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Original Article

Hepatic Dysfunction in Dengue Fever and Dengue Hemorrhagic Fever: A Cross-Sectional Study at A Tertiary-level Hospital, Bangladesh

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Abstract

Background: *Dengue is the most prevalent mosquito-borne viral infection, endemic in South-East Asia and found in tropical and subtropical regions worldwide, predominantly in urban and peri-urban areas. In Bangladesh, dengue has emerged as a significant public health concern since the mid-2000s. Beyond classical presentations, many patients with dengue infection present with liver dysfunction.* ***Objective:*** *The general objective of this study was to assess changes in liver function (AST, ALT, PT) in Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF). The specific objective was to evaluate whether changes in liver function could predict disease severity.* ***Study Design and Method:*** *This cross-sectional study was conducted over six months in the Medicine Wards of Sir Salimullah Medical College and Mitford Hospital, Dhaka, and included 50 patients diagnosed with DF or DHF. Results: Among the 50 patients, 34 (68%) had DF and 16 (32%) had DHF. Overall, 42% of patients had elevated AST and ALT levels. Most patients (58%) had AST and ALT levels within group 1 (≤46 U/L). AST elevation was observed in 32%, 4%, and 6% of patients in groups 2 (47–120 U/L), 3 (121–200 U/L), and 4 (>200 U/L), respectively. ALT elevation was observed in 26%, 10%, and 6% of patients in groups 2, 3, and 4, respectively. Elevated ALT levels were more frequent in DHF compared to DF, with a statistically significant difference ($p<0.05$). Serum bilirubin was >1 mg/dL in 18.75% of DHF patients compared to 6% of DF patients. Prothrombin time (PT) was prolonged by more than 3 seconds in 4 of 34 DF patients (11.76%) and in 6 of 16 DHF patients (37.5%), which was also statistically significant ($p<0.05$).* ***Conclusion:*** *Liver dysfunction is common in dengue infection and is more severe in DHF compared to DF. Monitoring liver function can help assess disease severity and guide clinical management.*

Key words: *DF, DHF, Hepatic, Dysfunction, Bangladesh*

Introduction: Dengue virus infection is now recognized as one of the most significant emerging infectious diseases worldwide.[1-3]. It is the second most common mosquito-borne illness after malaria,[4] and in the last two decades, the incidence of Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), and Dengue Shock Syndrome (DSS) has increased dramatically, often in epidemic form.[5] Currently, dengue is endemic in more than 100 countries across Africa, the Americas, the Eastern Mediterranean, Southeast Asia,

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and the Western Pacific, with an estimated 50–100 million cases of DF and over 500,000 cases of DHF annually. [6]

The disease is caused by one of four antigenically distinct serotypes (DEN-1 to DEN-4) of the Flavivirus genus.[7] Transmission occurs through Aedes mosquitoes, mainly Aedes aegypti and Aedes albopictus. Clinical manifestations vary widely, ranging from asymptomatic infection to DSS.[8] Liver involvement is increasingly reported as a complication of dengue.[9]

DF is usually an acute, self-limiting febrile illness characterized by fever, headache, myalgia, rash, leucopenia, and thrombocytopenia. Although disabling, its outcome is rarely fatal. In contrast, DHF is marked by plasma leakage, hemorrhage, and shock, with mortality rates of up to 5%, particularly among children[6]. In recent years, unusual systemic and organ-specific complications have become more common.[7] Although the liver is not the primary target organ, pathological findings such as centrilobular necrosis, fatty changes, Kupffer cell hyperplasia, and apoptotic hepatocytes have been documented, particularly in DSS. [10,11]

Most patients exhibit mild to moderate elevations of liver enzymes, with AST often higher than ALT.[15] While usually self-limiting, hepatic involvement may prolong the clinical course. In rare cases, fulminant hepatitis with high mortality has been reported.[12, 13] The mechanism of liver injury remains unclear, with evidence supporting both viral replication and immunemediated hepatocyte damage.[14,15] Unlike hepatitis B or C, dengue does not cause chronic liver disease.[16] However, in DHF, mortality may occur from prolonged shock, massive bleeding, respiratory failure, or encephalopathy.[17] Elevation of AST has been associated with severe disease and may serve as an early predictor of DHF. [18,19]

In Bangladesh, dengue continues to pose a major health challenge. Despite national guidelines based on WHO recommendations, differentiating dengue from other viral febrile illnesses and hepatitis remains difficult.[20]. Further research is needed to clarify the extent and clinical significance of hepatic dysfunction in dengue, which may improve diagnosis and management. Though dengue is a major public health problem in Bangladesh, there remain limitations in its identification and management. However, overlapping and confusing knowledge still exists in differentiating dengue from other viral fevers and acute viral hepatitis. In addition, our understanding of the type, extent, and consequences of hepatic involvement in dengue syndrome is still limited. Therefore, the present study aims to expand knowledge regarding dengue syndrome, with particular emphasis on the nature and extent of hepatic dysfunction in dengue fever and dengue hemorrhagic fever, assessed both clinically and biochemically. This may contribute to improved diagnosis and effective management of dengue syndrome in Bangladesh.

Materials and Methods

Study Design and Setting

This cross-sectional study was conducted among Bangladeshi patients with dengue fever and dengue hemorrhagic fever admitted to the medicine wards of Sir Salimullah Medical College (SSMC) and Mitford Hospital, Dhaka, from July 2011 to December 2011.

Patients

All febrile patients who were clinically suspected and serologically confirmed (IgM positive) as dengue fever or dengue hemorrhagic fever were considered for inclusion. A total of 50 patients were enrolled based on the defined criteria. Patients were selected using a convenient sampling method.

Inclusion and Exclusion Criteria

Inclusion criteria: Patients fulfilling the case definition of probable dengue fever and dengue hemorrhagic fever according to the *National Guidelines for Clinical Management of Dengue Syndrome* and those who voluntarily provided informed consent.

Exclusion criteria: Febrile patients below 12 years of age and patients suffering from other known hepatic disorders.

Laboratory Procedure

All patients underwent detailed clinical history taking and thorough physical examination. Laboratory investigations conducted in all patients included complete blood count (CBC) with total leukocyte count, total platelet count, and hematocrit; serum ALT, AST, bilirubin, and prothrombin time; and dengue serology (anti-dengue IgM and/or IgG antibodies). Selected patients additionally underwent chest X-ray, ultrasonography, serum albumin measurement, and testing for viral markers. All data were systematically recorded using a structured case record form

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Statistical Analysis

Data were meticulously checked, cleaned, and entered into a database prepared using SPSS software, for Windows. Both descriptive and inferential statistical analyses were carried out using SPSS. The data analysis process included compilation, validation, and systematic evaluation of clinical and biochemical parameters to assess hepatic dysfunction in dengue patients.

Ethical Review

The study protocol was reviewed and approved by the Institutional Ethics Committee of Sir Salimullah Medical College, Dhaka. The objectives, study procedures, potential risks, and benefits were explained in simple local language to each participant, and written informed consent was obtained. Confidentiality of all patient information and records was strictly maintained, and it was emphasized that the study would benefit both physicians and patients through improved clinical management.

Results

A total of 50 serologically confirmed dengue patients were included in this study. The cases were categorized into Dengue Fever (DF, n=34) and Dengue Hemorrhagic Fever (DHF, n=16), while Dengue Shock Syndrome cases were identified but not analyzed separately. Baseline demographic characteristics, presenting symptoms, physical signs, and laboratory findings were analyzed for both groups.

Demographic Characteristics

The mean age of patients was 26.76 ± 11.83 years in the DF group and 26.31 ± 10.30 years in the DHF group, with an overall mean age of 26.62 ± 11.26 years. Most patients (38%) were aged below 20 years (Table 1).

Table 1: Demographic Characteristics of DF and DHF Patients (n=50)

Characteristic Age (years)	DF (n=34)	DHF (n=16)	Total (n=50)	Percentage (%)
13–20	13	6	19	38
21–30	12	5	17	34
31–40	4	3	7	14
41–50	3	2	5	10
51–60	2	0	2	4
Mean ± SD	26.76±11.83	26.31±10.30	26.62±11.26	-
Gender				
Male	24	12	36	72
Female	10	4	14	28
Occupation				
Businessman	8	3	11	22
Service holder	4	1	5	10
Student	10	7	17	34
Housewife	6	1	7	14
Worker	6	2	8	16
Others	3	2	5	10

Among the study population, 36 (72%) were male and 14 (28%) were female, yielding a male-to-female ratio of 2.57:1. In the DF group, 24 (48%) were male and 10 (20%) female; in the DHF group, 12 (24%) were male and 4 (8%) female

Regarding socioeconomic status, 34 (68%) patients belonged to middle-class families, 15 (30%) to low-income families, and 1 (2%) to high-income families, indicating that dengue predominantly affected middle-class individuals. Occupationally, most DF patients were students (10) and businessmen (8), while in DHF, 7 were students and 3 businessmen. Overall, students represented the largest occupational group (28%)

Presenting Symptoms of Dengue Patients

A total of 50 serologically confirmed dengue patients were analyzed for clinical manifestations, divided into Dengue Fever (DF, n=34) and Dengue Hemorrhagic Fever (DHF, n=16). Fever was universal, present in 100% of patients in both DF and DHF groups. Headache was reported in 85% of DF patients and 88% of DHF patients, while myalgia/bodyache occurred in 88% of DF and 100% of DHF patients. Retro-orbital pain, a characteristic symptom of dengue, was observed in 40% of DF and 50% of DHF patients. Gastrointestinal symptoms, including abdominal pain, nausea, vomiting, and loose motion, were present in 62% of DF and 81% of DHF patients. Respiratory symptoms were less common, occurring in 30% of DF and 35% of DHF patients. Hemorrhagic manifestations were markedly more frequent in DHF (50%) than in DF (6%), reflecting the severity of vascular involvement in DHF (Figure 1).

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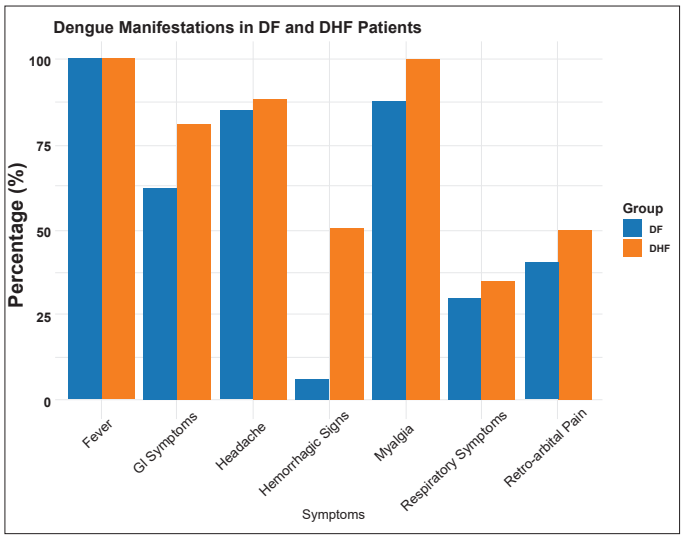

Figure 1 Presenting Symptoms of Dengue Patients

Fever patterns were further analyzed: 46 patients had high-grade fever, while 4 had low-grade fever. Continuous fever was observed in 28 patients, intermittent in 17, saddle-back in 10, and remittent in 5. Some patients exhibited mixed patterns combining high-grade with continuous, remittent, or saddle-back fever.

Median clinical parameters were as follows: systolic BP 100 mmHg, diastolic BP 70 mmHg, pulse rate 72 beats per minute, and body temperature 102ºF (Table 2).

Table 2: Clinical parameters of study population (n=50)

Parameter	Median	Range
Pulse rate/min	72	56–100
Systolic BP (mmHg)	100	80–140
Diastolic BP (mmHg)	70	60–110
Temperature (ºF)	102	99–105

Physical Signs

Rashes were observed in 41% of DF and 69% of DHF patients. Conjunctival hemorrhage occurred in 35% of DF and 44% of DHF patients. Positive tourniquet test was observed in 18% of DF and 75% of DHF cases. Hepatomegaly was noted in 6% of DF and 50% of DHF patients. No cases of jaundice were recorded. Ascites (12%) and pleural effusion (6%) were only present in DHF patients (Figure 2).

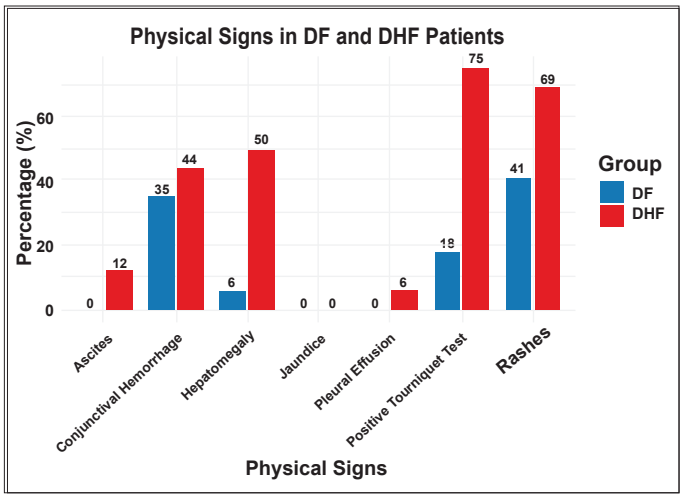

Figure 2 Physical Signs of dengue

Hemorrhagic Manifestations

In the DF group, melena was the only hemorrhagic manifestation, occurring in 2 patients (6%). In the DHF group, 8 patients (50%) exhibited hemorrhagic signs: melena (18.75%), gum bleeding (18.75%), hematemesis (6.25%), and epistaxis (6.25%) (Table 3)

Table 3: Hemorrhagic manifestations in DF and DHF patients (n=50)

Hemorrhagic Manifestation	DF (n=34)	DHF (n=16)	Total (n=50)
Epistaxis	0	1	1 (2%)
Gum bleeding	0	3	3 (6%)
Hematemesis	0	1	1 (2%)
Melena	2	3	5 (10%)
Absent	32	8	40 (80%)
Total	68%	32%	100%

Serum Bilirubin: Most patients (45/50) had levels below 1 mg/dl. Three DHF patients (18.75%) and 2 DF patients (6%) had bilirubin >1 mg/dl. The overall mean bilirubin was 0.75 mg/dl (range 0.2–2.0 mg/dl) (Table 4).

Table 4: Serum bilirubin in DF and DHF patients (n=50)

Serum Bilirubin (mg/dl)	DF (n=34)	DHF (n=16)	Total (n=50)
Below 1.0	32	13	45
Above 1.0	2	3	5
Total	34	16	50

ALT levels were ≤46 U/L in 29 patients (58%), 47–120 U/L in 13 (26%), 121–200 U/L in 5 (10%),

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and >200 U/L in 3 (6%). Elevated ALT was more pronounced in DHF, with three-fold elevations in 25% of DHF patients versus 3% of DF patients.

Table 5: AST distribution in DF and DHF patients (n=50)

AST (U/L)	DF (n, %)	DHF (n, %)	Total (n, %)
≤46 (Group 1)	23 (46%)	6 (12%)	29 (58%)
47–120 (Group 2)	9 (18%)	7 (14%)	16 (32%)
121–200 (Group 3)	1 (2%)	1 (2%)	2 (4%)
>200 (Group 4)	1 (2%)	2 (4%)	3 (6%)
Total	34 (68%)	16 (32%)	50 (100%)

Aminotransferases (AST and ALT): AST levels were grouped as ≤46 U/L (58%), 47–120 U/L (32%), 121–200 U/L (4%), and >200 U/L (6%) (Table 5).

Table 6: ALT distribution in DF and DHF patients (n=50)

ALT (U/L)	DF (n, %)	DHF (n, %)	Total (n, %)
≤46 (Group 1)	24 (48%)	5 (10%)	29 (58%)
47–120 (Group 2)	8 (16%)	5 (10%)	13 (26%)
121–200 (Group 3)	1 (2%)	4 (8%)	5 (10%)
>200 (Group 4)	1 (2%)	2 (4%)	3 (6%)
Total	34 (68%)	16 (32%)	50 (100%)

P-value calculated using Fisher's Exact Test (χ^2 = 9.678, p = 0.013).

*V*alues of ALT (U/L) were also divided into 4 groups. Most of the patients were in Group 1 and the numbers of patients were 29(58%). In group 2, total numbers of patients were 13 (26%). In Group 3, 5 patients had altered ALT value, of which 4 were in DHF group indicating that 3% of DF patients showed three-fold elevations of ALT value in comparison to 25% of DHF cases. In Group 4, 3 patients had found to have more than five-fold elevation of ALT value.

Chi square was done to find out the association ALT with Dengue Fever and Dengue Hemorrhagic Fever. It was presented with the statistical significant association of Dengue Fever and Dengue Hemorrhagic Fever with different levels of ALT (P=<0.05)

ALT levels were ≤46 U/L in 29 patients (58%), 47–120 U/L in 13 (26%), 121–200 U/L in 5 (10%), and >200 U/L in 3 (6%). Elevated ALT was more pronounced in DHF, with three-fold elevations in 25% of DHF patients versus 3% of DF patients.Fisher's exact test indicated a significant association between ALT levels and disease type (p=0.013) (Table 6).

Prothrombin Time (PT): PT prolongation >3 seconds occurred in 4/34 DF patients (11.76%) and 6/16 DHF patients (37.5%), with an overall 20% prevalence (Table 7).

Table 7: Prothrombin time prolongation in DF and DHF patients (n=50)

PT prolongation (sec)	DF (n=34)	DHF (n=16)	Total (n=50)
≤1	11 (22%)	4 (8%)	15 (30%)
2–3	19 (38%)	6 (12%)	25 (50%)
>3	4 (8%)	6 (12%)	10 (20%)
Total	68%	32%	100%

Independent sample t test was conducted to see the mean difference of ALT, AST and PT at statistical significant level between DF and DHF. The levels of ALT were significantly different (Not similar) in Dengue fever and Dengue Hemorrhagic Fever (t = -2.612, p = 0.012) whereas levels of AST was not different (similar) in DF and DHF (t = -1.562, p = 0.125). This result showed, ALT was lower value of 58.500 U/L in Dengue fever compare to Dengue Hemorrhagic fever which is statistically significant. Prothrombin time prolongation was also significantly different in DF and DHF (*t=-2.472 & p=0.017*) (Table 8).

Table 8: Independent samples t-test for ALT, AST, and PT

Parameter	t	p	Mean Difference	95% CI Lower	95% CI Upper
ALT (U/L)	-2.612	**0.012**	-58.500	-103.537	-13.463
AST (U/L)	-1.562	0.125	-87.493	-200.089	25.104
PT prolongation (sec)	-2.472	**0.017**	-2.540	-4.607	-0.474

These results demonstrate that hepatic dysfunction, reflected by elevated ALT and prolonged PT, is more pronounced in DHF compared to DF, while AST elevation is not significantly different between the two groups.

Discussion

A total number of 50 serologically confirmed (IgM Positive) patients were selected for the study. The cases of dengue patients in this study were divided into Dengue Fever (DF) and Dengue Hemorrhagic fever (DHF).3 cases of Dengue Shock Syndrome (DSS) were diagnosed in this study and were included with DHF group.

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Almost all the patients came from urban area. Only a few came from the rural area indicating either dengue viral vectors spread to rural settings or the infected patient travelled in the urban earlier.

Though, we took only those cases who were above 12 years, still majority of the subjects were under 20 years old age. The mean age (M± SD) among the study subject was 26.62± 11.26 years and the range of age was 14 -55 years. In DF the mean age (M± SD) was 26.76±11.83 and in DHF it was 26.31±10.30. The study of Safhan MNF *et al*, the mean age was 31±12 (SD) years[20] and Chareonsook 'O *et al*. showed–the age of highest incidence has increased and adults are now also being affected with dengue hemorrhagic fever/dengue shock syndrome [21] Wali JP et al. showed that contrary to the popular belief dengue hemorrhagic fever/dengue shock syndromeis not a disease of children only and the mean age of his study was 31 yrs ± 5.2(SD) [22], that are nearer to this study.

Male predominance was observed in this study and male and female ratio (2.57:1) was consistent with the study conducted by Itha S *et al*[23] where it was 1.8:1 . Total number of male patients were 36(72%) and female were 14 (28%). The male predominance might be due to increased risk of exposure to vectors or increase health care seeking behaviour. Further community based study will provide insight.

Occupational status of the respondents represents that, most of the patients with DF were students (20%) and businessmen (16%). In DHF group, it was found that 7(14%) patients were students, 3(06%) were businessmen. In total, it was found that most of the patients were students (28%).

In this study, 34 (68%) of the patients came from middle-class family, whereas 15 (30%) patients came from low-income family and the remaining 1 (2%) from high-class family. Both DF and DHF predominantly affect the middle-class family.

Different pattern of pains and aches were experienced by the study subjects. Almost all the patients of each group suffered from headache (86%), myalgia (92%), retro-orbital pain (54%). Anuradha S *et al.*[24] reported 96% of her study subjects suffered myalgia and other aches while Wali. JP et al.[25] showed Headache in 80.9%, myalgia 76.2% and these were the common symptoms which are similar to the findings in this study.

Median systolic and diastolic blood pressure of the study group was 100 mm Hg and 70 mm Hg, respectively. Median body temperature was found to be 101º F and median pulse rate was about 72 beats per minute. A similar report was reported by study[26] from Dengue patients that median temperature was 100.4 ºF, pulse rate was 94 beats per minute and median systolic and diastolic blood pressure was 107 mm Hg and 68 mm Hg, respectively.

Different patterns of rashes over the trunk, e.g., macular 42%, maculopapular 8%, totaling 50% of the study subjects, were observed. The tourniquet test was positive in 18% of DF cases and in 75% of DHF, respectively, while Nimmannitya S *et al*. reported 84% tourniquet test positive in all the study subjects of dengue hemorrhagic fever/dengue shock syndrome. [27] Kabra Sk *et al*. reported Tourniquet test was positive in 40% of dengue fever patients, 62% of dengue hemorrhagic fever[28].

About bleeding morbidity, Melena was the commonest hemorrhagic manifestation. In DHF, melena (18.75%), gum bleeding (18.75%), hematemesis (6.25%), and epistaxis (6.25%) were the presenting features. In DF, melena was the only hemorrhagic manifestation.

Liver damage is a common complication of dengue infection and aminotransferase levels are a valuable marker for monitoring these cases.[29] The result of this study showed that many patients with Dengue viral infection had some degree of mild to moderate hepatic dysfunction as indicated by hepatomegaly, abnormal hepatic enzyme levels and abnormal coagulation profile.

In this study, hepatomegaly was seen in 6% of DF and 50% of DHF patients. In a study by Moren,[30] hepatomegaly was observed in 60% of adult patients with dengue infection. Another study by Wahid *et al*. among 50 patients showed hepatomegaly seen in 60% of DHF patients and in 40% of DF patients.[31] However, in this study, hepatomegaly was consistent with DHF cases but was less common in DF cases.

Serum Bilirubin was found below 1 mg/dl in 45 out of 50 patients. 3 (18.75%) patients of DHF were found above 1 mg/dl (Highest 2 mg/dl) where 2 (6%) patients of DF were found so.

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In the study, the elevation of AST was higher in the DHF group (62.5%) than DF group (29.4%).out of 50 patient, 29(58%) were within normal level of AST. The rest of the 21(42%) had elevated serum AST levels. In groups 3 and 4, AST levels were elevated 3 to 5 times above the normal value, accounting for 10% of the total patients. An AST level was exceeding 5 times the upper limit in 35% of DF patients in the Shrivenu Itha study,[32] which is far greater than this study.

This study showed that the ALT level also changed. Elevation of ALT level occurred more in DHF group patients (68.75%) than DF group (29.4%). Out of 50 patients, 29(59%) were within normal values. Overall, 21(42%) patients had elevated ALT levels, which was statistically significant (p value <0.05). In groups 3 and 4, overall 8(16%) patients had the elevated ALT level that were 3 to 5 times above the normal value. Patients with five-fold or more elevation in ALT level were tested negative for viral markers. In Shrivenu Itha's study, [33] the ALT level was 5 times the upper normal limit in 9 (24%), which was closer to this study. Another study by Wahid et al[19] showed ALT above 200 U/L was seen in 16% of patients, which is similar to this study. So, the average levels of AST and ALT were greater in DHF than in DF. However, higher AST and ALT levels in DHF patients indicate that liver function derangement is closely related to the severity of dengue viral infection.

In this study, Prothrombin time (PT) was prolonged more than 3 seconds beyond the control in 4 of 34 DF patients (11.76%), whereas in DHF, PT was prolonged more than 3 seconds beyond the control in 6 out of 16 patients (37.5%). However, total 10(20%) out of 50 patients show PT prolongation more than 3 seconds beyond the control. In Shrivenu Itha study, [34] PT was prolonged more than 3 seconds beyond the control in 6 of the 37 patients (16%), which is consistent with this study.

So it should be noted that hepatomegaly and liver dysfunction are common and more severe in DHF compared to DF has been observed in the present study.

Limitation of the Study

This study was hospital-based and included only a small number of respondents. Patients from all socioeconomic backgrounds and regions of the country were not represented, as not all sought medical attention at the study site. Dengue diagnosis was based on clinical findings and anti-dengue IgM antibody testing, which may cross-react with other flaviviruses. Due to financial constraints, seasonal variation of the disease, and time limitations, the sample size was small, and confirmatory testing for acute precision and accuracy was limited. A larger, multi-institutional study over a longer period would provide more robust and generalizable findings.

Conclusion and Recommendation:

Dengue virus infection constitutes a significant proportion of hospital admissions in Bangladesh, particularly in Dhaka in recent years, and presents with varied clinical manifestations. This cross-sectional clinical study conducted over six months in the Medicine Wards of Sir Salimullah Medical College and Mitford Hospital, Dhaka, included 50 cases of Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF).

The study found that DF and DHF are usually associated with mild to moderate elevation of liver enzymes (AST and ALT), though the disease course is generally self-limiting and does not result in liver failure. Hepatic involvement is common in dengue infection, with hepatomegaly and mild to moderate enzyme elevation being more pronounced in DHF than DF.

Regular monitoring of liver function tests in dengue patients, especially those with DHF, is recommended to assess hepatic dysfunction and help predict disease severity.

Data Availability

N/A

Code Availability

Not applicable.

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Competing Interests

The authors declare that there are no commercial or financial relationships that could be perceived as potential conflicts of interest.

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