CLINICOPATHOLOGICAL PROFILE OF DENGUE FEVER AMONG CHILDREN ADMITTED IN A TERTIARY CARE HOSPITAL, DHAKA, BANGLADESH.

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ABSTRACT

Background: Dengue is not always manifested by its typical clinical features, its presentation may be atypical which may create confusion among physicians while making a diagnosis. The clinical profile that was seen in earlier epidemics has changed over time and various atypical features are found in day to day clinical practice. The trends in simple hematological and biochemical parameters are of utmost importance to evaluate the severity of the disease. **Aim:** This study was carried out to evaluate the clinico-pathological profile of dengue fever in children. **Materials and Method:** This cross-sectional study was conducted in the department of Paediatrics of Medical College for Women and Hospital, Uttara, Dhaka, from August to October 2023 following ethical clearance of the protocol. A total of 250 children aged 0-18 years who attended the study center with fever with positive NS1 (nonstructural protein 1) antigen or positive IgM (Immunoglobulin M) antibody of dengue were included after getting informed written consent from their legal guardians. Data were collected by using a structured questionnaire. Collected data were analyzed by the SPSS 26. **Results:** The mean±SD of age of the respondents was 7.12±4.26 year with male predominance (54.8%). All respondents had fever, wherein majority had low grade fever (67.2%). More than half of the respondents (52.4%) had vomiting. Oral thrush (42.8%), abdominal pain (34%), congestion of the eye (28.4%), runny nose (22.4%), cough (16%), headache (15.6%), rash (14.8%), lack of appetite (14%) and loose stool (13.6%) were the other common clinical features. Pleural effusion (15.6%) in Chest X-ray and respiratory distress (28.8%) and ascites (17.6%) were other common findings. Hepatomegaly, ascites, respiratory distress, pleural effusion and edematous gallbladder were significantly more in severe dengue than non-severe dengue fever. Besides, decreased Hb% (hemoglobin %), increased HCT (hematocrit) level, SGPT (Serum Glutamic Pyruvic Transaminase) >56U/L and SGOT (Serum Glutamic Oxalo-Acetic Transaminase) >45U/L were significantly higher in severe dengue fever than non-severe dengue. **Conclusion:** Dengue in children presented with diverse symptoms and severity. However, further multicenter study is recommended to verify the present findings.

INTRODUCTION

Dengue is a febrile illness caused by flavivirus which is transmitted by mosquitoes. This is endemic in Asia, the Pacific, Africa and the Americas.

Approximately, 400 million infections and 100 million clinically apparent infections occur annually[1]. Dengue remains endemic in Bangladesh since 2000.

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In a grossly under-reported setting, the reported cases and deaths in the country in 2000 were 5,555 and 93 respectively which came down gradually. This reduction in the number of deaths is certainly due to the improved and uniform management of the cases. Now, in last two years, there is again severe upsurge with complicated cases being observed more frequently[2].

The principal vector is the mosquito Aedes aegypti, which breeds in standing water, collection of water in containers, water-based air coolers and tire dumps are a good environment for the vector in large cities. There are four serotypes of dengue virus, all producing similar clinical syndrome, type specific immunity is lifelong but immunity against the other serotypes last only a few months[1].

Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) occur in individuals, immune to one dengue virus serotype, who subsequently become infected with a different serotype[3]. Previously, dengue was seen in small children and DHF/DSS in children 2-15 years old, but these conditions are now being seen in children less than 2 years old, and most frequently in those 16-45 years of age or older, in whom severe organ dysfunction is more common. Other epidemiological changes include the spread of dengue into rural communities and greater case fatality in women[1].

Dengue may be manifested by its typical clinical features, but its presentation may be variable making doctors confused[3]. Dengue virus infection produces a wide spectrum of signs and symptoms varying from subclinical disease to severe DHF or DSS, which is on the rise[4]. The clinical profile that was seen in earlier epidemics has changed over time and various atypical features are found in day to day clinical practice.

The trends in simple hematological and biochemical parameters are of utmost importance to evaluate the severity of the disease[4].Our present study was to evaluate the clinico-pathological profile of dengue fever in children.

MATERIALS AND METHOD

This cross-sectional study was carried out in Medical College for Women & Hospital (MCW&H) during the period from August to October 2023 to find out the clinico-pathological profile of dengue fever in children. The study included two hundred fifty (250) cases of children aged 0-18 years who attended the study center complaining of fever with positive NSI antigen or positive IgM antibody for dengue. Patient more than 18 years and patient with fever other than dengue were excluded from the study. All the clinical findings and investigations of the selected dengue fever patients were recorded in a predesigned questionnaire.

Written informed consent was taken and ethical clearance was taken from MCW&H ethical review committee. Frequencies and percentages were calculated for the qualitative variables. Arithmetic mean and standard deviation were used to describe the quantitative variables. Chi-square test was used to compare categorical variables. A p value of less than 0.05 was considered significant. Data entry and analysis were done using SPSS for windows version 26.0.

RESULTS

Table 1 : Distribution of age group of respondents (n=250)

Variable (age in years)	Frequency	Percentage (%)
0-5	105	42.0
6-10	76	30.4
11-16	69	27.6
Mean ± SD	7.12±4.26	

The age of the majority of the respondents were less than 5 years (42%) and mean age of the respondents was 7.12±4.26 year with the range of 0 to 16 years as displayed in Table 1.
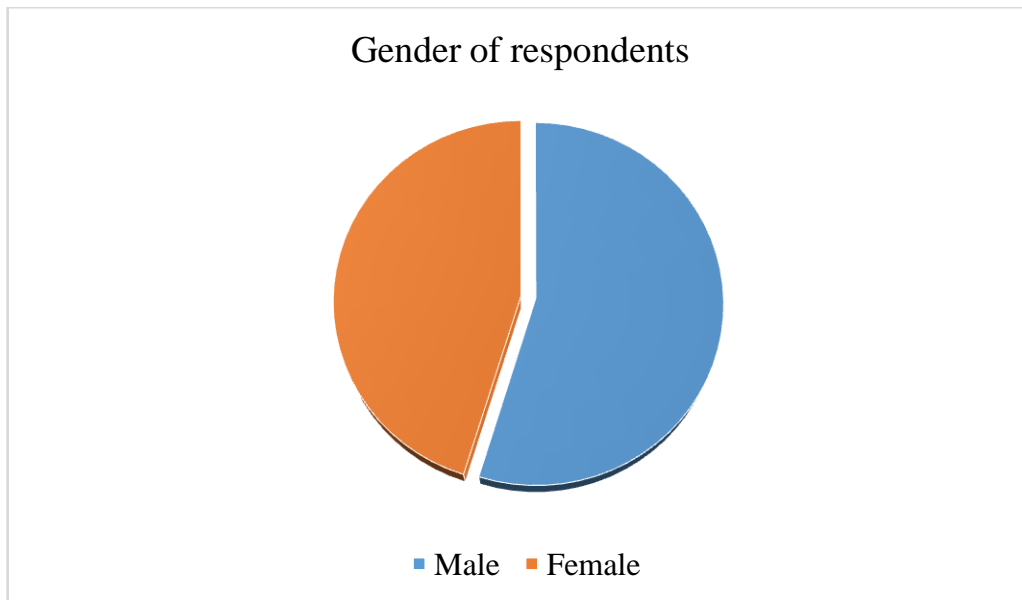

Figure 1 : Distribution of gender of respondents (n=250)

Figure 1 displays that more than half of the respondents were male (54.8%) and rest were female (45.2%).

Table 2: Sociodemographic status of respondents (n=250)

Variable	Frequency	Percentage
Residence		
● Urban	205	82
● Rural	45	18
Monthly family income		
● <10000 Taka	19	7.6
● 10000-30000 Taka	110	44
● >30000 Taka	121	48.4

Majority of the respondents were from urban residence (82%) and monthly family income was more than Taka 30000 (48.4%).

Table 3 : Clinical presentation of dengue fever (n=250)

Clinical presentation	Frequency	Percentage (%)
Fever	250	100
High fever	82	32.8
Low fever	168	67.2
Cough	40	16
Vomiting	131	52.4
Loose stool	34	13.6
Burning sensation during micturition	4	1.6
Lack of appetite	35	14
Headache	39	15.6
Retro-orbital pain	13	5.2
Body ache	29	11.6
Abdominal pain	85	34
Congestion of the eye	71	28.4
Oral thrush	107	42.8
Rash	37	14.8
Epistaxis	3	1.2
Runny nose	56	22.4

*Multiple responses were considered.

All respondents had fever, though majority of them had low grade fever (67.2%). More than half of the respondents (52.4%) had vomiting and less than half respondents had oral thrush (42.8%) (Table 3).

Table 4 : Common complications related to dengue fever (n=250)

Complications	Frequency	Percentage
Hepatomegaly	17	6.8
Splenomegaly	3	1.2
Respiratory distress	72	28.8
Pleural effusion	39	15.6
Ascites	43	17.2
Edematous gallbladder	23	9.2

According to chest Xray findings, respondents had respiratory distress (28.8%), ascites (17.2%) and pleural effusion (15.6%). Ultrasonography of the abdomen showed edematous gallbladder (9.2%), hepatomegaly (6.8%) and splenomegaly (1.2%) was also present among respondents. These findings are displayed by Table 4.

Clinicopathological profile of dengue fever among children

Table 5 : Biochemical and hematological parameters of patients with dengue fever (n=250)

Investigation	Mean±SD	Minimum	Maximum
Hb% (gm/dl)	11.85±1.47	7.20	16.4
WBC (/cumm)	6637.72±7507.29	1210.0	1114000.0
Platelet count (/cumm)	150052.4±78871.27	1100.0	475000
HCT (%)	37.04±5.91	22.0	56
SGPT (U/L)	44.25±24.81	7.0	222
SGOT (U/L)	45.03±22.98	4.2	166
Serum Albumin (gm/dl)	3.28±0.46	2.20	4.34

Hb: Hemoglobin; **WBC**: White Blood Cells; **HCT**: Hematocrit; **SGPT**: Serum Glutamic Pyruvic Transaminase; **SGOT:** Serum Glutamic Oxalo-Acetic Transaminase

Table 5 displays the laboratory parameters which showed mean Hb%, WBC, Platelet count, HCT, SGPT and SGOT values were within normal range.

Table 6: Frequency of biochemical and hematological parameters of dengue fever (n=250)

Variable	Frequency	Percentage
Hb level		
● Normal	187	74.8
● Decreased	63	25.2
Platelet level		
● <50000/cumm	21	8.4
● 50000-100000/cumm	37	14.8
● >100000/cumm	192	76.8
HCT level		
● Normal	120	48
● Decreased	52	20.8
● Increased	78	31.2
SGPT level		
● <56U/L	178	71.2
● >56U/L	72	28.2
SGOT		
● <45U/L	157	62.8
● >45U/L	93	37.2

Hb: Hemoglobin; **HCT**: Hematocrit; **SGPT**: Serum Glutamic Pyruvic Transaminase; **SGOT**: Serum Glutamic Oxalo-Acetic Transaminase.

According to Table 6, platelet count of 14.8 respondents had 50000-100000/cumm. Also, 25.2% respondents had decreased Hb% 31.2% had increased HCT level. Also, 28.2% had SGPT more than 56U/L and 37.2% had SGOT more than 45U/L.
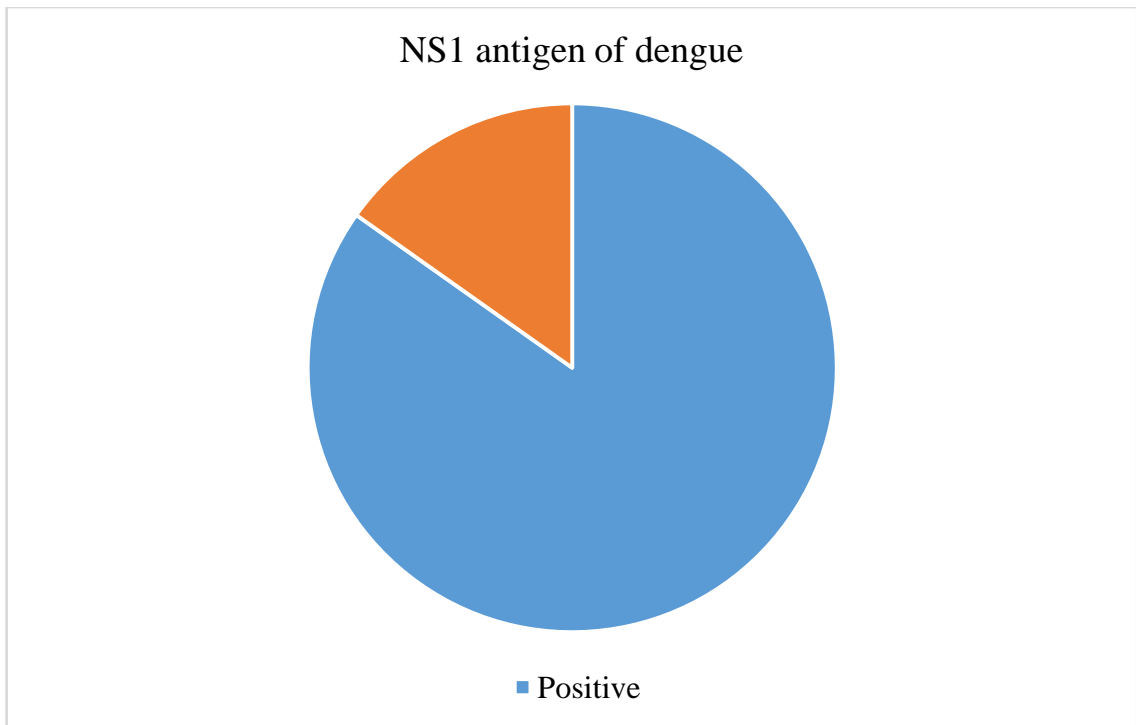
Figure 2 : Frequency of NS1Ag among respondents (n = 250)
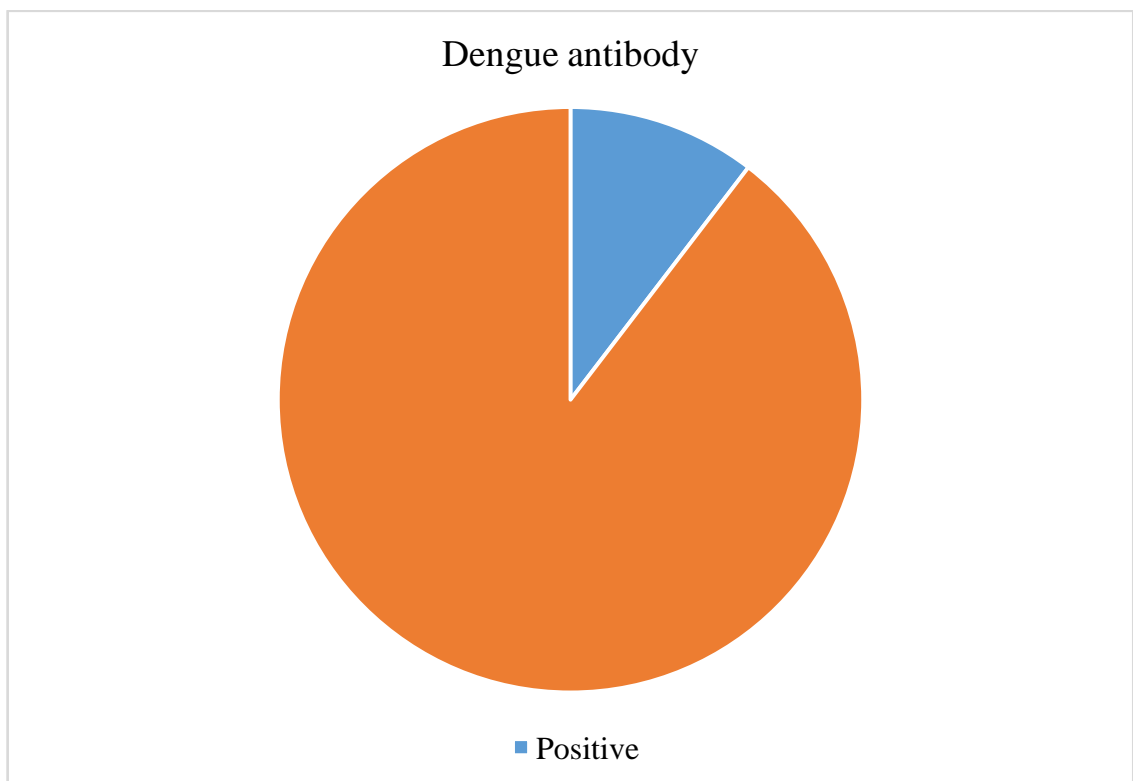NS1Ag was found positive among 84.8% of respondents as illustrated by Figure 2.

Figure 3 : Frequency of dengue antibody among respondents (n=250)
Figure 3 shows only 10.4% respondents had dengue antibody.

Clinicopathological profile of dengue fever among children

Table 7 : Pattern of dengue fever (n=250)

Variable	Frequency	Percentage
Severe dengue fever	68	27.2
Non-severe dengue fever	182	72.8
Dengue with warning sign	123	49.2
Undifferentiated dengue	59	23.6

Table 7 reported 68 out of 250 respondents had severe dengue fever. Among rest 123 respondents had dengue with warning sign and 59 respondents had undifferentiated dengue, which were categorized as non-severe dengue fever.

Table 8 : Association of complications of dengue fever with severity of disease (n=250)

Complications of dengue fever	Non-severe dengue n (%)	Severe dengue n (%)	p value
Hepatomegaly	7(3.8)	10(14.7)	0.002
Splenomegaly	1(0.5)	2(2.9)	0.122
Ascites	23(12.6)	20(29.4)	0.002
Abnormal respiratory system	35(19.2)	36(52.9)	<0.001
Pleural effusion	20(11)	19(27.9)	0.001
Edematous gallbladder	11(6)	12(17.6)	0.005

*Chi-square test was done. Values were expressed as frequency with percentage in parenthesis over column.

Hepatomegaly was significantly more severe dengue (14.7% and 3.8%) than non-severe dengue fever. Also, ascites, respiratory distress, pleural effusion and edematous gallbladder were significantly more in severe dengue respondents (Table 8).

Table 9 : Association of biochemical and hematological parameters of dengue fever with severity (n=250)

Variable	Non-severe dengue n (%)	Severe dengue n (%)	p value
Hb level			<0.001
Normal	154(84.6)	33(48.5)	
Decreased	28(15.4)	35(51.5)	
Platelet level			0.007
<50000/cumm	10(5.5)	11(16.2)	
>50000/cumm	172(94.5)	57(83.8)	
HCT level			<0.001
Normal	106(58.2)	14(20.6)	
Decreased	27(14.8)	25(36.8)	
Increased	49(26.9)	29(42.6)	
SGPT level			<0.001
<56U/L	147(80.8)	31(45.6)	
>56U/L	35(19.2)	37(54.4)	
SGOT			0.001
<45U/L	126(69.2)	31(45.6)	
>45U/L	56(30.8)	37(54.4)	
NS1Ag			0.793
Positive	155(85.2)	57(83.8)	
Negative	27(14.8)	11(16.2)	
Dengue antibody			0.369
Positive	17(9.3)	9(13.2)	
Negative	165(90.7)	59(86.8)	

*Chi-square test was done. Values were expressed as frequency with percentage in parenthesis over column. **Hb**: Hemoglobin; **HCT**: Hematocrit; **SGPT**: Serum Glutamic Pyruvic Transaminase; **SGOT**: Serum Glutamic Oxalo-Acetic Transaminase

Decreased Hb% was significantly higher in severe dengue fever than in non-severe dengue. Also, increased HCT level was higher in severe dengue fever compared to non-severe dengue fever. Though, 16.2% respondents with severe dengue fever had <50000/cumm platelet count and 5.5% respondents with non-severe dengue fever had <50000/cumm. Again, SGPT >56U/L and SGOT >45U/L was more in severe dengue fever patients (Table 9).

DISCUSSION

Dengue infections may be asymptomatic or can result in a wide spectrum of disease severity ranging from an influenza-like illness (dengue fever) to the life-threatening Dengue hemorrhagic fever (DHF)/Dengue shock syndrome (DSS) as observed by Islam et al. [5]. Classic dengue is more commonly seen among older children, adolescents, and adults and these are less likely to be asymptomatic[6].

In fact, children account for 90% of all dengue infections, and their risk of death during a secondary illness is roughly 15 times that of adults as reported by Islam et al.[6] and Sarkar et al.[7]

According to this study, the mean age of the respondents was 7.12 years though majority of the children were under 5 (42%), indicating that dengue affects a relatively young population and emphasizing the vulnerability of this age group to dengue fever. The gender distribution showed a slight predominance of males (54.8%), and a significant proportion of respondents resided in urban areas (82%). Swapna Reddy et al.[8] showed most commonly affected age group is 6-10 years of age in 47.9% of the cases in their study. Children ranged from age 1 month to 18 years with a mean of 5.6±4 years was found by Sarkar et al.[7] which was quite similar to our study.

The monthly family income was more than Taka 30000 (48.4%) among the parents of the children in this study. In 2022, Dhaka city and Chittagong were hit the hardest (incidence: 63.07% vs. 14.42%; morality: 63.34% vs. 24.16%), showing the relevance of population density in spreading of this fatal disease, which indicate most urban areas of Bangladesh were at risk for dengue outbreak as found in the study of Bhowmik et al.[9].

Clinical manifestations of the studied children had found that all respondents had fever, though majority of them had low grade fever (67.2%) and 32.8% had high grade fever in this study. Additionally common abdominal symptoms such as vomiting (52.4%), oral thrush (42.8%), abdominal pain (34%), lack of appetite (14%) and loose stool (13.6%) were found in this study. Khan et al.[10] revealed gastrointestinal symptoms were the most common associated feature of dengue infection, including mostly vomiting (80.4%), decreased appetite (79.5%), constipation (72.7%), and abdominal pain (64.9%).

Other severe clinical manifestations in the form of fever, pain abdomen, thrombocytopenia which correlated well with dengue serology were also found by Abhishek et al.[11]. These findings align with the typical clinical presentation of dengue fever, but the diversity of symptoms underscores the importance of considering dengue in a broad differential diagnosis.

According to chest x-ray findings of this study, respiratory distress (28.8%) was commonly found including ascites (17.6%), and pleural effusion (15.6%). However, edematous gallbladder (9.2%), hepatomegaly (6.8%) and splenomegaly (1.2%) were found in ultrasonography report of this study. Thickened and edematous gall bladder wall in 68.8%, unilateral pleural effusion 40.4%, bilateral pleural effusion 58.2 %, mild to moderate ascites 65.3%, splenomegaly 13.6% and, hepatomegaly 34.3 % was noted by Nahar at al.[12].

Also similar study showed pleural effusion was more common than ascites; (25.84%) and (12.35%) respectively as observed by Shultana at al.[13]. Hepatomegaly, ascites, respiratory distress, pleural effusion, and edematous gallbladder were significantly more prevalent in severe dengue cases, suggesting that these clinical parameters could serve as indicators of disease severity.

Laboratory results of this study revealed abnormalities in platelet count, hemoglobin levels, hematocrit levels, and liver enzymes. According to this study 8.4% respondents had less than 50000/cumm and 14.8% respondents had 50000-100000/cumm of platelet count. Also, 25.2% respondents had decreased Hb%, 20.8% had decreased HCT level and 31.2% had increased HCT level. Also, 28.2% had SGPT more than 56U/L and 37.2% had SGOT more than 45U/L. Kadadavar et al.[14] revealed hematological findings like raised hematocrit, platelet count and atypical lymphocytes were seen in majority of the dengue cases. A considerable percentage of respondents had thrombocytopenia, anemia, and elevated hematocrit levels. These hematological abnormalities are consistent with dengue fever and may contribute to the overall assessment of disease severity.

The presence of NS1Ag in a high percentage of respondents confirms the acute phase of dengue infection, while the relatively low prevalence of dengue antibodies suggests a population with limited prior exposure to the virus. In this study, NS1Ag was found positive among 84.8% of respondents. While, only 10.4% respondents had dengue antibody present in this study. Out of 198 samples of clinically suspected dengue cases of the study by Swapna Reddy et al.[8], 192 were found positive for Dengue NS1 antigen, 145 were found to be positive by IgG and 139 cases were positive for IgM. Hossain et al.[15] showed presence of NS1 Ag in 65 dengue cases and IgM and IgG for 32 dengue cases were positive.

Furthermore, pattern of dengue fever severity showed 68 out of 250 respondents had severe dengue fever. Among rest 123 respondents had dengue with warning sign and 59 respondents had undifferentiated dengue, which were categorized as non-severe dengue fever in this study. According to severity, about 20% fell under undifferentiated dengue fever, 51% with warning sign, and 29% suffered from severe dengue in the research done by Khan et al.[10]. Another study of Mishra et al.[16] suggested 13.4% had severe dengue fever and 54% had dengue fever with warning sign.

Hepatomegaly was significantly more in severe dengue (14.7%) than in non-severe dengue fever (3.8%). Also, ascites, respiratory distress, pleural effusion and edematous gallbladder were also significantly more in severe dengue respondents in this study. Mishra et al. showed the correlation between hepatomegaly and elevated SGOT was significant (p value 0.0346)[16]. Moreover, hepatomegaly, ascites, respiratory distress, pleural effusion, and edematous gallbladder were significantly more prevalent in severe dengue cases, suggesting that these clinical parameters could serve as indicators of disease severity following this study.

Also, decreased Hb% was significantly higher in severe dengue fever than non-severe dengue. Increased HCT level was higher in severe dengue fever compared to non-severe dengue fever. Though, 16.2% respondents with severe dengue fever had <50000/cumm platelet count and 5.5% respondents with non-severe dengue fever had <50000/cumm.

In the study of Islam et al. thrombocytopenia was present in nearly half of the cases of dengue fever patients[5]. Again, following this study, SGPT >56U/L and SGOT >45U/L was more in severe dengue fever patients. Frequent laboratory abnormalities in study by Khan et al.[10] were thrombocytopenia (87.2%), leucopenia (40.4%), and increased hematocrit (13.4%) and a decreased platelet count (<50,000/mm3) with increased hematocrit (> 20%) (AOR 4.94, 95%CI 1.48–17.31, p = 0.01) were significant predictors of severity of dengue fever.

LIMITATIONS

- The study had a relatively small final sample size due to restricted data collection and insufficient data curation.
- The study adopted a non-random convenience sampling, due to the fast changing nature of the outbreak.
- The clinical classification of dengue was applied to stratify severity, which may have resulted in misclassification bias due to the subjective nature of the assessment.

CONCLUSION

The findings of this study highlighted the diversity of symptoms associated with dengue infection and the potential severity of the disease. All these above information provided valuable insights into the demographic characteristics, clinical manifestations, and laboratory findings of a cohort of individuals diagnosed with dengue fever. These results correspond with the findings of previous studies with slight variations. However, further multicenter study with longer follow up is recommended.

CONFLICT OF INTEREST

There is no conflict of interest.

RECOMMENDATION

This study observed the clinical and bio-chemical profile of children with dengue fever in a single center and within small sample size. Further multicenter and longitudinal study is recommended to assess major complications and long term effect of dengue fever among children.

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