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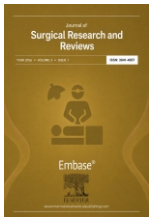

Research Article

Section: General Medicine

A Study on Cardiovascular Manifestations in Leptospirosis

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HIGHLIGHTS

- Cardiovascular involvement in leptospirosis
- Sinus tachycardia common ECG abnormality
- Reduced ejection fraction increased mortality
- Global hypokinesia indicated cardiac dysfunction
- Elevated CK-MB associated with mortality

Key Words:
Leptospirosis
Cardiovascular manifestations
Electrocardiography
Ejection fraction
CK-MB

ABSTRACT

Introduction: Leptospirosis is a zoonotic infection ranging from mild febrile illness to severe multiorgan dysfunction. Cardiovascular involvement may be apparent or subclinical and can include arrhythmias, conduction abnormalities, myocarditis, ventricular dysfunction, hypotension, and shock. **Aim & Objective:** To characterize cardiovascular manifestations in patients with leptospirosis, identify electrocardiographic abnormalities, assess the relationship between left ventricular ejection fraction and mortality, and evaluate the association of serum CK-MB levels with mortality. **Materials & Methods:** This prospective observational study was conducted in the Department of General Medicine, Justice K.S. Hegde Charitable Hospital, Mangalore, from January 2018 to June 2019. Fifty adults with positive Lepto card, IgM anti-Leptospira ELISA, or Modified Faine's score ≥25 were included, while patients with pre-existing cardiovascular disease were excluded. Clinical examination, ECG, echocardiography, ejection fraction, CK-MB, and in-hospital outcomes were assessed. **Results:** The mean age was 43.64 ± 14.94 years and 86% were males. Sinus tachycardia was the commonest ECG abnormality at 30%, followed by atrial fibrillation at 6%, ST-T changes at 4%, and multifocal atrial tachycardia, VPCs, and LBBB at 2% each. Ejection fraction was 51–60% in 88%, while global hypokinesia occurred in 8%. Overall mortality was 10%. Mortality increased with declining ejection fraction, reaching 100% in the single patient with EF ≤30%. Among patients with global hypokinesia, median CK-MB was significantly higher in non-survivors than survivors (100.55 vs 37.15; p=0.031). **Conclusion:** Cardiovascular involvement is clinically important in leptospirosis. ECG abnormalities, reduced ejection fraction, global hypokinesia, and elevated CK-MB may identify patients at higher risk and support monitoring and timely management.

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INTRODUCTION

Leptospirosis is an important zoonotic bacterial infection caused by pathogenic species of the genus *Leptospira*. The organism is maintained in nature through a wide variety of mammalian reservoirs, particularly rodents, cattle, dogs, and other domestic or wild animals, which may excrete leptospires in their urine for prolonged periods. Humans usually become infected through direct contact with infected animals or indirectly through exposure to water, mud, or soil contaminated with infected urine [1]. Entry commonly occurs through cuts or abrasions in the skin or through the conjunctival, oral, or nasal mucosa. The disease is particularly prevalent in tropical and subtropical regions where high rainfall, flooding, warm climate, inadequate sanitation, poor drainage, occupational exposure, and close contact with animals facilitate transmission [2].

Leptospirosis continues to represent a considerable public health problem because it is frequently underdiagnosed and can produce both sporadic infections and outbreaks following heavy rainfall or flooding. Agricultural workers, sewage workers, veterinarians, animal handlers, fishermen, sanitation workers, and persons exposed to floodwater are particularly vulnerable. Urban transmission is also increasingly recognized, especially in densely populated areas with poor waste disposal and substantial rodent infestation [3]. Globally, leptospirosis has been estimated to cause approximately 1.03 million cases and 58,900 deaths annually, with a particularly high burden in South and Southeast Asia, Oceania, parts of Latin America, and other resource-limited tropical regions [4]. The clinical presentation of leptospirosis is highly variable, ranging from a mild, self-limiting febrile illness to severe, life-threatening multiorgan dysfunction. The early phase commonly presents with abrupt fever, chills, headache, severe myalgia, conjunctival suffusion, nausea, vomiting, and generalized weakness. These manifestations are nonspecific and may mimic dengue, malaria, scrub typhus, enteric fever, viral hepatitis, and other acute febrile illnesses [5]. Severe leptospirosis may involve the liver, kidneys, lungs, central nervous system, and cardiovascular system. The severe icteric form, traditionally referred to as Weil disease, is characterized predominantly by jaundice, renal dysfunction, hemorrhagic manifestations, and circulatory disturbances. Pulmonary hemorrhage, acute respiratory distress syndrome, acute kidney injury, shock, and multiorgan failure may occur in critically ill patients and contribute substantially to mortality [6].

Cardiovascular involvement is an important but often underrecognized manifestation of leptospirosis. Cardiac abnormalities may be clinically apparent or may remain subclinical and become evident only after electrocardiographic, echocardiographic, or biochemical evaluation [7]. The cardiovascular spectrum includes sinus tachycardia, bradyarrhythmias, atrial & ventricular arrhythmias, atrioventricular conduction disturbances, nonspecific ST-segment and T-wave abnormalities, QT interval prolongation, myocarditis, myocardial dysfunction, pericardial involvement, pulmonary edema, hypotension, and circulatory shock. In severe cases, myocardial involvement may contribute to hemodynamic instability and multiorgan dysfunction. Importantly, cardiac abnormalities can occur even when classical cardiac symptoms such as chest pain or palpitations are absent, making systematic cardiovascular assessment clinically relevant [8].

The pathogenesis of cardiovascular involvement in leptospirosis is multifactorial and remains incompletely understood. Direct invasion or toxic effects of leptospires, myocardial inflammation, endothelial injury, vasculitis, capillary dysfunction, and immune-mediated mechanisms have all been proposed. Systemic inflammatory responses associated with severe infection may further cause myocardial depression and altered vascular tone [9]. In addition, accompanying hypoxemia, acidosis, hypotension, renal

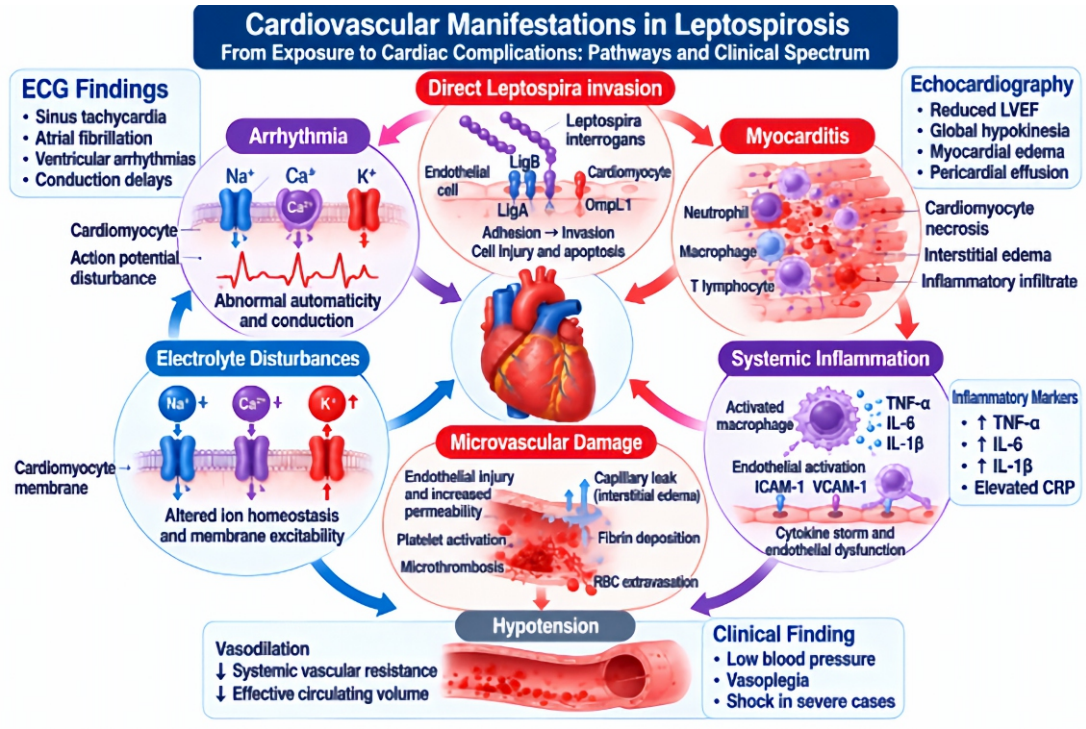

Figure 1: Cardiovascular manifestations and pathways in leptospirosis.

dysfunction, and disturbances of potassium and other electrolytes may precipitate or aggravate cardiac electrical abnormalities. Histopathological investigations have demonstrated myocardial inflammation and vascular changes in fatal leptospirosis, supporting the concept that genuine myocardial injury can occur during the disease rather than cardiac changes being solely secondary to systemic illness [10].

Electrocardiography represents one of the simplest and most readily available methods for detecting cardiovascular involvement. Sinus tachycardia is frequently associated with fever and systemic illness, but persistent or disproportionate tachycardia may indicate more significant cardiovascular involvement. Atrial fibrillation, premature atrial or ventricular contractions, atrioventricular block, bundle branch abnormalities, nonspecific ventricular repolarization changes, ST-T abnormalities, and prolonged QT intervals have also been described. Such abnormalities may result from myocarditis, autonomic disturbances, metabolic derangements, or electrolyte imbalance. Echocardiography provides additional information by evaluating ventricular systolic and diastolic function, regional wall motion, chamber dimensions, valvular abnormalities, and pericardial effusion. It may therefore assist in recognizing clinically apparent as well as subclinical myocardial dysfunction [8].

Cardiovascular manifestations in leptospirosis may indicate severe systemic disease and increased risk of adverse outcomes. Myocarditis, arrhythmias, conduction disturbances, and hypotension can impair cardiac function, while pulmonary involvement may increase right ventricular stress. Cardiac dysfunction may also worsen renal, hepatic, and pulmonary complications. Early recognition is therefore essential for identifying high-risk patients and guiding intensive monitoring and timely supportive management [8].

Cardiovascular involvement in leptospirosis may be overlooked because renal, hepatic, pulmonary, and hemorrhagic manifestations often dominate the clinical picture. Nonspecific features such as dyspnea, hypotension, and tachycardia may be attributed to sepsis or dehydration. Systematic evaluation with clinical examination, electrocardiography, echocardiography, and cardiac biomarkers can enable early detection, assess disease severity, improve risk stratification, and guide timely management and outcomes [11]. **Figure 1.** Cardiovascular manifestations of leptospirosis, illustrating the underlying pathophysiological pathways, including direct myocardial invasion, immune-mediated injury, endothelial dysfunction, electrolyte imbalance, and hypotension, leading to myocarditis and cardiac arrhythmias.

The study aimed to characterize cardiovascular involvement in patients with leptospirosis, with particular emphasis on identifying the common electrocardiographic abnormalities associated with the disease. It also sought to evaluate the relationship between left ventricular ejection fraction and mortality and to determine whether serum creatine kinase-MB (CK-MB) levels were significantly associated with mortality among patients diagnosed with leptospirosis during hospitalization period.

MATERIALS & METHODS

This prospective observational study was conducted in the Department of General Medicine, Justice K.S. Hegde Charitable Hospital, KS Hegde Medical Academy, Nitte (Deemed to be University), Mangalore, from January 2018 to June 2019. Fifty adults aged ≥18 years with positive Lepto card, IgM anti-Leptospira ELISA, or Modified Faine's score ≥25 were included. Patients with pre-existing hypertension, ischemic heart disease, congenital or rheumatic heart disease, cardiomyopathy, or other cardiovascular involvement were excluded. Sample size was calculated using an expected cardiovascular involvement of 37.1%, 14% precision, and 95% confidence, with allowance for non-participation. Institutional Ethics Committee approval was obtained before study initiation.

RESULTS

The study population had a mean age of 43.64 ± 14.94 years, with a median age of 42 years and a broad age range of 20–76 years, indicating involvement across adulthood. The close similarity between mean and median age suggests that the age distribution was relatively balanced without marked skewing. A clear male predominance was observed, with 43 (86.0%) males compared with 7 (14.0%) females. Thus, the cardiovascular manifestations of leptospirosis in this cohort were evaluated predominantly among middle-aged male patients, which should be considered while interpreting and generalizing the subsequent cardiovascular findings.

Agriculturists formed the largest occupational group (34.0%), followed by labourers (20.0%), while homemakers and shopkeepers each constituted 16.0%. This distribution indicates that leptospirosis was more frequent among individuals involved in occupations with greater environmental exposure, particularly to contaminated soil and water **(Table 1)**.

Fever was the most common symptom (94%), followed by myalgia (74%), vomiting (58%), yellow sclera (56%) and headache (52%). Oliguria (34%) and breathlessness (28%) were also noted, suggesting systemic involvement. Cough occurred in 22%, while hematemesis, altered sensorium and hemoptysis were relatively uncommon **(Figure 2)**. Icterus was the most common sign (56%), followed by tachycardia (30%), pallor (24%) and hypotension (20%). Tachycardia and hypotension indicate notable cardiovascular involvement in leptospirosis, while edema (14%) may reflect associated systemic dysfunction. Other signs such as clubbing, petechiae, cyanosis and lymphadenopathy were uncommon **(Table 2)**.

Sinus rhythm was the most common ECG finding (54%), while sinus tachycardia occurred in 30%, indicating frequent cardiovascular involvement. Atrial fibrillation was present in 6% and ST-T changes in 4%, suggesting rhythm and repolarization abnormalities. Multifocal atrial tachycardia, VPCs, and LBBB were uncommon, occurring in 2% each **(Figure 3)**.

Most patients had a preserved ejection fraction of 51–60% (88%), indicating that left ventricular systolic function remained normal in the majority. Reduced ejection fraction was observed in 12%, including 6% with EF 41–50%, 4% with EF 31–40%,

and 2% with EF ≤30%. These findings suggest that significant systolic dysfunction occurred only in a small proportion of leptospirosis patients **(Table 3)**.

Echocardiography was normal in the majority of patients (92%), indicating preserved cardiac function in most cases. Global hypokinesia was present in 8%, suggesting myocardial involvement in a small subset of leptospirosis patients. This supports that significant echocardiographic cardiac dysfunction was relatively uncommon in the study population **(Table 4)**. The mean CK-MB level was 46.2 ± 58.01, with a median of 23.0 and a wide range of 9.5–302.0. The marked difference between mean and median suggests a right-skewed distribution, likely due to a few patients with very high CK-MB values. This variability indicates that the degree of myocardial involvement differed considerably among patients with leptospirosis (**Table 5)**.

The majority of patients survived (45/50, 90%), while 5 patients (10%) were non-survivors. This indicates an overall favorable outcome in most patients with leptospirosis, although a clinically important mortality of 10% was observed. The findings emphasize that severe leptospirosis can still be associated with substantial risk of death, particularly when significant systemic or cardiovascular involvement occurs **(Figure 4)**.

Survival was highest among patients with ejection fraction 51–60%, where 42 of 44 (95.45%) survived. Mortality increased with declining ejection fraction, reaching 100% in the single patient with EF ≤30%. This pattern suggests that reduced left ventricular systolic function may be associated with poorer outcomes in leptospirosis. However, statistical significance could not be assessed because of small cell counts and a zero-value cell **(Table 6)**.

CK-MB levels were visibly higher among non-survivors than survivors, with a higher median and wider distribution. This suggests that greater myocardial injury may be associated with poorer outcomes in leptospirosis. However, without a reported statistical test or p-value, the significance of this difference cannot be confirmed **(Figure 5)**.

Among patients with global LV hypokinesia, median CK-MB was higher in non-survivors (100.55) than survivors (37.15). This difference was statistically significant (p = 0.031). The finding suggests that greater myocardial injury was associated with mortality in patients showing global hypokinesia. However, interpretation should remain cautious because only four patients were included in this subgroup **(Table 7)**.

Table 1: Descriptive Analysis of Occupation in the Study Population (N = 50)

Occupation	Frequency	Percentage
Agriculturist	17	34.0%
Labourer	10	20.0%
Homemaker	8	16.0%
Shopkeeper	8	16.0%
Chef	2	4.0%
Student	2	4.0%
Attender	1	2.0%
Boat worker	1	2.0%
Mechanic	1	2.0%
Total	**50**	**100.0%**

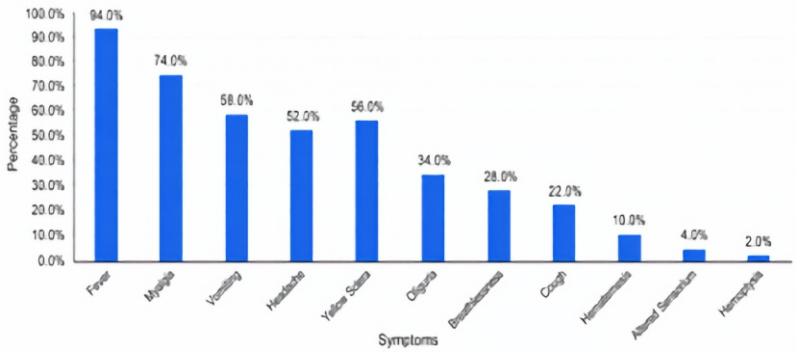

Figure 2: Bar Chart of Symptoms in the Study Population (N = 50)

Table 2: Summary of Signs in the Study Population (N = 50)

Signs	Frequency	Percentage
Icterus	28	56.0%
Tachycardia	15	30.0%
Pallor	12	24.0%
Hypotension	10	20.0%
Edema	7	14.0%
Clubbing	3	6.0%
Petechiae	2	4.0%
Cyanosis	1	2.0%
Lymphadenopathy	1	2.0%

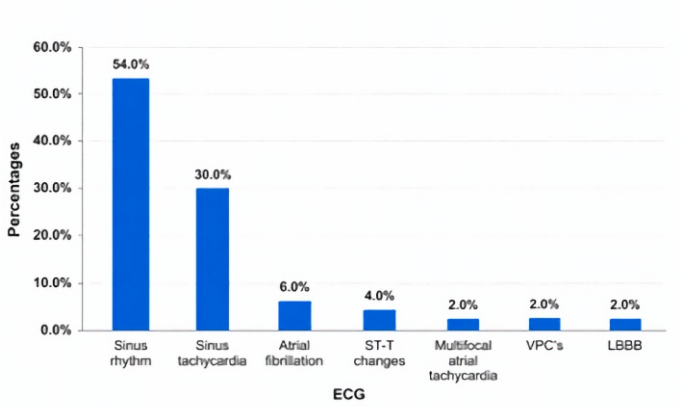

Figure 3: Bar Chart of ECG Findings in the Study Population (N = 50)

Table 3: Descriptive Analysis of Ejection Fraction in the Study Population (N = 50)

Ejection Fraction (%)	Frequency	Percentage
51 to 60	**44**	**88.0%**
41 to 50	**3**	**6.0%**
31 to 40	**2**	**4.0%**
≤ 30	**1**	**2.0%**
Total	**50**	**100.0%**

Table 4: Descriptive Analysis of ECHO in the Study Population (N = 50)

ECHO	Frequency	Percentage
Global hypokinesia	4	8.0%
Normal	46	92.0%
Total	**50**	**100.0%**

Table 5: Descriptive Analysis of CKMB in the Study Population (N = 30)

Parameter	Mean ± SD	Median	Minimum	Maximum	95% CI Lower	95% CI Upper
CKMB	46.2 ± 58.01	23.00	9.50	302.00	24.53	67.86

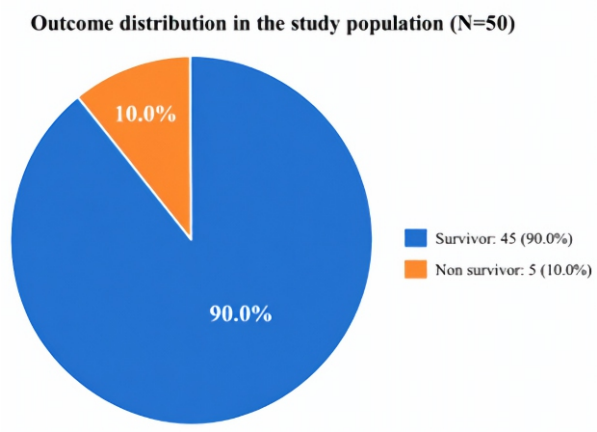

Figure 4: Outcome Distribution in the Study Population (N=50)

Table 6: Comparison of Ejection Fraction Between Outcome (N = 50)

Ejection Fraction (%)	Frequency	Survivor	Non-Survivor
51 to 60	44	42 (95.45%)	2 (4.54%)
41 to 50	3	2 (66.66%)	1 (33.33%)
31 to 40	2	1 (5%)	1 (50%)
≤ 30	1	0 (0%)	1 (100%)
No statistical test was applied due to 0 subjects in the cell.			

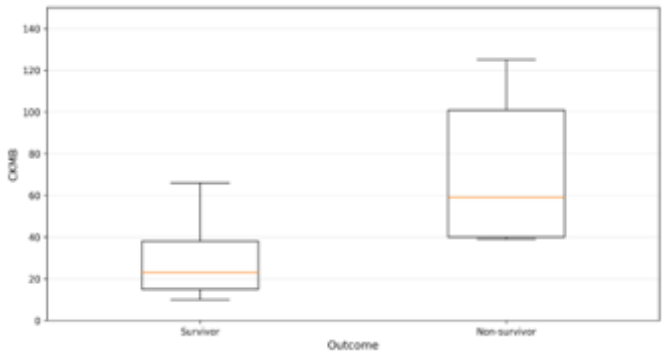

Figure 5: Box and Whisker Plot for Comparison of CKMB Between Survivors and Non-Survivors (N = 50)

Table 7: Comparison of Median CKMB Between Outcomes Among Patients with Global Hypokinesia of LV (N = 4)

Parameter	Survivor (N = 2), Median (IQR)	Non-Survivor (N = 2), Median (IQR)	Mann Whitney U Test (P value)
CKMB	**37.15 (7.12, 48.60)**	**100.55 (56.32, 110.70)**	**0.031**

DISCUSSION

Leptospirosis is a zoonotic infection caused by pathogenic *Leptospira* species and is particularly prevalent in tropical and subtropical regions. In India, it is increasingly recognized as an important public health problem. Several factors, including older age, oliguria, hyperkalemia, raised serum creatinine, acute respiratory distress syndrome, pulmonary hemorrhage, hyperbilirubinemia, hypotension, arrhythmias, & altered mental status, have been associated with adverse outcomes [12]. The present study included 50 patients to assess cardiovascular manifestations in leptospirosis.

The mean age of the study population was 43.64 ± 14.9 years, comparable to 45 ± 18 years reported by Abgueguen P et al. [13] and slightly higher than 37.3 ± 15.94 years reported by De Francesco Daher E et al. [14]. Males constituted 86% of cases, similar to the male predominance of 82.4% reported by De Francesco Daher E et al. [14] and 62% reported by Simi S et al. [15]. This predominance may reflect greater occupational and environmental exposure among males, particularly agricultural workers.

Fever and myalgia were the most frequent symptoms, occurring in 94% and 74% of patients, respectively, followed by vomiting (58%), headache (52%), oliguria (34%), and cough (22%). Simi S et al. [15] also reported fever and myalgia as prominent presentations, while Goswami R P et al. [16] documented fever, vomiting, oliguria, and cough in 100%, 41.6%, 34.7%, and 17.8% of cases. Similar symptom patterns were described by De Francesco Daher E et al. [17] and Katz A R et al. [18]. Agriculturists formed the largest occupational group (34%), supporting previous observations by Wang H K et al [19], Arumugam M et al. [20], and Katz A R et al. [18] that occupational exposure to contaminated soil, water, or infected animals increases the risk of leptospirosis. The common clinical signs were icterus (56%), tachycardia (30%), pallor (24%), hypotension (20%), edema (14%), clubbing (6%), and petechiae (4%). Comparable findings were reported by Arumugam M et al. [20] and Esen S et al. [21]. Electrocardiographic evaluation showed sinus rhythm in 54%, sinus tachycardia in 30%, atrial fibrillation in 6%, ST-T changes in 4%, and ventricular premature complexes in 2%. These findings closely corresponded with observations by Trivedi S et al. [22] and Chand P T et al. [23].

Mortality increased markedly with declining left ventricular ejection fraction, from 4.54% among patients with an ejection fraction of 51-60% to 100% among those with an ejection fraction below 30%. Chand P T et al. [23] similarly demonstrated increasing mortality with worsening ventricular function. Global hypokinesia was observed in 8% of patients. Overall mortality was 10%, compared with 16.7% reported by Esen S et al. [24]. CKMB levels were substantially higher among non-survivors, with a median of 57.65 compared with 21.45 among survivors, suggesting that elevated CKMB may indicate more severe cardiac involvement and could serve as a useful prognostic marker in leptospirosis.

CONCLUSION

This study demonstrates that cardiovascular involvement is an important component of leptospirosis and may influence clinical outcome. Sinus tachycardia was the commonest ECG abnormality, while atrial fibrillation, ST-T changes, ventricular premature complexes, and conduction abnormalities occurred less frequently. Most patients had preserved left ventricular systolic function, although global hypokinesia and reduced ejection fraction were observed in a minority. Mortality increased with declining ejection fraction, suggesting poorer prognosis with ventricular dysfunction. CK-MB levels were higher among non-survivors and were significantly elevated in non-survivors with global hypokinesia. Early cardiovascular assessment may therefore help identify high-risk patients and guide timely management during hospitalization.

LIMITATIONS & FUTURE PERSPECTIVES

The study's limitations include a single-centre setting, a relatively small sample size, and a short study duration, which may limit the broader applicability of the results. Future studies should incorporate multi-centre designs with larger population s to enhance validity, assess long-term outcomes, and investigate advanced

diagnostic & management approaches. Such efforts will improve overall patient care & help minimize complications.

CLINICAL SIGNIFICANCE

The clinical significance of this study lies in its potential to bridge the gap between research findings and practical health-care, diagnosis, and treatment outcomes. By highlighting real-care applications. It emphasizes the importance of translating scientific observations into meaningful improvements in patient world relevance, the study contributes to evidence based medical practice and supports informed clinical decision making. Ultimately, the findings aim to enhance patient quality of life, optimize therapeutic strategies, and promote better disease management in clinical settings.

ABBREVIATIONS

ECG: Electrocardiogram
EF: Ejection Fraction
CK-MB: Creatine Kinase-MB
VPCs: Ventricular Premature Complexes
LBBB: Left Bundle Branch Block
ELISA: Enzyme-Linked Immunosorbent Assay
IgM: Immunoglobulin M
LV: Left Ventricle
AF: Atrial Fibrillation
MAT: Multifocal Atrial Tachycardia
ST-T: ST-Segment and T-Wave

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AUTHOR CONTRIBUTIONS

All authors significantly contributed to the study conception and design, data acquisition, or data analysis and interpretation. They participated in drafting the manuscript or critically revising it for important intellectual content, consented to its submission to the current journal, provided final approval for the version to be published, and accepted responsibility for all aspects of the work. Additionally, all authors meet the authorship criteria outlined by the International Committee of Medical Journal Editors (ICMJE) guidelines.

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CONFLICT OF INTEREST

Authors declared that there is no conflict of interest.

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None

ETHICAL APPROVAL & CONSENT TO PARTICIPATE

All necessary consent & approval was obtained by authors.

CONSENT FOR PUBLICATION

All necessary consent for publication was obtained by authors.

DATA AVAILABILITY

All data generated and analyzed are included within this research article. The datasets utilized and/or analyzed in this study can be obtained from the corresponding author upon a reasonable request.

USE OF ARTIFICIAL INTELLIGENCE (AI) & LARGE LANGUAGE MODEL (LLM)

The authors confirm that no AI & LLM tools were used in the writing or editing of the manuscript, and no images were altered or manipulated using AI & LLM.

AUTHOR'S NOTE

This article serves as an important educational tool for the scientific community, offering insights that may inspire future research diretions. However, they should not be relied upon independently when making treatment decisions or developing public health policies.

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