



## Research article

## Dengue outbreak 2019: clinical and laboratory profiles of dengue virus infection in Dhaka city

Rudbar Mahmood<sup>a</sup>, Md. Shadly Benzadid<sup>a</sup>, Sophie Weston<sup>b</sup>, Ahmed Hossain<sup>a</sup>, Tanveer Ahmed<sup>c</sup>, Dipak Kumar Mitra<sup>a</sup>, Shakil Ahmed<sup>a,\*</sup><sup>a</sup> Department of Public Health, North South University, Dhaka, 1229, Bangladesh<sup>b</sup> British Heart Foundation Cardiovascular Epidemiology Unit, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK<sup>c</sup> Department of Cardiology, United Hospital Ltd, Dhaka, 1212, Bangladesh

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## ABSTRACT

**Background:** Dengue fever has been one of the most common mosquito-transmitted diseases in the world, affecting more than 128 countries in both tropical and subtropical regions. Bangladesh has been suffering from dengue outbreaks almost annually since 2000, and in 2019, Bangladesh faced the worst outbreak of dengue to date. This study aimed to provide clinical and biochemical profiles of Bangladesh's dengue-infected patients.**Methods:** This cross-sectional study was conducted from August through December 2019 in three tertiary private hospitals in Dhaka, Bangladesh. We collected information on demographic data, clinical characteristics, and laboratory profiles for 542 confirmed hospitalized acute dengue cases using a structured questionnaire.**Results:** The average age of the enrolled patients was 26.15 years, and about 50% of patients belonged to the age group of 20–40 years. The most frequent among the prevalent clinical symptoms were fever (93.1%), abdominal pain (29.5%), skin rash (25.3%), and diarrhea (19.7%). 316 patients had some complications, such as breathing problems (41.4%), pleural effusion (38.9%), gum bleeding (11.1%), etc. More than 90% of the patients showed seropositivity for the DENV-NS1 antigen.**Conclusions:** Over the last couple of years, dengue fever has become a major health issue for Bangladesh. To reduce the burden of this disease, timely diagnosis and prompt treatment are necessary. This analysis thus yields the clinical features, laboratory profiles, and seropositivity test results of dengue patients from Bangladesh. The research results may help clinicians understand the circumstantial diagnosis of dengue patients and facilitate early intervention.

## 1. Introduction

Dengue virus infection (DENV) is the most common mosquito-borne infectious disease worldwide. In more than 100 countries, dengue is considered an endemic disease. Around 2.5 billion people worldwide live in dengue-prone countries, and about 100 million new cases are reported annually [1]. The *Aedes aegypti* mosquito is the principal vector that transmits the dengue-causing virus. The pathogenic female *Aedes* mosquito transmits the virus to humans through bites and often acquires the virus when feeding on an infected person's blood. These mosquitoes breed in standing water, such as water tanks, puddles, old tires, and containers [2].

Over the past 50 years, dengue incidence has increased 30-fold, and Bangladesh has one of the highest burdens of dengue in the world [1],

[3]. Since 2000, Bangladesh has witnessed a dengue outbreak almost every year, with more than 3000 dengue cases in at least six of these annual outbreaks [4]. In 2019, more than 100,000 people in Bangladesh were hospitalized due to DENV infection, and among them, about 50% were from Dhaka City, the capital of Bangladesh [5]. 164 confirmed deaths due to dengue were reported by the Directorate General of Health Services (DGHS) in 2019 [5].

The signs and symptoms of dengue vary from non-specific febrile disease to classic dengue fever with hemorrhage and/or shock (Dengue Shock Syndrome) [6]. However, the earliest clinical features of the dengue are most commonly fever with nausea, vomiting, skin rash and body aches. Having said that, classic dengue fever is distinguished by rapid onset of high fever (up to 40 °C), extreme headache, nausea, and vomiting, severe joint and muscle pain, retro-orbital pain, and centrifugal

\* Corresponding author.

E-mail address: [sahmedshaon@gmail.com](mailto:sahmedshaon@gmail.com) (S. Ahmed).<https://doi.org/10.1016/j.heliyon.2021.e07183>

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maculopapular rash. On the other hand, the symptoms of the severe dengue develops 1–2 days after the fever disappears and the symptoms are tenderness and belly pain, minimum of 3 times vomiting in a day, epistaxis, hematemesis, melena, fatigue and restlessness [7], [8]. Most cases of dengue are self-limiting; however, if not treated and handled in the early stage of this disease, it can become a life-threatening condition [6]. The fatal emergency of the severe dengue could develop very rapidly i.e., within hours. Severe dengue causes internal hemorrhage and organ failure. The blood pressure of the patients drop severely and thus it causes shock. The dengue could also be responsible for pre-term birth, very low birth weight during pregnancy [9], [10]. The secondary dengue infection, old aged patients, high hematocrit values, low platelet count, and prolonged APTT (activated partial thromboplastin time) were identified as the potential risk factors for severe dengue fever. Thereby, these parameters demands emergency hospitalization to the patients [11,12,13]. Due to the rapid onset nature of the severe dengue, it is responsible for the hundreds of deaths of children and young adults in most of the Asian and Latin American countries of the world [1].

Thus, early diagnosis is crucial to prevent mortality due to dengue infection. Routine laboratory tests, i.e., complete blood count (CBC), blood culture, or serological examination, are used for differential and diagnostic confirmation. Usually, early diagnosis of dengue is based on the detection of NS1 antigen in the blood, as the IgM antibody can only be detected after the 6<sup>th</sup> day of the clinical manifestation of dengue [14]. However, clinical hints from history, physical examination, and routine laboratory tests are still relevant to diagnose dengue cases.

From the onset of fever, the blood profile of dengue patients starts to change. Usually, thrombocytopenia develops in 3–8 days and is followed by leukopenia and hemoconcentration due to plasma leakage [15]. Estimates suggest that dengue patients have an 87% rise in leukopenia as well as a positive tourniquet test in 52% of patients. Therefore, patients with acute febrile leukopenia and positive tourniquet tests were more likely to be diagnosed with dengue than influenza, enteroviruses, and leptospirosis [16]. For the accurate diagnosis and effective patient management, the precise clinical and laboratory profile is fundamental. So, this study attempts to clarify the clinical and laboratory profile of dengue cases, which are serologically confirmed in Bangladesh.

## 2. Materials and methods

### 2.1. Study design

This study was a prospective observational study performed in 3 private healthcare centers from August 2019 to November 2019 in Dhaka City. Dhaka was also the primary region of the dengue outbreak in 2019.

### 2.2. Study sites

This study was carried out in the inpatient department of 3 specialized tertiary private hospitals in Dhaka City; (a) Islami Bank Central Hospital, Kakrail Branch (b) Islami Bank Hospital, Motijheel Branch, and (c) Social Islami Bank Hospital, Panthapath Branch. All of these healthcare centers are located in the urban area of Dhaka District. All of these healthcare centers are non-teaching hospitals that had separate high dependency units (HDU), intensive care unit (ICU), enrich laboratory departments.

### 2.3. Study population

542 hospitalized dengue patients were recruited from the 3 participating study hospitals from August to December 2019. All patients had confirmed dengue based on NS1 (non-structural protein) antigen positivity. The hospitals were selected conveniently for data collection and due to their status as dengue specialized hospitals during the dengue outbreak. Admitted patients were carefully monitored, important clinical and laboratory details recorded regularly on a standard case report form. Clinical examination carried out meticulously including vital signs, skin

rashes, pleural effusion, breathlessness, ascites, hepatomegaly and splenomegaly etc. Patients were selected based on the laboratory confirmation of NS1 Ag or Anti-dengue IgM.

### 2.4. Inclusion and exclusion criteria

Patients who had an oral temperature  $\geq 100.4$  °F, <7 days of fever, and reported at least one particular symptom, i.e., headache, joint pain, backache, abdominal pain, vomiting, fatigue, anorexia, and diarrhea were recruited. Recruitment was done irrespective of patient age, gender, economic class, or ethnicity. Informed consent was taken from the patients who were not critically ill, and guardians provided assent for critically ill patients. Admitted patients who had a diagnosis other than the dengue were excluded from the study.

### 2.5. Blood sample collection and processing

3 mL of venous blood was collected from each patient by venipuncture. Blood was centrifuged, and plasma was inserted into EDTA tubes. Plasma aliquots were prepared and stored in cryovials at  $-20$  °C for subsequent analysis.

### 2.6. Laboratory test for dengue infection

Each of the patient's plasma was analyzed to detect the NS1 antigen. IgM antibodies were detected with the *Tell me fast*® Combo Dengue NS1-IgG/IgM Rapid Test (Biocan Diagnostics Inc. Canada). The analysis of the rapid dengue test was according to the manufacturer's guidelines. An indirect enzyme-linked immunosorbent (ELISA: EUROIMMUN diagnostics) assay was used to validate the IgM and IgG antibodies against the dengue virus. Confirmed acute dengue cases were defined as patients with samples positive for DENV NS1 protein alone or DENV NS1 protein with IgM antibodies or DENV NS1 protein with IgG antibodies against DENV and with febrile illness and at least one of the following symptoms: headache, backache, abdominal pain, joint pain, vomiting, anorexia, fatigue, or diarrhea. Routine hematological laboratory investigations such as complete blood cell count (CBC), hematocrit level were analyzed by an automated blood analyzer (Medonic M32M Cell Counter). Other biochemical tests like aspartate aminotransferase (AST), alanine transaminase (ALT) for liver function test, creatinine level, etcetera, were performed using an automated biochemistry analyzer (Vegasys).

### 2.7. Data collection

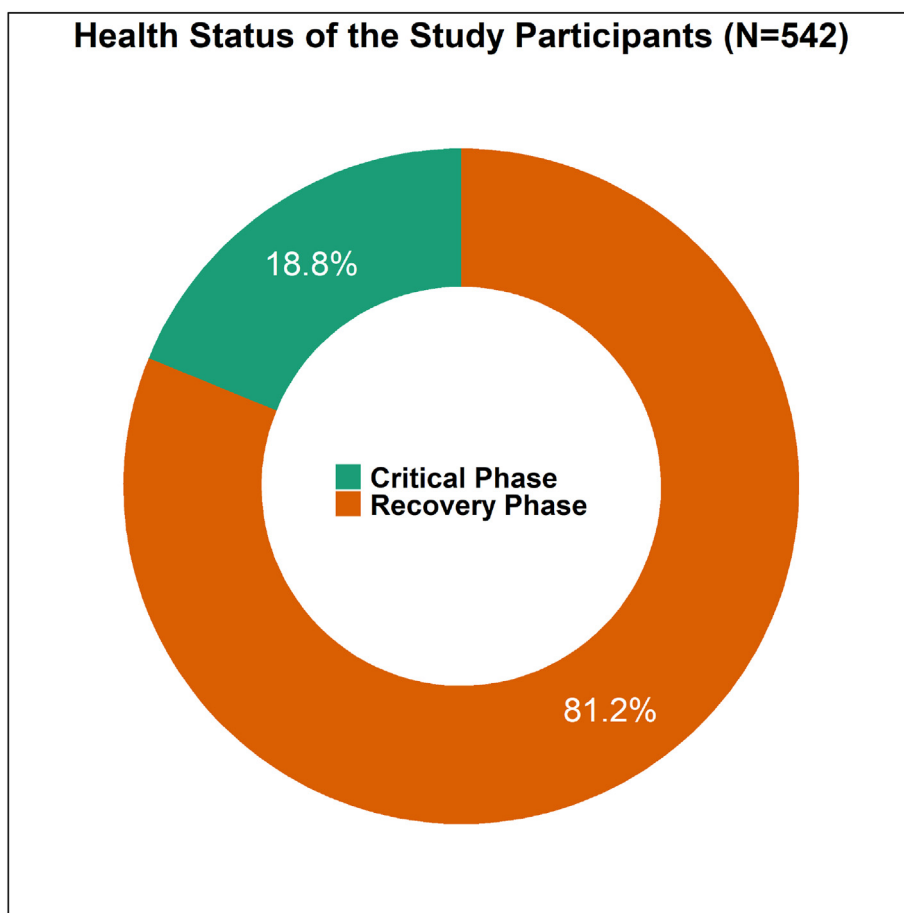
All the patients were clinically examined by a registered physician. Clinical features and lab parameters' data were administered by registered nurses using a structured questionnaire. The cutoff values for each investigation's results were based on reference ranges used by the laboratory.

### 2.8. Ethics approval and consent to participate

The ethical clearance of this study was obtained from the Ethics Review Committee (ERC) of North South University. Official permission from each of the study hospitals to carry out the study was obtained. Verbal and written consent was obtained from each of the patients. For patients who were in ICU or aged less than 16 years old, written assents were collected from the guardians.

### 2.9. Statistical analyses

Accuracy and completeness of the data were checked thoroughly. Data were entered from the questionnaire into Microsoft Excel 2013 edition. Data cleaning and analyses were done using statistical software R version 3.6.2. Descriptive statistics like mean, standard deviation, frequencies, and proportions were used to summarize the data.



\*Recovery Phase: The patients who had either less than three complications or no complication.

\* Critical Phase: The patients who were in the intensive care unit (ICU), and had more than 3 complications

**Figure 1.** Health status of the enrolled patients with DENV infection during data collection.

### 3. Results

In this study, a total of 542 patients were recruited, and all of them tested positive for seroprevalence of acute dengue virus (DENV) infection. All the listed patients were hospitalized and receiving treatment for DENV infection from the respective hospitals of our study. Our study enrolled patients from August 2019 to December 2019, which corresponds with the peak of the 2019 dengue outbreak in Dhaka City. Among the patients, 440 (81.2%) had been in the recovery phase, and 102 (18.8%) were in the critical phase (Figure 1).

#### 3.1. Socio-demographic information of the patients with DENV infection

Table 1 describes the socio-demographic data of the enrolled patient of this study. As shown in Table 1, out of 542 patients, 328 (60.5%) were male, and 214 (39.5%) were female. The mean ( $\pm$ SD) age of all patients was 26.15 ( $\pm$ 15.089). Approximately half of the patients (49.8%) were 20–40 years. 69 (12.7%) subjects of our study were children (<10 years), and 119 subjects (22.0%) were adolescents (10–19 years). Only 15.5% of the patients were >40 years. Of the 542 patients, around two-thirds (66.1%) had a nuclear family, and only 184 patients (33.9%) were from a joint family. The mean ( $\pm$ SD) number of family members patients have was 5.23 ( $\pm$ 2.3). Among all the patients, the majority had more than four family members (58.6%). Almost half of the patients were unemployed (49.6%), and only 29.2% of patients had a monthly income of more than 40,000 BDT (470 USD) [17]. A large portion of patients

lived in urban areas (69.9%), and only 30.1% of the patients hailed from either semi-urban or rural areas (Table 1).

#### 3.2. Clinical features of the patients with DENV infection

Table 2 presents the salient clinical features of the patients. A total of 505 (93.1%) patients had a fever, and the fever appears to be severe among the patients of our study. The mean ( $\pm$ SD) body temperature of the patients with fever was estimated to be 100.5 °F ( $\pm$ 2.1 °F). Myalgia was reported by 146 (26.9%) patients, and the pain was acute in nature. Maculopapular skin rash was ascertained in 137 (25.3%) patients, and 117 (21.6%) patients reported itchy skin. Nearly 30% of the patients complained of abdominal pain, and around 20% had suffered from diarrhea. Over 60% of the patients had nausea and vomiting problems, while 45.9% had been suffering from headaches. In addition to these clinical features, some less common signs and symptoms had been reported, such as retro-orbital pain in 27 (5.0%) patients, and conjunctival suffusion in 14 (2.6%) patients. In addition, some patients (6.9%) had other complaints such as anorexia, fatigue, and epistaxis (Table 2).

#### 3.3. Complications observed in patients with DENV infection

The complications that had arisen among the study patients due to the DENV infection are shown in Table 3a. Among the 542 patients, 316 (61.7%) had presented dengue complications. Hemorrhagic manifestations were found in 35 (11.1%) patients (16 male and 19 female), and all

**Table 1.** Socio-demographic characteristics of the patients with DENV infection.

Variables	Number of patients, n = 542	Percentage (%)
<b>Gender</b>		
Male	328	60.5
Female	214	39.5
<b>Age (in years)</b>		
	<b>Mean ± SD, 26.15 ± 15.089</b>	
<10	69	12.7
10–19	119	22.0
20–40	270	49.8
>40	84	15.5
<b>Family Type</b>		
Nuclear	358	66.1
Joint	184	33.9
<b>Number of family members</b>		
	<b>Mean ± SD, 5.25 ± 2.3</b>	
≤4	204	41.4
5	140	28.4
>6	149	30.2
<b>Occupation</b>		
Employed	273	50.4
Unemployed	269	49.6
<b>Residence</b>		
Semi-Urban/Rural	163	30.1
Urban	378	69.9
<b>Monthly Income (BDT)</b>		
	<b>Mean ± SD, 38531 ± 30184</b>	
≤20,000	102	33.1
20,001–40,000	116	37.6
≥40,000	90	29.2

of them mentioned gum bleeding. Pleural effusion was found among 123 (38.9%) patients (68 male and 55 female), and 131 (41.4%) patients (76 male and 55 female) reported having breathing problems. The ascitic fluid exudation was documented in 93 (29.4%) patients. Hepatomegaly and splenomegaly had been registered in 24 (7.6%) and 4 (1.3%) patients, respectively. 30 (9.5%) patients were suffering from multiple organ failure, and all of them were in life-threatening conditions (Table 3a & Table 3b).

### 3.4. Laboratory findings for the patients with the DENV infection

The laboratory findings for hospitalized patients with DENV infection of our study are shown in Tables 4 and 5. Table 4 illustrates the findings from routine laboratory tests, i.e., complete blood count (CBC), liver function test, etc., of the enrolled patients. The thrombocytopenia (Platelet count, <50,000/cumm) was the most common abnormality found in our patients. It was detected in more than two-thirds of the patients (73.2%). Data regarding leukocyte count could be retrieved from 417 patients. Of these 417 patients, 141 (33.8%) had been suffering from leukopenia (Leukocyte count <4000/cumm). The mean ( $\pm$ SD) value of the leukocyte count of the patients was 6263.3 ( $\pm$ 4828.9). Higher liver enzyme levels (AST, ALT, >45 IU/L) were identified in more than half (51.7%) of the patients. A marked increase in the hematocrit level (>45%) was identified among 279 (55.5%) out of 503 patients (Table 4).

Table 5 indicates the findings of serologic markers of acute DENV infection. It appears from Table 5 that 505 (93.2%) out of 542 patients were seropositive with the DENV-NS1 antigen alone. The dual seropositivity to DENV-NS1 plus anti-DENV IgM was detected among 503 (92.8%) out of 542 included patients. Only 38 patients (7.0%) showed dual seropositivity to DENV-NS1 plus anti-DENV IgG antibodies. However, a clinical diagnostic method, i.e., tourniquet test, had been applied to all the enrolled patients with DENV infection of this study, and 93 patients (17.2%) showed a positive result for the DENV infection (Table 5).

## 4. Discussion

Over the last couple of years, dengue has shown dynamic growth and has become a significant global burden. Dengue cases have risen in recent years as a result of increasing haphazard urbanization involving unregulated infrastructure development and inadequate sanitary facilities, ultimately leading to abundant mosquito breeding areas. In Bangladesh, dengue cases were recorded mostly in the monsoon period (50%) and in the post-monsoon season (49%) and from July to October, the peak season for dengue [18]. Like other Southeast Asian (SE) nations, Bangladesh is located in tropical and sub-tropical regions and has become an ideal habitat for the dengue vector and its increased transmission. Both vector types (*Aedes aegypti* and *Aedes albopictus*) were reported in Bangladesh during dengue outbreaks from 2000 to 2017 [19].

A snapshot of the dengue situation in Southeast Asia can provide an overview of how this emerging disease is causing a huge economic and social burden, especially in Southeast Asia and Bangladesh in particular. Like other low-and middle-income countries (LMICs), the current dengue situation in Bangladesh is causing economic burdens for our healthcare sector, as the allocation of the healthcare expenditure is steadily declining year on year [18]. At the same time, out-of-pocket expenditure (OOP) is raising (67%, the highest in the South - East Asia region) according to the findings of the Bangladesh National Health Accounts study (BNHA-V) [20].

Transmission of dengue peaks during the rainy season, in particular August to October, due to the optimal conditions for the *Aedes aegypti* mosquito [21]. Enrolled patients were selected in the present study during this peak time.

In the present study, the proportion of dengue fever was estimated to be greater in men than in women, which is consistent with the previous studies conducted in Saudi Arabia [22] and in Nepal [23] but contrasts with another study in Cameroon [24]. The differences between males and females might be explained by the fact that males are more exposed to virus-carrying mosquitoes either at the workplace or at the time of commuting to and from work. Most of the dengue cases (49.8%) occurred in the age group of 20–40 years in the present study. El-Gilany [22] found that dengue was most prevalent amongst people 16–44 years in Saudi Arabia, whereas M. Rahman *et al.* [25] reported the highest proportion of cases among 18–33 years age group in Bangladesh. Both studies indicate a higher occurrence in adults and are in line with our findings. We also noticed that young children under ten years of age were less affected (12.7%) by dengue fever. Similar observations were documented in Nepal [23], Nigeria [26] and Cameroon [24]. Lower prevalence of dengue infection among children than elderly people could be explained

**Table 2.** Clinical Features of patients with DENV infection.

Clinical Features	Number of patients, n = 542 (%)
Temperature	Mean ± SD, 100.5 °F ± 2.1 °F
Fever <sup>a</sup>	505 (93.1)
Abdominal Pain	160 (29.5)
Diarrhea	107 (19.7)
Skin Rash	137 (25.3)
Itching	117 (21.6)
Myalgia	146 (26.9)
Nausea/Vomiting	331 (61.1)
Headache	249 (45.9)
Conjunctival suffusion	14 (2.6)
Retro-Orbital Pain	27 (5.0)
Others <sup>b</sup>	37 (6.9)

Note:

<sup>a</sup> defined as a temperature  $\geq$ 100.4 °F.

<sup>b</sup> Anorexia, Fatigue and Epistaxis.



**Table 3a.** Complications experienced by patients with DENV infection.

Complications	Number of patients, n = 316 (%)
Bleeding	35 (11.1)
Pleural Effusion	123 (38.9)
Breathlessness	131 (41.4)
Ascites	93 (29.4)
Hepatomegaly	24 (7.6)
Splenomegaly	4 (1.3)
Seizures	10 (3.2)
Multiple Organ Failure	30 (9.5)

by the fact that children are given extra care by their parents. Also, all the participants of this study were recruited from the private health facilities and it could be assumed most of them belonged to the middle to high income group; therefore, most of the people lived in relatively clean and non-crowded area. This could also be relatable with the low infection rate among the children in this study.

The diagnosis of dengue requires either direct virus detection or the detection of specific antibodies, and rapid diagnosis is essential when considering the expeditious treatment of patients. Although the “gold standard” for diagnosis of dengue is the specific virus detection, isolation, and identification, the RT-PCR method (real-time reverse transcriptase-polymerase chain reaction) is gradually replacing this method because of its rapid diagnosis capability [27]. However, because of the relatively low cost and easy implementation in developing countries, the ELISA method for NS1 antigen or specific IgG and IgM antibodies detection (both single or combined) at present is a vital diagnostic tool compared to RT-PCR [24]. The additional advantage of combined DENV (NS1) with specific antibodies (IgM and IgG) is that they upgrade the rate of dengue diagnosis and bypass the false-positive results of a single test [28,29,30]. Hunsperger *et al* reported the sensitivity and specificity values of NS1 antigen method ranging from 60–75% and 71–80% respectively, and in the case of IgM anti-DENV ELISA the range was 96–98% and 78–91% respectively [31]. In another study V. Tricou *et al* [32] showed that the inclusion of IgM/IgG test result significantly increases the sensitivity of NS1 alone from 62.4% to 75.5% when NS1 and/or IgM was tested positive and 83.7% when NS1 and/or IgM and/or IgG became positive. Both single and combined NS1 antigen/IgG and IgM antibodies detection methods were used on 542 serum samples taken from febrile patients in the present study. We noticed that the Dengue cases were detected more in NS1 plus IgM antibodies test and NS1 antigen test alone compared to tourniquet test and NS1 plus IgG antibodies test in our study. These observations are in line with a previous study conducted by C. Palomares-Reyes *et al* [33] in Peru but in contrast with those of O. G. Oyero [34] in Nigeria and A. M. Ashshi *et al* [35] in Saudi Arabia.

The clinical profile of the enrolled dengue patients in this current survey shows that fever was the most common symptom (93.1%), which is consistent with studies from Pakistan [36], Saudi Arabia [22], and India [37]. Additionally, nausea-vomiting, headache, abdominal pain, myalgia, and skin rash were also identified among the patients.

Badreddine *et al*. [38] documented abdominal pain and vomiting as more common symptoms in their research. In another study, Abdel-Hady El-Gilany [22] found headache (74.60%) and myalgia (67.60%) as the most common symptoms after fever, suggesting a higher percentage than our study findings. Skin rash was identified in 25.3% of the dengue patients, which is similar to the previous study documented by El-Gilany [22] in Saudi Arabia and Ramabhata [37] in India. Ocular manifestations such as conjunctival suffusion and retro-orbital pain were less prevalent in this study than in other studies [22], [39]. It is noteworthy that, among the 542 participants included in this study, of them 37 patients who did not have any fever during the data collection session and 32 of them reported that they had a fever either on the previous day or a few hours earlier. This might be an effect of the antipyretic drugs that the patients were receiving.

In the current study, breathlessness (24.2%) was found as the most common complication of dengue, followed by pleural effusion (22.7%) and ascites (17.2%). V. Godbole [40] found pleural effusion and ascites in 11% of the dengue patients in India, which is comparatively lower than our results. Bleeding was noticed among 11% of the patients, which is higher than the current study findings (6.5%). Various studies have highlighted typical and atypical complications of dengue fever including acute respiratory distress syndrome (ARDS), dengue encephalopathy, encephalitis, lymphadenopathy, splenomegaly, myocarditis, anemia, multiple organ failure, hepatitis, febrile diarrhea, refractory shock, impaired consciousness, portal hypertension, appendicitis, pericardial effusion, myositis, acute kidney injury (AKI), and disseminated intravascular coagulopathy (DIC) [41, 42, 43].

After the evaluation of laboratory investigations in our study, results show that thrombocytopenia was the most common (73.2%) hematological abnormality among the patients. Similar findings were mentioned by Humayoun *et al*. [36] in Pakistan, R. P. Khetan *et al*. [44] in Nepal and R. Unnikrishnan *et al*. [45] in India. However, Kuna *et al*. [46] in Poland and A. Nigam [47] in India found thrombocytopenia among 20% and 60% of the patients, respectively, which is comparatively lower than the current study findings. Although the process of thrombocytopenia in dengue is the destruction of the bone marrow and the degradation of peripheral platelets, yet the precise cause is not yet understood [48]. Leukopenia was observed in the present study among 33.8% of the patients, which is higher than the findings of Kuna *et al*. (24.6%) [46]. Raised hematocrit level and higher AST, ALT, >45 IU/L level was also observed in our research, which is consistent with Humayoun *et al*. [36].

The clinical features along with the laboratory parameters that includes, the haematological and biochemical findings are very essential for the quick management of the dengue fever. The findings from this study indicated fever, nausea, vomiting, headache, abdominal pain, myalgia, skin rash, diarrhea are the most prevalent features. The high leukocyte count, low platelet count, raised AST, ALT value, and raised hematocrit value could be considered as vital parameters to diagnose dengue infected patients rapidly. However, More attention to DENV infection in Bangladesh is urgently required, as the peak period of dengue is coming soon. Furthermore, due to the heavy rainfall from April 2020 to May 2020 [49], [50], there is a possibility that new unexposed areas could be exposed to the dengue virus. To

**Table 3b.** Distribution of patients with complications according to their gender, febrile period, and lab parameters.

Complications due to DENV infection	Gender		Febrile Period		Platelet Count		Leukocyte Count		Liver Enzyme		Hematocrit	
	Male	Female	<3	>3	≤50,000	>50000	≤4000	>4000	Raised AST, ALT	Normal AST, ALT	Normal	Raised
Bleeding (n = 35)	16	19	3	17	13	22	17	18	19	16	21	14
Pleural Effusion (n = 123)	68	55	11	60	46	77	42	81	74	49	68	55
Ascites (n = 93)	44	49	8	66	31	62	41	52	52	41	54	39
Breathlessness (n = 131)	76	55	12	61	33	98	47	84	74	57	66	65
Seizures (n = 10)	7	3	1	4	3	7	6	4	1	9	6	4
Hepatomegaly (n = 24)	15	9	0	13	11	13	8	16	17	7	10	14
Multiple Organ Failure (n = 30)	16	14	5	19	6	24	15	15	15	15	17	30

**Table 4.** Lab parameters from the blood samples of patients with DENV infection.

Lab Parameters	Number of patients (%)
<b>Leukocyte Count (n = 417)</b>	
≤4000/cumm	141 (33.8)
>4000/cumm	276 (66.2)
<b>Platelet Count (n = 542)</b>	
<50000/cumm	397 (73.2)
≥50000/cumm	145 (26.8)
<b>Liver Enzyme (n = 542)</b>	
Raised AST, ALT <sup>a</sup>	280 (51.7)
Normal AST, ALT	262 (48.3)
<b>Hematocrit Value (n = 503)</b>	
Raised Hematocrit <sup>b</sup>	279 (55.5)
Normal Hematocrit	224 (44.5)

Notes:

<sup>a</sup> Raised AST, ALT >45 IU/L.<sup>b</sup> Raised Hematocrit >45%.**Table 5.** Pattern of seropositivity and clinical diagnostic method of patients with DENV infection.

Lab Parameters	Number of patients n = 542 (%)
<b>NS1</b>	
Positive	505 (93.2)
Negative	37 (6.8)
<b>NS1+IgM</b>	
Positive	503 (92.8)
Negative	39 (7.2)
<b>NS1+IgG</b>	
Positive	38 (7.0)
Negative	504 (93.0)
<b>Tourniquet Test</b>	
Positive	93 (17.2)
Negative	449 (82.8)

make matters worse, the two-month-long COVID-19 lockdown of Bangladesh slowed down the “Mosquito Eradication Campaigns” of the two city corporation areas of Dhaka [51]. As a consequence, there could be an increased number of dengue cases, and therefore a prompt and accurate diagnosis of dengue is essential. An explosive dengue outbreak amid the COVID-19 pandemic can be prevented, if local transmission could be identified promptly, followed by quick, effective vector control, and other public health measures. In this COVID-19 pandemic, the upcoming dengue fever epidemic will be an added burden for the country as both diseases share common clinical features, e.g., fever. Therefore, identifying, separating, and isolating dengue and COVID-19 patients will be difficult. It is our conviction that the data presented in this study could be a useful parameter for the early diagnosis of the dengue infection. Also, the findings would be helpful in demarcating the dengue infection from COVID-19. According to Ahmed et al. there is evidence of concurrent dengue and COVID-19 infections already, and they have suggested some dengue prevention strategies during the pandemic, such as i) a survey of *Aedes* mosquitoes should be performed along with the COVID-19 diligence; ii) the 2019 Wolbachia project of Bangladesh could be implemented to control the mosquito population; iii) the city corporations of all the divisions of Bangladesh should continue the destruction of the *Aedes* mosquito's breeding ground and spray insecticides in a regular manner; iv) by using the electronic and print media, awareness in the general population could be increased to prevent the mass spreading of the dengue virus infection. [52]; v) and, last but not the least, the government should take proper measures to reduce the cost for the

management of dengue not only in the government facilities, but also in the private health care facilities.

## Declarations

### Author contribution statement

Rudbar Mahmood: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

Shakil Ahmed: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Dipak Kumar Mitra: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Tanveer Ahmed: Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Ahmed Hossain and Md. Shadly Benzadid: Analyzed and interpreted the data; Wrote the paper.

Sophie Weston: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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### Data availability statement

Data will be made available on request.

### Declaration of interests statement

The authors declare no conflict of interest.

### Additional information

No additional information is available for this paper.

## References

- [1] World Health Organization, Dengue and Severe Dengue, 2020. <https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue>. (Accessed 15 May 2020).
- [2] H.F.L. Wertheim, P. Horby, J.P. Woodall, Atlas of Human Infectious Diseases, 2012.
- [3] P. Mutsuddy, et al., Dengue Situation in Bangladesh: an Epidemiological Shift in Terms of Morbidity and Mortality, 2019.
- [4] M.A. Mamun, J.M. Misti, M.D. Griffiths, D. Gozal, The dengue epidemic in Bangladesh: risk factors and actionable items, *Lancet* 394 (10215) (Dec 14 2019) 2149–2150. Lancet Publishing Group.
- [5] Directorate General of Health Services (DGHS) | Government of Bangladesh, Daily Dengue Status Report: 2019, 2019. Accessed: May 15, 2020. [Online]. Available: [https://www.dghs.gov.bd/images/docs/Notice/2019/dengue/Dengue\\_20191231.pdf](https://www.dghs.gov.bd/images/docs/Notice/2019/dengue/Dengue_20191231.pdf).
- [6] S.M. Halstead, Dengue and dengue hemorrhagic fever, in: *Handbook of Zoonoses*, Second Edition, Section B: Viral Zoonoses 11, CRC Press, 2017, pp. 89–99, 3.
- [7] I. Kautner, M.J. Robinson, U. Kuhnle, Dengue virus infection: epidemiology, pathogenesis, clinical presentation, diagnosis, and prevention, *J. Pediatr.* 131 (4) (1997) 516–524.
- [8] Centers for Disease Control and Prevention, Dengue symptoms and treatment, Nov 23 2020 (accessed Jan. 15, 2021), <https://www.cdc.gov/dengue/symptoms/index.html>.
- [9] Mayo Clinic, “Dengue Fever”, Nov 18 2020 (accessed Jan. 15, 2021), <https://www.mayoclinic.org/diseases-conditions/dengue-fever/symptoms-causes/syc-20353078>.
- [10] A. Wilder-Smith, E.E. Ooi, O. Horstick, B. Wills, Dengue, *Lancet* 393 (10169) (Jan 26 2019) 350–363. Lancet Publishing Group.
- [11] O. Wichmann, S. Hongsiriwon, C. Bowonwatanuwong, K. Chotivanich, Y. Sukthana, S. Pukrittayakamee, Risk factors and clinical features associated with severe dengue infection in adults and children during the 2001 epidemic in Chonburi, Thailand, *Trop. Med. Int. Health* 9 (9) (2004) 1022–1029. Sep.
- [12] M.A. Hegazi, et al., Risk factors and predictors of severe dengue in Saudi population in Jeddah, western Saudi Arabia: a retrospective study, *Am. J. Trop. Med. Hyg.* 102 (3) (2020) 613–621.
- [13] H.P. Tee, et al., Risk factors associated with development of dengue haemorrhagic fever or dengue shock syndrome in adults in Hospital Tengku Ampuan Afzan

- Kuantan - PubMed, Med. J. Malaysia 64 (4) (Dec 2009) 316–320. Accessed: Jan. 15, 2021. [Online]. Available: <https://pubmed.ncbi.nlm.nih.gov/20954558/>.
- [14] H.B.Y. Chan, C.H. How, C.W.M. Ng, Definitive tests for dengue fever: when and which should I use? Singap. Med. J. 58 (11) (Nov 2017) 632–635.
- [15] N. Ali, M. Usman, N. Syed, M. Khurshid, Haemorrhagic manifestations and utility of haematological parameters in dengue fever: a tertiary care centre experience at Karachi, Scand. J. Infect. Dis. 39 (11–12) (2007) 1025–1028.
- [16] C.J. Gregory, et al., Utility of the tourniquet test and the white blood cell count to differentiate dengue among acute febrile illnesses in the emergency room, PLoS Neglected Trop. Dis. 5 (12) (Dec 2011).
- [17] XE, “Convert USD/BDT. United States Dollar to Bangladesh Taka, 2020. <https://www.xe.com/currencyconverter/convert/?Amount=1&From=USD&To=BDT>. (Accessed 13 June 2020).
- [18] P. Mutsuddy, S. Tahmina Jhora, A.K.M. Shamsuzzaman, S.M.G. Kaisar, M.N.A. Khan, S. Dhiman, “Dengue situation in Bangladesh: an epidemiological shift in terms of morbidity and mortality”, Can. J. Infect. Dis. Med. Microbiol. 2019 (2019).
- [19] M. Ali, Y. Wagatsuma, M. Emch, R.F. Breiman, Use of a geographic information system for defining spatial risk for dengue transmission in Bangladesh: role for *Aedes albopictus* in an urban outbreak - PubMed, Am. J. Trop. Med. Hyg. 69 (6) (Dec 2003) 634–640. Accessed: Jan. 17, 2021. [Online]. Available: <https://pubmed.ncbi.nlm.nih.gov/14740881/>.
- [20] Ministry of Health and Family Welfare| Government of Peoples Republic of Bangladesh, “Bangladesh National Health Accounts 1997-2015 2015, 2018 no. September 2018, [Online]. Available: [https://www.researchgate.net/publication/327545331\\_Bangladesh\\_National\\_Health\\_Accounts\\_1997-2015\\_BNHA-V/citations](https://www.researchgate.net/publication/327545331_Bangladesh_National_Health_Accounts_1997-2015_BNHA-V/citations).
- [21] M. Anuradha, R. Dandekar, Screening and manifestations of seropositive dengue fever patients in Perambalur: a Hospital based study, Int. J. Med. Sci. Publ. Health 3 (6) (2014) 745.
- [22] A.H. El-Gilany, A. Eldeib, S. Hammad, Clinico-epidemiological features of dengue fever in Saudi Arabia, Asian Pac. J. Trop. Med. 3 (3) (Mar 2010) 220–223.
- [23] R.P. Khetan, et al., Profile of the 2016 dengue outbreak in Nepal, BMC Res. Notes 11 (1) (Jul 2018) 423.
- [24] S.B. Tchuandom, et al., A cross-sectional study of acute dengue infection in paediatric clinics in Cameroon, BMC Publ. Health 19 (1) (2019) 958.
- [25] M. Rahman, et al., First outbreak of dengue hemorrhagic fever, Bangladesh, Emerg. Infect. Dis. 8 (7) (2002) 738–740.
- [26] A.H. Fagbami, A. Fabiyi, T.P. Monath, Dengue virus infections in Nigeria: a survey for antibodies in monkeys and humans, Trans. R. Soc. Trop. Med. Hyg. 71 (1) (1977) 60–65.
- [27] A. Banerjee, U.K. Paul, A. Bandyopadhyay, Diagnosis of dengue fever: roles of different laboratory test methods, Int. J. Adv. Med. 5 (2) (2018) 395.
- [28] P. Dussart, et al., Evaluation of an enzyme immunoassay for detection of dengue virus NS1 antigen in human serum, Clin. Vaccine Immunol. 13 (11) (Nov 2006) 1185–1189.
- [29] S.M. Wang, S.D. Sekaran, Evaluation of a commercial SD dengue virus NS1 antigen capture enzyme-linked immunosorbent assay kit for early diagnosis of dengue virus infection, J. Clin. Microbiol. 48 (8) (Aug 2010) 2793–2797.
- [30] D. Hu, et al., Kinetics of non-structural protein 1, IgM and IgG antibodies in dengue type 1 primary infection, Virol. J. 8 (2011).
- [31] E.A. Hunsperger, et al., Evaluation of commercially available diagnostic tests for the detection of dengue virus NS1 antigen and anti-dengue virus IgM antibody, PLoS Neglected Trop. Dis. 8 (10) (2014).
- [32] V. Tricou, et al., Comparison of two dengue NS1 rapid tests for sensitivity, specificity and relationship to viraemia and antibody responses, BMC Infect. Dis. 10 (May 2010).
- [33] C. Palomares-Reyes, et al., Dengue diagnosis in an endemic area of Peru: clinical characteristics and positive frequencies by RT-PCR and serology for NS1, IgM, and IgG, Int. J. Infect. Dis. 81 (Apr 2019) 31–37.
- [34] O.G. Oyero, J.A. Ayukekbong, High dengue NS1 antigenemia in febrile patients in Ibadan, Nigeria, Virus Res. 191 (1) (Oct 2014) 59–61.
- [35] A.M. Ashshi, et al., Seroprevalence of asymptomatic dengue virus infection and its antibodies among healthy/eligible Saudi blood donors: findings from holy makkah city, Virol. Res. Treat. 8 (Feb 2017).
- [36] M.A. Humayoun, T. Waseem, A.A. Jawa, M.S. Hashmi, J. Akram, Multiple dengue serotypes and high frequency of dengue hemorrhagic fever at two tertiary care hospitals in Lahore during the 2008 dengue virus outbreak in Punjab, Pakistan, Int. J. Infect. Dis. 14 (SUPPL. 3) (Sep 2010) e54–e59.
- [37] S. Ramabhatta, S. Palaniappan, N. Hanumantharayappa, S.V. Begum, The clinical and serological profile of pediatric dengue, Indian J. Pediatr. 84 (12) (Dec 2017) 897–901.
- [38] S. Badreddine, et al., Dengue fever: clinical features of 567 consecutive patients admitted to a tertiary care center in Saudi Arabia, Saudi Med. J. 38 (10) (Oct 2017) 1025–1033.
- [39] H.K. Kapoor, S. Bhai, M. John, J. Xavier, Ocular manifestations of dengue fever in an East Indian epidemic, Can. J. Ophthalmol. 41 (6) (Dec 2006) 741–746.
- [40] V. Godbole, H. Rana, K. Mehta, F. Gosai, “Rising trend of cases of dengue fever admitted in a tertiary care hospital in Vadodara – a retrospective study, Apollo Med. 11 (4) (Dec 2014) 255–260.
- [41] D.E. Fujimoto, S. Koifman, Clinical and laboratory characteristics of patients with dengue hemorrhagic fever manifestations and their transfusion profile, Rev. Bras. Hematol. Hemoter. 36 (2) (2014) 115–120.
- [42] S. Pothapragada, B. Kamalakannan, M. Thulasigam, Clinical profile of atypical manifestations of dengue fever, Indian J. Pediatr. 83 (6) (Jun 2016) 493–499.
- [43] F.J. Carod-Artal, O. Wichmann, J. Farrar, J. Gascón, Neurological complications of dengue virus infection, Lancet Neurol. 12 (9) (Sep. 2013) 906–919. Lancet Neurol. 11 (1) (Jul 2018).
- [44] R.P. Khetan, et al., Profile of the 2016 dengue outbreak in Nepal, BMC Res. Notes 11 (1) (Jul 2018).
- [45] R. Unnikrishnan, P. Vijayakumar, B. Faizal, G. Paul, R. Sharma, Clinical and laboratory profile of dengue in the elderly, J. Fam. Med. Prim. Care 4 (3) (2015) 369.
- [46] K. A, et al., Clinico-laboratory profile of dengue patients returning from tropical areas to Poland during 2010–15, J. Vector Borne Dis. 53 (3) (2016).
- [47] A. Nigam, N. Gupta, P. Saxena, Clinical profile of dengue infection in pregnancy – a hospital-based study, Indian J. Med. Specialities 7 (4) (Oct 2016) 160–162.
- [48] V.J. Lee, D.C.B. Lye, Y. Sun, G. Fernandez, A. Ong, Y.S. Leo, Predictive value of simple clinical and laboratory variables for dengue hemorrhagic fever in adults, J. Clin. Virol. 42 (1) (May 2008) 34–39.
- [49] The Daily Star, Bangladesh Weather: More rain, nor'wester likely this week, Apr 25 2020 (accessed Jul. 02, 2020), <https://www.thedailystar.net/bangladesh-weather-more-rain-norwester-likely-this-week-1896607>.
- [50] The Daily Star, “Dengue amid Covid-19 Outbreak: with rain comes risk,” Dhaka, Apr 28 2020.
- [51] The Financial Express, Keeping Dengue in Mind, Apr 19 2020. Dhaka.
- [52] S. Ahmed, F. Tazmeem, First case diagnosed with both COVID-19 and dengue virus infections in Bangladesh: possible dengue prevention strategies amid COVID-19 outbreak, Public Health (May 2020).