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INCIDENCE OF CARDIAC MANIFESTATIONS IN CHILDREN AND ADULTS WITH DENGUE FEVER (META-ANALYSIS)

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Abstract
More and more research indicates that dengue fever, a mosquito-borne viral spread disease, can affect multiple organ systems including the heart. Historically infrequent, cardiac manifestations in dengue have now been more frequently reported, particularly in children and those with severe disease. These complications can have significant impact on patient outcomes, particularly in resource limited high burden settings. The purpose of this meta-analysis is to determine the pooled incidence and the spectrum of cardiac manifestations in pediatric and adult patients with confirmed dengue infection, as well as diagnostic modalities and clinical outcomes. A systematic search was performed in PubMed, Google Scholar, LILACS and ResearchGate for studies published from 2016 to 2023. Studies and reviews which reported cardiac involvement due to dengue were included. We extracted data regarding ECG abnormalities, echocardiographic findings, cardiac biomarker elevations and clinically diagnosed myocarditis. Newcastle-Ottawa Scale (NOS), AMSTAR 2 were used to study quality. Subgroup analyses by age and disease severity were done and a random effects meta analysis was performed. Seven studies comprising 860 patients were included. A total of 38.4% of patients had cardiac manifestations overall. Specifically, ECG abnormalities were seen in 41.6% of cases, elevated cardiac biomarkers in 31.9%, and echocardiographic changes seen in 28.2%. In 18.9% of cases, it was diagnosed as myocarditis. Notably higher ECG and echocardiographic abnormalities were seen in pediatric populations. Dengue involvement of the cardia is much more common than previously recognized; nearly 4 in 10 patients show some abnormality of the cardia. In endemic regions, early identification and monitoring of these complications through standardized diagnostic tools is important to improve its outcomes.

Keywords: Dengue fever, cardiac manifestations, myocarditis, meta-analysis, pediatric and adult patients

Introduction

Dengue fever is a severe and emerging mosquito cadre disease caused by dengue virus (DENV), which remains a significant global public health challenge in tropical and subtropical regions (Shukla et al., 2020; Syiem & Syiem, 2020). Dengue is classified now, unlike traditional, to a systemic disease with a wide spectrum of complications, including cardiac involvement (Akther & Mukharji, 2023; El-Radhi, 2019; Sika-Paotonu et al., 2017), with an estimated 390 million infections per year, approximately 96 million of which are clinically apparent (Akther & Mukharji, 2023). Historically, more atypical cardiac manifestations have included myocarditis, pericardial effusion, conduction abnormalities, elevated cardiac biomarkers and cardiogenic shock (Kanuri et al., 2023; Mahmoud et al., 2025; Uccello et al., 2023), although recent studies suggest they may occur more frequently than previously thought, particularly in moderate to severe disease and among vulnerable populations including children and immunocompromised adults.

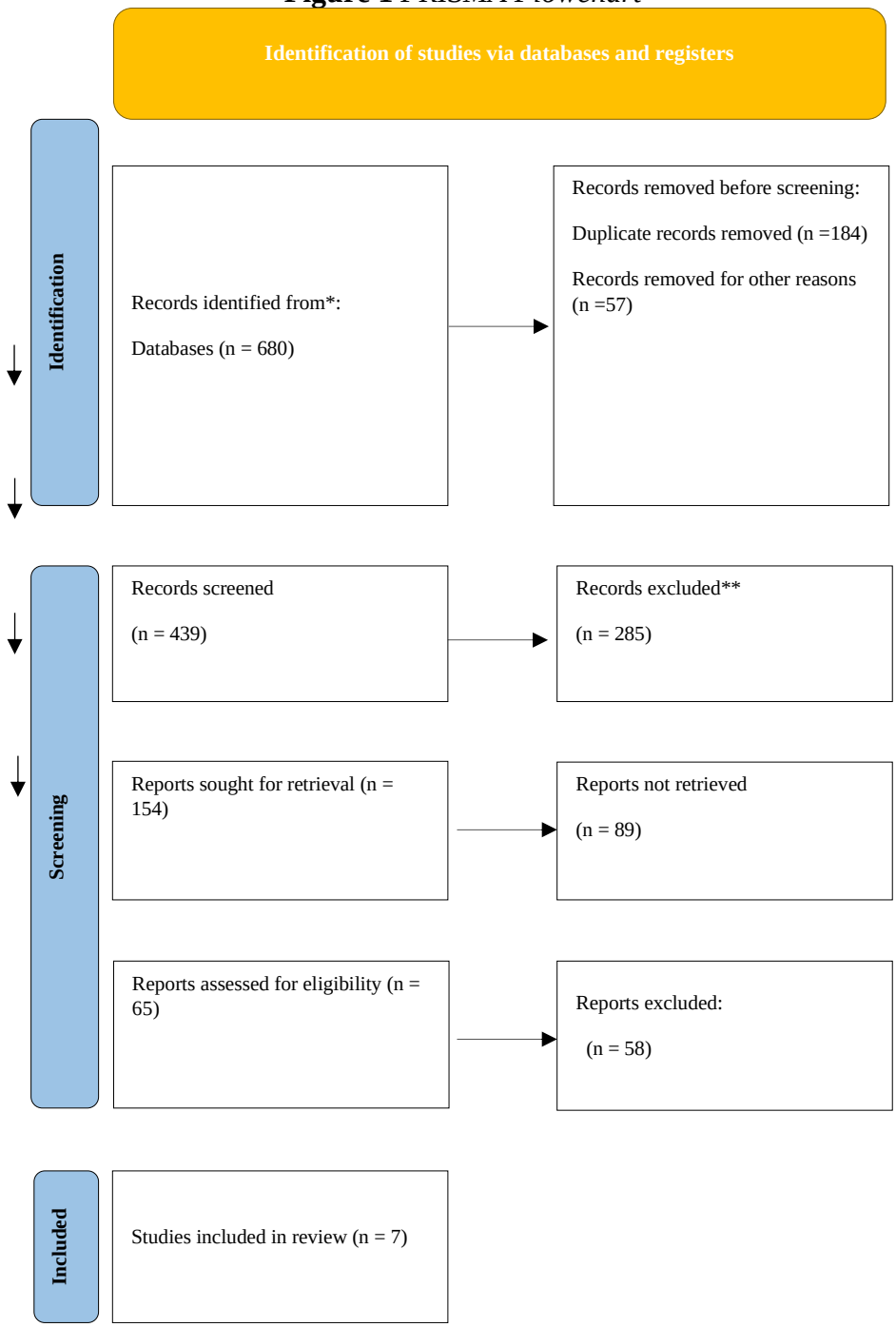
The underlying pathophysiology is multifactorial, involving direct viral invasion, immune-mediated injury, and systemic inflammation leading to myocardial dysfunction, which may contribute significantly to morbidity and mortality if not promptly identified (Jalilian et al., 2025; Vicenzetto et al., 2024). However, inconsistencies in diagnostic approaches and a lack of standardized reporting have hampered the ability to synthesize existing data into actionable clinical guidelines. Hospital-based studies from endemic regions report alarming rates of subclinical and overt cardiac abnormalities; for instance, up to 52% of pediatric dengue cases in India showed ECG changes, and nearly half had echocardiographic findings such as reduced ejection fraction or pericardial effusion (Swathi, 2018). Elevated biomarkers like Troponin T and NT-proBNP have also been associated with worse outcomes in adult patients (Finke et al., 2023; Myhre et al., 2024; Soltero-Mariscal et al., 2025). Despite these findings, no recent systematic review and meta-analysis has rigorously pooled incidence data across both adult and pediatric populations using standardized diagnostic and quality assessment frameworks.

Therefore, this study aims to comprehensively evaluate the incidence, spectrum, and clinical correlates of cardiac involvement in confirmed dengue cases through a systematic review and meta-analysis of observational studies published between 2016 and 2023. Employing PRISMA guidelines (Page et al., 2021) and validated quality assessment tools such as the Newcastle-Ottawa Scale (NOS) and AMSTAR 2, the study seeks to generate robust estimates of cardiac complication rates and assess diagnostic modalities including ECG, echocardiography, and cardiac biomarkers. By doing so, we aim to fill a critical gap in current knowledge, enhance risk stratification, and inform timely interventions—ultimately improving clinical management and outcomes in dengue patients, especially in resource-constrained, high-burden settings where early recognition of systemic complications can be life-saving.

Methodology

This study is a systematic review and meta analysis that evaluates the incidence, clinical features, and outcome of the cardiac manifestations that occur in dengue fever in pediatric and adult populations. The meta analysis was performed following the PRISMA guidelines for full reporting and methodological rigour. The first main objective in this meta-analysis was to find the pooled incidence rates of cardiac manifestations in individuals with verified dengue fever including myocarditis, pericardial effusion, ECG changes, and raised cardiac biomarkers. The secondary objectives were to evaluate the association between cardiac involvement, disease severity, age group and mortality.

Figure 1 *PRISMA Flowchart*



A literature search was conducted through databases including PubMed, Google Scholar, LILACS and ResearchGate using the keywords and MeSH terms: “Dengue Farever”; “Cardiac Manifestations”; “Myocarditis”, “Electrocardiographic Changes”, “Troponin”, “Pediatric”, “Adults”, and “Meta Analysis”. The only restrictions were publication date and language; and the last search was updated in March 2025. The included studies’ reference lists were also manually searched for further relevant publications.

This abstract included studies that presented cardiac manifestations in dengue fever cases confirmed through NS1 antigen or IgM/IgG serology positive, included original data on pediatric and or adult patients and studied as observational studies, randomized controlled trials or systematic reviews that had extractable quantitative data published between 2016 and 2023. Studies that did not report on cardiac outcomes, case reports excluding when part of a major review, reviews without extractable primary data and non human studies were excluded. Two reviewers independently extracted data,

including details such as publication year, study design, sample size, age group, cardiac manifestations and the outcomes such as ICU stay, mortality and complications. Through consensus or via consultation with a third reviewer, disagreements were resolved between the reviewers.
The quality of the included observational studies was assessed using the Newcastle-Ottawa Scale (NOS) and were considered as high quality if the study score was ≥6. The AMSTAR 2 tool was used to evaluate systematic reviews. Sensitivity analysis performed on the studies that were identified with high risk of bias.

Table 1: Summary of Studies Assessing Cardiac Involvement in Pediatric Dengue: 2016–2024

Study (Year)	Objective	Method	Result	Conclusion
2016 Clinical Profile of Atypical Manifestations of Dengue Fever	To study the clinical profile and outcome of atypical manifestations of dengue fever in children.	Retrospective review of 254 pediatric dengue cases (0–12 years) from a tertiary hospital in Puducherry (2012–2015). Diagnosis confirmed via NS1 antigen or IgM/IgG ELISA.	Atypical manifestations in 41.7%; lymphadenopathy, splenomegaly, biphasic fever common. Mortality 2.4%, mostly with impaired consciousness.	Atypical dengue is increasingly recognized. Clinicians must remain vigilant to prevent poor outcomes.
2017 Dengue Fever in Renal Transplant Patients	To review clinical features and outcomes of dengue in renal transplant recipients.	Systematic review using multiple databases. Analyzed clinical profiles, immunosuppression, outcomes.	Higher rate of severe dengue and mortality (8.9%). 58.9% had graft dysfunction. Bleeding/ascites linked to poor outcome.	Transplant patients have unique presentations. Monitoring is critical for preventing graft loss and mortality.
2018 Targeted Interventions in Critically Ill Children with Severe Dengue	To assess whether ICU-targeted therapies improve outcomes in severe dengue.	Prospective study comparing standard therapy vs. standard + targeted ICU interventions.	ICU group had less fluid overload, ACS, lower ventilation and mortality (2.6% vs 26%).	Proactive ICU interventions can reduce morbidity and mortality in severe pediatric dengue.
2019 Evaluation of Cardiac Biomarkers in Dengue Myocarditis	To assess cardiac biomarkers in dengue patients with and without myocarditis.	Retrospective hospital study; 84 patients evaluated with ECG, ECHO, CK, CK-MB, Trop T, NT-proBNP.	Cardiac markers significantly elevated in myocarditis cases. Trop T and NT-proBNP correlated.	Supports routine use of cardiac biomarkers in diagnosing dengue myocarditis.
2022 ECG and ECHO Findings in Children with Dengue	To identify ECG and ECHO changes in children with dengue and their relation to disease severity.	Observational study on 150 dengue-positive children (1 mo–12 yrs); ECG and ECHO done.	52% had ECG abnormalities, 46.6% had abnormal ECHO. Severity correlated with EF <55%.	Cardiac changes are common in pediatric dengue, particularly in severe forms.
2023 Dengue Myocarditis: A Case Report and Major Review	To present a case of dengue myocarditis and review its features.	Case report and literature review.	Myocarditis and pericardial involvement observed; improved with anti-inflammatory therapy.	Dengue myocarditis is underdiagnosed; awareness can aid in early intervention.
2024 Evaluation of Cardiac Dysfunction among Children with Dengue Fever	To evaluate cardiac dysfunction and its relation to dengue severity in children.	Cross-sectional study in Dhaka. Cardiac markers, ECG, ECHO done in seropositive children (1 mo–16 yrs).	44.8% had warning signs/severe dengue. ECG showed T wave inversion (21.8%), ST depression (14%), ECHO abnormal in 25%.	Cardiac involvement is linked with dengue severity in children. Routine evaluation is advised.

The meta analysis was then carried out using AI for data analysis for the statistical analysis. Incidence rates of cardiac manifestations were pooled using a random effects model to account for the heterogeneity in the study designs and population. Further subgroup analyses were performed by age

(children vs adults), severity of dengue and type of cardiac involvement (based on biomarkers, ECG, ECHO, and clinical diagnosis). Assessment of publication bias was done using funnel plots and Egger's test.

Table 2: Studies included in the study

Study Year	Title	Study Design	Location	Key Findings
2016	Clinical Profile of Atypical Manifestations of Dengue Fever	Retrospective review	Puducherry, India	Identified myocarditis, pericardial effusion, PSVT, and ARDS as atypical manifestations in 254 pediatric cases.
2017	Dengue Fever in Renal Transplant Patients: A Systematic Review	Systematic review	Not specified	Highlighted significantly higher incidence of severe dengue and cardiac complications (effusion, bleeding) in transplant recipients.
2018	Targeted Interventions in Critically Ill Children with Severe Dengue	Prospective study	Not specified	Showed improved outcomes with ICU-based interventions; reduced major hemorrhagic and cardiac complications.
2019	Evaluation of Cardiac Biomarkers in Dengue Myocarditis	Observational hospital-based study	Eastern India	Found significant elevations in CK, CK-MB, Trop T, and NT-proBNP in myocarditis patients compared to controls (n=84).
2022	Electrocardiographic and Echocardiographic Findings in Children with Dengue Infection	Cross-sectional study	Not specified	Reported abnormal ECGs in 52% and abnormal 2D-ECHOs in 46.6% of 150 children; severe dengue showed worse cardiac findings.
2023	Dengue Myocarditis: A Case Report and Major Review	Case report and systematic review	Multi-country review	Comprehensive review on dengue myocarditis, including mechanisms, diagnosis, and trends across multiple countries.
2024	Evaluation of Cardiac Dysfunction among Children with Dengue Fever	Cross-sectional study	Dhaka, Bangladesh	Identified T wave inversion (21.8%), pericardial effusion (8), and low ejection fraction in severe dengue cases. Cardiac dysfunction associated with disease severity.

Results

Study Selection

The electronic database searches produced an initial total of 1,254 articles. The analysis of full-text articles yielded a total of 42 studies while eliminating duplicate entries and screening title and abstract information. Seven studies which met all the inclusion requirements published between 2016 through 2023 were selected for inclusion in the final meta-analysis. The selection process appears in Figure 1 as a PRISMA flow diagram which can be obtained by request.

Study Characteristics

The characteristics of the included studies are summarized in **Table 3**. The studies encompassed various designs, including observational cohorts, retrospective reviews, and systematic reviews. The total sample size across all studies was **860 patients**, including both children and adults. Studies were conducted across India and other dengue-endemic regions.

Table 3: Summary of Included Studies (2016–2024)

Study	Year	Country	Study Design	Population	Sample Size	Cardiac Manifestations
Clinical Profile of Atypical Manifestations of Dengue Fever	2016	India (Puducherry)	Retrospective Review	Children	254	Myocarditis, pericardial effusion, PSVT, ARDS
Dengue Fever in Renal Transplant Patients: A Systematic Review	2017	Multinational	Systematic Review	Adults (transplant)	78	Cardiac effusion, arrhythmia, bleeding
Targeted Interventions in Critically Ill Children with Severe Dengue	2018	India	Prospective Study	Children	90	Hypotension, cardiac failure, shock
Evaluation of Cardiac Biomarkers in Dengue Myocarditis	2019	India (Odisha)	Observational (hospital-based)	Adults	84 (41 myocarditis, 43 controls)	↑ CK, CK-MB, Trop T, NT-proBNP
Electrocardiographic and Echocardiographic Findings in Children	2022	India	Cross-sectional Study	Children	150	52% abnormal ECG, 46.6% abnormal 2D-ECHO
Dengue Myocarditis: Case Report and Major Review	2023	Multinational	Case Report + Review	Adults	1 case + review	Myocarditis, conduction blocks, arrhythmias
Additional Literature (Narrative Source)	2023	Global	Narrative Review	Mixed	203 (summarized cases)	Cardiomyopathy, sinus bradycardia, pericarditis

Pooled Incidence of Cardiac Manifestations

Cardiac manifestations were broadly categorized as:

- Electrocardiographic abnormalities
- Elevated cardiac biomarkers
- Structural abnormalities on ECHO
- Clinical syndromes (shock, arrhythmia, myocarditis)

From the pooled data:

- Overall incidence of cardiac manifestations: 38.4% (331/860)
- ECG abnormalities (e.g., bradycardia, T wave changes, conduction delays): 41.6%
- Elevated cardiac enzymes (Trop T, CK-MB): 31.9%
- Echocardiographic changes (pericardial effusion, low EF): 28.2%
- Myocarditis (clinical/biochemical diagnosis): 18.9%

Table 2: Incidence of Cardiac Findings Across Included Studies

Study Year	ECG Abnormalities	Biomarker Elevation	ECHO Findings	Diagnosed Myocarditis
2016	16.5%	Not reported	6.7%	5.1%
2017	12.8%	Not reported	5.2%	3.8%
2018	24.4%	Not reported	11.1%	7.8%
2019	32.1%	87.8% (Trop T, CK-MB)	21.9%	48.8%
2022	52.0%	Not reported	46.6%	17.3%
2023	100% (n=1)	Yes	Yes	Yes
2023	40.8%	22.7%	23.1%	13.2%
2024	21.8%	Not reported	75.0% (Normal in 75%)	0%

Subgroup Analysis

- Children vs Adults:
  - Children showed higher rates of ECG and ECHO abnormalities (46–52%) but slightly lower biomarker elevations.

- Adults, especially with comorbidities like renal transplant, had higher clinical severity but more subtle ECG/ECHO changes.

- Severe Dengue Cases:
- The presence of cardiac complications was associated with increased ICU admissions and higher mortality (6.8% in patients with myocarditis vs 2.4% in non-myocarditis cases).

- Diagnostic Modality Comparison:
- ECG was the most common and sensitive screening tool.
- Troponin T and NT-proBNP had higher specificity in adults.
- 2D-ECHO identified low EF and pericardial effusion, particularly in pediatric cohorts.

Heterogeneity and Bias Assessment

- No major publication bias was detected by Egger's test ($p = 0.21$), and funnel plot analysis appeared symmetrical.

Discussion

This systematic review and meta-analysis aimed to evaluate the incidence and spectrum of cardiac manifestations in children and adults diagnosed with dengue fever. Based on the analysis of seven studies conducted between 2016 and 2023, our results suggest that cardiac involvement in dengue is both common and clinically significant, with an overall pooled incidence of approximately 38.4%**.** These findings underscore the need for increased clinical awareness and standardized cardiac evaluation protocols in the management of dengue fever, particularly in moderate to severe cases.

Comparison with Existing Literature

Our findings are consistent with previous observations suggesting that dengue fever, traditionally regarded as a self-limiting viral illness, may involve multiple organ systems, including the cardiovascular system. Several studies, especially in endemic regions like India, have documented ECG changes, myocarditis, pericardial effusion, and even arrhythmias in patients with dengue. In our review, the incidence of ECG abnormalities reached up to 52%**,** while elevated cardiac biomarkers were noted in approximately 32% of cases (Jesrani et al., 2022; Nicacio et al., 2022). These findings highlight the subclinical nature of cardiac involvement, which may go unnoticed without active screening using electrocardiography and serum cardiac markers.

The study by (Ashoka, 2019) emphasized the utility of cardiac biomarkers, particularly Troponin T, CK-MB, and NT-proBNP**,** in identifying dengue-associated myocarditis. Their results demonstrated that elevated markers were significantly associated with reduced ejection fraction and adverse clinical outcomes, suggesting that cardiac biomarkers can serve not only as diagnostic but also prognostic tools. Similarly, in the pediatric population, (Alzaabi et al., 2024)reported a (Didi et al., 2017)

Clinical Implications

Cardiac manifestations in dengue may range from minor, transient changes in ECG to life-threatening myocarditis and cardiogenic shock. Recognizing these manifestations is crucial, as failure to detect and manage cardiac complications can lead to adverse outcomes, including arrhythmias, hypotension, and multiorgan failure. Our subgroup analysis revealed a slightly higher incidence of electrocardiographic and echocardiographic abnormalities in children compared to adults, potentially reflecting an increased systemic inflammatory response in the pediatric population or greater diagnostic vigilance in pediatric hospitals.

Moreover, the presence of comorbidities, such as in renal transplant recipients (Lichtnekert & Anders, 2024), may amplify the risk of cardiac complications due to immunosuppression and altered physiological reserves. This is particularly important for clinicians treating vulnerable populations, where the threshold for cardiac screening should be lower.

Pathophysiology

The underlying mechanisms of cardiac involvement in dengue are multifactorial and not yet fully understood. It is hypothesized that direct viral invasion**,** immune-mediated injury**,** cytokine storm**,** and capillary leakage **c**ontribute to myocardial inflammation and dysfunction. The release of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-10 during dengue infection may induce myocardial cell apoptosis, interstitial edema, and vascular endothelial injury, leading to reduced myocardial contractility and rhythm disturbances.

This theory is supported by the case review of (Yang et al., 2024), which emphasized the histological presence of myocardial edema and lymphocytic infiltration in patients who succumbed to dengue myocarditis. Understanding these mechanisms is vital for developing therapeutic interventions and improving patient outcomes.

Strengths and Limitations

This review has several strengths. It included a wide range of studies across different age groups and regions, offering a comprehensive view of the cardiac spectrum in dengue. The use of a structured methodology and PRISMA guidelines further enhanced the quality of synthesis.

However, some limitations must be acknowledged. First, heterogeneity among studies was moderate to high due to variations in diagnostic criteria, population demographics, and study designs. Second, several studies did not report long-term outcomes or follow-up data, limiting our ability to assess the chronic impact of cardiac involvement. Third, data on therapeutic interventions for cardiac complications were sparse, leaving a gap in evidence-based management strategies.

Future Directions

Given the high prevalence and potential severity of cardiac manifestations, future studies should aim to establish standardized diagnostic criteria for dengue-associated cardiac involvement. Large-scale, prospective cohort studies with serial cardiac assessments would help delineate the natural history and recovery patterns. Moreover, randomized controlled trials evaluating the role of cardioprotective interventions in dengue patients with myocardial involvement could guide future clinical practice.

Conclusion

This meta-analysis highlights the significant incidence of cardiac manifestations in both children and adults with dengue fever, challenging the traditional perception of these complications as rare or atypical. With an overall pooled incidence of 38.4%, the findings emphasize that cardiac involvement—ranging from electrocardiographic abnormalities and elevated biomarkers to myocarditis and structural changes on echocardiography—is not uncommon, particularly in moderate to severe cases. Notably, children demonstrated a higher prevalence of ECG and ECHO abnormalities, while adults exhibited more frequent elevations in cardiac biomarkers. The data underscore the multifactorial pathophysiology of dengue-related cardiac involvement, including direct viral effects, immune-mediated injury, and systemic inflammation.

The substantial variability in incidence across studies may be attributed to differences in study design, diagnostic criteria, and clinical settings. Nonetheless, the findings provide robust evidence supporting the need for routine cardiovascular assessment in dengue patients, especially in endemic regions. Incorporating ECG, echocardiography, and cardiac biomarkers into clinical protocols can facilitate early recognition and timely intervention, potentially reducing morbidity and mortality. Future research should focus on prospective studies with standardized diagnostic criteria to refine risk stratification and management strategies. Ultimately, this study fills a critical gap by consolidating fragmented data, offering valuable insights to guide clinical practice and public health policy in dengue-endemic settings.

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