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GASTROINTESTINAL MANIFESTATIONS OF DENGUE FEVER IN CHILDREN OF BANGLADESH

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ABSTRACT

Background: Dengue is a mosquito borne viral fever and dengue epidemics are becoming more frequent over the time. Gastrointestinal (GI) manifestations usually the common manifestation and mostly missed due to lack of awareness and knowledge. This study is carried out the gastrointestinal manifestation and its correlation with the different types of dengue fever. **Methods:** This is a prospective observational study done on 103 serologically confirmed dengue virus infected children admitted in BSMMU. Children were examined clinically, and laboratory data was collected in respect of GI manifestation till they got discharged and analyzed by SPSS version 25, after approval from departmental review board. **Results:** The study participants were 103 (n=103) consecutive cases of dengue fever, out of which 59 (57%) cases were dengue fever, 27 (26%) were DHF and 17 (17%) were cases of DSS. Mean age was 8.44 ± 4.47 years and of them 58 (56.3%) were males and 45 (43.7) were females. Male to female ratio was 1.3:1. 81 (78.6%) patients were from urban and 22 (21.4%) came from rural areas. GI manifestations were noted in all cases of the study participants. Most common presentation were anorexia 80 (78%) & Vomiting 74 (72%) followed by abdominal pain 60 (58%) & diarrhea 25 (24%). GI bleeding manifesting as hematemesis and melena were found 9 (9%) and 7 (7%) patients. Ascites, Hepatomegaly and acute pancreatitis were found 20 (19%), 24 (23%) and 3 (3%) respectively. Among them GI bleeding (hematemesis & melena) (*p-0.001* & *p-0.000*), Ascites (*p-0.000*), hepatomegaly (*p-0.000*) were found significantly associated with dengue severity. Hypoalbuminemia, hypocalcaemia and electrolyte imbalance was found in 20(19.4%), 30 (29.1%) and 16 (15.5%) cases respectively and all are statistically significant with severe dengue fever (*p-value 0.000, 0.002* & *0.037* respectively). **Conclusion:** Gastrointestinal manifestations are very common in Dengue fever; in our study 100% of the patients had these symptoms. Atypical GI manifestations like hepatitis, acute pancreatitis are quite common than once thought of, are often missed. GI bleeding (hematemesis & melena), Ascites, hepatomegaly, hypoalbuminemia, hypocalcaemia and electrolyte imbalance might be used as predictors of severe dengue fever.

KEYWORDS: Dengue fever; GI manifestation; Hepatomegaly; Liver enzymes; Acute pancreatitis; Children.

INTRODUCTION

Dengue fever is a viral infection caused by the dengue virus (DENV), widespread arthropod born member of the genus Flavivirus is spread by day-biting Aedes mosquitoes, primarily Aedes aegypti and Aedes albopictus, two most important vectors and Aedes aegypti is highly domesticated.[1]

The incidence of dengue has increasing approximately 30-fold over the last 50 yrs and in tropical and subtropical countries about 400 million dengue infections occur in each year.[2,3] In worldwide live in 10 countries of the South-East Asia Region, about 52.0% of the people at risk of acquiring dengue infection.[4] The first reported dengue outbreak occurred in and around Dhaka of Bangladesh in 2000 with 5551 cases and 93 deaths and since then dengue cases has been reported yearly in all major cities of Bangladesh.[1]

According to World Health Organization, 3 categories of dengue infections were distinguishable: (1) classical dengue fever (DF), (2) dengue hemorrhagic fever (DHF) and (3) dengue shock syndrome (DSS). Classical DF are typically a mild flu-like illness, DHF and DSS are potentially fatal, and together are termed 'severe dengue'.[3,5] There are four DENV serotypes (DEN1-DEN4) which may cause dengue infection and mild disease usually occur after a primary infection and a

more severe disease manifestation occur following reinfection with a different DENV serotype.[6] Highest rates of infection occurring among infants and also they are at increased risk of severe infection like dengue shock syndrome due to the limited ability of the hemodynamic system in young children to compensate for capillary leakage.[3,7]

Wide ranges of clinical manifestations present in dengue fever and can range from an asymptomatic or mild febrile illness to a life-threatening hemorrhagic fever, shock, atypical manifestations like hepatic and neurological involvement which could be challenging for clinicians specially in non-endemic areas for diagnosis.[7] Atypical gastrointestinal manifestations like hepatitis, acute pancreatitis, GI bleeding, hepatomegaly, acute parotitis, ascites etc. is increased with rising disease burden due to rapid urbanization, growing population and inappropriate sanitary measures.[8,9,10]

This study aimed to study the spectrum of gastrointestinal symptoms, signs and laboratory parameters in child with dengue virus infection in our settings. There are very few study presents regarding this issue especially in children of Bangladesh.

MATERIALS AND METHODS

Study design: It was a prospective observational study conducted on serologically confirmed dengue virus infected children admitted in Bangabandhu sheikh mujib medical university (BSMMU), Dhaka, Bangladesh, from September to December 2019 contains 103 consecutive cases of child admitted with the diagnosis of dengue fever.

All suspected child with provisional diagnosis of dengue fever were admitted in dengue unit of BSMMU were taken into account. All children aged up to 17 years with positive dengue test either NS1 antigen, anti-dengue IgM antibody, anti-dengue IgG antibody were included in the study group. Children who are diagnosed with other disease like malaria, meningitis, typhoid fever and also previously diagnosed case of chronic liver disease, pancreatitis were excluded from the study.

Total 103 (n=103) child were included in the study. Cases were followed up daily for the clinical and laboratory parameters and information was collected in a preformed data sheet development by the investigators and included in the study. The patients were treated with oral paracetamol, oral or intravenous fluids, blood products transfusion according to the national guideline for clinical management of dengue syndrome, Bangladesh.[10]

Descriptive statistics was used for analysis. The quantitative variables were expressed as mean ± SD or median with IQR. The frequency of various signs, symptoms and lab parameter were compared with disease severity using *chi-square test* or *Fisher's exact test*. SPSS version 25.0.0 was used for data entry and analysis and p-value below 0.05 was considered significant. Written consent was taken and ethical clearance was taken from Departmental Review Board (DRB) of department of Pediatric Gastroenterology and Nutrition, BSMMU.

RESULT

The total number of our studied participants were 103 (n=103), out of which 59 (57%) cases were classical DF, 27 (26%) were DHF and 17 (17%) were DSS according to WHO guidelines [Figure 1]. [11] The age distribution was between 11-months-16 years with mean age was 8.44 ± 4.47 years [Table 1]. Most of the study participants belong to older group, 35.9% and 37.9% in between 5-10 year and more than 10 year respectively. 58 (56.3%) were males and 45 (43.7) were females in this study. Male to female ratio was 1.3:1. In both the groups of DF (33), DHF (20) male has high incidence but in DSS (12) group female were more and p-value was not significant [Table 1]. 81 (78.6%) patients were from urban and 22 (21.4%) came from rural areas. Most of them 76.7% belongs to middle socioeconomic background [Table 1]. Both socioeconomic condition and residential area of studied participant were not statistically significant with the severity of dengue fever.

Figure 2 outlines the distributions of various GI manifestations in dengue fever of the studied population. GI manifestations were noted in all the study participants. Most common presentation were anorexia 80 (78%), Vomiting 74 (72%) followed by abdominal pain 60 (58%) and diarrhea 25 (24%). GI bleeding manifesting with hematemesis and melena were found 9 (9%) and 7 (7%) patients. Ascites, hepatomegaly and acute pancreatitis were found 20 (19%), 24 (23%) and 3 (3%) respectively. In this study atypical GI manifestation acute pancreatitis was noted.

Table 3 outlines various GI manifestations and its correlation with different classification of dengue fever. Among them GI bleeding (hematemesis & melena), ascites, hepatomegaly were found significant with dengue severity.

Among the laboratory investigation median value of alanine transaminase was 37 (IQR: 25-62) and hypertransaminesemia was seen in 40 (38.8%) cases, which was not statistically significant with severity of dengue fever. Hypoalbuminemia, hypocalcaemia and electrolyte imbalance was found in 20 (19.4%), 30 (29.1%) and 16 (15.5%) cases respectively and all are statistically significant with severe dengue fever. Regarding electrolytes imbalance hyponatremia, hypokalemia and hyperkalemia were found in 12 (11.7%), 4 (3.9%) & 2 (1.9%) cases respectively. In 80 (77.7%) cases thrombocytopenia (<1, 50,000) was found, among them 26 and 15 cases were found in the DHF and DSS group and 39 cases found in DF group in this study [Table 3].

Most of the patients were positive for NS1 94 (91.3%) followed by anti dengue IgM antibody 9 (8.7%) as majority of the patients presented within 5 days of fever. Beside one dengue fever patient the entire patient of study population needed intravenous fluid management. Albumin was given in 12 (11.7%) cases, Platelet was transfused in 7 (6.8%) cases and 12 (11.7%) & 9 (8.7%) patient treated with intravenous calcium gluconate and steroid therapy and all of them belongs to sever dengue group [Table 4]. In this study all the cases were recovered.

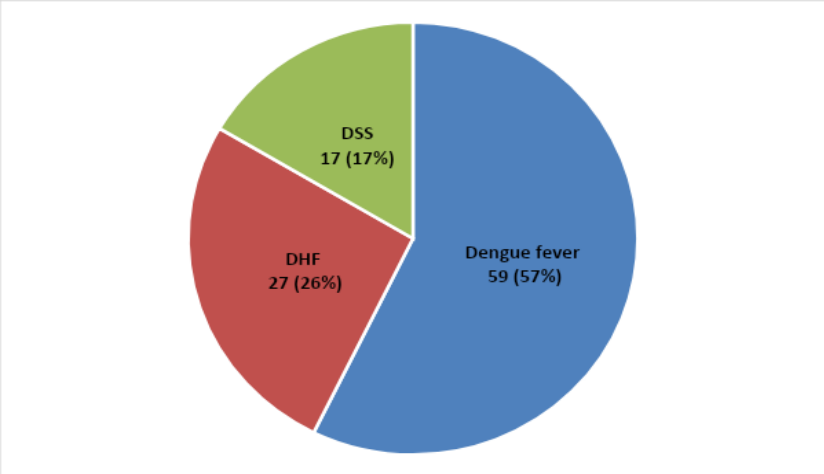

Figure 1 Patients classified according to different classification of dengue fever

Table 1: Demographic characteristics of the participants.

Parameter	Total No (%)	DF	Severe dengue		*p*-value
			DHF	DSS	
Age (Mean ± SD)	8.44 ± 4.47				
< 5 yrs	27 (26.2)	14	7	6	0.848
5-10 yrs	37 (35.9)	22	9	6	
>10 yrs	39 (37.9)	23	11	5	
Sex					
Male	58 (56.3)	33	20	5	1.000
Female	45 (43.7)	26	7	12	
Residence					
Urban	81 (78.6)	46	21	14	1.000
Rural	22 (21.4)	13	6	3	
Socioeconomic condition					
Low	7 (6.8)	4	2	1	0.167
Middle	79 (76.7)	49	20	10	
High	17 (16.5)	6	5	6	

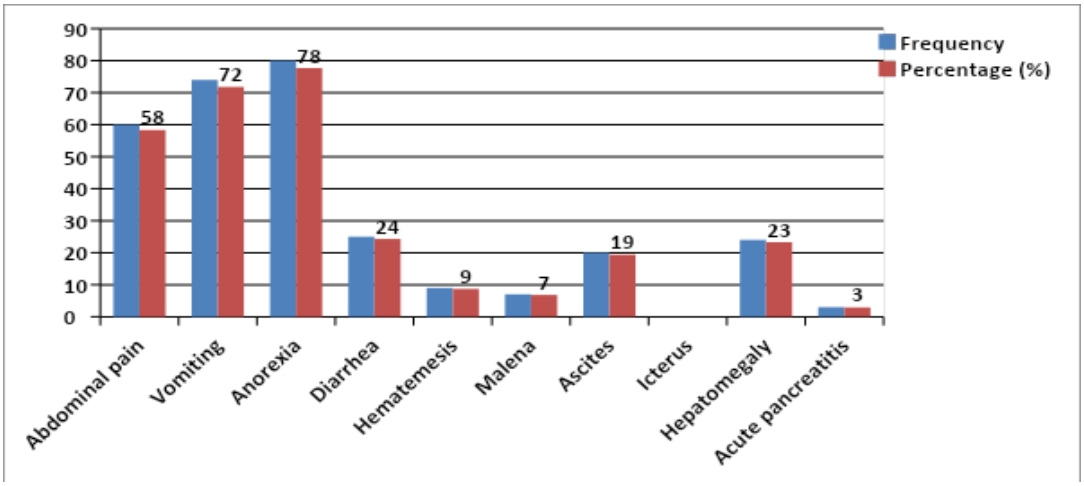

Figure 2 Distribution of GI manifestations in dengue fever of study participants.

Table 3: GI manifestation and laboratory findings with severity of dengue fever.

GI manifestation	No of study participants (n=103) No (%)	DF n=59 (57%)	Severe dengue		*p*-value
			DHF n=27 (26%)	DSS n=17 (17%)	
Abdominal pain	60 (58%)	30	18	12	0.204
Vomiting	74 (72%)	41	20	13	0.867
Anorexia	80 (78%)	44	22	14	0.759
Diarrhea	25 (24%)	14	7	4	1.000
Hematemesis	9 (9%)	0	8	1	0.001
Melena	7 (7%)	0	6	1	0.000
Ascites	20 (19%)	3	5	12	0.000
Hepatomegaly	24 (23%)	6	7	11	0.000
Acute pancreatitis	3 (3%)	1	1	1	0.390
Hypoalbuminemia	20 (19.4%)	3	10	7	0.000
Hypertransaminesemia	40 (38.8%)	21	10	9	0.429
Hypocalcemia	30 (29.1%)	9	13	8	0.002
Electrolyte imbalance	16 (15.5%)	5	6	5	0.037
Haematocrit (%) (mean ± SD)		39.29 ± 4.75			
<36.3%	25 (24.3%)	16	6	3	0.775
>36.3%	78 (75.7%)	43	21	14	
Platelet count					
0-10000	2 (1.9%)	1	1	0	0.007
>10000-50000	43 (41.7%)	17	14	12	
>50000-100000	23 (22.3%)	13	7	3	
>100000-150000	12 (11.7%)	8	4	0	
>150000	23 (22.3%)	20	1	2	

Table 4: Diagnosis, treatment modality and outcome of the study participants.

Parameter	Frequency (%)			
Diagnostic tests				
NS1 antigen	94 (91.3)			
IgM antibody	9 (8.7)			
IgG antibody	7 (6.8)			
Management parameter		**DF**	**DHF**	**DSS**
Fluid management				
Oral	1 (1%)	1	0	0
Intravenous	102 (99%)	58	27	17
Albumin transfusion	12 (11.7%)	0	4	8
Platelet transfusion	7 (6.8%)	0	5	2
Steroid (Dexamethasone)	9 (8.7%)	0	3	6
IV Calcium gluconate	12 (11.7%)	2	4	7
Outcome				
Recovery	103 (100%)			
Death	0 (0%)			

DISCUSSION

Dengue fever is a widely spread mosquito borne important tropical arboviral infection and has a global concern because of major outbreaks with mortality and morbidity in endemic countries.[10,12] In this study the clinical and laboratory profile related to GI system of children during an outbreak was observed.

The studied cases were divided into DF, DHF and DSS according to WHO TDR guidelines 2009 and national guidelines for clinical management of dengue fever of Bangladesh.[3,10] A total 103 dengue fever cases included in this study either based on NS1 antigen test or IgM and IgG antibody tests among them 59 (57%) were categorized as classical DF, 27 (26%) as DHF and 17 (17%) were DSS.

Most of affected children were belong to older group 35.9% in between 5-10 year and 37.9% in more than 10 year group with mean age 8.44±4.47 and it may be due to the school activity of these group and exposure to breeding places of mosquitoes during playing. These findings matched with other related studies.[13,14] Boys 58 (56%) are more affected than girls and boy to girl ratio

was 1.3:1; which is par with various studies and it may be due to the more exposure to mosquito bite during playing outdoor and traditional wearing of full slip cloth as well as less time spending outside by girls than boys.[14,15] Although dengue virus infection gradually shifted to rural areas according to WHO; in the present study urban child 81 (78.6%) still is more infected than rural child.

Dengue can be presented with various manifestations affecting different system of our body. In these study 100% child had GI manifestation which included both typical and atypical manifestations. Anorexia (78%), Vomiting (72%) followed by abdominal pain (58%) and diarrhea 25 (24%) are the most common GI symptoms. A study conducted by Mishra S. et. al. also found that abdominal pain, vomiting, and abdominal distension are most common GI manifestation which is matched with other various studies.[16,17]

Common bleeding manifestations of dengue fever are petechiae, purpura, ecchymosis, gum bleeding, GI bleeding (melena, hematemesis), and positive tourniquet test.[12] In these study melena 9% and hematemesis was found in 7% cases and these GI bleeding was commonly observed in severe dengue fever cases but some study reported GI bleeding manifestation also in non-severe dengue fever cases.[12,18] Bleeding in dengue is multifactorial, mostly due to decreased platelet function followed by other cause like fibrinogen consumption, prolongation of PT/aPTT, and vasculopathy.[17] In this study thrombocytopenia was found most of the cases 77.7% and in all class of dengue fever but mostly associated with the severe dengue group. Some study like Harris et al, Murge et al reported no significant correlation between platelet count and bleeding manifestations.[19,20] In this study no relation between thrombocytopenia and bleeding manifestation was found as 2 patients platelet count was below 10,000 without bleeding manifestation but some study differ with these statement.[12] The accurate indicator of plasma leakage and vascular permeability is raised hematocrit which is found in 78 (75.7%) cases but it was not associated with the severity of dengue which is different from the study conducted by Sharma NL et.al.[17]

Mild to moderately elevated alanine aminotransferase was found in 40 (38.8%) cases mostly in the dengue fever group and none of the child developed acute fulminant hepatitis. Which is not coincides with some previous study.[17] Hypoalbuminemia was observed in 19.4% cases which had significant association with the severity of dengue fever.

Other manifestations observed in this study were ascites (19%), hepatomegaly (23%), acute pancreatitis (3%), hypocalcaemia (29.1%), electrolytes imbalance (15.5%) cases. GI bleeding (hematemesis & melena), Ascites, hepatomegaly, hypoalbuminemia, hypocalcaemia and electrolyte imbalance were found significantly associated with dengue severity in this study.

There was no mortality in the present study group, it may be due to early diagnosis and improved management ability over the age, whereas previous study stated high case fatality rate of the South East Asian region like India, Bhutan, Nepal where case fatality rate (CFR) is more than 1%.[21] High CFR is usually due to delay in recognition of dengue epidemic in previous years or delay in seeking medical attention.

CONCLUSION

Dengue is very common in this continent and dreaded fevers for pediatric age group with various presentation and complications. Early diagnosis and adequate management can prevent significant mortality. GI manifestation is very common including both typical and atypical symptoms like hepatitis and acute pancretitis. GI bleeding (hematemesis & melena), Ascites, hepatomegaly, hypoalbuminemia, hypocalcaemia and electrolyte imbalance were found significantly high in severe dengue cases which may be used as possible markers of severe dengue after multicenter large scale study.

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