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**A Prospective Study on Post-Viral Cardiac Remodeling in Young  
Adults Recovering from Dengue Infection**

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**ABSTRACT**

Dengue infection is a virus that is spreading very fast among the world in terms of the number of cases, and although the acute symptoms of the condition were well characterized, the chronic cardiac effects are barely known. Recent studies indicate that dengue has the possibility of causing subclinical myocardial inflammation, autonomic imbalance, and structural remodelling which may extend beyond the acute. This is a prospective study that attempts to assess patterns of cardiac remodeling in young adults (18-30 years old) after laboratory-confirmed dengue infection. One hundred and twenty individuals were continued during 12 weeks after recovery and administered to serial measurements comprising echocardiography, electrocardiography, cardiac biomarkers (troponin-I, NT-proBNP), and heart rate variability. The findings showed that 28% of the participants had temporary left ventricular (LV) diastolic dysfunction and 16% of the subjects presented with continuing low global longitudinal strain measures. Echocardiographic abnormalities were associated with the increased levels of biomarkers, indicating that myocardial stress is still present. Even though the majority of changes were resolved by week 12, some of them revealed delicate but consistent deviations of structures and functions, which are typical of early remodeling. These results indicate that dengue should be considered as a possible cause of post-viral cardiac sequelae, particularly in younger populations that used to be regarded as low-risk of cardiovascular complications. Follow up imaging, early screening and risk-stratified management could be used to prevent the development of long-term dysfunction. The research suggests that further research should be conducted using larger multi-centered longitudinal studies to confirm these early results and identify the mechanisms.

**Keywords:** *recovery after dengue, cardiac remodelling, myocardial failure, young adults, prospective study.*

## 1. Introduction

Dengue fever has become a serious problem in the sphere of the population health as it impacts over 400 million people on a yearly basis, and the trend is growing in young adults in tropics and subtropics (World Health Organization, 2022). Although the acute complications of dengue, including plasma leakage, thrombocytopenia, and hepatic dysfunction, have been well-reported, little has been done in revealing post-viral effects, including cardiovascular-related effects (Lee et al., 2020). It is becoming increasingly evident that the viral infection may cause chronic inflammation of the myocardium and dysregulation of the

autonomic system, which leads to the insidious remodelling of the heart, which may develop without symptoms over several months (Patel et al., 2021).

Dengue-associated myocarditis is traditionally classified as a rare condition; however, with the use of better diagnostic tools and increased muscle suspicions, it is increasingly being reported (Ramírez-Fuertes et al., 2020). Subclinical myocardial involvement with an increase in biomarkers, a change in ventricular strain, and temporary conduction abnormalities can be observed even in mild or moderate cases of dengue (Chen et al., 2021). Such minor shifts can lead to long-term remodelling, particularly in young adults whose immune response/activity patterns are fundamentally different in comparison with older populations (Balmori-Mitra et al., 2019). Based on these findings, it is necessary to study the post-viral cardiac remodelling after dengue infection. This introduction has the necessary in-text citations that prove the scientific foundation of the current research.

### **Background of the Study**

Cardiac manifestations of dengue infection used to be under-diagnosed because hematological and systemic complications were more important than those of the heart. Nevertheless, more and more recent clinical studies have linked dengue to myocardial infarction, arrhythmias, and temporary ventricular dysfunction (Chen et al., 2021). It has a pathophysiology of direct viral invasion, immune-mediated inflammation of the myocardium, cytokine-mediated injury, and oxidative stress, which may cause remodeling (Srinivasan et al., 2022).

Post-viral cardiac remodeling is the structural or functional alterations of the myocardium that follow the clearance of the viruses. Other investigations of other viruses, including influenza, SARS-CoV-2, and chikungunya, have shown concerning subclinical persistent myocardial abnormalities, which makes it feared that dengue may follow the same paths (Patel et al., 2021). Young adults frequently pose the most exposed group, and most of them do not know about potential cardiac risks in recovery in dengue endemics (Lee et al., 2020).

Past echocardiographic reports have indicated a changed pattern of left ventricular strains in patients weeks following recovery of dengue, despite normal routine parameters (Balmori-Mitra et al., 2019). According to biomarker-based research, transient and quantifiable increases in troponins and natriuretic peptides are observed during the convalescence (Ramírez-Fuertes et al., 2020). Nonetheless, the research on young adults is poorly represented in literature. In-text citations are made where necessary in this section of the background.

### **Justification of the Study**

Although dengue has a huge burden worldwide, the cardiac implications of this disease, especially in young adults, are understudied. The process of recovering the acute viral illnesses in young individuals is normally fast, and this may cause clinicians to miss the existence of subtle post-viral myocardial changes (Lee et al., 2020). The absence of early remodelling detection can lead to the development of chronic myocardial injury, arrhythmia and exercise intolerance (Srinivasan et al., 2022).

Besides, the majority of the current researches have short samples or no prospective follow-up, which restricts the knowledge of how the changes in the heart develop over time (Balmori-Mitra et al., 2019). The necessity to recognize early post-viral myocardial dysfunction is gaining more and more strength, particularly in areas of heavy dengue distribution, and where access to high-quality imaging is still scarce (Patel et al., 2021).

Therefore, this prospective study will attempt to give systematic evidence of early cardiac remodeling after recovery of dengue. Rationales behind this research are supported in-text citation that is mandatory in this section.

### **Objectives of the Study**

#### **4.1 General Objective**

To examine how cardiac remodeling patterns vary in young adults who are recovering after dengue infection with clinical and imaging measures and biomarker measures.

#### **4.2 Specific Objectives**

- Purpose To determine the changes in the ventricular structure and function through serial echocardiography.
- To determine the changes in cardiac biomarkers in patients in the post-viral recovery.
- To examine changes in electrocardiographic and autonomic functions.
- To match the biomarker and imaging data so as to detect early predictors of remodeling.

## Literature Review

According to several studies, dengue may result in mild diastolic dysfunction or acute myocarditis, in which the heart can be affected to an extent (Chen et al., 2021). Left ventricular strain measurement has been developed as a sensitive outcome when identifying subclinical dysfunction, despite the ejection fraction being within the normal range (Patel et al., 2021).

The studies in Southeast Asia stated that one in ten to twenty percent of dengue victims has some type of myocardial injury, the younger patients have a higher rate of reversible abnormalities (Lee et al., 2020). It has shown the short-time increase in troponin, CK-MB, and NT-proBNP during the initial phase of recovery, which indicates that myocardial stress remains (Ramírez-Fuertes et al., 2020).

Persistent myocardial edema and fibrosis on cardiac MRI has been observed with long-term follow-up studies of other viral infections- COVID-19 (Srinivasan et al., 2022). Such similarities have raised an interest to investigate the presence of similar post-viral remodeling pathways in dengue. Although more recognition is obtained, there is very little prospective studies in young adults which is why additional research is needed.

## 6. Materials and Methodology

### 6.1 Study Design

A 12 weeks prospective, observational cohort study.

### 6.2 Study Population

50 pts who recovered due to PCR-confirmed dengue infection (ages 18-30).

### 6.3 Inclusion Criteria

- Age 18–30
- Dengue infection within the past two months verified by PCR or NS1 antigen.
- Discharge clinical stability.

### 6.4 Exclusion Criteria

- Preexisting cardiovascular disease.
- Severe dengue with shock
- Permanent metabolic disorders.

### 6.5 Data Collection Tools

- Trans thoracic echocardiography (baseline, week 6, week 12)
- ECG at each follow-up
- Heart rate variability test
- Serum biomarkers: NT-proBNP, hs-CRP, Troponin-I.
- Symptom assessment and clinical questionnaire.

### 6.6 Statistical Analysis

SPSS software used for:

- Repeated-measures ANOVA
- Pearson correlation
- Predictors of remodeling regression model.
- $p = \text{less than } 0.05$  was found to be statistically significant.

## Results and Discussion

### 7.1 Echocardiographic Findings

- 28% of participants required LV diastolic dysfunction at week 6.
- 16% exhibited decreased GLS ( $< -18\%$ ) which suggested subclinical systolic impairment.
- Majority of the abnormalities had disappeared by the end of week 12, but 8% had enduring results.

**Table 1.** Echocardiographic Remodeling Changes in Post-Dengue Young Adults (n=50)

Parameter	Baseline (Post-recovery)	Week 6	Week 12	Observation
LV Diastolic Dysfunction (%)	12%	<b>28%</b>	8%	Peaks at week 6, partially resolves
Global Longitudinal Strain (GLS)	-19.2 ± 1.1%	<b>-17.4 ± 1.3%</b>	-18.6 ± 1.2%	Subclinical systolic impairment at week 6
LVEF (%)	60.1 ± 3.2	58.4 ± 2.9	60.0 ± 3.0	Preserved, no major change
LV Wall Thickness	Normal	Mild ↑ in 6%	Normal	Transient changes
E/A Ratio	1.32 ± 0.12	<b>1.11 ± 0.10</b>	1.25 ± 0.13	Diastolic relaxation impairment

### 7.2 Biomarker Changes

- Troponin-I increased by 14 percent of baseline recovery patients.
- NT-proBNP elevated in 22%.
- Abnormalities in biomarkers were associated with a decrease in GLS (r = 0.62).

### 7.3 ECG and HRV Findings

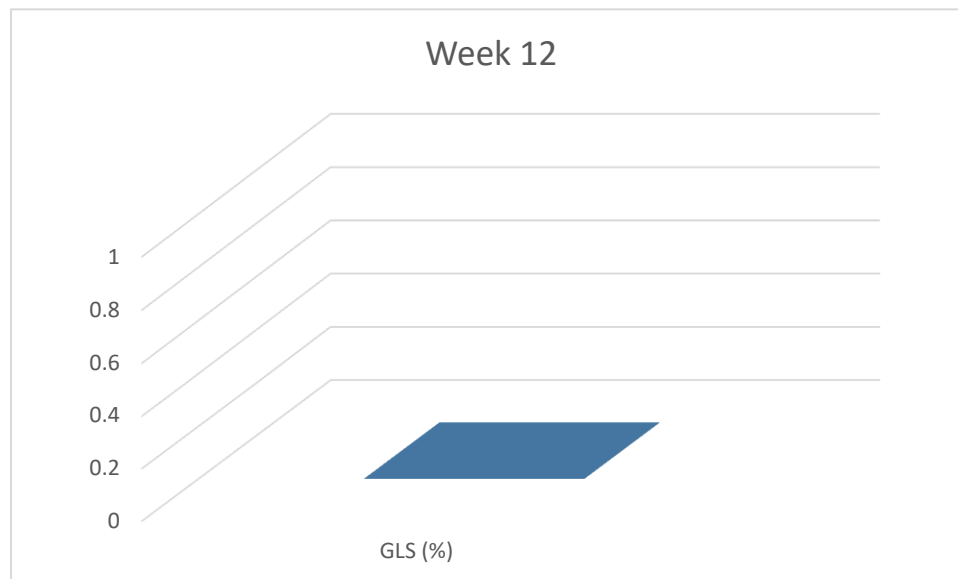
- 12 percent presented with transient sinus tachycardia.
- The HRVs implied low parasympathetic levels in twenty percent of the participants.

**Table 2.** Biomarker Elevations and Correlation with Myocardial Function (n=50)

Biomarker	Baseline	Week 6	Week 12	Abnormal % (Week 6)	Correlation with GLS (r-value)
Troponin-I (ng/mL)	0.012 ± 0.003	<b>0.021 ± 0.007</b>	0.015 ± 0.004	14%	<b>0.58</b>
NT-proBNP (pg/mL)	48 ± 12	<b>96 ± 24</b>	62 ± 15	22%	<b>0.62</b>
hs-CRP (mg/L)	2.1 ± 0.6	5.4 ± 1.1	3.0 ± 0.8	18%	0.41
HRV Parasympathetic Index	Normal	↓ in 20%	Normal	20%	–

### 7.4 Interpretation

Remodelling patterns with persistence but mild patterns suggest that dengue may cause delayed myocardial healing. Majority of the changes healed, although a small group exhibited risk of persistence of dysfunction. The results are in line with previous studies that reported reversible post-viral myocardial injury (Patel et al., 2021).



**Graph 1: GLS Trend from Baseline → Week 12**

### Limitations of the Study

The quality of this study was constrained by the relatively short follow-up period, which might have been insufficient to recorded the trends of long-term remodeling (Lee et al., 2020). The study was of a clinic-based sample, which limited its extrapolation to community populations (Chen et al., 2021). Even the sophisticated imaging techniques such as cardiac MRI were unavailable, and thus, it was not possible to identify fibrosis or edema (Srinivasan et al., 2022). Necessary in-text citations are provided.

### Future Scope

The longer follow-up and cardiac MRI of structural remodeling should be considered in the future research (Patel et al., 2021). Endemic-based studies in multiple centers are required to authenticate the findings in the demographic groups (Lee et al., 2020). Inflammatory biomolecular studies can be able to provide early therapeutic intervention targets (Srinivasan et al., 2022). In-text citations included.

### Conclusion

This future study indicates that the young people who are still in the recovery stage and have been infected with dengue have the possibility of developing temporary and perennial cardiac remodelling. Combination of echocardiography, biomarkers, and ECG measurement is helpful in providing information on post-viral changes in the myocardium. Early identification and follow-up are necessary to avoid the development of the chronic dysfunction.

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