Unveiling the Dual Threat: Myocarditis in the Spectrum of Dengue Fever

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Abstract: This meta-analysis aims to systematically review and analyze available studies on the association between myocarditis and dengue viral fever. A comprehensive literature search was carried out using several databases. Mantel-Haenszel odds ratios and associated 95% confidence intervals were produced to report the overall effect size using random effect models. Besides, random effects models were used to

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calculate the overall pooled prevalence. Data from 26 articles (6622 dengue patients) showed that pooled estimate of myocarditis in dengue fever was 12.4% (95% CI, 8.41-17.08). Higher prevalence was seen in reports from Asia (15.2%) compared to that from Latin America (3.6%). Besides, the pooled prevalence of severity and mortality was 34% (95% CI, 20.49-49.04) and 26.44% (95% CI, 18.07-35.78) respectively. Significantly higher prevalence rates of severe disease in the pediatric population (52.4%) and studies with a higher percentage of females (52.1%) were also observed. However, higher mortality rates were seen in the adult population (34.8%) compared with the pediatric age group. Further, myocarditis in dengue patients was associated with increased risk of severity (RR = 2.44, 95% CI 1.007-5.93, $P = 0.048$) and mortality (RR = 19.41, 95% CI 7.19-52.38, $P < 0.001$) compared with dengue patients without myocarditis. No significant publication bias was evident in the meta-analysis. The findings highlight the clinical significance of early identification and management of myocarditis in patients with dengue fever. (Curr Probl Cardiol 2024;49:102029.)

Introduction

Dengue viral infection is a major global health concern caused by the virus from the flavivirus family, with an estimated 390 million infections and approximately 20,000 deaths reported annually.[1] It has 4 serotypes (DENV-1 to DENV-4), often found in tropical and subtropical regions.[1] The Aedes aegypti mosquito is the principal carrier of the disease. In 2009, the WHO reclassified dengue infection: as "dengue without warning signs," "dengue with warning signs," and "severe dengue with and without hemorrhage."[2] The spectrum of dengue illness ranges from asymptomatic or mild forms to severe manifestations, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).[3]

Myocarditis, an inflammatory condition of the cardiac muscle, has received increased attention in recent years as one of the less common but potentially fatal dengue complications.[4] Researchers and medical professionals alike are becoming increasingly interested in myocarditis in relation to dengue infection. The involvement of the heart in dengue viral

infection creates a complex and difficult scenario because it can result in cardiac dysfunction, arrhythmias, and even heart failure.[5] Myocarditis caused by dengue is complex in pathogenesis and involves immune-mediated pathogenic pathways, direct viral invasion of cardiac tissues, and host immune response to the infection.[6] It is crucial to understand the occurrence and outcomes of myocarditis in dengue viral infection. Accurate knowledge of these factors can aid in early intervention approaches, the identification of high-risk individuals, and better patient outcomes.[6]

The true prevalence of myocarditis and its clinical consequences in the context of dengue infection, however, are still unknown, primarily because different study designs, sample sizes, and geographical locations have been used. A growing body of individual studies has reported varying estimates of myocarditis prevalence in dengue viral infection.[7-9] The variability in these study findings, however, highlights the need for a comprehensive and systematic evaluation to determine the true prevalence of dengue myocarditis and its impact on patient outcomes.

We present a rigorous meta-analysis that offers a thorough overview of the prevalence and outcomes of myocarditis in dengue viral infection in this article. We seek to provide a more thorough understanding of this dengue-related cardiac complication by combining and analyzing data from various sources, strengthening the knowledge base for clinicians to improve patient care and public health initiatives.

This meta-analysis aims to systematically review and analyze available studies on the association between myocarditis and dengue viral fever. The goals of this study were to (1) estimate the prevalence of myocarditis in patients with dengue fever; and (2) analyze the clinical outcomes of myocarditis in this cohort, such as severity, and mortality, by focusing on these goals, we want to offer insightful information about myocarditis effects on dengue patients and highlight areas that need more research.

Methods

Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines are followed in the communication and inscription of the present systematic review and meta-analysis.[10]

Search Strategy

A comprehensive literature search was conducted with PubMed and Embase until July 20th, 2023. The MedRxiv and SSNR preprint servers

were also filtered. We combined Medical Subject Headings (MeSH) terms and keywords, and subsequent search terms were, ([Dengue viral fever] or [Dengue hemorrhagic fever] or [Dengue infection] AND [Myocarditis] or [Heart] or [Cardiac complication] or [Outcomes] or [Shock] or [Mortality]). Investigations came from all over the world and there were no language barriers. We manually searched the relevant literature as well as the reference lists of the included studies to identify additional qualifying studies. Duplicate citations were eliminated, and the remaining articles were evaluated based on their titles and abstracts. The PRISMA flow diagram is depicted in Figure 1.

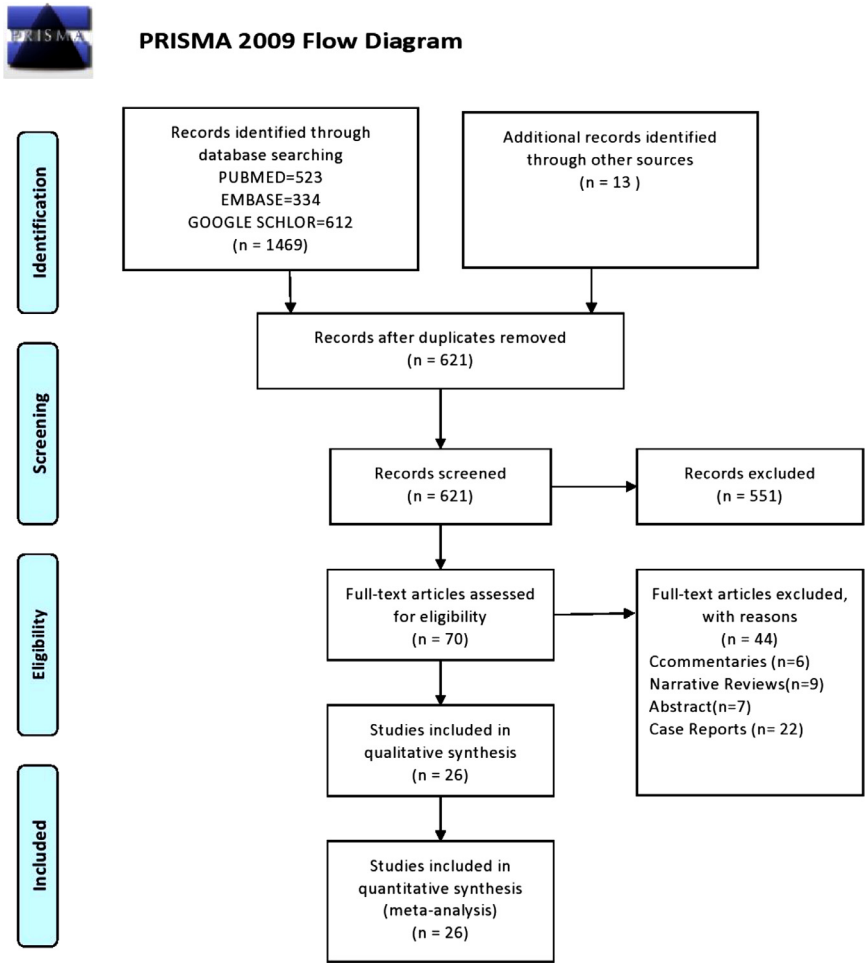

FIG 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram. (Color version of figure is available online.)

Eligibility Criteria

All qualified studies were comprised in this meta-analysis. To be competent for this meta-analysis, the article must fulfill the subsequent inclusion criteria: (1) an article describing myocarditis in dengue patients; (2) an article describing the prevalence or outcomes of myocarditis in the dengue patients' group. These studies were included irrespective of the patient's age, gender, ethnicity, and geographical region. Diagnosis of myocarditis was either based on ESC 2013 criteria or with a combination of markers of myocardial injury, ECG abnormalities, and imaging.

The exclusion requirements were established beforehand: (1) if no data regarding prevalence or outcomes is given, (2) duplicate publications, (3) letters to the editor, commentaries, reviews, case reports, and posters. Following the fulfillment of these requirements, an extensive interpretation of the residual studies and data extraction was accomplished in an Excel Table.

Study Selection and Quality Assessment

The titles and abstracts of the previously found papers were examined separately by the 2 authors. The predetermined eligibility standard was used to distinguish the studies by each author. Negotiation and a prior agreement that a third author would assess the difference in opinion aided in resolving the conflict. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of included observational studies and to assess the risk of bias.[11] Two authors independently utilized the Newcastle-Ottawa Scale (NOS) for assessing the individual quality of observational studies. The following sections were rated per study: low bias risk (8-9 points), moderate bias risk (5-7 points), and high bias risk (0-4 points).

Data Extraction

Data extraction for each study was advanced independently by 2 authors and then cross-checked to minimize errors. From each study, several details were retrieved, including the first author's name, year of publication, the origin country of the study, study design, dengue sample size, mean age, female proportion, Patients with myocarditis, severe dengue patients, and all-cause mortality.

Statistical Analysis

MedCalc Statistical Software version 19.6.4 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021) was utilized for all

statistical analyses. The pooled prevalence and associated 95% confidence interval (CI) were calculated using the random effect model. Subgroup analysis was done according to a variable such as the geographic location of the study, the patient's age group that is, age less than or more than 16 years, and the percentage of female patients in the sample size. Results for outcome analysis were presented as relative risk (RRs) with 95% CIs and pooled using the Mantel-Haenszel random-effects model. The I2 statistics were used to assess the heterogeneity of effect size estimates across these studies with I2 (low heterogeneity: I2≤25%; moderate: 25%-50%; high>75%). Publication bias was explored using funnel plots, Egger's regression test, and Begg-Mazumdar's rank correlation test.

Result

Characteristics of the Included Studies

Preliminary scans in numerous databases yielded 1482 articles. A total of 621 studies were evaluated from this group after removing duplicates. After taking into account the title and abstract, 551 articles were further eliminated, leaving 70 papers that could be considered plausible for this analysis after passing the article review. Based on thorough review and inclusion criteria, 26 articles totaling 6622 dengue patients were eventually included in this meta-analysis.[4-9,12-31] Table 1 summarizes the baseline characteristics of the studies that were included. Table 1 summarizes the demographics of the patients as well as the study characteristics.

Meta-Analysis for the Prevalence of Myocarditis in Dengue Viral Infection

Overall pooled random effects estimate of myocarditis in patients admitted with dengue fever across studies was 12.4% (95% CI, 8.41-17.08). Test statistics results revealed high heterogeneity ($I^2 = 96.07\%\%$, $p < 0.0001$). This effect was pooled from 25 studies incorporating 6583 patients admitted with dengue fever (Fig 2). Subgroup analysis was done for the data according to variables such as geographic region, patients' age group, and percentage of female patients in the sample. Analysis showed that the prevalence of myocarditis in Asia, Latin America, adult population, pediatric population (<16 years), studies with greater than 50% female patients, and studies with less than 50% female patients was 15.2%, 3.6%, 12.5%, 16.5%, 8.5%, and 16.7% respectively (Table 2). (Supplemental Fig 1).

TABLE 1. Baseline characteristics of included studies

Study	Year	Study type	Country	Sample size	Mean age (Years)	Female proportion, %	Diagnostic Criteria for Myocarditis	Myocarditis patients	Definition of severity
Baqi et al.[4]	2022	Retrospective	Pakistan	1008	NA	32	Marker of myocardial injury	42	Shock
Kaur et al.[9]	2022	Prospective	India	418	NA	24	NA	6	NA
Cabrera-Rego et al.[8]	2021	Prospective	Cuba	427	NA	NA	NA	1	NA
Buntubatu et al.[7]	2019	Prospective	Indonesia	50	8	30	Marker of myocardial injury	39	Shock
Lue et al.[12]	2022	Retrospective	Jamaica	339	6	50	NA	6	Hemorrhagic feature
Mansuanguan et al.[13]	2021	Prospective	Thailand	81	33	54	ESC myocarditis criteria	2	Hemorrhagic feature
Salgado et al.[14]	2010	Prospective	Colombia	102	6	NA	Marker of myocardial injury	11	NA
Miranda et al.[15]	2013	Prospective	Brazil	91	32	52	NA	4	NA
Shah et al.[5]	2021	Retrospective	India	320	NA	38	Marker of myocardial injury	56	Shock
Kularatne et al.[16]	2018	Case series	Sri Lanka	6	27	60	Marker of myocardial injury	1	NA
Arora et al.[18]	2013	Retrospective	India	120	33	30	NA	44	NA
Gupta et al.[17]	2022	Retrospective	India	150	36.7	65	ESC myocarditis criteria	41	Shock
Bhatt et al.[19]	2020	Prospective	India	182	30	31	ESC myocarditis criteria	13	Major bleeding
Li et al.[6]	2016	Retrospective	China	1782	NA	NA	ESC myocarditis criteria	201	Shock
Atmaja et al.[20]	2022	Retrospective	Indonesia	39	NA	NA	Marker of myocardial injury + ECG abnormalities	39	Shock
Weerakoon et al.[21]	2009	Prospective	Sri Lanka	319	NA	NA	Clinical diagnosis	45	NA
Satarasinghe et al.[22]	2007	Retrospective	Sri Lanka	217	NA	33	2D Echo	52	NA
Rivillas et al.[23]	2017	Cross-Sectional	Colombia	60	63	45	Marker of myocardial injury + ECG abnormalities	3	ICU Admission
Hussain et al.[24]	2017	Retrospective	Pakistan	128	32	33	NA	24	NA
Kularatne S et al.[25]	2005	Retrospective	Sri Lanka	190	30	NA	NA	5	Shock

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TABLE 1. (*continued*)

Study	Year	Study type	Country	Sample size	Mean age (Years)	Female proportion, %	Diagnostic Criteria for Myocarditis	Myocarditis patients	Definition of severity
Menwal et al.[26]	2020	Cross-Sectional	India	60	12	40	EF < 50%	5	NA
Bhat et al.[27]	2018	Case seies	India	11	36	20	ECG findings and clinical evaluation	6	Shock
Siddappa et al.[28]	2014	prospective	India	39	6.5	47	EF < 55%	10	NA
Kabra et al.[29]	1998	prospective	India	54	NA	NA	EF < 50%	9	Shock
Neeraja et al.[31]	2014	prospective	India	175	NA	39	Marker of myocardial injury + ECG abnormalities	16	Shock
Pothapregada et al.[30]	2016	Prospective	India	254	6.9	45	NA	5	Shock

NA- Not available.

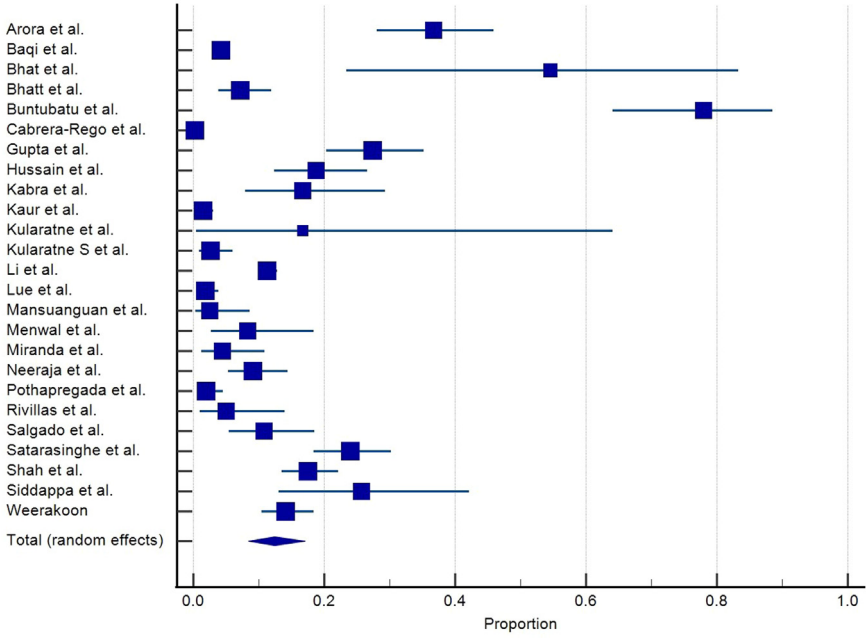

FIG 2. Forest plot for meta-analysis of the pooled prevalence of myocarditis in dengue patients. (Color version of figure is available online.)

Meta-Analysis for Severity Outcome

Overall pooled random effects estimate of severe disease in dengue viral infection presenting with myocarditis across studies was 34% (95% CI, 20.49-49.04). Test statistics results revealed high heterogeneity ($I^2 = 86.4\%$, $p < 0.0001$). This effect was pooled from 14 reports incorporating 429 dengue patients presenting with myocarditis (Fig 3). Subgroup analysis was done for the data according to variables such as patients' age group and percentage of female patients in the sample. Analysis showed that the prevalence of Severe disease in myocarditis patients in the adult population, pediatric population (<16 years), studies with greater than 50% female patients, and studies with less than 50% females was 30.2%, 52.4%, 52.1%, and 34.3% respectively (Table 2). (Supplemental Fig 2).

Meta-analysis results also indicated that myocarditis in dengue fever patients is associated with a higher risk of severe infection compared to patients without myocarditis. (RR = 2.44, 95% CI 1.007-5.93, $P = 0.048$). This outcome had moderate associated heterogeneity ($I^2 = 80.5\%$). The result was based on 1153 dengue patients' data (Fig 5A).

TABLE 2. Result of pooled prevalence outcome

Outcome	Number of studies (pooled sample)	Proportion %	95% CI	*P* (Test for heterogeneity)	*I2*
1.Pooled prevalence					
Overall	25 (6583)	12.419	8.410−17.081	$P < 0.0001$	96.07%
1.1 By geographic region					
Asia	20 (5883)	15.209	10.657−20.405	$P < 0.0001$	95.74%
Latin America	5 (1019)	3.671	0.919−8.152	$P < 0.0001$	87.88%
1.2 By age group					
Adult (>16 years)	10 (1515)	12.549	5.656−21.661	$P < 0.0001$	95.36%
Pediatric (<16 years)		16.571	4.837−33.453	$P < 0.0001$	96.85%
1.3 By female proportion in sample size					
Females greater than 50%	5 (667)	8.572	1.168−21.818	$P < 0.0001$	94.70%
Females less than 50 %	14 (3042)	16.709	9.675−25.202	$P < 0.0001$	96.67%
Severity outcome	Number of studies (Number of myocarditis patients)				
The pooled estimate of the severity	14 (429)	34.025	20.492−49.042	$P < 0.0001$	86.44%
2.1 By age group					
Adult (>16 years)	7 (86)	30.292	14.035−49.624	$P = 0.0078$	65.58%
Pediatric (<16 years)	4 (55)	52.405	39.721− 64.933	$P = 0.3943$	0.00%
2.2 By female proportion in sample size					
Females greater than 50%	3 (49)	52.146	6.828−95.176	$P = 0.0005$	86.71%
Females less than 50 %	8 (128)	34.376	20.689−49.539	$P = 0.0089$	62.74%

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TABLE 2. (*continued*)

Outcome	Number of studies (pooled sample)	Proportion %	95% CI	*P* (Test for heterogeneity)	*I2*
3. Mortality outcome	Number of studies (Number of myocarditis patients)				
The pooled estimate of mortality	7 (87)	26.447	18.071−35.782	*P* = 0.5602	0.00%
3.1 By age group					
Adult (>16 years)	3 (24)	34.884	18.393−53.501	*P* = 0.8077	0.00%
Pediatric (<16 years)	2 (17)	20.623	3.938−45.767	*P* = 0.2354	28.97%
3.2 By female proportion in sample size					
Females greater than 50%	2 (10)	41.492	16.404−69.232	*P* = 0.612	0.00%
Females less than 50 %	3 (61)	27.024	16.939−38.482	*P* = 0.4150	0.00%

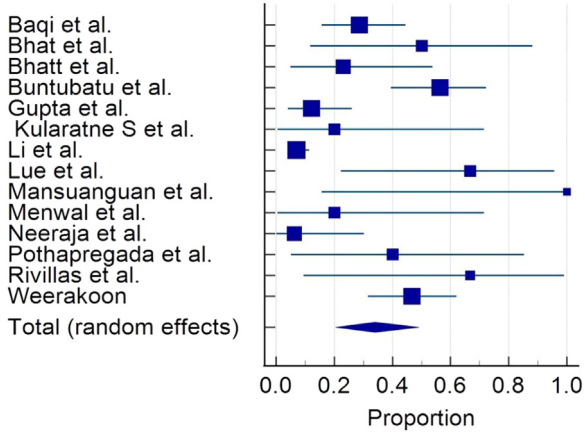

FIG 3. Forest plot for meta-analysis of the pooled prevalence of severe disease in dengue patients presenting with myocarditis. (Color version of figure is available online.)

Meta-Analysis for Mortality Outcome

Overall pooled random effects estimate of mortality in dengue viral infection presenting with myocarditis across studies was 26.44% (95% CI, 18.07-35.78). Test statistics results revealed moderate heterogeneity ($I^2 = 59.1\%$, $p < 0.0001$). This effect was pooled from 17 reports incorporating 87 dengue patients presenting with myocarditis (Fig 4). Subgroup analysis was done for the data according to variables such as patients' age group and percentage of female patients in the sample. Analysis

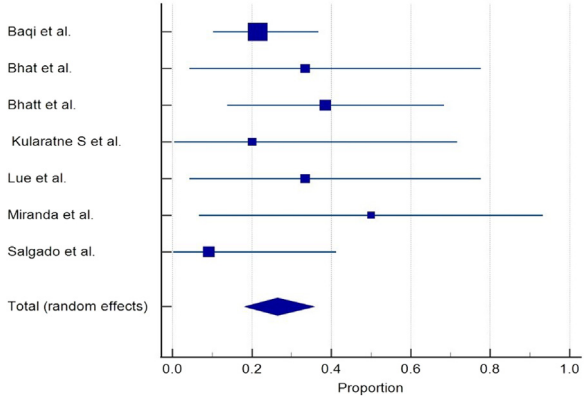

FIG 4. Forest plot for meta-analysis of the pooled prevalence of mortality in dengue patients presenting with myocarditis. (Color version of figure is available online.)

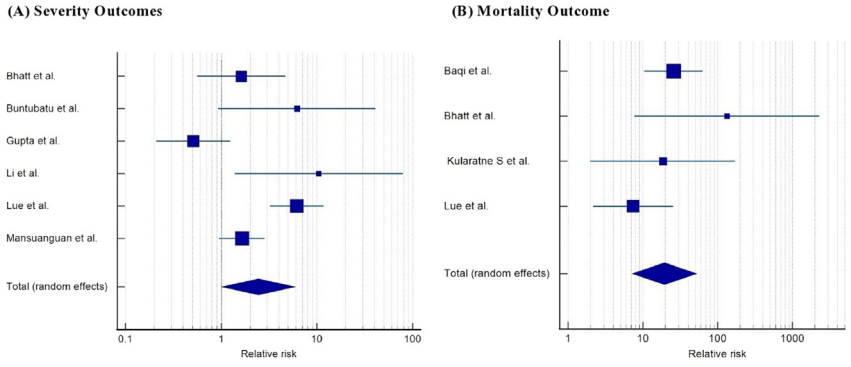

FIG 5. Forest plot for Risk ratio Meta-analysis of outcomes. (Color version of figure is available online.)

showed that the prevalence of mortality in myocarditis patients in the adult population, pediatric population (<16 years), studies with greater than 50% females, and studies with less than 50% females was 34.8%, 20.6%, 41.4%, and 27% respectively (Table 2). (Supplemental Fig 1).

Meta-analysis results also indicated that myocarditis in dengue fever patients is associated with a very higher risk of mortality compared to patients without myocarditis. (RR = 19.41, 95% CI 7.19-52.38, $P < 0.001$). This outcome had low associated heterogeneity ($I^2 = 39.8\%$). The result was based on 1719 dengue patients' data (Fig 5B).

Risk of Bias Assessment

The risk of bias assessment and quality assessment of incorporated observational studies were done with the aid of the Newcastle-Ottawa Scale (NOS). Out of 25 studies, 16 studies were of high quality, and 9 were of moderate quality, with an average score of 7.5. (Supplemental Table 1). Collectively, the evidence employed in these analyses was ascertained as being of good quality.

Publication Bias

Visual inspection of the standard funnel plots for all the analyses was identified as having low to Moderate symmetry. Correspondingly, the evaluation of publication bias was also escorted with the help of Egger's regression test and Begg-Mazumdar's rank correlation test. For both these tests, $p < 0.05$ was considered significant, and the analysis was considered to have publication bias. No evident publication bias was

witnessed for most analyses done in this study, however, Egger's regression test for severity prevalence outcomes had a *P* value less than 0.05, but the corresponding Begg-Mazumdar's rank correlation test showed no evidence of publication bias for this outcome. Hence, this analysis was almost without publication bias (Supplemental Table 2).

Discussion

Myocarditis caused by dengue viral infection is a potentially serious and emerging complication that requires close monitoring due to its impact on disease severity and mortality outcomes. For the purpose of this meta-analysis, we systematically assessed the incidence, severity, and mortality of myocarditis in patients admitted with dengue fever from various studies. Our meta-analysis findings shed light on the important clinical implications of myocarditis in dengue viral infection and provide valuable insights into the risk factors and outcomes associated with this complication.

Our meta-analysis revealed an overall pooled random effect estimate of myocarditis prevalence at 12.4% in patients admitted with dengue fever. The high heterogeneity observed ($I2 = 96.07\%$) among the included studies indicates considerable variability in the prevalence rates across different populations and regions. Subgroup analyses based on geographic region, patients' age group, and the percentage of female patients in the sample further highlighted the diversity in myocarditis prevalence. Notably, Asia exhibited the highest prevalence of myocarditis at 15.2%, while Latin America had a notably lower prevalence of 3.6%. Variations in dengue viral strains, genetic predisposition, and healthcare practices may all play a role in these regional disparities.[8] Age and gender were also identified as significant factors influencing the prevalence of myocarditis. The pediatric population showed a higher prevalence rate of 16.5% compared to 12.5% in the adult population. This discrepancy might be attributed to differences in immune response and myocardial susceptibility between age groups, as proposed by some reports.[12] Furthermore, studies with a higher percentage of female patients showed a lower prevalence rate of myocarditis (8.5%) compared to studies with a lower percentage of female patients (16.7%). Studies have reported a higher male percentage in surveillance data with dengue infection.[32] Besides, these gender-based disparities might be attributed to hormonal and immunological factors, which warrant further investigation.[33]

Furthermore, our meta-analysis indicated that the overall pooled random effects estimate for severe disease in dengue viral infection

presenting with myocarditis was 34%. The high heterogeneity observed (I2 = 86.4%) suggests that various factors such as age, gender, comorbidities, etc. might contribute to the variability in disease severity. Subgroup analysis based on patients' age group and the percentage of female patients revealed significantly higher prevalence rates of severe disease in the pediatric population (52.4%) and studies with a higher percentage of females (52.1%). These findings suggest that younger patients and females might be more vulnerable to severe outcomes when myocarditis is present alongside dengue viral infection. This is in accordance with a previously published report, which also reported a similar effect.[4,19] Likewise, our meta-analysis demonstrated a significant association between myocarditis and an increased risk of severe infection compared to patients without myocarditis, with a relative risk (RR) of 2.44. However, it is essential to interpret this result cautiously, considering the moderately associated heterogeneity (I2 = 80.5%). Similarly, the overall pooled random effects estimate of mortality in dengue viral infection presenting with myocarditis was 26.44%. Subgroup analysis based on patients' age group and the percentage of female patients highlighted higher mortality rates in the adult population (34.8%) and studies with a higher percentage of females (41.4%). Multiple factors might be responsible for this effect such as multiple comorbidities in the adult population, hormonal and immunological factors, etc.[32] These results emphasize how vital it is to take into account gender and age as risk factors for mortality in myocarditis patients who have a dengue viral infection. Moreover, our meta-analysis demonstrated a significant association between myocarditis and a substantially higher risk of mortality compared to patients without myocarditis, with a remarkably high relative risk (RR) of 19.41. The markedly increased risk of mortality might be attributed to the direct impact of myocarditis on cardiac function and the exacerbation of dengue-associated complications.[34]

The various cardiovascular manifestations of dengue infection are explained by complex pathophysiology. Myocarditis in these patient groups might be caused by a bunch of pathophysiologic mechanisms. (1) Direct cardiac tropism and viral replication: One of the causes of myocarditis in dengue infection might be due to the ability of the dengue virus to directly invade and replicate within cardiac cells, as seen with other viruses.[35] A study from Colombia showed that in a child with fatal DHF, myotubes were found to be infected with the dengue virus despite the myocardial sections having minor cellular infiltrates and appearing morphologically normal.[14] This was discovered utilizing immunofluorescence confocal microscopy on heart tissue. Besides, direct injury to

cardiac myocytes by NS1 antigen has also been reported.[15,19] This direct invasion has the potential to damage cells, impair the heart's ability to contract, and even cause cardiac dysfunction. (2) Immune response and cytokine storm: myocarditis caused by the dengue virus is frequently accompanied by a cytokine storm. Patients with dengue fever have higher levels of serum tumor necrosis factor, interleukins 6, 13, and 18, and cytotoxic factors, which enhance vascular permeability and cause shock.[36] Myocardial inflammation and injury are exacerbated by the unchecked inflammatory cascade, which also damages heart tissues. Consequently, the severity of myocarditis might be linked to the intensity and duration of the cytokine storm. (3) Viral virulence and strain variability: Variable levels of pathogenicity are present in various dengue virus serotypes and strains. It is possible that some strains have a stronger affinity for cardiac tissue, which can cause more severe myocardial inflammation and damage. When the DEN serotype was specified, only DEN-2 and DEN-3 were reported to be the responsible viruses in dengue patients with cardiac problems.[22]

In addition, the emergence of new dengue virus strains or mutations may also influence modifications in the disease's clinical manifestation, such as myocarditis.[37] (4) Host genetic factors and susceptibility: host genetic factors have been implicated in influencing the susceptibility to myocarditis in dengue-infected individuals. Polymorphisms in genes encoding various immune response molecules, such as human leukocyte antigen (HLA) and cytokines, may predispose certain individuals to a more severe immune reaction, exacerbating myocardial inflammation and injury.[38,39]

Besides, the immunological response to dengue infection may be weakened in those with pre-existing medical illnesses, such as chronic inflammatory disorders or immunodeficiencies, making them more vulnerable to serious cardiac involvement.[40] Understanding these complex pathways is crucial for early diagnosis, risk assessment, and individualized therapy strategies to reduce the potentially fatal effects of myocarditis in dengue-infected individuals. To enhance clinical outcomes, further research is needed to clarify our understanding of these determinants and design focused therapies.

A thorough strategy involving numerous medical principles and modalities is required for the diagnosis and treatment of myocarditis in dengue virus infection. Early detection is helped by clinical evaluation, which includes history and symptoms. Diagnostic data is typically obtained via laboratory tests like CBC, dengue serology, and cardiac-specific biomarkers.[6,18,26] Electrocardiography and echocardiography play

vital roles in assessing cardiac function and detecting myocardial abnormalities Cardiac MRI, with its superior tissue characterization capabilities, can aid in the diagnosis and assessment of myocarditis. Late gadolinium enhancement (LGE) on MRI can demonstrate areas of myocardial inflammation and fibrosis, aiding in prognosis.[17] Supportive care is necessary to ensure proper hydration and hemodynamic support. Anti-inflammatory drug use (NSAIDs, corticosteroids) is still debatable because of the possibility of worsening virus replication. It is crucial to treat dengue fever and its side effects, including heart failure and arrhythmias.[4,41,42] The prognosis depends on the severity of myocardial involvement. Monitoring cardiac recovery and any challenges requires long-term follow-up.[43] To achieve the best possible results for patients with myocarditis brought on by dengue virus infection, a multidisciplinary collaborative approach is required.

Our study has some limitations that need to be acknowledged despite its benefits and contributions. First off, the precision of our estimates may be impacted by the fact that some studies had relatively small sample sizes. Secondly, studies with all age groups, and all geographical regions were included, which might result in heterogeneity, although we tried to minimize that with subgroup analysis. Finally, because our analysis was based on published studies, the possibility of publication bias cannot be completely ruled out.

In conclusion, this meta-analysis provides comprehensive insights into the prevalence, severity, and mortality outcomes associated with myocarditis in dengue viral infection. The findings highlight the clinical significance of identifying and managing myocarditis in patients with dengue fever, particularly in pediatric populations and studies with a higher percentage of female patients. Clinicians should be vigilant in monitoring patients for signs of myocarditis and implementing appropriate therapeutic interventions to mitigate the risk of severe outcomes and mortality. Future research is warranted to elucidate the underlying mechanisms of myocarditis in dengue viral infection and identify potential targets for intervention and risk stratification.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Competing Interest

Authors have no potential conflicts of interest to disclose.

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None.

Supplementary materials

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