Profile of dengue patients admitted to a tertiary care hospital in Mumbai

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Dengue is a mosquito-borne arboviral infection that has become a public health concern in India and particularly Mumbai, where endemicity is on the rise. Fifty-seven children having dengue infection admitted over 12 months (2008) in a child health unit of a teaching hospital in Mumbai and who were positive for IgM antibodies by ELISA test were retrospectively studied for clinical profile and outcome. Common clinical findings were fever (100%), hepatomegaly (66.6%), vomiting (40.3%), and significant bleeding manifestations (38.5%). Common laboratory findings were thrombocytopenia (platelet <100,000/mm^3 in 96.5% patients), increased liver enzymes (59.6%), hypoalbuminemia (50.8%), hyponatremia (40.3%), and deranged prothrombin time/partial thromboplastin time (PT/PTT) (33.3%). Third spacing in the form of ascites and pleural effusion was present in 15.7% and 31.5% of patients, respectively. There was no correlation between platelet count and bleeding manifestation. Patients with dengue shock syndrome required more supportive therapy with blood products and inotropes and had a longer recovery time. Mortality in the study was 3.5%. PT/PTT, serum sodium, albumin, and white blood cell (WBC) counts were predictors of severity of dengue. To summarize, fever, hemorrhagic manifestations, hepatomegaly, thrombocytopenia, and evidence of plasma leakage (hemoconcentration, pleural effusion, ascites or hypoproteinemia) should lead a clinician to suspect dengue infection.

Key words: dengue, fever, bleeding.

Dengue is a public health problem in tropical and sub-tropical countries. It is an arboviral infection transmitted to humans through the bite of an infected Aedes mosquito[1]. In India, epidemics are becoming more frequent and are straining the limited resources of the public health system[1,2]. Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) are fatal forms of this disease, reported in India from Delhi, Calcutta and Chennai. DHF presents with fever, occasionally biphasic with bleeding (evidenced by at least one of the following: positive tourniquet test; petechiae, ecchymosis or purpura; bleeding from mucosa, gastrointestinal tract, injection sites or other locations; hematemesis or melena), thrombocytopenia (platelet ≤100,000 cells/mm^3), and evidence of plasma leakage due to increased vascular permeability (manifested by at least one: rise in hematocrit ≥20% above average, drop in hematocrit following volume replacement ≥20% of baseline, signs of plasma leakage such as pleural effusion, ascites and hypoproteinemia). DSS is said to be present when the criteria for DHF are fulfilled along with evidence of circulatory failure. Close monitoring and appropriate fluid therapy have resulted in a reduction in mortality to 1-5% in DHF/DSS patients[3]. In recent times, dengue has assumed epidemic proportions in Mumbai. This study was undertaken in Mumbai to evaluate the clinical and laboratory features and response to treatment and to find predictive markers of severity in patients hospitalized with dengue infection.

Material and Methods

This prospective study was undertaken in one of the three child health units of B. J. Wadia Hospital for Children, Mumbai over 12 months in 2008. B. J. Wadia Hospital for Children is a tertiary care teaching hospital, which had a total outpatient attendance of 22,221 for all three child health units in 2008. Our unit, which

has two admission days per week, hospitalized 2,514 patients in 2008, of which, 626 patients had febrile illnesses. Fifty-seven children, 3 months to 15 years of age, diagnosed with dengue infection and hospitalized for the same were studied. Detailed history was taken, and meticulous clinical examination was carried out daily. Tourniquet test, which is used in the clinical case definition of DHF, was done by inflating the blood pressure (BP) cuff on the upper arm to a point midway between systolic and diastolic BP for 5 minutes. If the resulting petechiae in an area of 6.25 cm^2 (2.5 x 2.5 cm) was ≥20, it was considered a positive test. Laboratory investigations carried out included hemoglobin, total and differential white blood cell (WBC) count, platelet count, hematocrit (Hct), prothrombin time (PT), partial thromboplastin time (PTT), liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT]), serum albumin, serum electrolytes, and chest X-ray. Renal function tests, ultrasonography (USG) of abdomen/chest and 2-dimensional (D) ECHO were done as required, and cerebrospinal fluid (CSF) analysis was done in patients with altered sensorium. All children were confirmed to have dengue infection by testing for dengue IgM antibodies by Panbio capture ELISA on their serum samples. The sensitivity and specificity of this test are 94.7% and 100%, respectively. Children with overlap infections with other organisms in addition to dengue were excluded. These patients were classified as dengue fever (DF), DHF and DSS as per World Health Organization (WHO) criteria[1].

Statistical analysis was done using the Statistical Program for the Social Sciences (SPSS) software. The clinical manifestations and laboratory findings of each illness group were compared using chi-square or Fisher's exact test for proportions and analysis of variance (ANOVA) for continuous data.

Results

Fifty-seven dengue seropositive cases were reported during this study period. Thirteen patients (22.8%) were infants between 2-8 months, 21 (36.8%) were between 1-5 years and 23 (40.4%) were between 6-15 years of age. The profile of dengue is shown in Table I, while the clinical manifestations and laboratory features are shown in Tables II and III, respectively. There were 34 (59.6%) males and 23 (40.4%) females. Fever (between 37.8-39.5°C) was the most consistent feature present in all patients. The majority of children (n=31, 54.3%) had fever of 4-7 days' duration before admission, while only 7 patients (12.3%) had fever for >7 days before admission. Six patients (10.5%) had biphasic fever. Tourniquet test was positive in 8 patients. Melena was present in 14 patients (63.6%), hematemesis in 6 (27.2%), petechiae in 7 (31.8%), epistaxis in 4 (18.2%), and pulmonary hemorrhage in 3 (13.6%). Laboratory investigations revealed thrombocytopenia (platelet count <100,000/mm^3 in 96.5% of patients) as the most consistent finding. Ascites and pleural effusion were present in 9 (15.7%) and 18 (31.5%) patients, respectively, while USG revealed increased gallbladder wall thickness/

Table I. Profile of Dengue (n=57)

Profile	Mean ± SD
Duration of fever (days)	5.1 ± 2.6
Age at onset (years)	4.9 ± 4
Recovery (days)	3.9 ± 2.3
Hemoglobin (g/dl)	11.1 ± 2.9
Hematocrit (%)	33.4 ± 8.9
WBC count (cells/mm^3)	8319 ± 4288
Platelet count (cells/mm^3)	47140 ± 38664
AST (IU/L)	371 ± 840
ALT (IU/L)	229 ± 492
PT (seconds deranged from control)	4.7 ± 8.5
PTT (seconds deranged from control)	17.8 ± 27
Serum albumin (g/dl)	3.3 ± 0.5.

Table II. Clinical Manifestations of the Dengue Cases

Symptoms/signs	No of patients: N (%)
Abdominal pain	18 (31.5%)
Headache	9 (15.8%)
Myalgia	7 (12.3%)
Retroorbital pain	4 (7%)
Vomiting	23 (40.3%)
Diarrhea	3 (5.2%)
Persistent irritability	4 (7%)
Oliguria	8 (14%)
Convulsions	7 (12.3%)
Altered sensorium	8 (14%)
Significant bleeding manifestations	22 (38.5%)
Hepatomegaly	38 (66.6%)
Splenomegaly	5 (8.7%)
Jaundice	6 (10.5%)
Erythematous maculopapular rash	6 (10.5%)
Periorbital puffiness	8 (14%)
Pedal edema	9 (15.7%)
Hypotension	16 (28%)

pericholecystic edema in 4 patients. 2D-ECHO was done in 10 patients, and 2 patients had myocardial dysfunction (ejection fraction <30%), 2 had myocardial dilatation, and 1 had pericardial effusion. CSF examination was normal in children with altered sensorium.

Twenty-eight patients (49.1%) had DF, 11 (19.3%) DHF and 18 (31.6%) DSS.

Twenty-six patients (45.6%) required intravenous fluids (6 ml/kg/hr - 20 ml/kg/hr), 9 patients (15.7%) inotropic support (dopamine/dobutamine) and 5 patients (8.7%) ventilator support. Twelve patients (21%) required blood products - platelets in 2 patients, frozen plasma (FFP) in 1, platelets and FFP in 3, FFP and packed red cells in 2, and all 3 blood products in 4 patients. A 3.5-year-old girl died within six hours of admission to hospital. She had presented with shock - feeble peripheral pulsations and hypotension. She was given fluid boluses and then 0.9% normal saline up to 20 ml/kg/hr and dopamine. The other patient was an 11-year-old boy who died within 48 hours of hospitalization. He had pleural effusion and ascites and was receiving high fluid volumes (up to 20 ml/kg/hr of 0.9% normal saline) and dopamine (10 mcg/kg/min) due to prolonged capillary refill time. Dobutamine (10 mcg/kg/min) was added due to low pulse pressure. He received packed cells, platelet and FFP transfusions because of persistent melena, severe thrombocytopenia and coagulopathy. Both of the above patients were put on ventilator and given soda-bicarb and adrenaline drip due to severe metabolic acidosis and persistent hypotension. However, they succumbed to their illness in spite of aggressive inotrope, vasopressor and ventilatory support due to refractory shock and massive pulmonary hemorrhage.

Discussion

The age group affected by dengue in our study is lower than in other Indian studies[4,5]. This supports the view that the endemicity of DF is increasing in Mumbai. Fever, vomiting, hepatomegaly, bleeding, thrombocytopenia, raised liver enzymes, deranged PT and PTT, hyponatremia, hypoalbuminemia, and third-space fluid loss (ascites and pleural effusion) were the chief clinical and laboratory features seen in our patients and also noted in other studies[1,4-6]. We found melena as the most common bleeding manifestation (68.6%), contrary to reports by Aggrawal et al.[4], Manjith et al.[5] and Zaki et al.[7], who reported hematemesis, whereas Kulkarni et al.[8] reported epistaxis as the common bleeding manifestation. Tourniquet

Table III. Laboratory Abnormalities of the Dengue Cases

Laboratory investigations	No. of patients: N (%)
Thrombocytopenia (<100,000/mm^3)	55 (96.5%)
Leukopenia	16 (28%)
Hemoconcentration (hematocrit >40%)	17 (29.8%)
Deranged PT/PTT	19 (33.3%)
Anemia	13 (22.8%)
Hyponatremia (serum Na<130 mmol/L)	23 (40.3%)
Raised transaminases (>twice of upper limit)	34 (59.6%)
Hypoalbuminemia (serum albumin <3 g/L)	29 (50.8%)
Raised serum creatinine	7 (12.2%)

test was positive in only eight patients, contrary to other studies[8,9], where it was positive in a significantly higher percentage of patients. Low proportion of positive tourniquet test in our patients may be due to the darker skin color or due to the different strain of dengue virus affecting the Indian subcontinent[5]. This test has a sensitivity of 41.6%, specificity of 94.4%, positive predictive value of 98.3%, and negative predictive value of 17.3% for dengue infection[10]. Other evidence of bleeding is frequently present, and the test provides additional information to aid in the diagnosis in only 5% of cases[10]. This was observed in seven patients who had other bleeding manifestations in addition to positive tourniquet test. Classic biphasic fever of dengue was seen in six patients (10.5%) only. Average duration of fever in our patients was 5.1 days, similar to the study by Manjith et al.[5] (4.9 days) and Ratageri et al.[11] (5.4 days). Headache and retro-orbital pain was common in older children (11-15 years old), whereas myalgia was common in 6-10- year-old patients (statistically significant). None of the patients had the feature of break-bone fever, i.e. joint and back pain classically described in dengue. Altered sensorium was present in eight patients having DHF/DSS, and convulsions were present in seven of these patients. These patients had hepatic encephalopathy (n=2), shock (n=2), severe hyponatremia (n=3), and intracranial bleed with pulmonary hemorrhage (n=1). Pancharoen[12], in his study, reported altered sensorium (83.3%) as the most common neurological finding, followed by seizures (45.2%), with these findings being observed in 75% of patients with DHF/DSS. Dengue infection can cause neurologic manifestations secondary to cerebral hypoperfusion due to shock, encephalitis/encephalopathy, hepatic dysfunction, metabolic derangements like hyponatremia and hypoglycemia, or rarely, due to acute disseminated encephalomyelitis or Guillain-Barré Syndrome (GBS)[12,13]. Hepatomegaly was more common in DF (44.7%) as compared to DHF (26.3%) and DSS (28.9%) patients, contrary to the study by Manjith et al.[5], in which DF patients had significantly less hepatomegaly.

Hemoconcentration (drop in Hct by 20% after treatment) was retrospectively diagnosed in nine patients (15.7%) who had normal or low Hct at presentation, while 29.8% of patients had hemoconcentration at the time of admission. Indian children with DHF have a lower than expected rise in Hct during the plasma leakage period; this has been attributed to the high prevalence of iron deficiency anemia in the general population[4, 14]. USG was helpful in detecting ascites and pleural effusion in three and six patients, respectively, not found on chest radiograph or clinical examination. USG has the highest sensitivity and negative predictive value in detecting plasma leakage in dengue[15].

Ninety-six percent of patients had platelet count <100,000/mm^3; 68.4% of patients had <50,000/mm^3 and 22.8% had <20,000/mm^3. Dhooria et al.[16] found thrombocytopenia (platelet <100,000/ mm^3) in all patients; 59% of patients had platelets <50,000/ mm^3 and 14.8% of patients had a very low count (<20,000/ mm^3). A platelet count <50,000/mm^3 in DHF has a six-fold higher mortality[16]. The two patients who died had very low platelet count (<20,000/mm^3). There was no correlation between platelet

counts and bleeding manifestations in our study. A similar finding was also noted in other studies[5,16], which suggests that bleeding in dengue is multifactorial. Various factors leading to bleeding in dengue, apart from thrombocytopenia, are decreased platelet function, fibrinogen consumption, prolongation of PT/PTT, and vasculopathy[17, 18]. Total WBC counts in our patients were variable. While the majority (70.2%) had normal counts, 28% of patients had leukopenia, and one patient had high count of 26,500/ mm^3. Lower WBC counts were associated with less severe grades of DHF, and normal counts were found in severe grades. Leukopenia was associated with increasing age at presentation. Raised liver enzymes were commonly seen in DHF and DSS patients (72.7% and 61.1%, respectively) than in DF patients (42.6%), similar to the study by Manjith et al.[5]. Predictive markers for severity found in one study [20] were younger age at onset, altered sensorium, paralytic ileus, and significantly deranged PTT, whereas we found PT/PTT, serum sodium, albumin, and WBC counts as predictors of severity of dengue.

The average recovery time was longer in DSS than DHF. Patients with DSS required more supportive therapy (blood products and inotropes). The overall mortality was 3.5%, and these patients had DSS, which is comparable with other Indian studies[4,5]. To conclude, dengue is becoming more prevalent in India. It is important to diagnose dengue among other common infections seen in Mumbai, like enteric fever, malaria, leptospirosis, and viral hepatitis. Symptoms like fever, vomiting, headache, and musculoskeletal pain associated with hemorrhagic tendencies, hepatomegaly, macular blanching rash, and third-space fluid loss (pleural effusion, ascites) supported by laboratory parameters like hemoconcentration, elevated liver enzymes and thrombocytopenia should increase the suspicion of dengue infection. Early diagnosis, monitoring and prompt supportive management can reduce mortality in dengue.

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