



Clinico-Pathological Profiles of patients with Dengue Fever in Dhaka, Bangladesh

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Abstract

Background: Dengue viral infections are among the most important mosquito-borne diseases of the Bangladeshi subcontinent and have become a major global public health concern. The spread of the disease has led to increased recognition of atypical manifestations apart from the classical clinical features of dengue infection. This study aimed to provide clinical and biochemical profiles of Bangladesh's dengue-infected patients. **Material & Methods:** This cross-sectional study was conducted from January 2021 to December 2021 in different government and private tertiary care hospitals in Dhaka, Bangladesh. We collected information on demographic data, clinical characteristics, and laboratory profiles for 271 confirmed hospitalized acute dengue cases using a structured questionnaire. **Results:** A total of 271 patients were hospitalized and received treatment for DENV infection from the respective hospital of our research. Table 1 describes the socio-demographic data of the enrolled patients in the study. As shown in Table-1, out of 271 patients, 164(60.52%) were male and 107(39.48%) were female. Almost half of the patients (135(49.82%)) were from the age group 20-40 years. Of the 271 patients, around 179(66.05%) patients had a nuclear family and 92(33.95%) patients had a joint family. Lab parameters of the blood samples of patients with DENV infection; from the report of leukocyte count, 134(66.01%) patients had >4000/cumm and 69(33.09%) patients had ≤4000/cumm. The pattern of seropositivity and clinical diagnostic method of patients with DENV infection of the study population. **Conclusions:** Over the last couple of years, dengue fever has become a major health issue in 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.

Keywords:- Clinico-pathological, Profiles, Patients, Dengue Fever.

INTRODUCTION

Dengue is an acute infection characterized by fever, headache, muscle, and joint pains, rash,

nausea, and vomiting. Dengue infections may also be asymptomatic or may lead to (a) "classical" Dengue fever (DF), (b) Dengue hemorrhagic fever (DHF) without shock, or (c)



Dengue hemorrhagic fever (DHF) with shock. It is caused by an arbovirus and spread by *Aedes* mosquitoes. Among all flaviviruses, it is the most common. The dengue virus is an RNA virus and is of 4 serotypes (DEN 1-4). The virus serotypes are closely related but antigenically distinct. Infection with one serotype of Dengue Virus (DENV) provides lifelong immunity to that serotype but results only in partial and transient protection against subsequent infection by the other three serotypes. A person can be infected as many as four times, once with each serotype. It is well established that re-infection with different DENV serotypes increases the risk of developing DHF. Since 2000, Bangladesh has experienced dengue fever every year. All four serotypes have been detected, with DENV-3 predominance until 2002.^[1] Approximately half of the world's population is at risk, especially people residing in tropical and subtropical climates. Dengue infection is a major challenge to public health, especially in South East Asia for several years. The incidence of dengue has increased dramatically around the world in recent decades. Bangladesh had a sporadic transmission of dengue virus from 1964 to 1999, but the first outbreak due to dengue virus type 3 occurred in 2001 with dengue outbreaks occurring at increasing frequency and magnitude since then. The rapid increase in dengue cases in 2019 became a public health concern in Bangladesh. Dengue has a wide geographical distribution and can present with a diverse clinical spectrum.^[2] Maximum patients present with fever and some directly present with bleeding manifestations. In recent years' gastrointestinal manifestations and shock is becoming more common. Over 50 million cases of dengue hemorrhagic fever (DHF) occur

in Asian countries.^[3] The reported case fatality rate is about 5%.^[4] For the reduction of morbidity and mortality, early diagnosis and prompt treatment are essential. Detailed evaluation of clinical and laboratory parameters will help in better understanding of the disease process and will help in the development of treatment and thus will improve the outcome of the disease. According to the WHO, dengue is one of the mosquito-borne viral diseases that poses a high medical burden in many regions worldwide recently. Before 1970, a limited number of countries reported severe dengue epidemics.^[5] However, the disease is now endemic in more than 100 countries in the regions of Africa, America, Eastern Mediterranean, South East Asia, and Western Pacific.^[6] America, South East Asia, and Western Pacific regions are the most seriously affected.^[5,6] In recent years, there is an increasing number of dengue infection cases detected predominantly in urban and semiurban areas and therefore has become a major international public health concern. Severe dengue has become a leading cause of hospitalization and death among children and adults in many regions, especially in Asian and Latin American countries.^[7,8] In Vietnam, dengue was first recognized in the 1960s, thanks to the dengue epidemics in Hanoi (North of Vietnam) and Cai Be (South of Vietnam). Recently, dengue has been reported to affect most provinces of the country, and the peak of infection is from June to October every year.^[9] Due to the wide geographic distribution of the mosquito vector and circulation of all four types of Dengue virus, dengue could rapidly spread across the country.^[10,11,12,13] This study aimed to attempt to clarify the clinical and laboratory



profile of dengue cases, which are serologically confirmed in Bangladesh.

MATERIAL AND METHODS

This cross-sectional study was conducted from January 2021 to December 2021 in different government and private tertiary care hospitals in Dhaka, Bangladesh. We collected information on demographic data, clinical characteristics, and laboratory profiles for 271 confirmed hospitalized acute dengue cases using a structured questionnaire. All of these healthcare centres are located in the urban area of the Dhaka District. All of these healthcare centres are non-teaching hospitals that had separate high dependency units (HDU), intensive care units (ICU), and enriched laboratory departments.

We collected information on demographic data, clinical characteristics, and laboratory profiles for 271 confirmed hospitalized acute dengue cases using a structured questionnaire. All patients had confirmed dengue based on NS1 (non-structural protein) antigen positivity. The hospitals were selected conveniently for data collection due to their status as dengue-specialized hospitals during the dengue outbreak. Admitted patients were carefully monitored, and important clinical and laboratory details were recorded regularly on a standard case report form. The clinical examination was carried out meticulously including vital signs, skin rashes, pleural effusion, breathlessness, ascites, hepatomegaly, splenomegaly, etc. Patients were selected based on the laboratory confirmation of NS1 Ag or Anti-Dengue IgM. Patients who had an oral temperature of 100.4° F. 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. 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 diarrhoea. Routine haematological laboratory investigations such as complete blood cell count (CBC) and 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). 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. 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. The accuracy and completeness of the data were checked thoroughly. Data were entered from the questionnaire into Microsoft Excel 2020 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.

RESULTS

This is a prospective observational study, a total of 271 patients were hospitalized and received treatment for DEVN infection from the respective hospital of our research. Table 1 describes the socio-demographic data of the enrolled patients in the study. As shown in [Table 1], out of 271 patients, 164(60.52%) were male and 107(39.48%) were female. Almost half of the patients (135(49.82%)) were from the age group 20-40 years. Of the 271 patients, around 179(66.05%) patients had a nuclear family and 92(33.95%) patients had a joint family. Among all the patients, the majority had more than 4 family members 112(41.33%). Approximately half of the patients were unemployed 134(49.45%) and only 79(29.15%) patients had a monthly income of more than 40,000 BDT.^[17] A large portion of patients lived in urban 190(70.11%) and only 81(29.89%) patients from

the semi-urban/rural areas [Table 1]. Among the patients, 81.18% of patients had been in the recovery phase and 18.82% of patients were in the critical phase [Figure 2]. [Table 2] presents the salient clinical features of the patients. A total of 252(92.99%) patients had a fever that appears to be severe the patients with a fever estimated to be 100.5° F (± 2.1 °F). There are 165(60.89%) patients who had nausea/vomiting, 124(45.76%) patients who had headaches, myalgia was reported by 79(26.94%) patients and 19(7.01%) patients had other features. [Table 3] shows the complication experienced by patients with DEVN infection, 131(48.34%) patients had a complication of breathlessness and 123(45.39%) patients had a pleural effusion these are the most common complication in this study. The distribution of patients with complications according to their gender, febrile period and lab parameters in [Table 4]; whereas 79 patients had breathlessness, 75 patients had pleural effusion, 56 patients had ascites, 21 patients had bleeding, 18 patients had multiple organ failure and only 6 patients had a seizure. [Table 5] shows the lab parameters of the blood samples of patients with DENV infection; from the report of leukocyte count, 134(66.01%) patients had $>4000/\text{cumm}$ and 69(33.09%) patients had $\leq 4000/\text{cumm}$. The pattern of seropositivity and clinical diagnostic method of patients with DENV infection of the study population in [Table 6].

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

Variables	Frequency	Percentage
Gender		
Male	164	60.52
Female	107	39.48

Age (in years)		
<10	34	12.55
10–19	60	22.14
20–40	135	49.82
>40	42	15.50
Family Type		
Nuclear	179	66.05
Joint	92	33.95
Number of family members		
≤4	112	41.33
5	77	28.41
>6	82	30.26
Occupation		
Employed	137	50.55
Unemployed	134	49.45
Residence		
Semi-Urban/Rural	81	29.89
Urban	190	70.11
Monthly Income (BDT)		
≤20,000	90	33.21
20,001–40,000	102	37.64
≥40,000	79	29.15

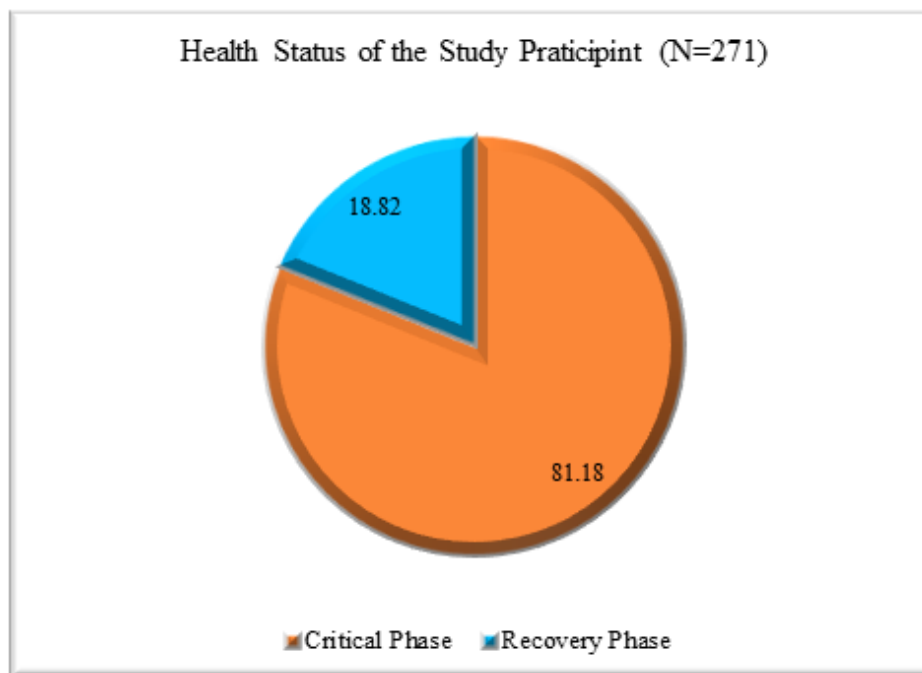


Figure 1: Health status of the enrolled patients with DENV infection during data collection.

Table 2: Clinical features of patients with DENV infection.

Clinical features	Frequency	Percentage
	Mean±SD, 100.5 °F±2.1 °F	
Fever	252	92.99
Abdominal pain	80	29.52
Diarrhoea	53	19.56
Skin rash	69	25.46
Latching	58	21.40
Myalgia	73	26.94
Nausea/Vomiting	165	60.89
Headache	124	45.76
Conjunctive suffusion	7	2.58
Retro-Orbital Pain	13	4.80
Others	19	7.01

Table 3: Complication experienced by patients with DENV infection.

Complications	Frequency	Percentage
Bleeding	35	12.92
Pleural Effusion	123	45.39
Breathlessness	131	48.34
Ascites	93	34.32
Hepatomegaly	24	8.86
Splenomegaly	4	1.48
Seizures	10	3.69
Multiple Organ Failure	31	11.44

Table 4: Distribution of patients with complications according to their gender, febrile period and lab parameter.

Complications due to DENV infection	Gender		Febrile Period		Platelet Count		Leukocyte Count	
	Male	Female	≤3	>3	≤50,000	>50,000	≤4,000	>4,000
Bleeding (n=21)	10	11	3	18	8	13	10	11
Pleural Effusion (n=75)	42	33	7	36	28	47	26	49
Ascites (n=56)	26	30	4	40	19	37	25	31
Breathlessness (n=79)	46	33	7	37	20	59	28	51
Seizures (n=6)	5	2	1	3	2	4	4	2

Hepatomegaly (n=14)	9	5	0	8	6	8	5	9
Multiple Organ Failure (n=18)	10	8	3	12	3	15	9	9

Table 5: Lab parameters from the blood samples of patients with DENV infection.

Lab Parameters	Frequency	Percentage
Leukocyte Count (n=203)		
≤4000/cumm	69	33.99
>4000/cumm	134	66.01
Platelet Count (n =271)		
<50000/cumm	198	97.54
≥50000/cumm	73	35.96
Liver Enzyme (n=271)		
Raised AST, ALTa	140	68.97
Normal AST, ALT	131	64.53
Hematocrit Value (n=250)		
Raised Hematocritb	139	68.47
Normal Hematocrit	111	54.68

Table 6: Pattern of seropositivity and clinical diagnostic method of patients with DENV infection.

Lab Parameters	Frequency	Percentage
NSI		
Positive	253	93.36
Negative	18	6.64
NS1pIgM		
Positive	251	92.62
Negative	20	7.38
NS1pIgG		
Positive	19	7.01
Negative	252	92.99
Tourniquet Test		
Positive	47	17.34
Negative	224	82.66

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 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.^[14] 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 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).^[15] Transmission of dengue peaks during the rainy season, particularly from August to October, due to the optimal conditions for the *Aedes aegypti* mosquito.^[16,21] 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 and Nepal but contrasts with another study in Cameroon.^[14,17,18,19] 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 found that dengue was most prevalent amongst people 16–44 years in Saudi Arabia, whereas M. Rahman et al. reported the highest proportion of cases among the 18–33 years age group in Bangladesh.^[17,20] 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, Nigeria and Cameroon.^[18,19,21] The lower prevalence of dengue infection among children than in older adults could be explained by the fact that children are given extra care by their parents. Also, all the participants of this study were recruited from private health facilities and it could be assumed most of them belonged to the middle to the high-income group; therefore, most of the people lived in relatively clean and non-crowded areas. This could also be relatable to 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.^[22] 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.^[19] 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.^[23,24,25] Hunsperger et al reported the sensitivity and specificity values of the 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.^[26] In another study V., Tricou et al. showed that the inclusion of IgM/IgG test results significantly increases the sensitivity of NS1 alone from 62.4% to 75.5% when NS1 and/or IgM were tested positive and 83.7% when NS1 and/or IgM and/or IgG became positive.^[27] 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 the 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. in Peru but in contrast with those of O. G. Oyero in Nigeria and A. M. Ashshi et al. in Saudi Arabia.^[28,29,30,35] 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, Saudi Arabia, and India.^[17,31,32] Additionally, nausea-vomiting, headache, abdominal pain, myalgia, and skin rash were also identified among the patients. Badreddine et al. documented abdominal pain and vomiting as more common symptoms in their research.^[33] In another study, Abdel-Hady El-Gilany found headache (74.60%) and myalgia (67.60%) as the most common symptoms after fever, suggesting a higher

percentage than our study findings.^[17] Skin rash was identified in 25.3% of the dengue patients, which is similar to the previous study documented by El-Gilany in Saudi Arabia and Ramabhata in India.^[17,37] Ocular manifestations such as conjunctival suffusion and retro-orbital pain were less prevalent in this study than in other studies.^[17,34] It is noteworthy that, among the 542 participants included in this study, of them, 37 patients who 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 found pleural effusion and ascites in 11% of the dengue patients in India, which is comparatively lower than our results.^[35] 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, anaemia, multiple organ failure, hepatitis, febrile diarrhoea, refractory shock, impaired consciousness, portal hypertension, appendicitis, pericardial effusion, myositis, acute kidney injury (AKI), and disseminated intravascular coagulopathy (DIC).^[36,37,38] After the evaluation of laboratory investigations in our study, results show that thrombocytopenia was the most common (73.2%) haematological abnormality among the patients. Similar findings were mentioned by Humayoun et al. in

Pakistan, R. P. Khetan et al. in Nepal and R. Unnikrishnan et al. in India.^[31,39,40]

Limitations of the study:

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSIONS

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 dengue infection. Also, the findings would be her help demarcate 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 regularly spray insecticides 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 of the management of dengue not only in the government facilities but also in the private health care facilities.

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