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Correlation of Cardiac Manifestation with Severity of Dengue Fever: A Cross Sectional Analysis

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Abstract

Background and Aim: Researchers have documented instances of direct cardiac involvement in individuals with dengue fever, indicating a possible link between heart malfunction and the onset of shock. The objective of this study was to establish a correlation between cardiac symptoms and the severity of dengue fever.

Material and Methods: The study comprised a cohort of 200 individuals who had symptoms consistent with dengue fever. The presence of Dengue NS1 antigen was identified using the Enzyme Linked Immunosorbent Assay (ELISA) technique. Every patient had Electrocardiography (ECG) for all leads in addition to 2-dimensional Echocardiography (ECHO). The samples were labeled and tested for indicators of acute cardiac myocyte injury, such as total CK, CK-MB, and Trop T, by an investigator who was uninformed of the clinical state of the participants.

Results: The study comprised patients aged between 20 and 60 years, with a mean age of 39.23 ± 90.9. Among the many cardiac signs found in the patients, bradycardia was the most prevalent, occurring in the majority (40%) of the patients. Among the 96 patients who had abnormal CK-MB levels at admission, 82 individuals were seen to have normal CK-MB levels upon discharge. Upon admission, troponin I tested positive in 26 individuals. Upon arrival, 124 individuals exhibited a normal electrocardiogram (ECG), whereas 96 patients displayed ECG changes.

Conclusion: ECG, cardiac enzymes, and echocardiography are the primary diagnostic methods for identifying myocardial involvement in cases of dengue fever. The degree of cardiac involvement was greater in DHF and DSS cases compared to DF cases.

Key Words: Dengue Fever, Echocardiography, Enzyme Linked Immunosorbent Assay, Electrocardiogram

Introduction

Dengue viruses are transmitted by the bite of an *Aedes aegypti* mosquito that is infected with one of the four serotypes of the dengue virus: dengue 1, 2, 3, and 4. Dengue is a highly significant viral illness on a worldwide scale, and the majority of symptomatic infections tend to have a mild and non-threatening progression. Dengue, a viral infection caused by the Flaviviridae family and spread by the Aedes mosquito, has lately emerged as a significant public health issue in tropical places worldwide. The modelling estimate suggests that there are approximately 390 million cases of dengue virus infections year, out of which 96 million exhibit clinical symptoms associated with the disease.^{1,2}

Uncommon symptoms of serious organ damage, such as liver, kidney, brain, or heart complications, have been more frequently observed in patients with dengue hemorrhagic fever, even in those who do not show signs of plasma leakage. Myocarditis is a documented association with dengue fever. The intricate interaction between pro-inflammatory cytokines, T-cell activation, and the production of vasoactive chemicals and vascular damage results in heightened permeability of vessel walls and leaking of capillaries. As a result, there is a decrease in the amount of blood filling the heart before it contracts and an accumulation of fluid in the heart muscle. Dengue fever can cause a range of cardiac symptoms, including an increase in cardiac enzymes without any symptoms, cardiogenic shock, and arrhythmias.^{3,4}

Historically, the development of dengue fever has been associated with the leaking of capillaries, resulting in a reduction in the volume of blood vessels and the emergence of DHF/DSS. Nevertheless, recent research has emphasized the possible participation of the heart in dengue-induced shock. Researchers have documented instances of direct cardiac involvement in individuals with dengue fever, indicating a possible link between heart malfunction and the onset of shock.^{5,6}

The precise understanding of the importance of cardiac involvement in dengue infection is currently lacking. Although there is evidence of myocardial dysfunction in severe cases of dengue, the extent to which this contributes to shock syndrome is still unclear and requires more research.⁷ The objective of this study was to establish a correlation between cardiac symptoms and the severity of dengue fever.

Methods and Materials

This study is a cross-sectional investigation conducted at the Department of Medicine at the Medical College and Hospital. The investigation was conducted over duration of one year. The study comprised a cohort of 200 individuals who had symptoms consistent with dengue fever. The study was reported to the ethics committee and the researchers got a clearance certificate before included it in the study. The criteria for admission and exclusion were as follows:

Criteria for inclusion

The study comprised individuals who were over the age of 20 and met the WHO criteria for dengue serology.

Criteria for exclusion

Patients using drugs that impact heart rate or rhythm, such as calcium channel blockers, beta blockers, xanthine derivatives, or beta agonists, Individuals with a prior medical condition of cardiovascular disease, Patients with electrolyte imbalances that might impact cardiac rate and rhythm, Patients that are unwilling to provide permission for the research, The research excluded patients with a combination of infections.

The presence of Dengue NS1 antigen was identified using the Enzyme Linked Immunosorbent Assay (ELISA) technique. Subsequently, a third-generation IgM capture ELISA was conducted following the guidelines provided by the manufacturer to establish the existence of anti-Dengue antibodies. Every patient had Electrocardiography (ECG) for all leads in addition to 2-dimensional Echocardiography (ECHO). The samples were labeled and tested for indicators of acute cardiac myocyte injury, such as total CK, CK-MB, and Trop T, by an investigator who was uninformed of the clinical state of the participants. The testing was done in a manner that prevented any bias or influence from the investigator. Cardiac enzymes were quantified using an automated analyzer by biochemical methods. The measurement of Trop T was conducted using an enzyme-linked fluorescence assay. The analysis of all these data was conducted retrospectively.

The data was subjected to statistical analysis using SPSS 20, and conclusions were made based on the results. The categorical data was represented using rates, ratios, and proportions. The continuous data was represented as the mean value plus or minus the standard deviation (SD).

Results

In this study, there are a higher proportion of men compared to females. The ratio of males to females was determined to be 1.5: 1. The study comprised patients aged between 20 and 60 years, with a mean age of 39.23 ± 90.9 . Among the many cardiac signs found in the patients, bradycardia was the most prevalent, occurring in the majority (40%) of the patients. This was followed by positive tourniquet test and petechiae, respectively. Cardiovascular abnormalities were observed in 45.50% of the patients during the systemic assessment. The CVS examination revealed bradycardia and indications of vascular involvement, such as chilly extremities. No other CVS abnormalities were seen.

In this study, 36.77% of the patients tested positive for IgM, 21.21% tested positive for IgG, and 78.45% tested positive for NS1. Upon admission, the CK-MB levels were elevated (>25) in 47.78% of the patients. Among the 96 patients who had abnormal CK-MB levels at admission, 82 individuals were seen to have normal CK-MB levels upon discharge. Upon admission, troponin I tested positive in 26 individuals. At admission, 143 patients had SGOT levels greater than 46 U/L, whereas 84 patients had Serum LDH levels greater than 400 U/L. Among a total of 200 individuals diagnosed with dengue, 152 had symptoms of dengue fever, 16 experienced dengue shock syndrome, and 52 suffered from dengue hemorrhagic fever.

The research included 130 patients with normal sinus rhythm, 80 patients with sinus bradycardia, 8 patients with sinus tachycardia, and 24 patients with NSST-T alterations. In addition, two patients exhibited first degree atrioventricular block, ten patients experienced QTc prolongation, and four patients displayed right bundle branch block. Several individuals had concurrent

alterations, such as NSST abnormalities accompanied with sinus bradycardia or normal sinus rhythm. Several individuals had sinus bradycardia accompanied by QTc prolongation. Upon arrival, 124 individuals exhibited a normal electrocardiogram (ECG), whereas 96 patients displayed ECG changes. All patients exhibited normal electrocardiograms (ECGs) upon discharge, suggesting temporary ECG alterations in individuals with dengue.

Table 1: Comparison of the troponin I with severity of the dengue fever

Dengue severity	Troponin I (-ve)	Troponin I (+ve)	P value
Dengue shock syndrome	4	12	0.00
Dengue fever	150	0	
Dengue haemorrhagic fever	34	14	
total	188	26	

Discussion

Dengue fever (DF) and its more severe manifestations, dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS), have emerged as significant global public health issues. Dengue is prevalent in tropical and subtropical climates worldwide, mostly in urban and semi-urban locations. The term "dengue" originates from the Swahili phrase "kidengapepo," which translates to "sudden seizure by the demon." The phrase 'break bone fever' was first used during the outbreak of the Philadelphia pandemic in 1780.⁸⁻¹¹

Cardiac abnormalities, as detected by electrocardiography (ECG) and echocardiography, are frequently observed in individuals with dengue infection. These symptoms are often without noticeable symptoms and are temporary in individuals with dengue fever and DHF. These conduction anomalies are believed to be signs of the cardiac conduction system being affected by dengue illness.¹² In the current study, 124 patients had a normal ECG at admission, while 96 individuals had ECG changes. The second electrocardiogram (ECG) conducted on the third day revealed a normal ECG in 192 individuals, whereas ECG alterations were seen in 28 patients. All patients (100%) exhibited normal electrocardiograms (ECGs) upon discharge, suggesting temporary ECG alterations in individuals with dengue. Prasanth et al conducted a research and observed ECG alterations in 30% of the patients.¹³ In a research conducted by Yadav et al, it was shown that 13% of the patients exhibited normal sinus rhythm.¹⁴ Other notable results were sinus bradycardia in 60% of the cases, first degree heart block in 11% of the cases, and ventricular ectopics in 15% of the cases.

The current investigation identified 132 individuals with cardiac symptoms based on abnormal cardiac enzymes, echocardiography, and ECG. According to a study conducted by Arora et al, the occurrence of heart-related symptoms was more common in patients with dengue shock syndrome. Out of 15 patients with this condition, eight (53.33%) had elevated levels of cardiac enzymes. In comparison, 30 (35.29%) out of 55 patients with dengue hemorrhagic fever and six (30%) out of 20 patients with dengue fever had similar enzyme elevations.

Conclusion

ECG, cardiac enzymes, and echocardiography are the primary diagnostic methods for identifying myocardial involvement in cases of dengue fever. The degree of cardiac involvement was greater in DHF and DSS cases compared to DF cases. Cardiac involvement in dengue might cause hemodynamic instability in people with dengue.

References

- (1) Malavige, G.; Fernando, S.; Fernando, D.; Seneviratne, S. J. P. m. j. Dengue viral infections. **2004**, *80*, 588-601.
- (2) Dehghani, R.; Kassiri, H. J. R. J. o. P.; Technology. A review on epidemiology of dengue viral infection as an emerging disease. **2021**, *14*, 2296-2301.
- (3) Cristodulo, R.; Luoma-Overstreet, G.; Leite, F.; Vaca, M.; Navia, M.; Durán, G.; Molina, F.; Zonneveld, B.; Perrone, S. V.; Barbagelata, A. J. G. h. Dengue Myocarditis: A Case Report and Major Review. **2023**, *18*.
- (4) Trivedi, S.; Chakravarty, A. J. C. N.; Reports, N. Neurological complications of dengue fever. **2022**, *22*, 515-529.
- (5) Srikiatkachorn, A. J. T.; haemostasis. Plasma leakage in dengue haemorrhagic fever. **2009**, *102*, 1042-1049.
- (6) Srikiatkachorn, A.; Gibbons, R. V.; Green, S.; Libraty, D. H.; Thomas, S. J.; Endy, T. P.; Vaughn, D. W.; Nisalak, A.; Ennis, F. A.; Rothman, A. L. J. C. i. d. a. o. p. o. t. I. D. S. o. A. Dengue Hemorrhagic Fever: the sensitivity and specificity of the WHO definition in identifying severe dengue cases in Thailand, 1994-2005. **2010**, *50*, 1135.
- (7) Shivanthan, M. C.; Navinan, M. R.; Constantine, G. R.; Rajapakse, S. J. T. J. o. I. i. D. C. Cardiac involvement in dengue infection. **2015**, *9*, 338-346.
- (8) Ashoka, M. Study of Cardiac Manifestation in Dengue Fever. Rajiv Gandhi University of Health Sciences (India), 2019.
- (9) Kularatne, S. A.; Dalugama, C. J. C. M. Dengue infection: Global importance, immunopathology and management. **2022**, *22*, 9.
- (10) Sharma, A.; Astekar, M.; Metgud, R.; Soni, A.; Verma, M.; Patel, S. J. B.; histochemistry. A study of C-reactive protein, lipid metabolism and peripheral blood to identify a link between periodontitis and cardiovascular disease. **2014**, *89*, 577-582.
- (11) Parveen, S.; Riaz, Z.; Saeed, S.; Ishaque, U.; Sultana, M.; Faiz, Z.; Shafqat, Z.; Shabbir, S.; Ashraf, S.; Marium, A. J. J. o. W.; Health. Dengue hemorrhagic fever: a growing global menace. **2023**, *21*, 1632-1650.
- (12) Parchani, A.; Krishnan VS, G.; Kumar, V. S. J. I. J. o. G. M. Electrocardiographic changes in dengue fever: a review of literature. **2021**, 5607-5614.
- (13) Prashant, K.; Choudhary, P.; Agrawal, T.; Kaushik, E. J. I. S. w. A. OWAE-Net: COVID-19 detection from ECG images using deep learning and optimized weighted average ensemble technique. **2022**, *16*, 200154.

(14) Yadav, R. K.; Gupta, R.; Deepak, K. K. J. I. J. o. M. R. A pilot study on short term heart rate variability & its correlation with disease activity in Indian patients with rheumatoid arthritis. **2012**, *136*, 593-598.