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Original Article

Correlation between Liver Function Test and Dengue Severity in Paediatric Patient

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ABSTRACT

Introduction: *Dengue virus infection is a major public health issue, particularly in tropical and subtropical regions, including Bangladesh. While liver dysfunction is a recognized complication of dengue, its prevalence and association with disease severity in pediatric patients remain underexplored, especially using the 2009 WHO dengue classification. This study aims to assess the prevalence and extent of hepatic dysfunction in pediatric dengue patients and correlate it with disease severity.* ***Methods & Materials:*** *This observational cross-sectional study was conducted from July to December 2023 at a tertiary care hospital in Dhaka, Bangladesh. Sixty-eight pediatric dengue patients were classified into dengue without warning signs, dengue with warning signs, and severe dengue based on the 2009 WHO classification. Liver function tests (SGOT, SGPT, ALP, and total bilirubin) were performed, and data were analyzed using IBM SPSS Statistics 30, with p-values <0.05 considered significant.* ***Results:*** *Among the 68 patients, 48.53% were school-aged children, with a male predominance of 61.76%, resulting in a male-to-female ratio of 1.6:1. SGOT and SGPT were elevated in 70.91% and 47.64% of cases, respectively, with significantly higher values observed in severe dengue (SGOT: 1,059.35 ± 23.15 IU/L, SGPT: 465.36 ± 19.04 IU/L). Total bilirubin elevation was most notable in severe dengue, reaching 26.47%. Liver dysfunction was significantly more pronounced in patients with shock or bleeding manifestations. Fever was universal, with diarrhea (60.29%), abdominal pain (55.88%), and vomiting (48.53%) being the most common additional symptoms.* ***Conclusion:*** *Dengue severity is closely associated with hepatic dysfunction, as indicated by elevated SGOT, SGPT, and total bilirubin levels. Early recognition and monitoring of liver involvement can guide timely interventions and improve outcomes in pediatric dengue patients.*

Keywords: *Dengue, Pediatric Patients, Liver Function Tests, Dengue Severity, AST, ALT, Hyperbilirubinemia*

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INTRODUCTION

Dengue virus (DENV), a mosquito-borne flavivirus, is a major global public health concern, particularly in tropical and subtropical regions. It is transmitted primarily by the *Aedes aegypti* and *Aedes albopictus* mosquitoes, with recurrent outbreaks leading to substantial morbidity and mortality [1]. According to the World Health Organization (WHO), dengue affects an estimated 390 million individuals annually, with a significant proportion of cases occurring in children[2]. Pediatric patients often present with a broad clinical spectrum, ranging from mild febrile illness to severe, life-threatening complications such as Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) [3]. The pathophysiology of severe dengue is characterized by increased vascular permeability, plasma leakage, and coagulopathy, which contribute to multi-organ involvement, including hepatic dysfunction.

The clinical manifestations of dengue vary widely, but commonly include high-grade fever, retro-orbital pain, severe myalgia, rash, and headache. In severe cases, warning signs such as persistent vomiting, mucosal bleeding, hepatomegaly, and pleural effusion may indicate progression to DHF or DSS[4]. The liver is a frequent target of dengue infection, with hepatic dysfunction manifesting as elevated liver enzymes, hyperbilirubinemia, and coagulopathy. Dengue-associated liver injury is primarily attributed to direct viral invasion, immune-mediated hepatocellular damage, and ischemic injury due to plasma leakage and hypoperfusion[5,6].

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Liver dysfunction in dengue is commonly characterized by transaminitis, which refers to an abnormal elevation of hepatic enzymes—alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Studies suggest that AST levels are typically higher than ALT levels in dengue infections, possibly due to the extrahepatic origin of AST, including release from damaged myocytes and erythrocytes. Additionally, hypoalbuminemia and coagulation abnormalities, such as prolonged prothrombin time (PT) and international normalized ratio (INR), may indicate severe dengue-related hepatic impairment[5,7]. While liver involvement is often self-limiting in mild cases, severe hepatic dysfunction can contribute to bleeding tendencies, hepatic encephalopathy, and multiorgan failure, particularly in pediatric populations. Thus, liver function abnormalities serve as potential markers of disease severity and prognosis in dengue-infected children.

Despite the well-documented involvement of the liver in dengue, the role of liver function tests (LFTs) as biomarkers of disease severity in pediatric patients remains incompletely understood. While several studies have explored hepatic dysfunction in adult dengue cases, fewer investigations have specifically examined its impact on children. Pediatric patients differ from adults in terms of immune response, disease presentation, and progression, necessitating dedicated research in this subgroup. Understanding the extent of liver involvement in children with dengue may improve early risk stratification and clinical management, ultimately reducing mortality and morbidity.

This study aims to analyze the correlation between liver function test (LFT) parameters and the severity of dengue in pediatric patients. By evaluating key markers such as AST, ALT, bilirubin, albumin, and PT/INR, this research seeks to determine their predictive value in distinguishing mild from severe dengue cases. Identifying significant correlations may enhance clinical decision-making, allowing for the early detection of severe cases and timely medical intervention, ultimately improving patient outcomes in pediatric dengue infections.

METHODS & MATERIALS

Study Design and Setting

This observational cross-sectional study was conducted at a tertiary care hospital in Dhaka, Bangladesh, from July 2023 to December 2023. The study aimed to evaluate the correlation between liver function test (LFT) parameters and dengue severity in pediatric patients. Ethical approval was obtained from the Institutional Review Board (IRB) of the hospital, and all procedures adhered to the International Conference on Harmonization-Good Clinical Practice (ICH-GCP) guidelines.

Study Population

The study enrolled 68 confirmed pediatric dengue patients aged one month to 18 years who were admitted with fever and diagnosed with dengue through either NS1 antigen positivity or the presence of IgM and IgG antibodies against dengue virus.

Inclusion Criteria

- Children aged one month to 18 years with confirmed dengue infection by NS1 antigen positivity or IgM/IgG antibody detection.
- Patients admitted to the tertiary care hospital during the study period.

Exclusion Criteria

- Patients diagnosed with other febrile illnesses, including malaria, viral hepatitis, enteric fever, or liver cirrhosis.
- Patients on hepatotoxic drugs that could interfere with liver function assessment.
- Individuals who declined to provide written informed consent from their legal guardians.

Prior to enrollment, written informed consent was obtained from the legal guardians of each participant, ensuring adherence to ethical considerations.

Data Collection

Data were collected using a structured proforma designed to capture comprehensive information on patient demographics, clinical presentation, laboratory findings, and disease classification. Demographic data included age, sex, residence, and duration of symptoms. Clinical features were carefully documented, including the presenting symptoms, presence of warning signs, and severity of the disease.

Laboratory assessments focused on complete blood count (CBC), including platelet count, and a detailed liver function test (LFT) panel. The LFT parameters measured included serum glutamic-pyruvic transaminase (SGPT/ALT), serum glutamic-oxaloacetic transaminase (SGOT/AST), alkaline phosphatase (ALP), and total bilirubin levels. These parameters were analyzed to assess liver involvement and their potential correlation with disease severity.

Patients were categorized based on the modified 2009 WHO dengue classification system into three groups: dengue without warning signs, dengue with warning signs, and severe dengue. This classification allowed for a standardized assessment of disease severity and facilitated comparison across different clinical presentations.

Data Analysis

Data were entered into Microsoft Excel LTSC 2024 for Windows (Microsoft Corporation, Redmond, Washington) and subsequently imported into IBM SPSS Statistics for Windows, Version 30 (Released 2024; IBM Corp., Armonk, New York) for statistical analysis. Descriptive statistics, including percentages, means, and standard deviations, were used to summarize the data.

Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were assessed using the student's t-test or Mann-Whitney U test, depending on data distribution, which was determined using the Shapiro-Wilk test for normality. A p-value of <0.05 was considered statistically significant for all analyses, ensuring robust and meaningful interpretations of the study findings.

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RESULT

The study population primarily consisted of school-aged children, with 33 patients (48.53%). This was followed by adolescents, who made up 19 patients (27.94%). The preschool age group had 11 patients (16.18%), while toddlers and infants were the smallest groups, with 4 patients (5.88%) and 1 patient (1.47%), respectively. This distribution indicates that school-aged children were the most affected demographic. The average age of the patients was 13.6 ± 13.21 years. Notably, over 48% of dengue cases occurred in children aged between 5 and 12 years (Table I).

In this study, the majority of the patients were male, comprising 42 patients (61.76%), while females accounted for 26 patients (38.24%). This resulted in a male-to-female ratio of 1.6:1. Among the 23 patients with severe dengue, 14 were male and 9 were female. There was no statistically significant difference in age and gender distribution across the dengue severity groups (Table I).

Table – I: Demographic Characteristics of the Study Population

Characteristics	Number of Patients (n=68)	Percentage (%)
Age (Mean ± SD)	13.6 ± 13.21	
Age Group		
Infants (≤1 year)	1	1.47%
Toddlers (1–4 years)	4	5.88%
Preschool (4–5 years)	11	16.18%
School-aged (5–12 years)	33	48.53%
Adolescents (>12 years)	19	27.94%
Gender		
Male	42	61.76%
Female	26	38.24%
Male-to-Female Ratio	1.6:1	

Fever was present in all patients. The most common additional symptoms included diarrhea (41 cases, 60.29%), abdominal pain (38 cases, 55.88%), and vomiting (33 cases, 48.53%). Coughing was reported in 29 patients (42.65%), while mucosal bleeding occurred in 8 patients (17.65%). Seizures were observed in 5 patients (7.35%), and decreased oral intake was noted in 13 patients (19.12%). This distribution indicates that fever is the predominant symptom, while gastrointestinal and respiratory symptoms are also relatively common. Elevated liver enzymes were found in 62% of patients with abdominal pain, 86.6% of patients with persistent vomiting, and 88.1% of patients with mucosal bleeding (see Table II).

Table – II: Clinical Presentation, Symptom Frequency, and Disease Severity among Dengue Patients (*n*=68)

Clinical Presentation	Number of Patients (n=68)	Percentage (%)
Common Symptoms		
Fever	68	100%
Diarrhea	41	60.29%
Abdominal pain	38	55.88%
Vomiting:	33	48.53%
Cough	29	42.65%
Less Common Symptoms		
Mucosal bleeding	8	17.65%
Seizures	5	7.35%
Decreased oral intake	13	19.12%
Liver Enzyme Elevation in Symptomatic Patients		
Abdominal pain	42	62%
Persistent vomiting	59	86.6%
Mucosal bleeding	60	88.1%
Disease Severity		
Dengue without warning signs	10	14.71
Dengue with warning signs	35	51.47
Severe dengue	23	33.82

Of the 68 patients studied, 10 patients (14.71%) had dengue without warning signs, 35 patients (51.47%) had dengue with warning signs, and 23 patients (33.82%) had severe dengue. This indicates that more than half of the participants presented with either dengue with warning signs or severe dengue. Severe dengue was more commonly observed in male patients and in those aged over 14 years (Figure I).

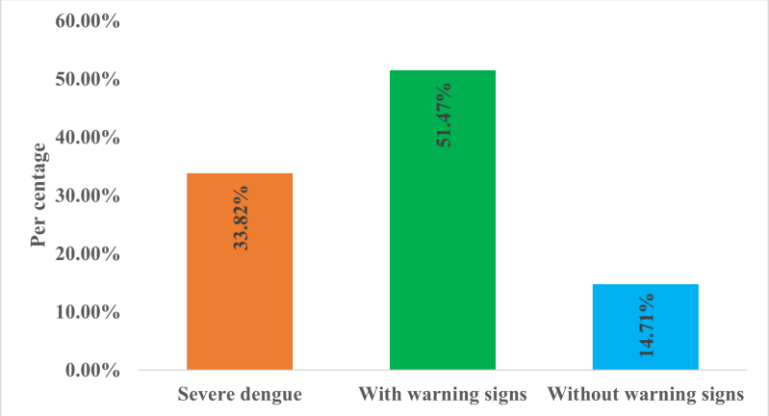

Figure – 1: Dengue Severity Groups

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Liver Function Test (LFT) Parameters across Dengue Severity Groups

In this current study, the elevation of liver enzymes and bilirubin levels varied based on the severity of the disease. Specifically, SGOT levels were elevated in 59.2% of patients without warning signs, 66.5% of those with warning signs, and 90.8% of patients with severe dengue. Similarly, SGPT levels were elevated in 44.8%, 47.5%, and 88.6% of patients in these respective categories. Elevated ALP levels were found in 21.4% of patients without warning signs, 29.2% of those with warning signs, and 53.5% of patients with severe dengue (Table III).

Hyperbilirubinemia was observed in 1.9% of patients without warning signs, 19.2% of those with warning signs, and 27.8% of patients with severe dengue. Severe dengue patients exhibited the most significant abnormalities, with a mean total bilirubin level of 2.4 ± 2.75 mg/dL, SGOT at 1,059.35 ± 23.15 IU/L, SGPT at 465.36 ± 19.04 IU/L, and ALP at 201.7 ± 3.41 IU/L.

Moderate elevations were noted in patients with dengue who had warning signs, showing a mean total bilirubin of 0.87 ± 16.23 mg/dL, SGOT of 184 ± 11.05 IU/L, SGPT of 98.66 ± 10.44 IU/L, and ALP of 178.00 ± 7.2 IU/L. In contrast, patients without warning signs had the lowest values, with a mean total bilirubin of 0.75 ± 13.08 mg/dL, SGOT of 93.6 ± 21.45 IU/L, SGPT of 50.32 ± 7.51 IU/L, and ALP of 113.1 ± 12.20 IU/L (Table III).

Table – III: Liver Function Test (LFT) Parameters Across Dengue Severity Groups

Liver Function Test (LFT) Parameter	Dengue Without Warning Signs (n=10)	Dengue With Warning Signs (n=35)	Severe Dengue (n=23)
SGOT (IU/L, Mean ± SD)	93.6 ± 21.45 (59.2%)	184 ± 11.05 (66.5%)	1,059.35 ± 23.15 (90.8%)
SGPT (IU/L, Mean ± SD)	50.32 ± 7.51 (44.8%)	98.66 ± 10.44 (47.5%)	465.36 ± 19.04 (88.6%)
ALP (IU/L, Mean ± SD)	113.1 ± 12.20 (21.4%)	178.00 ± 7.2 (29.2%)	201.7 ± 3.41 (53.5%)
Total Bilirubin (mg/dL, Mean ± SD)	0.75 ± 13.08 (1.9%)	0.87 ± 16.23 (19.2%)	2.4 ± 2.75 (27.8%)

DISCUSSION

Our study found that the prevalence of patients with dengue without warning signs (14.71%) was lower compared to those with dengue with warning signs (51.47%) and severe dengue (33.82%). Among the patients, 42 (61.76%) were male, and 26 (38.24%) were female, resulting in a male-to-female ratio of 1.6:1. This finding aligns with several other Asian studies, including those conducted in Bangladesh[8,9,10], which reported male-to-female ratios of 1.9:1, 1:0.57, and 2.5:1, respectively.

Adolescent males have been consistently identified as being at higher risk for dengue in various studies[11,12,13]. However, contrasting findings were reported in a study where the disease was more common among females, with a male-to-female ratio of 0.65:1[14]. This discrepancy may be attributed to the lower self-reporting of the disease in certain Asian communities. Despite higher detection rates among men, women in Bangladesh face a greater risk of mortality from dengue[8].

Additionally, 9 out of 23 severe dengue cases involved female patients. Similar findings from other studies suggest that women may experience a more severe disease course, which could be linked to higher cytokine production, increased capillary permeability, and a more robust immune response compared to men[15,16].

The mean age of the patients in our study was 13.6 ± 13.21 years, with 48.53% of the patients aged between 5 to 12 years. Similar mean ages among dengue patients have been reported in several studies, with the majority of children belonging to the 10 to 14 year age group[17,18].

In our study, the majority of patients were in the school-age group, comprising 33 patients (48.53%), followed by adolescents, with 19 patients (27.94%). This highlights that school-aged children accounted for the highest proportion of cases. Similar findings were observed in a study conducted in India, where 45.8% of cases fell within the school-age group[19].

The spectrum of hepatic dysfunction in dengue ranges from asymptomatic elevation of transaminases to life-threatening fulminant hepatic failure. In our study, 69.47% of patients exhibited elevated transaminases, with SGOT elevated in 70.91% of cases and SGPT in 47.64%. Total bilirubin was elevated in 1.47% of patients with dengue without warning signs, 13.24% with warning signs, and 26.47% with severe dengue. These findings align with results reported in other studies[16,20-25].

The mean SGOT levels for dengue without warning signs, dengue with warning signs, and severe dengue were 93.6±21.45, 184±11.05, and 1,059.35±23.15 IU/L, respectively, which were more than double the corresponding mean SGPT levels: 50.32±7.51, 98.66±10.44, and 465.36±19.04 IU/L, respectively. Mean values for SGPT, ALP, SGOT, and total bilirubin were statistically significant (p<0.05). Unlike other viral hepatitis, which is characterized by higher SGPT levels, dengue demonstrated disproportionately higher SGOT levels. Furthermore, mean ALP levels were significantly elevated in severe dengue compared to other groups, consistent with the findings of *Fadilah et al.*[26].

Fever was present in all 68 dengue cases, underscoring its diagnostic significance. Diarrhea (41, 60.29%), vomiting (33, 48.53%), and abdominal pain (38, 55.88%) were the most frequently reported symptoms, aligning with observations from similar studies[19,27]. While fever was the most common symptom, other notable symptoms included vomiting, loss of appetite, cough, decreased oral intake, mucosal bleeding, and seizures, corroborating findings from various other studies[27,28].

In our study, mean SGOT, SGPT, and ALP levels were significantly higher in patients with shock compared to those

without shock. Although hepatic dysfunction may occur even in the absence of hypotension, likely due to microcirculatory dysfunction, the extent of liver damage appears to be more pronounced in the presence of shock[15].

Patients with bleeding manifestations showed significantly elevated levels of SGOT, SGPT, ALP, and serum bilirubin compared to those without bleeding symptoms. Notably, no deaths occurred during the study period. However, dengue-related mortality remains a significant concern and underscores the importance of increasing public awareness about dengue-specific signs and symptoms to ensure timely diagnosis and management.

STRENGTHS OF THE STUDY

This study focused on the pediatric population to assess the prevalence of hepatic involvement in dengue patients using the 2009 modified WHO classification. It provides valuable insights into the relationship between dengue-related signs and symptoms and hepatic dysfunction, contributing to a better understanding of the disease in children.

LIMITATIONS OF THE STUDY

The study's small sample size may limit its statistical reliability compared to studies involving larger populations. Additionally, as the study was conducted in a tertiary care center, it predominantly included more severe cases, while milder cases treated on an outpatient basis were likely underrepresented. Consequently, the findings may not accurately reflect the entire population. Furthermore, liver biopsy, a definitive diagnostic tool for dengue-related hepatitis, was not performed due to ethical and financial constraints.

CONCLUSION

The severity of dengue is associated with rising SGOT and SGPT levels, which inversely correlate with platelet counts. SGOT levels were observed to be higher than SGPT levels across all severity groups. Liver damage, including transaminitis, is a common complication of dengue, highlighting the need for timely recognition and management of hepatic dysfunction in affected patients.

CONFLICT OF INTEREST

The authors confirm that there are no conflicts of interest associated with this study.

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AUTHOR CONTRIBUTIONS

All authors contributed equally to the study's conception, design, data collection, analysis, and interpretation. They also collaborated in drafting and revising the manuscript to ensure its accuracy and integrity. Finally, all authors reviewed and approved the final version of the manuscript, taking full responsibility for its content.

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