Clinical Profile of Dengue Infection

*Basak TB,[1] Talukder SI[2]

Dengue viral infections are among the most important mosquito-borne diseases of the Indian subcontinent and have become a major global public health concern. Spread of disease has led to increased recognition of atypical manifestations apart from the classical clinical features of dengue infection. A cross-sectional study of admitted patients suspected to have dengue infection was conducted during the monsoon and post-monsoon seasons in the year 2005 at the Department of Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. Patients who had serological confirmation of dengue infection were classified according to World Health Organization definitions of dengue fever and dengue hemorrhagic fever. Clinical and biochemical parameters were compared between the two groups. Out of 100 patients with suspected dengue fever enrolled in the study, 39(39%) had serologically confirmed dengue infection. Fifty eight (58%) patients were males and 42(42%) were females. Seventy (70%) patients had classical dengue fever while 30 (30%) had dengue hemorrhagic fever. The most common symptoms were headache 76(76%), abdominal pain 63(63%), vomiting 58(58%), rash 36(26%), and cutaneous hypersensitivity 16(16%). Hemorrhagic manifestations were present in 40(40%) patients. Atypical manifestations were recorded. Notably, 14% of patients had neurological involvement and 4% had acute hepatic failure. Overall mortality was 6% and all fatal cases were due to multi-organ failure. Dengue infection poses a huge burden to the health-care system; its spectrum ranges from mild self-limiting illness to severe fatal disease. It can have varied and multi-systemic manifestations which can go unrecognized. Clinicians should have a high index of suspicion for atypical manifestations.

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Key words: Dengue infection; dengue hemorrhagic fever; atypical manifestations of dengue fever; hepatic failure in dengue

Introduction

Dengue is a serious mosquito-borne viral disease which in recent years has become a major international public health concern. It is the most serious viral haemorrhagic fever in the world with an annual incidence of 100 million cases per year. Approximately 2.5 billion people, living mainly in urban areas of tropical and subtropical regions, are estimated to be at risk of acquiring dengue infection.[1] While dengue is endemic in more than 100 countries, most cases are reported from Southeast Asia and the western Pacific regions.[2] In Bangladesh the magnitude of dengue fever was largely unknown until it took a heavy toll in 2000 (5555 cases and 93 deaths were reported.[2] Nearly 90% of the dengue infections occur in children with risk

1. **Dr. Timir Baran Basak, Associate Professor, Department of Medicine, Dinajpur Medical College Hospital, Dinajpur*
2. *Dr. Sadequel Islam Talukder, Assistant Professor, Department of Pathology, Dinajpur Medical College Hospital, Dinajpur*

** For correspondence*

of dying during a secondary attack is nearly 15-fold higher than that of adults.[3,4] The present study was carried out in order to document the clinical manifestations of dengue infections in Bangladesh. Dengue infections vary in severity, ranging from influenza-like self-limiting illness to life-threatening dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) which, if left untreated, are associated with mortality as high as 20%.[2] The various manifestations of dengue may not have a distinct line of demarcation: apart from the classic features, reports of rare presentations have recently become more frequent.[5,6,7] Some presentations that are not classifiable under the World Health Organization (WHO) definitions may be potentially serious and may lead to increased morbidity and mortality of the disease. Many of these manifestations may remain unrecognized and unreported due to lack of awareness among primary care physicians. The most recent dengue outbreak was observed in the northern part of the country last year during the monsoon and post-monsoon period. We undertook this prospective study in the Department of Medicine, Bangabandhu Sheikh Mujib Medical University, from January to July 2005 to assess the clinical profile of dengue infection in hospitalized patients as well as to observe rare manifestations of dengue fever in the current outbreak and compare them with the WHO dengue classification.[8]

Methods

We included all suspected dengue patients of 14 years or older admitted to medicine wards and who appeared to have acute febrile illness with myalgia, arthralgia, headache, retro orbital pain, abdominal pain, nausea and vomiting, bleeding, hypotension or thrombocytopaenia. A detailed history as well as a general and systemic clinical examination was recorded. Haematological profiles and biochemical investigations were done at the time of admission and were followed by daily (or bi-daily) investigations as required until discharge. Signs of plasma leakage were assessed by chest radiograph and abdominal ultrasonography. Specific investigations were performed in patients who presented with neurological involvement (cerebrospinal fluid analysis, neuroimaging, electrodiagnostic studies or muscle biopsy) or hepatic failure (viral markers, peripheral smear and serology for plasmodium falciparum, typhoid fever and leptospirosis).

Patients were classified as dengue fever, dengue hemorrhagic fever or dengue shock syndrome according to WHO guidelines[8] and laboratory diagnosis of dengue was established by demonstration of specific IgM antibodies to dengue in serum. The study enrolled 100 patients of suspected dengue fever of whom 39% were serologically confirmed to have dengue infection. 58% patients were males and 42% were females. 76.9% patients had classic dengue fever while 23.1% fulfilled the criteria of dengue hemorrhagic fever. Of those patients with dengue hemorrhagic fever, 2 patients had developed dengue shock syndrome.

Statistical analysis was performed by Chi Square test done by using the Statistical Package for Social Sciences (SPSS 16.0) with $p < 0.05$ taken as statistically significant.

The study was approved by the Institutional Ethics Committee and written informed consent was obtained from all the patients

Results

Clinical diagnosis of dengue hemorrhagic fever was based on the presence of the following four criteria: (i) continuous high-grade fever lasting 2 to 7 days; (ii) hemorrhagic tendency as shown by a positive

tourniquet test, petechiae or epistaxis; (iii) thrombocytopenia < 100,000/µl; (iv) evidence of plasma leakage manifested by hemoconcentration (an increase in hematocrit 20% above the average for age, sex and population); pleural effusion and ascites, etc. Severity was graded from mildest to most severe depending on the basis of the presence of hypotension or circulatory failure, the presence of cold clammy skin and restlessness, tachycardia and weak pulse with pulse pressure < 20 mmHg from mildest to severe degree. Dengue shock syndrome was diagnosed if there was profound shock and pulse and blood pressure were not recordable.

Table I: Comparison of clinical parameters between dengue fever and dengue hemorrhagic fever

	Total dengue positive (n = 39)	Dengue fever (n = 30)	Dengue hemorrhagic fever (n=9)	P value
Headache/Myalgia	26 (70.21%)	18 (60.0%)	8 (88.87%)	0.22
Hemorrhagic manifestations	11 (28.21%)	2 (6.67%)	9 (100.0%)	0.01*
Rash	6 (15.38%)	4 (13.33%)	2 (22.22%)	0.51
Hepatomegaly	8 (20.51%)	5 (12.82%)	3 (33.33%)	0.55
Signs of plasma leakage	9 (23.1%)	-	9 (100.0%)	-

*p < 0.05 (significant)

Table II: Comparison of biochemical parameters between dengue fever and dengue hemorrhagic fever

	Total dengue positive (n = 39)	Dengue fever (n = 30)	Dengue hemorrhagic fever (n=9)	P value
Thrombocytopenia(platelet count <100,000/µl	28(71.79%)	19 (63.33%)	9 (100.0%)	0.04*
Abnormal PT/APTT	13 (33.33%)	5 (16.67%)	8 (88.9%)	0.01*
Elevation of transaminases	31 ((79.47%)	26 (86.67%)	5 (55.6%)	0.07
Hypoproteinemia (<5.5gm/dl)	12 (30.77%)	4 (13.33%)	5 (55.6%)	0.01*

*p < 0.05 (significant)

In our study the mortality rate was 6% (8) and all fatal cases were due to multi-organ failure. The most common symptoms were headache 26(70.21%), abdominal pain (63%), vomiting (58%), rash (26%), and cutaneous hypersensitivity (16%). Haemorrhagic manifestations were present in 11 (28.21%) patients in which epistaxis was the most common symptom. Per laboratory parameters, (86%) patients had leucopaenia; (89%) had thrombocytopaenia; 1 (92%) had elevation of liver enzymes; (48%) had raised serum bilirubin; an altered coagulation profile was found in (34%) patients; and 4% patients developed acute fulminant hepatic failure. The clinical and biochemical parameters in patients with dengue fever and dengue hemorrhagic fever are shown in Tables I and II.

Apart from the classical manifestations of the dengue infection, we particularly observed certain rare and atypical manifestations in this outbreak. Neurological complications were found in 14% of our patients compared to the previously reported 0.5-6%[9]. Neurological

involvement was present in the form of encephalopathy (6), hypokalaemic periodic paralysis (2), myositis (1) and Gullain-Barre syndrome (1). This neurological involvement can be related to the neurotrophic effect of the virus, the systemic effects of dengue infection, or the host immune response.[10]

Discussion

Liver enzyme elevation, a common feature in dengue infection[11,12] was also apparent in our study. In this study, AST levels were equal to or greater than those of ALT levels in all of dengue infected patients, a finding that has also been reported earlier.[13] Acute hepatic failure, a rarely reported manifestation of dengue hemorrhagic fever[14], was diagnosed in six of our patients. Deranged liver function in dengue infection can be a result of the direct effect of the virus on liver cells or the unregulated host immune response against the virus. Fulminant hepatic failure occurs because of acute severe hepatitis and massive necrosis of the liver, causing hepatic encephalopathy and even death.

A significant proportion of patients (63.33%) with classical or uncomplicated dengue fever had thrombocytopenia and 13% of them had an altered coagulation profile as well. Overall, an altered coagulation profile was observed in 33.33% patients in our study and is indicative of the activation of both coagulation and fibrinolysis during acute dengue infection, which is found to be particularly greater in patients with dengue hemorrhagic fever.[15]

The application of WHO the classification system is not as simple and straightforward as it seems and clinical features may overlap among different categories. The WHO classification system of dengue does not include unusual manifestations such as encephalopathy, acute hepatic failure, cardiomyopathy and acute respiratory distress syndrome, which might be life-threatening. Although these manifestations are rare, they have been reported from endemic regions.[6,16] Therefore, clinicians should have a high index of suspicion and knowledge of these atypical manifestations, particularly in view of the increasing burden of dengue on the health-care system.

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