Original Article

Clinical Presentation with Predictors of Severity of Dengue Fever in Children of 2019, Endemic in Bangladesh

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Abstract

Back ground: *Dengue fever is a serious public health problem with a wide range of clinical manifestations. In 2019, the clinical presentation of dengue infection was novel in relation to the conventional features of the previous years and also in degree of severity. So the study was done to see the varied clinical presentation, predictors of severity and outcome in pediatric population in 2019 endemic.*

Methods*: It was a cross sectional, descriptive study conducted among 100 cases of serologically positive dengue patients from department of Paediatrics of Shaheed Suhrawardy Medical College Hospital, Dhaka from July to October, 2019.The data were collected by preformed semi-structured questionnaires and analyzed using SPSS version 16.0.*

Results: *The mean age of the patients was 7.4 ± 3.4 years with equal male and female ratio. Children between 5-12 years were most (72%) commonly affected. Mean duration of fever was 4.5 ± 1.8 days and fever was present in 63% cases on presentation. Features of shock were present in 61% of patients who were designated as severe dengue. Most of the patients presented with abdominal pain (77%) followed by vomiting (70%), headache (35%), myalgia(32%) and retro-orbital pain(30%). Among the important clinical findings, tender hepatomegaly was present in 77% cases followed by ascites in 35% and pleural effusion in 4% cases. Melaena was found to be the most common form of bleeding manifestation. Risk factors for severe dengue were vomiting, abdominal pain, melaena, ascites and low platelet count. Majority of the patients (95%) were discharged, 4% were referred to ICU and only 1% died.*

Conclusion*: Majority of admitted pediatric dengue patients presented with severe Dengue (Dengue Shock Syndrome). Presence of vomiting, abdominal pain, ascites and low platelet count were found to be significant in predicting severity of dengue.*

Key Words:
Dengue; Severe dengue; Predictor.

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Introduction:

Dengue fever is an infectious mosquito-borne disease caused by dengue virus that occasionally develops into a potentially lethal complication called severe dengue which is a leading cause of severe illness and death among children.[1,2]

In Bangladesh, the first documented case of dengue like fever appeared in 1964 popularly known as "Dacca fever" which was later serologically proven as dengue fever.[3] After 36 years, this fever hit again Bangladesh in the year, 2000, claimed 93 deaths. After 3 years, the deaths gradually declined to almost zero. However, it struck again in 2018, killed 26 and affected 10,148 people.[4,5]

In 2019, Bangladesh experienced a nation-wise outbreak of dengue that began primarily in April 2019 and was on going up to October, 2019. According to Directorate General of Health Services (DGHS), majority of the affected were children and it surpassed all previous records, mostly in the capital city of Dhaka.[1,6,7] According to CDC unit of DGHS from April, 2019 to January, 2020, total 101,354 cases of confirmed dengue were diagnosed and at least 164 patients died from it during that period.[8] Dhaka was the worst-hit city in the country and the districts in Dhaka Division were among the most affected regions.[9]

Dengue Shock Syndrome (DSS) is a dangerous complication from dengue which is often caused by a secondary infection with a different virus serotypes.[4] Dengue patients usually go to the critical phase after 3 to 4 days of onset of fever. During this period, plasma leakage and hemo-concentration are documented and patients may develop hypotension and shock with or without severe organ impairment that may be fatal and life threatening.[10] Sometimes dengue may be manifested unusually with co-infections and co-morbidities which may result in diagnostic difficulty .[11]

Most of the people who died due to dengue fever in 2019, had been suffering from DSS with or without organ impairment. In this year, the clinical manifestations of dengue infection were novel in relation to the conventional features of the previous years. Most of the patients were presented with shock, but there was seldom any external bleeding manifestation specially skin rash, epistaxis or red eyes that were found in previous years. Most common presentation of bleeding was found in the form of melaena. Sometimes there was no history of documented fever, but the patients presented with shock with prior vomiting and abdominal pain. Although children are the main group affected by dengue, little published data are available in Bangladesh. As the exact clinical and laboratory profile are crucial for diagnosis and successful management of pediatric dengue patients. So, we aimed to analyze the variation in clinical spectrum, hematologic profile and outcome of pediatrics dengue patients admitted in pediatric ward of Shaheed Suhrawardy Medical College hospital, from the month of July to September, 2019.

Methods:

This is a hospital based descriptive cross-sectional study carried out among children having dengue infection admitted in Shaheed Suhrawardy Medical College Hospital, Sher-e-Bangla Nagar, Dhaka from 01/07/2019 to 31/10/2019. A total of 100 patients below the age of twelve years selected according to the clinical criteria mentioned in the National Guidelines for Dengue, were enrolled in the study. According to the guideline moderate dengue cases were categorized as dengue fever with warning signs like recurrent vomiting, abdominal pain, generalized weakness, lethargy/restlessness, mild pleural effusion/ascites, hepatomegaly and hematocrit >20% or dengue with co-morbid conditions. Severe dengue cases were defined as dengue fever with significant hemorrhage with or without shock, severe organ involvement or severe metabolic acidosis.

Convenient, purposive sampling was done in our study. Presence of fever or history of fever in last 7 days with or without features of shock with positive serology for dengue were included. Patients with any identified febrile illness more than 14 days and serologically dengue negative cases were excluded from the study. A total 100 serologically positive (NS1 antigen, IgM and IgG antibodies) were finally selected for our study. A written informed consent was taken from parents and a semi-stuctured questionnaire was used to collect data. Demographic variables, clinical and laboratory parameters were recorded. Dengue serology such as Rapid qualitative Immuno- chromatographic test (NS1 antigen detection) was done in patients who presented with fever for 3 days or lesser duration and anti- dengue IgM and IgG were done in those who came with fever for more than 5 days. Base line laboratory parameters such as complete blood count including white blood cell count (WBC), hematocrit (HCT), platelet count were done and repeated until significant clinical improvement appeared. In selected patients, SGPT, S. Creatinine, Chest–X-ray and Ultrasonography of abdomen were done and repeated when needed. The national guideline for Dengue, 2019 were used to classify the cases as mild, moderate and severe Dengue. All patients were treated according to the national guideline and outcome was measured as recovery, referral or death.

Statistical analysis:

The data were collected by preformed semi-structured questionnaires and were entered into Microsoft Excel for preliminary checking and editing. At every step of data collection, processing and analysis, monitoring was done by double checking.

Chi square test was done for qualitative variables and unpaired T test was done for quantitative variables. The results were calculated as mean±SD for quantitative variables and counts/percentages for qualitative variables. A p value <0.05 was considered to be statistically significant. All statistical analysis were performed using SPSS version 16.0.

Results:

Among 100 studied population, the mean age was7.4±3.4 years with equal male and female ratio. Children between 5-12 years were the most (72%) commonly affected population (Table-1). Mean duration of fever was 4.5±1.8 days. On admission, fever was present in 63% cases and 37% had a history of fever in 7 days prior to admission. Duration of fever was 4 days or more in most patients (73%). Most of the patients presented with abdominal pain (77%) followed by vomiting (70%), headache (69%), myalgia (42%) & retro orbital pain (40%). Among the clinical findings tender hepatomegaly was present in 77% cases followed by ascites in 35% and pleural effusion in 4% cases. Melaena (50%) was found to be the most common clinical finding followed by gum bleeding (8%), rash (14%), hematemesis (6%) and epistaxis (4%) (Table –II).

Severe dengue as per WHO classification is those with DHF with significant haemorrhage or DSS with or without organ involvement (61%) were predominant and moderate dengue fever with comorbidities and with warning signs were 39% of studied sample(Table-III).

Table-I

Demographic variables of study population (n-100).

Variables(AGE)	Number(n)	Percentage (%)
Mean age ±SD yrs	7.4±3.4 yrs	
<6 months	2	2.0
6 months -2	6	6.0
>2 yrs-5	20	20.0
>5yrs-12	72	72.0
Sex Male	51	51.0
Female	49	49.0
Male: Female=	1.04:1	

Table-II

Clinical Variables of Dengue patients (n-100).

Symptoms		No of patients	Percentage
Mean duration of fever± SD		4.5±1.8 days	
Fever at presentation	Present	63	63.0
	Absent	37	37.0
Duration of fever	<4 days	27	27.0
	≥4 DAYS	73	73.0
Body pain/ Abdominal Symptoms	Headache	69	69.0
	Retro-orbital pain	40	40.0
	Myalgia	42	42.0
	Arthralgia	27	27.0
	Vomiting	70	70.0
	Abdominal pain	77	77.0
Bleeding manifestation	Epistaxis	4	4.0
	Gum-bleeding	8	8.0
	Melaena	50	50.0
	Rash	14	14.0
	Hematemesis	6	6.0
Features of Shock	Present	58	58.0
	Absent	42	42.0
Features of plasma leakage	Ascites	35	35.0
	Pleural effusion	4	4.0
Enlarged tender liver	Present	77	77.0
	Absent	23	23.0
Expanded Dengue Syndrome	Heart failure	4	4.0
	Encephalopathy	2	2.0
Co-morbidities	Enteric fever	2	2.0
	Pneumonia	1	1.0
	UTI	2	2.0
	Hereditary Hemolytic Anemia	4	4.0

Table-III

Distribution of Dengue patients according to WHO classification (n=100).

Classification		No (n)	Percentage
Moderate Dengue	DF with co-morbid condition	9	9.0
	DF with warning signs	30	30.0
Severe Dengue	DSS with or without Organ involvement	61	61.0

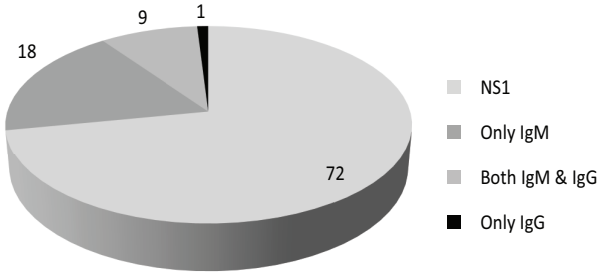

Fig-1: *Distribution of serologically positive dengue patients (n=100).*

The above table shows that age, vomiting, abdominal pain, melaena and ascites were found to be significantly higher in severe dengue than moderate dengue ($p<0.05$). Mean HCT was more in severe dengue than moderate dengue but statistically there is no significant difference ($p=0.07$). Mean TC was higher in moderate dengue than severe dengue but statistically no significant difference ($p=0.28$). Mean PC was higher in moderate than severe dengue with statistically high significant difference ($p<0.001$).

Table IV

Comparison of variables between severe dengue and Moderate dengue.

Variables	Severe dengue (n= 61)		Moderate dengue (n= 39)		p value
	Number	%	Number	%	
Age (>2 yrs – 12 yrs)	60	98.4	30	76.9	***0.001^{s}**
Vomiting	53	86.9	24	61.5	***0.006^{s}**
Abdominal pain	48	78.7	22	56.4	***0.02^{s}**
Melaena	38	62.3	12	30.8	***0.004^{s}**
Ascites	29	47.5	6	15.4	***0.001^{s}**
Hematocrit (HCT)(mean±SD)	34.8±3.9		32.8±6.4		**0.07^{ns}
Leucocyte count(TC)(mean±SD)	6254.5±2983.2		7620.3±9101.7		**0.28^{ns}
Platelet count(PC)(mean±SD)	81162.6±52042.5		143045.2±72462.1		****<0.00^{s}**

*p value reached from Chi Square test for qualitative variables.
**p value reached from unpaired t-test for quantitative variables.
s= Significant ($p<0.05$), ns = Not significant ($p>0.05$)

Table-V

Comparison of hematologic parameters of Dengue patients in 03 days (n=100).

Parameters	Day 01 mean±SD	Day 02 mean±SD	Day 03 mean±SD	p value
Haemoglobin (Hb) in gm/dl	11.6±1.6	11.7±1.5	12.4±8.9	0.71^{ns}
Hematocrti (Hct)	34.1±5.1	34.6±5.2	34.6±4.8	0.72^{ns}
Total leucocyte count(TC)	6792.5±6158.7	7068.7±11821.0	7958.9±8955.3	0.32^{ns}
Platelet count(PC)	105296.8±67654.6	80581.6±56213.4	78269.1±42367.6	**0.001^{s}**

The above table indicates that Hb, HCT and TC were found to be increasing in 03 days but the difference was not statistically significant (p>0.05). On the contrary, PC was found to be decreasing in 03 days with statistically significant difference (p<0.05). Here P value was calculated by ANOVA test.

Table-VI

Duration of Hospital stay of Dengue patients (n=100).

Duration of hospital stay in days	Number (n)	Percentage (%)
Mean duration of fever± SD	5.1±1.6 days	
≤3 days	10	10.0
4-5 days	65	65.0
>5 days	25	25.0

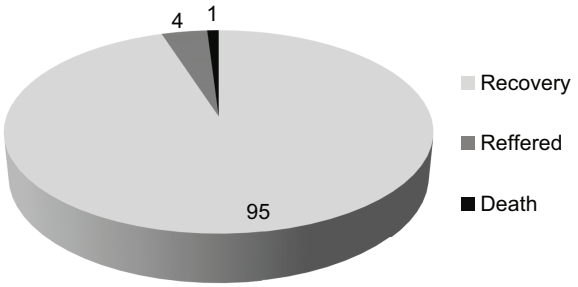

Fig-2: *Outcome pattern of dengue patients (n=100).*

Discussion:

In the present study, majority of patients of who suffered from moderate or severe dengue belong to the age group of 2-12 years that was statistically significant. Similar results were reported by other authors.[11,12,13] Reasons for dengue being common in more than 2 years may be due to more involvement of children in outdoor activities during this age whereas most of the infants are kept covered preventing them from mosquito bite. We found two infants below the age group of 6 months and they had history of maternal seropositive DENV infection.

Our study showed, equal amount of male and female affected by dengue which was found consistent with other studies[12,15] though differs with many studies[11,13] that indicate the similar possibility of both gender for being infected by dengue. This result is also not surprising because the primary vector, Aedes aegypti is active during day time and the pediatric patients including both sexes tend to have similar activities while going to school. Therefore, exposing both genders on a similar risk of being infected by dengue.[12,15]

In our study, majority (63%) of patients presented with fever at presentation and 37% patients had no fever at presentation with a history of fever within 1 week prior to admission. This results differs from other studies done by Sultana et al, Mobarak et al and Alam et al who showed 100% fever on presentation.[13,16,17]DENV infection is divided into three phases: febrile phase (2-7 days), critical or leakage phase(24-48 hrs) and convalescence phase(2-7 days)[10]. Here, 37 % of our patients who were afebrile were probably in leakage phase. Soegijanto et al showed pediatric patients in critical phase of the illness may not present with fever.[18] Mean duration of fever was 4.5 ± 1.8 days which is similar to other studies[15,16]. Abdominal symptoms were prominent in our series. Abdominal pain was the most common (77%) symptom followed by vomiting (70%) and melaena (50%). Bhave et al reported pain in abdomen as second most common clinical feature followed by vomiting[19]. Similarly, Cecilia et al, Hoque et al and Alam et al also showed abdominal pain is the second common symptom followed by other abdominal symptoms.[12,13,17] Among other features, patients presented with headache(69%), retro-orbital pain(40%), myalgia(42%) and arthralgia(27%) which are almost consistent with the studies done by Afroze et al, Alam et al and Mobarak et al.[11,16,17] On the other hand , these findings differ from that of Sultana et al. and Alam et al. where predominant symptoms was headache (85% and 91% consecutively) following fever. [13,17] As our study populations are of pediatric age group, so they might not be able to describe headache and retro-orbital pain clearly.[16]

In the present study, the most common bleeding manifestation was in the form of melaena followed by hematemesis which are not consistent with other studies where Alam et al found melaena in 8% cases and Gurdeep et al in 7.4% cases respectively.[17,20]A recent study also showed that the gastrointestinal bleeding was associated with DSS, although it is not a strong association (OR = 1.84.)[21] According to a meta-analysis, the two kinds of gastrointestinal bleeding that strongly predicted DSS were hematemesis and melaena while the other two kinds of bleeding (gum bleeding and epistaxis) were not significant risk factors[22]. In our series, skin rash was found only in 10 % cases which was mostly convalescent often associated with itching which is nearer to the study done by Gurdeep et al[20] who found petechiae in 18% cases. On the other hand, Alam et al found it in 75.9% cases, Mobarak et al in 55.35% cases and Sultana et al in 48.1% cases.[16, 17]

In our series, thrombocytopenia was found to be significant that was progressive in nature until patient settled. This result was in agreement with other studies with moderate

to severe thrombocytopenia in DHF.[23] Hemoglobin and hematocrit were found to be rising, a change most likely attributed to hemoconcentration consistent with other studies.[24,25] Data observed in this study showed NS1 antigen was found to be positive in 72 % of patients which is a little higher than the studies done by Kassim et al who found NS1 in 32.2%(67/208) cases and combined antigen and antibody test detected 62%(137/208) patients in their study.[26] Studies revealed the detection rate of NS1 antigen is higher in acute primary dengue infection than in acute secondary dengue infection. It's use has been suggested for early diagnosis of dengue infection after the onset of fever.[27,28] Most children stayed up to 4-5 days in 65% cases which is higher than the study done by Khalil et al and they found it was 72 hrs.[29] As we found recurrent shock in some patients so we waited until the patient became settled. All dengue patients in this study received standard care according to WHO guidelines. Mortality was found to be 1% similar to the study that was 1.2%.[29] Higher mortality in dengue is associated with older age and comorbidities which can explain our low mortality, in addition we referred four patients to pediatric intensive care unit due to development of heart failure, acute hepatic failure and dengue encephalopathy.

Conclusion:

In our study, majority of pediatric dengue patients presented with severe dengue (Dengue Shock Syndrome). Among the variables, patient's age, presence of vomiting, abdominal pain, and ascites and low platelet count were found to be significant in predicting severity of dengue. Meticulous management of Dengue shock syndrome according to national guideline reduced the mortality to 1%.

Limitations of the study: 1. The study populations were selected from only one hospital of Dhaka, so the result may not reflect the exact scenario of the country.

2. It was conducted over a short period of time.

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