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Original Research Article

Clinical and Laboratory Profile in Children with Dengue Viral Infection: A Single Centre Experience

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Abstract

Introduction: Dengue is a major health problem affecting Bangladesh. The number of cases has increased over the last few years with a large number of populations being children. However data regarding dengue among children is limited. ***Aim of the Study:*** Aim of the study was to highlight the most common clinical features and hematological and biochemical findings of patients with dengue fever. ***Methods:*** This hospital-based observational study was conducted at the Department of Pediatrics of Dhaka Shishu Hospital, Dhaka, Bangladesh. The study was carried out from 15th May to 14th Octobar 2022 with 220 patients. ***Result:*** Total 220 children were enrolled in the study. There was a slight male predominance where male constituted 125 (56.81%) of the study group, while female was 95 (43.19%). That gave a male to female ratio of 1.18:1. Out of 44 cases of raised prothrombin time dengue fever consists of 14 (31.82%), 28 (63.64%) cases of dengue Fever with warning and 2 (4.55%) of severe dengue. In our study 26 (21.7%) cases had complication that was more common in age group of less than of 4 years (31.8%). In our study, complication of dengue was more common in dengue with warning sign (35.6%). In our study 44 (18.63%) cases have complication that is more common in age group of less than of (5-8) years. ***Conclusion:*** Hepatic involvement is more common in severe dengue associated with significant rise of liver enzymes. Hepatomegaly is the most important clinical sign but alteration of liver profile can occur with or without hepatomegaly.

Keywords: Dengue, Liver profile, Hepatomegaly.

INTRODUCTION

Dengue is a mosquito-borne arboviral disease and a significant global public health threat prevalent in tropical and subtropical regions, primarily urban and semi-urban areas [1]. The WHO estimates that more than 2.5 billion individuals live at risk of dengue transmission in more than 100 countries, and approximately 50-100 million individuals have been infected with dengue annually [2]. Five hundred thousand severe dengue cases are diagnosed yearly, resulting in 24,000 deaths per year [3-6]. Dengue is endemic in the WHO regions of Africa, the Americas, the Eastern Mediterranean, South-East Asia, the Western Pacific regions, and the Caribbean [7]. In recent decades, the global incidence of dengue virus (DENV) infection has increased with increasing geographic expansion to new countries [8]. According to data from the National Guideline for Clinical Management of Dengue Syndrome, Government of People's Republic of Bangladesh, prior to 1970, only nine countries had experienced severe dengue epidemics, and today the disease is endemic ire than 100 countries around the world [9]. In Bangladesh, the first outbreak was in mid-2000, with the total number of reported cases being more than 5000. The case-fatality rate (CFR) was 1.7%, with 93 reported deaths, with the percentage of death being higher than in recent years [9]. According to WHO, the worst outbreak occurred in 2002, with 6,232 cases and 58 deaths [9]. From 2003 to 2015, there was a downward trend of dengue cases in this country, but in the last 3 to 4 years, the number of dengue cases has again started increasing at an alarming rate. In 2019 the total number of reported dengue cases was 101,354, and the case fatality rate was 0.16% [10].

Over the last 10-15 years, dengue fever (DF) and dengue hemorrhagic fever (DHF) has become the leading causes of hospitalization and deaths among children and adults in South-East Asian regions. The leading contributing factors for widespread and increasing dengue incidences are rapid unplanned urbanization and population migration to urban areas, poor sanitation facilities contributing to fertile breeding areas for mosquitoes, lack of vector control, and climatic changes [11]. As mosquitoes are widely distributed in Africa and can serve as vectors of the dengue virus, combined with rapid population growth, unplanned urbanization, and increased international travel, they could increase the epidemic risk in Asian countries. Specific treatment for dengue is not available, but early detection and fluid replacement therapy and the use of analgesics and antipyretics with good nursing care ensure a marked reduction of the mortality rates from 20% to less than 1% due to severe cases [12]. In clinical practice, as it is known, the patient's diagnosis and management are based on clinical manifestations and abnormal laboratory findings [13]. Initial DENV infection may be asymptomatic or result in a nonspecific febrile illness typically present with the sudden onset of fever, severe headache, bone, joint and muscular pains, mild bleeding manifestation, weakness, myalgia, and rash [14, 15]. All these clinical presentations are similar to many other febrile diseases prevalent in the country, such as malaria, Kala-azar, and typhoid fever which pose a diagnostic challenge of dengue [16]. Dengue is caused by infection with any of the four serotypes of DENV, an arbovirus single-stranded RNA virus of the genus Flavivirus [17]. Infection with one dengue serotype provides lifelong homotypic immunity to that particular serotype. Different serotypes can be circulated during an epidemic; thus, a person can eventually be infected as many as four times, once with each serotype [18]. It is well documented that subsequent infection with different DENV serotypes increases the risk of developing severe dengue [19, 20]. Infection with dengue can be diagnosed by using clinical presentations and laboratory tests. Of the laboratory tests, nonspecific tests; like hematological parameters, liver function tests, and serum protein concentration, and specific tests; such as viral antigen test, genomic sequence, and serology for antibody detection, are used [21, 22]. Therefore, this study aimed to highlight the most common clinical features and hematological and biochemical findings of dengue cases.

METHODOLOGY & MATERIALS

This hospital-based observational study was conducted at the Department of Pediatrics of Dhaka Shishu Hospital, Dhaka, Bangladesh. The study was carried out from 15th May to 14th Octobar 2022 with 220 patients. For each patient, basic demographics (name, age, sex, address) were collected. Presenting complaints (duration of fever, myalgia, headache, abdominal pain, vomiting, bleeding manifestations, rash, and petechiae) and examination findings (vitals, Hess test, pallor, organomegaly, urine output, signs of fluid retention, circulatory failure) were documented. A detailed history of clinical features, including the symptoms of dengue fever, was recorded on pre-designed proforma. Investigations like CBC, dengue NS1 antigen, dengue IgM and dengue IgG and serum bilirubin, SGPT, SGOT, ALP, prothrombin time, serum protein, serum albumin, USG abdomen were done as per the standard diagnostic workup followed in our hospital.

Inclusion Criteria

- The study included children up to 18 years of age presenting with IgM-positive and/or IgG-positive and/or dengue NS1 antigen-positive dengue fever.

Exclusion Criteria

- Patients with dengue-like illness who did not have supporting lab evidence, children with pre-existing liver diseases and parents who refused to participate were excluded from the study.

Serial laboratory investigations (hemoglobin, total leukocyte count, hematocrit and platelet count) Moreover, investigations like Serum glutamic pyruvic transaminase (SGPT), serum glutamic oxalic acid (SGOT), Prothrombin Time and serum albumin were recorded. Radiological investigations like ultrasound abdomen and chest X-ray were taken into consideration if available. Details of co-infections/alternate diagnoses considered at admission/discharge were also recorded. All data were presented in a suitable table or graph according to their affinity. A description of each table and graph was given to understand them clearly. All statistical analysis was performed using the statistical package for the social science (SPSS) program and Windows. Continuous parameters were expressed as mean ±SD and categorical parameters as frequency and percentage. Student's t-test made comparisons between groups (continuous parameters). Categorical parameters compared by Chi-Square test. The significance of the results, as determined by a value of $P<0.05$, was considered statistically significant.

RESULT

Total 220 children were enrolled in the study. There was a slight male predominance where male constituted 125 (56.81%) of the study group, while female was 95 (43.19%). That gave a male to female ratio of 1.18:1. The most common age group of presentation of dengue infection in children was 8-13 years. Mean age of children affected with dengue viral infection was 8.5 years and the gender distribution was not statistically significant. Clinically, 84(38.18%) patients had dengue fever 134 (60.91%) had dengue

with warning sign, and only2 (0.91%) had severe dengue. Dengue fever was the commonest presentation in 5-8 years group (64 patient-29.09%) while dengue with warning signs was the commonest presentation in 9-13-year-old (77 patients-35.00%). Less cases of severe dengue are probably because of public awareness (Table 1). All the children in the study group presented with vomiting (100%) and fever (100%) and abdominal pain was presented in 160 (72.73%). In our study, out of 220 patients, 49 (22.27%) cases had icterus. The most commonly affected age group is 9-13 years (35.00%). In our study 2 patient of severe dengue, had jaundice and out of 134 cases of dengue with warning signs, 27 patients (20.15%) had jaundice and 84 cases of dengue fever 20 patients (23.81%) had jaundice which is statistically insignificant (p=0.16) (Table 3). In our study, out of 220 patients 37(27.61%) cases had hepatomegaly. Out of 37 patients with hepatomegaly, the most commonly affected age group was 9-13 years (Table 4). In our study out of 220 cases 183 (83.18%) had thrombocytopenia. Out of 183 patients with thrombocytopenia, in 42 cases there was borderline thrombocytopenia and 54 had moderate thrombocytopenia and 4 patients had severe thrombocytopenia (Table 5). The 94 (42.72%) cases had hyperbilirubinemia (Table 6). The most common age group affected is 9-13 years i.e., 42.3%. However, this was less than clinical jaundice. Also, it did not statistically correlate with the occurrence of complications. Out of 142 cases with raised SGOT, 104 (73.24%) cases had dengue NS 1 antigen positive, 36 (25.35%) cases had dengue IgM positive and 2(1.41%) IgG positive. Out of 74 cases with raised SGPT, 55(74.32%) cases had dengue NS 1 antigen positive, 18 (24.32%) cases had dengue IgM positive and 1(1.35%) IgG positive. There was overlap of patients who had both SGOT and SGPT elevated. Out of 2 cases with raised ALP 2 (50%) was NS1 antigen positive and 2 (50%) was IgM positive. This is suggestive that serologically confirmed with NS1 antigen positive cases have more abnormal liver profile (Table 7). In our study 44 (20.00%) cases of dengue viral infection had elevated prothrombin time. The raised prothrombin time was most commonly seen in age group 4-8 years (Table 8). Out of 44 cases of raised prothrombin time dengue fever consists of 14 (31.82%), 28 (63.64%) cases of dengue Fever with warning and 2 (4.55%) of severe dengue. In our study 26 (21.7%) cases had complication that was more common in age group of less than of 4 years (31.8%). In our study, complication of dengue was more common in dengue with warning sign (35.6%) (Table 9). In our study 44 (18.63%) cases have complication that is more common in age group of less than of (5-8) years.

Table 1: Age distribution of the study population (N=220)

Age group (Years)	Frequency	Percentage
1-4	40	18.18
5-8	64	29.09
9-13	77	35.00
14-17	39	17.73
Total	**220**	**100.00**

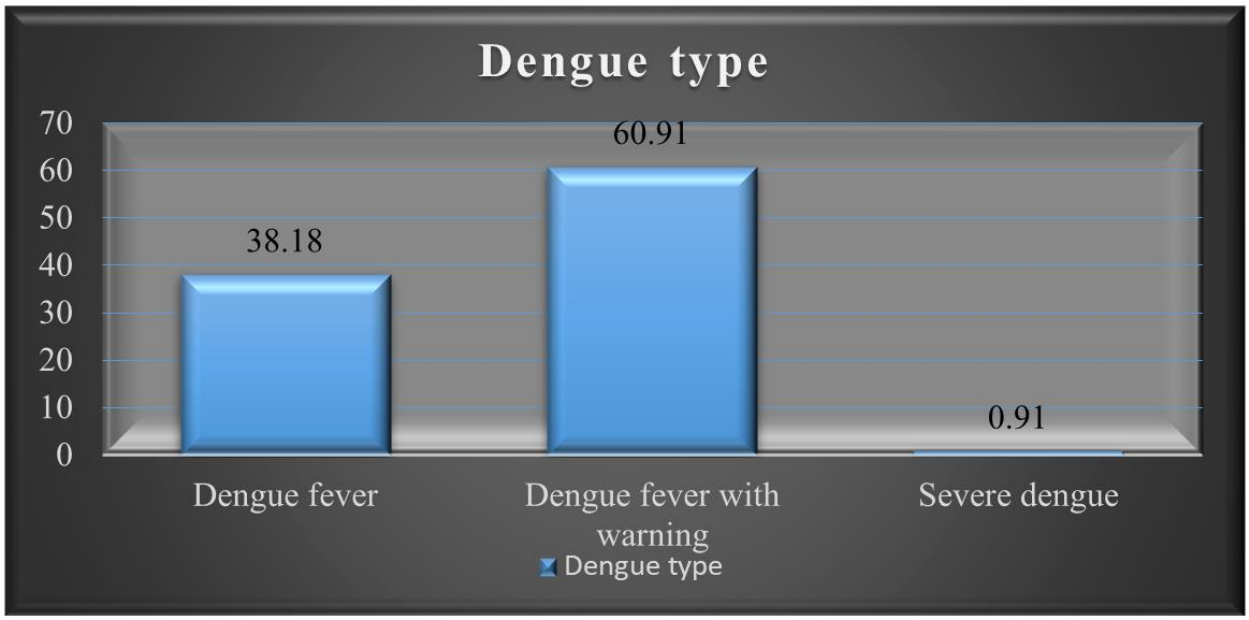

Figure 1: Type of dengue fever in study population

Table 2: Clinical features of patients with dengue

Clinical features	Frequency	Percentage
Fever	220	100.00
Vomiting	220	100.00
Abdominal pain	160	72.73
Jaundice	50	22.73
Pallor	42	19.09
Hepatomegaly	37	16.82
Thrombocytopenia	183	83.18
Hyperbilirubinemia	95	43.18
Elevated SGPT	104	47.27
Raised prothrombin time	38	17.27
Hypoproteinemia	42	19.09
Hypoalbumenemia	77	35.00

Table 3: Correlation between type of dengue and icterus

Icterus	Dengue fever (N=84)		Dengue fever with a warning (N=134)		Severe dengue (N=2)		Total
	N	%	N	%	N	%	
No	64	76.19	107	79.85	0	0.00	171
Yes	20	23.81	27	20.15	2	100.00	49
Total	**84**		**134**		**2**		**220**

Table 4: Correlation between type of dengue and hepatomegaly

Hepatomegaly	Dengue fever (N=84)		Dengue fever with a warning (N=134)		Severe dengue (N=2)		Total
	N	%	N	%	N	%	
Present	0	0	37	27.61	0	0	37
Absent	84	100	97	72.38	2	100	183
Total	**84**		**134**		**2**		**220**

Table 5: Correlation between complications and Thrombocytopenia

Dengue type	Normal (N=37)		Thrombocytopenia (N=183)		Total
	N	%	N	%	
Dengue fever (N=84)	28	33.33	56	66.67	84
Dengue fever with a warning (N=134)	9	6.72	125	93.28	134
Severe dengue (N=2)	0	0.00	2	100.00	2
Total	**37**		**183**		**220**

Table 6: Correlation between type of dengue fever and S.bilirubin level

S. bilirubin	Complication				Total
	No		Yes		
	N	%	N	%	
Hyper bilirubinemia	33	34.74	62	65.26	95
Normal bilirubinemia	15	12.00	110	88.00	125
Total	**26**		**94**		**220**

Table 7: Correlation between dengue type and liver enzyme

Liver enzyme	Dengue NS1 antigen +ve		IGM+ve		IGG+ve		Total
	N	%	N	%	N	%	
Elevated SGOT	104	73.24	36	25.35	2	1.41	142
Elevated SGPT	55	74.32	18	24.32	1	1.35	74
Elevated ALP	2	50.00	2	50.00	0	0.00	4
Total	**123**		**43**		**2**		**220**

Table 8: Correlation between dengue type and prothrombin time

Dengue type	Raised Prothombin Time		Normal Prothombin Time		Total
	N	%	N	%	
Dengue fever (N=84)	14	31.82	70	39.77	84
Dengue fever with a warning (N=134)	28	63.64	106	60.23	134
Severe dengue (N=2)	2	4.55	0	0.00	2
Total	**44**		**176**		**220**

Table 9: Correlation between age and complications of dengue

Age	No		Yes		Total
	N	%	N	%	
(1-4)	27	16.07	14	26.92	41
(5-8)	57	33.93	6	11.54	63
(9-13)	55	32.74	22	42.31	77
(14-17)	29	17.26	10	19.23	39
Total	**168**	**100.00**	**52**	**100.00**	**220**

DISCUSSION

Abdominal pain was most commonly seen in the age group of 8-12 years. In a study in Andhra Pradesh conducted on 100 children with dengue viral infection, abdominal pain was seen in 50% of cases [8]. In a study by WHO in Delhi, abdominal pain was seen in 40-50% of cases [23]. Dengue fever was the commonest presentation in 5-8 years group (64 patient-29.09%) while dengue with warning signs was the commonest presentation in 9-13-year-old (77 patients-35.00%). Severe dengue is most commonly seen in children less than four years, which may cause internal bleeding. Therefore, these patients have an increased incidence of pallor (Table 2). Patients with jaundice have a poor prognosis and are at a greater risk of developing severe dengue. In other studies, severe dengue cases were high because of less public awareness and delayed intervention. In a study conducted at Nagpur, out of 50 cases of severe dengue, 24% had jaundice [24]. In a study done in Indonesia, hepatomegaly was seen in 47.2% of cases [25]. In our study, out of 20 cases of hepatomegaly, all 20 patients had dengue with warning signs which is statistically significant (p=0.01). Patients presenting with hepatomegaly indicate increased severity of dengue viral infection. Out of 46 cases of dengue fever, 31(67%) had thrombocytopenia, and amongst cases with dengue with warning signs, 68 (93%) had thrombocytopenia. There was only one case with severe dengue and thrombocytopenia. Therefore, decreased platelet count predicts the severity of dengue viral infection. In the cell count analysis, most cases are associated with leucopenia, which is most common in the age group of 8-12 years. In a study in New Delhi, leucopenia was seen in 5.8% of cases, and leucocytosis was seen in 26.5% of cases (Table 5) [26]. In a study by Itha *et al.*, hyperbilirubinemia was seen in 30% of the cases [27]. In another study, hyperbilirubinemia was seen in 13.4% of cases of 52 cases of hyperbilirubinemia, 34 (65.3%) had complications, and 18 (34.7%) had no complications. this suggests that hyperbilirubinemia predicts the severity of dengue viral infection [28]. Out of 52 cases of hyperbilirubinemia, dengue fever consists of 3 (5.8%), 48 (92.3%) of dengue with a warning sign, and 1 (1.9%) of severe dengue. This also suggests that hyperbilirubinemia predicts the severity of dengue viral infection. In a study done at Assam, 1 out of 3 patients with severe dengue, 33.3% had hyperbilirubinemia [29]. In a study in Nagpur, out of 50 cases of severe dengue, 24% had hyperbilirubinemia [10]. In a study in Karnataka, India, 80.7% of cases had dengue NS1 antigen positive, and 26.3% had dengue IgM positive (Table 7) [30]. In a study conducted in Bangalore, Karnataka, India, 34% of patients had raised SGPT levels, 36% had raised SGOT, and 42% had raised ALP [31]. In a similar study which included 110 children between 2 months to 14 years, it was observed that 69.4% of the patients had raised SGPT levels, and 88% had raised SGOT levels [27, 32]. In our study, out of 120 children, 102(85%) had raised SGOT levels, and two patients (1.7%) had elevated ALP levels. The elevated level of SGOT is most commonly found in the age group of 8-12 years. The previous study shows that the most affected age group was 1-6 [31]. A study done at Nagpur suggests that among patients with elevated prothrombin time, dengue fever consists of (1.6%), (29.92%) cases of dengue fever with a warning, and (46%) of severe dengue [30]. Another study in Chennai shows that children under five years were most commonly affected by severe dengue (70%), with infants forming the largest group [33]. In our study, hypo-proteinemia was seen in 19.2% of 120 patients. The most common age group affected is 0-4 years (27.3%). In our study, hypo-proteinemia in severe dengue is 100%, dengue with warning signs is 26%, and dengue fever is 6.5%, which suggests that liver function is more abnormal in severe dengue. In our study, 35% of the patients had hypoalbuminemia. The most commonly affected age group is 12-16 years. In our study, hypoalbuminemia in severe dengue is 100%, 39.7% in dengue with warning signs, and 26.1% in patients with dengue fever, suggestive that liver function is more abnormal in severe dengue. The average hospital stay was 4.8 days (Maximum 11 days).

Patients with dengue fever with warning signs and severe dengue required a longer hospital stay. Out of 52 cases of hyper-bilirubinemia, dengue fever consists of 3 (5.8%), 48 (92.3%) of dengue with a warning sign, and 1 (1.9%) of severe dengue. This also suggests that hyperbilirubinemia predicts the severity of dengue viral infection. In our study, 91 (81.67%) cases had dengue NS1 antigen positive. 85.7% of cases with NS1 antigen positive fall within the 12-16 age group. This suggests that most patients presented in the first week of illness. In our study, out of 102 cases of elevated SGOT, 38 (37.2%) had dengue fever, 63 (61.7%) cases had dengue with a warning sign, and one (0.9%) had severe dengue. In our study, out of 53 cases of elevated SGPT, 10 (18.9%) had dengue fever, 42 (79.2%) cases had dengue with a warning sign, and one (1.9%) severe dengue. In our study, out of 2 cases of elevated ALP, 1 (50%) had dengue fever, 1 (50%) had dengue with a warning sign, and none had severe dengue.

Limitations of the Study

Every hospital-based study has some limitations and the present study undertaken is no exception to this fact. The limitations of the present study are mentioned. Therefore, the results of the present study may not be representative of the whole of the country or the world at large. The number of patients included in the present study was less in comparison to other studies. Because the trial was short, it was difficult to remark on complications and mortality.

CONCLUSION AND RECOMMENDATIONS

Hepatic involvement is more common in severe dengue. A significant rise in liver enzymes helps to recognize a severe dengue infection. Hepatomegaly is the most important clinical sign, but alteration of liver profile can occur with or without hepatomegaly. Further studies with large sample size needed to explore more about the presentations of Dengue fever.

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