

Original Article

Gastrointestinal and Hepatic Manifestation of Dengue and its Role in Prediction of Severity in Children

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Abstract:

Dengue fever is a communicable disease having variable clinical manifestations. Gastrointestinal manifestations also occur in dengue. Diagnosis of the disease may be missed without proper knowledge about these presentations. This study was carried out to explore Gastrointestinal manifestations of dengue fever and define its role in identification of severe dengue. This cross-sectional observational study was conducted at Chattogram Medical College Hospital, Bangladesh from November, 2022 to December, 2022. After detailed history, examinations and investigations total 101 children of dengue fever were divided into two groups naming dengue fever with or without warning sign and severe dengue fever. Comparison was done in between groups in context of GI symptoms and investigations. Among total 101 patients about 24 (23.76%) got severe dengue fever. Mean age was 6.83 ± 3.9 years with a Male: Female ratio of 1.5:1. Majority (86.1%) having GI symptom. Common presentations were vomiting (69.3%), abdominal pain (59.4%), nausea (25.7%), anorexia (22.8%), diarrhea (17.8%). Other observed GI manifestations were ascites (8.91%), melena (7.92%), hematemesis (1.98%), jaundice (0.99%) hepatomegaly (1.98%), acute pancreatitis (0.99%) and acute liver failure (0.99%). Among these diarrhoea, ascites, melena were found significant with dengue severity ($p=0.00$). Raised S. ALT was seen in 39.6% cases which significantly corresponds with SDF ($p=0.00$). In conclusion, GI manifestation is very common in dengue fever and often appears as main presenting symptom associated with fever. Among various typical and atypical GI symptoms diarrhea, ascites, melena, transaminasemia can be used as a predictor of severe dengue.

Key words: Dengue fever, Ascites, Gastrointestinal symptom, S.ALT.

Introduction:

Dengue fever is an ancient mosquito-borne viral infection which is clinically recognized for more than

200 years¹. But now a days it has emerged as a major public health concern. According to the World Health

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Organization (WHO), dengue fever ranks among the top ten hazards to world health. Given that dengue has increased thirty times more frequently worldwide in the past fifty years, it is also the virus that is most rapidly

spreading^{2,3}. It is widespread throughout the world's tropical and subtropical climates. As a tropical country practically since 2000 Bangladesh is experiencing dengue outbreak in each successive year with a changing pattern of presentations in each outbreak^{4,5}. As of December 31, 2022, there had been 60,078 cases of dengue and 266 dengue-related deaths, making the outbreak the second worst since 2000⁶. Dengue virus (DENV) has four serotypes (DEN 1-4). Infection with any of the four dengue viral serotypes may present as asymptomatic infection or may cause variable presentations like fever, generalized body ache, retro orbital pain and other systemic presentations. It has been categorized in different ways by different organizations. According to WHO, it is described as classical dengue fever (DF), dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS)³. However it may turn into severe dengue syndrome characterized by increased vascular permeability, thrombocytopenia, and deranged haemostasis ultimately circulatory compromise to shock followed by multi organ failure and death^{7,8}. Dengue fever does not have a specific antiviral treatment, but the physiologic abnormalities are temporary, and most patients recover completely if appropriate fluid management is provided during the peak vascular leakage period. Under skilled hands, the current DSS mortality rate is less than 1%^{9,10,11}.

Now a day besides typical presentations of fever, rash, body ache other unusual symptoms of multiple organ system are predominating. Gastrointestinal and hepatic manifestations are well known in dengue fever. But with increasing disease burden atypical presentations from these systems like diarrhoea, hepatitis, fulminant hepatic failure, acalculous cholecystitis, acute pancreatitis etc. are seen more often in dengue fever. Sometimes liver involvement may manifested only by the elevation of transaminases. Hepatic involvement may be attributed to the direct effect of the virus on liver cells or as a result of dysregulated host immune responses against the virus^{12,13}. Ultimate fate of hepatic and kuffer cell involvement is cellular apoptosis which sometimes turns into fatal acute liver failure¹⁴. Without proper knowledge about these variable presentations dengue cases can be missed out where early recognition can be lifesaving. There is limited study in children regarding this problem from our country. This study aims to serve at this issue by exploring variable gastrointestinal and hepatic presentations of dengue as well as their significance in prediction of dengue severity.

Materials and Methods:

This cross-sectional observational study was conducted at Chattogram Medical College Hospital, Chattogram, Bangladesh. Data was collected from November 2022 to December 2022. A total of 101 consecutive cases of serologically diagnosed dengue fever of either gender, aged < 12 years were studied. It was diagnosed by recent onset high-grade fever and serological confirmation by positive NS1 antigen or IgM by ELISA method. Patients with pre-existing liver disease or co-infection with other hepatotropic virus and who were unwilling to give consent were excluded from the study. The study was approved by the Ethics Committees of Department of Pediatrics, Chattogram Medical College Hospital, Chattogram, Bangladesh. Informed written consent was obtained from each patient or his/her parents. Detailed history and clinical examinations were done. For all patients CBC, S.SGPT/ S.ALT were done. Patients were divided into two groups; dengue fever with or without warning sign and severe dengue fever according to national guidelines for clinical management of dengue fever in Bangladesh⁵. After collection, data were checked manually, processed and analyzed by computer based program IBM SPSS Statistics, version 21 (Statistical Package for Social Science, Chicago, Illinois) for Windows XP. Results were expressed as mean \pm standard deviation (SD) or number or percentage. Data for clinical characteristics and laboratory results were compared between different patient groups by using the chi-square test or Fisher's exact test for categorical variables and the Mann-Whitney test for continuous variables. ROC curve was drawn to determine the significance of S.ALT. P value <0.05 was considered as significant.

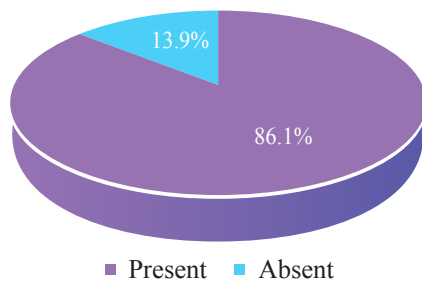
Results:

A total number of 101 (n=101) diagnosed cases of dengue fever were analyzed, out of which 77 (76.23%) having DF with or without warning sign and remaining 24 (23.76%) were cases of SDF. The age distribution was between 3 months-12 years with a mean age of 6.83 \pm 3.9 years. Most of them 42(41.6%) were in the older age group (9-12 years). There were 30 children below 5 years, 29 children between 5 to 8 years. Males were predominant 62(61.4%) over females 39(38.6%) in this study and M: F ratio was 1.5:1 (Table 1). Most of the patients come from urban areas 69(68.3%) and rest of them were from rural areas 32(31.7%). During the comparison of demographic characteristics (age, sex, residence) with the severity of dengue fever there was no statistical significance in between groups (Table I).

Table I: Distribution of patients according to demographic variables (n=101)

Characteristics	Total No (%)	Dengue Fever	Severe Dengue Fever	P value
Age				0.62
1-4	30(29.7)	22	8	
5-8	29(28.7)	24	5	
9-12	42(41.6)	31	11	
Sex				0.72
Male	62(61.4)	48	14	
Female	39(38.6)	29	10	
Socioeconomic				0.76
Urban	69(68.3)	52	17	
Rural	32(31.7)	25	7	

In our study population GI manifestations were very much likely (86.1%). Only a small number of patients (13.9%) did not have any GI symptoms (Figure 1).

**Figure-1:** Distribution of patient according to presence or absence of GI symptoms

Among various GI manifestations vomiting was most common 70(69.3%) followed by abdominal pain 60(59.4%) nausea 26(25.7%), anorexia 23(22.8%), diarrhea 18(17.8%) and ascites 9(8.91%). Other observed GI manifestations were melena 8(7.92%), hematemesis 2(1.98%), jaundice 1(0.99%) hepatomegaly 2(1.98%), acute pancreatitis 1(0.99%) and acute liver failure 1(0.99%). We correlated all the GI manifestations with different groups of dengue fever. Among them diarrhea, ascites, melena were found significant ($p=0.00$) with dengue severity (Table II).

Table II: Distribution of patients according to gastrointestinal manifestations of study populations (n=101)

Characteristics	Total No (%)	Dengue Fever	Severe Dengue Fever	P value
Anorexia	23(22.8)	16	7	0.27
Nausea	26(25.7)	19	7	0.42

Vomiting	70(69.3)	52	18	0.34
Abdominal pain	60(59.4)	43	17	0.14
Diarrhoea	18(17.8)	8	10	0.00
Constipation	5(4.95)	4	1	0.66
Melena	8(7.92)	7	1	0.00
Jaundice	1(0.99)	0	1	0.24
Hepatomegaly	2(1.98)	0	2	0.05
Ac. Pancreatitis	1(0.99)	0	1	0.24
Hematemesis	2(1.98)	0	2	0.05
Ascites	9(8.91)	0	9	0.00
Acute liver failure	1(0.99)	0	1	0.24

In 54 (53.4%) cases thrombocytopenia ($<1,50,000/\text{cmm}$) was found, and this corresponds significantly ($p=0.01$) with dengue severity (Table III).

Table III: Distribution of patients according to complete blood count (n=101)

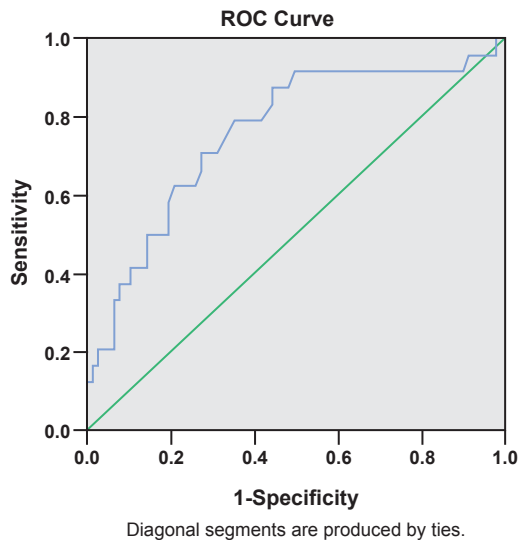
Parameter	Dengue Fever (n=77)	Severe Dengue Fever (n=24)	P value
PLT (/cmm)			0.01
>150000	42	5	
100000-150000	12	6	
50000-99000	17	7	
<50000	6	6	
Hct (%)			0.17
<30	14	8	
30-40	51	11	
>40	12	5	
Hb (gm/dl)			0.26
<6	2	1	
6-9	7	5	
>9	68	18	

Among the laboratory investigations hypertransaminasemia was seen in 40 (39.6%) cases, which was statistically significant ($p=0.00$) with severity of dengue fever (Table IV).

Table IV: Distribution of patients according to S. ALT values (n=101)

S. ALT (U/L)	Dengue Fever (n=77)	Severe Dengue Fever (n=24)	P value
<40	54	7	0.00
40-120	18	10	
120-400	5	4	
>400	0	3	

In ROC curve the AUC for S.ALT was 0.76 (95% CI: 0.65–0.88) (Figure 2).

**Figure-2:** ROC curve for S.ALT against dengue severity

Discussion

Dengue is an alarming arboviral disease with a wide range of manifestations affecting multiple organ systems. GI manifestations are highly noticeable in Dengue fever besides other presentations. Present study point focuses on different GI manifestations of Dengue fever and its significance in prediction of disease severity. Here we distributed our 101 assigned children into 2 groups naming DF with or without warning sign and severe DF according to national guidelines for clinical management of dengue fever in Bangladesh⁵. Among them about one fourth of the patients (23.76%) having severe dengue in this study. Children are prone to develop severe dengue due to their weak immune system and also hemodynamic instability. Our finding is similar to other studies where Bokade et al.¹⁵ and Yashwanth et al.¹⁶ found (22.7%) and (25%) severe dengue patients respectively. About half (41.6%) of the

affected children were older in age group with mean age 6.83 ± 3.99 years. It may be as a result of their more exposure to mosquito bite as they spend more time in crowded places such as school, park etc. These findings are similar to related study¹⁶. Boys (61.4%) are more affected than girls and boy to girl ratio was 1.5:1; which is par with other study and it may be due to the more exposure during playing outdoor and also traditional more health seeking behavior for male child¹⁷. According to WHO now-a-days dengue is expanding in rural areas but still most of the children (68.3%) is from urban areas in this study.

Most of the patients (86.1%) having GI manifestations in present study which is comparable to study done by Akram et al.¹⁸ where about 90% having GI symptoms. In present study commonest presentation is vomiting (69.3%). Similar findings were narrated in another study¹⁸. Abdominal pain (59.4%) is another common one. There are a large number of causes responsible for abdominal pain in dengue fever such as acute hepatitis, acalculus cholecystitis, acute pancreatitis, appendicitis, spontaneous bacterial peritonitis, enteritis, peptic ulcer disease and gastric erosions etc¹⁹. It may be the cause for abdominal pain being a common symptom. Another study shows equal findings where about 58% patients suffered from abdominal pain¹⁷. Some patients presented with nausea (25.7%), anorexia (22.8%), and diarrhea (17.8%). Diarrhea may be cytokine mediated as IL8 is involved in pathophysiology of both dengue and diarrhoea²⁰. In another study 13% patient having diarrhea¹⁸. We found ascites in 8.91% cases. Actually dengue ns1 protein and cytokines are involved in endothelial damage ultimately plasma leakage and development of ascites²¹. Other observed GI manifestations were melena (7.92%), hematemesis (1.98%), These findings are similar to other study¹⁷. Haemorrhage in dengue is multifactorial, mostly may be due to decreased platelet function but other causes like fibrinogen consumption, coagulopathy and vasculopathy etc. also may present²². We correlated all the GI manifestations with different groups of dengue fever. Among them diarrhea, ascites, melena were found significant with dengue severity. These finding are as per other related article¹⁷. Other presentations were Jaundice (0.99%) hepatomegaly (1.98%) and acute pancreatitis (0.99%). Hepatic involvement is known in dengue fever since 1950s. Dengue hepatitis may be symptomatic with hepatomegaly, jaundice or may have asymptomatic hypertransaminasemia but in severe cases it can turn into fulminant hepatic failure. In our study only one patient was diagnosed as a case of acute liver failure and treated at PICU. Fortunately the patient survived with proper supportive treatment and gained complete recovery. However multiple mechanisms may

be responsible for development of liver injury in dengue fever such as direct viral cytopathic effects, immune related injury or hypo perfusion etc. Sometimes dengue infection causes microcirculatory dysfunction by causing venular or sinusoidal endothelial injury which can lead to hepatocyte ischemia, in the absence of hypotension²³. In present study Jaundice (0.99%) and hepatomegaly (1.98%) were found in small number but asymptomatic hypertransaminasemia was seen in (39.6%) cases. Hypertransaminasemia was present in all groups of dengue fever but mostly associated with the severe dengue fever. Similar finding was narrated in another study²⁴. During correlation with different groups of dengue fever it was also significantly correlated with dengue severity. We also drew ROC curves for ALT against severe dengue to determine the reliability of ALT values in defining dengue severity. The area under the ROC curve (AUC) for S.ALT was 0.76 (95% CI: 0.65–0.88). The AUC for a diagnostic curve ranging from 0.70 to 0.80 indicate an acceptable level of the test. This demonstrates that raised ALT level can be used as a marker for prediction of severe dengue. In (53.4%) cases we found thrombocytopenia ($<1,50,000/\text{cmm}$) and this corresponds significantly ($p=0.01$) with dengue severity. During our study period only one patient died, others achieved complete recovery.

Conclusion:

GI manifestation is very common in dengue fever and often appears as the main presenting symptom associated with fever. Among various typical and atypical GI symptom diarrhea, ascites, melena are significantly associated with severe dengue. Transaminasemia was seen in all forms of dengue cases but more common in severe dengue fever group. These parameters may be used in prediction of severe dengue. So, strong suspicion of dengue fever should be made if a patient presents with fever and GI symptoms like vomiting, abdominal pain, diarrhoea, acute pancreatitis etc, specially during dengue epidemic. Diarrhea, ascites, melena, transaminasemia can be used as a predictor of severe dengue. This study was a single center study with a small sample size, further large scale study can be done for better results.

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Conflicts Of Interest: None.

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