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ORIGINAL ARTICLE

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Profile of Newly Diagnosed Hypertensive Patients at a Tertiary Care Hospital in Himachal Pradesh

Priya Jamwal, Ram Chander Negi**, Rajesh Sharma***, Vijay Kumar Barwal****, Jatinder Kumar Mokta*****, Prem Machhan******

Abstract

***Background and Aim:** Hypertension is an important public health problem in India and one out of every five adults has hypertension. It's continuously rising incidence and prevalence emphasises the need for studying factors contributing to this pandemic. The consequences of hypertension can be devastating for the patient, healthcare provider and the country as a whole.*

***Material and Methods:** This was an observational, cross-sectional study done in 70 patients aged 18 years and above with newly detected hypertension at a tertiary care institute in North India. A pre-designed proforma was used to collect data, like socio-demographic factors with the various clinical parameters, investigations and biochemical parameters.*

***Results:** Most subjects (42.9%) were in the age group of 40 - 59 years. Majority of the patients (58.6%) presented with systolic blood pressure (SBP) 140 - 179 mmHg. Family history of hypertension was present in nearly one-third (35.7%) and most of the patients (51.4%) had a sedentary lifestyle. Increased Waist to hip ratio (WHR) was seen in 61.4 % and 27.1% of the females and males, respectively. Overall, on ECG, 25.7% had evidence of LVH. Deranged serum protein level was seen in 18.6%, dyslipidaemia in 47.1% and HbA1c was in the diabetic range in 22.9% of our subjects.*

***Conclusion:** This study reinforces the importance of regular screening to alter the natural history of hypertension, permit more effective treatment and thus help in reducing the morbidity and mortality.*

***Key words:** Newly diagnosed hypertensive, clinical profile, biochemical profile.*

Introduction

It is estimated that hypertension affects one-third of the world's population[1,2]. It is an important public health problem in India and one out of every five persons has hypertension, while 50% of people above 50 years have hypertension. Ultimately by the age of 78 years, 90% people develop hypertension[3]. Around 7.7 - 10.4 million annual deaths are attributable to elevated blood pressure (BP) levels. It is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India. Research also shows that each 10 millimeters of mercury (mmHg) rise of systolic BP is associated with 45% higher risk for ischaemic heart disease (IHD) and 65% higher risk of cerebrovascular accident (CVA) in those aged 55 - 64 yrs[4,5]. Complications of hypertension are either due to atherosclerosis leading to coronary artery disease (CAD), peripheral artery disease (PAD) and aortic disease or due to pressure changes like left ventricular failure (LVF), intracerebral haemorrhage (ICH) and hypertensive encephalopathy[6].

In the last twenty years prevalence of hypertension in urban locations has stabilised to about 25 - 30%, but it has increased in rural populations from 15 to 25%. This is due to rapid urbanisation of rural populations with consequent changes in lifestyles and increase in overweight and obesity[7,8]. Most research suggests a common pattern, i.e., increasing prevalence of hypertension and strong association with various risk factors.

Himachal Pradesh is rapidly climbing up the hypertension ladder. Various studies report a prevalence of hypertension from 11.3% in adolescents with additional 22.3% pre-hypertensives and 35.9% in rural communities[9,10]. Above all, the Longitudinal Ageing Study of India (LASI), says that a whopping 54.1% of the population (above 45 years) suffers from hypertension and 42.1% are in pre hypertension stage in the state. These figures are much higher than the national average of 44.9% (hypertension) and 39.7% (pre-hypertension)[11,12]. This worrisome and rapidly rising incidence and prevalence of the disease in our state as well as in India emphasises the need for studying factors contributing to this pandemic. On extensive literature review, we could not find any studies from Himachal Pradesh on clinical and biochemical profile of "newly diagnosed" hypertensive patients. Therefore, we

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conducted this study on newly diagnosed hypertensive patients presenting in a tertiary care hospital in Himachal Pradesh.

Material and Methods

This was an observational, cross-sectional study conducted in the Medicine department of Indira Gandhi Medical College and Hospital (IGMCH), Shimla, a tertiary care institute in North India, from August 2023 to February 2024, with the primary objective of studying the clinical and biochemical profile of newly diagnosed hypertensive patients. The sample size consisted of all the consecutive patients who presented to the department of Medicine, IGMCH, Shimla during the study period. All patients aged 18 to ≥90 years were included in the study. Written informed consent was obtained from all participants. In patients who were unconscious, consent was obtained from the next of Kin.

A pre-designed proforma was used to collect data of all newly diagnosed hypertensive patients. All relevant information including personal and demographic details, clinical parameters including vitals, Body Mass Index (BMI), Waist Hip Ratio (WHR), Electrocardiogram (ECG), Chest X-ray (CXR), 2-Dimensional echocardiography (2D-ECHO), fundoscopy and Ankle Brachial Pressure Index (ABPI) were recorded. The lab parameters including, complete haemogram (CHG), liver function test (LFT), Renal Function Test (RFT), high-sensitivity C-reactive protein (hs-CRP), Calcium, Phosphorus, Lipid profile, Haemoglobin A1c (HbA1c), fasting plasma glucose (FPG), serum proteins, Uric acid, Thyroid profile, Vitamin D3, and urine albumin creatinine ratio (UACR) for degree of albuminuria were also collected.

Newly diagnosed hypertension was defined as the average of two consecutive measurements with a 5 minutes gap on the dominant arm with patient sitting (feet touching the ground) and supine, with blood pressure (BP) apparatus at the level of heart, as per Joint National Committee VIII (JNC VIII) guidelines (systolic BP ≥140 mmHg and/or diastolic BP ≥90 mmHg). Before measuring the BP, it was ensured that the patient had taken rest for at least 10 minutes, and did not smoke, or had any tea/coffee, exercise, and other stimulants for at least 30 minutes beforehand. We used the BMI cut-offs as per the Asia-Pacific classification[13] and abdominal obesity, i.e., waist-hip ratio (WHR) cut-offs used were >0.90 in males and >0.85 in females. The cut-offs taken for Ankle Brachial Pressure Indices (ABPI) were given by Qasi *et al* in their study on Society for Vascular Technology's interpretation of resting ABPI measurements[14].

Statistical analysis

The data of all enrolled subjects was collected on a pre-designed proforma and entered in Microsoft Excel 2007 (Microsoft Corp, Redmond, WA) software spreadsheet. It was further cleaned and checked for any transcription errors. The results are presented as means, standard deviations, frequencies and percentages along with their 95% confidence intervals. The statistical software Epi Info version 7.2.6.0 (Centre for Disease Control (CDC), Atlanta, USA)[15]; was used for statistical analysis.

Results

A total of 70 patients were included in the study. Male subjects account for about two-third, i.e., 46 (65.7%) of the total study population. The mean (Standard deviation) age of the study participants was 58.4 (16.4) years. Maximum subjects, i.e., 30 (42.9%), were in the age group of 40 - 59 years. According to the Census 2011, in Himachal Pradesh, 10.03% of the population lived in urban areas while 89.9% lived in rural areas. Although this might have changed since the past 13 years due to increasing urbanisation, but this still may have an impact on the findings of our study population as we had majority of patients, i.e., 48 (68.6%) from rural areas. A family history of hypertension was present in nearly one-third, i.e., 25 (35.7%) of our study population. We found that 36 (51.4%) patients had a sedentary lifestyle or light activity levels. Only 13 (18.6%) had moderate to vigorous activity levels. Mixed diet was consumed by 38 (54.3%), disturbed sleep was present in 16 (2.9%), and alcohol use disorder was reported by 20 (8.6%), while 37.1% of the study participants were smokers. Most of the patients had neurological complaints 24 (34.3%) in the form of acute stroke, 23 (32.8%) presented with cardiovascular complaints such as symptoms of heart failure or myocardial infarction and 10 (14.3%) presented with respiratory symptoms. Surprisingly, 13 (18.6%) patients also presented with gastrointestinal complaints (Table I).

Majority of the patients, i.e., 41 (58.6%) presented with systolic blood pressure (SBP) 140 - 179 mmHg and surprisingly 29 (41.4%) directly arrived with a SBP of 180 mmHg or more. Diastolic blood pressure of most subjects (54.3%) was in the category 90 to 120 mmHg. Thirty six (51.4%) study subjects were found to be either overweight 15 (21.4%) or obese 21 (30%). Only eight (11.4%) had a normal WHR, while out of the remaining 89.6%, increased WHR was seen in 19 (27.2%) males and 43 (61.4%) females. On ECG, 14 (25.7%) had evidence of left ventricular hypertrophy (LVH), 10 (18.6%) had left axis deviation and only two patients had asymmetrical ST-T changes. Most subjects, i.e., 46 (65.7%) had a normal 2D ECHO, 17 (24.3%)

had mild-to-moderate left ventricular systolic dysfunction (LVSD), 6 (8.5%) had severe LVSD and only one patient had concentric LVH. Hypertensive retinopathy of grade I, II and III was present in 16 (22.9%), 11 (15.7%) and three (4.3%) participants, respectively. On chest X-rays, around 15 (21.4%) had cardiomegaly while two (2.9%) presented with fluid overload secondary to heart failure. The Ankle Brachial Pressure Indices (ABPI) detected in our study was normal in 55 (78.6%) participants. Eight (11.4%) study subjects had ABPI above 1.3, which was suggestive of calcification of arteries (Table II).

Laboratory investigations revealed deranged serum protein levels in 13 (18.6%), dyslipidaemia in almost half, i.e., 33 (47.1%), hypothyroidism in 10 (14.3%), deranged fasting plasma glucose level in 24 (34.3%), HbA1c in prediabetic range in 19 (27.1%) and in diabetic range in 16 (22.9%) of our subjects. Micro albuminuria was seen in 15 (21.4%) and macro albuminuria in six (8.6%) of our total study subjects (Table III).

Table I: Socio-demographic profile and presenting complaints of the study participants (N = 70).

Variable	Classification	n (%)
Gender	Male	46 (65.7)
	Female	24 (34.3)
Age Group	18 - 39 years	8 (11.4)
	40 - 59 years	30 (42.9)
	60 - 79 years	24 (34.3)
	80 years and above	8 (11.4)
Residence	Rural	48 (68.6)
	Urban	22 (31.4)
Family history of Hypertension	Absent	45 (64.3)
	Present	25 (35.7)
Level of Physical activity	Low	36 (51.4)
	Moderate	21 (30.0)
	Vigorous	13 (18.6)
Dietary History	Vegetarian	32 (45.7)
	Mixed	38 (54.3)
Sleep	Adequate	54 (77.1)
	Disturbed	16 (22.9)
Alcohol intake	No	50 (71.4)
	Yes	20 (28.6)
Smoking	No	44 (62.9)
	Yes	26 (37.1)
Presenting Complaints	Gastrointestinal	13 (18.6)
	Neurological	24 (34.3)
	Cardiovascular	23 (32.8)
	Respiratory	10 (14.3)

Table II: Clinical parameters and investigations of study participants (N = 70).

Investigation	Classification	n (%)
Systolic BP	≥140 - 179	41 (58.6)
(mmHg)	≥180	29 (41.4)
Diastolic BP	80 - 89	20 (28.6)
(mmHg)	>90 - 119	38 (54.3)
	≥120	12 (17.1)
BMI	Underweight (<18.5)	5 (7.1)
(Kg/m^2)	Normal (18.5 - 22.9)	29 (41.4)
	Overweight (23 - 26.9)	15 (21.4)
	Obese (≥27)	21 (30.0)
WHR	Normal (Both males and females)	8 (11.4)
	Females >0.85	43 (61.4)
	Males >0.90	19 (27.1)
ECG	Normal	44 (62.9)
	Left axis	10 (14.3)
	LVH	14 (20.0)
	ST-T changes	02 (2.9)
ECHO	Normal	46 (65.7)
	Mild-to-moderate LVSD	17 (24.3)
	Severe LVSD	6 (8.6)
	Concentric LVH	1 (1.4)
Fundoscopy	Normal	40 (57.1)
	Hypertensive Retinopathy Grade I	16 (22.9)
	Hypertensive Retinopathy Grade II	11 (15.7)
	Hypertensive Retinopathy Grade III	3 (4.3)
	Hypertensive Retinopathy Grade IV	0 (0)
Chest X-Ray	Normal	53 (75.7)
	Cardiomegaly	15 (21.4)
	Fluid Overload	2 (2.9)
Ankle Brachial	Likely normal (>1.3)	55 (78.6)
Pressure Indices	Probable calcification (1 to 1.3)	8 (11.4)
(ABPI)	Mild disease (0.9 - 1.0)	4 (5.7)
	Claudication (0.5 - 0.9)	3 (4.3)
	Severe occlusive disease or critical limb ischaemia (<0.5)	0 (0)

Table III: Lab Parameters of study participants (N = 70).

Lab parameter	Range	n (%)	95% CI
Haemoglobin (g/dL)	>12	52 (74.3)	62.4 - 84.0
	10-11.9	18 (25.7)	16.0 - 37.6
	<10	0 (0)	-
TLC (per microlitre)	<4,000	58 (82.9)	71.9 - 90.8
	4000 - 11000	02 (2.9)	0.4 - 9.9
	>11000	10 (14.3)	71. - 24.7
Platelet count (per micro litre)	<150000	61 (87.1)	76.9 - 93.9
	150000 - 300000	9 (12.9)	6.1 - 23.0
	>300000	0 (0)	-
hs-CRP (mg/dL)	<1	39 (55.7)	43.3 - 67.6
	1 - 3	10 (14.3)	7.1 - 24.7

	>3	21 (30.0)	19.6 - 42.1
RFT	Normal	54 (77.1)	-
	Deranged	16 (22.9)	-
Electrolytes	Normal	53 (75.7)	-
	Deranged	17 (24.3)	-
Calcium	Normal	38 (54.3)	-
	Deficiency	32 (45.7)	-
Phosphorus	Normal	59 (84.3)	-
	Hyperphosphataemia	11 (15.7)	-
Vit D3 (ng/dL)	≥ 20	27 (38.6)	21.2 - 50.9
	≤ 20	43 (61.4)	49.0 - 72.8
LFT	Normal	59 (84.3)	-
	Deranged	11 (15.7)	-
Serum Protein	Normal	57 (81.4)	-
	Deranged	13 (18.6)	-
Lipid Profile	Normal	37 (52.9)	-
	Deranged	33 (47.1)	-
Thyroid Profile	Normal	60 (85.7)	-
	Hypothyroidism	10 (14.3)	-
FPG	Normal	46 (65.7)	-
	Deranged	24 (34.3)	-
HbA1C (%)	<5.7	35 (50.0)	37.8 - 62.2
	5.7 - 6.4	19 (27.1)	17.2 - 39.1
	>6.4	16 (22.9)	13.7 - 34.5
Urine ACR	Normal	49 (70.0)	-
	Microalbuminuria	15 (21.4)	-
	Macroalbuminuria	06 (8.6)	-

Discussion

The mean (SD) age of our newly diagnosed hypertensive patients was 58.4 (16.4) years. Similar studies by Varghese *et al* and Kaur *et al* found that mean age was lower at 41.6 and 47 years respectively[16,17]. Our study found that the largest proportion of patients (42.9%) were in the age group of 40 - 59 years; similarly Pokkuluri *et al* in Telangana also found that 69.8% patients belonged to 30 - 60 years age group[18]. This implies that most of the population lying in this age group is negligent about their health and arrive in hospital due to development of complications secondary to newly diagnosed hypertension. Gender-wise distribution is suggestive of male dominance (65.7%) in newly diagnosed hypertensive patients. Contrary to this, Varghese *et al* found that females (52.6%) were more than males in their study[16]. Referring to the level of physical activity in our study subjects, 51.4% were sedentary or had low physical activity, i.e., they avoided any kind of exertion. A similar study in Telangana[18] found that 29.1% study subjects had no physical activity. These results highlight the association of hypertension with physical inactivity, indirectly suggesting the importance of physical activity in avoiding the development of hypertension. On enquiring about the patients' personal history, more than half, i.e., 54.3%, consumed mixed diet, nearly one fourth, i.e., 22.9% had disturbed sleep habit, 28.6% consumed alcohol and more than one third, i.e., 37.1% were smokers. Almost similar findings were seen by Pokkuluri *et al*[18]. These are suggestive of significant impact of one's personal choices on his/her predisposition to develop hypertension.

Most patients presented with neurological symptoms, primarily stroke (34.3%) and cardiovascular complaints, mainly myocardial infarction, and heart failure. Similar findings were seen by Vinayak *et al*[19] in South India. Contrary to this, Singh *et al*[20] in North India found headache (58%) and giddiness (44%) to be the commonest presenting complaints. We also found respiratory symptom, mainly dyspnoea in 14.3% patients, which was less than 20.5% seen by Vinayak *et al* (20.5%) in their study[18]. However, we saw gastrointestinal symptoms in 18.6% of our patients, which were not seen in both of the above studies[19,20].

41.4% of our study subjects presented with hypertensive crisis, which was lower than 66% found by Singh *et al*[20] in Haryana. Considering the BMI, a significant chunk of our patients, i.e., 51.4% were either overweight or obese. Moderate increases in BMI have been shown to be associated with diastolic hypertension in men[21]. Discussing about waist hip ratio, only 11.8% of the subjects had a normal waist hip ratio. Canada Fitness Survey data for people aged 20 to 69 years were analysed by White *et al* in 1986, in which they found waist hip ratio to be in close association in hypertensive men of age 40 - 59 years, and women of age 40 - 69 years[21].

Nearly one-fifth of our study participants (21.7%) were found to have left ventricular hypertrophy changes as diagnosed by the Sokolow Lyon criteria. In 2019, Cao *et al* studied ECG-LVH and cardiovascular disease (CVD) mortality. They found that ECG-LVH prevalence rates (2.40%, 4.45%, 5.75%, 8.51%, 14.38%) increased exponentially as systolic blood pressure increased from 120 to 160 mmHg in individuals with a positive family history of hypertension[22].

Nearly one third of patients, i.e., 30%, were found to have CRP levels in the high-risk range, highlighting the role of inflammation in the development of hypertension. Published literature has also shown that raised CRP levels are associated with development of hypertension[23,24]. RFT's were found to be deranged in about one fourth, i.e., 22.9% of our study subjects which is suggestive of either renal aetiology of hypertension or renal parameters derangement because of hypertension itself and this has also been corroborated in a study done by Adamczak *et al*[25]. Serum calcium levels were found to be deficient in 45.7% patients and even higher number of subjects (61.4%) had vitamin D deficiency. Siddiqee *et al* in their systematic review and

meta-analysis from five South Asian countries also found an overall 68% pooled prevalence of vitamin D deficiency. The highest prevalence of vitamin D deficiency was found in Pakistan (73%) followed by Bangladesh (67%), India (67%), Nepal (57%) and Sri Lanka (48%) respectively[26]. Contrary to this, another study[27] found a higher prevalence of vitamin D deficiency among school children in Himachal Pradesh. This can be explained by inadequate sun exposure due to work profile of study subjects.

Lipid profile was found to be deranged in nearly half (47.1%) of our study subjects implying that dyslipidaemia has a strong association with hypertension. Studies in United States and Taiwan have also concluded the same[28,29]. Both these studies also concur with our findings that prevalence of high blood pressure and mean levels of systolic and diastolic blood pressure increased as BMI increased. Effect of thyroid disorder was also studied in our subjects and only 14.3% were found to have hypothyroidism. This was contrary to findings of Åsvold *et al*[30] and Berta *et al*[31] which demonstrated that elevated diastolic and systolic blood pressure is present in around one-third of patients with overt hypothyroidism. Fasting plasma glucose was found to be deranged in nearly one third, i.e., 34.3% of our study participants. Prediabetic or diabetic range of HbA1c was found in 50% of the subjects. A significant proportion of the population is unaware of their diabetic status and is aware of it once incidentally newly diagnosed with hypertension. Alderman *et al*[32] found an even higher percentage with 54% having elevated baseline plasma glucose, giving no history of diabetes. Urine ACR is an indicator of relative speed of progression to chronic kidney disease. Glomerular hyperfiltration initiates a cycle of progressive increases in intraglomerular pressure and repetitive renal injury. In our study, 21.4% of our patients were found to have macroalbuminuria and 8.6% had microalbuminuria. Wang *et al* in their study have also supported the premise that microalbuminuria is an early finding in individuals with a predisposition to hypertension[33].

Conclusion

This study results highlight the fact that one or more co-morbidities like diabetes mellitus, dyslipidaemia, hypothyroidism etc., may exist in patients newly diagnosed with hypertension, suggesting that multifactorial interplay leads to the development of cardiovascular disease in these patients. A large proportion of the population presented with sequelae of hypertension like stroke, heart failure, renal failure and myocardial infarction showing that they were unaware of their hypertension status or did not know about its complications. They came to know about these co-morbidities or complications incidentally when work up was done for hypertension.

The study reinforces the importance of making the population aware about hypertension and holding regular screening camps in rural as well as urban areas so that we can diagnose hypertension and intervene at a point where permanent damage has not been done. Early intervention and treatment offer a chance to alter the natural history of the disease, permit more effective treatment and thus help in reducing the morbidity and mortality from the disease.

Ethical considerations

The study ensured that ethical considerations were met by obtaining approval from the Institutional Ethics Committee of Indira Gandhi Medical College Shimla, Himachal Pradesh vide their letter no. IEC/IGMC/83/2023-24, dated 9th June 2023. Before enrollment, written and informed consent was taken for the study from each participant. Privacy and confidentiality of all the study participants were maintained as per the ethical principles for medical research involving human subjects as mentioned in the Indian Council of Medical Research (ICMR) as well as those in the Declaration of Helsinki guidelines.

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ORIGINAL ARTICLE

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Clinical Profile and Outcomes of Patients of Decompensated Chronic Liver Disease

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Abstract

Background: Decompensated chronic liver disease (DCLD) is a major cause of morbidity and mortality worldwide, with a significant burden in India. Understanding its clinical profile, aetiological spectrum, and mortality predictors is essential for improving the outcomes.

Methods: A prospective, observational study was conducted among 150 adults admitted with DCLD over 18 months. Demographic data, clinical features, laboratory parameters, and radiological findings were documented. Disease severity was classified using the Child-Pugh scoring system. In-hospital mortality was the primary outcome.

Results: The majority of patients were aged 41 - 50 years (51.3%) with male predominance (74.7%). Alcohol-related liver disease was the leading aetiology (44.7%), followed by hepatitis B (28.7%), hepatitis C (12.7%), and non-alcoholic fatty liver disease (9.3%). Most patients had Child-Pugh Class B (55.3%) or C (44.7%). Common presentations included moderate ascites (72%), jaundice (60.7%), splenomegaly (50.7%), and hepatic encephalopathy (39.4%). In-hospital mortality was 20.7%, significantly higher in Child-Pugh Class C (90.3%) versus Class B (9.7%, p <0.001). Mortality was highest in alcohol-related CLD (48.4%) but showed no significant association with aetiology (p = 0.763).

Conclusion: DCLD predominantly affects middle-aged males, with alcohol and hepatitis B virus as major aetiologies. Advanced disease (Child-Pugh Class C) strongly predicts in-hospital mortality, highlighting the need for early detection and intervention.

Key words: Decompensated chronic liver disease, alcohol-related liver disease, Hepatitis B, Hepatitis C, Child-Pugh class, in-hospital mortality.

Introduction

Decompensated chronic liver disease (DCLD) represents the advanced stage of chronic liver injury, characterised by complications including ascites, hepatic encephalopathy, variceal bleeding, and jaundice[1,2]. Decompensation is associated with increased morbidity and mortality[3].

Globally and in India, chronic liver disease remains a major public health concern. Indian hospital-based studies have consistently demonstrated that patients often present late[4]. Alcohol-related liver disease remains the predominant cause of cirrhosis and decompensation in most parts of India, reflecting rising alcohol consumption patterns[5,6]. Chronic viral hepatitis, particularly hepatitis B virus (HBV) and hepatitis C virus (HCV) infection, continues to contribute substantially to the disease burden, despite the availability of effective antiviral therapies[7].

Metabolic dysfunction-associated steatotic liver disease (MASLD) has emerged as an increasingly important aetiology of chronic liver disease in India, driven by the growing prevalence of obesity, diabetes mellitus, and metabolic syndrome[8]. Although MASLD-related cirrhosis constitutes a smaller proportion of hospitalised DCLD cases, its contribution is expected to rise in the coming years. Patients with DCLD frequently present with complications such as ascites, jaundice, upper gastrointestinal bleeding, infections, renal dysfunction, and hepatic encephalopathy, all of which adversely affect short-term outcomes[9].

Disease severity at presentation is a critical determinant of outcome in DCLD. Prognostic scoring systems such as the Child-Pugh classification are widely used to stratify disease severity and predict mortality. Multiple studies have demonstrated a strong association between higher Child-Pugh class and increased in-hospital and short-term mortality among patients with decompensated cirrhosis[10,11].

Data describing the clinico-etiological profile and short-term outcomes of DCLD patients from Central India remain limited. Given regional variations in aetiology and healthcare access, understanding local disease patterns is essential for improving patient management. The present study was therefore undertaken to evaluate the clinical profile,

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aetiological spectrum, and in-hospital outcomes of patients with decompensated chronic liver disease admitted to a tertiary care center in Central India, with particular emphasis on the relationship between disease severity and in-hospital mortality.

Material and Methods

This prospective, observational study was carried-out at the Department of Medicine at a tertiary care centre in Central India. The study was conducted over an 18-month period, from July 2023 to December 2024. The study protocol was approved by the Institutional Ethics and Scientific Committee, and all participants provided written informed consent in their native language.

A total of 150 patients admitted to the medical wards with a diagnosis of decompensated chronic liver disease (DCLD) were enrolled based on specific inclusion and exclusion criteria. The study included patients who were 18 years or older, had a confirmed diagnosis of DCLD, and were willing to provide informed consent. Patients under the age of 18, pregnant females, those with hepatocellular carcinoma or other malignancies, and individuals who declined to participate were excluded from the study.

Data collection involved a comprehensive evaluation of each participant upon admission. Demographic data such as age, sex, occupation, and place of residence were recorded. A detailed clinical history was taken to document presenting symptoms like jaundice, abdominal distension, gastrointestinal (GI) bleeding, and altered sensorium, along with risk factors such as alcohol use, intravenous drug use, and a history of blood transfusions. A thorough general and systemic examination was also performed, including the recording of vital signs and a detailed examination of the gastrointestinal, cardiovascular, respiratory, and central nervous systems.

Baseline laboratory and radiological investigations were conducted to support the clinical evaluation. Haematological tests included a complete blood count (CBC), Erythrocyte Sedimentation Rate (ESR), and C-Reactive Protein (CRP). Liver function was assessed through serum bilirubin, SGOT, SGPT, ALP, total protein, and albumin, while renal function was evaluated using blood urea and serum creatinine. Other key tests included serum electrolytes, urinary albumin, lipid profile, and PT/INR. Serological markers for Hepatitis B (HBsAg) and Hepatitis C (Anti-HCV) were also analysed. Radiological investigations included an abdominal ultrasound and a chest X-ray. For relevant cases, ascitic fluid was analysed to determine its nature and rule-out infection.

The prognosis and severity of the disease were assessed using the Child-Pugh scoring system, which integrated five key parameters: serum bilirubin, serum albumin, INR, and the presence of ascites and hepatic encephalopathy. The primary outcome measured was in-hospital mortality. Other outcomes assessed included the length of hospital stay, clinical improvement or deterioration, and the need for ICU admission or ventilatory support.

For statistical analysis, all collected data were tabulated in a master chart using Microsoft Excel. The analysis was performed using SPSS version 27.0. Quantitative variables were presented as mean ± standard deviation, while qualitative variables were summarised as frequencies and percentages. Appropriate statistical tests, including the chi-square test, were used to determine the significance of associations, with a p-value of less than 0.05 considered statistically significant.

Results

A total of 150 patients with chronic liver disease (CLD) were analysed to assess clinical profiles, aetiologies, and their association with in-hospital outcomes. The study population predominantly comprised Child-Pugh class B and C cases, with a notable proportion presenting with complications such as ascites and hepatic encephalopathy. Mortality patterns, aetiological distribution, and correlations with clinical severity were evaluated using appropriate statistical tests.

Table I: Baseline demographic, clinical, and laboratory characteristics of the study population (N = 150).

Age Group (years)	Frequency (n)	Percentage (%)
≤ 20	1	0.7
21 - 30	6	4
31 - 40	16	10.7
41 - 50	77	51.3
51 - 60	40	26.7
>60	10	6.7
Gender		
Female	38	25.3
Male	112	74.7
Co-morbid Conditions		
Absent	107	71.3
Hypertension	34	22.7
Diabetes Mellitus	22	14.7
Obesity	11	7.3
Hyperlipidaemia	6	4
History of Alcohol Consumption		

Absent	73	48.7
Present	77	51.3
H/O Blood Transfusion/ IV Drug Abuse/ High Risk Behaviour		
Absent	92	61.3
Blood Transfusion	41	27.3
High-Risk Occupation	8	5.3
IV Drug Abuse	5	3.3
IV Drug Abuse and Blood Transfusion	3	2
Present (unspecified high-risk behaviour)	1	0.7
HBsAg Status		
Non-reactive	106	70.7
Reactive	44	29.3
HCV Status		
Non-reactive	131	87.3
Reactive	19	12.7
Ascites		
Mild Ascites	5	3.3
Moderate Ascites	108	72
Gross Ascites	37	24.7
Splenomegaly		
Absent	74	49.3
Present	76	50.7
Jaundice		
Absent	59	39.3
Present	91	60.7
Upper GI Bleed		
Absent	86	57.3
Present	64	42.7
Encephalopathy		
Absent	91	60.7
Minimal	28	18.7
Advanced	31	20.7
Laboratory parameters	**Mean**	**Std. Deviation**
Haemoglobin (g/dL)	9.26	1.97
TLC (/µL)	10,318.05	4,511.32
Platelets (L/µL)	1.65	0.87
RBS (mg/dL)	143.55	51.37
Urea (mg/dL)	65.67	36.14
Creatinine (mg/dL)	1.51	0.86
PT (sec)	26.11	10.98
INR	1.74	0.34
Total Bilirubin (mg/dL)	5.14	10.15
Direct Bilirubin (mg/dL)	2.01	1.46
SGOT (U/L)	117.84	64.91
SGPT (U/L)	99.04	60.98
ALP (U/L)	149.48	84.72
Total Protein (g/dL)	5.7	0.73
Albumin (g/dL)	2.49	0.42
Serum Sodium (mmol/L)	133.74	5.73
Serum Potassium (mmol/L)	4.42	0.58

Table I summarises the baseline demographic, clinical, and laboratory characteristics of 150 patients with chronic liver disease (CLD). The majority of patients were aged 41 - 50 years (51.3%), with a male predominance (74.7%). Hypertension (22.7%) and diabetes mellitus (14.7%) were the most common co-morbidities. A history of alcohol consumption was present in 51.3% of cases, while 27.3% had a history of blood transfusion. Hepatitis B surface antigen (HBsAg) was reactive in 29.3% of patients, and hepatitis C virus (HCV) infection was reactive in 12.7%. Moderate ascites was the most frequent presentation (72%), with splenomegaly present in 50.7% and jaundice in 60.7%. Upper gastrointestinal (GI) bleed was observed in 42.7%, and hepatic encephalopathy in varying degrees was seen in 39.4% of patients (18.7% minimal, 20.7% advanced).

Laboratory investigations revealed anaemia (mean haemoglobin 9.26 ± 1.97 g/dL), thrombocytopenia (mean platelet count 1.65 ± 0.87 L/µL), elevated liver enzymes (SGOT 117.84 ± 64.91 U/L, SGPT 99.04 ± 60.98 U/L), hyperbilirubinaemia (mean total bilirubin 5.14 ± 10.15 mg/dL), hypoalbuminaemia (2.49 ± 0.42 g/dL), and hyponatraemia (mean sodium 133.74 ± 5.73 mmol/L).

Table II: Distribution of patients by aetiology, Child-Pugh class, and clinical outcome in chronic liver disease (N = 150).

Child-Pugh Class	Frequency (n)	Percentage (%)
A	0	0
B	83	55.3
C	67	44.7
Aetiology for CLD		
Autoimmune Hepatitis	5	3.3
HBV-Related	43	28.7
HCV-Related	19	12.7
Alcohol-Related	67	44.7
Wilson's Disease	1	0.7
Budd-Chiari Syndrome	1	0.7
MASLD Associated	14	9.3

Outcome		
Discharge	119	79.3
Death	31	20.7

More than half of the patients were classified as Child-Pugh Class B (55.3%), while 44.7% were in Class C; no patients belonged to Class A. Alcohol-related liver disease was the most common aetiology (44.7%), followed by HBV (28.7%) and HCV (12.7%). MASLD (9.3%) and autoimmune hepatitis (3.3%) contributed to a smaller proportion, whereas Wilson's disease and Budd-Chiari syndrome each accounted for 0.7%. The majority of patients (79.3%) were discharged, while 20.7% succumbed to the disease (Table II).

Table III: Association between Child-Pugh class and in-hospital mortality (N = 150).

Child-Pugh Class	Death n (%)	Discharge n (%)	Total n (%)	p value
A	0 (0.0)	0 (0.0)	0 (0.0)	**<0.001**
B	3 (9.7)	80 (67.2)	83 (55.3)	
C	28 (90.3)	39 (32.8)	67 (44.7)	
Total	31 (100)	119 (100)	150 (100)	

In-hospital mortality was significantly higher among patients with Child-Pugh Class C (90.3%) compared to Class B (9.7%), while no deaths occurred in Class A. The association between Child-Pugh class and mortality was statistically significant (p <0.001) (Table III).

Table IV: Association between aetiology of chronic liver disease and in-hospital outcome (N = 150).

Aetiology of CLD	Death n (%)	Discharge n (%)	Total n (%)	p value
Alcohol Related	15 (48.4)	52 (43.7)	67 (44.7)	0.763
Autoimmune Hepatitis	1 (3.2)	4 (3.4)	5 (3.3)	
Budd-Chiari Syndrome	0 (0.0)	1 (0.8)	1 (0.7)	
HBV-Related	7 (22.6)	36 (30.3)	43 (28.7)	
HCV-Related	3 (9.7)	16 (13.4)	19 (12.7)	
MASLD-Associated	5 (16.1)	9 (7.6)	14 (9.3)	
Wilson's Disease	0 (0.0)	1 (0.8)	1 (0.7)	
Total	31 (100)	119 (100)	150 (100)	

Alcohol-related CLD (44.7%) and HBV-related CLD (28.7%) were the most common aetiologies among the study participants. Mortality was highest in alcohol-related CLD (48.4%), followed by HBV-related (22.6%) and MASLD-associated cases (16.1%). However, the association between aetiology and in-hospital outcome was not statistically significant (p = 0.763) (Table IV).

Discussion

The present study evaluated the clinico-aetiological profile and in-hospital outcomes of 150 patients with decompensated chronic liver disease admitted to a tertiary care center in Central India. The majority of patients were middle-aged, with peak incidence in the 41 - 50 year age group, and a marked male predominance. Similar age and sex distributions have been reported in earlier Indian studies, highlighting that DCLD predominantly affects males in their economically productive years[4,5].

Alcohol-related liver disease was the most common aetiology in the present cohort, accounting for nearly half of all cases, followed by HBV- and HCV-related chronic liver disease. This aetiological pattern closely mirrors findings from other Indian hospital-based studies, where alcohol has consistently emerged as the leading cause of cirrhosis and decompensation[6,7]. MASLD constituted a smaller but significant proportion of cases, reflecting the rising burden of metabolic liver disease in India[8].

Ascites was the most frequent clinical manifestation observed in this study, followed by jaundice, splenomegaly, upper gastrointestinal bleeding, and hepatic encephalopathy. Similar clinical profiles have been documented in previous studies, underscoring the central role of portal hypertension and reduced hepatic reserve in the pathophysiology of decompensated cirrhosis[9].

In-hospital mortality in the present study was 20.7%, which is comparable to mortality rates reported in other Indian and Asian studies of hospitalised DCLD patients[10]. Mortality was significantly higher among patients with Child-Pugh Class C disease compared to those with Class B disease, reaffirming the prognostic value of the Child-Pugh classification in predicting short-term outcomes. Similar associations between advanced Child-Pugh class and increased mortality have been consistently demonstrated in earlier studies[11].

Although mortality was numerically higher among patients with alcohol-related liver disease, no statistically significant association was observed between aetiology and in-hospital outcome. This finding suggests that disease severity at presentation, rather than underlying aetiology alone, plays a more decisive role in determining short-term prognosis[11].

The findings of this study emphasize the ongoing burden of alcohol- and viral hepatitis-related liver disease in Central India and highlight the importance of early diagnosis, aetiological treatment, and timely referral before the onset of advanced decompensation. Public health strategies focusing on alcohol moderation, viral hepatitis screening and treatment, and metabolic risk factor control are essential to reduce progression to decompensated cirrhosis and improve patient outcomes.

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ORIGINAL ARTICLE

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Aetiological Spectrum of Hospital-Acquired Hypernatraemia

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Abstract

***Background:** In critically ill, hospitalised patients, hypernatraemia has been an independent predictor of mortality. Hospital acquired hypernatraemia (HAH) is a frequently overlooked entity and knowledge of common risk factors for hypernatraemia can help early identification of HAH and fluid management to be modified accordingly.*

***Methods:** This cross-sectional, observational study enrolled 100 adult patients who developed hypernatraemia (Na^+ >145 mEq/L) after 48 hours of admission. Amount of enteral feed, its mode of administration and net tonicity of intravenous (IV) fluids were calculated. Administration of sodium containing drugs were recorded. Factors leading to renal and extrarenal free water loss were assessed. Patients were classified as having mild hypernatraemia (146 - 149 meq/L), moderate (150 - 159 meq/L) and severe hypernatraemia (>160 meq/L). The assessment of risk factors in patients with mild (Group I) vs moderate + severe hypernatraemia (Group II) were done.*

***Results:** The mean age of the study cohort was 52.83 ± 16.9 years with M: F ratio of 3.34. Hypertension was the most common co-morbidity (23%) with neurological diseases (40%) being the most common reason for hospital admission. 42% patients developed hypernatraemia on day 3, 36% on day 4 and 22% after 5 days. The mean serum sodium levels were 150.97 ± 4.88 mEq/L. 51% had mild hypernatraemia, 42% had moderate and 7% had severe hypernatraemia. Among the various causes of hypernatraemia, hypertonic fluids and sodium containing drugs contributed in 63% and 75% of patients respectively. Extrarenal water loss and factors with potential to cause renal water loss were observed in 51% and 43% of patients respectively. 78% of patients did not have free access to water.*

***Conclusion:** HAH is multifactorial and a close vigilance on various risk factors can aid in risk stratification and institution of prompt measures to prevent hypernatraemia and improve quality of health care.*

***Key words:** Hypernatraemia, Osmolality, intravenous fluids, drugs.*

Introduction

Sodium and water disorders are frequently seen in critically ill, hospitalised patients with hypernatraemia as an independent predictor of mortality[1]. It has been classified as community or hospital acquired hypernatraemia (CAH or HAH) with HAH defined as serum sodium concentration above 145 mEq/L occurring during hospitalisation among patients having normal serum sodium on admission[2]. The reported prevalence of HAH varies from 1 - 6% which is higher than reported for CAH (0.2%) stressing an iatrogenic component in its evolution[3-7].

In critically ill, hospitalised patients, hypernatraemia develops because of gain of sodium, due to loss of free water from the body or from combination of both. Gain of sodium usually occurs due to administration of hypertonic intravenous fluids, sodium containing drugs. Secondly, loss of free water from body can occur due to renal or extrarenal causes contributing to hypernatraemia. Renal free water loss may be accounted by various factors, viz., diabetes insipidus, hyperglycaemia, use of loop diuretics or mannitol whereas extrarenal free water loss can occur via several routes viz., enteral fluid loss (diarrhoea/vomiting) or increased insensible water losses (sweat or respiratory losses as seen during fever or mechanical ventilation respectively)[8]. Thirst is a protective mechanism against development of hypernatraemia which is often supressed or rendered ineffective by inadequate access to free water owing to underlying medical condition viz., cerebrovascular accidents, acute pancreatitis, etc.

HAH is frequently overlooked by treating physicians amidst management of more urgent medical issues of patients. The knowledge of common clinical risk factors for hypernatraemia can help identifying HAH early and fluid management to be modified accordingly. Literature is limited on this topic from this part of world and moreover had shown varied factors in different settings; so with this study, we planned to explore the aetiological causes of HAH at our tertiary care centre.

Material and Methods

The study was a cross-sectional, observational study carried out at the Department of Medicine, Pt. B.D. Sharma

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PGIMS, Rohtak from November 2023 to October 2024 and a total of 100 adult patients who developed hypernatraemia (Na^+ >145 mEq/L) after 48 hours of admission were included in the study. The demographic profile and relevant clinical details including day on which hypernatraemia developed after hospitalisation, clinical diagnosis and presence of other co-morbidities were noted. Serum sodium levels were estimated using ion selective electrodes. Normal serum osmolality was taken between 280 to 295 mOsm/kg[9]. Amount of enteral feed and its mode of administration (Ryles tube or oral) was noted. Net tonicity of the parenteral fluids administered over prior 48 hours was calculated after dividing total number of osmoles infused by total volume of fluid administered. Concomitant potassium chloride administration was also considered for calculating tonicity of fluids. Administration of commonly used sodium containing drugs, viz., antibiotics (Ampicillin, Amoxycillin/clavulanic acid, Piperacillin, Ceftriaxone, Cefazolin, Ceftazidime, Ciprofloxacin), antifungals (Fluconazole, Voriconazole, Foscarnet), antiepileptics (Sodium Valproate, Phenytoin) and sodium bicarbonate (injection or tablets) over the 48 hours preceding the development of hypernatraemia were recorded. Extrarenal free water loss due to diarrhoea (stools of loose consistency with frequency more than 4 times daily), vomiting, fever (oral temp >38^0 C) was assessed. Factors leading to renal free water loss (glycosuria, mannitol, loop diuretics) in 48 hours preceding the development of hypernatraemia were recorded. Daily urine output of the patients was recorded. Polyuria was defined as 24-hour urine volume exceeding 3 L/day[9]. The Study was approved by the institutional Ethical Committee vide letter no BREC/23/TH-Medicine-13 dt 05.10.2023.

Definitions

Hypernatraemia: Patients with serum sodium levels of > 145 meq/L were diagnosed to have hypernatraemia and were further divided into three subgroups having mild (145 - 149 meq/L), moderate (150 - 159 meq/L) and severe (>160 meq/L) hypernatraemia[10].

Tonicity of Fluids: Intravenous fluids administered in 48 hours preceding the development of hypernatraemia were classified based on calculated net tonicity (Hypertonic: >/300/mOsmol/kg; Isotonic: 280 - 300/mOsmol/kg; Hypotonic </280/mOsmol/kg).

Statistical analysis

The data was recorded in predesigned proformas. The data entry was done in Microsoft Excel for windows and data analysis was done using Quickcals (GraphPad Software; San Diago, CA). The presentation of categorical variables was done in the form of number and percentage (%). For the quantitative data, the normally distributed variables were expressed as mean ± standard deviation (SD) and the continuous variables with skewed distribution as median (interquartile range).

Results

Demographic Profile of Patients (n=100)

The study participants age ranged between 18 to 86 years. The mean age of the cohort was 52.83 ± 16.9 years with male: female ratio of 3.34. Hypertension was the most common co-morbidity (23%) with neurological diseases (40%) being the most common reason for hospital admission. 42% patients developed hypernatraemia on day 3 as compared to 36% on day 4 and 22% developing hypernatraemia after 5 days of hospital stay. The trends have been shown in Table I.

Table I: Baseline parameters and time to develop hypernatraemia in patients.

Parameters	N = 100
Age (Mean + SD)	52.83 ± 16.9 years
Gender (M: F)	3.34
Co-morbidities	
Hypertension	23
Chronic liver disease	11
Diabetes mellitus	11
Neurological diseases	9
Chronic kidney disease	7
Pulmonary diseases	6
Cardiovascular diseases	4
Others	7
Multiple comorbidities	18
Reason for Admission	
Neurological disease	40
Gastrointestinal tract and Liver disease	23
Respiratory disease	10
Renal disease	6
Cardiovascular disease	3
Others	18
Time of Onset of Hypernatraemia (Days)	
3	42
4	36
>5	22

Serum electrolytes in study population

The serum sodium levels ranged 146 - 168 mEq/L with a mean value of serum sodium level being 150.97 ± 4.88 mEq/L. Fifty one patients had mild hypernatraemia, 42 had moderate and 7 had severe hypernatraemia as shown in Table II, (Fig. 1a and 1b).

Table II: Grades of hypernatraemia.

Grades of Hypernatraemia	No. of Subjects (100)
Mild hypernatraemia (146 - 149 meq/L)	51
Moderate hypernatremia (150 - 159 meq/L)	42
Severe hypernatremia (>160 meq/L)	7

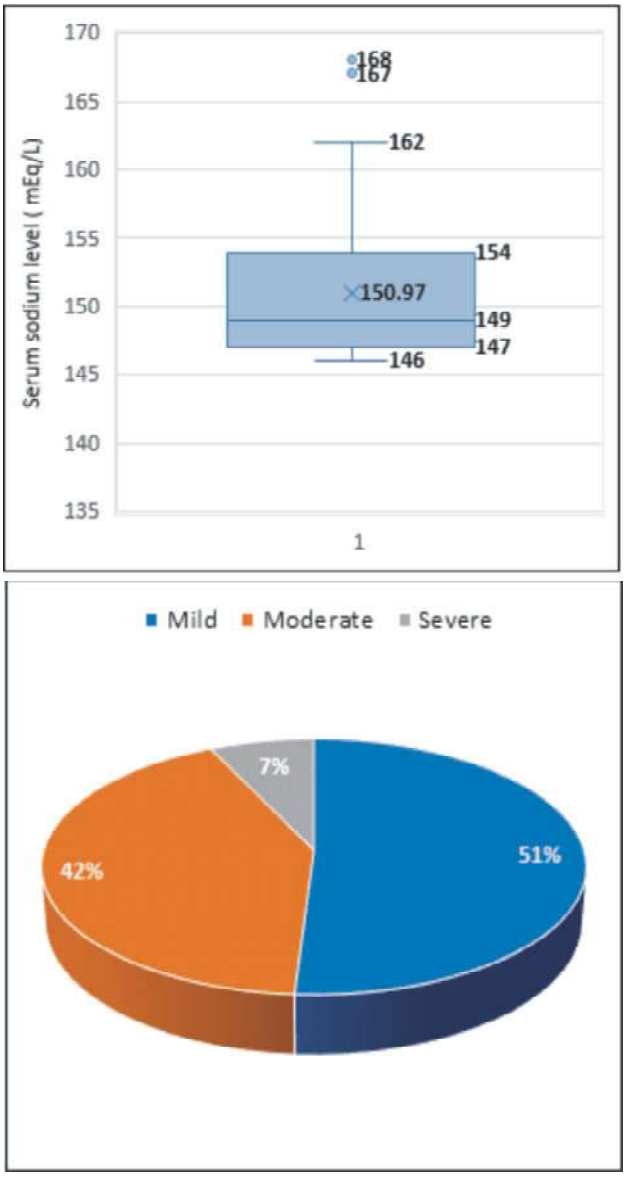

Fig. 1a, 1b: *Serum sodium levels in patients.*

Risk factors for hospital acquired hypernatraemia (HAH) in study population

Hypertonic IV fluids and sodium containing drugs were used in 63% and 75% of patients respectively. Extrarenal water loss and factors with potential to cause renal water loss as risks were observed in 51% and 43% of patients respectively. 78% of patients did not have free access to water as shown in Table III.

Table III: Risk factors for HAH.

IV Fluids	100
Hypertonic (>300 mOsm/kg)	63
Isotonic (280 - 300 mOsm/kg)	19
Hypotonic (<280 mOsm/kg)	16
No IV fluids	02
Sodium Containing Drug	75
Antibiotics	68
Antiepileptics	15
Sodium bicarbonate	13
More than one sodium containing drug	21
Extra renal Water Loss	51
Fever	41
Gastrointestinal tract loss	18
Diarrhoea	11
Vomiting	7
>1 factor	8
Factors having potential to cause renal water loss	43
Mannitol	20
Loop diuretic	18
Glucose	10
Diabetes insipidus	0
More than one factor	5
Free access to water	100
Yes	22
No	78

Risk factors among different grades of hypernatraemia

Fifty one patients had mild hypernatraemia and 49 patients had moderate to severe hypernatraemia. Presence of various risk factors among different subgroups has been shown in Table IV, (Fig. 2).

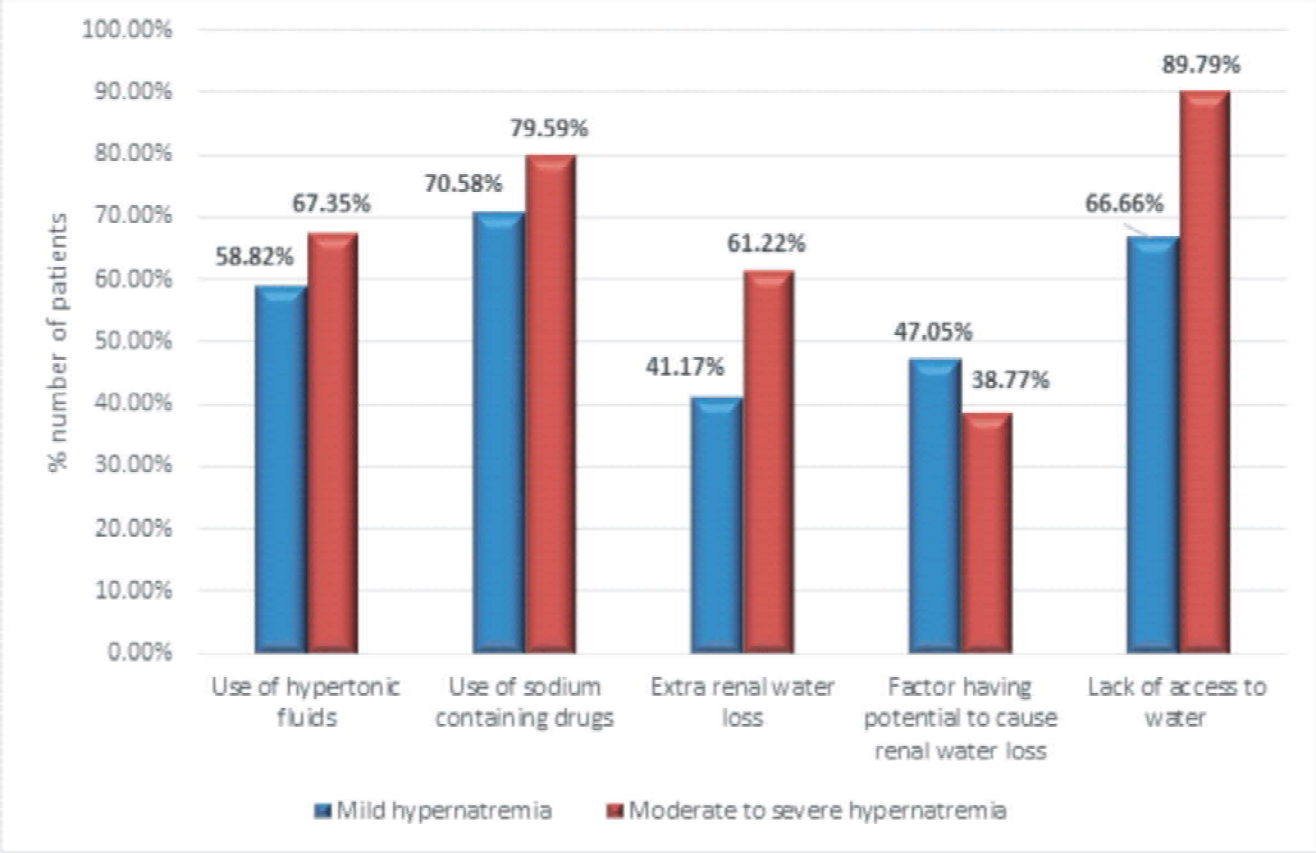

Fig. 2: *Various risk factors among different grades of hypernatraemia.*

Table IV: Risk factors among different grades of hypernatraemia

Risk Factor	Mild Hypernatraemia (n = 51)	Moderate + Severe Hypernatraemia (n = 49)
Use of hypertonic fluids	30 (58.82%)	33 (67.35%)
Use of sodium containing drugs	36 (70.58%)	39 (79.59%)
Extra renal water loss	21 (41.17%)	30 (61.22%)
Factors with potential to cause renal water loss	24 (47.05%)	19 (38.77%)
Lack of access to water	34 (66.66%)	44 (89.79%)

Discussion

Hypernatraemia in critically ill hospitalised patients has a high mortality rate than patients with normal sodium levels (43% *versus* 24%)[11]. Plasma sodium level reflects ratio of sodium and water in the body with hypernatraemia being actually an indicator of relative deficiency of free water compared to sodium[12]. As many critically ill patients have impaired level of consciousness, their water balance is no longer regulated by thirst but is ill-managed, often by the physician or caretaker, leading to iatrogenic hypernatraemia. Attention to risk factors associated with development of HAH has the potential to prevent its occurrence, decrease mortality rates and improve quality of healthcare. With this study, we tried to explore various clinical risk factors for development of HAH.

The average age of patients was 52.8 ± 16.9 years with a male predominance. More than half of the patients (57%) had pre-existing chronic medical illness. The reason for hospitalisation, organ system involvement showed wide diversity, with predominance of neurologic diseases (40%). The mean duration of hospital stay before the onset of hypernatraemia was 4.27 ± 1.83 days. These observations get strength from other study showing average onset of hypernatraemia on day 5.9 ± 4.3 of ICU stay with almost all patients requiring 2 days to develop hypernatraemia[8].

The mean value of serum sodium level was 150.97 ± 4.88 mEq/L. About half of the study participants (51%) had mild hypernatraemia and this finding can be accounted by the fact that fluid management is a dynamic and ongoing process rather than being a single intervention. We hypothesize that the treating physicians increased the number of hypotonic fluids after looking at the trends of serum sodium thereby preventing the development of moderate-to-severe hypernatraemia but the amount was

not sufficient for the prevention of mild hypernatraemia.

Intravenous fluids were given to 98% of patients with use of hypertonic IV fluids in 63% patients, which is much higher than reported from another study using IV hypertonic solutions in only 27% patients preceding the onset of hypernatraemia[8]. Normal saline and dextrose normal saline (DNS) were the predominant fluids used (osmolality of 308 mOsmol/kg), thus making them hypertonic as compared to normal serum osmolality of 280 - 295 mOsmol/kg[9,10,12]. Further potentiating HAH was the use of potassium chloride, which was added to intravenous fluids in 38% of patients to correct either hypokalaemia or to meet daily requirement. Addition of potassium chloride to intravenous fluids increased the osmolality of intravenous fluids resulting in osmolality of IV fluids in hypertonic range in 86.8% patients. Previous studies had also reported increased tonicity of IV fluids with addition of potassium[8,14], further highlighting importance of potassium as iatrogenic cause of HAH.

75% patients were given sodium containing drugs which included antibiotics (68%), antiepileptics (15%) and sodium bicarbonate (13%). Since the list of sodium containing drugs is vast and moreover it is difficult to quantify sodium content of these drugs; we could not find any study deciphering the exact role of this class of drugs in causation of HAH. However, causation of HAH with use of sodium bicarbonate has been studied earlier with usage ranging from 12.5 - 18% of patients prior to the onset of hypernatraemia[8,15,16]. The use of sodium bicarbonate was in 13% of patients in our study.

Extrarenal water losses prior to development of hypernatraemia were observed in 51% patients. Fever was recorded in 41% while increased gastrointestinal tract fluid losses were seen in 18%. These findings were similar to a study reporting fever in 56% and enteral losses in 40% patients developing HAH[17]. An interesting fact was that in 4% of cases, diarrhoea was caused by overzealous use of lactulose in hepatic encephalopathy patients and we emphasize on its judicious use to cause only 3 - 4 semisolid stools per day as described earlier in a study[18].

Average urine output was 1001.3 ± 394.87 ml in the study population. None of the patients had polyuria, which is in sharp contrast to a previous study reporting polyuria in 38% patients (diuretics in 50%, osmotic diuresis in 30% and diabetes insipidus in 20%)[8]. In our study, none of the patients had diabetes insipidus. Loop diuretics were used in 18%, mannitol in 20% and 10% patients had glycosuria. Loop diuretics have been shown to cause defect in urine concentrating abilities of kidneys during hypernatraemia, however as we did not quantify urine osmolality in our study, so we cannot compare our findings with previous data. However, we stress that daily assessment of water balance in hospitalised ill patients is crucial. Urine electrolyte free water should be calculated and added to daily fluid requirement of patients to replenish free water loss, especially in patients receiving diuretics and mannitol to prevent hypernatraemia.

Enteral feeding was present in 62% patients and 38% patients had no enteral intake. Liquid feed was given to patients either orally or through Ryles tube. The average enteral intake in these patients was 424.75 mL and 88.7 % of these patients received enteral feed below 1000 mL. The details on tonicity of enteral feed were not recorded, so the current study cannot make comment on free water intake via enteral feed.

78% of patients in this study cohort lacked free access to water. Thirst is a powerful protective mechanism against hypernatraemia and lack of access to water might have contributed to the development of hypernatraemia in these patients[19]. Palevsky *et al* reported lack of access in 86% of patients having hospital acquired hypernatraemia[17]. In our study, the reason behind lack of free access to water was either impaired thirst perception due to altered mental status or prohibited enteral feeding due to enteral diseases. All patients with GCS score below 15 lacked free access to water which highlights the tendency of treating physicians to preclude oral intake in critically ill patients with possible high-risk of aspiration, serious illness or sepsis[12]. Further complicating the scenario, out of 22 patients who had free access to water, only 5 patients had enteral intake above 1000 mL which might be attributed to loss of appetite and nausea from illness or medications side effects. The current study highlights the early recognition of at-risk patients (patients with low GCS) and appropriate free water administration to be made an integral part of comprehensive continuum of care for critically ill patients.

The study had some inherent limitations. It was an observational study, hence causative association of risk factors with development of hypernatraemia cannot be established concretely. Due to lack of standardisation of enteral feed, only amount of enteral feed was evaluated and free water content of feed cannot be commented. Since renal concentrating defect (urine osmolality) was not assessed, only the presence of risk factors which can cause renal free water loss were recorded and their contribution to HAH cannot be comment upon concretely.

In conclusion, we stress that clinicians need to consider ongoing hypotonic fluid loss from renal or extrarenal route, judicious use of sodium containing drugs and appropriate amount of electrolyte free water to prevent development of hypernatraemia. Moreover, oral intake in critically ill patients should be encouraged and iatrogenic suppression

of protective thirst mechanisms needs to be avoided. In resource-limited hospital settings where daily calculation of tonicity balances in all patients is not possible, knowledge of these clinical factors can aid in risk stratification and treatment planning to prevent hypernatraemia and improve quality of healthcare.

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Impact of A Communication Skills Module for First Year Medical Residents

Kothai Gnanamoorthy, Prasanna Karthik Suthakaran**, Jagadeesan Mohanan**, Mahendrakumar Kalappan***

Abstract

***Background:** Communication skills were for a long time a part of the "hidden curriculum" in medical education. In India, communication skills were not taught as a separate skill to medical students. This study was designed to measure the improvement in communication skills of first year medical residents after implementation of a communication skills training module.*

***Methods:** Twenty-nine first year medical residents were enrolled in this training module. They underwent a 6-week long training module in communication skills which covered various scenarios faced in day-to-day practice. They were evaluated both before and after the module using the Kalamazoo Essential Elements Communication Checklist (Adapted) (KEECC - A). They also underwent another evaluation after 6 months of completing the module. Feedback was also obtained from participants and trainers.*

***Results:** The mean scores of the pre-test, post-test and follow-up were 14.30 ± 3.31, 25.60 ± 3.94 and 23.69 ± 5.35 respectively. The improvement in scores between pre-test and post-test was + 11.30 (95% CI 10.30 - 12.30, p <0.0001) and the decrease of the follow-up score from the post-test was - 1.91 (95% CI - 2.86 to - 0.97, p = 0.003). Both these changes were statistically significant. There was a positive feedback from participants and trainers.*

***Conclusions:** There is a definite need for improvement of communication skills among first year medical residents in India. The use of standardised check lists helps in easy assessment and reproducibility across different settings. This training has to be constantly reinforced to prevent regresssion of skills.*

***Key words:** Communication checklist, doctor – patient relationship, KECC-A, Kalamazoo.*

Introduction

In 2018, the National Medical Commission of India notified the Competency Based Medical Education for Undergraduates[1]. According to this document, one of the roles that an Indian Medical Graduate (IMG) has to play is that of a "communicator". According to Accreditation Council for Graduate Medical Education (ACGME), training in medical education involves training in communication skills like listening effectively to patients, eliciting relevant information about them with effective questioning skills, providing disease related information back to them using effective explanatory and interpersonal skills like building and maintaining a therapeutic relationship, and demonstrating caring and respectful behaviours towards patient and their caregivers[2].

Communication skills were for a long time a part of the "hidden curriculum" in medical education. There were many initiatives by different agencies responsible for medical education across the world to improve the communication skills of medical residents. In May 1999, twenty one members from various major medical education and professional organisations attended a conference held in Kalamazoo, Michigan, USA sponsored jointly by the Bayer Institute for Healthcare Communication and the Fetzer Institute. This meeting involved discussions on various methods used in training medical residents in communication skills. At the end of this conference, the consensus arrived at, called the Kalamazoo Consensus Statement (KCS) I was released[3]. This statement highlighted 7 key elements of communication in clinical encounters which were building the doctor – patient relationship, opening the discussion, gathering information, understanding the patient's perspective, sharing information, reaching an agreement and providing closure. In April 2002, the American Academy on Physician and Patient (AAPP) held a conference on patient - physician communication at the Fetzer Institute in Kalamazoo, Michigan. The discussions in the conference lead to the release of the Kalamazoo Consensus Statement (KCS) II which concluded that the assessment of communication and interpersonal skills can be conducted using checklists

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of observed behaviors during interactions with real or simulated patients, by surveys of patients' experiences in clinical interactions and by examinations using oral, essay, or multiple-choice response questions[2]. The discussions in KCS II lead to the development of a checklist called Kalamazoo Essential Elements Communication Checklist (Adapted) (KEECC - A)[4]. This checklist has been used as an assessment tool and found to be effective in evaluating communication skills of medical residents[5,6]. The use of the Kalamazoo Essential Elements of Communication Checklist – Adapted (KEECC - A) or other dedicated communication skills checklists has made a definitive impact on improving in communication skills of residents being trained in the West[6].

In India, communication skills were not taught as a separate skill to medical students till the Medical Council of India/ National Medical Commission guidelines were formed on the implementation of Attitude, Ethics, Communication (AETCOM) module for undergraduate medical students[7]. However most of the current set of first year resident doctors have not fully benefited from this change. In this scenario, this study was designed to measure the improvement in communication skills of first year medical residents after implementation of a communication skills training module.

Methodology

After obtaining clearance from the Institutional Ethics Committee, faculty members, (Assistant and Associate Professor cadre) from the Department of Medicine of our institution underwent a two week training program for proper use of the Kalamazoo Essential Elements of Communication Checklist – Adapted (KEECC - A) under the guidance of the primary investigator and members of the Medical Education Unit (MEU) using role play and pre-determined standardised patient scenarios. The KEECC - A checklist used 7 different elements for evaluation of the student. Each of these elements were rated on a Likert scale of 1 - 5 (1 = poor, 2 = fair, 3 = good, 4 = very good, and 5 = excellent). The scores obtained in each of the individual elements were totalled to arrive at the score for that particular interaction. The maximum possible marks that could be attained was 35. Once the faculty members were deemed to have been trained, the authors and the other trained members of the Department of General Medicine, along with guidance from the senior faculties, developed 40 standardised patient scenarios covering aspects of communication skills like obtaining consent, explaining a diagnosis/condition to the patient, breaking bad news to a patient, explaining about terminal stage of a relative and interpersonal skills like handling an angry patient/relative, handling an error by a colleague.

Twenty nine first year medical residents who provided informed consent to participate in the study were enrolled. They underwent a baseline evaluation of their communication skills with the help of KEECC - A checklist using a standardised patient scenario and were rated by two independent trained evaluators. The arithmetic mean of the scores of the two evaluators was taken as the pretest score. After the pretest was over, the residents underwent training in the communication skills module over a period of 6 weeks.

In this module, trainers first demonstrated techniques of communication skills in a few standardised encounters using role play with one trainer playing the role of a standardised patient and another trainer playing the role of a resident doctor. The trainers highlighted specific areas of the communication scenarios and clarified doubts of students. The students were then divided into small groups of 6 members each, for practice. Each group was assigned a trained faculty member as an observer/evaluator. For every training session, three of the previously prepared scenarios were chosen. One student was then asked to perform the role of resident doctor as mentioned in the scenario with a standardised patient. The other members observed the entire interaction. The observer/evaluator observed the entire interaction and rated the student using the KECC - A checklist. At the end of the communication scenario, the participant was asked to give their insights on the overall communication process and also their impression on the successful completion of the tasks they set out to achieve. The other students also gave their inputs on what went well and what could have been done better. At the end, the observer/evaluator gave his feedback on the performance of the student and clarified areas where mistakes were made. The process was repeated with a different scenario and a different student. Each of the groups underwent a similar training.

The same process was repeated for a total of 6 sessions over a period of 6 weeks. The small groups were assigned a different trainer/evaluator for each session. At the end of 6 weeks, a post-test evaluation was done. Each student underwent evaluation twice, using two different standardised patient scenarios, and rated by two independent evaluators. The arithmetic mean of all four scores obtained was taken as the post-test. Individual feedback was provided to the candidates about their strengths and weaknesses. After a period of 6 months, the students were again evaluated by a process similar to the post test. The arithmetic mean of these scores were taken up as the follow-up score. Feedback from participants and faculty members was obtained at the end of the training programme using a pre-validated questionnaire.

Data was recorded in Microsoft Excel 2019. Charts were prepared using the same. Statistical analysis was done with Quickcalcs by Graphpad. p value of <0.05 was taken as statistically significant. Paired t-test analysis was used for testing changes in scores.

Results

In this study, there were 16 male residents and 13 female residents. All of them had completed their undergraduate training including internship prior to April 2019. Their ages ranged from 24 - 29 years (Median - 27 years).

The mean score of the pretest was 14.30 ± 3.31 and the mean score of the post test was 25.60 ± 3.94. The improvement in scores was + 11.30 (95% CI 10.30 - 12.30) and this change was statistically significant (p <0.0001). The mean score at follow-up was 23.69 ± 5.35. The decrease of the score from the post-test was - 1.91 (95% CI - 2.86 to - 0.97) and this change was also statistically significant (p = 0.003) (Table I). Fig. 1 shows the distribution of scores in the three settings for each individual student.

Fig. 2 shows the median scores in the individual elements of the KECC - A checklist in three different settings. The median scores in all the elements showed an increase after the training programme. The change was the highest in the "providing closure" element followed by "building relationship" and "opening the discussion elements". In all these elements, the median score reached the maximum possible score of 5. The "reaching an agreement" element also showed good improvement after the training program. All elements of the KEECC - A showed a similar or lower median score an follow-up when compared to the post-test except the element of "gathering information" which showed a higher score.

91.42% of the respondents (n = 32) agreed or strongly agreed that the current undergraduate curriculum laid less emphasis on communication skills. 94.28% of the respondents (n = 33) agreed or strongly agreed that there was a definite unmet need for training in communication skills for residents. 100% of the respondents (n = 35) agreed or strongly agreed that the communication module improved skills of the residents and that the same course be conducted for subsequent post-graduate resident batches.

Discussion

There exists a strong need for improvement of communication skills among first year residents in India[8]. The development of various models for enhancing communication skills have shown promise in improving skills of the residents[8,9]. The findings of these studies are similar to the finding of our study; that training improves communication skills of residents. Porcerelli *et al* also found that the use of KECC – A as a training tool improved communication skills among post-graduate residents and also improved their own self-rating of communication skills[7]. The advantages of the KEECC -A checklist is that it provides a structured method for assessment of communication skills and the assessment can be standardised across assessors and assessments. The challenges in using KEECC-A checklist is that it provides a broad framework for assessment of the communication skills subject to interpretation by the assessor and there is a need for pre-assessment standardisation of the marking scheme to be used when there is more than a single assessor.

The results of this study are similar to the findings of Chavda *et al* and Nayak *et al* who found that the use of a communication module improved skills when using KEECC – A for evaluating these skills among undergraduate students in different settings[10,11]. Chavda *et al* showed that among their students, the mean score in communication skills improved from 49.86 to 75.45 and the increase was statistically significant. Similarly, Nayak *et al* showed an increase in the median score from 9 to 40 which was statistically significant.

In this study, before the training module, the median scores in the first five elements of KEECC – A, namely, building the doctor – patient relationship, opening the discussion, gathering information, understanding the patient's perspective, and sharing information were higher than the median scores in the last two elements, namely reaching an agreement and providing closure. This showed a lack of training and importance given to reaching an agreement to the treatment plan with the patient and providing closure to the discussion. The training also helped to improve the "providing closure" element followed by "building relationship" and "opening the discussion" elements the most as these elements showed the most increase in median scores after training. The changes in scores in other elements showed that the residents required further training to achieve the highest possible score in each element. The "sharing of information" element and "understanding patient perspective" element were the ones with the lower median score, possibly indicating their current stage of medical training.

This study also showed that some of the skills learned by training decreased and some others increased over a period of time in the absence of a continuous training module. This finding is similar to the findings of Taveira- Gomes *et al* who found that among clerkship students, who were trained in communication skills during their second year of training, some skills like empathy and ability to collect information improved whereas their interview structure

and non-verbal behaviour declined[12]. This again reiterates the need for continuous efforts to maintain these skills at a higher level.

During this study, the need for training assessors in the correct technique of implementing the KEECC-A checklist for assessment of communication was challenging. This was necessitated by the need for inter-assessor reproducibility of scoring. First year medical residents had a definite lack of communication skills prior to this training module and the areas that had to be trained required extensive training on an individual basis making it a time-consuming process.The lack of video recording during assessment hindered the training process as feedback was based on recall by the assessor and resident. The implementation of video recording could have possibly enhanced the remedial measores needed in non-verbal communication skills.

Conclusions

Communication skill is one of the most important skills that a doctor should possess. First year residents should learn this soft skill at the earliest so as to enhance their patient – doctor relationship and should continuously hone this skill over the years to achieve a high standard. The current resident students have a definite need for training on communication skills as it has not been taught to them formally in their undergraduate years. The use of a validated tool like KEECC – A helps in measuring these skill sets over multiple occasions in a standardised manner. These skills also need constant reinforcement to ensure they do not decay.

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ORIGINAL ARTICLE

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Financial Burden of Gynaecologic Cancers: Out-of-Pocket Expenses in Pre-Treatment Evaluation

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Abstract

Objective: With the increasing incidence of gynaecologic cancers, there has been an increase in financial burden on patients. Out-of-pocket expenditure (OOPE) affect patients' households and their ability to comply with treatment. The purpose of this study was to calculate the out-of-pocket expenditure and catastrophic health expenditure borne by patients during gynaecologic cancer diagnostic work-up.

Methods: A total of 200 patients with various gynaecological cancers were enrolled from the outpatient department, and data were collected regarding cost incurred by patients and caregivers under the headings of 'Direct medical', 'Direct non-medical', and 'Indirect' costs.

Results: The average OOPE for diagnostic evaluation of a patient receiving care for gynaecologic cancer in this institute was found to be INR 25550.34 with a standard deviation (SD) of INR 27292.73. The average Direct medical cost, Direct non-medical cost, and Indirect costs were INR 7899.21 (SD 9257.46), INR 3865.98 (SD 5320.14), and INR 13785.15 (SD 20501.72), respectively. Patients suffering from ovarian cancer had the highest OOPE, which was statistically significant (INR 33007.4, p <0.05). The Indirect cost was also maximum in ovarian cancer patients (INR 18740). It was observed that 23.5% of them had to bear 'catastrophic health expenditure', which is when OOPE exceeds 40% of the total non-food expenditure of the family.

Conclusion: This study gives insight into the financial burden of patients, in terms of OOPE, in gynaecologic cancer diagnosis, which further delays health-seeking behaviour and thereby increases morbidity and mortality. Policy makers should give special attention to these patients and take remedial measures to reduce their cost burden.

Key words: Gynaecologic cancers, out-of-pocket expenditure, direct medical cost, direct non-medical cost, indirect cost, catastrophic health expenditure.

Introduction

India is facing a surge in non-communicable diseases, with cancer emerging as a significant global health problem, as highlighted by The Global Cancer Observatory (GLOBOCAN) 2022[1]. India ranks third in cancer incidence globally, next to China and the United States (USA)[2]. An estimated 2.5 million individuals are living with cancer in India (double the population of Hawaii), with an increase of nearly 700,000 new cases annually, as per the Indian Council of Medical Research (ICMR) report[3]. Gynaecological cancers account for 12.5% of all tumours in women. There has been an increasing incidence of ovarian and endometrial cancer, and recently, cervical cancer and endometrial cancer are being diagnosed in younger age groups also[4]. The economic burden endured by patients and their families due to the high cost of cancer diagnosis has become an emerging concern. High out-of-pocket expenditure (OOPE) and the Indirect costs involved in cancer diagnosis and treatment frequently lead to financial burden and toxicity[5-7], medication non-adherence, changes in spending habits, and the need to borrow money in 25% cases[8].

Due to a lack of comprehensive government health insurance policies in India, a large part of the financial burden of cancer diagnosis and treatment is endured by patients and families. According to a survey, only 18% (government funded 12%) of the urban population and 14% (government funded 13%) of the rural population were covered under any form of health insurance[9]. The Ayushman Bharat-Pradhan Mantri Jan Arogya Yojana (AB-PMJAY) is India's largest public health insurance scheme. It is estimated to cover approximately 50 - 55 crore poor and vulnerable individuals, constituting the bottom 40% of India's population.

Out-of-pocket expenditure (OOPE) is defined as the total amount of money spent by the patient or family during diagnosis/treatment, which includes direct medical and non-medical costs as well as indirect costs. Direct medical expenditure includes costs of investigations, medicines,

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consultation charges, etc. Direct non-medical expenditure includes costs incurred on travel, food, and accommodation[10]. Indirect cost is defined as the loss of income due to the absence from work of a patient/caretaker while being investigated or treated. Catastrophic health expenditure (CHE) is deemed to be present if the health expenditure of the family on the cancer-related illness, i.e., total OOPE, is more than or equal to 40% of the annual Capacity to Pay (CTP). CTP is defined as the total non-food expense of the family (household expenses minus the food expenses per month). The monthly CTP is multiplied by 12 to get the annual CTP[11].

According to the National Sample Survey Organisation (2015), around 60% of healthcare expenditure is paid out-of-pocket by patients in India[12]. This causes an immense burden on household finances. Even before reporting to a tertiary care hospital, patients spend money going to small or private health facilities. To our knowledge, there have been very limited studies done in India that estimated the OOPE borne by cancer patients[13-16]. We conducted this study to estimate the OOPE from onset of symptoms till diagnosis for various types of gynaecological cancers at a tertiary care hospital in Delhi, India. We surveyed the socio-demographic profile of cancer patients seeking care at our hospital, along with a detailed evaluation of economic factors till the cancer diagnosis was made.

Methodology

This cross-sectional study was conducted at a tertiary care government hospital in Delhi from July 2023 to March 2026. We regularly receive referrals from smaller government hospitals, private clinics in and around Delhi, and other states as well. This was a pilot study, approved by the ethical committee of the hospital (GTBHEC 2024/P-201), and was registered under ClinicalTrials.gov (Reg. No.-CTRI/2024/07/070008). Patients visiting the outpatient department and diagnosed with/suspected of having gynaecologic cancer were included in the study. The exclusion criteria were non-gynaecologic cancer and patients unwilling to participate in the study. Women were enrolled, and data was analysed for 200 participants. Written consent was taken from all participants, and a pre-designed performa was used to collect data from patients and/or family members in a comfortable private place. Complete confidentiality of the information collected was ensured. We only took details of the cost incurred during the diagnostic workup of gynaecologic cancer, i.e., from onset of first symptoms till final diagnosis of cancer. The histopathological reports of gynaecologic cancers were collected later on and recorded to confirm the final diagnosis. The study used a bottom-up micro-costing method to estimate the OOPE (Direct and Indirect costs) associated with diagnosing gynaecologic cancer. Micro-costing or bottom-up costing is defined as a method of cost calculation in which each component of resource use (e.g., laboratory tests, drugs, travel, food expenses) is estimated, and a unit cost is derived for each. This is used for precise calculation of the economic costs of health interventions. Here, cost was calculated for each element of an intervention.

Data collection was done by the principal investigator and/or co-investigator. Demographic characteristics of the study population were noted. Details of money spent under various headings, e.g., laboratory investigations, imaging, drugs, blood transfusion and medical materials, transportation, food expenses during hospital visit, and accommodation expenses for both the patient and caretakers, were collected based on recall by the patient and/or relatives. Details of the patient's total family income from all sources were noted. The total family expenditure breakdown was obtained to calculate the capacity to pay. The CHE rate, i.e., the proportion of patients who experienced catastrophic expenditure out of the total patients included in the study, was also calculated. All costs were reported in Indian National Rupees (INR).

Statistical analysis: Data was entered and managed using Microsoft Excel and subsequently analysed using SPSS version 31. Quantitative variables were summarised as mean and standard deviation (SD), while qualitative variables were presented as frequencies and percentages.

The normality of quantitative data was assessed using the Kolmogorov-Smirnov test. For comparison between two groups, based on a quantitative variable, the independent samples t-test was applied for normally distributed data, whereas the Mann-Whitney U test was used for non-normally distributed data.

For comparisons involving more than two groups, based on quantitative variables, one-way analysis of variance (ANOVA) was used for normally distributed data, while Kruskal-Wallis test was employed for non-normally distributed data.

A p-value of less than 0.05 was considered statistically significant.

Results

A total of 200 cases of gynaecologic cancers were recruited in the current study. An interim analysis of this study was published previously, which included 89 cancer patients[17]. Results show a similar trend in the outcome parameters, with minor differences. The baseline demographic characteristics are shown in Table I. Mean age of study participants was 49.2 years. Around 69.55% of participants were from an urban background. More than half (64%) of

the participants received no formal education.

Table I: Socio-Demographic characteristics of study group.

Characteristics		Summary measures n (%)
Mean Age (years)	49.2 years	
Marital status	Unmarried	9 (4.5%)
	Married	174 (87%)
	Widow/ Divorced	17 (8.5%)
Religion	Hindu	144 (72%)
	Muslim	54 (27%)
	Other	2 (1%)
Education	Illiterate/Primary	128 (64%)
	Senior Secondary	61 (30.5%)
	Graduate	11 (5.5%)
Occupation	Unskilled	164 (82%)
	Semiskilled/Skilled	36 (18%)
Type of family	Nuclear	122 (61%)
	Joint	78 (39%)
Locality	Urban	139 (69.5%)
	Rural	61 (30.5%%)

The disease characteristics of participants are mentioned in Table II. The majority of patients were of ovarian cancer, followed by cervix, endometrial, vulva, and other (vaginal and choriocarcinoma). More than half of them (65%) presented in stage II disease and above. Usually, cancer patients first approach the nearby private or small government hospital for their symptoms before being referred to a tertiary care hospital. During this time, they spend a lot of time and money until the final cancer diagnosis and treatment are initiated. The mean time duration from the onset of symptoms till reporting to the tertiary care hospital was 9.16 months for all cancers. This could be the reason for late presentation in the advanced stage. It was observed that almost 50% of participants showed up in other smaller government hospitals before coming to our hospital, and the rest were seen by private clinics, practitioners of alternative medicine or unqualified quacks.

Table II: Disease characteristics of cancer patients.

Stage (%)	Ovarian n (82)	Cervix n (67)	Endometrial n (44)	Vulval n (5)	Others n (2)
I (35%)	28	17	22	2	1 (Choriocarcinoma)
II (33%)	18	30	15	2	1 (Vaginal)
III (23%)	27	15	3	1	
IV (9%)	9	5	4	–	
Mean duration from onset of symptoms till hospital visit (months)	9.5	11.04	7.18	10.2	3.5
Type of Previous consultation					
Private (50%)	47	25	24	2	2
Government (50%)	35	42	20	3	–

Table III gives insight into the socio-economic characteristics of the study participants. Among the 200 participants, 63% had a ration card above poverty line. Awareness regarding various government health schemes was very limited, and only 23% of participants were aware of the Ayushman Bharat Scheme. Only 3% of women reported utilisation of any health insurance scheme.

As mentioned in Table IV, the average OOPE for diagnostic evaluation of a patient receiving care for gynaecologic cancers in this institute was estimated to be INR 25550.34 with a SD of INR 27292.73. The average Direct medical, Direct non-medical, and Indirect costs were INR 7899.21(SD 9257.46), INR 3865.98 (SD 5320.14), and INR 13785.15 (SD 20501.72), respectively. Patients having ovarian cancers spent the highest OOPE, which was statistically significant (INR 33007.4, $p < 0.05$). The average money spent by patients on Direct medical and Direct non-medical costs was highest with other types of cancer (choriocarcinoma and vaginal cancer). Indirect cost was highest in ovarian cancer patients (INR 18740) as shown in Table IV. There were significant differences in all cost parameters of OOPE among various types of gynecologic cancers ($p < .05$).

Table III: Socio-economic characteristics of participants.

Characteristics	n (%)	
Type of Ration Card	Above Poverty Line	126 (63%)
	Below Poverty Line	49 (24.5%)
	No Ration Card	25 (12.5%)
Awareness of the Ayushman Bharat Scheme	Yes	46 (23%)
	No	154 (77%)
Recipient of any Government Health Benefit	Yes	7 (3.5%)
	No	193 (96.5%)
Recipient of any Health Insurance	Yes	6 (3%)
	No	194 (97%)

Table V gives the section-wise Direct (medical and non-medical) and indirect expenses experienced by participants. Direct medical and Direct non-medical costs for each of the above-discussed independent variable categories were summarised as means with standard deviation (SD). Overall, total OOPE was also calculated and presented as the mean with SD. Direct medical and non-medical costs were higher in the 41 - 50 year age group (INR 10588.3, INR 4843.5), whereas Indirect cost and OOPE were highest in the <30 year age group of INR 18609.3 and INR 32145.9,

respectively, statistically significant (p <0.01). The difference in total OOPE by urban and rural patients in various occupational groups was not found to be statistically significant.

The educated group of patients (graduates) spent the highest average OOPE of INR 33321.1 with statistical significance (p <0.05). The OOPE for upper class of Modified Kuppuswamy Classification was highest at INR 59275 than other classes (p <0.05). This was due to high Direct medical and non-medical costs. The OOPE was statistically higher in patients having an above poverty line ration card (INR 28377.6). Although only six patients utilised health insurance, making no significant difference in OOPE in comparison to patients not utilising health insurance. Patients who were aware of the Ayushman Bharat Scheme spent a higher OOPE of INR 33907.8 when compared to those who were unaware of this scheme (p-value <0.005).

Catastrophic health expenditure calculation

The data on household expenditure patterns and OOPE were analysed to explore the proportion of households suffering catastrophic health expenditure from the ongoing cancer evaluation and diagnosis. It was observed that 23.5% of individuals were found to have borne catastrophic health expenditures. When data was analysed based on the type of cancer, it was observed that 34.9% patients of ovarian cancer had CHE as mentioned in Table VI.

Table IV: Out of pocket expenditure (OOPE) in INR for different cancer types.

Type of cancer	Ovarian (82)	Cervix (67)	Endometrial (44)	Vulval (5)	Others (2)	p-value	Overall
Direct Medical Mean (SD)	9870.51 (9651.5)	5537.01 (9624.8)	7599.5 (6943.4)	8300 (11934.4)	11800 (4949.7)	**<0.05**	7899.21 (9257.46)
Direct Non-Medical Mean (SD)	4396.9 (4476.1)	3802.1 (7009.7)	2850.6 (2724.4)	1795 (667.6)	11750 (15202.7)	**0.03**	3865.98 (5320.14)
Indirect Mean(SD)	18740 (22849.3)	10232.0 (19689.3)	11304.5 (16687.2)	6180 (5745.6)	3250 (4596.1)	**0.01**	13785.15 (20501.72)
Total OOPEMean (SD)	33007.4 (27365.0)	19571.2 (29549.7)	21754.77 (21949.3)	16275 (15714.0)	26800 (14849.2)	**<0.05**	25550.34 (27292.73)

**OOPE: Out of Pocket Expenditure. *Direct (medical) cost includes costs of investigations, medicines, consultation charges, etc. *Direct (non-medical) costs include costs on travel, food, and accommodation expenses. *Indirect cost is defined as the loss of income due to the absence from work of a patient/ caretaker while being investigated/treated.*

Table V: Patient characteristics and financial burden of gynaecological cancers expressed in INR.

	Direct (Medical) Mean (SD)	p-value	Direct (Non-medical) Mean (SD)	p-value	Indirect Mean (SD)	p-value	Total OOPE Mean(SD)	p-value
Age (Yrs)								
<30	8872.8 (6616.0)	0.11	4663.7 (5169.7)	0.36	18609.3 (17885.9)	0.01	32145.9 (21252.6)	**0.01**
31 - 40	7962.3 (7102.5)		3602.8 (3821.7)		15792.8 (19537.3)		27358.0 (24533.0)	
41 - 50	10588.3 (13462.4)		4843.5 (7797.4)		15128.8 (2719.2)		30560.7 (33133.1)	
51 - 60	6087.1 (7648.6)		3335.7 (4261.2)		12267.4 (19607.4)		21690.3 (24694.6)	
>60	6098.4 (6252.4)		3198.0 (3688.0)		10144.57 (20472.9)		19441.0 (25630.81)	
Occupation								
Unskilled (164)	7877.09 (9571.7)	0.51	3752.42 (5091.4)	0.24	12810.24 (20027.2)	0.01	24439.75 (27136.9)	0.06
Skilled (36)	8000.00 (7783.0)		4383.33 (6314.0)		18226.39 (22296.9)		30609.72 (27812.8)	
Locality								
Rural (61)	9157.2 (11354.9)	0.41	4714.8 (5174.4)	0.01	12619.3 (15053.4)	0.65	26491.3 (20396.8)	0.06
Urban (139)	7347.1 (8155.8)		3493.4 (5358.6)		14296.7 (22510.5)		25137.3 (29878.2)	
Education								
Illiterate	7352.3 (8933.3)	0.01	3823.0 (5869.1)	0.01	11707.9 (21356.6)	<0.05	22883.4 (29039.0)	**<0.05**
Senior secondary	8405.4 (10345.3)		3394.8 (2858.9)		18170.9 (19277.5)		29971.1 (24154.1)	
Graduate	12250 (3279.2)		7726.6 (8489.1)		13344.4 (10260.6)		33321.1 (15946.9)	
Socio-economic status								
Lower	6040.8 (7197.2)	**0.01**	3925.0 (5828.4	**0.01**	6291.0 (15788.6)	**<0.05**	16256.9 (19712.2)	**<0.05**

Lower-middle	7325.1 (7424.7)		3223.7 (3597.1)		15494.2 (19091.1)		26043.1 (24370.1)	
Upper-lower	7399.2 (8783.1)		3916.3 (61775.9)		15280 (23041.7)		26595.5 (33004.6)	
Upper-middle	10100.0 (6036.8)		4230.9 (3820.3)		21276.1 (25578.7)		35607.1 (30292.7)	
Upper	35625.0 (29101.9)		13150.0 (7113.13)		10500 (16441.8)		59275 (26417.0)	
Ration card								
Above poverty line (126)	7756.4 (8998.6)	0.65	3827.8 (4162.9)	0.09	16793.2 (21993.4)	**<0.05**	28377.6 (27522.1)	**0.01**
Below poverty line (49)	7467.1 (8915.0)		4414.8 (8067.6)		7373.0 (17202.5)		19255.0 (29136.8)	
No card (25)	9465.4 (11263.1)		2982.4 (3579.5)		11192.0 (153)		23639.8 (20166.1)	
Health Insurance utilisation								
Yes (6)	11066.6 (8224.5)	0.18	6337.1 (6033.6)	0.27	9091.6 (7479.3)	0.91	26495.5 (17300.5)	0.43
No (194)	7801.2 (9289.2)		3789.56 (5295.7)		13930.3 (20766.1)		25521.1 (27572.9)	
Awareness about Ayushman Bharat Scheme								
Yes (46)	10642.7 (7847.9)	**0.05**	5316.2 (5841.5)	**0.01**	17948.9 (21359.4)	**0.01**	33907.8 (26494.2)	**<0.05**
No (154)	7079.7 (9508.5)		3432.8 (5094.7)		12541.4 (20142.9)		23053.9 (27113.1)	

Table VI: Catastrophic health expenditure calculation in various gynaecologic cancers in INR.

Type of cancer	Ovarian (82)	Cervix (67)	Endometrial (44)	Vulval (5)	Others (2)	Overall
Mean Annual Capacity To Pay (CTP) in INR	130495.7	104479.8	128082	147717.6	119496	121569.96
Number of patients exceeded 40% of annual CTP	29(34.9%)	10(15.1%)	8(18.18%)	0	0	23.5%

Discussion

The mean age of study subjects was 49.2 years. The age distribution is younger in comparison to previous studies conducted among head and neck cancer (HNC) patients in North India[18]. Most of the study population (69.5%) lived in urban areas and belonged to lower middle class. The utilisation of health insurance was very low (only six patients among 200), which is much less than reported in the study of Chauhan *et al*[18]. In the present study, 77% of patients were un-aware of the Ayushman Bharat Scheme.

The socio-demoraphic and economic stratum of patients visiting and government hospital can exptian the low levels of awareness.

The average Direct medical cost, Direct non-medical cost, and Indirect costs in the current study were INR 7899.21(SD 9257.46), INR 3865.98 (SD 5320.14), and INR 13785.15(SD 20501.72), respectively. The Indirect cost was highest at INR 13785.15. The estimation of OOPE for cancer diagnosis and treatment depends on various factors, i.e., study period, type of cancer, and cost components. The present study showed a total OOPE of INR 25550.34, which was much less than the OOPE reported for various solid cancer treatments from South India (INR 35,817)[19]. The reported OOPE was INR 36,812 for HNC from New Delhi in 2006. In 2017, Chauhan *et al* from Chandigarh reported that OOPE for HNC was around INR 37,845[18]. Our study calculated OOPE from symptom onset till final diagnosis was made and did not include the treatment aspect in the cost analysis. This was becaues treatment is free in our hospital. Also, as many cancer patients are referred to our attached oncology center (Delhi State Cancer Institute) for further chemo radiation, follow-up of these patients would have been difficult.

The OOPE for all types of cancer in India, done in 2006 - 2007, was INR 36,812. By 2017 - 2018, the average OOPE for cancer treatment had further increased, exceeding INR 2,895 for outpatient care and INR 52,393 for inpatient care[20]. In 2018 - 19, the average OOPE for hospitalisation-related to cancer treatment in India was estimated at INR 85,595[21]. In 2023, the average Direct medical cost for an outpatient consultation was approximately INR 8,053, while the cost for each hospitalisation was around INR 39,085[21]. The high cost of cancer treatment, unfortunately forces many households to borrow money or sell assets to cover expenses[22]. A recent Indian study done at a tertiary care hospital of Uttar Pradesh, including 120 cancer patients attending surgical OPD from July 2020 to November 2021, estimated an average OOPE in cancer treatment of INR 79925.5. The Direct medical expenditure was INR 45151, and the Indirect non-medical expenditure was INR 10,000[23].

In the current study, patients with ovarian cancers spent the highest OOPE, which was statistically significant (INR 33007.4, $p < 0.05$). This may be due to the nonspecific and

overlapping nature of symptoms of ovarian cancer, leading to multiple specialist consultations and more investigations. The disease is already in an advanced stage at the time of diagnosis in most cases. The lower mean value of total OOPE in the present study (as compared to other studies) can be explained by the fact that we calculated the OOPE spent by patients from the onset of symptoms till the diagnosis was made, while other studies included the whole treatment cost of cancer. We focused on the expenses of diagnostic evaluation during outpatient and inpatient care received by gynaecologic cancer patients, including indirect cost estimation. The Indirect cost estimation has not been studied in many previous studies. In fact, the major part of OOPE was in the Indirect domain, followed by direct medical costs. This can be explained by the fact that, even though diagnostic modalities are free of cost, patients and/or caregivers need to leave their daily jobs for their hospital visits. This loss of income due to absence from work is directly proportional to the number of visits and time spent in hospital. Sometimes patients have to take loans or sell their fixed assets. This financial burden is also reflected by the significantly higher direct (medical and non-medical) and indirect costs among individuals who sought consultations from private practitioners before reporting to this hospital. Due to proximity and/or convenience, patients prefer to visit small or private health facilities for evaluation of symptoms. Long queues for consultation, lack of super-specialty doctors, and advanced investigations in government hospitals are deterrents to health-seeking behaviour. Patients sometimes fall prey to quacks who encash on their ignorance and illiteracy, further adding to the cost burden. The richer households belonging to upper socio-economic class were spending more on management of cancer, which is similar to studies by Rajpal and Chauhan *et al*[13,18]. The OOPE was not significantly different between urban and rural patients. While in other studies, individuals from urban settings spent more than those from rural settings[18].

Catastrophic health expenditure

The 40% cut-off on the CTP was used to calculate the incidence of CHE in present study. The prevalence of Catastrophic health expenditure (CHE) in the current study was 23.5%, as compared to 34% prevalence reported by Chauhan *et al*[18]. In fact, lower CHE in the present study could be again explained by the fact that our study took into account OOPE in the diagnostic part of gynaecologic cancers. The prevalence of CHE was 34.9% in ovarian cancer, followed by 18.18% in endometrial cancer and 15.1% in cervical cancer.

The overall OOPE was contributed mainly by Indirect costs. In a tertiary care hospital setting, unnecessary OPD visits by both patients and caretakers can be avoided by utilizing telemedicine. Further research should focus on developing protocols for follow-up visits, along with establishing specialised cancer clinics in tertiary care hospitals and satellite follow-up clinics in Primary care centres near homes of patients.

Strengths and Limitations

There are few studies in literature regarding the cost analysis of gynaecologic cancers. Moreover, the present study is the only study to look into cost by gynaecologic cancer type. The indirect costs under various headings (loss of income due to the absence from work of a patient/caretaker while being investigated/treated) were collected, which has not been done in most previous studies. This would reflect the expenditure pattern in calculating OOPE. An important finding was that cancer patients paid substantial out-of-pocket costs under the category of Indirect cost. Patients with higher socio-economic class and higher education (graduates) had the highest direct medical and direct non-medical expenditure. Only 23% were aware of government schemes like the Ayushman Bharat Scheme; however, almost all patients (97%) were not covered by any health insurance scheme.

Limitations

We collected information-related to economic burden, based on the recall method. It was the patient's perspective for capturing the cost incurred during diagnoses of gynaecologic cancers. The calculation of OOPE was dependent on self-reported costs by patients, but lacked verification (e.g., bills or receipts). Information was not collected about coping strategies used by patients and families to overcome catastrophic health expenditure. It was a cross-sectional study to quantify OOPE among selected cancer patients attending the OPD of a tertiary care center. Therefore, the results of the study may not be representative of all cancers in the general population. The sample size was small, so further studies with large sample size may give more insight into the health-related economic burden on patients suffering from gynaecologic cencers.

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ORIGINAL ARTICLE

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Evaluation of the Relation between Dialysis Vintage, Cognitive Functions and Functional Status in CKD Patients

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Abstract

***Background:** Patients on haemodialysis are particularly vulnerable to cognitive impairment because of their advanced age, which inherently raises the risk of cognitive decline. Furthermore, stroke is frequently quite common in this population, which is a major factor in cognitive dysfunction. Cognitive impairment risk is further increased by cardiovascular risk factors, which are prevalent in haemodialysis patients. Haemodialysis also may be linked to cognitive problems because of blood pressure variations and it's effects on brain perfusion.*

***Aim:** To evaluate the relation between dialysis vintage, cognitive functions and functional status in CKD (chronic kidney disease) patients undergoing haemodialysis. We assessed cognitive function using Montreal Cognitive Assessment (MOCA) and the functional decline using Barthel Index (BI).*

***Methods:** Using a prospective observational study, the authors measured cognitive function and daily activity level in 60 haemodialysis patients between the age of 18 years and 80 years at Aarupadai Veedu Medical College. The study data for cognitive function and functional status was captured using Montreal cognitive assessment (MOCA) and Barthel index (BI), respectively.*

***Result:** This study suggests that as the vintage of dialysis increases, the Barthel Index score tends to decrease, implying a decline in the patient's functional status. The correlation was statistically significant, with a p-value of 0.001. The study demonstrated a strong association between longer dialysis vintage and lower MOCA scores. These findings suggest that individuals on dialysis for a longer duration are more likely to exhibit cognitive decline as measured by the MOCA scale. The statistical significance of this correlation was p <0.01.*

***Conclusion:** The study confirmed a strong positive relationship between a longer dialysis vintage and a higher risk of cognitive impairment. The study also showed a positive association between a decline in functional status and extended dialysis treatment.*

***Key words:** Cognitive function, functional status, dialysis vintage, MOCA, Barthel index.*

Introduction

Millions of people worldwide suffer from chronic kidney disease (CKD), with end-stage renal disease (ESRD) frequently requiring dialysis treatment in order to sustain life[1]. Dialysis is a useful treatment for the symptoms and side-effects of end-stage renal disease (ESRD); however, long-term dialysis exposure, sometimes known as "dialysis vintage," has been linked to a number of unfavourable health outcomes, such as reductions in cognitive function and general functional status[2]. Furthermore, decreased quality-of-life, greater reliance on others for daily tasks, and increased death rates have all been linked to cognitive impairment in people with chronic kidney disease (CKD)[3]. In addition to cognitive function, dialysis patients are at high-risk for physical functional decline, which encompasses mobility, self-care, and the ability to perform activities of daily living[4]. Older dialysis patients are more likely to experience functional impairment, and research indicates that a longer dialysis history is associated with worsening functional results[5]. Numerous factors, such as vascular disease, anaemia, and inflammation, which worsen neurocognitive deficits, influence the loss in cognitive and functional abilities in dialysis patients[6,7]. Furthermore, another risk factor for poor cognitive and physical results is the existence of frailty in dialysis patients, which frequently develops along with extended dialysis duration[8]. The precise processes by which dialysis vintage leads to a loss in

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cognition and functionality, however, are still being studied. Building on earlier research, this study intends to assess the association of dialysis vintage with cognitive function, and functional status in patients with chronic kidney disease (CKD). It also seeks to identify possible variables that may guide treatment measures aimed at enhancing patient outcomes.

The study was commenced after obtaining ethics clearance from the IEC of the institute.

Material and Methods

This prospective observational study was conducted in the Department of Nephrology at Aarupadai Veedu Medical College and Hospital, Puducherry, over a period of two months. The aim was to evaluate the relationship between dialysis vintage, cognitive function, and functional status in 60 chronic kidney disease (CKD) patients undergoing intermittent haemodialysis. The sample size of 60 was arrived based on the formula for cross-sectional studies. The participants were recruited consecutively as they arrived to the haemodialysis centre. Eligible patients were between 18 and 80 years old, had been on haemodialysis for at least three months, and provided informed consent. Patients with a history of psychological disorders, cerebral or cardiovascular injuries, acute illness, or those unwilling to participate were excluded from the study. Cognitive function was assessed using the *Montreal Cognitive Assessment (MoCA)*, a validated tool for detecting mild cognitive impairment, while functional status was measured using the *Barthel Index (BI)*, which evaluates a patient's ability to perform basic activities of daily living. Both assessments were conducted during dialysis sessions by trained personnel to ensure accuracy and minimise patient fatigue. Dialysis vintage, defined as the duration of time the patient had been undergoing haemodialysis, was recorded, and its relationship with cognitive and functional outcomes was analysed. The primary objective was to evaluate the correlation between the length of time on dialysis and declines in cognitive and functional status. The data analysis was performed using SPSS version 21.

Results

The study included a total of 60 patients undergoing haemodialysis. The majority of participants were male (73.3%), followed by females (26.7%). The age distribution was relatively diverse, with participants ranging from 21 to 80 years old. The most common age group was 41 - 50 years (33.3%), followed by 51 - 60 years (25.0%). The duration of dialysis vintage varied among participants, with the majority (25%) having been on dialysis for 0 - 6 months. The longest dialysis vintage recorded was 120 months (10 years). The most common dialysis frequency was twice a week (91.7%), followed by three times a week (8.3%). The functional status of the participants was assessed using the Barthel Index. The majority of participants (48.3%) fell within the 61 - 90 range, indicating moderate functional dependence. A smaller proportion (29%) exhibited severe functional dependence (21 - 60 range), while 35% demonstrated a high level of functional independence (91 - 100 range). Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA). The majority of participants (48.3%) scored within the 11 - 17 range, suggesting mild cognitive impairment. A smaller group (38.3%) scored between 18 - 25, indicating borderline cognitive impairment. Only a small percentage (3.3%) achieved scores above 25, indicating normal cognitive function. A correlation analysis was conducted to examine the relationship between dialysis vintage and functional status (Barthel Index) as well as cognitive function (MoCA score). Results indicated a significant negative correlation between dialysis vintage and Barthel Index scores ($r = -0.428$, $p < 0.001$), suggesting that longer dialysis duration was associated with decreased functional status. Additionally, a significant negative correlation was found between dialysis vintage and MoCA scores ($r = -0.501$, $p < 0.001$), indicating that individuals on dialysis for longer durations were more likely to exhibit cognitive decline.

Table I: Demographic and clinical characteristics.

Parameters	Value
Age (years)	49.5 ± 13.52
Gender	
Male	44 (73.33%)
Female	16 (26.67%)
Weight (kgs)	53.92 ± 11.38
Frequency	
2/week	55 (91.67%)
3/week	5 (8.33%)
Vintage	
Less than 1 year	30 (50%)
More than 1 year	30 (50%)
Vascular Access	
AVF	52 (86.67%)
Catheter	8 (13.33%)

Table II: Score distribution.

Parameter	Value
Barthel Index	
Independent	7 (11.7%)
Slightly dependent	21(35.0%)
Moderately dependent	29(48.3%)
Severely dependent	3(5.0%)
Montreal Cognitive Assessment Scale	
Normal	2(3.3%)

Mild cognitive function	23(38.3%)
Moderate cognitive function	29(48.3%)
Severe cognitive function	6(10.0%)

Table III: Correlation between dialysis vintage and Barthel index score.

Variable	Pearson Coefficient (r)	p-value
Dialysis Vintage and Barthel Index Score	-0.428**	**0.001**
Dialysis Vintage and MOCA Score	0.501**	**0.001**

***Correlation was significant at the 0.01 level (2-tailed), 95% C.I.*

Discussion

Our study demonstrates a significant relationship between dialysis vintage and both cognitive function and functional status in patients with chronic kidney disease (CKD). As the duration of dialysis increases, we observed a statistically significant decline in the Barthel Index score ($p = 0.001$), which implies a corresponding decrease in functional capacity. This association between dialysis vintage and functional decline is well-supported by existing literature, which has established that prolonged exposure to dialysis can lead to diminished physical performance due to a combination of factors, including cumulative physical stress, nutritional deficiencies, and chronic inflammation[9,10]. Given that the Barthel Index measures the ability to perform activities of daily living (ADLs), this decline suggests that patients who remain on dialysis for extended periods become increasingly dependent, which severely impacts their quality-of-life.

Functional decline in long-term dialysis patients is a multifactorial issue. Several studies have identified sarcopenia, frailty, and the cumulative effects of co-morbid conditions such as cardiovascular disease and diabetes as key contributors to the deterioration of functional status in dialysis patients[11,12]. Sarcopenia, in particular, has been noted to progress more rapidly in CKD patients due to chronic inflammation and oxidative stress, both of which are exacerbated by the dialysis process. Furthermore, frailty, which encompasses physical weakness, weight loss, and reduced endurance, is highly prevalent in CKD patients and is significantly associated with poor functional outcomes[13]. Thus, the decline in Barthel Index scores observed in our study reflects not only a deterioration in physical capacity but also the broader impact of these systemic factors on the ability to maintain independence.

Cognitive decline, as indicated by lower Montreal Cognitive Assessment (MOCA) scores, was also significantly associated with longer dialysis vintage ($p = 0.01$). This finding is consistent with previous research that has highlighted the increased prevalence of cognitive impairment in CKD patients, particularly those who have been on dialysis for extended periods[14]. Several mechanisms have been proposed to explain the cognitive decline in CKD patients, particularly those on long-term dialysis. One of the most widely accepted explanations involves the chronic exposure to uraemic toxins, which accumulate due to reduced renal clearance and contribute to neurotoxicity. Uraemic toxins, such as indoxyl sulfate and p-cresyl sulfate, are known to induce oxidative stress and inflammation, which can damage the blood-brain barrier and lead to neuronal injury[15]. This is further compounded by the presence of traditional cardiovascular risk factors, such as hypertension, diabetes, and dyslipidemia, which are prevalent in CKD patients and are themselves linked to cognitive decline[16,17]. Moreover, the process of dialysis itself, while essential for maintaining life in end-stage renal disease (ESRD) patients, may exacerbate these issues by contributing to fluctuations in blood pressure and cerebral perfusion, thereby increasing the risk of cerebrovascular events.

Another potential contributor to cognitive decline in dialysis patients is anaemia, which is common in CKD due to the kidney's reduced ability to produce erythropoietin. Anemia can lead to cerebral hypoxia, which has been associated with both cognitive impairment and an increased risk of dementia in older adults[18]. Additionally, CKD patients often experience metabolic imbalances, such as disturbances in calcium and phosphate homeostasis, which may contribute to vascular calcification and cognitive dysfunction[19]. Our findings suggest that these factors may interact to accelerate cognitive decline in patients with prolonged dialysis vintage, further emphasizing the need for early intervention to mitigate these risks.

In addition to physical exercise, maintaining proper nutritional status is also crucial for preventing functional decline in dialysis patients. Malnutrition is highly prevalent in CKD patients due to a combination of factors, including reduced appetite, metabolic acidosis, and protein-energy wasting, all of which can contribute to muscle loss and frailty. Nutritional interventions, such as dietary supplementation with protein and amino acids, have been shown to improve muscle mass and physical performance in CKD patients and should be considered as part of a comprehensive strategy to mitigate functional decline[20]. Similarly, cognitive interventions, such as structured cognitive training programs, may help to slow the progression of cognitive impairment in dialysis patients, particularly those who are at high-risk for dementia[21].

While our study provides valuable insights into the relationship between dialysis vintage, cognitive function, and functional status, there are several limitations that should be acknowledged. First, our study is cross-sectional

in nature, which limits our ability to establish causality between dialysis vintage and the observed declines in cognitive and functional abilities. Longitudinal studies are needed to confirm these findings and to better understand the temporal relationship between dialysis duration and cognitive and functional outcomes. Second, while we used the Barthel Index and MOCA to assess functional and cognitive status, respectively, these tools may not capture the full range of impairments experienced by CKD patients. Future research should consider the use of more comprehensive assessments, such as the Instrumental Activities of Daily Living (IADL) scale, which evaluates higher-order functional abilities, and domain-specific cognitive tests that can provide a more detailed understanding of cognitive decline[22].

Another limitation of our study is the potential for selection bias, as patients with severe cognitive or functional impairments may be less likely to participate in the study or may have discontinued dialysis. This could result in an underestimation of the true prevalence of cognitive and functional decline in long-term dialysis patients. Additionally, we did not control for certain co-morbid conditions, such as depression and anxiety, which are common in CKD patients and may influence both cognitive function and quality-of-life[23]. Future studies should include a more comprehensive assessment of psychological factors to better understand their role in the observed declines.

Conclusion

Our study highlights a significant association between dialysis vintage and both cognitive function and functional status in patients with chronic kidney disease (CKD). As the duration of dialysis increases, patients experience notable declines in both cognitive performance and functional capacity, as measured by the Montreal Cognitive Assessment (MOCA) and the Barthel Index, respectively. These findings are consistent with existing literature and underscore the multifaceted nature of the challenges faced by long-term dialysis patients, including sarcopenia, frailty, chronic inflammation, and exposure to uraemic toxins.

The observed declines in cognitive and functional abilities reflect the cumulative impact of prolonged dialysis on both physical and mental health. The interplay of factors such as nutritional deficiencies, anaemia, metabolic imbalances, and co-morbid conditions further exacerbates these issues. Consequently, there is a critical need for comprehensive, multidisciplinary approaches to address these challenges. Strategies should include regular monitoring of cognitive and functional status, targeted nutritional and cognitive interventions, and management of comorbid conditions.

Given the limitations of our cross-sectional study, future research should employ longitudinal designs to better understand the temporal dynamics between dialysis vintage and cognitive and functional outcomes. Additionally, more comprehensive assessment tools and considerations of psychological factors are necessary to capture the full spectrum of impairments and to develop effective strategies for improving the quality-of-life in long-term dialysis patients. Ultimately, our findings emphasize the importance of early intervention and holistic care to mitigate cognitive and functional decline and enhance patient outcomes in the CKD population.

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ORIGINAL ARTICLE

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Prevalance and Clinical Profile of Pulmonary Hypertension in Chronic Liver Disease: A Tertiary Care Hospital-Based Study

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Abstract

***Introduction:** Chronic liver disorders (CLDs) have significantly increased global mortality. With 1.6 billion affected by conditions like alcoholic liver disease (ALD), hepatitis B and C, and non-alcoholic fatty liver disease (NAFLD), complications such as cirrhosis, hepatopulmonary syndrome (HPS), and portopulmonary hypertension (PoPH) are prevalent. This study investigates the prevalence and clinical profile of pulmonary hypertension (PH) in patients with CLD.*

***Objectives:** This study aims to evaluate the clinical profile and prevalence of pulmonary hypertension in patients with CLD and assess its correlation with the severity of liver disease.*

***Methods:** This cross-sectional study involved 150 patients with CLD with PH, from January 2023 to June 2024. Patients aged >14 years with CLD and PH were included, excluding those with malignancies, recent surgeries, or other causes of PH.*

***Results:** The mean patient age was 45.55 ± 9.8 years, predominantly male (79.3%), with most from lower socio-economic backgrounds (65.3%). Alcohol use was prevalent (78.7%), and 32.0% tested positive for HBsAg. Ascites varied in severity, and 20.0% of patients had PH (6.7% mild, 13.3% moderate). A significant correlation was found between Child-Pugh scores and PH prevalence (p <0.001).*

***Conclusion:** Pulmonary hypertension is observed in 20.0% of patients with CLD, with severity correlating strongly with liver disease severity. Trans-thoracic echocardiography is non-invasive diagnostic tool for PH in patients with CLD. Alcohol remains a major preventable cause of CLD. Further research is needed to confirm these findings and explore management strategies.*

***Key words:** Chronic liver disease; pulmonary hypertension; alcoholic liver disease; hepatopulmonary syndrome; portopulmonary hypertension; Child-Pugh score; trans-thoracic echocardiography.*

Introduction:

Chronic liver disorders (CLDs) are a significant public health concern due to their rising global morbidity and mortality. From 1980 to 2013, global mortality from CLDs increased by 46%, with most deaths occurring in LMICs (low- and middle-income countries), predominantly in Asia as well as Africa, where vital event reporting systems are inadequate[1]. This underreporting may obscure the true burden of CLDs, necessitating improved methods to assess their impact on health systems. In 2017, 1.6 billion people suffered from CLDs, primarily caused by HCV (hepatitis C virus), ALD (alcoholic liver disease), NAFLD (non-alcoholic fatty liver disease), and HBV (hepatitis B virus). Cirrhosis contributed to 132 million deaths globally, with a significant increase from 1990. In East and Southeast Asia, cirrhosis incidence is notably high, with a 13% increase in prevalence since 2000.

Pulmonary hypertension (PH), a severe condition affecting the cardiovascular system, has become better understood over the past 25 years, yet remains challenging to study due to its varied causes and treatment approaches. Specialised PH clinics are recommended to enhance patient outcomes and research. Portopulmonary hypertension (PoPH), as well as hepatopulmonary syndrome (HPS), are serious issues in patients with CLD, impacting functional status and survival. HPS is characterised by pulmonary vasodilation and hypoxaemia, while PoPH develops right heart failure through rising pulmonary vascular resistance[2].

Despite the advances in understanding PH and its link to CLD, complications like ascites and hepatic encephalopathy remain prevalent. Identifying and managing pulmonary arterial hypertension (PAH) in patients with CLD is crucial, and The purpose of this study is to determine the prevalence along with clinical characteristics of PH in this population.

Aim and Objectives

To estimate the prevalence of pulmonary hypertension and compare its clinical profile in patients with chronic liver disease in a tertiary care hospital.

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Methods

This hospital-based cross-sectional investigation had been performed with 150 patients diagnosed with chronic liver disease with pulmonary hypertension who attended the outpatient and inpatient department of the Medicine Department, over 18 months from January 2023 to June 2024, after obtaining consent from the patients.

Inclusion Criteria

Age >14 years with patients of chronic liver disease with pulmonary hypertension. Chronic liver disease is diagnosed in patients using both clinical evaluation and radiological criteria.

Exclusion Criteria

Patients of chronic liver disease with associated malignancy other than hepatocellular carcinoma, Budd-chiari syndrome, recent abdominal surgery (within 3 months.), abdominal trauma, patients having pulmonary artery hypertension due to any other cause.

All patient data was preceded and entered in an Excel sheet and examined utilizing SPSS (Statistical Package for Social Sciences) version 23.0 for the Windows. The arithmetic mean ± standard deviation was employed to display quantitative data. Qualitative data was presented as frequencies (percentages). For variables, parametric and non-parametric tests were applied as required. The two groups' category variables were compared employing the chi-square test. Student t test or else ANOVA (Analysis of variance) was used to assess group variation over time. P-values less than 0.05 had been regarded as statistically significant.

Table I: Distribution of the studied patients based on variables.

Variable		Number of patients (n=150)	Percentage
Alcoholic	Yes	118	78.7
	No	32	21.3
HCV	Positive	0	0.0
	Negative	150	100.0
HBsAg	Positive	48	32.0
	Negative	102	68.0

Table II: Child-Pugh score of patients.

Child-Pugh Score	Number of patients (n=150)	Percentage
Grade A	39	26.0
Grade B	39	26.0
Grade C	72	48.0

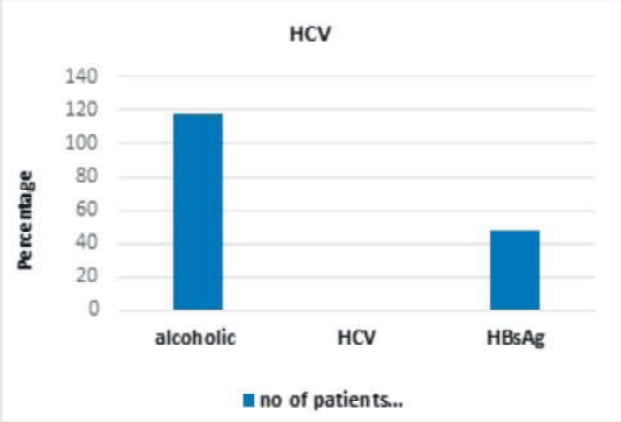

Fig. 1: *Distribution of the studied patients based on variables.*

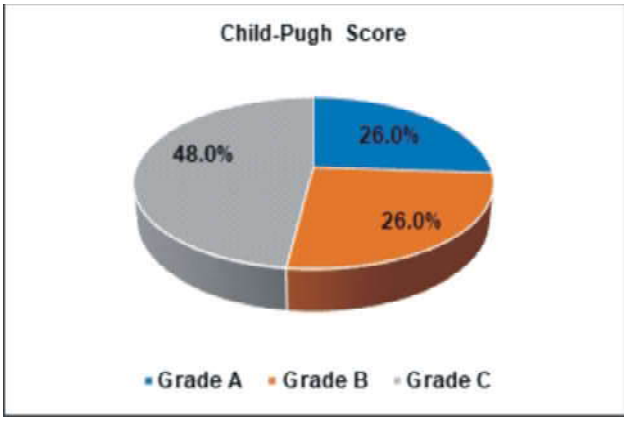

Fig. 2: *Child-Pugh Score of patients.*

Table III: Pulmonary hypertension prevalance in patients with chronic liver disease.

Pulmonary hypertension (Echo Findings)		Number of patients (n = 150)	Percentage
No		120	80.0
Yes	Mild	10	6.7
	Moderate	20	13.3

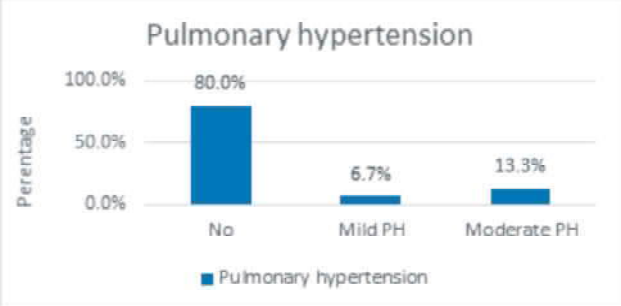

Fig. 3: *Pulmonary hypertension.*

Table IV: Compare the clinical profile of pulmonary hypertension with chronic liver disease

Pulmonary hypertension (Echo Findings)	Child-Pugh Score			p-value
	Grade A (n=39)	Grade B (n=39)	Grade C (n=72)	
No	39 (100.0%)	27 (69.2%)	54 (75.0%)	**<0.001**
Mild	0 (0.0%)	2 (5.1%)	8 (11.1%)	
Moderate	0 (0.0%)	10 (25.6%)	10 (13.9%)	

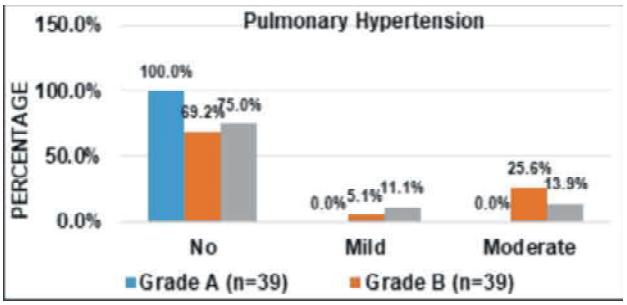

Fig. 4: *Clinical profile comparison of pulmonary hypertension with chronic liver disease.*

Results

- The study analysed 150 patients, revealing that maximum had been aged 41 - 50 years (40.7%), having mean age of 45.55 ± 9.8 years. Most patients were male (79.3%).
- Socio-economically, most patients were from the lower class (40.0%), followed by upper lower (25.3%), lower middle (17.3%), and upper middle (17.3%) classes, with no patients in the upper class.
- The majority lived in rural areas (75.3%).
- Alcohol use was prevalent in 78.7% of patients, while HCV was absent and 32.0% tested positive for HBsAg. (Table I) (Fig. 1).
- 46.0% of cases had mild ascites, 39.3% had moderate ascites, 13.3% had severe ascites, and 1.3% had no ascites at all.
- According to the Child-Pugh score, 26.0% of patients were in Grade A and Grade B, while 48.0% were in Grade C (Table II) (Fig. 2).
- USG findings indicated splenomegaly in 86.6% of cases, and altered liver echotexture in all patients.
- Portal vein diameter averaged 13.17 ± 17 mm. 64.0% of cases with upper GI endoscopy had Grade 1 oesophageal varices, 31.3% had Grade 2, as well as 4.7% had Grade 3.
- Pulmonary hypertension was present in 20.0% of patients, with 6.7% having mild and 13.3% moderate PH (Table III) (Fig. 3).
- The prevalence of pulmonary hypertension was substantially correlated with rising Child-Pugh scores; a p-value of less than 0.001 indicated statistical significance (Table IV) (Fig. 4).

Discussion

In our study, 78.7% were alcoholics and there were no HCV-positive cases whereas HbsAg-positive were in 32.0% of cases. Also, mild ascites were in 46.0% followed by moderate in 39.4%, absent in 13.3% and severe in 1.3%. Our findings were supported by Khadka *et al* reporting that Ascites were present in 4 (10.53%) cases, and coagulopathy in 2 (5.26%) cases[4]. Enenche *et al* reported that 40.0% of cases had ascites[5]. Rekha and Sushmitha reported that many patients had a history of chronic alcohol usage[6].

In our study, patients are distributed on the basis of child-pugh score and it had been found that Grade A and Grade B cases had been 39.0% each whereas Grade C was in the majority of cases with 48.0%. Also, it was found that splenomegaly was positive in 130 (86.6%) of the studied cases and altered liver echotexture was in all the cases. The mean portal vein was 13.17 ± 17 mm. Our findings were in concordance with outcomes of Lamba *et al* who made reporte that class B child-pugh score was in majority of the cases (54.5%) followed by A and C with 22.7% each[3]. Likewise, Gurghean AV and Tudor IA reported that utilizing the child-pugh functional classification, the degree of hepatic cirrhosis was evaluated[7].

In this study, upper GI endoscopy shows that oesophageal varices (grade 1) were in 64.0% followed by large oesophageal varices (grade 2) in 31.3% and small oesophageal varices (grade 3) in 4.7%. Chaudhary *et al*[1] have investigated the results in the upper gastrointestinal tract of individuals who have portal hypertension and liver cirrhosis. 51 (57.3%) of the patients in their research, oesophageal varies, had upper gastrointestinal haemorrhage, which is a significant cause[8].

In our study, pulmonary hypertension was seen in 30 cases out of 150 cases (20.0%) out of those positive cases 6.7% had mild PH and 13.3% had moderate PH. The association between pulmonary hypertension and child-pugh score shows that if the child-pugh score increases (indicating more severe liver disease), the likelihood of having pulmonary hypertension also increases. This is particularly evident in the transition from Grade A to Grades B and C, with many patients in Grades B and C experiencing mild-to-moderate PH. The p-value of <0.001 confirms that these differences

are statistically significant. Our findings were in concordance with outcomes of Lamba *et al* who made reporte that three of the19 patients with CPS Grade C had moderate-severe PAH, and fourteen of the patients had mild PAH. Compared to child classes B and A, it was shown that child class C had higher rates of pulmonary arterial hypertension[3]. In comparison to prior research, the strong and clinically correlated relationship between CPS and PAH was discovered Punekar *et al* discovered class A comprised 43.0% of cases, class B included 45.0%, and class C included 12% of cases based on the CPS for the severity of cirrhosis. The length of chronic liver illness increases the frequency of heart problems[9].

Gurghean AV and Tudor IA in their study concluded that Twenty per cent of the patients suffering from portal hypertension – that is, 27 from a total of 116 – developed pulmonary hypertension[7].

According to Enenche *et al* of the subjects, 64 (30.5%) had pulmonary hypertension. Ten (4.8%) of the 64 (30.5%) patients with pulmonary hypertension had moderate pulmonary hypertension, and 54 (25.75%) had mild pulmonary hypertension. Severe pulmonary hypertension was not present in any subject[5].

Duration of chronic liver illness increases the frequency of heart problems. In Lamba *et al* study, among the instances of PAH, pericardial effusion was observed to occur in just 3% of cases and diastolic dysfunction in about 42.0% of cases, which is greater than the research conducted by Punekar and Thakur[94] where the incidences of pericardial effusion (22.0%), systolic dysfunction (6.0%), diastolic dysfunction (32.0%), and pulmonary arterial hypertension (6.0%) were recorded[3,9]. Balde discovered that among individuals with liver cirrhosis, there was no meaningful relation between CPS and echocardiographic alterations[10]. The results aligned with the research conducted by Ghayumi where he observed that 40.0% of patients had diastolic dysfunction, 32.7% had pulmonary artery hypertension, 47.3% had left ventricular hypertrophy, and 3.6% had pericardial effusion. This might be a result of the reduced sample size we used[11].

Conclusion

According to the study's findings, pulmonary hypertension is rather common among patients with CLD. There was a 20.0% prevalence. A straight forward and non-invasive method for identifying pulmonary hypertension In patients with CLD is trans-thoracic echocardiography. In the Uttar Pradesh area, alcohol addiction is the most frequent cause of CLD (preventable cause). Further research is needed to validate the strong correlation between the severity of underlying liver illness and the prevalence of pulmonary hypertension.

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REVIEW ARTICLE

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Prognostic Role of Dynamic Serum Lipid Profile Alterations in Acute Respiratory Failure: A Scoping Review

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Abstract

Background: Acute respiratory failure (ARF) is a critical condition commonly triggered by infectious or inflammatory insults to the lungs. Recent studies have highlighted that systemic inflammation during ARF can lead to significant alterations in serum lipid metabolism, yet their prognostic utility remains underexplored.

Objectives: To systematically map the current evidence on serum lipid profile alterations in ARF and assess their prognostic significance.

Methods: A scoping review was conducted following PRISMA-ScR guidelines. Literature searches were performed in PubMed, Scopus, Embase, and Web of Science for studies published between January 2015 and March 2025. Eligible studies included those reporting changes in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), or triglycerides (TG) in ARF patients, including COVID-19-associated ARDS. Extracted data focused on lipid trends, disease severity, inflammatory markers, and mortality outcomes.

Results: Eighteen studies involving over 6,000 patients were included. Most studies reported significant reductions in HDL-C and LDL-C during acute illness, particularly in severe COVID-19. Low HDL-C levels were frequently associated with elevated inflammatory markers, increased ICU admission, mechanical ventilation, and mortality. Some studies identified composite ratios like monocyte-to-HDL-C and platelet-to-HDL-C as stronger prognostic indicators than individual lipids. Triglyceride changes were inconsistent but appeared to correlate with cytokine activation. Persistently low lipid levels during recovery were linked to adverse outcomes.

Conclusion: Alterations in serum lipids, especially reduced HDL-C and LDL-C, may serve as valuable prognostic markers in ARF. Incorporating lipid monitoring into clinical protocols could enhance risk stratification and patient management.

Key words: Acute respiratory failure, lipid profile, HDL-C, LDL-C, prognosis, scoping review.

Introduction

Acute respiratory failure (ARF) is a life-threatening condition characterised by the failure of lungs to maintain adequate oxygenation or carbon dioxide elimination, resulting from diverse pulmonary or systemic insults such as pneumonia, acute respiratory distress syndrome (ARDS), or sepsis[1,2]. It remains a leading cause of intensive care unit (ICU) admissions globally and is associated with high rates of morbidity and mortality, particularly in vulnerable populations with co-morbidities like diabetes and cardiovascular disease[3].

In recent years, especially during the COVID-19 pandemic, there has been a growing interest in identifying reliable, cost-effective prognostic biomarkers that could assist in early stratification of ARF severity and outcomes. While traditional indicators like the PaO_2/FiO_2, ratio, APACHE II, and SOFA scores are widely used, they may not fully capture the complex metabolic and immunological changes that occur during acute illness[4].

Among emerging biomarkers, alterations in serum lipid profiles have drawn significant attention. Lipids, including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG), are known to undergo marked changes during systemic inflammatory responses[5-7]. HDL-C, in particular, plays an essential role in modulating inflammation, neutralizing endotoxins, and protecting against oxidative damage. Hypocholesterolaemia, especially low HDL-C, has been repeatedly associated with worse clinical outcomes in patients with severe infections and respiratory failure[8-10].

These lipid alterations may occur rapidly and are thought to

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be mediated by inflammatory cytokines, altered hepatic synthesis, and increased vascular permeability. Figure 1 illustrates the proposed mechanistic pathways linking systemic inflammation in ARF to dynamic changes in lipid metabolism and immune dysregulation.

The COVID-19 pandemic further underscored the clinical relevance of lipidomics. Studies consistently report that patients with severe SARS-CoV-2 infection experience profound reductions in HDL-C and LDL-C, which often correlate with inflammatory marker elevation, critical illness, and increased mortality[11-13]. Moreover, composite indices such as monocyte-to-HDL-C and platelet-to-HDL-C ratios have been proposed as novel prognostic markers, offering additional insight beyond conventional lipid values[14-16].

Despite emerging evidence, data remain scattered across different populations and ARF aetiologies. To date, no synthesis has comprehensively mapped the spectrum of lipid profile alterations in ARF or critically examined their prognostic value across diverse clinical settings.

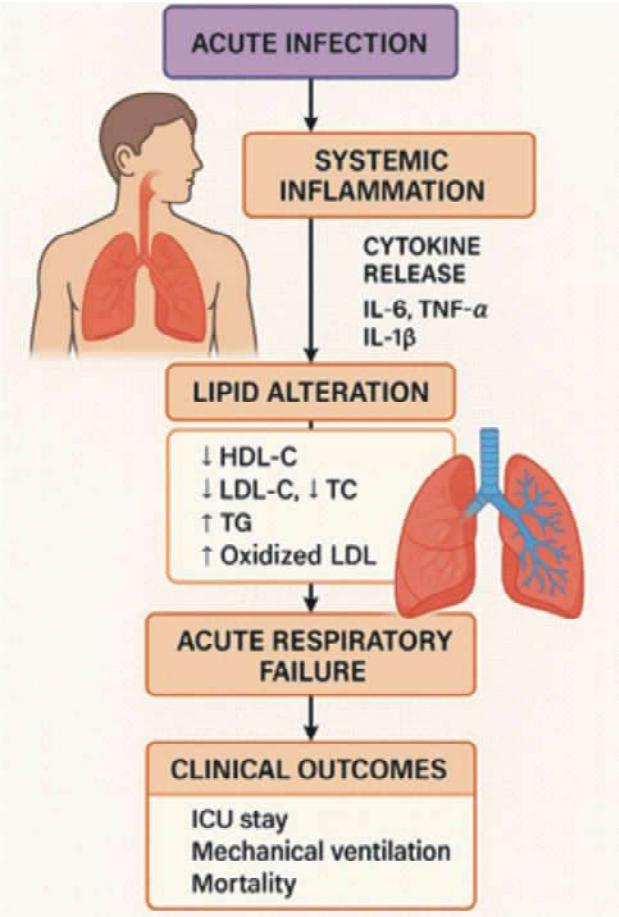

Fig. 1: *Illustrates how acute infections trigger systemic inflammation affecting lipid profiles by lowering HDL-C, LDL-C, TC levels while raising TG levels; these changes interfere with surfactant function and alveolar-capillary integrity leading to ARF.*

This scoping review aims to consolidate available research on dynamic serum lipid changes in ARF, evaluate their association with clinical outcomes, and highlight knowledge gaps requiring future investigation.

Methods

This review was structured as a scoping study using the PRISMA-ScR checklist to ensure transparency and methodological rigor. The review question was framed using the Population-Concept-Context (PCC) strategy recommended by the Joanna Briggs Institute. We focused on identifying and mapping research that explored changes in lipid profiles – such as HDL-C, LDL-C, total cholesterol, triglycerides, and ApoA-I – and their link to outcomes in patients with acute respiratory failure (ARF) and related lung conditions including COVID-19, COPD, asthma, and interstitial lung disease. Studies were included if they were published in English between 2005 and 2025, involved human participants, and provided original data on serum lipid values along with relevant clinical outcomes such as ICU admission, ventilation requirement, or death. Review articles, animal studies, and those lacking lipid data or prognostic endpoints were excluded. We searched four electronic databases – PubMed, Scopus, Embase, and Google Scholar – using specific keywords and controlled vocabulary related to lipid biomarkers and respiratory failure. The search strategy was refined to retrieve both recent and foundational studies. Two reviewers screened all articles independently, reviewing titles, abstracts, and full texts. Any disagreements were resolved through discussion or consultation with a third reviewer. Additional studies were identified by reviewing the references of selected papers. A data charting form was used to extract key study details. Due to variability in study designs and outcome measures, a descriptive synthesis was conducted. No ethical approval was necessary as only publicly available literature was used.

Results

Study Selection: Out of 4,310 records from PubMed/MEDLINE (n = 1,230), Scopus (n = 1,500), Embase (n = 1,020), and Google Scholar (n = 560), 1,160 duplicates were removed. After title and abstract review, 3,150 articles were excluded for not meeting inclusion criteria. A total of 185 full-text articles were screened for eligibility. Of these, 166 were excluded based on criteria such as no serum lipid data (n = 54), no prognostic outcomes (n = 48), non-original studies (n = 32), ineligible study types (n = 21), and duplicated cohorts (n = 11). Ultimately, 18 studies met all inclusion criteria for the final review.

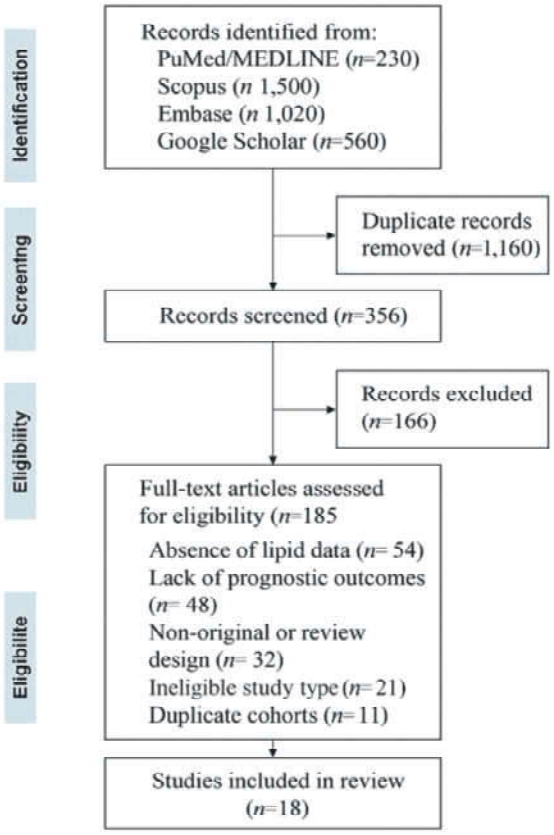

Fig. 2: *PRISMA 2020 flow diagram showing the study selection process[9].*

Overview of Included Studies: All the 18 studies included (from 2005 through 2025) were published during this period indicating a worldwide interest in the prognostic value of lipid-based biomarkers in respiratory diseases. These were conducted in a wide variety of clinical settings and with a range of patient populations, including those with COVID-19, asthma, COPD, ILD, lung cancer, LRTIs, diabetic retinopathy, and NAFLD. A minority of studies looked at the relationship between lipid levels and severe COVID-19, progression and mortality (HDL-C, LDL-C, TC and TG) (Table I).

Table I: Overview of included studies.

Parameter	Details
Number of studies included	18
Timeframe	2005 - 2025
Geographic spread	Studies from North America, Europe, Asia, and the Middle East
Study designs	Observational (n = 16); Prospective cohort (n = 1); Retrospective/cross-sectional (n = 2)
Clinical settings	ICU, inpatient wards, outpatient pulmonary clinics
Sample sizes	Ranged from 60 to over 3,000 patients
Target populations	COVID-19, asthma, COPD, ILD, lung cancer, LRTIs, diabetic retinopathy, NAFLD

Characteristics of Included Studies: The 18 studies reviewed were diverse in design, population, and clinical focus, mostly observational, examining serum lipid biomarkers (TC, LDL-C, HDL-C, TG) in lung-related diseases. Geographically, they spanned the US, China, Turkey, Mexico, Sweden, India, and more. Settings ranged from ICUs and emergency wards (mainly for COVID-19 and ARF) to outpatient clinics for chronic diseases like asthma, COPD, diabetic retinopathy, and NAFLD. Prognostic parameters included mortality, ICU admission, ventilation, severity scores (SOFA, APACHE II), and hospital stay. Emerging biomarkers like monocyte-HDL-C and platelet-HDL-C ratios were also noted.

Distribution by Diagnosis of Respiratory Disease: Underlying disease was the unit of analysis, yielding 18 studies included for analysis. The majority (n = 9) focused on COVID-19, featuring uniformly low levels of HDL-C, LDL-C, and TC, and high levels of TG-associated with death, risk of ICU admission, and need for ventilation. In asthma-based studies (n = 2) LDL-C was inversely correlated with mortality, monocyte-to-HDL-C and platelet-to-HDL-C ratios were strong predictive factors. One study on COPD identified stage-specific lipidomics signatures. Two studies on ILD and one on LRTI (n = 2) found decreased HDL-C and ApoA-I as predictors of dryness and death. The lung cancer study found modified TG/HDL-C ratios, whereas DR and NAFLD studies focused on systemic lipid derangements influencing respiratory consequences. These findings reinforce the potential utility of lipid biomarkers as prognostic markers in a broad range of respiratory diseases (Table III).

Patterns of Lipid Alteration and Prognostic Implications: Lipid changes had uniformly significant relationships with the severity of disease type under different respiratory diseases. HDL-C, LDL-C, and total cholesterol were decreased significantly in most cases with severe symptoms, which was indicative of systemic inflammation and obvious hepatic impairment. Higher triglycerides implied a higher inflammatory load and multiorgan failure. Interestingly, composite ratios such as monocyte: HDL-C and platelet:HDL-C showed better predictive performance, with more improvements seen in the asthma population. These findings emphasize the importance of lipid indices in clinical risk assessment (Table IV).

Table II: Characteristics and key findings of the 18 included studies.

Author (Year)	Study Design	Setting/Population	Lipid Biomarkers Studied	Outcomes Assessed	Key Findings
Mireia *et al* (2021)	Observational study	Patients with LRTIs (CAP and COVID-19)	TC, LDL-C, HDL-C, TG	Prognosis and mortality	Low TC, LDL-C, HDL-C linked to worse outcomes, esp. COVID-19
Wen *et al* (2024)	Retrospective cohort study	3,233 asthmatic adults (NHANES 2005 - 2018)	LDL-C, HDL-C, TG, TC	All-cause mortality	1 mmol/L ↑ in LDL-C = 17% ↓ mortality
Barman *et al* (2022)	Retrospective cross-sectional study	COVID-19 patients in Turkey (n >200)	TC, LDL-C, HDL-C, TG	Mortality and in-hospital outcomes	TC, LDL-C, HDL-C lower in COVID-19; HDL-C predictive of mortality
Ochoa-Ramírez *et al* (2024)	Observational study	100 COVID-19 patients	TC, HDL-C	Disease severity and mortality	Low HDL and high TC linked to COVID-19 mortality
Ochoa-Ramírez *et al* (2020)	Observational study	COVID-19 patients in Mexico	TC, LDL-C, HDL-C, TG	Clinical diagnostic significance	Significant lipid changes suggest diagnostic use in COVID-19
Gruber, Maja *et al* (2009)	Observational study	LRTI patients	TC, HDL-C	Prognosis	Low HDL-C and TC predict poor outcomes in LRTIs
Guyi *et al* (2020)	Observational study	COVID-19 patients	HDL-C	Severity and survival	Low HDL-C linked to COVID-19 severity/mortality
Arslan *et al* (2021)	Observational study	COVID-19 patients	TC, LDL-C, HDL-C, TG	Disease severity	Lipid alterations correlate with COVID-19 severity
Karolyn *et al* (2021)	Observational study	COVID-19 patients	TC, LDL-C, HDL-C, TG	Mortality	LDL <50 mg/dL and TG >150 mg/dL linked to COVID-19 mortality
Radwan *et al* (2024)	Prospective cohort study	Cancer patients with LRTIs	TC, HDL-C	Mortality	Low HDL-C linked to mortality in cancer + LRTIs
Zhang *et al* (2025)	Cohort study	Asthma patients	Monocyte-HDL-C ratio	Mortality	High monocyte/HDL-C ratio linked to higher asthma mortality
Liu *et al* (2024)	Observational study	Diabetic retinopathy patients	LPAR3, Calponin	Disease progression	LPAR3 and CNN1 levels differ in diabetic retinopathy
Barbara *et al* (2022)	Observational study	COVID-19 patients	Various lipid biomarkers	Medium-term clinical outcomes	Lipid profiles altered post-COVID with persistent symptoms
Zhao *et al* (2025)	Cohort study	Asthma patients	Platelet-HDL-C ratio	Elevated BEOC levels	High platelet/HDL-C ratio linked to elevated BEOC in asthma
Jiang *et al* (2024)	Observational study	NAFLD patients	Various lipid biomarkers	Lipid profile alterations	Gut therapy alters lipids in NAFLD patients
Fang *et al* (2020)	Observational study	Marine phytoplankton	Lipid biomarkers	Microbial community structure	Lipid output varies by environment in phytoplankton
Ding *et al* (2022)	Observational study	Swedish cohort	Blood lipid levels	Atrial fibrillation	Midlife lipid levels linked to atrial fibrillation
Liu *et al* (2021)	Observational study	COPD patients	Serum lipid species	Disease progression	Lipidomic profile changes linked to COPD stages

Patterns of Lipid Alteration and Prognostic Implications: Lipid changes had uniformly significant relationships with the severity of the disease type under different respiratory diseases. HDL-C, LDL-C, and total cholesterol were decreased significantly in most cases with severe symptoms, which was indicative of systemic inflammation and obvious hepatic impairment. Higher triglycerides implied a higher inflammatory load and multiorgan failure. Interestingly, composite ratios such as monocyte: HDL-C and platelet:HDL-C showed better predictive performance, with more improvements seen in the asthma population. These findings emphasize the importance of lipid indices in clinical risk assessment (Table IV).

Table III: Included studies by disease category, main lipid findings, and outcomes.

Disease Category	No. of Studies (n=18)	Key Lipid Biomarkers Affected	Observed Trends	Primary Prognostic Outcomes
COVID-19	9	HDL-C, LDL-C, TG, TC	↓ HDL-C, ↓ LDL-C, ↓ TC in severe cases; ↓ TG	Mortality, ICU admission, ventilator support
Asthma	2	LDL-C, HDL-C, Monocyte-HDL-C ratio, Platelet-HDL-C ratio	LDL-C inversely related to mortality; ↓ Monocyte/HDL-C and Platelet/HDL-C ratios	Mortality, eosinophilia (BEOC)
COPD	1	Serum lipidomic signatures	Distinct lipid patterns by disease stage	Stage-based progression monitoring
ILD/LRTI	2	HDL-C, ApoA-I, TC	↓ HDL-C and ApoA-I; ↓ TC as inflammatory marker	Fibrosis, mortality
Lung Cancer	1	TG, HDL-C	↑ TG/HDL-C ratio	Systemic inflammation, clinical deterioration
DR/NAFLD	2	Lipidomic-inflammatory pathways	Altered lipid profiles linked to metabolic-pulmonary dysfunction	Increased respiratory vulnerability, inflammation

Table IV: Summary of lipid alteration patterns and associated prognostic outcomes.

Lipid Marker / Ratio	Trend Observed	Clinical Associations	Notable Studies
HDL-C	↓ in most severe/fatal cases	ICU admission, mortality, ventilation	Gruber (2021), Wu (2021), Arslan (2021)
LDL-C	↓ in advanced stages	Systemic inflammation, poor outcomes	Wen (2024), Barman (2022), Ochoa-Ramírez (2021)
Total Cholesterol (TC)	↓ in COVID-19 and ILD	Fibrotic progression, stress response	Mosaad (2021), Liu D (2020)
Triglycerides (TG)	↑ in inflammatory states	ICU need, multiorgan dysfunction	Wu (2021), Ding Liu (2020), Arslan (2021)
Monocyte-to-HDL-C Ratio	↑ in asthma	Mortality risk, immune activation	Zhang Q (2025)
Platelet-to-HDL-C Ratio	↑ in asthma	Eosinophilic inflammation, poor prognosis	Zhang Y (2025)

Timing of Lipid Measurements: The timing of lipid assessments varied significantly across studies, affecting comparability and clinical interpretation. Most studies measured lipid levels at hospital or ICU admission, providing early prognostic insights. However, few studies included longitudinal profiling, which could better reflect disease dynamics and treatment responses. Studies like Wu (2021), Liu D (2024), and Barbara J (2022) showed that serial lipid measurements offered valuable information on disease progression and recovery. The lack of standardised timing across studies remains a key limitation (Table V).

Table V: Timing of lipid measurements and longitudinal assessment in included studies.

Study Author (Year)	Timing of Lipid Measurement	Longitudinal Assessment
Gruber M (2021)	At hospital admission	No
Wen J (2024)	Baseline (NHANES registry)	No
Barman HA (2022)	At admission + pre-infection values	Partially
Mosaad (2021)	At hospital admission	No
Ochoa-Ramírez (2021)	Acute phase (hospitalisation)	No
Ding Liu (2020)	Acute infection phase	No
Lee C (2020)	At admission	No
Arslan (2021)	At admission	No
Wu M (2021)	Admission + ICU course	Yes
Radwan S (2024)	Hospital stay	Yes
Zhang Q (2025)	Baseline registry values	No
Liu D (2024)	Longitudinal trends (DR progression)	Yes
Barbara J (2022)	Pre- and post-COVID recovery	Yes
Zhang Y (2025)	Registry baseline values	No
Jiang H (2024)	Before and after microbial therapy	Yes
Fang M (2020)	During environmental exposure	No
Ding M (2022)	Midlife baseline	No
Liu D (2021)	Stage-based comparison	Yes

Clinical Outcomes Assessed

The prognostic utility of serum lipid alterations was examined across various clinical outcomes in the included studies. Mortality was the most frequently assessed endpoint (n = 14), with consistent associations observed between reduced HDL-C and LDL-C levels and increased death risk. ICU admission (n = 6) was commonly linked to elevated triglyceride levels and low HDL-C, indicating heightened disease severity. The requirement for mechanical ventilation (n = 5) was associated with significant dyslipidemia, particularly hypertriglyceridaemia. Additionally, composite severity scores – such as SOFA and APACHE II – were used in 7 studies to objectively quantify systemic involvement; patients with abnormal lipid profiles often exhibited

higher scores. These findings highlight the value of lipid parameters not only in disease monitoring but also in early prognostic risk stratification across a range of respiratory conditions. The distribution of these clinical outcomes across the reviewed studies is visually represented in Fig. 3.

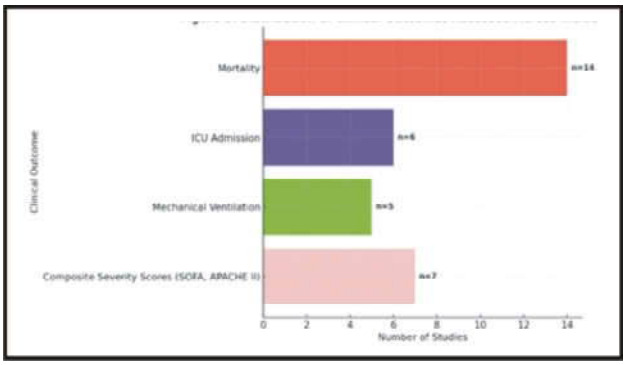

Fig. 3: *Distribution of clinical outcomes assessed across included studies.*

This horizontal bar chart highlights the frequency with which each clinical outcome was assessed across the 18 included studies. Mortality was the most evaluated endpoint (n = 14), followed by composite severity scores (n = 7), ICU admissions (n = 6), and the need for mechanical ventilation (n = 5). Lipid biomarkers – especially HDL-C, LDL-C, and TG – were significantly associated with these outcomes, reinforcing their prognostic value in acute respiratory conditions.

Geographical and Ethnic Variability: The 18 studies included were conducted in various regions of the world: most in China (n = 5), followed by the USA and Turkey (n = 2 per country). LDL-C and TG were different between ethnic groups in only one study (Wen *et al*, 2024). The majority did not have subgroup analysis, thereby restricting generalisability. HDL-C, TG were low in the regional trends of Chinese COVID-19/asthma cases and TC was abnormal in Turkish and Egyptian ones. These tendencies reveal the necessity for ethinicity-based cut-off points of lipid parameters (Table VI).

Emerging Biomarkers and Techniques

Novel lipid biomarkers have been recently identified in respiratory diseases. Lipidomics, composite ratios (monocyte/HDL-C, platelet/HDL-C) and ApoA-I have been found to have prognostic significance in asthma, COPD, and post-COVID states. Combined lipidomic-transcriptomic approaches may complement precision diagnostics and risk stratification irrespective of the disorder (Table VII).

Table VI: Geographical and ethnic variability in lipid biomarker studies.

Study Author (Year)	Country/ Region	Ethnic Stratification Reported	Comments on Baseline Lipids
Gruber M (2021)	Austria	No	Lower HDL-C in severe COVID cases
Wen J (2024)	USA	Yes (NHANES multiracial)	Ethnic differences noted in LDL-C and TG
Barman HA (2022)	Turkey	No	Low HDL-C in Turkish ICU patients
Mosaad (2021)	Egypt	No	Elevated TC predictive in Egyptian cohort
Ochoa-Ramírez (2021)	Mexico	No	TC/LDL-C patterns in Latin American population
Wu M (2021)	China	No	Low TG and HDL-C in COVID/asthma
Zhang Q (2025)	China	No	Novel HDL-C ratios in asthma cohort
Barbara J (2022)	USA	No	Persistent dyslipidemia in post-COVID survivors
Zhang Y (2025)	China	No	Eosinophil-lipid ratio in Chinese asthma group
Liu D (2024)	China	No	Longitudinal lipid data in DR with respiratory overlap
Liu D (2021)	China	No	COPD-specific lipidomics in Chinese patients
Arslan (2021)	Turkey	No	Severe dyslipidemia patterns in Turkish patients

Evidence Gaps Identified: Despite growing interest in lipid-based prognostic markers for respiratory diseases, significant gaps persist. Studies employed diverse lipid panels without standardised thresholds, hindering comparability and clinical application. Most relied on single-timepoint measurements, lacking longitudinal data. Advanced tools like lipidomics and AI are underutilized in practice. Ethnic stratification was infrequent, and key groups – such as pediatric and ILD subpopulations – were underrepresented. These gaps underscore the need for multicenter, standardised, and technology-driven research to validate lipid biomarkers for clinical use.

Table VII: Emerging biomarkers and diagnostic techniques in lipid-based respiratory research.

Study Author (Year)	Biomarker/Technology Investigated	Clinical Disease Context	Methodological Platform	Key Findings / Clinical Utility
Liu D (2021)	Lipidomics profiling (mass spectrometry)	COPD	Mass spectrometry-based lipidomic mapping	Stage-specific lipidomic signatures correlated with COPD severity
Zhang Q (2025)	Monocyte-to-HDL-C ratio	Asthma	Integrated immuno-lipid composite marker	Stronger mortality prediction in asthma
Zhang Y (2025)	Platelet-to-HDL-C ratio	Asthma	Inflammatory platelet-lipid interaction index	Prognostic implications for eosinophilic asthma

				phenotypes
Liu D (2024)	LPAR3 expression and CNN1 co-expression	Diabetic retinopathy with respiratory overlap	Transcriptomic and lipidomic co-analysis	Experimental targets linking metabolic inflammation to pulmonary vulnerability
Barbara J (2022)	ApoA-I and HDL subfractions	Post-COVID-19 syndrome	Serological proteomics and HDL subfractionation	Correlated with persistent post-COVID inflammation

Discussion

This scoping review highlights the emerging importance of dynamic alterations in serum lipid profiles as potential prognostic markers in patients with acute respiratory failure (ARF). Across various clinical contexts – including bacterial pneumonia, viral pneumonitis, COVID-19-related ARDS, asthma, and chronic obstructive pulmonary disease – consistent patterns of lipid disturbances have been documented. These alterations reflect both the metabolic consequences of systemic inflammation and the body's acute phase response to severe illness.

A predominant finding across studies is the significant decline in high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) during the acute phase of respiratory failure. These changes are not merely incidental but correlate with markers of disease severity, including higher inflammatory burden, increased need for mechanical ventilation, prolonged ICU stay, and increased mortality. The reduction in HDL-C, in particular, appears to be an early and sensitive indicator of poor prognosis, as this lipoprotein exerts anti-inflammatory, antioxidant, and endothelial-stabilizing effects that are critical during systemic illness. Its depletion suggests ongoing immune dysregulation and impaired vascular protection[17-21].

In contrast, triglyceride levels demonstrate greater variability, influenced by nutritional status, hepatic insulin resistance, and the degree of cytokine activation. In some cohorts, elevated triglyceride levels are associated with worse outcomes, potentially indicating underlying metabolic derangement and heightened systemic inflammation. Total cholesterol levels also tend to decline significantly during acute illness, and persistent hypocholesterolemia beyond the acute phase has been linked with delayed recovery and chronic inflammation[22,23].

Emerging research suggests that composite lipid-immune indices – such as the monocyte-to-HDL-C ratio or platelet-to-HDL-C ratio – may serve as more powerful prognostic tools than single lipid measurements. These indices integrate immune cell dynamics with lipid metabolism and have shown better correlation with mortality and disease progression in several forms of ARF, including those driven by COVID-19 and asthma[24]. Such ratios reflect a broader inflammatory phenotype and may guide risk stratification in the critical care setting.

Mechanistically, acute inflammation and infection lead to significant alterations in lipid metabolism through multiple pathways[25-28]. Pro-inflammatory cytokines downregulate hepatic production of apolipoproteins, suppress lipoprotein synthesis, and enhance lipid oxidation. Simultaneously, acute phase reactants such as serum amyloid A displace structural proteins on HDL particles, rendering them dysfunctional and pro-inflammatory. These dysfunctional HDL particles lose their protective role and may contribute to worsening endothelial injury and oxidative stress[29-31].

Lipidomic studies further extend this understanding by revealing specific changes in lipid subclasses, including sphingolipids, phospholipids, and ceramides, which are associated with immune activation, lung injury, and coagulation abnormalities. Such findings suggest that lipidomic profiling may not only serve diagnostic and prognostic roles but also reveal therapeutic targets in ARF management[32,33]. A few recent studies have shown that certain lipidomic signatures correlate strongly with ICU mortality, disease severity, and systemic inflammatory response, even outperforming traditional clinical markers[34,35].

Despite promising findings, several challenges limit the clinical translation of lipid biomarkers. The timing of lipid measurement in relation to disease onset varies across studies, and longitudinal data on lipid normalisation or persistence post-illness is limited. Moreover, differences in assay methods, patient populations, and concurrent treatments introduce variability in results. It is also unclear how medications commonly used in ARF management – such as corticosteroids, immunosuppressants, or lipid-modifying agents – affect these lipid changes and their interpretability[36-39].

Future studies should prioritize standardised measurement protocols, incorporate serial lipid profiling, and evaluate the additive prognostic value of lipid indices when combined with established clinical scoring systems. There is also a need to explore whether modifying lipid profiles therapeutically can influence outcomes in ARF, such as through the use of statins, omega-3 fatty acids, or reconstituted HDL formulations.

Conclusion

This review highlights the prognostic value of dynamic serum lipid changes (HDL-C, LDL-C, TGs, and composite ratios) in acute respiratory infections (ARI) and related conditions. Lipid abnormalities were linked to outcomes like death, ICU admission, mechanical ventilation, and severity scores. Despite promising findings, the literature is heterogeneous with nonuniform lipid profiles and measurement times. Novel biomarkers and tools like lipidomics show promise but need validation. Future research should focus on standardisation, longitudinal follow-up, and leveraging omics-based findings for improved patient outcomes.

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REVIEW ARTICLE

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Cardiac Sarcoidosis: A Clinical Review

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Abstract

Cardiac sarcoidosis represents one of the most consequential manifestations of systemic sarcoidosis, associated with significant morbidity and mortality. This review examines the epidemiology, pathophysiology, clinical presentation, diagnostic approach, and management of cardiac sarcoidosis, illustrated by a clinical case. We challenge the traditional framing of sarcoidosis as primarily a respiratory disease and highlight the importance of recognising cardiac involvement, which may occur in isolation or precede pulmonary manifestations. Contemporary diagnostic advances, particularly cardiac magnetic resonance imaging and 18 F-fluorodeoxyglucose positron emission tomography-computed tomography (FDG-PET/CT), have transformed our ability to detect and monitor cardiac disease. Management remains largely eminence-based, though emerging evidence supports aggressive immunosuppression with corticosteroids and steroid-sparing agents. We discuss the role of implantable cardiac defibrillators, risk stratification using advanced imaging, the importance of serial monitoring with soluble interleukin-2 receptor and FDG-PET/CT imaging, and the emerging use of tumour necrosis factor inhibitors for refractory disease.

Case Presentation

A 44-year-old man was brought to the emergency department following an out-of-hospital cardiac arrest. Paramedics reported ventricular tachycardia responsive to defibrillation. Initial investigations were largely unremarkable: chest radiograph was normal, electrocardiogram showed non-specific T-wave changes, and routine blood tests were within normal limits apart from mildly elevated C-reactive protein and raised troponin.

A further episode of ventricular tachycardia in the emergency department proved refractory to initial defibrillation, necessitating amiodarone infusion. Following stabilisation, computed tomography (CT) of the chest revealed bilateral hilar lymphadenopathy without parenchymal lung abnormalities. Transthoracic echocardiography demonstrated mild left ventricular systolic impairment with an ejection fraction of 45%, basal septal hypokinesis, and normal right ventricular function.

Coronary angiography showed no significant atherosclerotic disease. Cardiac magnetic resonance imaging (cMRI) demonstrated multifocal late gadolinium enhancement (LGE) in a non-ischaemic pattern, predominantly affecting the basal interventricular septum with extension to the right ventricular aspect – a distribution highly characteristic of cardiac sarcoidosis. There was associated myocardial oedema on T2-weighted imaging, suggesting active inflammation. Soluble interleukin-2 receptor was markedly elevated at 4,322 U/mL.

He was commenced on pulse methylprednisolone followed by oral prednisolone 40 mg daily. An implantable cardiac defibrillator was inserted. Endobronchial ultrasound-guided biopsy of an enlarged mediastinal lymph node revealed non-caseating granulomatous inflammation, supporting a diagnosis of cardiac sarcoid. 18 F-fluorodeoxyglucose positron emission tomography/CT (FDG-PET/CT) demonstrated high avidity within the myocardium corresponding to the areas of LGE on MRI, along with avid lymph nodes in the mediastinum alongside multiple skeletal, splenic, and hepatic lesions. Notably, there was no significant atrial FDG uptake.

Detailed occupational and environmental history revealed that he had worked in the building industry for over twenty years, with frequent exposure to silica insulation dusts, often without appropriate respiratory protection. He was a non-smoker with no family history of autoimmune disease or cardiomyopathy.

He was discharged on methotrexate 20 mg weekly with a tapering prednisolone regimen. At three-month follow-up, his implantable defibrillator had not discharged and echocardiography showed improvement in left ventricular ejection fraction to 52%. However, soluble interleukin-2 receptor remained elevated, and repeat FDG-PET/CT demonstrated persistent myocardial avidity, indicating inadequate suppression of inflammation. Treatment was escalated by adding intravenous infliximab at a dose of 5 mg/kg every eight weeks.

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At 12-month follow-up, FDG-PET/CT demonstrated complete suppression of myocardial avidity with resolution of extracardiac lesions, and soluble interleukin-2 receptor had fallen to within the normal range. Left ventricular ejection fraction had normalised at 58%. At two years of follow-up, he remains well with no ICD discharges and no symptoms on combination maintenance infliximab and 10mg weekly methotrexate.

Epidemiology

Population Incidence and Prevalence

The epidemiology of cardiac sarcoidosis has changed substantially in recent decades due to advances in diagnostic imaging. Data from Finland demonstrate a greater than 20-fold increase in annual detection rates between 1988 and 2012, with prevalence reaching approximately 2.2 per 100,000 adults[1]. By 2021, estimated prevalence had risen to 14 cases per 100,000 population[2].

In the United States, systemic sarcoidosis prevalence is approximately 35.2 cases per 100,000 population, with substantial geographic clustering[3]. The incidence is significantly higher in Black Americans compared with White Americans (35.5 versus 10.9 per 100,000 annually), with the Black Women's Health Study reporting an annual incidence as high as 71 per 100,000 and prevalence approaching 2%[4,5].

In England, a recent population-based study using linked primary care data identified 18,554 incident cases between 2003 and 2023, with age- and sex-standardised incidence increasing from 6.65 to 7.73 per 100,000 person-years[6]. Mortality was significantly elevated compared with the general population, with standardised mortality ratios of 1.8 in males and 2.1 in females.

A Danish registry study comparing 11,834 patients with sarcoidosis to matched population controls demonstrated excess cardiovascular risk at the population level[7]. Ten-year risks were elevated for heart failure (3.18% versus 1.72%), ventricular arrhythmias and cardiac arrest (0.96% versus 0.45%), pacemaker implantation and conduction disease (0.94% versus 0.51%), and atrial fibrillation (3.44% versus 2.66%). All-cause mortality was also increased (10.88% versus 7.43%). These data underscore the importance of cardiac surveillance in all patients with sarcoidosis.

Limited epidemiological data are available from South Asia. Sarcoidosis was historically considered rare in India, though increasing recognition suggests this may reflect under-diagnosis rather than true low prevalence[8]. Most available evidence comes from hospital-based series in tertiary centres, which may not be population-representative. These reports indicate that extrapulmonary manifestations, including cardiac involvement, may be more common than previously appreciated.

Challenging the Respiratory-Centric View

Historically, sarcoidosis has been framed as primarily a respiratory disease. This perspective warrants re-examination. The traditional emphasis on pulmonary disease reflects significant surveillance bias: sarcoidosis has been diagnosed predominantly by respiratory physicians, and the literature reflects patients seen in respiratory services.

Contemporary data suggest that a substantial proportion of patients do not have parenchymal lung disease but have significant involvement of other organs. The Finnish data, where two-thirds presented with clinically isolated cardiac disease, exemplify this point[1]. Importantly, cardiac involvement carries major prognostic significance and may surpass pulmonary disease in its impact: in an older study from Japan, cardiac sarcoidosis was found to account for up to 85% of sarcoidosis-related death[9].

The proportion of patients with systemic sarcoidosis who have cardiac involvement depends critically on detection methods. Clinical manifestations are encountered in only approximately 5% of patients[10]. However, when advanced imaging is employed, 20 - 25% demonstrate cardiac involvement[11]. Autopsy studies reveal even higher rates: 20-29% in the United States and 58-70% in Japanese series[9]. This discrepancy underscores the occult nature of much cardiac disease.

Importantly, up to half of cardiac sarcoidosis cases present as isolated cardiac disease without clinically apparent extracardiac involvement at diagnosis[1]. With systematic investigation, however, more than 80% of what are initially thought to be isolated cardiac cases are ultimately found to have extracardiac disease[12].

Environmental and Occupational Exposures

The aetiology of sarcoidosis remains incompletely understood, though epidemiological evidence suggests a role for environmental exposures in genetically susceptible individuals. Occupational exposures to inorganic dusts merit particular attention. The ACCESS study identified elevated odds of sarcoidosis among individuals with occupational exposure to insecticides, agricultural employment, and mould or mildew[13]. A Swedish registry study demonstrated increased risk among workers exposed to silica and other mineral dusts[14]. In the United States, sarcoidosis clusters have been reported among firefighters, particularly following the World Trade Center disaster[15].

The case presented illustrates the importance of obtaining a detailed occupational history. The patient's prolonged

exposure to inorganic dusts in the building industry, without adequate respiratory protection, represents a plausible environmental trigger. While such exposures cannot be proven to be causative in individual cases, identifying them serves two purposes: it may support the diagnosis of sarcoidosis in ambiguous cases, and it has implications for occupational health advice regarding future exposure avoidance.

Clinicians should actively enquire about occupational exposures to dusts (particularly silica and construction materials), agricultural work, and firefighting. A history of working in environments with poor ventilation or inadequate respiratory protection is relevant. These exposures are not included in diagnostic criteria but may increase clinical suspicion for sarcoidosis in patients presenting with compatible syndromes.

Pathophysiology

Cardiac sarcoidosis results from granulomatous infiltration of the myocardium. The non-caseating granulomas comprise epithelioid cells, multinucleated giant cells, and a surrounding rim of lymphocytes. These granulomas arise from a dysregulated T-cell immunological response with activation of type 1 T-helper cells and upregulation of cytokines including tumour necrosis factor-alpha, interferon-gamma, and interleukin-2[2]. The disease progresses through an active inflammatory phase, which may evolve to fibrosis and scarring.

The clinical manifestations depend upon location and extent of infiltration. Granulomas involving the basal interventricular septum may cause conduction abnormalities. Ventricular myocardial infiltration creates a substrate for arrhythmias through both active inflammation and scar formation. Extensive involvement may lead to ventricular dysfunction and heart failure.

Anatomical Distribution

The interventricular septum is the most frequently affected region in cardiac sarcoidosis. The basal septum is involved in approximately one-third of cases at autopsy and represents the most common site of involvement on cardiac MRI, where it may be the sole site of involvement[16,17]. The predilection for the basal septum explains the strong association between cardiac sarcoidosis and atrio-ventricular conduction disease. Enhancement involving the right ventricular aspect of the septum may produce a characteristic "hook" appearance, while a "basal inferoseptal triangular" pattern is considered highly suggestive of cardiac sarcoidosis[18]. In terms of myocardial layer distribution, subepicardial and mid-wall patterns predominate (approximately 40% and 30% respectively), while subendocardial and transmural enhancement are less common[19]. Crucially, the pattern does not correspond to coronary artery territories, helping to distinguish cardiac sarcoidosis from ischaemic heart disease. Differentiation from other forms of myocarditis is more challenging; sarcoidosis tends to favour the basal septum, whereas viral myocarditis more often involves the inferolateral subepicardial wall[20,21].

The most typical pattern on FDG PET/CT is a heterogeneous, multifocal distribution of focal inflammation throughout the left ventricle, with or without right ventricular involvement, that does not conform to a coronary artery territory (Fig. 1). Perfusion imaging can be used as an adjunct to interpretation and typically demonstrates reduced perfusion at sites of active inflammation. Although this multifocal pattern is most characteristic, a wide range of distributions may occur. Less common patterns, such as diffuse right ventricular and multifocal septal involvement, are rare but recognised manifestations of cardiac sarcoidosis and have been described on both cardiac MRI and FDG-PET/CT(Fig. 2)[22,23].

Pericardial involvement is uncommon and usually occurs through direct extension from adjacent myocardial inflammation, while clinically significant pericarditis is rare[24]. Atrial involvement may occur and is associated with an increased risk of atrial arrhythmias, particularly atrial fibrillation[25]. Involvement of the papillary muscles can lead to valvular dysfunction.

Patient Characteristics

Sarcoidosis classically presents between 25 and 60 years. Recent studies have identified two incidence peaks: the third and fourth decades, and women over 50 years[26]. Cardiac sarcoidosis presents at a mean age of around 50 years. Age is clinically important when evaluating rhythm disturbances; in younger patients, idiopathic fibrosis of the conduction system is uncommon, therefore high-grade atrioventricular block in individuals under 60 years should prompt investigation for secondary causes, including sarcoidosis.

Ethnicity plays a significant role in both occurrence and phenotypic expression. Cardiac involvement appears particularly prevalent in Japanese populations, where autopsy studies demonstrate higher rates of cardiac granulomas[9]. In the United States, Black patients are more likely to present with symptomatic heart failure compared with White patients, while ventricular arrhythmias are more frequent in males[27]. Black patients have more frequent multiorgan involvement, with odds ratios exceeding 3 for multiple organ system disease[28]. The reasons for these disparities remain largely unknown.

Clinical Presentation

The clinical manifestations of cardiac sarcoidosis can be categorised into three broad syndromes: conduction abnormalities, arrhythmias, and heart failure. Many patients remain asymptomatic, with cardiac involvement detected only through screening or incidentally.

Conduction Abnormalities

Conduction disease represents the most common clinical manifestation, found in 23 - 30% of patients with myocardial involvement[29]. High-grade atrioventricular block (Mobitz II or complete heart block) is characteristic. The predilection for the basal interventricular septum, which contains the atrioventricular node and bundle of His, explains this prevalence. At diagnosis, right bundle branch block is seen in 26 - 43% of cases[2].

A key clinical question is how often unexplained conduction block in young and middle-aged adults is due to sarcoidosis. The Finnish pacemaker registry provides compelling data: among 72 patients aged 18 - 55 years with initially unexplained second- or third-degree atrioventricular block, biopsy-verified cardiac sarcoidosis or giant cell myocarditis was found in 19% and 6% respectively[30]. A Canadian study found cardiac sarcoidosis in 34% of patients aged 18 - 60 years with unexplained high-grade block[31].

These data carry important implications: any patient under approximately 60 years presenting with unexplained high-grade atrioventricular block should be systematically evaluated for cardiac sarcoidosis. The Heart Rhythm Society specifically recommends screening in patients younger than 60 with unexplained Mobitz II or third-degree block[32].

Ventricular Arrhythmias

Ventricular tachycardia and ventricular fibrillation are life-threatening manifestations. As illustrated by the case presented, ventricular tachycardia may be the presenting feature, including in the context of cardiac arrest. These arrhythmias arise from re-entrant circuits created by patchy myocardial scarring interspersed with areas of inflammation

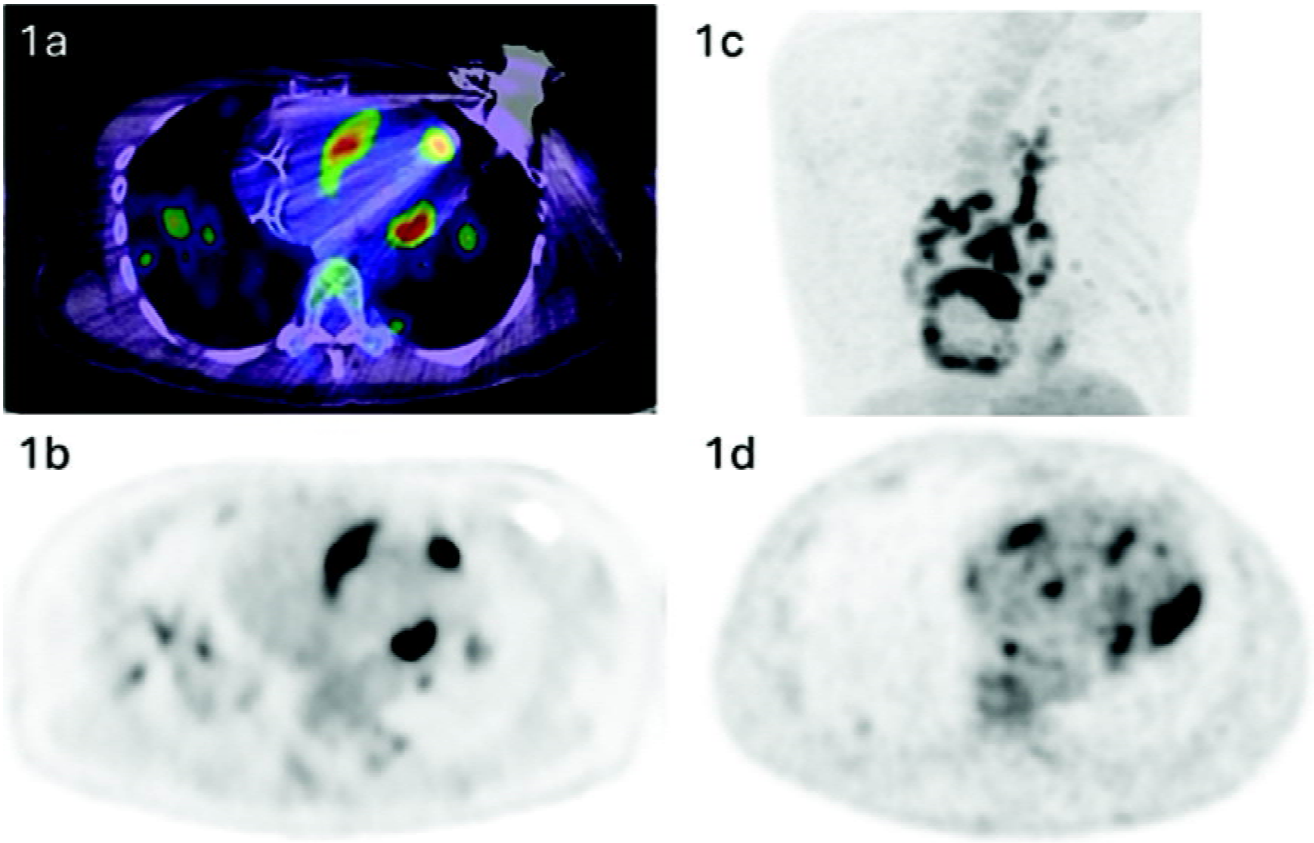

Fig. 1: *FDG-PET/CT patterns in cardiac sarcoidosis. (a) Axial fused PET/CT and (b) axial PET images from a patient with an implantable cardioverter-defibrillator (ICD), demonstrating multifocal left ventricular FDG uptake with FDG-avid pulmonary nodules. The presence of an ICD precludes cardiac MRI assessment, highlighting the role of serial FDG-PET/CT in monitoring treatment response and disease activity. (c) Maximum intensity projection (MIP) and (d) axial PET images from a second patient, showing the typical pattern of heterogeneous, multifocal biventricular FDG uptake with foci of atrial involvement. FDG-avid mediastinal and hilar lymphadenopathy is also seen, illustrating the ability of PET to identify extracardiac biopsy targets.*

and normal tissue. Right ventricular free wall involvement and multifocal myocardial enhancement on cardiac MRI are associated with a substantially increased risk of ventricular arrhythmias.

Sudden cardiac death may be the first manifestation of sarcoidosis, which is an under recognised cause of sudden death in young adults. Data from the Finnish registry indicate a 9% five-year risk of sudden cardiac death even in patients presenting solely with atrioventricular block and preserved left ventricular ejection fraction greater than 50%[33]. This finding has important implications for device therapy decisions, as discussed below.

Atrial Arrhythmias

Although ventricular arrhythmias dominate discussions of cardiac sarcoidosis, supraventricular arrhythmias do occur and can be clinically significant. In a retrospective study of 100 patients with definite or probable cardiac sarcoidosis followed for a mean of 5.8 years, the prevalence of supraventricular arrhythmias was 32%, with atrial fibrillation being the most frequent[34]. Left atrial enlargement on echocardiography was the strongest predictor of supraventricular arrhythmia development.

Recent data suggest that FDG-PET/CT may identify patients at risk of atrial fibrillation. In a study of 118 patients who were in sinus rhythm at cardiac sarcoidosis diagnosis, atrial FDG uptake was an independent risk factor for incident atrial fibrillation: 55% of those with atrial uptake developed atrial fibrillation within five years compared with 18% of those without[35]. This observation has potential implications for anticoagulation decisions and rhythm monitoring strategies.

Heart Failure

Heart failure may result from extensive granulomatous infiltration causing ventricular dysfunction. Both dilated and restrictive patterns can occur. Left ventricular systolic dysfunction is present in approximately half of patients with cardiac sarcoidosis at the time of their diagnosis[1]. Right ventricular dysfunction may result from direct infiltration or pulmonary hypertension, which may be secondary to pulmonary disease or left ventricular failure. Importantly, heart failure has the potential to improve with immunosuppressive therapy when active inflammation predominates over irreversible scarring, a distinction that can be assessed by cardiac MRI and perfusion imaging.

Heart failure appears more prevalent among Black patients and women compared with White patients and men[27]. Clinicians should consider cardiac sarcoidosis in cases of unexplained cardiomyopathy, particularly in younger patients.

What Cardiac Sarcoidosis Does Not Typically Cause

Equally important is understanding atypical features. Pericarditis and clinically significant pericardial effusions are uncommon (although autopsy evidence of silent

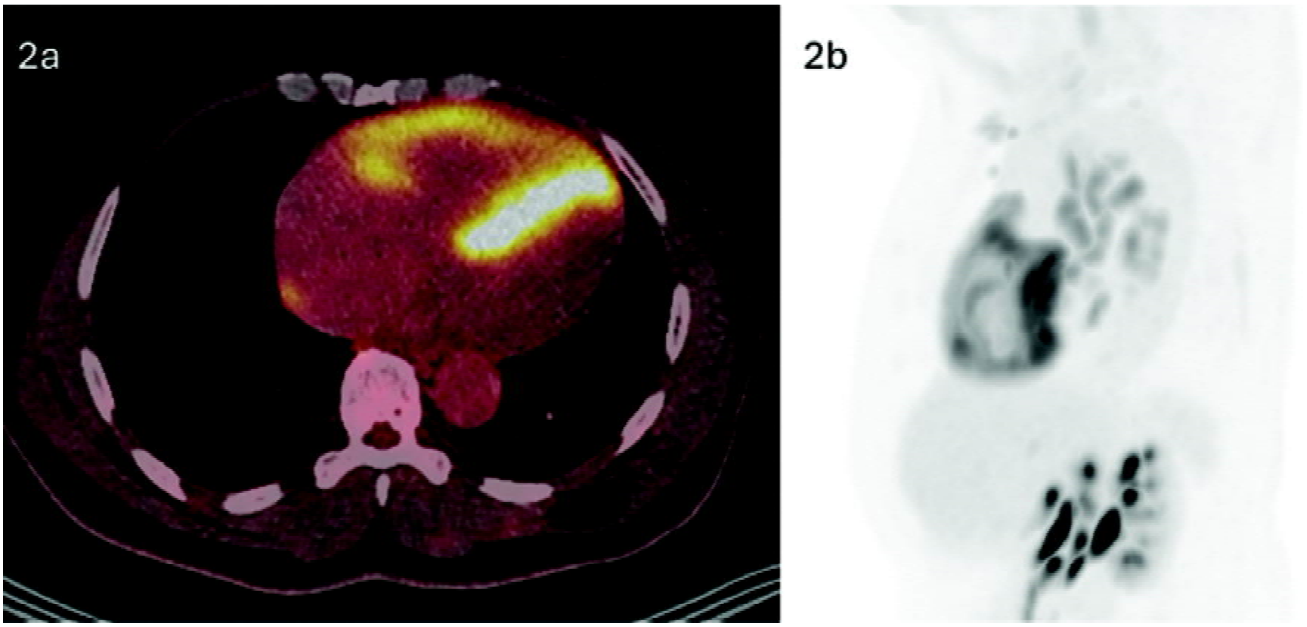

Fig. 2: *FDG-PET/CT in cardiac sarcoidosis demonstrating a rare but recognised pattern of diffuse right ventricular and septal FDG uptake. (a) Axial fused PET/CT image showing intense FDG avidity along the right ventricular free wall and interventricular septum. (b) Maximum intensity projection (MIP) image confirming diffuse cardiac uptake and demonstrating FDG-avid mediastinal and hilar lymphadenopathy.*

pericardial involvement is not infrequent)[24,36]. Valvular lesions are rare. Coronary arteritis does not typically occur and coronary angiography, in the absence of concurrent cardiovascular risk factors, is characteristically normal. Large vessel involvement such as aortitis is unusual. Significant aortitis should prompt consideration of alternative diagnoses including giant cell arteritis, Takayasu arteritis, and IgG4-related disease[37].

Diagnostic Approach

The diagnosis of cardiac sarcoidosis is supported by the demonstration of non-caseating granulomatous inflammation in involved tissue, combined with a compatible clinical syndrome. In practice, obtaining cardiac tissue confirmation is challenging, and clinicians frequently rely upon extra-cardiac tissue diagnosis with compatible cardiac findings.

Recognising the Possibility of Cardiac Sarcoidosis

Several features should heighten clinical suspicion. Cardiac manifestations typically follow a non-ischaemic pattern, with abnormalities that do not respect coronary artery territories on imaging. Age is also informative: a younger patient with high-grade atrioventricular block or unexplained ventricular arrhythmias warrants active investigation. Extracardiac clues are frequently present. Mediastinal or hilar lymphadenopathy and inflammatory eye disease (particularly uveitis) should strengthen suspicion. All patients in whom cardiac sarcoidosis is suspected should undergo formal ophthalmic examination.

Systematic Assessment for Multiorgan Involvement

If cardiac sarcoidosis is suspected, systematic search for involvement of other organ systems is warranted. FDG-PET/CT imaging allows comprehensive mapping of disease activity across multiple organs. PET/CT may reveal uptake in lung parenchyma, lymph nodes, liver, spleen, bone, joints, muscles, salivary glands and other organs. In our service, we additionally screen for endocrine involvement, in particular hypothalamic-pituitary involvement.

This systematic approach serves two purposes: it may identify more accessible sites for tissue diagnosis than the heart, and it defines the extent of systemic disease with implications for prognosis and management.

The Diagnostic Pitfall: Coincidental Granulomas

A critical diagnostic hallenge relates to interpretation of granulomatous inflammation. Sarcoidosis may present asymptomatically with mediastinal lymphadenopathy and can remain clinically silent for many years without consequence. This becomes particularly important when evaluating cardiac presentations. Consider a patient presenting with heart failure and mediastinal lymphadenopathy showing granulomas. It would be tempting to conclude cardiac sarcoidosis is the cause. However, the underlying cardiac pathology could instead represent an inherited cardiomyopathy in an individual with coincidental, previously asymptomatic extra-cardiac sarcoidosis. The presence of extracardiac granulomas should therefore be regarded as supportive evidence within the appropriate clinical context, rather than definitive proof of cardiac involvement.

Cardiac Imaging

Cardiac MRI and FDG-PET/CT have transformed diagnosis and management. Cardiac MRI with gadolinium-based contrast agents may demonstrate myocardial oedema on T2-weighted sequences (suggesting active inflammation), LGE (reflecting fibrosis or inflammation), wall motion abnormalities, and impaired left ventricular function. Sensitivity is 75 - 100%, and specificity is 76 - 78%[38].

FDG-PET/CT detects metabolically active inflammatory tissue. Suppression of physiological cardiac glucose uptake through dietary preparation and fasting to induce a mild ketotic state and suppress physiological myocardial glucose uptake via insulin dependent GLUT-4 transporters is essential. 24 hours of ketogenic diet should suppress myocardial FDG uptake in 80% of patients and 72 hours of ketogenic diet will achieve 95% suppression rates. FDG-PET/CT has the advantage of imaging the whole body, revealing extracardiac disease and providing biopsy targets.

A key distinction relates to monitoring treatment response. Cardiac MRI demonstrates fibrosis through LGE, which represents established scar and does not regress with immunosuppression. MRI can also detect myocardial oedema on T2-weighted imaging reflecting active inflammation however, its sensitivity and reproducibility for serial monitoring are more limited. In contrast, FDG-PET directly demonstrates metabolically active inflammation and is generally preferred for assessing inflammatory activity and monitoring response to immunosuppressive therapy. The joint Society of Nuclear Medicine and Molecular Imaging and American Society of Nuclear Cardiology 2017 Expert Consensus[39] the 2024 American Heart Association (AHA) position statement[2] recommend the use of repeat FDG PET/CT to ensure adequate response to therapy within 3 - 6 months of commencing immunosuppression.

Perfusion imaging can help identify areas of reduced perfusion due to inflammation and/or scar that do not correspond to a coronary artery territory. In the 2024 AHA scientific statement on cardiac sarcoidosis imaging, the

sensitivity and specificity of any FDG uptake pattern are reported as 100% and 33%, respectively[2]. In contrast, more typical imaging patterns, such as multifocal non-contiguous FDG-avid perfusion defects or myocardial FDG uptake in the presence of typical extracardiac sarcoidosis, have a sensitivity of 83% and specificity of 100%. In the absence of biopsy confirmation or extracardiac features of sarcoidosis, our experience is that diagnostic uncertainty often remains, and neither 100% sensitivity nor specificity is achieved with PET or other advanced imaging modalities.

Endomyocardial Biopsy

Endomyocardial biopsy (EMB) remains the gold standard but has important limitations. Patchy distribution means sensitivity is only 20 - 30% even with multiple biopsies[32]. Yield can be improved by targeting imaging abnormalities or using electro-anatomical mapping. Major complications include cardiac perforation, tamponade, and arrhythmia (1 - 5% risk)[40]. Given the low sensitivity and associated risks, EMB is typically reserved for uncertain cases.

In practice, diagnosis is usually established by demonstrating non-caseating granulomas in extra-cardiac tissue combined with compatible cardiac imaging. This approach is endorsed by the Heart Rhythm Society consensus statement[32]. However, awareness of the aforementioned diagnostic pitfalls is crucial; this is part of the art of diagnostic medicine.

Soluble Interleukin-2 Receptor

Soluble interleukin-2 receptor (sIL-2R) has emerged as a useful biomarker. Serum levels are elevated in active sarcoidosis and correlate with disease activity[41]. Sensitivity and specificity for diagnosing sarcoidosis are approximately 88% and 85% respectively, superior to angiotensin-converting enzyme[42]. In cardiac sarcoidosis, elevated sIL-2R is associated with worse outcomes. We measure soluble sIL-2R levels at diagnosis and monitor them serially during treatment as a biomarker of disease activity and therapeutic response.

Differential Diagnosis

The differential diagnosis of cardiac presentations attributable to sarcoidosis requires a systematic evaluation for alternative causes, including other granulomatous diseases, inherited conditions, infections, and malignancy.

Tuberculosis: The Critical Distinction

In endemic regions including the Indian subcontinent, the most important differential diagnosis is tuberculosis. Both conditions cause granulomatous inflammation and distinguishing them has profound implications for management. The histopathological distinction rests on caseation: tuberculous granulomas classically demonstrate central caseous necrosis, whereas sarcoid granulomas are non-caseating. However, this distinction is not absolute. Non-caseating granulomas may be seen in tuberculosis, particularly in early or treated disease.

Clinical and laboratory features aid differentiation. Tuberculosis is typically associated with greater burden of constitutional symptoms, positive tuberculin skin test or interferon-gamma release assay, and identification of acid-fast bacilli on microscopy or culture. In practice, when tuberculosis cannot be excluded, many clinicians will commence anti-tuberculous therapy before considering immunosuppression for sarcoidosis. Immunosuppressing a patient with unrecognised tuberculosis carries serious consequences.

Although pulmonary involvement is most typical, tuberculosis can also affect the heart. Cardiac involvement may manifest as pericarditis or, less commonly, myocarditis. Pericardial involvement is more characteristic of tuberculosis than sarcoidosis[43]. Large pericardial effusions and constrictive physiology should raise particular concern for a tuberculous aetiology.

Other Infectious Causes

Several other infections warrant consideration. Rheumatic fever, though declining in developed countries, remains an important cause of cardiac disease in India and other parts of South Asia[44]. Rheumatic carditis primarily affects the valves rather than the myocardium, but differentiation may be required in patients with both valvular and myocardial abnormalities.

Viral myocarditis can present with ventricular arrhythmias and cardiomyopathy, though the acute presentation and preceding viral prodrome usually distinguish it from sarcoidosis[45]. In patients from Latin America, Chagas disease should be considered[46]. Lyme carditis is relevant in endemic regions of North America and Europe, presenting with fluctuating high-grade atrioventricular block[47].

Inherited Cardiomyopathies

With increasing availability of genetic testing, inherited cardiomyopathies have become essential considerations in the differential diagnosis of cardiac sarcoidosis. This is particularly relevant for patients presenting with apparent isolated cardiac disease without extracardiac manifestations.

Desmoplakin cardiomyopathy is an excellent example. Caused by mutations in the gene encoding desmoplakin, this arrhythmogenic cardiomyopathy is characterised by episodic myocardial injury, left ventricular fibrosis, and high

incidence of ventricular arrhythmias – features that overlap substantially with cardiac sarcoidosis[48]. Crucially, desmoplakin cardiomyopathy can present with myocarditis-like episodes associated with troponin elevation and myocardial inflammation on FDG-PET/CT, leading to misdiagnosis as cardiac sarcoidosis. The cardiac MRI findings can be similar, with subepicardial and mid-wall LGE.

Lamin A/C cardiomyopathy also shares clinical features with cardiac sarcoidosis, including conduction system disease, atrial arrhythmias, ventricular arrhythmias, and dilated cardiomyopathy[49]. The combination of atrioventricular block with atrial arrhythmias and mild ventricular dilatation in a younger patient should prompt consideration of laminopathy.

Distinguishing features favouring inherited cardiomyopathy over cardiac sarcoidosis include family history of cardiomyopathy or sudden death, absence of extracardiac sarcoidosis despite thorough investigation, and certain ECG patterns (low-voltage QRS complexes and poor R-wave progression may suggest laminopathy).

We are increasingly incorporating genetic testing for arrhythmogenic and dilated cardiomyopathy genes in patients with suspected cardiac sarcoidosis when extracardiac disease cannot be demonstrated, when family history suggests inherited disease, or when the clinical picture is atypical for sarcoidosis. The identification of a pathogenic variant fundamentally changes management, prognosis, and necessitates consideration of cascade screening and risk assessment in family members.

Malignancy

Lymphoma is an important differential, particularly given that both conditions can present with mediastinal lymphadenopathy and cardiac involvement. Pericardial effusion, which is common in cardiac lymphoma but unusual in sarcoidosis, provides a helpful distinguishing feature[50]. Extensive lymphadenopathy, hepato-splenomegaly, and constitutional symptoms should heighten suspicion for lymphoma. When lymph node biopsy is performed, the pathologist should specifically exclude lymphomatous involvement.

Others

In addition to inherited cardiomyopathies and infectious myocarditis, other potential causes of a false positive cardiac sarcoidosis imaging diagnosis include ischaemic hibernating myocardium, recent myocardial infarction, other infiltrative or autoimmune causes of dilated cardiomyopathy and incomplete suppression of physiological myocardial glucose uptake prior to scanning.

Management

The management of cardiac sarcoidosis remains predominantly eminence-based. There are no randomised controlled trials specifically addressing immunosuppressive treatment. Nonetheless, clinical experience strongly supports immunosuppression, and contemporary management involves a tiered approach.

The Case for Immunosuppression

Most clinicians agree that immunosuppression is necessary. In our experience patients with ventricular arrhythmias treated with device therapy alone often continue to experience recurrent discharges, whereas the addition of immunosuppression is associated with improved arrhythmia control. Dramatic improvement in left ventricular function and reversal of atrioventricular block have been reported following immunosuppressive treatment.

A systematic review of 34 retrospective studies found that corticosteroid therapy improved atrioventricular conduction in 43% of treated patients compared with none among untreated patients[51]. Data quality was insufficient to draw firm conclusions regarding impact on ventricular arrhythmias or mortality, but the direction of effect supports treatment. The American Heart Association endorses corticosteroids as first-line treatment for cardiac sarcoidosis with active inflammation[2].

Induction Therapy with Corticosteroids

Our approach for induction therapy involves pulse methylprednisolone, typically 500 mg to 1 g intravenously daily for three days, followed by oral prednisolone. The pulse dose is individualised based on patient factors including diabetes, body weight, and age.

The optimal maintenance dose of oral corticosteroid is uncertain. Practice varies considerably between centres. Some experts recommend starting at 30 mg daily, citing concerns that higher doses (40 - 60 mg daily) are associated with greater adverse effects without clear evidence of superior efficacy. Others, including our group, favour higher initial doses (40 - 60 mg daily, approximately 0.5 - 1 mg/kg) in patients with significant inflammation or clinical instability, tapering to 10 - 15 mg daily over subsequent months. A systematic review found insufficient data to compare dosing regimens[51].

In the case presented, we initiated prednisolone at 40 mg daily given the severity of presentation with cardiac arrest. More modest presentations might reasonably be treated with lower initial doses. What is clear is that prolonged

high-dose corticosteroid therapy should be avoided: the adverse metabolic, skeletal, and infectious consequences are substantial, and steroid-sparing agents should be introduced early to facilitate dose reduction.

Steroid-Sparing Therapy: Methotrexate

Our first-line steroid-sparing agent is methotrexate. The PREDMETH trial demonstrated non-inferiority of methotrexate compared with prednisone for pulmonary sarcoidosis[52]. Evidence from neurosarcoidosis similarly supports efficacy. In a retrospective study of 28 patients with cardiac sarcoidosis treated with methotrexate, 88% demonstrated an initial reduction in cardiac FDG uptake, with complete resolution observed in 60%[53].

We aim for a target dose of 20 mg orally methotrexate once weekly. Dose adjustments are required based on patient characteristics; Japanese patients may require lower doses due to pharmacogenomic factors. Renal function must be carefully considered given methotrexate's renal excretion. Folic acid supplementation is standard. Mycophenolate mofetil represents an alternative steroid-sparing agent with some supporting data, though methotrexate is favoured as first-line[54].

Escalation to Tumour Necrosis Factor Inhibitors

For patients failing corticosteroids and methotrexate, we escalate therapy to a TNF inhibitor, typically infliximab. A multicentre study demonstrated significant reduction in prednisone dose and improvement in cardiac FDG uptake with TNF inhibition[55]. Prednisone decreased from 21.7 mg at initiation to 7.3 mg at 12 months. Among patients with cardiac FDG uptake, 62% showed complete or partial resolution. In the study by Rosenthal and colleagues, adalimumab was added in 19 patients with persistently active disease or methotrexate intolerance, with FDG uptake improvement in 84% and resolution in 63%[53].

An important caveat relates to TNF inhibitors in heart failure. The ATTACH trial demonstrated increased mortality when infliximab was used for non-sarcoid heart failure[56]. However, this concern may not apply to sarcoidosis, where treating the underlying inflammation may improve function. We use infliximab in cardiac sarcoidosis including patients with reduced ejection fraction, with close monitoring with echocardiography and serum NT-proBNP levels, and specialist cardiology input. Cost and availability may limit access to biologic therapy in some settings.

Implantable Cardiac Defibrillators

Implantable cardiac defibrillators play a central role in the management of cardiac sarcoidosis given the substantial risk of ventricular arrhythmias and sudden cardiac death. The indications for ICD implantation have been codified in the 2017 American Heart Association/American College of Cardiology/Heart Rhythm Society guideline, which includes specific recommendations for patients with cardiac sarcoidosis[57].

Secondary Prevention

ICD implantation is unequivocally indicated for secondary prevention in patients who have survived sustained ventricular tachycardia or cardiac arrest, as in the case presented. This group carries the highest risk of recurrent events with annualised rates of recurrent arrhythmia or sudden death approaching 80% in this population[58].

Primary Prevention

For primary prevention, ICD implantation is recommended in patients with cardiac sarcoidosis and left ventricular ejection fraction ≥35% despite optimal medical therapy[59]. This threshold aligns with indications for non-ischaemic cardiomyopathy. However, cardiac sarcoidosis presents a particular challenge: patients with preserved ejection fraction remain at significant risk of sudden death, and reliance on conventional ejection fraction thresholds may be inadequate for risk stratification.

The Heart Rhythm Society consensus statement recommends considering ICD implantation in patients with cardiac sarcoidosis who have syncope of suspected arrhythmic origin or imaging evidence of significant myocardial scar, even with preserved ejection fraction[32]. A study of 290 patients with biopsy-proven sarcoidosis found that LVEF >35% with any LGE had an annualised event rate of 2.1%, rising to 12.0% when LGE exceeded 5.7% of LV mass[58].

Risk Stratification Using Advanced Imaging

Contemporary risk stratification increasingly relies upon advanced imaging findings. LGE on cardiac MRI is associated with increased risk of death and ventricular arrhythmias. Importantly, the pattern of LGE may be as significant as extent: involvement of the right ventricular free wall, multifocal distribution, and subepicardial patterns are associated with particularly high arrhythmic risk[60].

Right ventricular abnormalities on cardiac MRI carry independent prognostic significance. In a study of 290 patients, reduced right ventricular ejection fraction was independently associated with all-cause death, whilst right ventricular LGE was independently associated with sudden cardiac death and significant ventricular arrhythmia[61].

FDG-PET/CT findings also predict adverse events. Patients with both abnormal myocardial FDG uptake and resting perfusion defects have substantially higher rates of ventricular tachycardia and death than those with normal imaging[62]. Right ventricular FDG uptake appears to confer particularly high risk.

Role of Electrophysiological Study

For patients without a clear indication for ICD implantation, electrophysiological study may inform risk stratification. Inducible sustained ventricular tachycardia predicts future arrhythmic events, and some centres use this to guide ICD decision-making in patients with preserved ejection fraction and equivocal imaging findings[63,64]. However, the added value of electrophysiological testing beyond imaging findings remains uncertain and is not routine in our centre.

Pacemaker Indication

For patients with cardiac sarcoidosis requiring permanent pacemaker implantation for high-grade atrioventricular block, our practice is to favour implantation of a device with ICD functionality rather than a pacemaker alone. The Finnish registry demonstrated a 9% five-year risk of sudden cardiac death even among patients presenting with atrioventricular block and preserved ejection fraction above 50%[33]. This risk justifies the additional complexity and cost of an ICD in most cases.

Monitoring Treatment Response

Assessment requires a comprehensive approach that integrates clinical, biochemical, and imaging parameters. We routinely evaluate symptom burden, arrhythmia events, and heart failure status. Device interrogation provides objective documentation of arrhythmia frequency and burden, while serial measurement of sIL-2R serves as a biomarker of inflammatory activity.

FDG-PET/CT is the imaging modality of choice for monitoring. We typically perform FDG-PET/CT at approximately four to six months after treatment initiation to assess response. Persistent cardiac avidity despite treatment indicates inadequate control and should prompt escalation.

Duration of Treatment

The optimal duration of immunosuppressive treatment remains uncertain and represents an important knowledge gap. Unlike some phenotypes of pulmonary sarcoidosis that may remit spontaneously or tolerate treatment withdrawal, cardiac sarcoidosis carries significant risk of relapse upon treatment cessation.

Current evidence and clinical guidelines suggest that treatment should continue for at least one to two years[54]. Our approach is to continue treatment long-term, with shared decision-making regarding the risks and benefits. Serial FDG-PET/CT imaging guides treatment decisions, and treatment de-escalation should not be carried out if myocardial FDG avidity persists. If inflammation has resolved and remains suppressed on serial imaging, cautious de-escalation may be considered. We favour a phased approach: for patients on combination therapy, we would first withdraw the biologic agent while maintaining background methotrexate, with close monitoring for disease recurrence using sIL-2R levels and repeat FDG-PET/CT at approximately six months. Complete treatment withdrawal is undertaken with great caution and close surveillance, typically only after at least two years of sustained remission.

The patient in the case presented remains on maintenance infliximab and low-dose methotrexate at two years, with stable imaging appearances. We have not yet attempted treatment de-escalation given the severity of his initial presentation.

Prognosis

Cardiac sarcoidosis carries significant morbidity and mortality, though outcomes are highly variable depending on clinical presentation, extent of disease, and response to treatment.

Survival Data

The most comprehensive survival data come from the Finnish nationwide study. Among 110 patients with histologically confirmed cardiac sarcoidosis diagnosed between 1988 and 2012, overall transplant-free survival was 99.1% at one year, 93.5% at five years, and 89.3% at ten years[1]. However, outcomes varied substantially by presentation. Patients presenting with heart failure had markedly worse prognosis: transplant-free survival of 90%, 75%, and 52.5% at one, five, and ten years respectively. Patients presenting with arrhythmias or conduction disease had more favourable outcomes.

Prognostic Factors

Several factors predict adverse outcomes in cardiac sarcoidosis. New York Heart Association functional class and left ventricular end-diastolic dimension are independent predictors of death[65].

Advanced imaging findings carry prognostic significance independent of ejection fraction. LGE on cardiac MRI predicts death and ventricular arrhythmias even in patients with preserved ejection fraction[38]. FDG-PET/CT

abnormalities, particularly the combination of perfusion defects with increased FDG uptake, predict adverse cardiac events[62].

Right ventricular involvement, whether manifest as reduced right ventricular ejection fraction or right ventricular LGE, independently predicts adverse outcomes[61]. History of sustained ventricular tachycardia or cardiac arrest identifies patients at highest risk of recurrent arrhythmic events, justifying aggressive device and immunosuppressive therapy.

Prognosis with Treatment

While randomised data are lacking, observational evidence suggests that immunosuppressive therapy improves outcomes in cardiac sarcoidosis. Resolution of inflammation on FDG-PET/CT following treatment is associated with reduced arrhythmic events[66]. Improvement in left ventricular function following immunosuppression is well documented and, in our experience, can be dramatic when treatment is initiated before extensive fibrosis has developed.

The case presented illustrates the potential for excellent outcomes with aggressive multimodality management. Despite presenting with cardiac arrest and multiorgan disease, the patient achieved complete suppression of inflammation, normalisation of ventricular function, and remains free of arrhythmia at two years. Such outcomes are achievable but require prompt recognition, thorough staging, aggressive immunosuppression, appropriate device therapy, and meticulous longitudinal follow-up.

Conclusions

Cardiac sarcoidosis represents a challenging but increasingly recognised manifestation with substantial implications for morbidity and mortality. We must move beyond the traditional framing of sarcoidosis as primarily a respiratory disease. A substantial proportion of patients have significant extrapulmonary involvement, and cardiac disease may occur without parenchymal lung disease.

Clinicians should maintain a high index of suspicion, particularly in younger patients with unexplained arrhythmias, conduction disease, or cardiomyopathy. A detailed occupational history may reveal relevant environmental exposures. In endemic regions, distinguishing sarcoidosis from tuberculosis is the critical first step; immunosuppressing unrecognised tuberculosis carries serious consequences. The finding of granulomatous inflammation should support but not define the diagnosis of cardiac sarcoidosis; genetic cardiomyopathies must be considered when extracardiac disease cannot be demonstrated.

Management centres on immunosuppression combined with device therapy for arrhythmia protection. While evidence from randomised trials is lacking, clinical experience strongly supports corticosteroids, methotrexate, and TNF inhibitors. Risk stratification using advanced imaging informs ICD decisions, particularly in patients with preserved ejection fraction. Serial monitoring with sIL-2R and FDG-PET/CT guides therapy escalation and, eventually, cautious de-escalation.

Future research should focus on evidence-based treatment protocols through randomised trials, biomarkers predicting treatment response, and optimal strategies for treatment duration. In the meantime, a thoughtful, patient-centred approach combining aggressive immunosuppression with careful monitoring can achieve excellent outcomes, as exemplified by the case presented.

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REVIEW ARTICLE

JIACM 2026; 27 (1): 65-68

Approach to A Patient with Vertigo: A Guide For Physicians

Swati Tandon, Vikram Wadhwa**, Ravi Meher****

Abstract

The vestibular system helps to maintain balance and stabilise gaze. Balance is controlled primarily by the cerebellum, which receives input from the vestibular nuclei in the brain stem. This, in turn, receives input from the visual pathway, proprioception and inner ear. The vestibular apparatus (labyrinth) of the inner ear consists of three semicircular canals, and two otolith organs called the utricle and the saccule. Displacements and linear accelerations of the head, are detected by the two otolith organs. Receptors in the semicircular canals respond to the rotational movements of the head. When the head tilts to one side, receptors on the ipsilateral ear are stimulated and receptors in the contralateral ear are inhibited. These receptors send impulses to the brain stem and cerebellum via the vestibular nerve to control balance. Any disruption of this pathway can lead to vertigo[1].

Abnormalities in the vestibular/visual/proprioceptive system can cause symptoms of vertigo. Vertigo due to vestibular system abnormalities may result from damage or dysfunction in parts like the vestibular labyrinth or the vestibular nerve (peripheral causes), or occur due to disturbances in the central vestibular system, specifically in the brainstem and cerebellum[2].

Patients with abnormalities of vestibular system can present with symptoms of vertigo (spinning sensation), dysequilibrium (feeling of imbalance), light-headedness (sensation of giddiness/dizziness) and falls. Targeted history taking, clinical bedside examinations, functional testing of the vestibular system, and imaging are instrumental for correct diagnosis and therapy management. This article will act as a quick guide to help physicians evaluate dizzy patients.

Accurate diagnosis of a patient with vertigo, dizziness, or unsteadiness can be challenging, ranging from acute symptoms in emergency departments to chronic symptoms in outpatient settings. One of the challenges is the heterogeneity of symptoms on clinical presentation and the wide range of etiologies underlying these leading symptoms[3]. Vestibular symptoms can all be caused by a range of general medical, (e.g., hypoglycaemia, anaemia), neurological, (e.g., migraine, epilepsy, dysautonomia, cerebellar and extrapyramidal disorders), cardiovascular, (e.g., orthostatic hypotension, arrhythmias) and psychiatric conditions (e.g., panic attacks, generalised anxiety). These should be kept in mind while evaluating a patient with vestibular symptoms.

According to the International Classification of Vestibular Disorders (ICVD)created by Classification Committee of the Bárány Society (CCBS), a patient presenting with vestibular symptoms can be grouped into three syndromes[4]. These are:-

(i) acute vestibular syndrome (AVS) comprised of monophasic diseases of acute onset lasting days to weeks,

(ii) episodic vestibular syndrome (EVS) encompassing illnesses manifesting recurrent attacks of vestibular symptoms each lasting seconds to days, and

(iii) chronic vestibular syndrome (CVS) including conditions in which symptoms persist for a minimum of 3 months.

The acute vestibular syndrome (AVS) is usually defined as the rapid onset of dizziness or vertigo, nausea or vomiting, head motion intolerance, gait instability, and often nystagmus lasting for at least 24 hours[5]. AVS is the result of an acute unilateral, peripheral or central, vestibular lesion that causes a sudden asymmetry of the normal vestibular nuclei neuronal firing rate[6]. Although most cases of definite AVS are likely to be either vestibular neuritis or stroke, the differential diagnosis can include labyrinthitis, first attack of Meniere's disease or vestibular migraine. It is important, therefore, not to miss stroke as all other are relatively benign causes. Stroke is suspected if the patient presents with associated neurological symptoms such as weakness, dysarthria, sensory changes, ataxia or confusion. Risk factors for vascular disease, including smoking, diabetes, obesity, hypertension and hyperlipidaemia, need to be assessed to rule-out stroke and CVAs, which can lead to vertigo from ischaemia or infarction[1].

Additional symptoms associated with vertigo may originate from a peripheral lesion[7], such as recent viral infection that

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can cause acute labyrinthitis and vestibular neuritis. Finally, it is essential to review a patient's medication prescriptions and social history for any substance or alcohol use. Medications that can impact vestibular function include anticonvulsants, antidepressants and antihypertensive agents.

Episodic vestibular syndrome (EVS) patient presents with recurrent episode of vertigo lasting seconds to days. The differential diagnosis include: BPPV, labyrinthine dehiscence, Meniere's disease and vestibular migraine. These can be due to some trigger or can be spontaneous. Trigger refers to a specific act or situation that provokes or aggravates the symptoms[8]. Bending over, lying down, rolling over in bed, may all trigger short vertigo attacks, typical for BPPV (Benign paroxysmal positional vertigo). Vestibular problems due to BPPV should cause vertigo in particular lying down position, and may also during the upright movement. If problems only occur during the erecting phase, it could be due to orthostatic hypotension. Valsalva manoeuvre, coughing, or loud sounds that cause vertigo can be attributed to perilymphatic fistula or a third mobile window lesion, e.g., the superior semicircular canal dehiscence. Some vertigo attacks occur completely spontaneously, such as those caused by Meniere's disease or vestibular migraine. Presence of associated aural symptoms such as tinnitus and hearing loss suggests Meniere's disease. Clinicians should also enquire about symptoms such as headache, photophobia, and visual auras, as these frequently accompany vestibular migraines.

Distinguishing various timing and triggers of dizziness in patients helps to narrow the differential diagnosis and focus on serious treatable causes. Many medical causes commonly present with episodic dizziness or vertigo, (e.g., cardiac arrhythmia, orthostatic hypotension, transient hypoglycaemia).

Chronic vestibular Disorders (CVS) include Vestibular migraine and Bilateral vestibulopathy which could be due to ototoxic medications, idiopathic, infection, age-related or autoimmune conditions. These patients present with dizziness, postural instability and oscillopsia.

When combined with a comprehensive history, a focused physical examination can help further differentiate between various causes of vertigo. Examination should involve the following[1]:-

- **Eye examination:**
  - **Nystagmus testing:** Nystagmus is quick, jerky, involuntary movements of the eye. Nystagmus has a slow phase (vestibular driven) and fast phase (corrective saccade). Direction of nystagmus is denoted by the direction of fast component. In peripheral lesions, the predominant direction of nystagmus remains the same regardless of the direction of gaze, while central lesions may present with nystagmus that reverses direction[9]. Horizontal gaze direction changing nystagmus, (i.e., right beating nystagmus in right gaze and left beating nystagmus in left gaze) is a hallmark of a central lesion. In addition, the presence of vertical or purely torsional nystagmus is suggestive of central lesions as well[10].
  - **Head Impulse Test (HIT):** A functional vestibular system allows one to maintain gaze during rotation through vestibulo-ocular reflexes (VOR). The head impulse test is a physical examination technique to test VOR. In this exam, patients are asked to fix their gaze on a target such as examiner's nose. The head is turned quickly to the right or left by about 15 degrees. A typical response occurs when the eyes remain on the target. An abnormal response is when the eyes are dragged off the target in the direction of head turning, followed by a corrective saccade back to the target. This response implies a peripheral lesion resulting in a deficient vestibulo-ocular reflex on the side of the head turn (Fig. 1).
  - **Skew Test:** This test involves the examiner covering one eye and observing for a vertical or horizontal shift in the uncovered eye. Central lesions sometimes produce a slight skew deviation (Fig. 2).
    - When the head impulse test is combined with an examination of nystagmus and a test for skew, this is referred to as the Head Impulse-Nystagmus-Test for Skew (HINTS)[6]. A normal head impulse test on both sides with direction-changing nystagmus and/or skew deviation is suggestive of a central lesion. An abnormal head impulse test with unidirectional nystagmus and absent skew deviation strongly suggests a peripheral lesion.

      Note: The HINTS test may be more sensitive for diagnosing acute stroke than magnetic resonance imaging (MRI) within the first 48 hours following symptom onset[6].

    - Neurological examination: A focused neurological examination including gait, balance and coordination needs to be performed. The gait, balance assessment (Romberg's test, Untenberger's test and foam test), and examination for cerebellar signs (such as finger nose test, test for

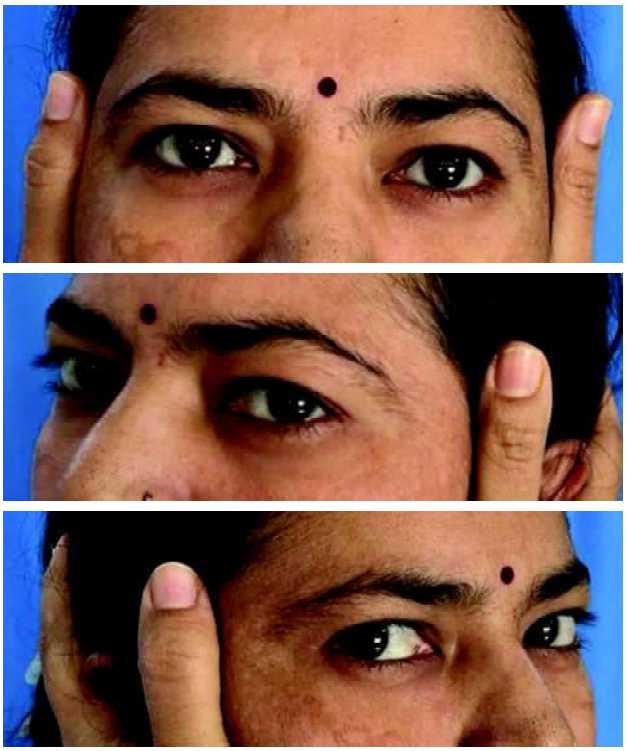

Fig. 1: *Head Impulse Test. 1A): Patient is asked to fix gaze on a target such as examiner's nose. 1B), 1C): The head is turned quickly to the right or left by about 15 degrees. A typical response occurs when the eyes remain on the target.*

dysdiadokinesia) can exclude central causes.

- ❖ Ear examination: An otoscopic examination should be performed to visualise the tympanic membrane for any retraction pockets as seen in cholesteatoma or vesicles on the pinna that can be seen in a Herpes zoster infection. Vertigo triggered by applying intermittent pressure on the tragus (Fistula test - Fig. 3) or with the Valsalva manoeuvre is seen in a perilymphatic fistula. A hearing assessment should be performed in such cases to look for sensorineural hearing loss.

- ❍ **Cardiovascular examination:** Pulse, blood pressure, heart rate and rhythm should be checked. Orthostatic blood pressure measurement must be done in suspected cases.

Neuroimaging is indicated[1] if:-

- Clinical examination is not consistent with a peripheral lesion
- prominent risk factors for CVA are present
- associated with neurological signs and symptoms such as diplopia, dysarthria.

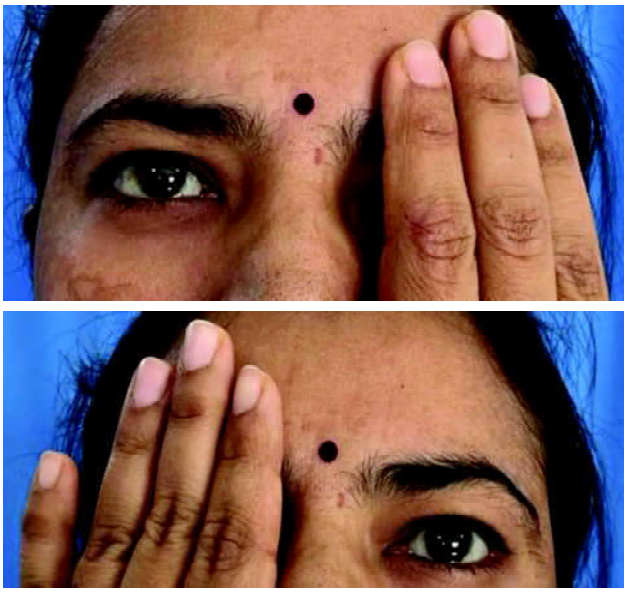

Fig. 2: *Test for Skew. 2a), 2b): This test involves the examiner covering one eye and observing for a vertical or horizontal shift in the uncovered eye*

The preferred methods of imaging are brain MRI and magnetic resonance (MR) angiography, as computed tomography (CT) scan is less sensitive than MRI for detecting and evaluating central lesions due to their limited resolution of posterior fossa structures. However, if a brain MRI is unavailable or contraindicated, a CT scan with thin cuts may be used, primarily through the brainstem and cerebellum[11]. In these cases, referral to a neurologist is recommended[12].

Treatment

The management of vertigo depends on its aetiology, and addressing the underlying cause often alleviates the symptoms. Pharmacological interventions may help suppress vestibular symptoms during acute episodes, which can persist for several hours to days. It is important to make healthcare professionals aware that vestibular suppressants (such as prochlorperazine) should be used for a limited duration, as excessive use may unnecessarily hinder the brain and central nervous system's natural compensatory mechanisms for peripheral vertigo. Steroids can be beneficial in some instances such as vestibular neuritis. Therapeutic repositioning manuvres such as Epley's manouvre is the recommended treatment for BPPV. Additional non-pharmacologic treatments for patients with permanent unilateral or bilateral vestibular dysfunction include physical therapy with vestibular rehabilitation.

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CASE REPORT

JIACM 2026; 27 (1): 69-71

Imatinib-Induced Interstitial Lung Disease Successfully Switched to Nilotinib

Kamran Chaudhary, Chandan Kumar***

Abstract

Imatinib mesylate (IM) is a tyrosine kinase inhibitor (TKI) approved for treating Philadelphia-positive chronic myeloid leukaemia (Ph+ CML). Although it is mostly well tolerated, IM-induced interstitial lung disease (ILD) is a rare phenomenon and consensus regarding its management is lacking. We describe a case of IM-induced ILD in a patient with CML, that demonstrated significant clinico-radiological resolution after discontinuation of IM, and switching to Nilotinib along with oral corticosteroid therapy.

Key words: Imatinib, Interstitial Lung disease, Nilotinib, CML.

Introduction

Imatinib mesylate (IM) was the first approved tyrosine-kinase inhibitor (TKI) that revolutionised the treatment of Philadelphia-positive, Ph+ chronic myeloid leukaemia (Ph+ CML). Imatinib competitively blocks the adenosine triphosphate (ATP) binding site of several tyrosine kinases that are responsible for clonal cell proliferation. It is also approved for the treatment of acute lymphoblastic leukaemia (Ph+ALL), Gastro-intestinal stromal tumour (GIST), myelodysplastic/myeloproliferative diseases, systemic mastocytosis and hypereosinophilic syndrome[1,2].

Imatinib is generally well tolerated. Pleural effusions have been reported in 1 - 6% of cases, with resolution after withdrawal of the drug[1]. Interstitial lung disease with Imatinib is considered rare. Although the mechanism of ILD with TKI is unclear, recent evidence suggests a role of T-helper cell-mediated hypersensitivity reaction and immune complex deposition[3]. Here we describe a patient with CML who developed imatinib-induced ILD, with significant clinico-radiological resolution after discontinuation of the drug, adding corticosteroids and switching to Nilotinib.

Case history

A 49-year-old male was diagnosed with Ph+ CML, in January 2022. He was commenced on Imatinib (IM) therapy at a dose of 400 mg daily. The patient tolerated the medication well and had achieved complete haematological remission at 6 months. He presented to the respiratory medicine outpatient clinic in October 2023 with gradually progressive breathlessness on exertion, modified medical research council (MMRC) grade three, dry cough for two months, with no history of fever. He did not have any other co-morbid condition. He was a former smoker of twenty pack years. On examination, his room air saturation was 94%, no clubbing, bibasal inspiratory crackles on auscultation. A chest X-ray showed bilateral diffuse reticular shadows (Fig. 1). A high-resolution computed tomography scan (HRCT) of the chest showed bilateral ground glass opacities, with interstitial septal thickening and traction bronchiectasis involving bilateral lower lobes with diffuse centriacinar and paraseptal emphysematous changes (Fig. 2).

His routine laboratory investigations including acute phase reactants were within normal limits. He was started on broad-spectrum antibiotics. His sputum culture, acid-fast bacilli (AFB) smear, sputum Gene Xpert, fungal stain and fungal culture reports were negative. Anti-nuclear antibody (ANA) and a complete autoimmune profile panel were also negative. Spirometry showed a forced expiratory volume in one second (FEV1) of 3.19 L (80% predicted), forced vital capacity (FVC) of 3.2 L (66% predicted) and reduced diffusion capacity of lungs for carbon monoxide (DLCO) of 4.1 mmol/min/Kpa (51% predicted). Thus, imatinib-induced interstitial lung disease was suspected on clinical and radiological grounds, after ruling-out infectious causes, and imatinib was stopped. Oral corticosteroids were started at 40 mg once daily and then slowly tapered over 3 months. Nilotinib was started as an alternative to Imatinib at a dosage of 400 mg twice daily, which was well tolerated and haematological remission was sustained at three months follow-up. The patient was also provided with bronchodilators for underlying emphysema. A repeat HRCT chest scan in December 2023 showed significant resolution of ground glass opacities and septal thickening (Fig. 3). The

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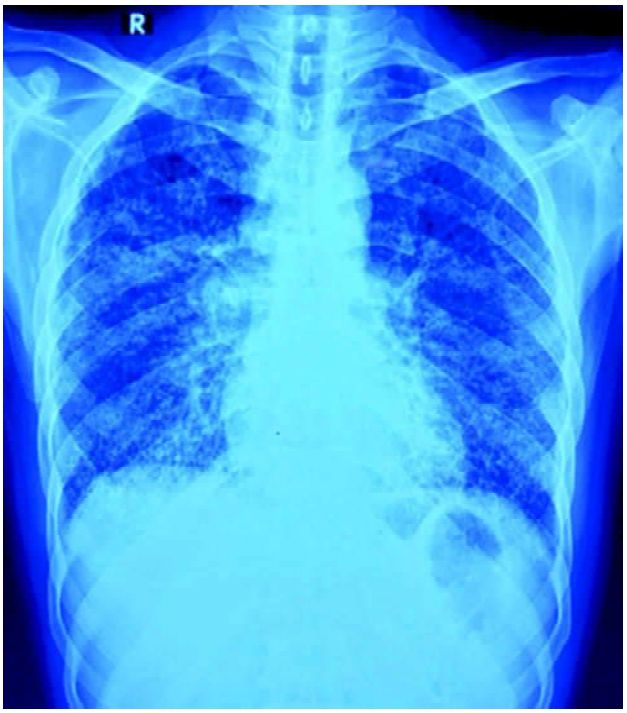

Fig. 1: *Chest X-ray on presentation showing bilateral diffuse reticular shadows.*

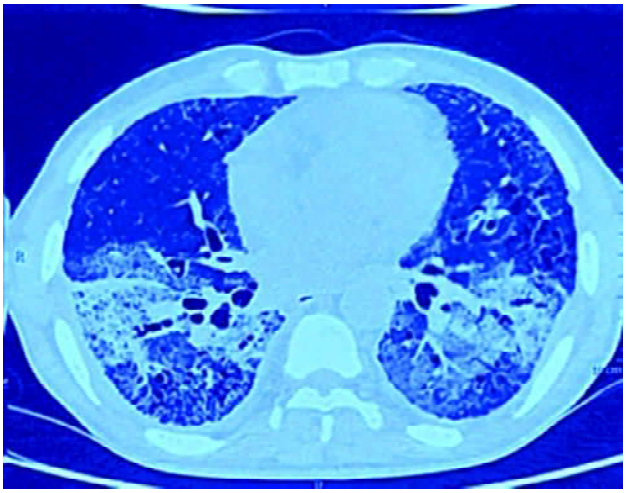

Fig. 2: *CT chest (October 2023) shows bilateral ground glass opacities, septal thickening and traction bronchiectasis.*

patient also reported improvement in dyspnoea with a room air saturation of 96%. Oral corticosteroids were tapered off at three months and Nilotinib was continued for CML.

Discussion

Imatinib is mostly well tolerated with mild adverse reactions including gastrointestinal disturbances, fluid retention and myalgias. IM-induced interstitial lung disease (ILD) is rare, with a median onset of 49 days (14 - 282 days). One study

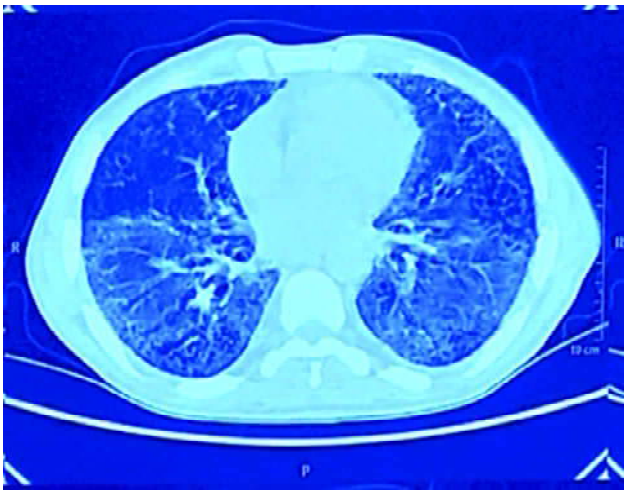

Fig. 3: *CT chest (December 2023) shows significant resolution of ground glass opacities.*

reported an onset of 2 weeks after discontinuation of IM, with clinico-radiological improvement after treatment with corticosteroids[1,3]. Commonly reported radiological features include bilateral nodular, interstitial or ground glass opacities or organising pneumonia[1]. In a large Japanese case series involving 27 cases of IM-induced ILD, 24 patients received corticosteroids. Most patients recovered, while five patients showed no improvement. A pre-existing lung disease was identified as a risk factor for the development of IM-induced lung disease[4]. In this case, emphysema was considered to be the pre-existing pulmonary disease predisposing to IM-induced ILD.

Nilotinib, a second-generation TKI, has a twenty-fold higher affinity for BCR-ABL kinases. It has been approved for the treatment of CML in patients with imatinib resistance or intolerance. There have been few reports of the development of pleural effusions and interstitial pneumonitis with Nilotinib[2]. However, many studies have shown substituting Nilotinib for imatinib to be favourable in the management of IM-induced interstitial lung disease in patients with CML. A study by Zhang *et al* reported worsening clinical symptoms after re-introducing imatinib in a patient with CML and IM-induced ILD one month after it had been stopped. The clinical symptoms subsided, lung functions improved and sustained remission was achieved after substitution with Nilotinib[5]. Another case of IM-induced ILD that had developed in a previously treated patient of pulmonary tuberculosis, was successfully switched to Nilotinib. The patient demonstrated sustained remission with lung function improvement and partial radiological resolution after 8 months of follow-up[6]. However, one study by Cho *et al* reported nilotinib-induced irreversible fibrotic ILD that responded to corticosteroids and a change of medication to ponatinib for CML treatment[7].

The mainstay of treatment involves discontinuation of Imatinib. Most studies have reported initiation of corticosteroids followed by gradual tapering over two to three months, resulting in clinical, radiological and lung function improvement. However, development of a fibrotic pattern of ILD, that is likely related to the duration of imatinib exposure, usually does not respond to corticosteroid treatment and is associated with poor outcomes[7]. Switching to Nilotinib or an alternate TKI can be considered in patients who develop ILD associated with Imatinib.

Conclusion

Imatinib-induced interstitial lung disease is an uncommon but serious condition with varied radiological patterns. Hence, it is important to monitor patients regularly for IM-induced ILD, especially those with underlying chronic lung disease. Discontinuation of Imatinib along with initiation of corticosteroids and switching to a different TKI has demonstrated favourable clinical and radiological outcomes.

Key Messages: *Imatinib-induced interstitial lung disease is an uncommon but serious condition. Patients on Imatinib therapy should be regularly monitored especially those with an underlying chronic lung disease. Withdrawal of the drug, switching to a different TKI along with corticosteroid therapy should be considered in patients developing ILD due to Imatinib.*

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CASE REPORT

JIACM 2026; 27 (1): 72-75

Acute Motor Sensory Axonal Neuropathy following Viral Encephalitis: Sequential Immune Dysregulation

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Introduction

Guillain-Barré Syndrome(GBS) is recognised as an acute, post-infectious, immune-mediated polyneuropathy. It often occurs after an antecedent mucosal infections such as respiratory or gastrointestinal infection[1]. Triggers for the development of GBS include *Campylobacter jejuni*, Cytomegalovirus (CMV), and influenza[2]. Based on electrodiagnostic findings and pathological features, GBS can be broadly subclassified into Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), Acute Motor Sensory Axonal Neuropathy. Other related variants include Miller-Fischer Syndrome, Bickerstaff Brainstem encephalitis, Cervico-Pharyngeal-Brachial variant[3].

The proportional incidence of GBS subtypes varies significantly; while the demyelinating form is predominant in North America and Europe, the axonal variants are more prevalent in Asia and Central/South America. AMSAN is one of the rarest forms of GBS, accounting for less than 5% of all cases[4]. The axonal variants present with more profound deficits having a less favourable prognosis compared to demyelinating forms as the recovery in axonal variants involves incomplete axonal regeneration rather than simple remyelination[5].

Case Presentation

A 77-year-old female, presented with a 4-day history of fever followed by altered mental status, characterised by irrelevant speech, and aggressive behaviour. Physical Examination revealed a conscious delirious patient with positive signs of meningeal irritation such as neck rigidity. Motor strength in all four limbs was found to be MRC grade 5/5. The initial Diagnostic Workup including routine labs and fever panel were unremarkable, ruling out common bacterial or septic causes. Magnetic Resonance Imaging (MRI) of brain with contrast showed no acute intraparenchymal lesions or significant leptomeningeal enhancement (Fig. 1). Cerebrospinal Fluid (CSF) Analysis demonstrated lymphocytic pleocytosis (250 cells/μL) with an elevated protein level (95.4 mg/dL) Table I.

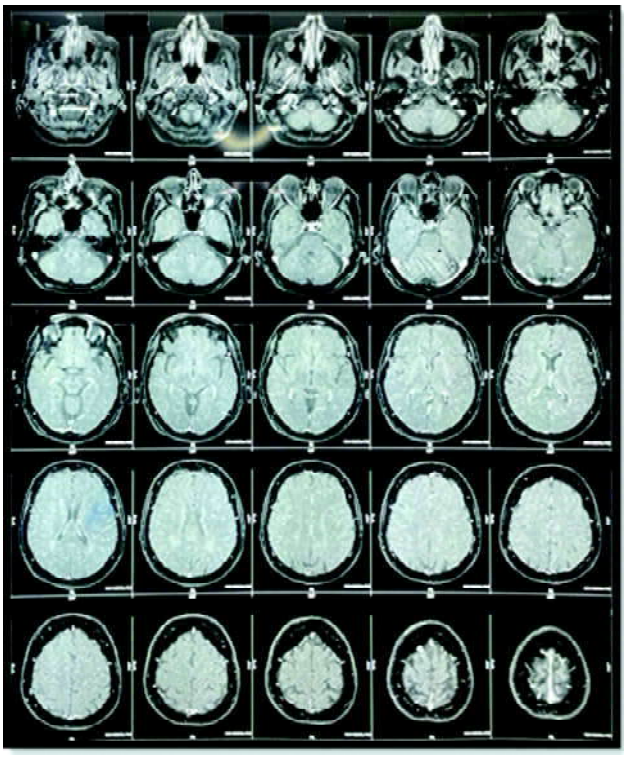

Fig. 1: *Initial MRI Brain with contrast study.*

Table I: CSF analysis.

Initial CSF analysis			
Parameter	**Patient result**	**Reference range**	**Unit**
CSF cell count	250	0 - 5	cells/μL
CSF protein	95.4	15 - 45	mg/dL
Repeat CSF analysis			
Parameter	**Patient result**	**Reference range**	**Unit**
CSF cell count	50	0 - 5	cells/μL
CSF protein	98.6	15 - 45	mg/dL

**Abbreviations* CSF: Cerebrospinal fluid.*

Based on the clinical syndrome (fever, encephalopathy, meningeal signs) and the CSF profile with elevated proteins

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and cell count, a presumptive diagnosis of Viral Encephalitis was made. Intravenous Acyclovir (10 mg/kg body weight) was initiated. By day 2 of hospitalisation the patient responded well to Acyclovir. Her mental status had improved, she was oriented and obeying commands. The patient was shifted to ward and continued on intravenous Acyclovir.

On Day 7 of hospitalisation, the patient experienced an acute-onset ascending motor weakness. She subsequently developed urinary retention requiring catheterisation and labile blood pressure (indicating an autonomic dysfunction).

On examination: hypotonia was noted in all 4 limbs with reduced Motor Strength: Bilateral Lower Limbs MRC Grade 3/5 and Bilateral Upper Limbs MRC Grade 4/5. The new symptom constellation prompted re-evaluation for a post-infectious process. MRI Brain with whole spine was performed and the study remained unremarkable, excluding acute stroke, myelitis or compressive lesions (Fig. 2, 3). Repeat CSF analysis was performed and the analysis showed protein: 98.6 mg/dL and WBC Count: 50 cells/μL (Table II).

Table II: Nerve conduction study.

Motor Nerve Conduction Study					
Nerve	**Recording Site (Muscle)**	**Stimulation Site**	**Latency (ms)**	**Amplitude (mV/μV)**	**Conduction Velocity (m/s)**
Median (L)	APB	Wrist	3.25	4.38 mV	68.97
		Elbow	6.88	3.48 mV	68.97
Median (R)	APB	Wrist	3.13	2.44 mV	68.97
		Elbow	6.75	1.62 mV	68.97
Peroneal (L)	EDB	Ankle	0.00	0.00 μV	–
		Knee	0.00	0.00 μV	–
Peroneal (R)	EDB	Ankle	2.50	0.91 mV	54.90
		Knee	8.88	0.68 mV	54.90
Tibial (L)	EHL	Ankle	0.00	0.00 μV	–
		Popliteal Fossa	0.00	0.00 μV	–
Tibial (R)	EHL	Ankle	14.00	2.83 mV	95.48
		Popliteal Fossa	17.88	0.73 mV	95.48
Sensory Nerve Conduction Study					
Nerve	**Side**	**Recording Site**	**Peak Latency (ms)**	**Amplitude (mu\μV)**	**Interpretation**
Superficial Peroneal	Left	Ankle	NR	0.0	Absent Response (Severe Axonal Loss)
Superficial Peroneal	Right	Ankle	NR	0.0	Absent Response (Severe Axonal Loss)
Sural	Left	Ankle	2.15	11.4	Normal
Sural	Right	Ankle	NR	0.0	Absent Response (Severe Axonal Loss)
Median	Left	Digit 2	2.40	30.7	Mild slowing, Amplitude preserved
Median	Right	Digit 2	2.80	30.6	Mild slowing, Amplitude preserved
Ulnar	Left	Digit 5	2.45	26.3	Mild slowing, Amplitude preserved
Ulnar	Right	Digit 5	2.70	24.4	Mild slowing, Amplitude preserved
Radial	Left	Forearm	1.20	25.0	Normal
Radial	Right	Forearm	1.60	18.1	Normal

The combination of rising protein and resolving pleocytosis formed the basis for albuminocytological dissociation, a cardinal feature of GBS. Electrophysiological studies (Table III, IV) revealed uniformly absent or reduced muscle action potential amplitudes in Peroneal and Tibial nerve and reduced sensory nerve action potential in the superficial peroneal and sural nerves. These findings are consistent with acute motor and sensory axonal polyradiculoneuropathy, a severe axonal variant of GBS.

A final diagnosis of Post-Viral Encephalitis AMSAN variant of GBS was established. The patient was initiated

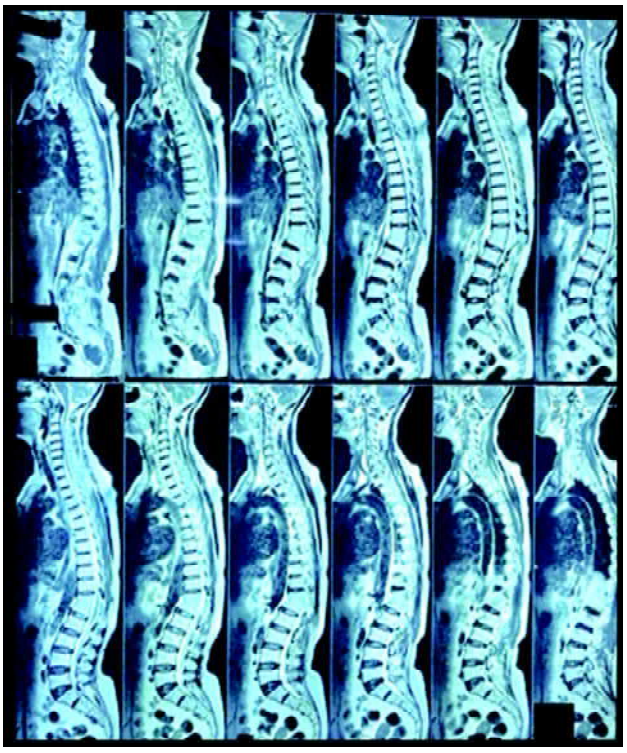

Fig. 2: *MRI whole spine screening.*

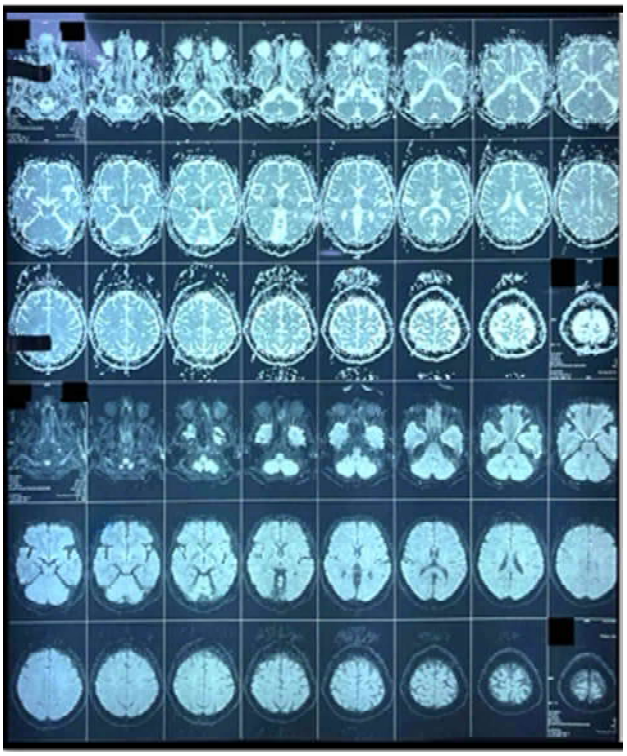

Fig. 3: *Repeat MRI brain study.*

Intravenous Immunoglobulin (IVIg)(at the standard total dose 2 g/kg body weight, totalling 120 g) administered over 5 days. By the completion of the IVIg course, the patient demonstrated gradual clinical improvement in motor strength in the bilateral lower limbs with power of MRC Grade 4/5.

Discussion

The occurrence of GBS following severe CNS inflammation as seen in our patient, challenges the conventional mucosal para-infectious paradigm.

The rapid transition noted in our patient from encephalitis to the AMSAN variant of GBS can be speculated to be a result of either a shared antigenic determinant between the CNS and PNS or a profound immune response resulting in disruption of the blood brain barrier thus allowing a CNS inflammation to trigger a secondary cascade in the periphery.

The hypothesis of 'immune spillover' is further strengthened by case reports documenting development of GBS following intense CNS insults such as cerebrovascular accidents. The common pathological link in these analogous cases is disruption of blood brain barrier hypothesised to permit an immune spillover[6].

A study conducted by Yang *et al* demonstrated varying degrees of axonal degeneration and demyelination in sciatic nerve of a mouse model infected with Japanese encephalitis. This study established a link between and a primary CNS inflammation triggering an immune response in the periphery[7]. Similarly, Tan *et al* conducted a sural nerve biopsy on a patient who developed GBS one week after traumatic brain injury. The presence of foamy macrophages in the endoneurium provided a direct histopathological evidence of immune mediated destruction in PNS following an acute CNS insult[8].

The most instructive element of our case is the evolution of the CSF profile. The initial CSF analysis, characterised by marked lymphocytic pleocytosis (250 cells/muL) and elevated protein (95.4 mg/dL), strongly indicated an active viral neurotropic infection despite lack of leptomeningeal enhancement in the MRI study. Improvement in patient's sensorium following Acyclovir also strengthened the diagnosis of viral encephalitis. A study conducted by Sukumaran *et al* (2024) demonstrated that 38.1% patients with infectious encephalitis presented with normal MRI findings, underscoring the importance of biochemical assessment, especially in hyperacute phase of illness[9].

The new onset neurological deterioration on day 7 of hospitalisation in the backdrop this unique CSF picture of resolving CNS inflammation juxtaposed with rising protein effectively ruled out ongoing encephalitis as the cause of the new weakness. Furthermore, the Electrodiagnostic

study revealed an absent motor and sensory responses in left peroneal and tibial nerve, with reduced amplitude in the right leg confirming the diagnosis of Acute Motor and Sensory Axonal Neuropathy.

The constellation of progressive ascending flaccid quadriparesis (MRC Grade 3/5), intense dysesthesia, and rapid progression was consistent with the severe axonal pathology. The development of urinary retention with labile blood pressure highlights significant autonomic dysfunction – an indicator of the severity of the disease. Autonomic dysfunction occurs in approximately 70% of patients with axonal variants of GBS[10].

The rapid clinical response following IVIG, with bilateral lower limb power improving from MRC Grade 3/5 to MRC Grade 4/5 by the end of the treatment course underscores the importance of high clinical suspicion and timely intervention.

Conclusion

This case expands the clinical spectrum of GBS from a mucosal para-infectious immune-mediated response by documenting AMSAN variant GBS following viral encephalitis in an elderly patient. The temporal evolution from an initial CNS pleocytosis to a subsequent albumino-cytological dissociation supports the possibility of CNS mediated immune response contributing to a PNS injury. Though such causality cannot be established from a single case, such observations highlight the need to explore the spectrum of post CNS insult immune dysregulation as an uncommon but possible pathway of GBS.

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CASE REPORT

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Fulminant Multisystem Thrombosis in a Middle-Aged Male: A Case Report

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Abstract

Fulminant multisystem thrombosis is a life-threatening condition that requires rapid diagnosis and aggressive management due to its high morbidity and mortality. We describe a 44-year-old male with no prior autoimmune or thrombotic history who presented with dyspnoea, abdominal pain, haematuria, and chest discomfort. Imaging revealed widespread simultaneous arterial and venous thromboses involving the pulmonary arteries, inferior mesenteric artery, renal vasculature, and deep veins of the right lower limb. Antiphospholipid antibody testing demonstrated a positive lupus anticoagulant and elevated β2-glycoprotein I IgM, raising strong suspicion for catastrophic antiphospholipid syndrome (CAPS). Despite prompt initiation of anticoagulation, immunomodulatory therapy, and supportive care, the patient developed anterior spinal artery thrombosis causing paraparesis, followed by a fatal acute myocardial infarction due to presumed coronary thrombosis. This case underscores the fulminant nature of multisystem thrombosis, highlights the diagnostic challenges of de novo CAPS, and emphasizes the need for early recognition and aggressive multimodal treatment to improve outcomes, while also noting that although CAPS is more common in females, it can rarely occur in males as demonstrated in this case.

Introduction

Antiphospholipid syndrome (APS) is an acquired autoimmune thrombophilia defined by recurrent arterial or venous thrombosis and pregnancy morbidity associated with persistent antiphospholipid antibodies (aPLs), including lupus anticoagulant (LA), anticardiolipin (aCL), and anti-β2-glycoprotein I antibodies (aβ2GPI)[1]. APS may occur as a primary condition or secondary to systemic autoimmune diseases, most commonly systemic lupus erythematosus. Catastrophic antiphospholipid syndrome (CAPS), first described by Asherson in 1992[2], is an uncommon but severe APS variant that occurs in fewer than 1% of APS patients[3]. It is characterised by rapidly progressive thrombosis involving multiple organ systems over days to weeks. Despite advances in anticoagulation and immunomodulatory therapy – including corticosteroids, intravenous immunoglobulin (IVIG), and plasma exchange – mortality remains between 30% and 50%[4]. Although CAPS typically affects middle-aged women with known APS or autoimmune disease, it can arise *de novo* without identifiable triggers, and atypical presentations pose significant diagnostic challenges. It may affect men rarely, as in our case.

Case Presentation

A 44-year-old male with a history notable only for hypertension and no previous thrombotic, autoimmune, or inflammatory illness presented with 5 - 6 days of progressive shortness of breath, mild haemoptysis, atypical chest pain, diffuse abdominal pain accompanied by nausea and vomiting, and macroscopic haematuria. On arrival, he appeared acutely ill and dyspnoeic, with tachycardia, tachypnoea, normotension, and an afebrile status. Physical examination revealed decreased breath sounds in the left hemithorax and diffuse abdominal tenderness without guarding or rebound. Initial cardiovascular and neurological evaluations were unremarkable. Laboratory investigations (Table I) demonstrated neutrophilic leucocytosis (20 x 10^3/μL), thrombocytosis (556 x 10^3/μL), elevated alkaline phosphatase (176 U/L), hypoalbuminaemia (2.1 g/dL), and preserved renal function (blood urea 35.6 mg/dL, serum creatinine 1.2 mg/dL, uric acid 7.1 mg/dL). Coagulation profile was normal, with a Prothrombin Time (PT) of 12.5 seconds, an Activated Partial Thromboplastin Time (aPTT) of 30.0 seconds, and an International Normalised Ratio (INR) of 1.0. Additionally, fibrinogen levels were measured at 300 mg/dL, and the peripheral smear showed no schistocytes, making disseminated intravascular coagulation (DIC) unlikely.

Different imaging studies revealed extensive multiorgan thrombosis. Doppler ultrasound of both lower limbs identified acute thrombosis of the right femoral, popliteal,

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and peroneal veins (Fig. 1). CT pulmonary angiography demonstrated thrombi in the right lower lobe segmental pulmonary arteries and a large embolus in the left main pulmonary artery (Fig. II). Contrast-enhanced CT of the abdomen revealed multiple renal infarcts, and CT angiography identified thrombosis of the inferior mesenteric artery. Given the presence of multiple simultaneous arterial and venous thromboses affecting several organ systems within a short interval, a systemic hypercoagulable disorder was strongly suspected, and evaluation for APS was pursued. The patient had no history of thrombosis, surgery, trauma, or infection, and no evidence of disseminated intravascular coagulation, which increased the suspicion of catastrophic antiphospholipid syndrome.

Antiphospholipid testing revealed a positive β2-glycoprotein I IgM level (>20) and a positive lupus anticoagulant, with negative anticardiolipin antibodies, supporting an antiphospholipid-mediated thrombotic process. On hospital day 4, he experienced sudden onset sensorimotor paraparesis. MRI of the whole spine demonstrated acute anterior spinal artery thrombosis corresponding to his neurological deficits. The rapid development of widespread arterial and venous thromboses affecting the pulmonary, renal, mesenteric, venous, and spinal circulations within one week fulfilled the diagnostic criteria for CAPS.

Table I: Investigations reports.

Investigation	Result	Normal Range/Reference
Complete Blood Count (CBC)	Neutrophilic leucocytosis: $20 \times 10^3/\mu L$ Thrombocytosis: $556 \times 10^3/\mu L$	WBC: $4.0 - 11.0 \times 10^3/\mu L$ Platelets: $150 - 400 \times 10^3/\mu L$
Liver Function Tests (LFTs)	Elevated alkaline phosphatase: 176 U/L	Alkaline Phosphatase: 30 - 120 U/L
Renal Function Tests (RFTs)	Blood urea: 35.6 mg/dL Serum creatinine: 1.2 mg/dL Uric acid: 7.1 mg/dL	Urea: 10 - 20 mg/dL Creatinine: 0.6 - 1.2 mg/dL Uric acid: 3.5 - 7.2 mg/dL
Coagulation Profile	Prothrombin Time (PT): 12.5 seconds Activated Partial Thromboplastin Time (aPTT): 30.0 sec International Normalised Ratio (INR): 1.0 Fibrinogen: 300 mg/dL	PT: 11.0 - 14.0 seconds aPTT: 25.0 - 35.0 seconds INR: 0.9 - 1.1 Fibrinogen: 200 - 400 mg/dL
Peripheral Blood Smear	No schistocytes	No schistocytes
ESR	ESR- 12 mm/hr	ESR- 0 - 15 mm/hr
CRP	CRP- 2 mg/L	CRP- less than 3mg/L

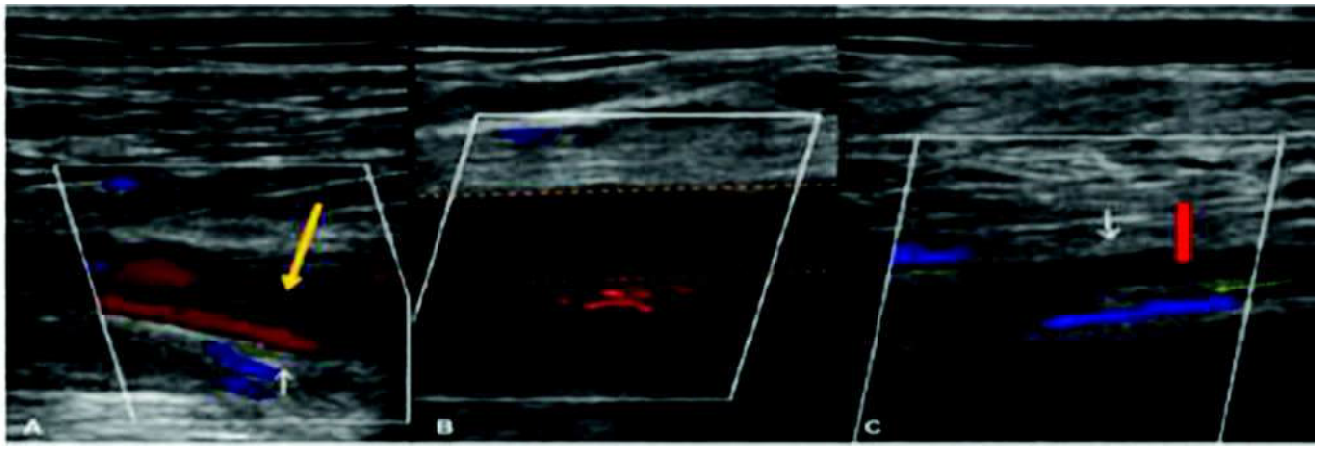

Fig. 1: *Doppler venous ultrasound demonstrating thromboses in the right (A) femoral, (B) popliteal, and (C) peroneal veins.*

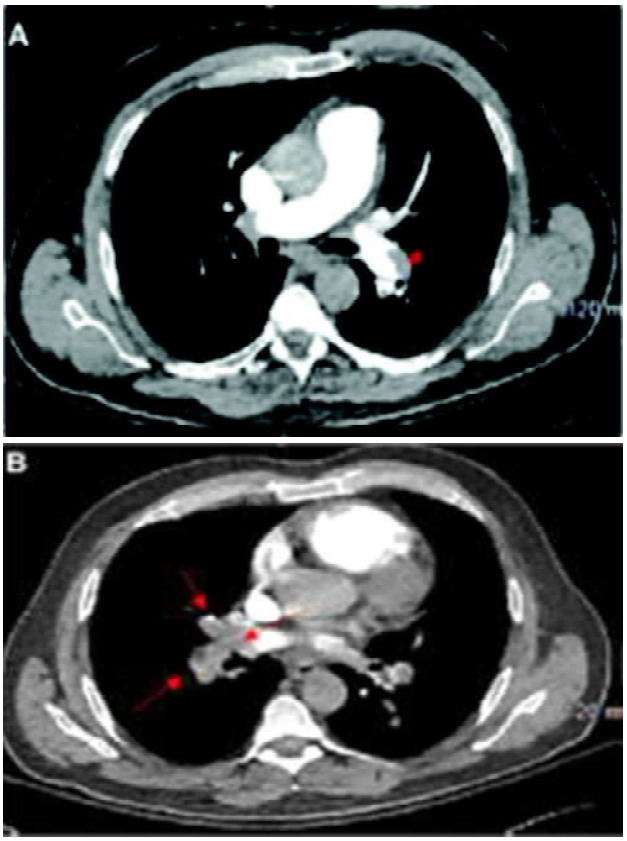

Fig. 2: *CT chest angiogram demonstrating pulmonary emboli in (A) the left main pulmonary artery, (B) the right main pulmonary artery and right lobar branches.*

Differential Diagnosis

The patient's abrupt and widespread arterial and venous thromboses prompted consideration of several critical differential diagnoses (Table II). Sepsis-induced coagulopathy was initially considered, as severe infection may trigger widespread endothelial injury and thrombosis. However, the patient exhibited no fever, haemodynamic instability, leucocytosis typical of infection, or positive cultures, making this diagnosis unlikely. Disseminated intravascular coagulation was also evaluated given the multiorgan ischaemia, but normal fibrinogen levels, preserved platelet count, and the absence of schistocytes argued against consumptive coagulopathy. Primary inherited thrombophilias such as factor V Leiden mutation, prothrombin gene mutation, or deficiencies of antithrombin III, protein C, or protein S were considered but deemed unlikely because they rarely cause simultaneous arterial and venous thrombosis in multiple territories and typically do not present with such explosive progression. Thrombotic microangiopathies, including thrombotic thrombocytopenic purpura and atypical Haemolytic uraemic syndrome, were considered but were inconsistent with the absence of haemolysis, normal platelet count, preserved renal function at presentation, and initially normal neurological findings. Vasculitis disorders such as ANCA-associated vasculitis and polyarteritis nodosa were also evaluated, but there was no evidence of systemic inflammation, characteristic vascular abnormalities, or supportive serologies. Ultimately, the simultaneous involvement of large and small vessels across multiple organ systems over a short time frame, combined with positive antiphospholipid antibodies, was most consistent with catastrophic antiphospholipid syndrome.

Table II: Differential diagnosis.

Differential Diagnosis	Points in Favor	Points Against
Sepsis-induced coagulopathy	– Presence of multiorgan thrombosis. – Elevated white blood cell count (neutrophilic leucocytosis).	– No fever or haemodynamic instability. – No positive cultures or evidence of infection – No systemic inflammation, which is usually seen in sepsis.
Disseminated Intravascular Coagulation (DIC)	– Multiorgan thromboses could indicate disseminated thrombosis. – The presence of thrombosis in multiple organs suggest DIC.	– Normal fibrinogen levels (usually decreased in DIC). – Normal platelet count, no schistocytes seen in peripheral smear. – Absence of haemolysis or significant anaemia.
Inherited Thrombophilias	– No prior history of thrombosis or autoimmune disease to suggest APS. – The abrupt nature of thrombosis affecting multiple vascular territories could suggest hypercoagulability	– Rarely causes both arterial and venous thrombosis simultaneously. – The explosive progression of thrombosis seen here is not typical of inherited thrombophilias – Inherited thrombophilias do not generally involve the spinal arteries, as in this case.
Thrombotic Microangiopathies (TTP or aHUS)	– Multiorgan involvement, including renal ischaemia, could suggest a microvascular pathology.	– No evidence of haemolysis, which is typical in TTP or aHUS. – Normal platelet count at presentation. – Preserved renal function and lack of neurological findings initially.

Vasculitis Disorders (ANCA-associated vasculitis, Polyarteritis nodosa)	– Systemic vascular involvement and thrombosis could mimic vasculitis. – Thrombosis in multiple vascular beds is common in vasculitis	– No evidence of systemic inflammation (e.g., elevated CRP or ESR). – No characteristic vascular abnormalities on imaging
Catastrophic Antiphospholipid Syndrome (CAPS)	– Widespread arterial and venous thrombosis across multiple organ systems. – Positive antiphospholipid antibodies (lupus anticoagulant, a2-GPI IgM).	– Initially, no prior history of autoimmune disease or thrombotic events – Diagnosis is rare, and initial symptoms overlap with common conditions. – It is more common in females and rarely seen in males
Myeloproliferative Neoplasm with neutrophilic leukocytosis	– Marked leukocytosis and thrombocytosis – Known association with thrombosis (arterial and venous) – Can cause hypercoagulable state	– No splenomegaly reported – No prior history suggestive of chronic MPN – Acute fulminant presentation atypical – No confirmatory tests (e.g., JAK2 mutation)
Hyperhomocysteinaemia	– Can predispose to arterial and venous thrombosis – May explain multisite thrombosis	– Usually causes chronic/recurrent thrombosis, not fulminant – No homocysteine levels reported – Does not typically cause such rapid progression
Occult systemic malignancy (paraneoplastic thrombosis)	– Malignancy is a known cause of hypercoagulability (Trousseau syndrome) – Can present with unexplained thrombosis	– No weight loss or constitutional symptoms – No mass lesions on imaging – Abrupt catastrophic course less typical – No prior cancer history

Management

Management focused on stabilizing the patient's respiratory status, controlling the thrombotic process, and addressing potential triggers. He was provided supplemental oxygen and immediately initiated on therapeutic low molecular weight heparin to prevent further thrombus formation. Because infection is a common precipitant of CAPS and could not initially be excluded, empirical broad-spectrum antibiotics were administered. IVIG was initiated early due to strong suspicion for CAPS, and antiplatelet therapy was added to help mitigate thrombus propagation. Despite these measures, the patient's clinical condition deteriorated, and the development of acute paraparesis prompted urgent imaging, confirming anterior spinal artery thrombosis and signalling ongoing catastrophic vascular involvement.

Advanced immunosuppressive and complement-targeted therapies, including cyclophosphamide (often used in SLE-associated CAPS) and eculizumab (which has demonstrated benefit in complement-mediated or refractory CAPS)[5], were considered. However, the rapid pace of his clinical decline precluded timely initiation.

Despite aggressive anticoagulation and initiation of immunomodulatory therapy, the patient's condition continued to deteriorate. On hospital day 6, he developed new-onset central chest pressure radiating to the left arm, accompanied by diaphoresis, nausea, and worsening dyspnoea. His clinical status declined rapidly, progressing to hypotension and tachyarrhythmia. A 12-lead ECG demonstrated acute ST-segment elevations in the anterior precordial leads, consistent with an extensive anterior wall ST-elevation myocardial infarction, a known but rare manifestation of CAPS-related coronary thrombosis. Concurrent bedside cardiac ultrasound revealed new severe left ventricular systolic dysfunction with regional wall motion abnormalities. Despite immediate initiation of advanced cardiac life support, including vasopressor support and antithrombotic escalation, he suffered recurrent ventricular arrhythmias culminating in pulseless ventricular tachycardia. Prolonged resuscitative efforts were unsuccessful, and the patient was pronounced deceased. The abrupt onset of myocardial ischaemia in the setting of active, uncontrolled systemic thrombosis underscores the fulminant nature of CAPS and highlights the challenge of preventing fatal macrovascular events even with timely and appropriate therapy.

Discussion

Catastrophic antiphospholipid syndrome represents the most severe form of APS, characterised by rapidly evolving, widespread thrombosis affecting multiple vascular beds within days. The underlying pathogenesis involves a self-amplifying cycle of endothelial activation, cytokine release, platelet aggregation, and complement activation, leading to uncontrolled microvascular and macrovascular thrombosis[5]. Although APS itself is relatively uncommon, CAPS occurs in fewer than 1% of APS patients[3] and carries a mortality rate of 30 - 50% despite early recognition and treatment[4]. Importantly, nearly one-third of CAPS cases occur *de novo*, without prior APS diagnosis or underlying autoimmune disease[6-8], contributing to diagnostic delays.

This patient's initial symptoms – including dyspnoea,

abdominal pain, and haematuria – were nonspecific and overlapped with far more common conditions such as pulmonary embolism, nephrolithiasis, or mesenteric ischemia from atherosclerotic disease. Such nonspecific presentations often obscure the diagnosis until multiorgan involvement becomes evident. The rare combination of deep vein thrombosis, pulmonary embolism, renal infarction, mesenteric artery thrombosis, and spinal artery thrombosis arising within days is highly unusual and strongly characteristic of CAPS.

Management of CAPS is centered around early initiation of triple therapy consisting of therapeutic anticoagulation, high-dose corticosteroids, and either IVIG or plasma exchange[9]. This multimodal approach aims to attenuate immune-mediated vascular injury, reduce circulating pathogenic antibodies, and halt propagation of thrombosis. In recent years, complement inhibitors such as eculizumab have emerged as promising adjunctive therapies in refractory cases[5]. However, the aggressiveness of CAPS in some patients, as demonstrated in this case, limits the opportunity to introduce additional therapies.

Epidemiologically, APS is more prevalent in women than men, and male patients presenting with fulminant or early-onset APS may represent a distinct phenotypic subgroup with potentially different risk profiles or disease trajectories[6-8]. The absence of identifiable triggers, the extraordinary tempo of disease progression, and the involvement of multiple major arterial and venous systems contributed to the poor prognosis in this case. Spinal arterial thrombosis, a rare manifestation even within APS, underscores the severity of vascular compromise occurring in catastrophic presentations.

In CAPS, myocardial infarction (MI) can occur due to coronary artery thrombosis, a result of the pro-thrombotic effects of antiphospholipid antibodies (aPLs). These antibodies promote endothelial dysfunction, platelet aggregation, and clot formation, not only in small vessels but also in larger arteries like the coronary vessels. While MI is less common in APS compared to venous thromboembolism, its occurrence in CAPS is significant, as it can rapidly lead to severe myocardial ischaemia and cardiac arrest. The hypercoagulable state in CAPS, coupled with complement activation, increases the risk of arterial thrombosis, including in the coronary circulation. This underscores the need for early detection and aggressive management, as coronary involvement can contribute to high mortality in these patients[10].

This case is exceptional due to the combination of male sex, absence of prior autoimmune disease, absence of identifiable precipitating factors, and the rapidly progressive nature of multisystem arterial and venous thrombosis that developed within a matter of days. The sudden onset of anterior spinal artery thrombosis, along with the subsequent fatal myocardial infarction, underscores the fulminant nature of CAPS and its capacity to rapidly compromise multiple vascular territories. These unique and severe manifestations highlight the diagnostic challenges in recognizing CAPS early, particularly when presented without a prior history of autoimmune disease or typical risk factors. Furthermore, this case emphasizes the clinical variability of CAPS and the therapeutic difficulties in managing such an aggressive and rapidly progressing condition, contributing valuable insights into the complexity of diagnosing and treating this rare but devastating syndrome.

Conclusion

Catastrophic antiphospholipid syndrome is a rare but devastating thrombotic emergency that requires high clinical suspicion, particularly when patients present with rapidly evolving thromboses across multiple vascular beds. This case highlights the importance of early recognition of CAPS even in patients without pre-existing autoimmune disease, conventional risk factors, or identifiable triggers. The patient's fulminant presentation despite timely anticoagulation and immunomodulatory therapy illustrates the limitations of current treatment strategies and the need for improved diagnostic tools and more effective targeted therapies.

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