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Association of Aminotransferase Levels with Disease Severity in Dengue: A Prospective Observational Study

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Abstract **Original Research Article**

Background: Prompt identification of the progression to severe dengue, utilizing straightforward and quantifiable tests, is essential for guiding appropriate supportive treatment. This study sought to evaluate whether aminotransferase levels could serve as a predictive marker for disease severity in dengue patients. ***Methods:*** This prospective observational study was conducted within a hospital setting, involving 70 patients admitted to the Bangladesh Shishu Hospital & Institute. Dengue diagnoses were established by detecting NS1 antigen between days 2 and 3, and/or IgM antibody positivity between days 6 and 10. Serum aminotransferase levels were quantified upon patient admission to evaluate the severity of the dengue infection. ***Results:*** The mean age was 5.5 ± 4.02 years, with 42.9% of patients aged between 1 and 5 years, and a male majority (62.9%). Dengue shock syndrome manifested in 28.6% of the patients. The average SGOT level (85.71 ± 67.80) was higher than the average SGPT level (58.27 ± 51.22). Notably, the mean SGOT level was significantly elevated in dengue shock syndrome cases (129.73 ± 97.42 U/L) compared to other dengue classifications ($p = 0.004$). Similarly, the mean SGPT level was also significantly higher in patients with dengue shock syndrome (101.58 ± 75.20 U/L) than in those with other forms of dengue fever ($p < 0.001$). A direct correlation was observed between SGOT levels and disease severity, indicated by a correlation coefficient (r) of 0.394 and a p-value of 0.001. ***Conclusion:*** The findings suggest that hepatic dysfunction is a frequent occurrence in dengue fever. An early elevation in transaminase levels can therefore assist in predicting the severity of the illness. This predictive capability is valuable for facilitating close monitoring of patients prone to developing severe forms of dengue and for enabling the timely initiation of appropriate therapeutic interventions.

Keywords: Dengue Shock Syndrome (DSS), Aminotransferases (SGOT & SGPT), Disease Severity Prediction, Hepatic Dysfunction, Pediatric Dengue, Biomarkers.

INTRODUCTION

The dengue virus (DENV), a type of flavivirus, is transmitted to humans through the bites of Aedes aegypti and Aedes albopictus mosquitoes. It is widespread across more than 100 nations globally. The virus is categorized into four distinct serotypes—DENV1, DENV2, DENV3, and DENV4—which exhibit genetic and antigenic variations [1,2]. DENV1 and DENV3 are generally considered less severe compared to DENV2 and DENV4, with DENV4 being less virulent than DENV2. While infection with one serotype confers lasting protection against that specific type, subsequent infection with a different serotype can lead to a heightened risk of complications. Dengue represents a significant cause of sickness and fatalities among children in Southeast Asian countries [1,2]. According to the World Health Organization (WHO), there are approximately 50-100 million new dengue infections worldwide annually, with 50,000 severe cases requiring hospitalization and a fatality rate approaching 2.5%. Over the past two decades, the occurrence of cases has escalated nearly eight-fold, rising from 505,430 cases in 2000 to roughly 5.2 million in 2019 [3,4].

In Bangladesh, the first significant surge of dengue hemorrhagic fever was observed in mid-2000, with 5,551 recorded dengue cases reported from the cities of Dhaka, Chittagong, and Khulna. Of these cases, 4,385 (62.4%) were identified as Dengue Fever (DF) and 1,186 (37.6%) as Dengue Hemorrhagic Fever (DHF). The case fatality rate stood at 1.7%, resulting in 93 recorded deaths. By 2019, 101,354 dengue cases were reported, accompanied by 179 associated deaths [5].

The spectrum of dengue illness ranges from a mild fever to more severe manifestations like dengue hemorrhagic fever and dengue shock syndrome [6]. Dengue fever typically presents as an acute febrile illness lasting 2 to 7 days, characterized by symptoms such as headache, pain behind the eyes, muscle pain, joint pain, rash, and bleeding complications [7]. For diagnosing dengue fever during the initial five days of fever, the NS1 antigen presence is detected via the enzyme-linked immunosorbent assay (ELISA) method. Within the first two to three days of the illness, the NS1 test shows a diagnostic sensitivity exceeding 90%. However, this sensitivity progressively declines and markedly reduces after the fifth day [8]. Dengue virus-specific IgM can be identified and is useful for diagnosing dengue virus infections with high sensitivity and specificity. In individuals with a primary infection, a gradual IgM response is observed, increasing to 50% within three to five days, 80% after more than five days, and achieving 100% by ten days [9,10]. According to the WHO, severe dengue is classified as dengue hemorrhagic fever and dengue shock syndrome [11].

The liver is a frequently affected organ in dengue, with dengue-associated liver injury first documented in 1967 [12]. An enlarged liver (hepatomegaly) serves as a warning sign in dengue. Hepatic dysfunction in dengue can vary from minor increases in transaminases to severe liver failure. The exact mechanism of liver function impairment is not precisely understood, attributed either to the direct viral action or an uncontrolled host immune response [13]. The clinical presentation of Dengue fever is highly diverse [14], making it challenging to predict which pediatric patients will develop severe dengue infection, particularly in the initial phases [15]. Elevated levels of liver enzymes are frequently observed in the early stages of dengue infection, and several studies indicate that increased transaminases at admission can serve as indicators for assessing the severity of dengue infection [16]. Therefore, this study aims to evaluate the utility of liver enzymes as early indicators of severity and their predictive value for patient outcomes. The rise of serum aminotransferase levels is considered important for assessing the seriousness of dengue fever. This study seeks to establish the correlation between dengue illness severity and aminotransferase levels.

MATERIALS & METHODS

This hospital-based prospective observational study was conducted in wards of Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh, from November 2024 to August 2025 to determine the association between serum aminotransferases level and the severity of dengue. The sample size was determined using the following formula: n=z2 pq/d2. A total 70 children were included in this study. Subjects with Dengue fever with warning sign and aged between 1 month to 15 years was included in this study. Patient with dengue shock syndrome, Dengue haemorrhgic fever, the presence of severe chronic disease, Recent blood transfusion & Children with pre-existing liver disease were excluded from this study. The study included patients who met the WHO 2012 definition of dengue fever along with dengue warning sign. Febrile patients with serology-positive dengue from outside labs were also included in the study. Patients were excluded if they refused to give consent for participation in the study. Participants who met the inclusion and exclusion criteria and gave informed consent to participate in the study were enrolled. Patients with NS1 positivity on days one to three and/or positive IgM on days 6 to 10 were defined as dengue cases; those with other confirmed diagnoses were labeled as other febrile illnesses. Severe dengue was marked by severe thrombocytopenia, significant bleeding, plasma leakage, Shock, and multi-organ failure. Other cases were marked as non-severe dengue. The outcome of this study was to see an association between serum aminotransferases and severity of illness.

Statistical Analysis:

Data analysis was done using the Statistical Package for the Social Science (SPSS) Version 25. Continuous variables were summarized using mean and standard deviation (SD) and categorical variables as frequencies and percentages. Comparison of multiple means across disease severity was done using ANOVA test. Pearson´s correlation coefficient test was used to calculate the correlation between variables. A probability value of <0.05 (95% CI) was accepted as the level of statistical significance.

RESULTS

Table 1 show the mean age was found 5.5 ± 4.02 years among them 42.9% was between 1-5 years of age and males were predominant (62.9%).

Table 1: Demographic profile of the study subjects (N=70)

	Frequency (n)	Percentage (%)
Age (years)		
< 1	8	11.4
1 - 5	30	42.9
>5 - 10	22	31.4
>10 - 15	10	14.3
Mean ± SD	5.50 ± 4.02	
Min - max	0.33 - 15	
Gender		
Male	44	62.9
Female	26	37.1

During admission, dengue cases presented with variety of clinical features. Fever was present in 100% patients and mean duration of fever was 4.52 ± 2.51days. Table 2 show that, along with fever other predominant clinical presentations were characteristic rash (32.8%), vomiting (18.6%), abdominal pain (18.6%), reduced urine output (12.9%) and diarrhea (7.1%).

Table 2: Symptoms of dengue of the study subjects (N=70)

Symptoms	Frequency (n)	Percentage (%)
Fever	70	100.0
Rash	23	32.8
Joint pain/Arthralgia	1	1.4
Persisting vomiting	13	18.6
Headache	3	4.3
Constipation	1	1.4
Diarrhea	5	7.1
Abdominal pain	13	18.6
Retro-orbital pain	4	5.7
Urine output reduced	9	12.9
Duration of illness (days)		
Febrile [Mean ± SD]	4.52 ± 2.51	

Regarding serological tests, Dengue NS1 was found positive (evidence found before admission) in 60% affected children whereas 35.7% had positive result for dengue IgM and 4.3% had both IgM & IgG.

Table 3: Dengue NS1 antigen of the study subjects (N=70)

	Frequency (n)	Percentage (%)
Dengue NS1		
Positive	42	60.0
ICT for Dengue		
IgM (positive)	25	35.7
IgG (positive)	3	4.3

Table shows 28.6% study subject developed Dengue shock syndrome, 10% developed Dengue hemorrhagic fever, 4.3% developed Expanded dengue syndrome and 57.1% remain as Dengue fever with warning sign.

Table 4: Type of dengue (N=70)

	Frequency (n)	Percentage (%)
Dengue Fever with warning sign	40	57.1
Dengue Hemorrhagic fever	7	10.0
Dengue shock syndrome	20	28.6
Expanded dengue syndrome	3	4.3

Baseline liver function were observed in the study population. On admission Mean SGOT (85.71 ± 67.80) was more than Mean SGPT (58.27 ± 51.22).

Table 5: Aminotransferases level of the study subjects (N=70)

	Mean ± SD	Min - max
AST (Alanine aminotransferase)	85.71 ± 67.80	12 - 367
ALT (Aspartate aminotransferase)	58.27 ± 51.22	14 – 298

According to the findings, both enzymes are increased in dengue of all kinds, with dengue shock syndrome showing the highest levels. The mean AST level is 62.73 ± 35.16 U/L in dengue fever with warning signs, 83.43 ± 36.21 U/L in dengue hemorrhagic fever, and 129.73 ± 97.42 U/L in dengue shock syndrome. The average AST level in expanded dengue syndrome is 95.67 ± 97.30 U/L. Comparably, the mean ALT level is 37.91 ± 17.58 U/L in dengue fever with warning signs, 55.43 ± 37.60 U/L in dengue hemorrhagic fever, 101.58 ± 75.20 U/L in dengue shock syndrome, and moderately elevated at 57.00 ± 45.31 U/L in expanded dengue syndrome.

Table 6: Aminotransferases (AST, ALT) level according to dengue type (N=70)

Aminotransferases	Dengue Fever with warning sign	Dengue Hemorrhagic fever	Dengue shock syndrome	Expanded dengue syndrome	p-value
AST (U/L)	62.73 ± 35.16	83.43 ± 36.21	129.73 ± 97.42	95.67 ± 97.30	0.004
ALT (U/L)	37.91 ± 17.58	55.43 ± 37.60	101.58 ± 75.20	57.00 ± 45.31	<0.001

ANOVA test was done

There was a positive correlation between AST levels and disease severity, with a correlation coefficient (r) of 0.394 and a p-value of 0.001. This means that the relationship was statistically significant. ALT levels also had a positive and statistically significant relationship with disease severity, with a r value of 0.459 and a p value of less than 0.001.

Table 7: Correlation of aminotransferases parameters with severity of dengue of the study subjects (N=70)

Severity of dengue	r	p-value
AST (Alanine aminotransferase)	0.394	0.001
ALT (Aspartate aminotransferase)	0.459	<0.001

Pearson's correlation test was done.

DISCUSSION

Currently, reliable tests for monitoring or predicting dengue's severity and patient outcomes are unavailable. Consequently, this study aimed to investigate the association between serum aminotransferase levels and the severity of dengue illness, hoping to uncover new avenues for developing improved therapeutic targets. This correlation between aminotransferases and patient outcomes was examined at a tertiary care hospital.

Within our study population, males constituted the majority (44 patients, 62.9%). This observation aligns with findings from other research; for instance, a study in Singapore reported that 71% of PCR-positive dengue fever patients were male [17], and Nadeem M *et al.,*similarly identified a male predominance in their patient group [16]. The median duration of the febrile phase in our cohort was 4.52 ± 2.51 days. This is consistent with findings by Chaiyaratana W et al., who reported a comparable median febrile stage of five days (with a range of 1 to 10 days and an interquartile range of 4 to 6 days) [17].

Our investigation identified Dengue Hemorrhagic Fever in 7 (10%) participants, Dengue Shock Syndrome in 20 (28.6%) participants, and Dengue Fever with Warning Signs (DFWS) in 40 (57.2%) participants. This distribution aligns with other research; Shankar RB *et al.,*[18] reported that DFWS constituted the majority of dengue cases (70.83%), and studies by Dr. Lakshmanaswamy A *et al.,*[19] and Manohar *et al.,*[20] also indicated a higher prevalence of DFWS.

In our cohort, the mean AST level (85.71 ± 67.80) surpassed the mean ALT level (58.27 ± 51.22). This pattern mirrors the findings of Srinivasulu DM et al., who also reported higher mean AST (186.52 IU/L) compared to ALT (129.91 IU/L) [21]. Notably, mean AST levels were significantly higher in patients with Dengue Shock Syndrome (DSS) (129.73 ± 97.42 U/L) compared to other dengue classifications (p=0.004). A similar statistically significant elevation was observed for mean ALT levels in DSS patients (101.58 ± 75.20 U/L) when compared to other dengue fever types (p<0.001). These results are consistent with Shankar RB et al.'s work, which also demonstrated significantly raised AST and ALT levels in DSS [18]. A positive correlation was identified between AST levels and disease severity (r=0.394, p=0.001). This finding is reinforced by studies from Dr. Siddappa F.D *et al.,*[22], Amrita Roy *et al.,*[23], and Manohar *et al.,*[20], all of whom similarly demonstrated a positive association between increased transaminase levels and the severity of dengue.

Conflict of interest

There are no conflicts of interest associate with this study.

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CONCLUSION

Liver impairment is frequently observed in dengue infection. Elevated liver enzyme levels early in the disease course serve as an early indicator of disease severity. This insight facilitates enhanced surveillance of individuals at higher risk of developing severe manifestations, thereby permitting the timely initiation of appropriate therapeutic interventions.

LIMITATIONS

1. The study's inability to differentiate between compensated and decompensated dengue shock syndrome might have limited a more comprehensive understanding of disease progression.
2. Furthermore, the absence of dengue virus genotyping consequently restricted the ability to establish correlations between specific serotypes and aminotransferase level, as well as overall disease severity.

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