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Original Research Article

Prevalence and clinical impact of heart failure in dengue-infected patients with Clarkson's disease

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ABSTRACT

Background: Dengue fever is a mosquito-borne viral infection with significant public health implications, especially in tropical regions. Capillary leakage syndrome (CLS), a severe complication of dengue, may lead to circulatory failure and multi-organ dysfunction. Emerging evidence links dengue to cardiac complications, yet the prevalence of heart failure in dengue patients with CLS remains underexplored. This study assessed the prevalence and clinical impact of heart failure in dengue patients with CLS.
Methods: A cross-sectional observational study was conducted at Government Medical College, Srikakulam, from September 2023 to February 2025. A total of 350 adult dengue patients were included. Patients were categorized based on the presence of heart failure and CLS. Laboratory parameters (hematocrit, serum albumin, NT-proBNP, troponin I) and cardiac assessments (ECG, echocardiography, chest X-ray) were analyzed. Statistical analysis identified predictors of heart failure in dengue patients with CLS.
Results: Heart failure was diagnosed in 44 patients (12.5%) with concurrent CLS. Patients had elevated hematocrit (48.5%±5.2), low serum albumin (1.8±0.4 g/dl) and raised NT-proBNP (1500±324 pg/ml) and troponin I (0.56±0.22 ng/ml). Echocardiography revealed reduced ejection fraction (28%), myocarditis (22%), pulmonary congestion (18%) and arrhythmias (16%). Significant predictors of heart failure included NT-proBNP>500 pg/ml, hypoalbuminemia <3.0 g/dl, hyponatremia <135 mmol/l and myocarditis on echocardiography.
Conclusions: Heart failure is an underrecognized but significant complication in dengue patients with CLS. Biomarker screening and early cardiac evaluation are vital for timely intervention and improved outcomes.

Keywords: Cardiac dysfunction, Capillary leakage syndrome, Dengue, Heart failure, Myocarditis, NT-proBNP

INTRODUCTION

Dengue fever, a mosquito-borne viral disease caused by the dengue virus (DENV), remains a significant global public health challenge, with an estimated 390 million infections occurring annually across more than 100 countries.[1] The disease is particularly prevalent in tropical and subtropical regions, where the Aedes aegypti and Aedes albopictus mosquito vectors thrive, creating an environment conducive to recurrent outbreaks.[2] Countries in South and Southeast Asia, Latin America and parts of Africa have witnessed a rising incidence of dengue fever, often leading to severe clinical outcomes and straining healthcare infrastructure.[3] India, among the most affected nations, has experienced frequent dengue epidemics in

recent decades, with a growing burden of severe dengue cases leading to increased morbidity and mortality.[4] Dengue fever presents with a diverse spectrum of clinical manifestations, ranging from asymptomatic or mild febrile illness to life-threatening complications such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[5] The progression to severe dengue is driven by complex pathophysiological mechanisms, including endothelial dysfunction, cytokine storms and heightened immune responses that result in increased vascular permeability and plasma leakage.[6] Systemic capillary leakage syndrome (CLS), a key feature of severe dengue, significantly contributes to circulatory collapse, multi-organ failure and, in some cases, death.[7] Despite advancements in dengue management, the unpredictability of CLS progression remains a major clinical concern.

Emerging evidence suggests that dengue virus infection may also lead to significant cardiovascular complications, a relatively underexplored aspect of the disease.[8] While dengue primarily affects the hematologic and vascular systems, recent studies have identified cardiac involvement in severe cases, including myocarditis, arrhythmias, pericardial effusion and acute heart failure.[9] Several mechanisms have been proposed to explain dengue-associated cardiac dysfunction, including direct viral invasion of myocardial cells, immune-mediated injury, systemic inflammation and electrolyte imbalances.[10] The interplay between CLS and heart failure further complicates the clinical picture, as fluid resuscitation essential in the management of dengue-induced capillary leakage can inadvertently exacerbate myocardial dysfunction in patients with compromised cardiac function.[11]

The burden of dengue-related cardiac complications is increasingly recognized worldwide, yet it's true prevalence remains uncertain due to underreporting and lack of routine cardiac assessment in dengue management protocols.[12] Studies from endemic regions have reported varying rates of myocarditis and heart failure among hospitalized dengue patients, with some suggesting that cardiac involvement is a strong predictor of adverse outcomes.[13]

Echocardiographic abnormalities, elevated cardiac biomarkers such as NT-proBNP and troponin and electrocardiographic changes have been observed in severe dengue cases, highlighting the need for enhanced cardiac surveillance in dengue patients.[14] Despite these findings, there remains a gap in systematic research evaluating the impact of CLS on cardiac function and its potential role in worsening dengue prognosis.

From a global health perspective, dengue continues to challenge healthcare systems, particularly in low- and middle-income countries, where outbreaks overwhelm hospital capacities and contribute to substantial economic burdens.[15] Inadequate healthcare resources, limited access to advanced diagnostics and high treatment costs disproportionately affect vulnerable populations, making early identification of high-risk patients crucial for improving outcomes.[16] The ongoing expansion of dengue into previously non-endemic regions due to climate change and urbanization further underscores the urgency of developing comprehensive management strategies that incorporate both infectious disease and cardiovascular care principles.[17]

Recognizing the clinical overlap between CLS and heart failure in dengue patients is essential for optimizing treatment approaches and reducing mortality. Given the limited data on the prevalence and predictors of heart failure in dengue patients with CLS, this study aims to address this gap by systematically evaluating the incidence of cardiac dysfunction in severe dengue cases. Through improved clinical awareness, early diagnostic markers and a multidisciplinary approach, this research seeks to enhance patient management and contribute to global efforts in mitigating dengue-related complications.

METHODS

Study design

This study is a cross-sectional observational study conducted to evaluate the prevalence and clinical characteristics of heart failure in dengue patients with concurrent capillary leakage syndrome (CLS).

Study place

The study was conducted in the Department of Medicine at Government Medical College Srikakulam, Andhra Pradesh, India.

Study duration

The study over a period of one and half years, from September 2023 to February 2025.

Study population

The study included adult patients diagnosed with dengue fever based on clinical presentation and laboratory-confirmed dengue infection. Patients were categorized based on the presence or absence of heart failure and CLS.

Sample size

A total of 350 dengue patients were enrolled in the study, of which 50 patients were diagnosed with both heart failure and CLS.

Inclusion criteria

Participants eligible for this study were adults aged 18 years or older who had a confirmed diagnosis of dengue fever, established through either NS1 antigen positivity or IgM serology. Additionally, patients were required to

exhibit evidence of capillary leakage syndrome (CLS), characterized by a hematocrit rise greater than 20% or clinical manifestations of plasma leakage, such as pleural effusion or ascites. Only those individuals who showed echocardiographic or biomarker-based indications of heart failure were considered. Furthermore, informed consent was a prerequisite for inclusion in the study and only patients who willingly provided written consent were enrolled.

Exclusion criteria

Patients were excluded from the study if they had any pre-existing cardiac conditions, including chronic heart failure or ischemic heart disease, as such conditions could confound the assessment of dengue-related cardiac dysfunction. The presence of concurrent illnesses, particularly sepsis or chronic kidney disease, also served as exclusion criteria due to their potential to interfere with accurate cardiac evaluation. Pregnant women were not included in the study owing to the physiological changes during pregnancy that might affect study parameters. Finally, individuals who declined to participate or failed to provide informed consent were excluded from enrolment.

Data collection

The collection of data encompassed a range of demographic and clinical parameters. This included the patient's age, gender, area of residence (urban or rural), socioeconomic status and clinical history. Detailed notes were taken on the duration of fever and the presence of any warning signs or symptoms suggestive of cardiac involvement, such as palpitations, dyspnea or chest discomfort. These data were recorded systematically at the time of admission using a standardized data collection form.

Laboratory investigations

Laboratory confirmation of dengue infection was performed using NS1 antigen testing along with IgM and IgG serologies. Markers indicative of capillary leakage syndrome included measurements of hematocrit and serum albumin levels. Cardiac function was assessed using biomarkers such as N-terminal pro-brain natriuretic peptide (NT-proBNP) and troponin I or T, which provided insight into myocardial strain or injury. Additionally, serum sodium and potassium levels were evaluated to detect electrolyte imbalances that may accompany severe dengue and contribute to cardiac dysfunction.

Cardiac assessment

Cardiac function was evaluated using a combination of imaging and electrophysiological modalities. Echocardiography was utilized to determine the left ventricular ejection fraction (LVEF), identify myocardial wall motion abnormalities and detect features suggestive of myocarditis. Electrocardiography (ECG) was employed to observe arrhythmic patterns and conduction disturbances. Furthermore, chest radiography was conducted to assess the presence of pulmonary congestion or pleural effusion, which could reflect volume overload or ongoing plasma leakage.

Diagnostic criteria for heart failure

The diagnosis of heart failure in this study was established through a combination of clinical, biochemical and imaging criteria. The Framingham criteria were used as the foundational clinical guideline for diagnosis. This was complemented by echocardiographic evidence of reduced LVEF below 50% and the presence of segmental or global wall motion abnormalities. Biochemically, heart failure was confirmed by elevated NT-proBNP levels equal to or exceeding 500 pg/mL, along with a concurrent rise in cardiac troponins, indicative of myocardial injury.

Ethical considerations

Ethical approval for this study was obtained from the Institutional Ethics Committee of Government Medical College Srikakulam. Written informed consent was obtained from all participants before enrolment.

Statistical analysis

Data were analyzed using SPSS version 22. Continuous variables were presented as mean±standard deviation and categorical variables were expressed as percentages. Comparisons between groups were performed using the chi-square test for categorical variables and the t-test for continuous variables. A p value <0.05 was considered statistically significant.

RESULTS

This study included a total of 350 participants diagnosed with dengue fever, with a mean age of 35.4±12.6 years. A male predominance (64%, p=0.036) was observed and urban residency accounted for 76% (p=0.017). The average duration from fever onset to presentation was 6.2 days and 30% of participants reported a prior history of dengue (p=0.025).

Prevalence of heart failure and CLS

Among the 350 dengue patients, 44 (12.5%) were identified as having heart failure with concurrent capillary leakage syndrome (CLS), while 306 (87.5%) had dengue without these complications. These findings suggest that while heart failure is not a universal complication of CLS, its presence in 12.5% of cases highlights the necessity for focused cardiac monitoring in dengue patients.

Laboratory findings

The laboratory results revealed significant abnormalities consistent with CLS and cardiac dysfunction. The mean

hematocrit was 48.5±5.2% (p=0.012), indicative of haemoconcentration. Serum albumin levels were reduced to 1.8±0.4 g/dl (p=0.001), reflecting plasma leakage. Cardiac biomarkers were notably elevated, with troponin I at 0.56 ng/ml (p=0.003) and NT-proBNP at 1500 pg/ml (p=0.007), indicating myocardial injury and cardiac stress. The mean serum sodium level was 131.5±4.6 mmol/l (p=0.038), showing hyponatremia, a common complication in severe dengue cases.

Echocardiographic and ECG findings

Echocardiographic assessments showed that 28% of patients had reduced left ventricular ejection fraction (LVEF<50%) (p=0.041), while 22% exhibited signs of myocarditis. Pulmonary congestion was detected in 18% of cases and arrhythmias were observed in 16% of patients on ECG. These findings emphasize the cardiac burden associated with CLS in dengue patients.

Predictors of heart failure in dengue patients with CLS

A multivariate analysis identified strong predictors of heart failure among dengue patients with CLS. Serum albumin <3.0 g/dl (OR 3.5, 95% CI: 1.8–6.9, p=0.004), NT-pro BNP>500 pg/ml (OR 4.2, 95% CI: 2.1–8.5, p=0.002), sodium <135 mmol/l (OR 2.8, 95% CI: 1.4–5.4, p=0.012) and myocarditis features on echocardiography (OR 5.1, 95% CI: 2.4–10.7, p=0.001) were significantly associated with heart failure risk.

Overall clinical impact

Heart failure was diagnosed in 5% of participants, while 6.25% had CLS without heart failure. These results underscore the need for early cardiac screening and multidisciplinary management in dengue patients presenting with CLS to improve outcomes.

Table 1: Demographic and clinical characteristics of study participants (n=350).

Characteristics	Frequency (N)	%	P value
Age (in years, Mean±SD)	35.4±12.6	-	-
Sex			
Male	220	62.9	0.036
Female	130	37.1	
Residence			
Urban	266	76	0.017
Rural	84	24	
Days of fever onset (Mean±SD)	6.2±2.1	-	-
Previous dengue history			
Yes	105	30	0.025
No	245	70	

Table 2: Laboratory parameters in the study participants (n=350).

Parameter	Mean±SD	Normal range	P value
Hematocrit (%)	48.5±5.2	36-44	0.012
Serum albumin (g/dl)	1.8±0.4	3.4-5.4	0.001
Troponin I (ng/ml)	0.56±0.22	0-0.04	0.003
NT-proBNP (pg/ml)	1500±324	<125	0.007
Sodium (mmol/l)	131.5±4.6	135-145	0.038

Table 3: Predictors of heart failure in dengue patients with CLS (n=44).

Predictor variable	Odds ratio (95% CI)	P value
Serum albumin<3.0 g/dl	3.5 (1.8–6.9)	0.004
NT-proBNP>500 pg/ml	4.2 (2.1–8.5)	0.002
Sodium<135 mmol/l	2.8 (1.4–5.4)	0.012
Myocarditis features on echo	5.1 (2.4–10.7)	0.001

DISCUSSION

This study investigated the prevalence and clinical impact of heart failure (HF) in dengue patients with capillary leakage syndrome (CLS) at Government Medical College, Srikakulam, India. Among 350 dengue patients, 44 (12.5%) were diagnosed with HF with concurrent CLS, underscoring the significance of cardiac involvement in severe dengue cases. Dengue is primarily recognized as a vascular disorder, but cardiac manifestations are

increasingly acknowledged. Myocarditis, arrhythmias and heart failure have been reported in severe dengue cases, suggesting direct viral myocarditis or systemic inflammatory effects.[18] The CLS observed in dengue results from vascular endothelial dysfunction, plasma leakage and hemoconcentration, which may contribute to myocardial stress and dysfunction.[19]

Demographic and clinical findings

This study identified a male predominance (62.9%), similar to previous reports highlighting a higher incidence of dengue in urban male populations due to greater vector exposure.[20] The mean age of participants was 35.4±12.6 years, with 76% residing in urban areas. These trends align with regional epidemiological data, which indicate that dengue outbreaks are more frequent in urbanized settings.[21]

The study also revealed that 30% of participants had a prior history of dengue, emphasizing the possibility of recurrent infections contributing to severe complications. The average time from fever onset to hospital presentation was 6.2 days, suggesting that delayed medical attention may contribute to severe outcomes, particularly in individuals with pre-existing cardiac risks.[22]

Laboratory and cardiac findings

Key laboratory parameters reflective of CLS and cardiac involvement were significantly altered. Hemoconcentration (elevated hematocrit), hypoalbuminemia and hyponatremia were present in a substantial proportion of patients, while raised levels of NT-proBNP and troponin I indicated myocardial stress and possible subclinical myocarditis. Cardiac imaging further supported this with reduced ejection fraction, evidence of myocarditis, pulmonary congestion and arrhythmic changes.

Notably, multivariate regression identified hypoalbuminemia, elevated NT-proBNP, hyponatremia and echocardiographic signs of myocarditis as statistically significant predictors of heart failure. These markers, particularly NT-proBNP and myocardial imaging findings, may provide clinicians with early tools for identifying patients at high risk of developing cardiac complications. These findings align with previous reports where dengue myocarditis was associated with impaired cardiac function and arrhythmic complications.[25]

Predictors of heart failure in dengue patients with CLS

The interplay between fluid resuscitation, a mainstay of CLS management and the risk of exacerbating heart failure presents a key clinical dilemma. A tailored management strategy emphasizing early biomarker screening, controlled fluid therapy and close cardiac monitoring could help reduce morbidity and mortality in such patients.

While these findings are insightful, they are limited by the single-centre design and lack of long-term follow-up data. Larger, multi-centre and longitudinal studies are needed to validate the predictors and understand the natural course of dengue-associated cardiac dysfunction.

Clinical implications and challenges

This study underscores the significant burden of cardiac complications in severe dengue and highlights the need for systematic cardiac screening in patients presenting with CLS. The coexistence of capillary leakage and heart failure poses a therapeutic challenge, as fluid resuscitation a mainstay of dengue management can exacerbate cardiac decompensation.

A balanced approach involving careful fluid management, electrolyte correction and cardiac monitoring is crucial in preventing worsening myocardial dysfunction. The use of biomarkers like NT-proBNP and early echocardiographic assessments can aid in early detection and targeted intervention.[24]

This study was conducted at a single-center tertiary care hospital, which may limit its generalizability to broader populations. Additionally, long-term follow-up data were unavailable, restricting the ability to assess the progression of cardiac dysfunction in dengue patients. Future multi-center studies with larger sample sizes and prospective follow-up are needed to further explore the relationship between CLS and heart failure.[25]

CONCLUSION

This study highlights the significant prevalence of cardiac dysfunction in dengue patients with CLS, emphasizing the need for early detection, biomarker-based diagnostics and multidisciplinary management. Elevated NT-proBNP, hypoalbuminemia and myocarditis emerged as strong predictors of cardiac complications, reinforcing the importance of proactive cardiac surveillance in severe dengue cases. A multidisciplinary approach involving infectious disease specialists, cardiologists and intensivists is essential to optimize management strategies and reduce morbidity and mortality in dengue patients with cardiac involvement.

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