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# Atypical Clinical Features in Paediatric Dengue Patients: Is There a Changing Trend?

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## Abstract

**Background**: Dengue fever is the most rapidly spreading mosquito borne viral disease worldwide. It is estimated that the incidence has increased 30-fold over the last five decades. Recently, the reappearance of dengue in the pediatric population is a matter of concern among pediatricians, especially due to the presence of atypical features, leading to delayed diagnosis. There are few studies regarding the changing trend of paediatric dengue patients due to under reporting of the cases. **Material & Methods:** This prospective study was conducted among forty-five paediatric dengue patients below 15 years of age (n=45) at MH Samorita Hospital & Medical College, Dhaka over a period of 6 months from July 2021 to December 2021. Neonates and patients with co-infection were not included in the study. All clinical and laboratory details were collected during their hospital stay in a structured questionare form. **Results:** Forty-five paediatric dengue patients below 15 years of age were enrolled in the study (n=45). Out of the 45 cases 35 patients were non-severe dengue (undifferentiated fever, dengue fever with warning signs, and dengue fever without warning signs) and 10 patients were of severe dengue (DHF and DSS) according to WHO guidelines. The male to female ratio was 1.6: 1 in our study group. The majority of the cases 25 (55.5%) were within 6 to 10 years of age. Patients having features of severe dengue were also seen mostly (17.7%) in this age group. The mean age of hospitalized patients was 8.9 years. In our study there were 16 patients (35.6%) with classical dengue fever, 23 (51.1%) patients with dengue hemorrhagic fever without shock and 6 patients (13.3%) with features of dengue shock syndrome. Atypical clinical features were seen in 17 cases (37.8%). The most common atypical features found in twelve children were acalculous cholecystitis (26.7%). Renal impairment and hepatitis were present in 17.8% and 13.3% of patients. Among neurological manifestations two patients (4.4%) developed impaired consciousness and one patient (2.2%) had seizure. **Conclusion:** Atypical manifestations of DF can be fatal in many paediatric patients. There should be a high index of suspicion among clinicians for timely detection and management of atypical manifestation of severe dengue infection to prevent mortality.

**Keywords**:- Dengue, Infection, Hemorrhage, Shock.

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## INTRODUCTION

Dengue fever is the most rapidly spreading mosquito borne viral disease worldwide. It is estimated that the incidence has increased 30-fold over last five decades as a result of growing population, rapid urbanization and lack of appropriate sanitary measures, proliferation of mosquitoes and subsequent dengue infections.[1] The clinical spectrum of Dengue fever range from asymptomatic infection to undifferentiated febrile illness, classical Dengue fever (DF), dengue hemorrhagic fever (DHF), dengue shock syndrome ( DSS) , and expanded dengue syndrome which include neurological, hepatic, renal, cardiovascular and other isolated organ involvement.[1] According to the WHO dengue virus infection is classified as; probable dengue, dengue with warning signs and severe dengue (dengue with severe plasma leakage, severe bleeding, or multi-organ failure).[2] Dengue fever in the children has recently created concern among pediatricians, especially due to the increased incidence of atypical features, leading to delayed diagnosis and increased mortality. Nearly 95% of paediatric dengue cases are children aged less than 15years.[3] As their hemodynamic system is immature, children specially infants, are prone to develop severe dengue disease.[4,5] According to National surveillance data from Asian countries infants and children aged 4–9 years are consistently at the highest risk for severe dengue disease.[5] It is essential that clinical presentations of dengue in the pediatric population are categorized into typical and atypical clinical features for early detection of severity. Early detection and appropriate management of severe dengue can reduce dengue-associated mortality.[6] The first major dengue outbreak in Bangladesh occurred in 2000. In 2019 there was another outbreak where over 100,000 people suffered with a high incidence of dengue shock syndrome (DSS) and secondary dengue infections.[7] With increase in epidemics of dengue, atypical manifestations are also on the rise. In many studies clinical presentations of dengue in the pediatric population have been described but detailed profiling of atypical clinical features of dengue in the pediatric population is lacking. In this study we describe the unusual (atypical) manifestation of dengue fever among paediatric patients along with their clinical profile at a tertiary care hospital during the recent outbreak in 2021.

## MATERIAL AND METHODS

This prospective study was conducted at MH Samorita Hospital & Medical College, Dhaka over a period of 6 months from July 2021 to December 2021. All probable dengue cases aged 15 years and below in whom diagnosis was confirmed by enzyme linked immune-absorbent (ELISA) based dengue antigen detection test (NS1 antigen) and antibody detection test immunoglobulin M capture ELISA (MAC- ELISA) were included in the study. Neonates and patients with co-infection and fever lasting for more than 10 days were excluded from the study. Detailed history was obtained, physical examination and baseline investigations were done and the children were followed-up till discharge. All clinical and laboratory details were carefully studied and noted in a structured questionnaire during hospital stay. Data of atypical neurological, gastrointestinal, respiratory, cardiovascular, renal, hematologic manifestations in dengue

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fever were recorded and analyzed. The laboratory investigations such as complete blood count, liver function test, renal function test, chest X-ray, and ultrasonography were analyzed. Institutional approval for the study and informed consent from the patients were taken.

## RESULTS

Forty-five paediatric dengue patients below 15 years of age were enrolled in the study (n=45). Due to presence of co-infection with UTI in one patient and enteric fever in another, two cases were excluded from 47 dengue cases admitted during the study period. Diagnosis was confirmed by either a positive dengue NS1 within three days of onset of fever or by positive dengue IgM antibody done after 5 days of onset of fever. Out of the 45 cases 35 patients were non-severe dengue (undifferentiated fever, dengue fever with warning signs, and dengue fever without warning signs) and 10 patients were of severe dengue (DHF and DSS) according to WHO guidelines. There were 28 male (62.2%) and 17 females (37.7%). The male to female ratio was 1.6: 1 in our study group. Non severe dengue and dengue with atypical features were seen higher in males and severe dengue was found higher in females. The majority of the cases 25 (55.5%) were within 6 to 10 years of age. Patients having features of severe dengue were also seen mostly (17.7%) in this age group. The mean age of hospitalized patients was 8.9 years. 24 patients (53.3%) stayed in the hospital for 4 to 6 days. Only 9 (20.6%) patients stayed up to 3 days and 12 (26.6%) patients needed hospital admission for more than 6 days. The mean duration of hospital stay was 5.5 days. [Table 2]

In our study there were 16 patients (35.6%) with classical dengue fever, 23 (51.1%) patients with dengue hemorrhagic fever without shock and 6 patients (13.3%) with features of dengue shock syndrome. [Figure 1] Atypical clinical features were seen in 17 cases (37.8%). The most common atypical features found in twelve children were acalculous cholecystitis (26.7%). Renal impairment and hepatitis were present in 17.8% and 13.3% of patients. Among neurological manifestations two patients (4.4%) developed impaired consciousness and one patient (2.2%) had seizure. Acute pancreatitis was apparent in 2 (4.4%) patients and pericarditis was evident in 2 (4.4%) patients. Only one patient with dengue fever developed myositis and another child had parotitis during the febrile phase. [Figure 2]

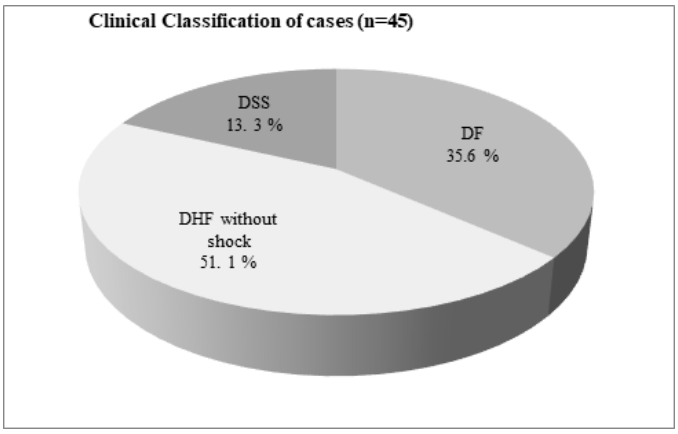


**Figure 1:** Figure showing distribution of cases according to the clinical classification of dengue fever.

Patients with dengue fever presented with following features during admission with decreasing order of frequency – fever (100%), headache (46.6%), abdominal pain (40%), right hypochondriac tenderness (31%), ascites (31%), lethargy (26.6%), hypotension (24.4%), myalgia

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(22.2%), itching (22.2%), cough (20%), right sided pleural effusion (17.7%) and shock (17.7%). Among the patients 15.5 % had with persistent vomiting, pharyngeal congestion, restlessness, conjunctival congestion and arthralgia. 11.1 % of the patients had macular rash, retro-orbital pain, diarrhea and oliguria. Bilateral pleural effusion was present in 3 (6.6%) patients, 3(6.6%) patients had hepatomegaly and 2 (4.4%) patients had splenomegaly. [Table 2]

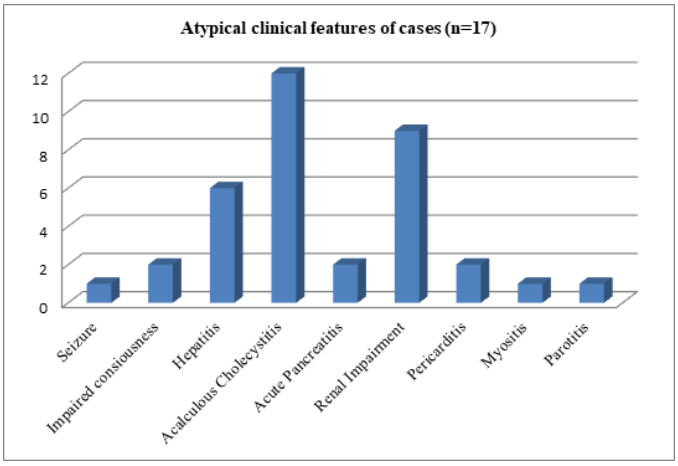


**Figure 2:** Figure showing frequency of atypical manifestations among dengue patients associated with expanded dengue syndrome.

**Table 1:** Epidemiological characteristics of patients with dengue fever (N=45)

| Variables | Categories | n= (%) | Dengue Fever ± warning signs (%) | Severe Dengue (%) | Stats |
|---|---|---|---|---|---|
| Age | 1-5 years | 5 (11.1) | 5 (11.1) | 0 | Mean age 8.9 years |
| | 6-10 years | 25 (55.5) | 17 (37.7) | 8 (17.7) | |
| | 11-15 years | 15 (33.3) | 13 (28.8) | 2 (4-4) | |
| Sex | Male | 28 (62.2) | 24 (53.3) | 4 (8.8) | Male : Female 1.6 : 1 |
| | Female | 17 (37.7) | 11 (24.4) | 6 (13.3) | |
| Duration of hospital stay | < 4 days | 9 (20.6) | 5 (11.1) | 0 | Mean duration 5.5 days |
| | 4-6 days | 24 (53.3) | 22 (48.8) | 1 (2.2) | |
| | > 6 days | 12 (26.6) | 8 (17.7) | 9 (20.0) | |
| Atypical manifestation | | 17 (37.7) | 13 (28.8) | 4 (8.8) | |

**Table 2:** Clinical profile of patients with dengue fever (N=45)

| Clinical Variables | Numbers | Percentage (%) |
|---|---|---|
| Fever | 45 | 100 |
| Rash | 5 | 11.1 |
| Conjunctival congestion | 7 | 15.5 |
| Coryza | 3 | 6.6 |
| Headache | 21 | 46.6 |
| Retro orbital pain | 5 | 11.1 |
| Myalgia | 10 | 22.2 |
| Arthralgia | 7 | 15.5 |
| Lethargy | 12 | 26.6 |
| Itching | 10 | 22.2 |

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| | | |
|---|---|---|
| Bleeding from mucosa | 4 | 8.8 |
| Cough | 9 | 20.0 |
| Respiratory distress | 2 | 4.4 |
| Pharyngeal congestion | 7 | 15.5 |
| Right sided pleural effusion | 8 | 17.7 |
| Bilateral pleural effusion | 3 | 6.6 |
| Persistent vomiting | 7 | 15.5 |
| Diarrhea | 5 | 11.1 |
| Abdominal pain | 18 | 40.0 |
| Right hypochondriac tenderness | 14 | 31.1 |
| Hepatomegaly | 3 | 6.6 |
| Spleenomegly | 2 | 4.4 |
| Ascites | 14 | 31.1 |
| Restlessness | 7 | 15.5 |
| Hypotension | 11 | 24.4 |
| Oliguria | 5 | 11.1 |
| Shock | 8 | 17.7 |

## DISCUSSION

In this study there was a distinct higher incidence observed among the younger age group (6-10 years) accounting for (55.5%) of the total cases with a male preponderance and the male to female ratio was 1.6: 1. Patients having features of severe dengue were also seen mostly (17.7%) in this age group. The mean age of hospitalized patients was 8.9 years. In a study by Choudhury,[8] the commonest age group was above 10 years with male predominance and male to female ratio was 2:1. Similarly, male predominance was observed in other studies like Agarwal et al,[9] Narayana et al,[10] and Gomber et al.[11] All patients in this study were from urban area which was also noticed in a study by Srinivasa,[12] though WHO has reported shift of Dengue to rural areas. A seasonal pattern was observed in this study and the highest incidence was recorded in the monsoon (May-August) and the postmonsoon (September-December) seasons during the one year study period. Wongkoon S et al,[13] have also described the seasonal pattern of Dengue, mostly in the rainy season due to abundance of mosquito breeding in the season. In a case control study in Thailand,[14] the primary Dengue infection was noticed in (9.5%) and (11.4%) in case and control group respectively, whereas in this study, (77.7%) cases having no previous history of Dengue infection. Fever was noted among (100%) patients. Macular rash and vomiting were the next common symptoms followed by abdominal pain representing (11.1%), (15.5%) and (40%) respectively. Agarwal et al [9] in their study in Delhi showed fever, abdominal pain and vomiting as the commonest symptoms. In one more study by Wang et al,[15] vomiting (60.5%) and abdominal pain (32.5%) were the commonest presenting symptoms in Dengue

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infected children. Headache was seen in (46.6%) studied children whereas about (28.8%) observed in Narayanan et al,[10] (77%) in Kalyanarooj et al,[16] and (22%) in Ratageri et al studies.[17] In our study there were 16 patients (35.6%) with classical dengue fever, 23 (51.1%) patients with dengue hemorrhagic fever without shock and 6 patients (13.3%) with features of dengue shock syndrome. The most common bleeding manifestation noted in study by Srivastava and Ahmed et al which was similar to this study.[18,19] In our study right hypochondriac tenderness (31%), ascites (31%), lethargy (26.6%), hypotension (24.4%), myalgia (22.2%), itching (22.2%), cough (20%), right sided pleural effusion (17.7%) and shock (17.7%). In another study by Ratageri et al,[17] the common bleeding manifestations were GI bleeding (22%) and petechiae (18%). A study by Shubhankar Mishra,[20] detected (25.77%) cases having pleural effusion which is quite similar (17.7%) to our study. Among the patients 15.5 % had with persistent vomiting, pharyngeal congestion, restlessness, conjunctival congestion and arthralgia. 11.1 % of the patients had macular rash, retro-orbital pain, diarrhea and oliguria. Bilateral pleural effusion was present in 3 (6.6%) patients, 3(6.6%) patients had hepatomegaly and 2 (4.4%) patients had splenomegaly cases respectively whereas other studies showed hepatomegaly in (86.9%),[18] ascites (93.4%), pleural effusion (82.6%) and facial puffiness in (84.7%) study population. Setiwan et al,[21] and Mehdi SA et al,[22] noted (95%) and (60%) ascites in severe Dengue and (34%) and (17.7%) in mild Dengue cases respectively. Atypical clinical features were seen in 17 cases (37.8%). The most common atypical features found in twelve children were acalculous cholecystitis (26.7%). Renal impairment and hepatitis were present in 17.8% and 13.3% of patients. Among neurological manifestations two patients (4.4%) developed impaired consciousness and one patient (2.2%) had seizure. Acute pancreatitis was apparent in 2 (4.4%) patients and pericarditis was evident in 2 (4.4%) patients. Only one patient with dengue fever developed myositis and another child had parotitis during the febrile phases. Other than few case reports, there are no such prospective studies from this part of the country in the previous literature on increasing incidence of such varied neurological manifestations among dengue cases in pediatric population.[23] As of now, three pathogenic mechanisms are there to explain the different neurological complications associated with dengue infection.[24] Some workers suggest that neurological manifestations are secondary to metabolic or hematological derangement related with the disease process itself, where the cerebrospinal fluid (CSF) analyses, including measurements of protein, glucose, and cell count, are usually normal.[25] In a study by Mishra tourniquet test was found to be negative in majority of the cases whereas studies in other countries especially Southeast Asian countries reported tourniquet test positivity as the commonest bleeding manifestation.[20]

## CONCLUSIONS

Atypical manifestations can sometimes present with Classical dengue fever. In some cases it can be an isolated manifestation or can have warning signs as well. This should raise a concern among the treating physians to provide better management of patients. Dengue fever presenting with atypical features

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particularly with neurological manifestations can be fatal. Further studies on patterns of paediatric dengue infection in different regions would help clinicians and health administrators to make more informed and evidence-based health planning decisions.

**Limitation**

This study with a limited number of samples which can't reflect the scenarios of whole country.

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