



## Gastrointestinal Manifestations of Dengue Fever among Children: A Multicenter Cross-Sectional Study in Bangladesh

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### Abstract

**Background:** Dengue fever is an arboviral illness spread by mosquitoes and is now a major public health issue on a global scale. Unfortunately, only few studies have documented unusual clinical characteristics of dengue among children. **Objective:** The objective of this study was to describe the gastro intestinal manifestations of dengue infected children during 2019 dengue outbreak in Dhaka city. **Methodology:** This cross-sectional study was conducted at Department of Virology at National Institute of Laboratory Medicine and Referral Center, Dhaka, Bangladesh among confirmed cases of dengue fever (Children aged less than 12 years) admitted in the pediatric ward of Dhaka Medical College Hospital, Kurmitola General Hospital, Sir Sallimullah Medical College Hospital, Dr M R Khan Sishu Hospital and BSMMU in Dhaka from June 2019 to November 2019 for period of six months. Data was collected using a structured questionnaire via face-to-face interview from guardian of the children. The investigation profile was collected from their hospital records. **Results:** Out of confirmed 200 pediatric dengue patients, children with dengue had an average age of  $9.8 \pm 2.7$  years with a slight female predominance. The majority (36.5%) of the children belonged to the age group of 5 to 9 years. Among 200 patients, 42 patients diagnosed as severe Dengue according to WHO classification. Gastrointestinal symptoms were the most common associated feature, including mostly Nausea/vomiting (81.0%), abdominal pain (61.0%), ascites (29.0%), hepatomegaly (19.0%), diarrhoea (13.0%) and others. Elevation of transaminases was found in 40.0% of the children. About 30% of the patients had platelet count more than or equal to 50000 and hematocrit more than 40 was observed in 12% patients. Atypical manifestations such as acalculous cholecystitis, acute fulminant hepatitis, acute pancreatitis, parotitis, AKI and paralytic ileus were noted in small number of patients. **Conclusion:** In conclusion, fever with vomiting and abdominal pain are common presentations of dengue fever.

**Keywords:** Dengue; children; febrile; 2019 outbreak

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### Introduction

Dengue viruses are arthropod-borne flaviviruses which is transmitted by *Aedes aegypti* mosquito<sup>1</sup>. In most

tropical and subtropical countries, Dengue has become a global public health concern<sup>2</sup>. Almost 75.0% of the dengue global disease burden is in the Southeast Asia and Western Pacific regions. Throughout the past five decades, dengue cases have dramatically increased on a global scale<sup>1</sup>. An estimated 500,000 people with severe dengue infection require hospitalization annually and 90.0% of them are children less than 5 years of age<sup>3</sup>. Over the last few decades, with growing population, rapid urbanization and inappropriate sanitary measures, the epidemics and subsequent

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dengue infections have increased rampantly. With rising disease burden, atypical manifestations have increased as well, which are most often missed due to lack of awareness<sup>4</sup>.

Some cases of febrile illness found in 1964 in Dhaka, later which was identified as Dengue<sup>5</sup>. In 2000 a major outbreak occurred in Bangladesh, mostly in three large cities of Bangladesh<sup>5</sup>. In 2019 the most extensive and fatal outbreak of dengue occurred in the history of Bangladesh and circumstances was worse than previous outbreak<sup>6</sup>. Over 101354 people were reported, and 179 deaths were recorded<sup>7</sup>. The unofficial number of cases and deaths might be higher due to lack of country's inadequate health reporting system. The high mortality was associated with not only dengue shock syndrome (DSS) but also secondary dengue infections<sup>8</sup>. Approximately 95.0% of cases are less than 15 years and mortality rate of most of the countries is 5% cases<sup>9</sup>. As children have immature hemodynamic system, they tend to develop severe form of dengue disease. National surveillance data from Asian countries show that infants under 1 year of age and children aged 4 to 9 have consistently been at the highest risk for severe dengue disease<sup>8</sup>.

Although, liver abnormalities have been described as a manifestation of DHF, the prevalence of other gastrointestinal manifestations is unknown. Atypical gastrointestinal manifestations of dengue reported are hepatitis, fulminant hepatic failure, acalculous cholecystitis, acute pancreatitis, and diarrhea. Upper GI bleed, ascites can occur as a consequence of plasma leakage in severe dengue. Hepatomegaly and few cases of splenomegaly have been reported in dengue infection. Hepatic dysfunction is a crucial feature seen in DENV infection. The prime targets for DENV infection are Hepatocytes and Kupffer cells, as confirmed in biopsies and autopsies of fatal cases. For infecting cells, the major rate limiting step is the viral attachment to the receptors present on surface of host cell. An eventual outcome of hepatocyte infection by DENV is cellular apoptosis, a phenomenon demonstrated both in vivo and in vitro<sup>10</sup>. This study was aimed to describe the gastro intestinal manifestations of dengue infected children during 2019 dengue outbreak in Dhaka city.

## Methodology

**Study Settings and Population:** This study was conducted at department of virology, NILMRC on 200 confirmed cases of dengue fever (aged 0-12 years) who were admitted in the pediatric ward of Dhaka

Medical College Hospital (N=40), Kurmitola General Hospital (N=38), Sir Sallimullah Medical College Hospital (N=51), Dr M R Khan Sishu Hospital (N=53) and BSMMU from June 2019 to November 2019. Children admitted during this time with a confirmed diagnosis of DF (Positive to Dengue NS1 antigen and/or anti-dengue IgM antibodies) were included in the study. Data was collected from all the 5 hospitals. The case definition, diagnosis, and management for dengue fever were as per the revised World Health Organization (WHO) guidelines 2011. Children were classified as severe and non-severe dengue infection. Children with plasma leakage, organ involvement, and severe thrombocytopenia were categorized as severe dengue infection. The diagnosis was confirmed by NS1 or dengue serology for IgM and IgG antibodies during the acute phase and convalescent phase of illness.

**Sample Collection Procedure:** Detailed history was taken and clinical evaluation and examination was performed on admission and subsequently during the stay in the hospital. According National Guideline 2018, Dengue cases were classified. The laboratory investigations like complete blood count including-hemoglobin level, Platelet count and PCV, was done in all the cases and repeated. Chest X-ray, ultrasonography of the abdomen and chest, Liver and renal function tests were done when needed. These patients were managed according to national guideline. Patients were discharged from hospital when fever subsided and/or vital signs became normal.

**Statistical Analysis:** Statistical analyses was performed with SPSS software, versions 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.). Continuous data that were normally distributed were summarized in terms of the mean, standard deviation, median, minimum, maximum and number of observations. Categorical or discrete data were summarized in terms of frequency counts and percentages. When values are missing, the denominator was stated. Chi-square test was used for comparison of categorical variables. Every effort was made to obtain missing data. A two-sided P value of less than 0.05 was considered to indicate statistical significance.

**Ethical Clearance:** All procedures of the present study were carried out in accordance with the principles for human investigations (i.e., Helsinki Declaration) and also with the ethical guidelines of the Institutional research ethics. The study protocol was approved by the Institutional Review Board of

NILMRC. Participants in the study were informed about the procedure and purpose of the study and confidentiality of information provided. All participants consented willingly to be a part of the study during the data collection periods. All data were collected anonymously and analyzed using the coding system.

**Results**

Out of confirmed 200 pediatric dengue patients, 149 (74.5%) cases were positive for NS1 antigen, and 51 (25.5%) cases for IgM antibody. Overall, children with dengue had an average age of 9.8±2.7 years with a slight female predominance (Figure I).

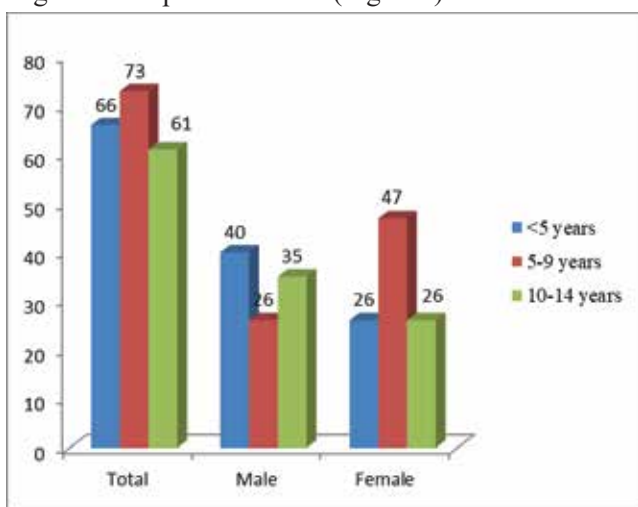


Figure I: Gender and Age group distribution of study population

The majority (36.5%) of the children belonged to the age group of 5 to 9 years (Table 1). Among 200 patients, 42 patients diagnosed as severe Dengue according to WHO classification (Figure II).

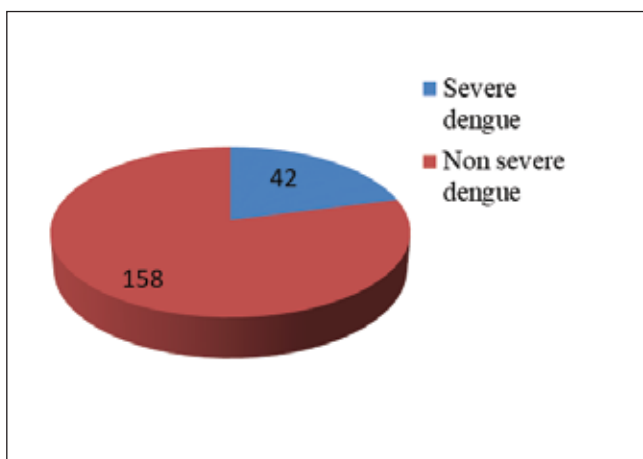


Figure II: Patient Classified According to Severity

Table 1 describes the various GI manifestations in dengue fever in the study population. Almost 90.0% of the patients presented with gastrointestinal manifestations. Most common GI symptom noted was nausea/vomiting seen in 81.0% of the patients followed by pain in abdomen in 61.0%. Ascites was present in 28.0% patients, diarrhea occurred in 13.0% patients and some others complications also seen. In our study Atypical manifestations such as acalculous cholecystitis, acute fulminant hepatitis, acute pancreatitis were noted in small number of patients.

Table 1: Distribution of various GI manifestations

GI Manifestations	Frequency	Percent
Nausea/Vomiting	163	81.5
Abdominal Pain	123	61.5
Transaminase Increased	80	40
Ascites	56	28
Hepatomegaly	39	19.5
Diarrhoea	27	13.5
Jaundice	25	12.5
Fulminant Hepatitis	13	6.5
Splenomegaly	12	6
Bleeding manifestations	12	6
Cholecystitis	9	4.5
Acute Pancreatitis	8	4

Table 2 represents manifestations in Dengue other than GI symptoms. Fever was the most common manifestation noted (100%) followed by myalgia (89%). Few other manifestations were headache, retro orbital pain, arthralgia and rash. In this study bleeding manifestations (Hematemesis and Malena commonly) were seen in 25% of population. Encephalopathy, and AKI was seen among 0.5% cases. Respiratory distress syndrome and Paralytic Ileus was seen among 1% cases and Parotitis was seen in 2.5% cases (Table 2).

Table 2: Other clinical manifestations in Dengue

Clinical Manifestations	Frequency	Percent
Fever	200	100.0
Myalgia	178	89.0
Headache	161	80.5
Retro orbital pain	123	61.5
Arthralgia	75	37.5
Rash	73	36.5
Bleeding manifestations (Hematemesis/ Malena)	51	25.5
Encephalopathy	1	0.50
Respiratory distress	2	1.0
AKI	1	0.50
Paralytic Ileus	2	1.0
Parotitis	5	2.5

## Discussion

With a high rate of morbidity and mortality, dengue fever is a serious public health concern. The most recent outbreak has revealed a variety of clinical manifestations as well as unpredictable clinical progression and prognosis<sup>11</sup>. This was a multicenter retrospective study of dengue among children, which reports mainly gastrointestinal presentations of dengue in Bangladesh. In this study, children 5-9 years were the most commonly affected age group and were more at risk to develop severe dengue infection and similar to the previous studies by Faridi et al., and Wichmann et al<sup>11-12</sup>.

Nausea with or without Vomiting and abdominal pain are commonly reported gastrointestinal features in our study. Few atypical gastrointestinal features were found like acalculous cholecystitis, acute fulminant hepatitis, acute pancreatitis in some patients.

This study found one case of encephalopathy- a rare manifestation of dengue infection<sup>9</sup>. However, only 1.8% of children had a past history of dengue indicating that the severe cases cannot be explained by the secondary infection by a different serotype alone. Dengue outbreak in Bangladesh after 2018 has increased fatality rate after introduction of DENV-3 into the region where preexisting DENV-1 and DENV-2 were already circulating<sup>1,13</sup>.

The majority of the patients were cases of non-severe dengue and only 21% cases were severe dengue. Among the hospitalized patients' other studies also reported similar pattern with majority of cases with non-severe dengue infection<sup>12</sup>. In the present study among all clinical presentations, fever was most common. Following fever, abdominal pain was the next common symptom abnormal aminotransferase level followed by hepatomegaly which is also seen at another study of Bangladesh<sup>14</sup>. In this study elevation of transaminases was found in 40.0% of the children. However, the severity of hepatitis was mild to moderate in the majority of the patients. Acute fulminant hepatitis was seen in 6.5% of children.

Bleeding manifestations were seen in 6.0% of cases and much lower in comparison to the previous studies<sup>15-16</sup>. The most common hemorrhagic manifestations in our study was Hematemesis and Malena. But few Petechiae and Gum bleeding were also reported. However, hematemesis was the most common manifestations in the study by Narayanan et al<sup>17</sup>, whereas epistaxis was most common in the study by Faridi et al<sup>18</sup>. The tourniquet test in our study was

positive in 10% of cases and was much lower compared to the previous studies<sup>19</sup>. The tourniquet test did not correlate well with bleeding manifestations or with thrombocytopenia, similar to the finding reported by Wali et al<sup>19</sup> and Narayanan et al<sup>17</sup>.

About 30.0% of the patients had platelet count  $\leq$  50000 and hematocrit more than 40 was observed in 12.0% patients. Bleeding manifestations were highly variable and did not always correlate with the platelet counts as it occurred in 23.0% of cases with normal platelet counts.

AKI appears to be a common severe dengue consequence that raises the morbidity and mortality of those who are infected<sup>20,21</sup>. Laoprasopwattana et al<sup>22</sup> reported an incidence of 0.9% among children in Thailand, and Lee et al<sup>23</sup> reported an incidence of 3.3% among adults in Taiwan. But in this study we reported only 0.5% cases. Acute parotitis is a common clinical symptom of numerous autoimmune, metabolic, viral, and drug-related diseases, however it typically occurs bilaterally<sup>24</sup>. We described an uncommon occurrence of unilateral parotid gland involvement following dengue illness among 2.5% cases. Due to their quick onset, acute infections that involve the parotid glands can be mistaken for the measles.

The study has some limitations. Due to insufficient data collection and inadequate data curatio n, we first had a small sample size. Due to the fact that data on pediatric dengue cases were gathered concurrently with adult cases from the multifunctional tertiary care facilities, our data collection was constrained.

## Conclusion

In conclusion most of the children presents with high grade, continued fever and characteristic rashes followed by vomiting and abdominal pain. Gastrointestinal symptoms were the most common presentation along with fever. Atypical manifestations were few. Some are suffering from severe form of dengue either haemorrhage or shock. Strict supervision and also surveillance is needed.

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## Conflict of Interest

The authors have no conflicts of interest to disclose.

## Financial Disclosure

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**Authors' contributions**

Arifa Akram, Shaidur Rahman conceived and designed the study, analyzed the data, interpreted the results; Arifa Akram contributed to the analysis of the data, interpretation of the results and critically reviewing the manuscript; Lubana Akram wrote up the draft manuscript; Uzzal Kumar Ghosh, MF Abiduzzaman involved in the manuscript review and editing; All authors read and approved the final manuscript.

**Data Availability**

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

**Ethics Approval and Consent to Participate**

Ethical approval for the study was obtained from the Institutional Review Board. As this was a prospective study the written informed consent was obtained from all study participants. All methods were performed in accordance with the relevant guidelines and regulations.

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