinations** — On examination, the patient had frontal bossing, a prominent jawline and acral thickening of both hands and feet (Figs 1&2), suggestive of acromegaly. The patient had normal hair and nails and had no ulcers in and around the mouth. The patient had no pallor, icterus, cyanosis, or clubbing but had Grade 3 edema. The patient had locomotor brachialis. There was no swelling in the neck, palpable lymph nodes and prominent neck veins. There were no signs of muscle wasting. There was no redness of the hands or skin discolorations or signs of petechial hemorrhage. The pulse was 84 beats/min, regular in rhythm, normal in volume and character, with no radio-radial and radio-femoral delay. All peripheral pulses were normal. Systolic and diastolic

blood pressures were within normal limits. She had a normal respiratory rate with no signs of respiratory distress. On examining the abdomen, it was distended with no signs of umbilical herniation. The patient had no flapping tremors. There was no prominence in the abdominal veins. However, fluid thrill was present and there was no palpable liver or spleen. The routine eye examination was within normal limits. On testing for visual acuity, 6/36 in the right eye and 6/60 in the left eye and fundoscopy were also normal. Slit-lamp examination of the eye showed no signs of Kayser-Fleisher rings or any other abnormality. Perimetry was unremarkable for both eyes. Intra-ocular pressure was 12 mmHg of both eyes, measured using Goldmann Applanation Tonometer. Ocular Coherence Tomography was also within normal limits for both eyes, measured using Topcon 3D OCT-1 Maestro 2 system (Fig 3). The patient was although, advised refraction of -1.5 D for Right eye and -1.75 D for Left eye and +1.5 D for near vision for both eyes.

Routine blood investigations were done for the patient and are tabulated in Table 1. Routine urine examination yielded 4+ protein but otherwise was normal. Peripheral Blood Smear study was suggestive of microcytic hypochromic anaemia. Ascitic fluid analysis showed 185(87.2%) mononuclear cells and 27(12.8%) polymorphonuclear cells with an Ascitic Fluid Sugar of 20 mg/dL, a Protein of 4.56 mg/dL, and an Adenosine Deaminase of 16.77 U/L. Ascitic culture suggested no growth of organisms. There was no evidence of malignant cells in the ascitic fluid. HbsAg, anti-HCV and HIV turned out to be negative. Anti-Nuclear Antibodies (ANA), Anti-Smooth Muscle Antibodies (ASMA) and Anti-Liver-Kidney-microsomal Antibodies (Anti LKM) were negative. The hormonal assays were also done and are given in Table 2.

Ultrasonography of the abdomen suggested chronic liver parenchymal disease with massive ascites with a portal vein diameter of 14.7 mm. The patient also had a left renal complex cyst and a right renal simple cyst with hydronephrotic changes. Upper GI endoscopy suggested antral ulcer with multiple polypoid growths around the greater and lesser curvature of the stomach, leading to gastric outlet obstruction with no features of esophageal or gastric varices. A Doppler study of the bilateral lower limbs showed the patient to have Deep Vein Thrombosis. The D-Dimer of the patient was done following the Doppler study and came out to be 7.11 g/mL (N = 0–0.4 g/mL). An X-ray of both the feet showed elevated heel pad thickness



Fig 1

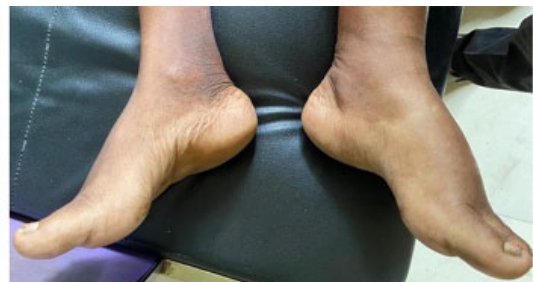


Fig 2



Fig 3

Table 1 — Showing Blood Parameters		
Lab Parameters	Patient'S Value	Normal Value
Hemoglobin	9 g/dL	12-15 g/dL
Total count	6120/mm <sup>3</sup>	4000-11000/mm <sup>3</sup>
MCV	89.3 fL	80-100 fL
Platelet count	1.4*10 <sup>5</sup> /mm <sup>3</sup>	1.5-4.5*10 <sup>5</sup> /mm <sup>3</sup>
AST	48.40 U/L	14-36 U/L
ALT	26.20 U/L	<35 U/L
S Urea	34.91 mg/dL	15-36 mg/dL
S Creatinine	0.81 mg/dL	0.52-1.04 mg/dL
S Sodium	133 mmol/L	137-145 mmol/L
S Potassium	3.10 mmol/L	3.5-5.10 mmol/L
S Albumin	2.67 g/dL	3.5-5.0g/dL
Blood sugar(Random)	92 mg/dL	70-139 mg/dL
S Iron	30.40 g/dL	37-170 g/dL
Prothrombin time	25.2 sec	10.7-14.1 sec
INR	2.12	0.9-1.16

Table 2 — Showing Hormone Assay			
Hormone Assay	Patient's Value	Normal	Method Used
IGF-1	29.5 ng/mL	94-252 ng/mL	Chemiluminescent Competitive Immunoassay
TSH	5.91 mIU/mL	0.465-4.680 mIU/L	Immunometric
fT4	0.86 ng/dL	0.78-2.19 ng/dL	Competitive Immunoassay
Prolactin	51.40 ng/mL	3.34-26.72 ng/mL	Immunometric
FSH	<0.66 mIU/mL	16.74-113.59 mIU/mL	Immunometric
LH	<0.216 mIU/mL	10.87-58.64 mIU/mL	Immunometric
Cortisol (8 am)	22.7 mcg/dL	4.82-19.50 mcg/dL	Electrochemiluminescent immunoassay
ACTH	20.8 pg/mL	≤46 pg/mL	Chemiluminescent Immunometric assay

of 30.7 mm and 26.4 mm on the left and right sides, respectively (Fig 4). Ultrasonography of the neck showed hypoechoic lesions with regular margins but with no echogenic foci and internal vascularity in both the thyroid lobes suggestive of TIRADS 2 lesion. A non-contrast CT scan of the brain revealed a hyperdense lesion around the pituitary fossa along with calcification of bilateral basal ganglia. A T1/T2 iso-intense lesion of size measuring approximately 13 mm was noted in the suprasellar region

showing homogenous enhancement on post contrast MRI study; however, there were no blooming foci on the GRE/SWI sequence. The bilateral frontal sinus and jaw appear enlarged. The findings suggest pituitary macroadenoma. (Figs 5,6,7,8) She was commenced on treatment with Bromocriptine 10 mg/day, as she was unwilling to undergo pituitary surgery and radiotherapy and because somatostatin analogues and pegvisomant were not routinely available at our hospital. She was also started on LMWH for Deep Vein Thrombosis. She was referred to a higher gastroenterology centre as she had gastric polyps causing Gastric Outlet Obstruction.

**DISCUSSION**

It has long been known that serum IGF-I levels are correlated with disease activity in acromegaly. Clemmons, *et al* demonstrated that IGF-I concentrations correlated with heel pad thickness, fasting blood sugar concentrations, and response to an Oral Glucose Tolerance Test (OGTT) in patients with acromegaly. Also, the changes in IGF-I levels in 15 patients who were followed for a year after treatment matched the amount of clinical improvement<sup>3,4</sup>.

Our case in point showed that acromegaly can cause hepatic and endocrine disorders. Acromegaly disrupts glucose and lipid metabolisms, increases free fatty acids, and causes hepatic and extra-hepatic insulin resistance and fat distribution alterations. Growth hormone promotes muscle and liver gluconeogenesis and glycogenolysis. It releases free fatty acids through lipolysis. High release of free fatty acids and insulin resistance are well established NAFLD risk factors. Conversely, enhanced lipolysis may prevent NAFLD in acromegaly patients.

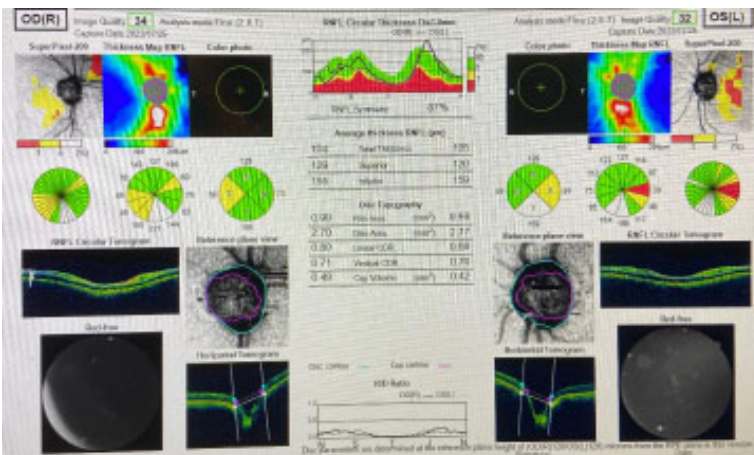


Fig 4



Fig 5

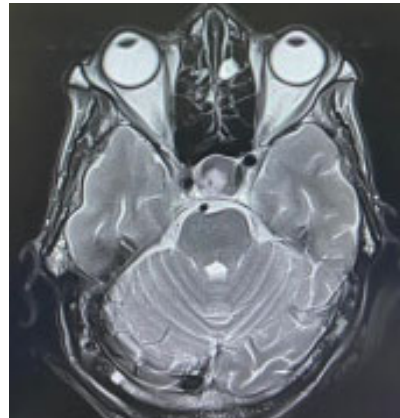


Fig 6

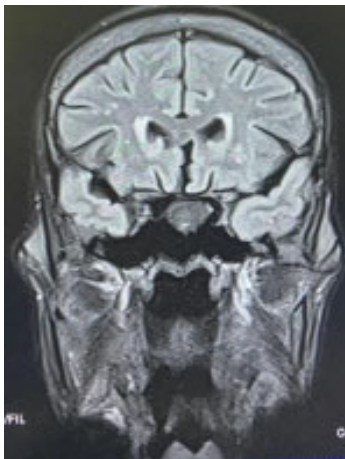


Fig 7

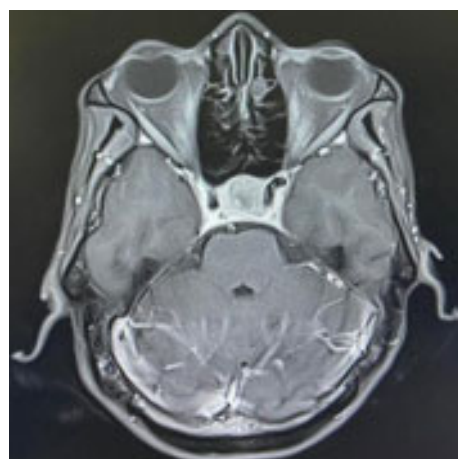


Fig 8

Henceforth, the complex metabolic actions of GH make debatable link between NAFLD and acromegaly<sup>5</sup>.

Chronic Liver Disease frequently exhibit occult endocrine dysfunction, which correlates directly with the severity of liver dysfunction. Previous research indicates that 10-25% of cirrhotic patients had thyroid problems.<sup>2</sup> In people with acromegaly, goitre is predominately nodular, and the incidence of thyroid cancer is also elevated. Most likely, the cause of goitre in people with acromegaly is a high insulin-like growth factor-1 (IGF-1) that binds to its specific receptor on thyrocytes. In contrast, Thyroid Stimulating Hormone (TSH), another essential component related to goitre formation, is reduced or missing in certain patients with acromegaly. This is primarily due to secondary hypothyroidism, which is induced by adenoma compression, pituitary surgery, or irradiation<sup>6</sup>.

Our patient showed dipstick proteinuria, which may be caused by Focal segmental Glomerulosclerosis (FSGS) in acromegaly patients. These patients may develop renal hypertrophy and enlarged kidneys than controls with significant rise in renal plasma flow and glomerular filtration. However, our patient did not undergo kidney biopsy for the confirmation of diagnosis. Clinical cases of glomerular lesions caused by high GH production are rare

and have only been documented twice. Yoshida, *et al* described a 46-year-old acromegaly-FSGS in 1999. The administration of corticosteroids resulted in partial remission but after tapering of dosages, relapses were observed. The subcutaneous administration of Octreotide acetate, and removal of pituitary adenoma via trans-sphenoidal surgery was done. After normalising creatinine clearance, steroids were gradually reduced to maintain remission. The case suggested that increased GH secretion might worsen renal glomerular disease. Another case by Takai, *et al* of a 53-year-old man with mild proteinuria for 6 years and acromegaly for 15 years showed renal biopsies having FSGS and enlargement of glomerular tufts. Trans-sphenoidal microsurgery of the adenoma did not eliminate proteinuria, despite normalised GH and IGF-1 levels. These two examples implied the development and progression of FSGS might be involved in patients with acromegaly. The intensity and duration of glomerulonephritis while undergoing treatment for acromegaly, may affect the outcome. There is strong evidence that GH and IGF-1 secretion may affect renal function and growth due to the expression of GH receptor, IGF-1 and IGF-1 binding proteins in different nephron segments, having unique anatomy and function<sup>7</sup>.

Portal hypertension, which is generally asymptomatic until problems occur, was present in the patient. 80–90% of asymptomatic cirrhosis patients have high portal pressure, 40% of whom have oesophageal varices. Depending on portal hypertension severity, they may develop at 6-10% every year in persons without varices.<sup>8</sup>

Low IGF-1 in the context of clinical acromegaly may also indicate a later stage of a disease process that was once linked to high IGF-1 and caused the clinical signs of acromegaly but has now “burnt out” (this is called “burnt-out acromegaly”). In addition, burnt-out acromegaly is frequently accompanied by additional hypopituitarism<sup>1</sup> symptoms, which were present in our patient. IGF-1 is mostly made in the liver and having CLD may cause IGF-1 levels to be low.

There are functional pituitary adenomas in which the cell type that makes them causes increased secretion of one or more anterior pituitary hormones. Nonfunctioning adenomas, on the other hand, do not secrete hormones but can potentially compress the anterior pituitary, resulting in hormonal deficiencies. Pituitary adenoma patients should be evaluated by a multidisciplinary team that includes endocrinology, ophthalmology and



Neurosurgery<sup>9-11</sup>. Low FSH and low LH with relatively preserved TSH and ACTH in this patient may be due to the compression effect of the macroadenoma causing low gonadotropins.

Recent research has shown that acromegaly patients have a wide variety of coagulation abnormalities in their serum. These abnormalities have the potential to lead to hypercoagulable states and, as a result, increase the risk of Thrombosis<sup>12</sup>. Few VTE instances in acromegalic patients have been reported since Coffey and Cummins described the first in 1912<sup>13</sup>. Al Dahmani, *et al* reported three VTE cases in uncontrolled acromegaly patients without risk factors in 2015<sup>14</sup>. Dal, *et al* examined Danish health registries of acromegaly patients to predict sequelae. The patients in this group experienced more VTE overall<sup>15</sup>. The link between serum IGF-1 and Thrombosis risk is uneven and unclear. In certain studies, higher IGF-1 levels were linked to early carotid artery atherosclerosis<sup>16</sup>, whereas low levels were linked to increased intima-media thickness and atrial fibrillation<sup>17,18</sup>. Besides serum coagulation abnormalities, malignancy and obstructive sleep apnea can increase hypercoagulability risk in acromegaly. Studies also show that acromegaly increases the risk of colon, thyroid and kidney malignancies<sup>12</sup>. Our study's strength is its assessment of all hormonal axes in this patient; relatively few studies from our nation have been reported. We did not do a GH suppression test following the OGTT, we did not measure free Testosterone, TBG, or SHBG, and we did not perform colonoscopy to rule out polyps in the colon. The relationship between endocrine dysfunction and underlying Chronic Liver Disease could not be determined from our study.

### CONCLUSION

Serum IGF-I concentration is a sensitive measure of integrated GH levels in patients with acromegaly that closely correlates with clinical and biochemical markers of disease activity. Renal or Hepatic Disease or impaired nutritional status should be viewed as confounding conditions. These conditions may cause alterations in IGF-I production and/or bioactivity, such that the IGF-I concentration may no longer accurately reflect disease activity. We describe a case of liver dysfunction in an elderly patient with acromegaly and low IGF-1 levels. In a patient with supportive clinical findings, a low IGF-1 test does not rule out acromegaly. It is imperative that a high index of suspicion be kept at all times in order to avoid losing out on this crucial diagnosis.

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## Short Communication

# A Research Protocol on Efficacious Evaluation of Thrombus Recanalization Techniques Employing Pigtail Catheter versus Spray Catheter for Vessel Patency in Acute Iliofemoral Deep Venous Thrombosis — A Randomized Controlled Trial

Sakshi Pritam Arora<sup>1</sup>, Gaurav V Mishra<sup>2</sup>, Pankaj Banode<sup>3</sup>, Abhilasha Dass<sup>4</sup>, Priyanka Banode<sup>5</sup>, Waqar M Naqvi<sup>6</sup>, Rajkiran Kanhaiya Rathi<sup>7</sup>

**Background :** Iliofemoral Deep Vein Thrombosis involves either partial or total occlusion of iliac and/or common femoral vein led by intravascular thrombus causing obstruction of resultant lumen. Venous valvular incompetence is one of the common factors leading to Deep Venous Thrombosis making it a vicious circle. Now-a-days, the concept of pharmacomechanical catheter directed thrombolysis is being utilised to treat Deep Venous Thrombosis of the lower limbs. The present study compares two thrombus recanalization techniques in iliofemoral deep vein thrombosis with respect to vessel patency.

**Materials and Methods :** In a randomised controlled parallel group trial, subjects (n=80) with acute iliofemoral Deep Venous Thrombosis will be enrolled into two groups A and B with 1:1 ratio of allocation. Group A will be subjected to spray catheter thrombus recanalization and group B will be subjected to pigtail catheter thrombus recanalization techniques. Follow-up will be on a periodic basis till 9 months. Primary outcome will be vascular patency representing antegrade flow across thrombosed vascular segment.

**Purpose of the study :** The outcomes of the current study will analyse the patency percentage of thrombosed iliofemoral venous segments after spray catheter and pigtail catheter thrombus recanalization techniques with respect to antegrade vascular flow.

**Expected clinical implications :** This study attempts to investigate the outcomes of two thrombus recanalization techniques at different points in the timeline up to 9 months with reference to vascular patency in terms of the antegrade flow across the thrombus site.

[J Indian Med Assoc 2024; 122(11): 66-9]

**Key words :** Thrombus Recanalization, Pigtail Catheter, Spray Catheter, Vessel Patency, Acute Iliofemoral, Deep Venous Thrombosis.

Iliofemoral Deep Vein Thrombosis involves either partial or total occlusion of iliac and/or common femoral vein led by intravascular thrombus causing obstruction of resultant lumen. This leads to elevation

<sup>1</sup>PhD Scholar, Department of Interdisciplinary Sciences, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra 442107

<sup>2</sup>PhD Scholar, Professor, Department of Radiodiagnosis, Jawaharlal Nehru Medical College, Wardha, Maharashtra 442005 & Pro Vice Chancellor, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra 442107 and Corresponding Author

<sup>3</sup>PhD, Professor and Head, Department of Interventional Radiology, Jawaharlal Nehru Medical College, Wardha, Maharashtra 442005

<sup>4</sup>MDS, Associate Professor, Department of Conservative Dentistry and Endodontics, Sharad Pawar Dental College & Hospital, Wardha, Maharashtra 442001

<sup>5</sup>MDS, Professor, Department of Periodontics and Oral Implantology, Sharad Pawar Dental College & Hospital, Wardha, Maharashtra 442001

<sup>6</sup>PhD, Assistant Professor, Department of Faculty of Interdisciplinary Sciences, Datta Meghe Institute of Higher Education and Research, Wardha, Maharashtra 442107

<sup>7</sup>MD, Assistant Professor, Department of Radiology, Dr Ulhas Patil Medical College & Hospital, Jalgaon, Maharashtra 425309

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### Editor's Comment :

- This study protocol has been designed to examine the effectiveness of 2 methods for Deep Venous Thrombolysis - Conventional method using the spray catheter and the novel method which employs the pigtail catheter ie, Banode Mishra Thrombolysis technique.
- The main findings which are akin to the present study are to examine the vascular patency of the affected iliac vessels over a period of time to ensure long term effects.
- Any statistically significant difference in between the conventional and novel methods over the course of study will be key to indicating desired procedure selection for deep venous thrombosis.

of venous blood pressure thereafter due to decreased luminal diameter. Resultant functional disability of affected leg is known to cause pain, cramps, hyperpigmentation, heaviness etc<sup>1,2</sup>. Post thrombotic syndrome thereafter is a known and notorious sequel due to functional disability along with antegrade venous flow obstruction<sup>3-7</sup>.

Literature states that the more distal the thrombus is located, the better recanalization potential of the involved vessel there is if treated with anticoagulant therapy alone<sup>8,9</sup>. This may be attributed to the fact

that the more proximal the site of thrombus in the venous vasculature, the more venous Blood Pressure it takes to propel the blood for the veins towards the heart and again, this puts the venous valves at extreme pressure. Venous valvular incompetence is one of the common factors leading to Deep Venous Thrombosis making it a vicious circle. Main outcome in question apart from long term follow up remains vessel patency at different points in the timeline<sup>10-13</sup>.

It is stated clearly in literature that one of the most important factors contributing towards post thrombotic syndrome along the timeline is residual thrombus as a result of an incomplete thrombolysis treatment<sup>14,15</sup>. However, the recent advances mark the concept of utilising pharmacomechanical catheter directed thrombolysis to treat lower limb Deep Venous Thrombosis. Hence, the null hypothesis states that the thrombus recanalization techniques employing pigtail catheter will not be more efficacious than spray catheter for vessel patency in acute iliofemoral deep venous thrombosis and the alternate hypothesis states vice-versa.

The present study compares two thrombus recanalization techniques in the setting of iliofemoral deep vein thrombosis with respect to vessel patency in terms of the anterograde flow across the thrombus site.

## MATERIALS AND METHODS

### Ethical Approval :

The study proposal was approved on consideration of ethical grounds by Institutional Ethics Committee, Datta Meghe Institute of Medical Sciences (deemed to be university) on 15<sup>th</sup> July, 2022 with letter reference number DMIMSU(DU)/IEC/2022/03. The present study has been registered in the Clinical Trial Registry India with the registration number CTRI/2022/12/047888. <https://ctri.nic.in/Clinicaltrials/rmaindet.php?trialid=76868&EncHid=15032.46177&modid=1&compid=19>

### Study Design :

The present study will be carried out in the Department of Interventional Radiology, Acharya Vinoba Bhave Rural Hospital, Jawaharlal Nehru Medical College after approval obtained from Institutional Ethics Committee, Datta Meghe Institute of Higher Education and Research (declared as deemed to be university), formerly known as Datta Meghe Institute of Medical Sciences (deemed to be university). The participants will be duly informed about the aim, objectives and procedure pertaining to this research and will be included only after obtaining a statement of informed consent from them. A total of 80 cases will be enrolled and divided into 2 groups of 40 each.

### Trial Design :

The study is a randomized parallel group controlled trial. The patients included for the research will be distributed into two independent groups – Group A and Group B. Group A will include patients getting the spray catheter based Deep Venous Thrombolysis while Group B will be assigned to be getting the pigtail catheter based Deep Venous Thrombolysis. The allocation of patients into these two groups will be based on computer generated randomization with concealment/blinding to be carried out by usage of sequentially numbered sealed envelopes.

### Participants :

Those patients aged 16 to 75 years with acute ilio-femoral Deep Venous Thrombosis reporting to Department of Interventional Radiology, Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha with absence of contraindications to thrombolytic treatment or no other cerebrovascular pathology related to fibrinolytic therapy, having life expectancy more than 6 months with no history of malignancy or addiction, those having given the statement of informed consent with symptoms of 21 days or less time duration will be enrolled<sup>4,12</sup>. Those patients with the history of recent major surgery, cerebrovascular accident and pregnancy will be considered under the exclusion criteria.

### Sample Size Consideration :

Sample size was calculated using the Superiority (Parallel Design) Formula Using Proportion Difference as follows<sup>16</sup> :

$$n1 = \frac{(Z\alpha + z\beta)^2 (p1(1-p1) + p2(1-p2))}{(\epsilon - \delta)^2}$$

$$Z\alpha = 1.64$$

$$\alpha = \text{Type I error}$$

$$Z\beta = 0.84$$

$$\beta = \text{Type II error rate at 20\%}$$

$$\text{Power } (1-\beta) = 80\%$$

$$\epsilon = \text{True proportional difference}$$

$$\delta = \text{Clinically Relevant difference (25\%)}$$

Considering true proportional difference  $\epsilon = 0$

$$P1 = 60\%, P2 = 80\% \text{ (Assumed)}$$

Here, True proportion difference Luminal Obstruction opening (Difference in Proportion  $\epsilon$ ) = 0 % = 0

Clinically acceptable for Superiority ( $\delta$ ) single tail = 25% = 0.25 (Expected)

$$P1 = 60\% = 0.60$$

$$P2 = 85\% = 0.85 \text{ (Assumed)}$$

$$n1 = (1.64 + 0.84)^2 \cdot [(0.60 \cdot (1 - 0.60)) + (0.85 \cdot (1 - 0.85))] / (0.00 - 0.25)^2 = 36 \text{ for one group superiority}$$

$$\text{Total} = 36 + 36 = 72, \text{ considering 10\% Drop out rate } \sim 8 = 40 + 40 = 80$$

Therefore, the total number of cases which will be enrolled for the present study is 80, thereby including

40 cases in each study group.

### Intervention Design :

#### Group A :

All the patients in Group A will be subjected to spray catheter (Cook Medicals LLC, USA) thrombus recanalization technique. The patients will be lying in prone position after the deployment of a filter in the inferior vena cava near the left renal vein's origin. The popliteal vein will be accessed by ultrasonography and punctured followed by insertion of a 7 French sheath (Translumina Therapeutics LLP, India). This will be followed by introduction of 0.035 hydrophilic guidewire (Blueneem Medical Devices Pvt Ltd., India) and intravascular catheter (Cook Medicals LLC, USA) over it and a venogram will be taken to assess the level and extent of intravascular thrombus load on digital subtraction angiography. A 5 French Cobra or Headhunter catheter (Cook Medicals LLC, USA) will be advanced over the guidewire up to the level of inferior vena cava crossing the thrombotic section. Then, there will be exchange of Cobra or Headhunter catheter with spray catheter over the hydrophilic guidewire through the sheath. The proximal tip of spray catheter will stay at the site of thrombus. Through the spray catheter, there will be administration of alteplase (10 ml alteplase in 50 ml normal saline). After 4 hours, spray catheter is exchanged over the hydrophilic guidewire with Judkins catheter (Translumina Therapeutics LLP, India) and mechanical aspiration of thrombus is carried out using a 50 ml syringe immediately followed by a post procedural venogram.

#### Group B :

All the patients in Group B will be subjected to pigtail catheter thrombus recanalization technique. The patients will be lying in prone position after the deployment of a filter in the inferior vena cava near the left renal vein's origin. The popliteal vein will be accessed by ultrasonography and punctured followed by insertion of a 7 French sheath. This will be followed by introduction of 0.035 hydrophilic guidewire and intravascular catheter over it and a venogram will be taken to assess the level and extent of intravascular thrombus load on digital subtraction angiography. A 5 French Cobra or Headhunter catheter will be advanced over the guidewire up to the level of inferior vena cava crossing the thrombotic section. Then, there will be exchange of Cobra or Headhunter catheter with pigtail catheter (Cook Medicals LLC, USA) over the hydrophilic guidewire through the sheath. The proximal tip of pigtail catheter will stay at the site of thrombus. This will be followed by forceful injection of alteplase (10 ml alteplase in 50 ml normal saline) through the pigtail catheter with rotation of the

pigtail catheter by an angle of 90 degree and withdrawal by 1.5 to 2 cm distally. These steps will be repeated in succession till the entire thrombotic segment has been covered. After 4 hours, pigtail catheter is exchanged over the hydrophilic guidewire with Judkins catheter and mechanical aspiration of thrombus is carried out using a 50 ml syringe immediately followed by a post procedural venogram.

### Outcome Measures :

The primary outcome for the present study will be extent of vessel recanalization and patency percentage based on the degree of luminal reduction. The success of catheter directed thrombolysis will be classified as success (>90%), partial success (more than 50% but <90%) and failure (<50%) where the said percentages are referring to the luminal area where venograms reveal robust antegrade flow across the thrombus site.

### Follow-up :

Once the immediate pre-procedural ( $t_0$ ) and post-procedural ( $t_4$ ) venograms will have been taken, subsequent venograms will be recorded at further future patient visits at one ( $t_1$ ), three ( $t_2$ ), six ( $t_3$ ), and nine ( $t_4$ ) months as shown in Fig 1 after the discharge on colour doppler ultrasound or digital subtraction angiography. The follow-up measurements will be preserved electronically. During the trial, in case of the drop outs, the reasons will be recorded along with getting in contact with them as soon as possible and subjecting them to the projected follow up subsequently. The data regarding patient withdrawal as well as drop-out will be recorded and reflected in the final data analysis under the intention to treat principle of the analysis.

### Blinding :

The intervention and outcome measure will be implemented by the Principal Investigator under the supervision of co-investigator.

### Data Management :

The recorded data of the present trial will remain secured with restricted access upon permission for further analysis and reference by the researcher, the supervisor or the biostatistician.

### Statistical Analysis :

The statistical analysis of the recorded data will be carried out by IBM SPSS Statistics software (Version 27). Group effect will be calculated and compared by two-way analysis of variance (ANOVA). Significant difference thus shown, students t-test will be applied to calculate and compare in-group changes. Determination of significance will be made by a two-sided p value of less than 0.05. Baseline comparison

TIMEPOINT**	STUDY PERIOD						
	Recruitment	Allocation	Post-allocation				Close-out
	-t <sub>0</sub>	Baseline t <sub>0</sub>	t <sub>1</sub>	t <sub>2</sub>	t <sub>3</sub>	t <sub>4</sub>	t <sub>4</sub>
<b>ENROLLMENT:</b>							
Eligibility screen	X	X	X			X	X
Informed consent	X						
Allocation		X					
<b>INTERVENTIONS:</b>							
[Group A]		X	X	X	X	X	
[Group B]		X	X	X	X	X	
<b>ASSESSMENTS:</b>							
[Extent of Vessel Recanalization]		X	X	X	X	X	X
[Patency Percentage]		X	X	X	X	X	X

Fig 1 — SPIRIT Schedule for randomized parallel-group controlled trial, interventions, and assessments where t<sub>0</sub> is pre-procedural, t<sub>1</sub> is one month, t<sub>2</sub> is three months, t<sub>3</sub> is six months, and t<sub>4</sub> is nine months follow-up

will be carried out using Fisher’s exact test, t-test or Mann-Whitney U test. Comparison of primary outcome will be carried out by application of Mann-Whitney U test upon the recorded data at the post-procedural venogram, 1 month, 3 months, 6 months and 9 months as per future patient visits. Intention to treat analysis principle will be used for the present study.

**DISCUSSION**

Venous Thromboembolism has been a considerable concern in public health domain with high rates of pulmonary thromboembolism therein<sup>17-19</sup>. Deep venous thrombosis stands for approximately 66% of venous thromboembolism cases. A trial on Adjunctive Catheter-Directed Thrombolysis for Thrombus Removal (ATTRACT) demonstrated that catheter-directed pharmaco-mechanical thrombolysis (PCDT) did not lessen the frequency of post thrombotic syndrome but lowered its intensity during a 24-month period of follow-up and accelerated resolution of acute symptoms<sup>12</sup>. In a trial, the Catheter-Directed Venous Thrombolysis in Acute Iliofemoral Vein Thrombosis (CAVENT), thrombolysis was directed with catheter to reduce the post-thrombotic syndrome risk 2 and 5 years<sup>10</sup>. Pharmacomechanical catheter directed thrombolysis has been employed in various studies and randomized trials<sup>10,12</sup> noting its significant utility in easing the severity of acute symptoms<sup>20</sup>. This study attempts to investigate the outcomes of two thrombus recanalization techniques at different points in the timeline up to 9 months with reference to vascular patency in terms of the anterograde flow across the thrombus site.

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## Pictorial CME

### Elephantiasis : A Reappraisal with Special Reference to Nuclear Scan

Rudrajit Paul<sup>1</sup>

**E**lephantiasis, or lymphatic filariasis, is a neglected tropical disease in India<sup>1</sup>. It is a vector borne disease with the parasite lingering in the lymphatic system for decades (if untreated) and causing an irreversible disfiguring and debilitating damage to the limbs and other organs<sup>1</sup>. Although elephantiasis is most commonly caused by chronic infection with *Wuchereria* or *Brugia* species, there are rare some non-infectious causes also, like podoconiosis, caused by chronic exposure to irritants in the soil<sup>2</sup>. Very rarely, congenital absence of lymphatics can cause a similar appearance or lymphatic obstruction in lepromatous leprosy can cause a condition called Elephantiasis nostras verrucosa<sup>3</sup>. Whatever the aetiology, elephantiasis has become extremely rare in India presently, due to a spectacular socio-economic development, mass anti-filarial drug prophylaxis programs and a general improvement in medical services. However, medical students need to be aware of the clinical picture because occasionally such cases may be encountered. This article presents the pictorial presentation of such a rare case.

#### CASE REPORT

A 68-year-old woman from Kolkata came to the OPD with massive swelling of both legs (left>right). There were non-healing ulcers on the lower legs (Fig 1) with foul smelling discharge and pus. She could not bend the knees. The skin had a leathery feel with peau d' orange. The patient had never visited a proper medical facility in the last three decades and had only been attended by alternative medicine practitioners. In childhood, she had stayed in lower Assam for a few years after which the family moved to Kolkata.

Routine blood works were normal including a normal eosinophil count. Ultrasonographic venous doppler did not show any venous thrombosis. There was massive interstitial edema. Radioisotope lymphangioscintigraphy (Fig 2) showed almost complete absence of dye flow from distal to proximal limb. Blood for IgG anti-Filaria antibody came positive.

The patient was treated for cellulitis and pyoderma and discharged with explanation of the prognosis. Surgical colleagues found the case inoperable.

#### DISCUSSION

Elephantiasis is a chronic debilitating condition with profound implications for social status, mobility and professional capability of the patient. It is chronic massive irreversible lymphedema. Besides the apparent cosmetic effect, the most common complication of chronic lymphedema is recurrent skin and soft tissue infections, which was present in our patient. Such infections are not only the effect of lymphedema but also a contributor to further



Fig 1 — lower leg of the patient with cellulitis and pus

Fig 2 — Lymphangioscintigraphy of both legs showing absence of dye flow

progression of the lymphatic blockage<sup>4</sup>. Our patient had suffered from recurrent pyoderma and cellulitis over decades.

Medical treatment in the initial stages of filariasis with Diethyl Carbamazine Citrate can help in clearing the infection. But once the infection becomes chronic with lymphatic fibrosis, anti-parasite treatment is generally unhelpful. There are some surgical options for lymphedema like debulking of skin, lympho-venous anastomosis creation or laser treatment<sup>4</sup>. But again, those are useful in initial stages only, not the advanced stage seen here. There are certified lymphedema therapists available, who can help the patient with appropriate advice about exercise, hygiene, footwear, wound care and complex decongestive physiotherapy<sup>5</sup>.

There are specific geographical regions endemic for filariasis. But, as the present case shows, such severe cases may be encountered in non-endemic regions too. In those cases, it is important not only to take present address, but also a detailed history of dwellings from childhood.

We present this case to highlight the clinical presentation of this rare condition. Since the infection has become very rare in India, physicians may miss the diagnosis initially. But a missed diagnosis can result in future devastating consequences.

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<sup>1</sup>MD, MRCP, DNB, Consultant Physician, Department of Medicine, Ruby General Hospital, Kolkata, West Bengal 700107 and Corresponding Author

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## Commentary

# Headache Algorithm : A Guide to Differential Diagnosis and Management of Headache Disorders by Indian Medical Association

K Ravishankar<sup>1</sup>, Tapas Kumar Banerjee<sup>2</sup>, A V Srinivasan<sup>3</sup>, Dharmesh Kumar Patel<sup>4</sup>,  
A V Jayakrishnan<sup>5</sup>, Jayesh Lele<sup>6</sup>, Bimal Shah<sup>7</sup>, Rajen Shah<sup>8</sup>

Headache, characterized by pain or discomfort in the cephalic or facial regions, can manifest with or without accompanying symptoms. Most cases of headache encountered in clinical practice are primary in origin and are often benign. Yet, they are the most prevalent cause of temporary disability in patients of all age groups. The presence of more serious and life-threatening if untreated secondary causes make the situation worse. The current review focuses on developing algorithms for differential diagnosis of various headache disorders, so that secondary causes can be addressed promptly, while providing an accurate approach towards diagnosis of primary headaches. This review will also provide guidance regarding the management and treatment options available for primary and secondary headaches. The review is developed and reviewed by eight panel members of the Indian Medical Association (IMA).

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**Key words :** Headache, Indian Medical Association (IMA).

**H**eadache is a painful and disabling feature of multiple conditions including primary headaches like migraine, tension type headache and cluster headache or a secondary symptom of underlying condition. It is estimated that headache disorders affect approximately 40% of the population and are more common in females compared to males<sup>1</sup>. According to Global Health Estimates (2019), headache disorders were found to be the third highest cause of Disability-adjusted Life Years (DALYs) worldwide, after stroke and dementia<sup>1</sup>. Headache disorder was the most prevalent neurological disorder in India in 2019, affecting 488 million<sup>2</sup>. The

International Classification of Headache Disorders (ICHD-III) classifies headaches into three categories: primary headache disorders (includes tension type headache, migraine, and cluster headaches), secondary headache (includes headaches due to potentially life-threatening etiologies such as traumatic brain injury, vascular cranial disorders, substance abuse, infection etc) and cranial neuropathies, such as trigeminal neuralgia<sup>3</sup>. Primary headaches are more common in practice than secondary headaches. The scope of the current review is to provide algorithms for differential diagnosis and management of headache disorders. The review is developed and reviewed by eight panel members of the Indian Medical Association (IMA). The IMA recommended panel members included headache experts from different specialties including neuro-physicians, neurosurgeons, clinical physicians, ENT, and general practitioners, who discussed issues related to the stepwise management of headache.

### Primary Headache :

In routine practice primary headaches comprise more than 90% of all headache cases<sup>4</sup>. Primary headaches are generally not life-threatening but can cause pain, discomfort and decrease the overall Quality of Life (Table 1).

### Migraine :

Migraine is a chronic neurological disease with episodic acute attacks of head pain and is characterized by attacks of moderate-to-severe headache and reversible neurological and systemic

<sup>1</sup>MD (Internal Medicine), Consultant In-charge of The Headache and Migraine Clinics, Jaslok & Lilavati Hospitals & Research Centre 15, Pedder Rd, IT Colony, Tardeo, Mumbai 400026

<sup>2</sup>MD, FRCP (Lon), FRCP (Edin), FAAN, FIAN, Medical Director & Chief Consultant Neurologist, National Neurosciences Centre, Kolkata, 2nd Floor, Peerless Hospital Campus, Kolkata 700094 and Corresponding Author

<sup>3</sup>MD, DM, PhD (Neuro), D Sc, FRCP, FAAN, FIAN, Emeritus Professor, The Tamil Nadu Dr MGR Medical University, Guindy, Chennai 600032

<sup>4</sup>DM (Neuro), Consultant Neurologist, Neuro Care Clinic & Research Center Naranpura, Ahmedabad 380013

<sup>5</sup>MS (Ortho), Mch (Neuro), Head of The Department, Neuro & Spine Surgeon, EMS Memorial Co-operative Hospital & Research Centre Ltd, Malappuram, Kerala 679322

<sup>6</sup>MBBS, General Practitioner, Senior Consultant, Dr Jayesh Lele Clinic, Mumbai, Maharashtra 400064

<sup>7</sup>MS (ENT), D ORL, ENT & Head-Neck Surgeon, Bhartiya Arogya Nidhi Hospital, Mumbai 400049

<sup>8</sup>MS (ENT), Director, Synergy ENT & Eye Hospital, Mehsana, Gujrat 384002

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	Migraine	Tension Type Headache	Cluster Headaches
Pain Description	Throbbing, moderate to severe, worse with exertion/daily activity	Pressure, tightness, waxes and wanes	Abrupt onset, deep, continuous, excruciating, explosive
Associated Symptoms	Photo/phono- phobia, nausea & vomiting, aura	None	Tearing, congestion, rhinorrhoea, pallor, sweating
Location	Unilateral	Bilateral	Unilateral
Duration	4-72 h	Variable	0.5-3 h, many per day
Patient Appearance	Resting in quiet dark room	Remains active or prefers to rest	Remains active, prefers hot shower
Patient profile	Young female	-	Male, smoker

Table 1 — Common types of Primary Headaches

symptoms in some patients. Many epidemiological studies have documented its high prevalence and socio-economic and personal impacts. In India, the prevalence of migraine is 214 million and it is the second largest contributor to the disability due to neurological disorders (Fig 1)<sup>2</sup>.

While migraine was previously regarded as primarily vascular, the importance of sensitization of pain pathways and neurogenic origin of attacks in the CNS, have gained increasing attention. Several internal and external factors, called as triggers, either induce or exacerbate migraine and associated symptoms via activating trigemino-vascular system. Some common triggers include nuts, chocolate, processed foods, wine, coffee, tea, cheese, weather changes, bright light, odours, travel, missed meal or fasting, dehydration, stress, sleep disturbances, menstruation and menopause. Identification of these triggers can help in the management of migraine<sup>5</sup>. However, it is important to note that different patients have different triggers for migraine; a migraine patient need not have all possible triggers.

Increasing headache intensity and frequency are associated with comorbidities related to psychiatric disorders (depression, anxiety), sleep conditions (insomnia) and inflammation (IBD). People with migraine were significantly more likely to report

insomnia, and depression, anxiety among other conditions<sup>6</sup>.

**Abortive Treatment of Migraine :**

Patient life style modifications and trigger avoidance can help reduce the migraine frequency and severity. These include sitting in dark isolated places to avoid light and sound, avoiding work and exertion, taking rest and trying to sleep<sup>7</sup>.

Abortive drug therapy targets individual headache episodes in patients with episodic and chronic migraine. NSAIDs are first line abortive treatment of migraine along with simple and combination analgesics.

Naproxen sodium is found to be effective in the treatment of migraine, when given in dosage 500 mg, it relieved the symptoms of migraine and reduced the severity in a time dependent manner<sup>8</sup>. Antiemetics like domperidone alleviate incapacitating symptoms of nausea and vomiting and enhance the bioavailability of the co-prescribed NSAIDs<sup>9</sup>. Paracetamol and aspirin (ASA) have a longstanding history in the treatment of migraine attacks.<sup>10</sup> Ibuprofen, a propionic acid derivative, is a widely used antimigraine drug. Doses of 800 mg to 1,200 mg or 400 mg as an arginine salt were superior to placebo<sup>10</sup>.

Sumatriptan (oral, SC and nasal), and the newer triptans (zolmitriptan (oral and nasal), naratriptan (oral), rizatriptan (oral), eletriptan (oral), almotriptan (oral) and frovatriptan (not available in India)) display high agonist activity at mainly the serotonin 5-HT1B and 5-HT1D receptor subtypes. Triptans are most effective when taken early in an attack, when the headache is still mild. Upon relapse, triptan treatment can be repeated or combined with fast-acting NSAIDs eg, naproxen sodium, ibuprofen lysine or diclofenac potassium<sup>11</sup>. Triptans are contraindicated in patients with Coronary Artery Disease (CAD).

Ergotamine oral because of their erratic absorption and frequent side effects of nausea, vomiting, muscle cramps and vasoconstriction and cardiac effect ergotamine are rarely used now. Lasmiditan is newly introduced centrally and peripherally acting 5-HT1F receptor specific agonist. Dose is 50 mg and 100 mg tablets per day<sup>12</sup>. A patient should refrain from driving for at least 8 hours after taking<sup>13</sup>.

**Prophylactic Treatment of Migraine :**

Recurrent migraines are often functionally disabling and can impair Quality of Life. Prophylactic therapy may decrease the frequency, severity and duration of migraine attacks, increase responsiveness

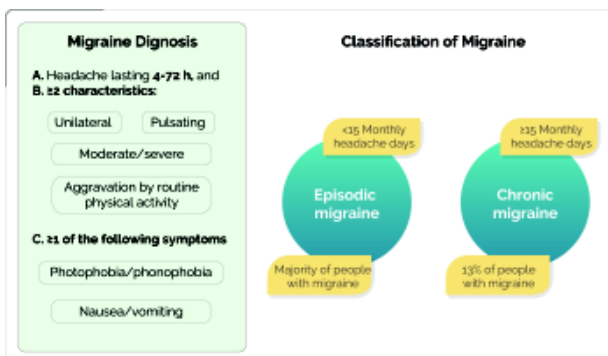


Fig 1 — Migraine Diagnosis and Classification



to acute migraine therapy and improve Quality of Life.

Lifestyle modifications have been suggested as a potential preventive countermeasure for the prophylaxis of migraine and include dietary, sleep and stress management. Avoiding known triggers for migraine headache may play an important role in reducing the severity and frequency of migraine episodes<sup>7</sup>. Some studies suggest low fat and high protein in diet as a putative preventive measure against migraine. Ketogenic diet for reducing the occurrence of migraine attacks have been suggested<sup>14</sup>. Certain nutraceuticals like riboflavin, magnesium and coenzyme Q10 may be well tolerated and effective in the adult prophylaxis of migraine<sup>14</sup>. Daily Walk and moderate cardiovascular/ aerobic exercise have been shown to be effective in reducing the frequency of migraine<sup>15</sup>.

Amitriptyline, a tricyclic antidepressant, is commonly used in the prophylaxis of migraine and Tension Type Headache (TTH) and treatment of depression and neuropathic pain<sup>15</sup>. It is also prescribed in medication overuse headache. Because of its multimodal actions, many international guidelines and an Indian expert consensus

recommend that amitriptyline is useful in migraine with co-morbidities<sup>16-20</sup>.

Propranolol, a beta-blocker, reduces central hyperexcitability through  $\beta$ 1- adrenoceptor-mediated inhibition of noradrenaline release, thus reducing central catecholaminergic hyperactivity. Some other prophylactic medications are flunarizine, topiramate, and divalproex.

In a network meta-analysis done by Jackson, *et al* in 2015, they found amitriptyline to be better than several other medications including candesartan, fluoxetine, propranolol, topiramate and valproate and no different than atenolol, flunarizine, clomipramine or metoprolol<sup>21</sup>. Although, the literature indicates amitriptyline to be more effective than other prophylactic drugs, in real World the efficacy of a particular prophylactic medication varies from one individual to another.

Second line prophylactic therapy includes botulinum toxin, monoclonal antibodies (eg, Only Erenumab is available in India) and, neuro-modulation methods like remote electro-neuro-modulation devices (eg, Nerivio) and vagus nerve stimulation (Table 2)<sup>22</sup>.

Diagnosis										
IF lasting from 4-72 hours AND ≥ 2 features: Unilateral, Pulsating, Moderate/severe or Aggravation by routine physical activity AND ≥ 1 of the following symptoms: Photophobia/Phonophobia or Nausea/Vomiting										
Abortive Treatment										
<b>1st Line</b> Naproxen sodium 250/500 mg SOS Paracetamol 1000 mg SOS, Ibuprofen 400 mg SOS, Aspirin 1000 mg SOS If, nausea vomitings are one of the most bothersome symptoms then, Naproxen + Antiemetic drugs (Domperidone 10 mg or Metoclopramide 10 mg) BD/SOS If no optimal response on above therapy then refer to headache specialist for further treatment. 2nd line: Triptans, Triptan + Naproxen; 3rd line: Lasmiditan										
Prophylactic Treatment										
Provide prophylactic drug treatment, if any of the following is present: Attacks significantly interfere with patients' daily routines despite acute treatment/ Frequent attacks/ Contraindication to, failure, or overuse of acute treatments/ Adverse Events with acute treatments/ Patient preference.										
Migraine without Co-morbidities										
Amitriptyline		Propranolol			Flunarizine		Topiramate		Divalproate sodium	
Starting Dose: 5-30 mg at OD bedtime Maximum tolerated dose: Up to 25-50 mg Duration of therapy: 3-6 Months		Starting dose- 20 mg BD Maximum Tolerated dose- Up to 80 mg BD Duration of therapy 3-6 Months			5-10 mg at bedtime, for 3-6 months		25-50 mg BD		500-1000mg daily, for 3-6 months	
Migraine with Co-morbidities										
Anxiety	Depression	Insomnia	Tension type Headache	Neuropathic Pain	Diabetes	Asthma	Hypertension	Epilepsy	Obesity	Kidney Disease
Amitriptyline*, Topiramate, Divalproate Na	Amitriptyline*, Topiramate, Divalproate Na	Amitriptyline	Amitriptyline	Amitriptyline*	Amitriptyline	Amitriptyline	Propranolol	Topiramate, Divalproate Na	Topiramate	Propranolol, Flunarizine
Avoid										
Propranolol, Flunarizine	Propranolol, Flunarizine	Propranolol			Propranolol	Propranolol		Amitriptyline	Flunarizine, Amitriptyline, Divalproate Na	Topiramate
* Starting Dose: 20-25 mg at OD bedtime; Max. dose: Up to 50-75 mg										

Table 2 — Diagnosis and management of Migraine

**Secondary Headaches :**

A secondary headache is caused by underlying structural or infection conditions that trigger pain-sensitive areas in the neck and head. Secondary headaches are uncommon, but they are more serious than primary headaches.

The ICHD-3 provides a list of eight categories and 46 subcategories for causes of secondary headaches including trauma or injury to the head and neck; cranial and cervical vascular disorders; nonvascular intracranial disorders including neoplasm; a substance or its withdrawal; infection; disorders of homeostasis; disorders of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cervical structure and psychiatric disorders<sup>3</sup>.

**Approach to a suspected case of secondary Headache :**

- Check vital signs.
  - Perform focused history and examination:
- If red flags (Fig 2) are present: refer to The right specialist.

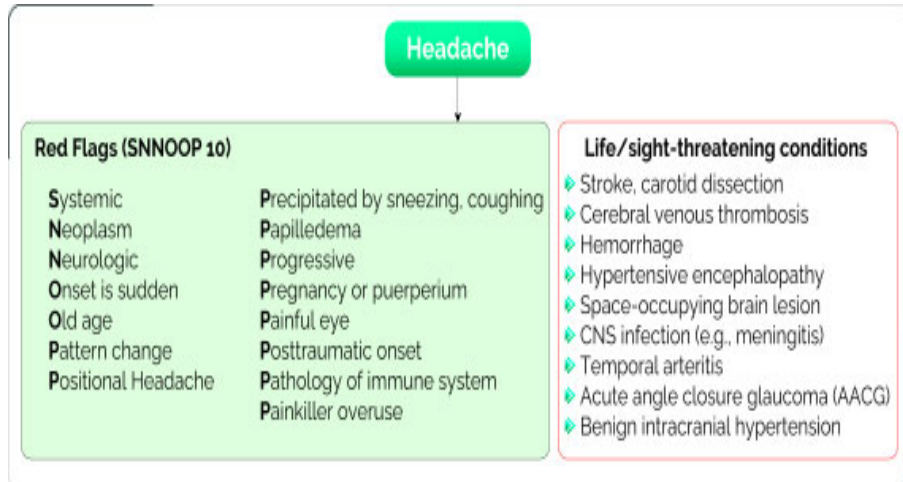


Fig 2 — Red flag signs of Secondary Headaches<sup>23</sup>

Tension Type Headache	Cluster Headache	Menstrual Headache	Medication Overuse Headache	Sinus Headache	Hypertension Headache	Exertional Headache	Head-Injury Headaches
<b>Etiology</b>							
Cause: Various factors, such as nutrition, muscle tension, environment, and genetics.	Pathology in trigeminal nerve.	Hormonal changes during and around menstruation in female leading to migraine headache.	Chronic medication overuse is the most significant risk factor. The risk from lowest to highest is: triptans, ergotamine, NSAIDs, paracetamol, and combination analgesics containing opiates or barbiturates.	Referred pain originated from intense mucosal irritation (DNS, polyps and septal sinus (polyps or edematous turbinates).	High blood pressure (greater than 180/120) can cause a headache in some patients.	Strenuous physical exercise, with the following triggers: running, jumping, weightlifting, sexual intercourse, bouts of coughing or sneezing.	Headache immediately or soon after a head injury. Headaches can also develop months after the original head injury.
<b>Signs and Symptoms</b>							
Recurring bilateral headaches with mild to moderate, dull, pressing sensation in the temporal and forehead area, neck, shoulder, and occasionally retro-orbital. Not exacerbated by routine physical activity.	Severe, unilateral headache lasting from 15 to 180 minutes, with symptoms concentrated around the orbit, supraorbital, and/or temporal regions. Autonomic symptoms on the side of headache: redness and tearing in the eye, a stuffy or runny nose, sweating, constricted pupils, drooping eyelids, or swelling around the affected area.	Symptoms of migraine during a 5-day menstrual period in at least 2 of every 3 menstrual cycles (Pure Menstrual migraine). Menstrually-related migraine: Pure Menstrual migraine and additionally at other times of the month outside the cycle.	Symptoms of any primary headache- Migraine, tension type headache or Cluster headache.	A dull, throbbing pain around the eyes, cheeks, and forehead with or without history of allergy.	A hypertension headache usually occurs on both sides of your head and is typically worse with any activity. It often has a pulsating quality.	Usually very short-lived but can sometimes last up to 2 days. They present as throbbing pain throughout the head and are more common in those with a family history of migraine.	Headache with or without warning symptoms including unconsciousness, seizures, vomiting, memory loss, confusion, vision or hearing problems.
<b>Management</b>							
<b>Abortive treatment:</b> Paracetamol, Aspirin, NSAIDs (Ibuprofen, Naproxen) or their combinations with caffeine. <b>Preventive Treatment:</b> Amitriptyline (10-50 mg OD at bedtime) is the primary choice for preventive treatment, followed by Mirtazapine and Venlafaxine.	<b>Refer to headache specialist. Abortive treatment:</b> Primary: Subcutaneous sumatriptan and high-flow oxygen. Alternate: intranasal triptans. <b>Preventive Treatment:</b> First line-Verapamil and lithium. Second line: Melatonin and topiramate.	Abortive (eg, Naproxen + Dexamethasone) and preventive treatment (Amitriptyline 10 mg) are same as that for migraine. <b>Refractory patient shall be referred to headache specialist.</b> The hormonal treatment may also be offered.	<b>Refer to headache specialist.</b> Amitriptyline (10-75 mg OD at bedtime) may help.	<b>Primary care:</b> Antihistamines, Anticholinergics, Oral Decongestants (not >3 days), Steam inhalation and warm compresses. <b>If no resolution, refer to Otorhinolaryngologist.</b> Mucociliary clearance is obtained with medical and/or surgical interventions.	<b>Primary care:</b> Antihypertensive Agents as per patients' medical and drug history. <b>It can be an emergency and refer to higher center if following is present-</b> changes in vision, numbness or tingling, epistaxis, chest pain, shortness of breath.	Headache is usually very short-lived but <b>frequent, longer and chronic exertional headaches should be referred to headache specialist.</b>	Imaging tests may be required. <b>If warning symptoms are seen, after a primary care, always call emergency and refer to specialist.</b>

Table 3 — Common Headaches other than Migraine

- If no red flags are present and suspicion for life-threatening causes is low: identify the underlying cause through appropriate investigation. CT/MRI imaging or CSF analysis or lab testing may be necessary for secondary headaches.

- Provide supportive care.

All clinically relevant headaches other than migraine are listed in Table 3 along with their etiology, signs, symptoms and management options.

### Conclusion :

Effective management of headache disorders is dependent on accurate differentiation between primary and secondary headaches. This review emphasizes the importance of a structured approach to diagnosis and outlines management strategies, including pharmacological and non-pharmacological therapies, to improve patient outcomes. Triggers identification and use of prophylactic agents play an important role in reducing clinical burden of primary headache.

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**Conflict of Interest (if any) :** Nil

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## Drug Corner

# Exploring the Efficacy and Safety of Lincomycin 1000 mg SR Tablets in ENT Infections : A Clinical Investigation

Anish Desai<sup>1</sup>, Priyanka Das<sup>2</sup>, Sreeni Nair<sup>3</sup>, Anuja Sakpal<sup>4</sup>

ENT conditions contribute to over 11% of the total cases in an accident and emergency department with acute ENT infections accounting for a significant portion of these presentations. Over the past decade, there has been a rise in hospital admissions for conditions like tonsillitis, peritonsillar abscess and deep neck space infections. Previous microbiology studies on admitted acute ENT infections have consistently identified Group A-beta-haemolytic Streptococcus (GABHS) (13.7%) as the most common isolate, followed by *Fusobacterium necrophorum* (13.6%) and *Staphylococcus aureus* (8.0%).

Lincomycin has shown its effectiveness in addressing a range of ENT infections<sup>11-13</sup>. A meta-analysis conducted by Desai, *et al* suggests that lincomycin has proven beneficial in treating various infections caused by gram-positive and anaerobic organisms.

This study aimed to evaluate the safety and effectiveness of a 1000 mg sustained-release tablet of lincomycin hydrochloride for the treatment of ENT infections caused by susceptible pathogens. The overall effectiveness of lincomycin treatment was evaluated using the PGA scale. A total of 460 (99.14%) patients achieved clinical success with lincomycin, while clinical failure was observed in only four (0.86%) cases. These findings support the idea that lincomycin is an effective and well-tolerated treatment option for diverse ENT indications.

[J Indian Med Assoc 2024; 122(11): 76-80]

**Key words :** Staphylococcus Aureus, Ent Infections, GABHS, Lincomycin, Tonsillitis.

Infections affecting the Ear, Nose and Throat (ENT) or Upper Respiratory Tract Infection (URTI) are widespread and can affect individuals across all age groups, from children to adults. These infections, particularly those prevalent in children, necessitate early diagnosis and appropriate management to guarantee optimal growth and development. They can manifest as either acute or chronic conditions<sup>1</sup>. ENT constitutes a significant proportion of the cases seen by general practitioners, as well as by otorhinolaryngologists, both on an outpatient and an inpatient basis<sup>2</sup>. Common ENT infections that can be effectively treated with medications include Acute Rhinitis, Sinusitis, Adenoiditis, Tonsillitis, Pharyngitis, Acute and Chronic Suppurative Otitis Media (CSOM), Otitis externa, Laryngitis and Epiglottitis<sup>3</sup>.

ENT conditions contribute to over 11% of the total cases in an accident and Emergency Department, with acute ENT infections accounting for a significant portion of these presentations. Over the past decade,

there has been a rise in hospital admissions for conditions like Tonsillitis, Peritonsillar Abscess and Deep Neck Space Infections. Previous microbiology studies on admitted acute ENT infections have consistently identified Group A-beta-haemolytic streptococcus (GABHS) (13.7%) as the most common isolate, followed by *Fusobacterium necrophorum* (13.6%) and *Staphylococcus aureus* (8.0%)<sup>4</sup>.

Most often, these infections are the primary cause for prescribing antibiotics, such that recovery usually occurs spontaneously. Some of these infections can progress to severe complications with a life-threatening potential. Swift therapeutic measures are necessary in these situations, involving hospitalization and the commencement of initial intravenous (IV) antibiotic therapy<sup>5</sup>. Several studies have demonstrated that patients who received antibiotics before admission exhibited a higher proportion of cultures with either no growth or normal flora. Additionally, there was a decrease in the number of isolates of Penicillin-susceptible organisms<sup>2,6</sup>.

Risk factors associated with ENT infection include accidental aspiration or ingestion of foreign bodies, crowding, low socio-economic status, poor parental educational level, smoking, anaemia and poor nutrition<sup>7,8</sup>. The presentation of foreign bodies in the Ear, Nose and Throat is common in primary and emergency care settings<sup>1,9</sup>.

<sup>1</sup>MD, FCP, PGDHEP, Director, Medical Affairs, Intellimed Healthcare Solutions, Mumbai 400071

<sup>2</sup>PhD Molecular Biology, Deputy General Manager - Medical Writing, Intellimed Healthcare Solutions, Mumbai 400071

<sup>3</sup>Doctor of Pharmacy, Assistant Manager - Medical Affairs, Intellimed Healthcare Solutions, Mumbai 400071

<sup>4</sup>Doctor of Pharmacy, Executive-Medical Affairs, Intellimed Healthcare Solutions, Mumbai 400071

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The initial guidance from the Groupe de Pathologie Infectieuse Pédiatrique de la Société Française de Pédiatrie (GPIP-SFP) and the Société de Pathologie Infectieuse de Langue Française (SPILF), as incorporated into the 2021 Haute Autorité de Santé (HAS) guidelines, emphasizes the recommendation against prescribing antibiotics for common cold, Non-streptococcal Tonsillopharyngitis, Laryngitis, Congestive Acute Otitis Media, or Otitis media with effusion<sup>5</sup>. Antimicrobial prescription patterns vary by location and are influenced by factors such as antimicrobial susceptibility, physician preferences, and costs. The irrational use of antimicrobials, including prescribing antibiotics for non-bacterial infections, administering inadequate dosages, and choosing improper routes, has resulted in ineffective treatment, prolonged illness, higher incidence of adverse drug reactions, suboptimal therapy, therapeutic failure, and polypharmacy. This eventually contributes to an increased burden of medical costs and the emergence of antibiotic resistance<sup>3</sup>.

Lincomycin, the pioneering antibiotic in the lincosamide class, was initially discovered in 1964 in the actinomycete *Streptomyces lincolnensis*<sup>10</sup>. It has been extensively researched and applied in various outpatient and hospital-based settings and is available in both oral and injectable forms. Lincomycin is commonly prescribed for treating a spectrum of infections, including ENT and URTI, Skin and Soft Tissue Infections (SSTI) such as surgical wound infections, bone and joint infections (Osteomyelitis and septic arthritis), and oro-dental infections. Its antibacterial action targets gram-positive bacteria, such as *Staphylococcus*, *Streptococcus* (pyogenes, viridans, and pneumonia), *C diphtheriae*, and anaerobic bacteria, including *Clostridium Propionibacterium*<sup>11</sup>.

Lincomycin has shown its effectiveness in addressing a range of ENT infections<sup>11-13</sup>. A meta-analysis conducted by Desai et al., suggests that lincomycin has proven beneficial in treating various infections caused by gram-positive and anaerobic organisms. It has demonstrated efficacy in managing Acute Upper Respiratory Tract and ENT infections, including Tonsillitis, Pharyngitis, Sinusitis and Acute Otitis Media (AOM)<sup>11</sup>. In another study trial, thirty-seven (100%) cases of gram-positive infections seen in an active general practice were treated successfully with lincomycin orally or intramuscularly<sup>12</sup>.

Furthermore, the safety profile of lincomycin in a meta-analysis revealed that an oral dose of lincomycin (1-2 g/day) showed no signs of toxicity, with only mild transient adverse effects, including allergic contact

dermatitis, anaphylaxis, bowel upset, occasional diarrhea, or other non-bothersome side effects<sup>11</sup>. Another study by Guslits showed that lincomycin 600 mg had no toxic effects with only a mild disruption of bowel function and occasional diarrhea being observed as side effects<sup>12</sup>. Therefore, this study was conducted to evaluate the effectiveness and safety of sustained released tablets of lincomycin 1000 mg in ENT infections.

## MATERIALS AND METHODS

### Study Design :

This was an open-label, retrospective, observational study. This study aimed to evaluate the safety and effectiveness of a 1000 mg sustained-release tablet of lincomycin hydrochloride for the treatment of ENT infections caused by susceptible pathogens. Patients willing to follow the procedures as per the study protocol voluntarily signed an informed consent form.

### Patient Criteria :

The study included individuals of age groups, from paediatric to elderly patients over 80 years of age and had been diagnosed with various infections, including URTI, such as Laryngopharyngitis, Tonsillitis, Bacterial Rhinosinusitis, Otitis Media and others. Participants who had not been part of a similar investigation within the preceding four weeks were included in the study.

Individuals who were pregnant, lactating, allergic to lincomycin antibiotics, had pre-existing renal, liver, or cardiac conditions, or other conditions as determined by the investigator (such as uncontrolled Diabetes and uncontrolled Hypertension), or who were already on antibiotic treatment or unable to follow the study procedures and protocol were excluded from the study.

### Study Intervention :

A 1000 mg sustained-release tablet of lincomycin hydrochloride was administered once daily for 5 days.

### Outcome Measures :

The primary outcome measures were adverse events and causality assessment.

The secondary outcomes were Total Symptom Score (TSS) and Physician's Global Assessment (PGA) scale. The TSS evaluated the clinical cure, while the PGA was used to assess the successful treatment outcome at the end of lincomycin treatment.

### Data Analysis :

A sample size of 464 patients was considered appropriate. Categorical data were expressed as numbers and percentages. Effectiveness was tested

using the Wilcoxon signed-rank test. All adverse events were recorded and causality was evaluated using the causality assessment tool. Causality was categorized as definite, probable, possible, or unlikely.

**RESULTS**

**Demographic Details :**

A total of 464 patients were enrolled in the study, covering a broad spectrum of age groups, from paediatric to elderly patients over 80 years of age, all presenting with ENT infections. Most patients were male, accounting for 268 patients (57.76%). Individuals belonging to the 31-40 years (27.59%) age group contributed to the highest percentage of patients (Table 1).

**Indications for Lincomycin :**

This study included 39 ENT indications for which lincomycin was prescribed. Among these groups, patients diagnosed with Acute Pharyngitis, Cough, Csom, Throat Pain, Tonsillitis and URTI accounted for more than 5% each of the total indications (Fig 1). The other indications are summarized in Table 2.

**Effectiveness of Lincomycin Based on Symptom Severity Score :**

The effectiveness of lincomycin was assessed by using the total symptom severity score. The symptoms evaluated were ear pain, running nose, throat pain, nasal pain and discharge, deafness, voice hoarseness and painful swallowing. At baseline, 165(35.56%) and 248 (53.45%) patients had moderate and severe symptoms, respectively (Fig 2). A reduction in the average TSS score was observed on day 5 versus baseline (Fig 3). Following the 5-day lincomycin regimen, there was a notable decrease in the number of patients with moderate and severe symptoms (Fig 2), with a significant reduction in TSS ( $p=0.0000000092$ ) (Table 3).

**Overall Treatment Outcome of Lincomycin :**

The overall effectiveness of lincomycin treatment was evaluated using the PGA scale. A total of 460 (99.14%) patients achieved clinical success with lincomycin, while clinical failure was observed in only four (0.86%) cases (Fig 4). Additionally, no fatal outcomes were observed throughout the study.

Age Group	No of Patients	Percentage
< 10 Years	8	1.72%
11-20 Years	27	5.82%
21-30 Years	127	27.37%
31-40 Years	128	27.59%
41-50 Years	93	20.04%
51-60 Years	51	10.99%
61-70 Years	23	4.96%
71-80 Years	5	1.08%
> 80 Years	2	0.43%
Total	464	100.00%

**Safety Outcomes of Lincomycin Treatment :**

After lincomycin treatment, 457 patients (98.49 %) reported no adverse reactions. Only a minority of patients, accounting for 7 (1.51%), experienced adverse drug reactions primarily related to Gastrointestinal (GI) disturbance, including Diarrhoea (0.22%), nausea (0.43%) and Abdominal pain (0.86%) (Fig 5).

**Causality Assessment of Lincomycin Treatment :**

The causality assessment scale employed in this study was used to determine the probability of adverse events associated with lincomycin administration. A total of 20 patients (46.51%) reported a causal relationship between lincomycin and GI disturbances as unlikely, while an equivalent percentage of patients (46.51%) reported it as certain.

**DISCUSSION**

In the present study, the assessment of lincomycin's effectiveness demonstrated a significant

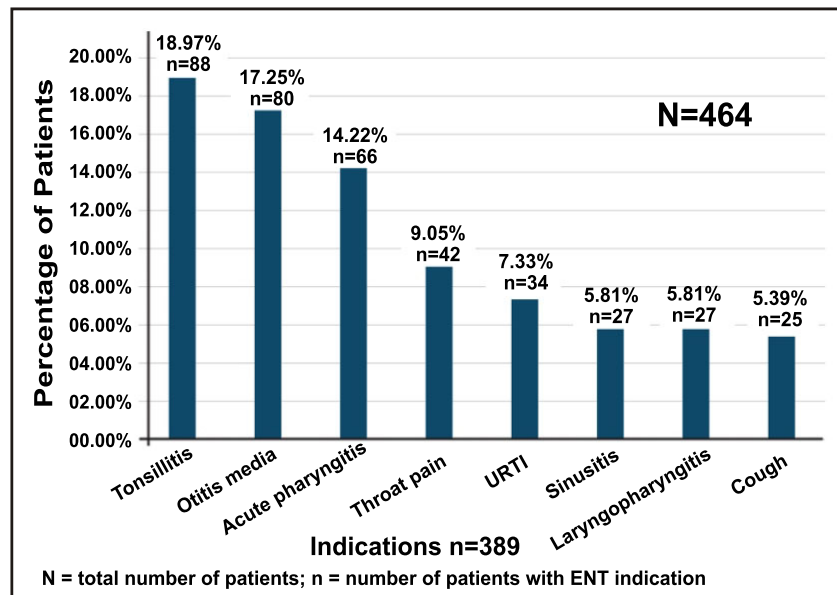


Fig 1 — ENT Indications in each group of patients contributing to more than 5% of the total population

Table 2 — Indications in each group of patients contributing to less than 5% of the total population

ENT Indications (N=464)	Other indications(N=464)
Respiratory tract infection (n=14, 3.03%)	Acute vestibular pain (n=1, 0.22%)
Rhinitis (n=13, 2.8%)	Granuloma (n=1, 0.22%)
Folliculitis (n=7, 1.51%)	Headache (n=5, 1.08%)
Dysphagia (n=4, 0.86%)	Furunculitis (n=3, 0.65%)

N=total number of patients; n=number of patients with ENT indication

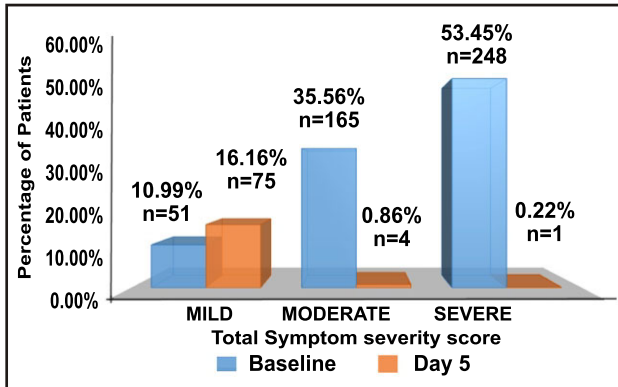


Fig 2 — Total symptom severity score of patients at baseline versus 5 days of lincomycin treatment

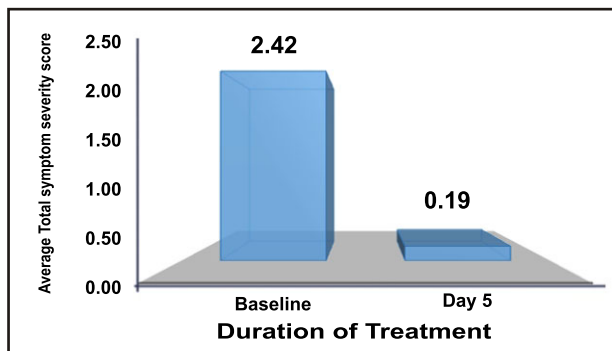


Fig 3 — Average total symptom score of patients at baseline versus day 5 of lincomycin treatment

reduction in symptoms by day 5 versus baseline. This finding is consistent with that of a recent Indian study indicating the prompt and effective action of lincomycin in alleviating ENT symptoms<sup>13</sup>. A multicentre postmarketing study evaluated the comparative efficacy and safety of multidose treatments using 500 mg capsules of lincomycin hydrochloride versus 200 mg tablets of cefpodoxime proxetil in 41 patients with tonsillitis and sinusitis. The

Table 3 — Summary of total symptom scores of patients at baseline versus 5 days of lincomycin treatment

TSS	Mean	N	Median	SD	SE	Wilcoxon W	P-Value	% Effect	Result
Baseline	2.42	464	3.00	0.68	0.0317	-18.911 <sup>b</sup>	0.0000000092	92.36	Significant
Day 5	0.19	464	0.00	0.43	0.0198				

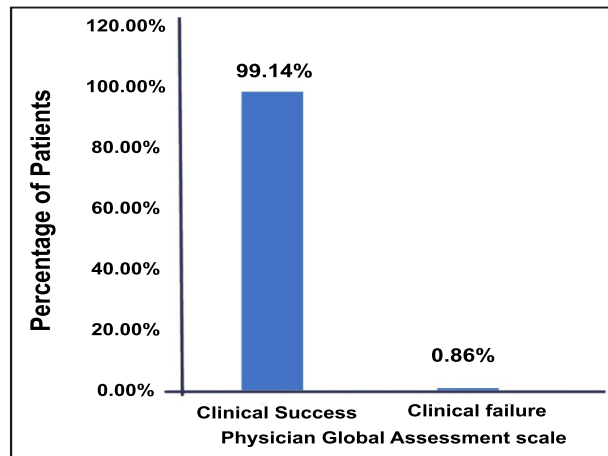


Fig 4 — Outcome assessment of lincomycin treatment using the PGA scale

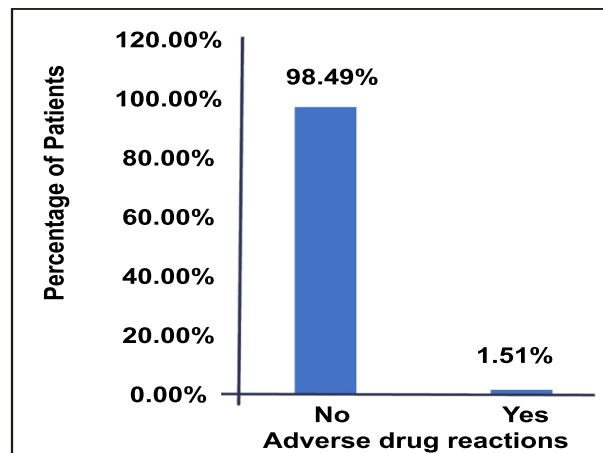


Fig 5 — Incidence of adverse drug reactions due to lincomycin treatment

results revealed that 67.89% and 52.27% of the patients in the lincomycin and cefpodoxime groups, respectively, achieved complete relief from all clinical symptoms. The findings suggest that lincomycin hydrochloride capsules, a conventional antibiotic, demonstrate effective treatment for alleviating tonsillitis and sinusitis compared to the newer third-generation antibiotic<sup>13</sup>. The minimal incidence of clinical failure observed in our study further serves as a testament to the overall effectiveness of lincomycin in the treatment of ENT infections.

The impact of ENT infections extends beyond specific age groups and influences both adults and children. This prevalent issue often leads to substantial disruptions in the daily lives of affected individuals, posing a growing health concern.

A study focusing on pediatric ENT disorders in India revealed that otitis media was most commonly observed in male children (53.2%). The majority of these affected children were from lower socio-economic backgrounds, living in combined-family setups and had mothers with limited educational backgrounds<sup>14,15</sup>.

A crucial aspect of our findings pertains to the safety profile of lincomycin. The low frequency of reported adverse reactions is a noteworthy observation, emphasizing the favorable safety profile associated with lincomycin use in the context of ENT infections. Among the reported adverse reactions, gastrointestinal disturbances emerged as the singular event, consistent with the well-documented side effect profile of lincomycin. The causality assessment indicated a well-balanced perception among patients concerning the probability of these occurrences being linked to lincomycin treatment, with an equal number of patients reporting no connection between lincomycin use and adverse events. In conclusion, the collective evidence presented in this study significantly adds to our understanding of the effectiveness and safety of lincomycin in the treatment of ENT infections.

#### Limitations of the Study and Prospects :

This study had some limitations, including the assessment period of 5 days for lincomycin's effectiveness is relatively short, potentially not capturing any long-term effects or complications that may arise with its extended use. To gain a more comprehensive understanding, further research, including randomized controlled trials, long-term follow-up, and comparative studies with other antibiotics, is necessary to provide additional insights into the sustained effectiveness and safety of lincomycin.

#### CONCLUSION

Our study highlights the broad applicability of a 1000 mg lincomycin sustained-release tablet in the management of ENT infections, with significant improvements in symptom severity, clinical success rates, and minimal adverse reactions. These findings support the idea that lincomycin is an effective and well-tolerated treatment option for diverse ENT indications.

**Declaration :** Article is not published / submitted in any other journal.

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## Book Review

**HIV-AIDS in India & Developing Countries**  
 by Dr. Yanamadala Murali Krishna, MD,  
 4-50, Main Road, Indrapalem, Kakinada 533006,  
 Andhra Pradesh, India,  
 e-mail : [peopleagainstaids@yahoo.co.in](mailto:peopleagainstaids@yahoo.co.in).  
 First Published : May, 2024, Pages iv + vi + 122,  
 Price : Rs.155.00, Outside India : US\$ 7.99.

### Overview :

Dr. Yanamadala Murali Krishna's *HIV-AIDS in India & Developing Countries* offers an in-depth, authoritative examination of the HIV-AIDS epidemic, with a particular focus on the Indian subcontinent and other developing nations. The book carefully traces the origins, transmission, and global ramifications of the HIV virus while addressing the specific socio-economic challenges faced by these regions in combating the disease. Divided into comprehensive chapters, it delves into the medical, social, and political dimensions of HIV-AIDS and provides a roadmap for both understanding the disease and implementing effective interventions.

### Book Structure and Content :

The book begins with a historical account of the origins of HIV, followed by a detailed exploration of the global impact of the disease, as highlighted in the early chapters. Chapters 1 to 4 set the stage by exploring the epidemiology and biological mechanisms of the virus, offering a global perspective on the HIV pandemic. Dr. Krishna's writing style is clear, concise, and devoid of unnecessary medical jargon, making it accessible to a wider audience, including policymakers, healthcare workers, and public health students.

One of the most compelling aspects of the book is the chapter on HIV-AIDS in India, where Dr. Krishna examines the unique trajectory of the disease within the subcontinent. This section not only emphasizes the high-risk groups and cultural factors influencing the spread of the disease but also highlights the significant progress India has made through its generics industry and global contributions to HIV treatment equity.

The author places great emphasis on prevention strategies and treatment protocols, particularly the section on Two-Drug Antiretroviral Therapy, which is a crucial read for healthcare professionals in resource-limited settings. In the Indian context, the narrative successfully addresses the cultural stigmatization of the disease and the lack of adequate healthcare infrastructure, making a strong case for global collaboration in both prevention and treatment efforts.

### Highlights :

The chapters on HIV and Tuberculosis, HIV and Pregnancy, and the role of UNAIDS in coordinating a global response to AIDS are particularly noteworthy. Dr. Krishna carefully analyzes the co-infection of HIV and TB, an urgent issue in India and other developing nations, and outlines diagnostic approaches like the Tuberculin Response for better management of HIV-TB patients.

Moreover, the book dedicates a thoughtful chapter to HIV Cure Research and the promise of an AIDS vaccine, discussing the scientific, financial, and ethical challenges of vaccine development. The reader gains valuable insight into the global fight against AIDS, emphasizing how innovations in HIV treatment, including generic drug production in India, have substantially contributed to making antiretroviral therapy accessible to low-income countries.

The final chapters focus on women and children, a segment disproportionately affected by the AIDS epidemic, and explore the societal implications of living with HIV, including the fight for rights of those affected by the disease. The author advocates for a more robust legal and social framework to protect the rights and dignity of HIV-positive individuals.

### Critical Evaluation :

One of the book's greatest strengths lies in its ability to weave together scientific information with

real-world applications. Dr. Krishna's deep understanding of the epidemiological and clinical aspects of HIV-AIDS is evident throughout, as is his concern for the socio-economic contexts that hinder effective treatment in developing countries. The section on Indian generics and global HIV treatment equity presents a balanced view of the complex global pharmaceutical landscape and India's critical role in ensuring access to life-saving medications at an affordable cost.

However, while the book is comprehensive in scope, it occasionally assumes a level of pre-existing knowledge that may alienate non-specialist readers. A more detailed glossary of medical terms or an expanded introduction to antiretroviral therapies could enhance accessibility for a broader audience.

### Conclusion :

*HIV-AIDS in India & Developing Countries* is a meticulously researched and thoughtfully presented work that offers valuable insights into one of the most critical global health challenges of our time. Dr. Yanamadala Murali Krishna's book is not only a significant academic contribution but also an essential guide for policymakers and healthcare professionals involved in the global fight against HIV. Its particular emphasis on India and other developing nations fills a crucial gap in HIV literature, making it a must-read for anyone interested in global public health.

**Dr. Shambo S. Samajdar**

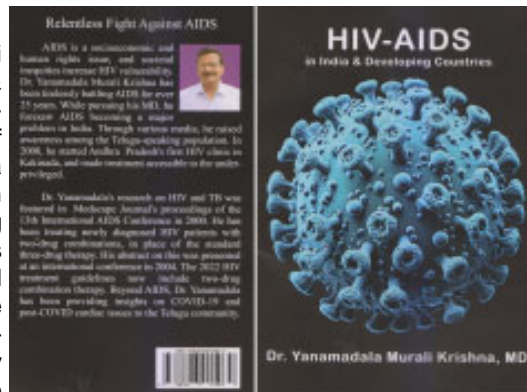
MD DM (Clinical Pharmacology)

FIPS, Fellow Diabetes India, Fellowship Respiratory and Critical Care (WBUHS)

PG Dip Endo & Diabetes (RCP), Dip Allergy Asthma Immunology (AAAAI)

Consultant, Diabetes and Allergy-Asthma Therapeutics Specialty Clinic, Kolkata

Faculty, JMN Medical College and Hospital, Nadia



## Letter to the Editor

[The Editor is not responsible for the views expressed by the correspondents]

### An Unusual Case of Flagellate Pigmentation Following Chemotherapy

SIR, — Flagellate pigmentation is a relatively uncommon but specific cutaneous adverse effect of bleomycin observed in clinical practice<sup>1</sup>. A 14 years old female having non seminomatous germ cell tumor of ovary was referred to dermatology out-patient department for some skin lesions after 7 days of taking first dose of chemotherapy. She was given intravenously bleomycin (30 units) single dose, etoposide 100mg/m<sup>2</sup> on day 1 to 5 and cisplatin 20mg/m<sup>2</sup> on day 1 to 5. On examination, the patient had multiple, mild pruritic, non tender, hyperpigmented, linear lesions over trunk, extremities, neck along line of pressure or scratching (Figs 1&2). The lesions ranged from 2to3mm in width and 2cm to10cm in length. Routine blood investigations were normal. Nails and hairs were normal. No clinical features of dermatomyositis, still's disease, no history of shiitake mushroom ingestion, child abuse were present. Dermatographism could not be elicited. Patient was treated with topical steroid and oral antihistamines. Causality assessment was carried out using the World Health Organisation-Uppsala Monitoring Centre criteria and Naranjo's Scale. The scale shows bleomycin was the probable cause of this adverse drug reaction. Other two drugs were not found to be the culprit drug.

Bleomycin is a chemotherapeutic antibiotic. Its mode of action is to block DNA uptake of thymidine in the S-phase of the cell cycle. It was first isolated by Umezawa in 1965 from soil fungus *Streptomyces verticillus* near coal mine in Japan<sup>2</sup>. It has been used for Hodgkin's lymphoma, certain germ cell tumor, sclerosis of recurrent pleural effusion. It has been used in various skin conditions like wart, hemangiomas, vascular malformations, cutaneous malignancies, condyloma accuminata, leishmaniasis cutis<sup>3</sup>. Bleomycin is inactivated by enzyme, bleomycin hydrolase, which cleaves ammonia group from bleomycin. Skin and lung tissue lack this enzyme which may account for most susceptible organ for bleomycin toxicity<sup>4</sup>. Skin toxicity includes Raynaud's phenomenon, hyperkeratosis, nailbed changes, palmoplantar desquamation<sup>5</sup>.

Flagellate dermatitis is occurrence of multiple whipped out lesions over multiple body areas. The term flagellate was derived from latin term *flagellum* due to its typical presentation<sup>6</sup>. Flagellate pigmentation due to bleomycin is specific but rare cutaneous adverse effect which appears 12-24 hours to 6 months after first exposure. Other drugs like peplomycin, docetaxel, bendamustine, trastuzumab can also cause flagellate dermatitis<sup>6</sup>. The exact pathogenesis is still unknown and different theories like

accumulation of toxic level of bleomycin due to low level of hydrolase, microtrauma due to scratching, increased melanogenesis, heat recall and reduced epidermal turnover allowing prolonged melanocyte -keratinocyte contact are proposed. It is usually dose dependant and occurs irrespective of route of bleomycin administration or malignancy being treated. It usually occurs after 90 to 285 units cumulative dose of bleomycin but very few cases have been reported with dose as low as 15 units given perenterally<sup>5,6</sup>. In this case the patient developed flagellate pigmentation after 30 units of intravenous bleomycin which is a rare occurrence. So, physician must be aware of this



Fig 1 — Flagellate pigmentation over back and neck



Fig 2 — Flagellate pigmentation over abdomen

characteristic cutaneous adverse effect of bleomycin even in low dose perenteral administration. We are reporting this case due to its rarity in a very low dose of bleomycin.

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Department of Dermatology,  
IPGME&R, Kolkata 700020  
<sup>1</sup>MBBS, Postgraduate Trainee  
<sup>2</sup>MD, Assistant Professor  
<sup>3</sup>MD, Professor

**Pramit Nandy<sup>1</sup>**  
**Olympia Rudra<sup>2</sup>**  
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