

Gastrointestinal and Other Atypical Presentations of Dengue Fever: A Multicenter Study in the Northern Region of Bangladesh

MS Hossain¹, M Nuruzzaman², Maknunnahar³, MMU Anwar⁴, MS Alam⁵, MN Ali⁶, AHMS Rana⁷, MM Rashid⁸, KM Alam⁹, MM Alam¹⁰

Abstract

Background: Dengue is a global problem, but has a greater impact on developing and tropical countries. Dengue is surging due to increasing Aedes mosquitoes in overcrowded areas. Atypical presentations of dengue are a challenge during management. That's why we intended to determine the pattern, prevalence, and outcome of gastrointestinal and other atypical presentations of dengue fever during the 2023 epidemic in Bangladesh.

Materials and Methods: This was a multicenter hospital-based cross-sectional study held in two tertiary medical college hospitals in the northern part of Bangladesh: Rangpur Medical College Hospital and Dinajpur Medical College Hospital. All the patients who were admitted with laboratory-confirmed dengue cases from June 2023 to October 2023 were included in this study.

Results: Out of a total of 160 patients, majority were between 21-40 years of age (57%), and the predominant study subjects were male, 120 (75%). We found that 73 (45.6%) patients presented with gastrointestinal and atypical manifestations, while rest 87 (54.4%) patients had only classical presentation. The atypical manifestations are acute watery diarrhea (17.5%), acute acalculus cholecystitis (8.1%), ascites (4.4%), acute hepatitis (3.1%), pleural effusion (2.5%), pneumonia (2.5%), acute pancreatitis (1.3%), GIT bleeding (1.3%), Encephalitis (1.3%), meningitis and myocarditis.

Conclusions: Looking for these atypical features of dengue fever at least during the outbreak season of dengue may save health resources and many valuable lives.

Key words: Dengue fever, Outbreak, Gastrointestinal manifestations

Authors:

Md. Shakhawat Hossain, MBBS, MD (Gastroenterology), Assistant Professor, Department of Gastroenterology, Rangpur Medical College, Rangpur, Email: drshparvez@gmail.com.

Md. Nuruzzaman, MBBS, FCPS (Medicine), Associate professor, Department of Medicine, Dinajpur Medical College, Dinajpur, Email: drzaman78@gmail.com.

Maknunnahar, BDS, MPH, Ph. D Research Fellow, School of Science and Technology, Bangladesh Open University, Gazipur, Email: drauna89@gmail.com.

Md. Mahfuj-Ul-Anwar, MBBS, FCPS (Medicine), Assistant Professor, Department of Medicine, Rangpur Medical College, Rangpur, Email: mahfujrnc@gmail.com.

Md. Shafiul Alam, MBBS, FCPS (Medicine), FCPS (Gastroenterology), Associate Professor, Department of Medicine, Rangpur Medical College, Rangpur, Email: shafiulssmc23@gmail.com.

Md. Naushad Ali, MBBS, FCPS (Medicine), MD (Gastroenterology), Associate Professor, Department of Gastroenterology, Rangpur Medical College, Rangpur, Email: dr.naushadali74@gmail.com

Abu Hena Md. Shohel Rana, MBBS, MD (Gastroenterology), Assistant Professor, Department of Gastroenterology, Rangpur Medical College, Rangpur, Email: shohel4gastro@gmail.com

Md. Mamunur Rashid, MBBS, MD (Gastroenterology), Assistant Registrar, Department of Gastroenterology, Rangpur Medical College, Rangpur, Email: drshparvez@gmail.com

Khondoker Monirul Alam, MBBS, FCPS (Medicine), FCPS (Gastroenterology), Consultant (Medicine), Rangpur Medical College, Rangpur, Email: russelrnc35@gmail.com.

Md. Makhsumul Alam, MBBS, MD (Gastroenterology), Professor, Department of Gastroenterology, Rangpur Medical College, Rangpur, Email: makhsumulalam@hotmail.com.

Corresponding Author: Md. Shakhawat Hossain, MBBS, MD (Gastroenterology), Assistant Professor, Department of Gastroenterology, Rangpur Medical College, Rangpur; Email: drshparvez@gmail.com; mobile-+8801973223892

Introduction:

Dengue fever (DF) is a vector-borne disease, transmitted by various species of female Aedes mosquitoes. Amazingly, Bangladesh has achieved tremendous success in controlling communicable diseases at present. But, it is also true that we are passing a decade of up surging dengue and other vector-borne diseases like Chikungunya and Zika virus. In South East Asia, particularly in Bangladesh, this emerging disease causes a huge social and financial burden, as well as cuts the ongoing health budget.¹ Earlier this year, WHO mentioned dengue fever as a potential threat among ten diseases for 2019, and recent outbreaks in many countries confirm this observation. The WHO on 2008 proposed a new classification of DF. This revised classification divides dengue into three types: 1) Dengue without warning signs (D-W), 2) Dengue with warning signs (D+W), and 3) Severe dengue fever.^{2,3} Classically, dengue cases presented as either asymptomatic or fever, body aches, and malaise, like other viral illnesses. But about one-third of cases may develop severe complications such as dengue hemorrhagic fever and dengue shock syndrome. However, it may present with the involvement of other systems such as gastrointestinal, neurological, renal, respiratory, cardiac, or other systems.^{4,5} Dengue clinical features vary in presentation and extension of disease according to age, geography, the season of an epidemic, and host factors. In the few recent outbreaks, it was observed that new and atypical features are increasing.⁶ So, global awareness regarding the atypical manifestation of dengue fever is a burning issue for early diagnosis and adequate management, as well as to prevent unwanted death. This study aimed to determine the pattern, prevalence, and outcome of gastrointestinal (GI) and other atypical presentations of dengue fever during the 2023 epidemic in Bangladesh to enrich our current management strategy.

Materials and Methods:

This was a descriptive type of cross-sectional study held in two tertiary-level Medical College Hospitals, Rangpur Medical College Hospital and Dinajpur Medical College Hospital, located in the northern part of Bangladesh.

All the patients who were admitted with laboratory-confirmed dengue cases from June 2023 to October 2023 were included in this study. Dengue patients with pregnancy, bleeding disorders, viral hepatitis, malaria, and leptospirosis were excluded from the study to maintain uniformity. After taking a detailed history and clinical examination by a respective physician or focal persons few investigations were given to patients. Complete blood count, RBS, Serum creatinine, Liver function test- serum bilirubin, ALT, AST, alkaline phosphatase were done for all patients. Ultrasound of the Abdomen was done for patients who presented with abdominal pain. Chest X-Ray and ECG were done for patients who complained of chest pain or dyspnea. CSF examination, CT scan/MRI of the brain was done for patients who presented with altered consciousness or focal neurological deficits.

All patients were reviewed and assessed daily for any new changes till discharge from the hospital. Data were collected using a self-structured and pretested questionnaire containing demographic variables, investigations, clinical manifestations, complications, and mortality. We included symptoms of DF as follows: 1) General symptoms; 2) Gastrointestinal symptoms; 3) Respiratory; 4) Cardiovascular; 5) Neurological; 6) Renal symptoms; and 7) Severe features. Data were analyzed by statistical software SPSS Version 15.0 (IBM Corp., Armonk, NY, USA). Statistical analyses were performed to determine: 1) the Frequency of different typical, gastrointestinal, and other atypical features of Dengue fever; 2) the Association of age and sex with atypical features; and 3) the Association of atypical features and hospital outcomes of admitted patients. All continuous variables were analyzed using Student's t-test, and categorical variables using the Chi-square test. P-values of < 0.05 were considered as significant. Ethical permission was taken from the respective authority of both Medical College hospitals.

Results:

In this multicenter study, 97 patients were from Rangpur Medical College Hospital, and the remaining 63 were from Dinajpur Medical College Hospital (Figure 1). Out of a total of 160 patients, majority of the patients were between 21-40 years of age (57%), and the predominant study subjects were male, 120 (75%).

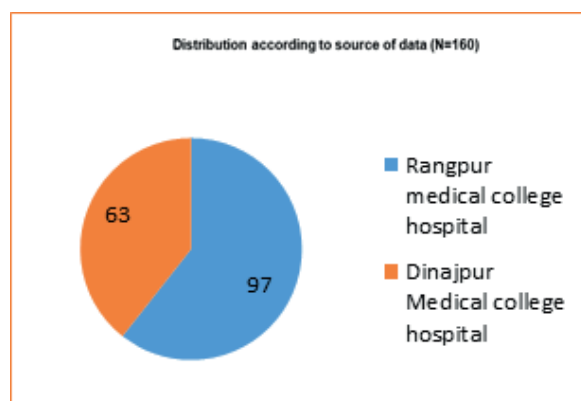


Figure 1: Distribution of the study subjects according to source of data (N=160)

Almost all patients had fever, and the majority of them experienced general symptoms. However, a good number of people also suffered from less common and easily overlooked symptoms that are not usual in dengue. Among GI symptoms, 33.1% had abdominal pain, 23.8% had diarrhea, and 08% from GIT bleeding. Moreover, 14.4% and 13.1 % had chest pain and cough, respectively. Only 04 % suffered from renal symptoms, and 20% of patients had severe features like spontaneous bleeding and shock. Figure 2 depicts the frequency of symptoms of the study subjects.

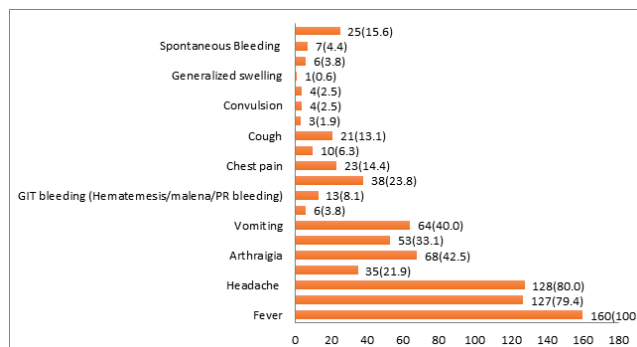


Figure 2: Distribution of patients according to clinical features (n=160)

In this epidemic, we noticed that more than half of the patients, 84 (52.5%) patients, have leucopenia, and 130 (81 %) patients have low platelet count. Among abnormal ultrasound reports of 21 patients (13.13%), 13 (8.12%) had acalculous cholecystitis, 07(4.37%) had ascites, and 01 patient (0.62%) had hepatomegaly. Only 04 (2.5%) patients showed pleural effusion on chest X-Ray reports. (Table-1)

Table 1: Distribution of patients according to investigation reports (n=160)

Investigation reports	Frequency (%)
Biochemical Reports	
ALT (elevated)	38 (23.8)
AST (elevated)	12 (7.5)
Blood urea (elevated)	8 (5.0)
S. Creatinine (elevated)	15 (9.4)
Electrolyte imbalance	15 (9.4)
Ultrasonogram of abdomen	
Normal	139 (86.87)
Acalculous cholecystitis	13 (8.1)
Hepatomegaly	1 (0.62)
Ascites	7 (4.37)
Chest X-Ray findings	
Normal	154 (96.3)
Pleural effusion	4 (2.5)
Not done	2 (1.3)

So, finally out of 160 dengue cases 73(45.60%) patients were presented with atypical manifestation and among them 45(61.64%) patients had severe dengue features. Figure-3 shows the frequency of typical and all atypical manifestations among the study subjects. Table 2 depicts the details of gastrointestinal and atypical manifestations of study populations.

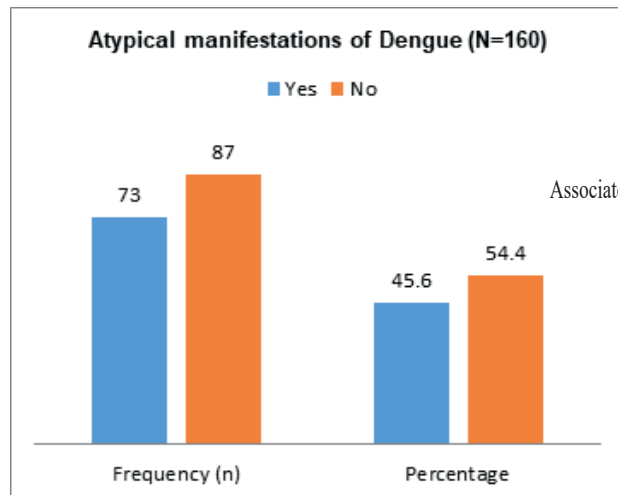


Figure 3: Distribution of patients according to frequency of typical and atypical manifestations (n=160).

Table 2: Distribution of patients according to gastrointestinal and other atypical manifestations (n=160)

Manifestations	Frequency (%)
Gastrointestinal	
Acute acalculous cholecystitis	13(8.1)
Acute diarrhea	28(17.5)
Acute hepatitis	5(3.1)
Ascites	7(4.4)
Acute pancreatitis	2(1.3)
GIT bleeding	2(1.3)
Respiratory	
Pleural effusion	4(2.5)
Pneumonitis	4(2.5)
Neurological	
Encephalitis	2(1.3)
Meningitis	1(0.6)
Transverse myelitis	1(0.6)
Myocarditis	1(0.6)
Severe manifestations	
DHF	20(12.5)
DSS	21(13.1)
DIC	3(1.9)
Sepsis	1(0.6)

In this study, 152 (95%) of those admitted patients were managed conservatively and 04 (2.5%) patients needed ICU support, and 04 patients needed medical intervention like dialysis. While 158 (98.8%) patients were cured completely and only 02 (1.2%) of them died during hospital admission.

Table 3: Association of Gastrointestinal and other atypical manifestations of Dengue with age and Gender (n=160)

Age	GI and other atypical manifestations		Total(160)	*p-value
	Yes	No		
<20	22 (51.1)	21 (49.1)	43 (26.9)	0.297
20 - 40	45 (47.36)	50 (53.64)	95 (59.4)	
41 - 60	5 (26.8)	14 (73.2)	19 (11.9)	
60 - 80	1 (33.33)	2 (66.66)	3 (1.9)	
Gender	GI and other atypical manifestations		Total(160)	p-value
	Yes	No		
Male	58 (48.33)	62 (52.66)	120 (75.0)	0.234
Female	15 (37.5)	25 (53.5)	40 (25.0)	

*Chi-square test was done to see the level of significance ($p \leq 0.05$).

There was no significant association found between atypical manifestations with age and gender in our study (Table. 3). The same results were also depicted regarding the association with the outcome of dengue patients in both places (Table 4).

Table 4: Association of Gastrointestinal and other atypical manifestations of Dengue with outcome (n=160)

Outcome	GI and other Atypical manifestations		Total(160)	*p-value
	Yes	No		
Cured	71 (44.3)	87 (55.7)	158 (98.8)	0.207
Died	2 (100)	0 (0.0)	2 (1.2)	

*Chi-square test was done to see the level of significance ($p \leq 0.05$).

Discussions:

Dengue fever has been reported from all regions of the world, including Africa, Southeast Asia, the Eastern Mediterranean, the Western Pacific, and the Americas.⁷ Dengue is a communicable disease like tuberculosis and malaria that is also increasing day by day, especially in developing countries. Its endemic area and epidemic seasons are also changing. The pattern of presentation and age group is also different from previous reports.⁸ All these changes made the diagnosis of dengue a notorious challenge, especially in the early periods of the disease. Delayed diagnosis is the cause of delayed lifesaving interventions and more loss of life. In this multicenter hospital-based study, we studied 160 dengue-infected patients admitted to both medical college hospitals within our study period. In this study, males were predominantly affected (75%), and nearly half (48.33%) of them presented with GI and other atypical manifestations. This study is very similar to a study conducted by Antony et al. conducted in India in 2014.⁸ Another study by Perez R et al. also shows that in Manila, Philippines, male were more affected by dengue fever than

female in 2011.⁹ Related study in Bangladesh by Azad AK et al. also found male predominance in 2006.¹⁰ However, A South American study conducted by Kaplan et al. showed in their study that females were more infected than males.¹¹

Our main focus was to identify the prevalence of gastrointestinal and atypical manifestations of dengue fever in Bangladesh. We found that 73 (45.6%) patients presented with atypical manifestations, while the rest 87 (54.4%) patients had only a classical presentation of dengue fever. This proves that nearly half of them had atypical presentations. Ahlawat et al. in India found 39.3% of their patients had atypical manifestations.¹² Acute watery diarrhea was the most common atypical feature in our study (17.5%). Others were acute acalculous cholecystitis (8.1%), ascites (4.4%), acute hepatitis (3.1%), pleural effusion (2.5%), pneumonia (2.5%), acute pancreatitis (1.3%), GIT bleeding (1.3%), Encephalitis (1.3%), meningitis and myocarditis. Natarajan et al. found 85.5% of patients have febrile diarrhea, 28.3% of patients have acalculous cholecystitis, and acute pancreatitis was observed in 1.8% of dengue patients.¹³ Diarrhea and acalculous cholecystitis were also common atypical features in a study by Azad et al. in Bangladesh.¹⁰ However, some other researchers found acalculous cholecystitis as the most common atypical presentation, such as Ahlawat et al.¹² 32.7%, Bhatti et al. 16.36%¹⁴, and Sai PMV et al. 85%.¹⁵ Acute diarrhea and pancreatitis in dengue fever may be due to widespread cytokine release in the body due to inflammatory response. Acalculous cholecystitis may be due to cholestasis and cystic duct spasm.¹⁶

Neurological manifestations are also not uncommon in dengue fever. Altered consciousness, subdural hematoma, and signs of raised intracranial pressure have been reported in many studies. The other rare presentations are the weakness of limbs and cranial nerve palsies.^{17,18} Ahlawat et al. found 8.1% neurological presentation in their study.¹²

In our study, 1.2% of patients died, and all of them presented with atypical features of dengue. If we analyze dengue patients with only atypical features, 2.7% died and 97.3% recovered. A study by Antony et al. showed a case fatality rate of 1.2%, with 0.97% in males and 1.49% in females,⁸ which is very similar to ours.

Conclusions:

Dengue is a disease that has no drugs or vaccines yet to be invented. So, prevention of spread and early diagnosis is the mainstay of successful management. As it is a tropical disease, every year we face a surge of dengue at the beginning of the rainy season. This is our small effort to identify the rate of atypical manifestations of dengue infection, which are less common but easily overlooked by physicians. So, keeping in mind these atypical features of dengue fever at least during the peak season of dengue we may detect dengue fever early, save many lives and health resources.

Conflicts of interest: There is no conflict of interest.

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References:

1. Amin MMM, Hussain AMZ, Nahar K, Chowdhury IA, Murshed M, Chowdhury MA. Sero-diagnosis of dengue infections in four metropolitan cities of Bangladesh. *Dengue Bull.* 2000;24:29–33. Available from: <https://policycommons.net/artifacts/486926/searo-diagnosis-of-dengue-infections-in-four-metropolitan-cities-of-bangladesh/1461730/>
2. World Health Organization. Dengue: guidelines for diagnosis, treatment, prevention and control. New ed. Geneva: WHO; 2009. Available from: <https://apps.who.int/iris/handle/10665/44188>
3. Directorate General of Health Services (DGHS), Ministry of Health and Family Welfare (MOHFW), Bangladesh. National guideline for clinical management of dengue syndrome. 4th ed. Dhaka: Communicable Disease Control, DGHS; 2018. Available from: <https://drive.google.com/file/d/1Xzz6XsnBzAd8nyskk2EWX0kv7BwQ6ymL/view>
4. Khanna S, Vij JC, Kumar A, Singal D, Tandon R. Dengue fever is a differential diagnosis in patients with fever and abdominal pain in an endemic area. *Ann Trop Med Parasitol.* 2004 Oct;98(7):757–760. doi:10.1179/000349804X3153
5. Kyle JL, Harris E. Global spread and persistence of dengue. *Annu Rev Microbiol.* 2008;62:71–92. doi:10.1146/annurev.micro.62.081307.163005
6. Karim MN, Munshi SU, Anwar N, Alam MS. Climatic factors influencing dengue cases in Dhaka city: a model for dengue prediction. *Indian J Med Res.* 2012 Jul;136(1):32–39.
7. World Health Organization. Global strategy for dengue prevention and control 2012–2020 [Internet]. Geneva: WHO; 2012. p. 16–17 [cited 2023 Jan 26]. Available from: <https://apps.who.int/iris/handle/10665/75303>
8. Antony J, Celine TM. A descriptive study on dengue fever reported in a Medical College Hospital. *Sahel Med J.* 2014;17:83–6. doi:10.4103/1118-8561.140285.
9. Perez R. Males more prone to dengue than females – DOH. *Inquirer.net* [Internet]. 2011 Sep 6 [cited 2023 Jan 26]. Available from: <https://newsinfo.inquirer.net>
10. Azad AK, Mohammad H, Billal A, Saha AK, Ahmed T. Clinical presentation of dengue in 150 admitted cases in Dhaka Medical College Hospital. *J Med.* 2006;7(1):3–9. doi:10.3329/jom.v7i1.1355
11. Kaplan JE, Eliason DA, Moore M, Sather GE, Schonberger LB, Cabrera-Coello L, et al. Epidemiologic investigations of dengue infection in Mexico, 1980. *Am J Epidemiol.* 1983 Mar;117(3):335–43. doi:10.1093/oxfordjournals.aje.a113546
12. Ahlawat RS, Kalra T. Atypical manifestations of dengue fever in a recent dengue outbreak. *Ann Trop Med Public Health.* 2017;10:1448–1452. doi:10.4103/ATMPH.ATMPH_18_17.
13. Natarajan N, Cugati S, Tirupathi RP, Padmapriya N. Patterns and trends in atypical manifestations of dengue among inpatient adults in tertiary care teaching institute of South India. *Int J Contemp Med Res.* 2017;4(10):2152–2156. Available from: <https://www.ijcmr.com>
14. Bhatti S, Shaikh NA, Fatima M, Sumbhuani AK. Acute acalculous cholecystitis in dengue fever. *J Pak Med Assoc.* 2009 Aug;59(8):519–521.
15. Venkata Sai PM, Dev B, Krishnan R. Role of ultrasound in dengue fever. *Br J Radiol.* 2005 May;78(929):416–418. doi:10.1259/bjr/54704044
16. Premaratna R, Bailey MS, Ratnasena BG, de Silva HJ. Dengue fever mimicking acute appendicitis. *Trans R Soc Trop Med Hyg.* 2007 Jul;101(7):683–685. doi:10.1016/j.trstmh.2007.02.006
17. Gupta N, Srivastava S, Jain A, Chaturvedi UC. Dengue in India. *Indian J Med Res.* 2012 Sep;136(3):373–390.
18. Neeraja M, Lakshmi V, Dash PK, Parida MM, Rao PV. The clinical, serological and molecular diagnosis of emerging dengue infection at a tertiary care institute in southern India. *J Clin Diagn Res.* 2013 Mar;7(3):457–461. doi: 10.7860/JCDR/2013/4786.2798