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Emerging Problems in Infectious Diseases

Cardiac involvement in dengue infection

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Abstract

Introduction: Dengue is endemic in the tropics, and complications involving organ systems are seen with varying incidence.
Methodology: We performed a systematic review. MEDLINE, EMBASE, Scopus SciVerse, Google Scholar, and LILACS were searched for papers providing information on cardiac involvement in dengue.
Results: Cardiac involvement is not uncommon in dengue infection and is often transient, but may be associated with significant morbidity and even mortality. Direct viral invasion, immune mechanisms, electrolyte imbalance, derangement of intracellular calcium ion storage, lactic acidosis, and ischemia due to hypotension all play a role in myocardial dysfunction. The manifestations of cardiac involvement include clinical, electrocardiographic, echocardiographic, cardiac enzyme, and histopathologic abnormalities. Echocardiography appears to be a useful tool for detecting myocardial involvement and should be performed in patients with electrocardiographic abnormalities or hemodynamic instability. Treatment is largely supportive, though there are some anecdotal reports of improvements with specific agents.
Conclusions: Knowledge on cardiac manifestations in dengue is limited, and further studies are needed to establish the exact pathophysiology and role of specific agents in the prevention and treatment of cardiac complications in dengue.

Key words: dengue; myocarditis; pericarditis; shock; heart; cardiac; calcium.

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Introduction

Dengue is one of the most important mosquito-borne illnesses worldwide [1]. It is a caused by a flavivirus with four distinct serotypes (DENV1, DENV2, DENV3, and DENV4). Current estimates project that 390 million infections occur annually, in over 100 countries, of which 96 million result in clinical disease with a case fatality rate of around 1% [2]. Infection with one of the serotypes is thought to result in lifelong serotype-specific immunity. Serious disease is thought to occur mainly, though not exclusively, as a result of a second infection by a different serotype [3]. The mechanisms that result in the development of the severe, life-threatening dengue shock syndrome remain an enigma. The primary pathophysiological phenomenon of the disease that occurs is acute vascular leakage, which lasts for 24–48 hours after its onset.

Despite being traditionally considered a disease of children, dengue is now known to affect individuals of any age, and results in significant economic impact. Dengue infection is difficult to control; no specific treatment or vaccine is available, and vector control is fraught with difficulties. There is no specific treatment for dengue [4].

The natural history of dengue infection usually follows a clear pattern. The majority of infections are asymptomatic and subclinical. Symptomatic disease follows an incubation period of four to seven days, and begins as an acute febrile illness with high temperature, malaise, retro-orbital headache, myalgia, backache, nausea, loss of appetite, and vomiting [5]. For management purposes, clinical illness is divided into three phases: the febrile phase, the critical phase, and the recovery phase. Around the third to seventh day of illness, the critical phase, which is associated with a dropping platelet count, recovery of leukopenia, and defervescence, may begin. The critical phase is defined by the occurrence of features of plasma leakage: rising hematocrit, clinical or radiological evidence of third-space fluid leakage, and, in some cases, hypotension. A proportion of patients develop severe clinical shock, of which a minority proceed to develop relentless severe intractable shock, coagulopathy with bleeding, and multi-organ failure, which can culminate in death [6].

As the incidence of dengue increases, reports of atypical manifestations are also on the rise, although these may be underreported because of lack of awareness and under-diagnosis of dengue [7]. The incidence of various complications, in both serologically diagnosed patients and those with merely a clinical diagnosis without supporting serology, is quite similar [8]. A variety of atypical manifestations of dengue have been described [7]. In one study of 913 schoolchildren with dengue, a wide variety of complications were observed: hepatitis (27%), neurological alterations (25%), renal impairment (7%), cardiac involvement (8%), pulmonary changes (9%), acalculous cholecystitis (9%), hemophagocytic syndrome (2.5%), pancreatitis (1%), and acute abdominal pain (11%) [9].

Cardiac involvement is not uncommon and is encountered in centers handling large numbers of dengue cases. Clinical manifestations of cardiac involvement can vary widely, from silent disease to severe myocarditis resulting in death. Rhythm abnormalities, hypotension, arrhythmias, myocarditis, myocardial depression with symptoms of heart failure and shock, and pericarditis have been reported. Involvement of multiple organs as well as the presence of metabolic derangement can further confuse the picture [10,11]. Still, the significance of cardiac involvement in dengue infection is not fully understood. Myocarditis, pericarditis, and cardiomyopathy after dengue have been reported in the literature from the 1970s [12-15]. During outbreaks, incidence of myocarditis as high as 13% has been reported; electrocardiographic changes have been noted in up to 62.5% of patients [16-17]. In this paper, we review the published literature on the pathophysiology, clinical features, and investigation findings of cardiac involvement in dengue, and identify implications for treatment and future research.

Methodology

MEDLINE, EMBASE, Scopus SciVerse, Google Scholar, and LILACS were searched for papers containing the keyword dengue with any of the following: cardiac, myocarditis, myocardial, myocard*, pericarditis, pericardial, pericard*, echocardiogram, ECG, electrocardiogram, electrocard*, or heart in the abstract or text. The search was restricted to the past four decades. There were 178 abstracts found during the combined search. Endnote X5 was used to filter the papers. All authors read through the abstracts and identified relevant papers; the full text was read through in these. Related references were also included. Sixty-seven papers provided relevant information. The key studies showing evidence of cardiac involvement in dengue are summarized in Table 1.

Dengue virus serotypes and the heart

Dengue fever is caused by four dengue virus serotypes, DENV1, DENV2, DENV3, and DENV4 [18-19]. DENV2 is associated with unusual manifestations of dengue and asymptomatic myocarditis [20,21], and has also been shown to cause myocardial dysfunction in children who had dengue hemorrhagic syndrome (DHF) or dengue shock syndrome (DSS) in a series of 17 patients in India [22]. Kularatne *et al*. [23] described three cases of myocarditis caused by DENV3 in Sri Lanka. Although there are no reports of cardiac involvement in DENV1 or DENV4, there is inadequate evidence to determine whether a particular serotype is preferentially associated with cardiac involvement. Although severe dengue is said to occur mostly with secondary infection by a different serotype [24], whether cardiac involvement is more common with secondary infection is also not known. Further studies are needed to establish the relationship between serotypes, antigenicity, and cardiac involvement. The variability of cardiac involvement between epidemics [25] is possibly a reflection of variations in antigenicity in relation to serotypes.

Difficulties in defining cardiac involvement in dengue

The main difficulty in describing the manifestations and frequency of cardiac involvement in dengue is the lack of clear criteria to define cardiac involvement. Hypotension, shock, arrhythmias, and pulmonary edema have all been described in severe cases of dengue. However, patients with severe dengue can have gross derangement of hemodynamics and homeostasis as a consequence of plasma leakage and tissue hypoperfusion. For example, shock and pulmonary edema occur as a result of plasma leakage or volume overload due to acute kidney injury. Thus, even if concurrent cardiac involvement were present, it would be difficult to differentiate it in the clinical setting. The degree to which myocardial dysfunction contributes to shock is not clearly known. In a cohort of dengue patients on whom echocardiographic assessments were performed, mean left ventricular ejection fraction (LVEF) was similar in patients with and without shock; furthermore, depressed left ventricular function was more commonly seen in patients without shock [26].

Table 1. Studies of cardiac dysfunction in dengue

Reference	Study population	Findings/outcomes/conclusions
Kularatne *et al*. 2005 [16]	n = 404; 13–85 years	Myocarditis diagnosed by ECG in 5 cases; 1 death due to arrhythmia (total 3 dengue deaths).
Satarasinghe *et al*. 2007 [21]	n = 217; 12–65 years	185 subjects had echocardiography; 24% had echo evidence of myocarditis; all myocarditis cases had bradycardia; 1 patient had Wenckebach phenomenon. No mortalities. Echo abnormalities absent on long-term echocardiographic follow-up.
Wali *et al*. 1998 [22]	n = 17; 14–58 years	ECG, echo, radionucleotide ventriculography, and Tc pyrophosphate imaging utilized. ECG showed ST and T wave changes in 5/17 patients. Global hypokinesia in 12/17. Mean LVEF in DSS 39.6%.
Khongphatthanayothin *et al*. 2007 [26]	n = 91; 10.5 ± 2.9 years	DF = 30, DHF = 36, DSS = 25. EF by echo < 50% in 6.7% DF, 13.8% DHF, and 36% DSS patients (p = .01). Troponin not elevated (11/91 evaluated).
Lateef *et al*. 2007 [28]	n = 39; 32.8 ±10.8 years; Matched controls	Mean HR lower in the dengue group: 87.6 (± 12.5)/min (dengue) 104.6 (± 14)/min (controls). (p < 0.0001). All in sinus rhythm.
La-Orkhun *et al*. 2011 [39]	n = 35; 11.7 ± 2.3 years	24-hour Holter done on defervesence. 29% had rhythm abnormalities. Sinus pauses (1); first-degree AV block (2) and Mobitz type I second-degree AV block (Wenckebach) (3); atrial (4) and ventricular ectopic beats (5). Abnormalities unrelated to severity of dengue.
Salgado *et al*. 2009 [41]	n = 102; Children ≤ 13 years	11 (10.7%) with myocarditis. 10 needed inotropes. 9 bradyarrhythmias, 2 tachyarrhythmias, echo-pericardial leakage in 2 and diminished LVEF in 1. Myocarditis in relation to the severity of dengue statistically significant (p = 0.0004).
Khongphatthanayothin *et al*. 2003 [44]	n = 23; 10.8 ± 2.8 years	Echocardiography performed during toxic, convalescent stages and 2 weeks after discharge. LVEF lower during toxic stage than after recovery. End-diastolic volume low during toxic stage and normalized during convalescence and recovery. Cardiac index low during the toxic stage due to decreased preload and depressed LVEF. Cardiac index subnormal during convalescence due to sinus bradycardia.
Kabra *et al*. 1998 [46]	n = 54; 6.3 ± 2.9 years	LVEF < 50% = 9/54. Repeat echocardiography in 3 children after 2 months showed improved LVEF.

Sengupta *et al*. 2013 [49]	n (DF) = 20;
	23 ± 8 years;
	n (control) = 20;
	23 ± 5 years
		LVEF reduced in patients with DHF at presentation compared with controls (51.25 ± 0.96% vs. 59.32 ± 1.26%; p = 0.032). Compared to controls, DHF patients had attenuated peak longitudinal strain in subendocardial region, increased circumferential strain evident only in the subepicardial region (p = 0.009), and higher radial strain (p < 0.001).

Yadav *et al*. 2013 [51]	n = 67; 3 months – 14 years	Tei index showed myocardial involvement in 70%. Tei index improved on discharge but did not normalize. 1 fatality.
Yacoub *et al*. 2012 [48]	n = 79; 8–46 years	Echo tissue Doppler imaging showed 45% with systolic and 42% with diastolic impairment. Patients with severe dengue have more severe systolic and diastolic cardiac dysfunction. 51/79 had ECGs, of which 18 were abnormal; 3/10 (30%) in dengue, 11/32 (34%) in dengue+ and 4/9 (44%) in the severe group; abnormalities included first-degree AV block, sinus bradycardia, T wave changes, and ST segment abnormalities.
Salgado *et al*. 2010 [68]	n = 102; DF = 23; DHF = 79; 1–13 years	Myocarditis in 11/79 (14%) with DHF. ECG showed sinus bradycardia (9/11), tachycardia (2/11), and T-wave inversions 7/11. 7 had echo: pericardial effusion in 5, diastolic function impairment in 2. Elevated CPK-MB found in 6 patients with myocarditis.
Miranda *et al*. 2013 [45]	n = 81; 32 ± 21 years; DF = 54 (67%); DHF I-II = 26 (32%); DHF III-IV = 1; 4 months to 81 years	Troponin I elevated in 6 (7%), NT-proBNP elevated in 10 (12%). 8 (10%) had clinical heart involvement: heart failure (4), shock and chest pain, 3 each. 2 deaths from refractory cardiogenic shock. Echocardiography abnormal 4/10: abnormal wall motion with preserved LVEF 2/4, abnormal wall motion and reduced LVEF 1/4, pericardial effusion 1/4. Cardiac involvement was confirmed by CMR in the 4 patients with abnormal echo.

ECG: electrocardiogram; echo: echocardiogram; DF: dengue fever; DHF: dengue hemorrhagic fever; DSS: dengue shock syndrome; LVEF: left ventricular ejection fraction; AV: atrioventricular; CMR: cardiac magnetic resonance imaging; NT-proBNP: N-terminal pro-brain natriuretic peptide; CPK-MB: creatine phosphokinase myocardial band

However, lower LVEF did correlate with increased need for fluid replacement and increased third-space fluid loss. Metabolic derangement, including abnormalities of sodium, potassium, and calcium are seen in severe dengue shock, and arrhythmias could occur as a result. Thus, separating secondary cardiac effects from primary cardiac involvement is fraught with difficulties, and this may have led to under-reporting of cardiac involvement in the past. Clinical features, electrocardiographic abnormalities, abnormal cardiac biomarkers, and echocardiographic findings have been evaluated in various studies as possible markers of cardiac involvement in dengue.

Clinical and electrocardiographic abnormalities

The presence of electrocardiogram (ECG) abnormalities has been used by some authors to denote cardiac involvement in dengue [16]. A diverse range of ECG abnormalities have been reported with dengue, including rate and rhythm abnormalities, heart block, wave form abnormalities, and voltage abnormalities [27-41]. Reported rhythm abnormalities include relative bradycardia [28], sinoatrial block [29], disorders of atrioventricular conduction (junctional rhythm [29-31], second-degree [32] and complete heart block [27,33], and monomorphic premature ventricular contractions on a background of heart block [32]), atrial flutter [34], transient [27,35] and persistent [36] atrial fibrillation, self-limiting tachy-brady arrhythmia [37], sinoatrial block, and uniform ventricular ectopics progressing to ventricular bigemini [38]. Electrocardiographic features mimicking acute myocardial infarction have also been reported [40].

ECG abnormalities may be asymptomatic or go undetected. In a prospective study in Thailand, 18- to 24-hour Holter monitoring was performed on 35 children at least 24 hours after defervescence; 10 patients (29%) had abnormalities of rhythm (sinus pause [n = 1], first-degree AV block [n = 2], Mobitz type I second-degree AV block [n = 3], atrial ectopics [n = 4], ventricular ectopics [n = 5]) [39]. No relationship was demonstrated between the clinical severity of dengue and the incidence of rhythm abnormalities. In another prospective study in a cohort of children with DHF, 102 patients were followed up to identify signs of possible myocarditis. Eleven children had signs of myocarditis; all of them had ECG changes (supraventricular and ventricular tachycardia, sinus bradycardia, and low voltage complexes) [41]. In another case series of 120 patients with dengue, 62.5% showed ECG abnormalities (T inversions, ST depression, bundle branch blocks) [16].

Clinical manifestations suggesting cardiac involvement in dengue are diverse and include chest pain, palpitations, pleurisy, irregularities of pulse, bradycardia, hypotension, pulmonary edema, and features of shock [30,37]. Kularatne *et al*. [16], in a case series, classified patients into two groups: cardiac and non-cardiac, based on the presence or absence of ECG abnormalities (T inversion, ST depression, bundle branch blocks). ECG changes were seen in 75 of 120 (62.5%) patients (cardiac group) and these patients were found to be more susceptible to fatigue, dyspnea, low peripheral oxygen saturation in room air ($p = 0.001$), chest pain ($p = 0.001$), and flushing of skin ($p = 0.05$) compared to 45 (37.5%) patients with normal ECGs (non-cardiac group). Based on whether just IgM or both IgM and IgG were positive, patients were categorized as primary or secondary dengue, respectively. In the cardiac group, there were 31 primary and 44 secondary dengue patients. In the cardiac group, 17 (23%) patients had hypotension and 58 (77%) developed tachycardia and bradycardia ($p < 0.001$) compared to four (9%) in the non-cardiac group. The design of this study had flaws; first, classification was based on the presence or absence of ECG changes, thus misclassification could occur if ECG changes were a result of metabolic derangement or if these ECG changes were pre-existent. Second, only two patients were said to have developed shock, while 17 patients developed hypotension; the definitions of shock or hypotension were not provided. It is known that tachycardia and hypotension is more frequently seen in DSS [42]. Thus, although this study provides some evidence that patients with ECG changes were more likely to develop hypotension and tachycardia or bradycardia, it does not provide convincing evidence that cardiac involvement was present. Further, the patients in this study appear to be stable dengue patients; the study did not include patients with more severe dengue. We suggest that the use of ECG changes alone to denote cardiac involvement is inaccurate, although the ECG is a quick and useful test to screen for cardiac abnormalities.

Cardiac biomarkers in dengue

Cardiac biomarkers may indicate the presence of cardiac involvement in dengue. A prospective study in Sri Lanka evaluated several cardiac biomarkers (myoglobin, creatine kinase-muscle brain-type, N-terminal pro-brain natriuretic peptide, heart-type fatty

acid-binding protein, troponin T) in patients with dengue; 25% of patients had abnormal results in one or more biomarkers [43]. However, the correlation between biomarkers and cardiac function has not been clearly demonstrated; troponin T was shown to correlate poorly with left ventricular function [26].

Echocardiography and cardiac imaging

Echocardiographic evidence of myocardial involvement in dengue has been clearly demonstrated [21,22,26,44,45]. In a study of 91 children with dengue, LVEF < 50% was observed in 6.7%, 13.8%, and 36% of patients with DF, DHF, and DSS, respectively [26]. Troponin was measured in just nine patients and was normal in all of them. Rapid recovery took place within 24–48 hours, and there were no deaths. Tachycardia and respiratory symptoms, pleural effusions, and lower cardiac outputs were more likely to occur in patients with low LVEF, and their fluid requirements were greater. In another study of 54 children under 12 years of age, LVEF was reduced (< 50%) in nine cases, and two had LVEF below 35% [46]. However, no real correlation was seen with severity of dengue and reduction in LVEF occurring in all stages of clinical severity. Constantine *et al*. [47] described echocardiographic features of myocarditis in 8 out of 37 adult and pediatric patients with dengue, and all of these patients belonged to the category of DHF. Reduced LVEF below 60% was noted only in four patients.

Wali *et al*. [22] assessed cardiac function using echocardiography and radionuclide ventriculography in 17 patients with severe dengue. LVEF less than 40% was detected in 7 patients, and global hypokinesia in 12 patients. No evidence of myocardial necrosis was detected on 99mTc-pyrophosphate imaging. All cardiac changes were fully reversed on reassessment three weeks later. Satarasinghe *et al*. [21] demonstrated echocardiographic evidence of myocarditis in 24% of patients with dengue; myocarditis was twice as common in men, and none of the patients had cardiac symptoms. Cardiac dilatation, the most commonly demonstrated echocardiographic evidence of myocarditis, more commonly affected the right ventricle (57%), and was associated with tricuspid regurgitation. Left ventricular dilatation was seen in 21% of patients, and biventricular dilatation in 16%. Irregular jerky movement of the anterior wall was also a feature. All patients had DENV2 infection. Full echocardiographic recovery was seen in all patients. The authors stated that CPK-MB levels were not useful in detecting myocarditis, but did not indicate whether these tests were done on all patients. Yacoub *et al*. [48] also demonstrated that systolic and diastolic abnormalities were increasingly seen with more severe grades of dengue; segmental wall motion abnormalities, involving the septum and right ventricular wall were observed. Sengupta *et al*. [49] also demonstrated similar evidence of myocarditis in patients with dengue, and suggest that two-dimensional (2D) speckle tracking echocardiography may be a more sensitive tool for the detection of early and subtle myocarditis. However, the clinical relevance of early detection of asymptomatic and clinically benign myocarditis is questionable; in fact, it could be an inefficient use of resources and result in unnecessary transfers to intensive care units. Both systolic and diastolic dysfunction may occur in myocarditis, and the picture is often confounded by low diastolic filling pressures because of plasma leakage. The Tei index [50] has been suggested to be a better index of global myocardial function. Yadev *et al*. [51] compared the sensitivity of LVEF by echo with the Tei index in a cohort of 67 children with dengue. LVEF was low in 42% of patients on admission, and low Ejection fraction (EF) was seen in half of the patients with shock. In comparison, the Tei index was abnormal in 72% of patients. While 83% of all patients had normal LVEF on discharge, 69% of patients with shock had abnormal Tei index on discharge. Thus, myocarditis may be underestimated by echocardiography.

Echocardiographic studies provide insight into the hemodynamic changes in patients with dengue. In patients with DSS, preload, LVEF, and cardiac index are significantly lower during the critical phase compared to the recovery phase. Mean arterial blood pressure appears to be maintained by increased systemic vascular resistance compensating for reduced cardiac index [44]. It has been postulated that transient sympathetic failure may occur in some patients, resulting in bradycardia and hypotension [52].

Despite the evidence of myocardial dysfunction in severe dengue, the degree to which this contributes to shock syndrome is yet unclear and warrants further study. The limited available evidence suggests that, at least in patients with shock unresponsive to fluid resuscitation, the possibility of concurrent myocarditis should be considered. Importantly, these studies were performed in patients with varying degrees of illness severity, including dengue shock, but did not include those *in extremis*; in severe relentless dengue, gross myocardial depression with very low LVEF has been reported, though whether this is a part of terminal

multi-organ failure with severe metabolic derangement remains to be determined [53,54]. Cardiac magnetic resonance (CMR) imaging, where available, may be of value in confirming the diagnosis of myocarditis, with a positive predictive value of 95% if at least two of the three diagnostic criteria are present [45].

Pericardial involvement

Acute pericarditis, characterized by chest pain, has been reported in dengue [55]. Pericardial effusions are also known to occur, and these are often of little clinical significance, identifiable only by echocardiogram [56]. It could be postulated that these are a result of plasma leakage. There is a single case report of pericardial tamponade in a patient with dengue and lupus nephritis; there was diagnostic confusion as to whether this was a result of dengue or the underlying connective tissue disorder [57].

Pathophysiology of cardiac involvement in dengue

The pathophysiology of cardiac involvement in dengue is poorly understood. Myocardial involvement in dengue may result either from direct viral invasion of cardiac muscles or cytokine-induced immune damage, or both [58,59]. Increased levels of serum tumor necrosis factor-α, interleukins 6, 13 and 18, and cytotoxic factors in patients with dengue illness lead to increased vascular permeability and shock [60,61]. Whether these cytokines play a role in the development of myocardial cell injury is uncertain [37]. Cardiac involvement, although often mild, can be severe enough to result in progressive and intractable acute heart failure with global hypokinesia and acute cardiac dilatation [22,26,46]. Lactic acidosis, which occurs [62] as a result of the sluggish circulation, possibly contributes to myocardial depression in severe cases.

Dengue viral antigen has been demonstrated in inflammatory cells in the heart [45,63], and dengue virus has been shown to produce cardiac injury experimentally [64]. Virus or RNA have been detected in various tissues, including kidney, heart, lung, and brain in deaths due to dengue [24,65,66]. It has been proposed that derangements of Ca^{2+} storage in the infected cells may directly contribute to the causation of myocarditis [67,68].

Histopathology

Dengue antigen has been demonstrated with immunohistochemistry in fatal dengue with clinical myocarditis despite normal light microscopy with hematoxylin and eosin (H&E) stain [68]. Damage to cardiac muscle tissue has also been demonstrated in patients dying of dengue, although there is evidence from just four patients [63,69]. Severe tissue damage with hemorrhage, interstitial edema with inflammatory cell infiltration, and necrosis of myocardial fibers have been noted [69]. Both focal and diffuse myocarditis have been demonstrated in patients dying of dengue, with inflammation and infiltration by lymphocytes, neutrophils, and eosinophils [70]. Pericarditis has also been demonstrated. Whether these changes indicated direct viral damage to the myocardium, or whether the changes were part of a widespread non-specific immunological response occurring in terminal dengue, is unknown. Nonetheless, the presence of viral antigen in the heart muscle, coupled with evidence that the dengue virus can cause myocardial damage in the experimental setting, suggests that, at least to some extent, direct viral-induced tissue damage does take place.

Management

Clinical features suggestive of myocarditis are lacking in sensitivity and specificity. Myocarditis is asymptomatic in the majority of patients with dengue, and diagnosis or treatment in the absence of clinical features is unnecessary. Thus, routine echocardiography is not warranted. Patients with ECG changes and those with features of clinical heart failure should have an echocardiogram done. The biggest dilemma is determining whether, in a patient with shock, myocarditis is playing a contributory role. There are no clear guidelines regarding this; the presence of ECG changes should alert the treating clinician to the possibility of associated myocarditis. On most occasions, myocarditis occurring in dengue is not clinically significant. Where suspicion is strong, echocardiography will be helpful if available. Supportive care includes optimal intravascular volume maintenance with intravenous fluids, judicious use of diuretics where indicated [37], and inotropic support where necessary. In particular, if myocardial involvement is suspected, care should be taken not to cause iatrogenic fluid overload [71]. The place of invasive cardiac monitoring to guide the clinician in this is not known. Much of the evidence suggests that myocarditis is transient and self-limiting. A case of dramatic recovery following a single dose of intravenous methyl prednisolone in a 14-year-old with dengue complicated by myocarditis was reported by Premaratna *et al*. [54]. However, the current evidence base does not support the use of corticosteroids or immunoglobulins in treating severe dengue [4].

Correction of serum calcium derangements to optimize cardiac status is usually carried out, especially in the presence of myocarditis. However, there is currently no evidence of its benefit.

Conclusions

Dengue is a serious problem in the tropics. Cardiac involvement is worrisome for both the clinician and patient. Asymptomatic myocarditis appears to be common in dengue, and spontaneous uneventful recovery is the norm. Patients manifest with a variety of clinical features suggesting cardiac involvement, many of which overlap with other complications of the condition. A high index of suspicion is needed to identify cardiac involvement early. The presence of electrocardiographic abnormalities may suggest possible cardiac involvement; however, echocardiography is currently the most useful investigation. Further studies are needed to evaluate the hemodynamic impact of myocardial involvement in patients with severe dengue. Most forms of treatment currently are purely supportive, but with better understanding of the pathophysiology of dengue, targeted treatment may become possible.

Authors' contributions

All authors participated in the design of the review, the article search and information coding, drafting of the manuscript and critically revising the review. All read and approved the final manuscript. SR is the guarantor of this paper.

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