Dengue Epidemic in Jamshedpur-Tata Main Hospital (TMH) Experience
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Abstract

Background: Dengue is the most rapidly spreading mosquito-borne viral disease in the world. There have been few case reports on the clinical and laboratory data in patients with dengue from the eastern part of the subcontinent.

Aim: This study was aimed to evaluate the clinical profile and laboratory data of patients admitted in TMH, Jamshedpur in order to understand better the clinical pattern and severity of the disease and to identify the factors associated with bad outcome.

Methods: A retrospective study of the case records of confirmed dengue fever cases admitted to the medical wards of TMH, Jamshedpur (Jharkhand), from September to December 2013 was done. The data analyzed included demographic profile, clinical presentation, biochemical parameters, hematological profile, treatment strategy and clinical outcomes.

Results: A total of 431 patients were studied. The clinical features observed in this study in the order of frequency were fever (81%), vomiting (43%), myalgias (38%), headache (37%), abdominal pain (15%), haemorrhagic manifestations (15%), skin rash (13%), diarrohea (12%), ascites (3%), and polyserositis (3%). Pleural effusion (2.8%) and hepatomegaly (1.8%). Atypical presentations observed were encephalitis, acute pancreatitis and ARDS. Gastrointestinal bleeding in the form of melena and hematemesis were the most common haemorrhagic manifestations seen. Thrombocytopenia followed by leucopenia was the most common haematological abnormality found. Severity of thrombocytopenia directly correlated to the haemorrhagic manifestations (P<0.0001) and mortality (P<0.001). Hepatic dysfunction was seen in 40 (9%) patients which included all 16 patients of DHF and 4 patients of DSS. The case-fatality rate observed was 8(1.9%) patients. Deaths were due to disseminated intravascular coagulation (DIC), acute kidney failure, Acute Respiratory Distress Syndrome (ARDS), Multi Organ Dysfunction Syndrome (MODS) and resistant shock. The risk factors that appeared predictive of the bad outcome of the disease and thus of prognostic importance were abdominal pain (RR 8.48, 95% CI 6.36-11.32, P<0.0001), vomiting (RR 1.72, 95% CI .56 to 2.36, P<0.0003), gastrointestinal bleed (RR 10.9, 95% CI 4.8 to 16.62, P<0.0001), thrombocytopenia (RR 5.6, 95% CI 3.33-5.63, P<0.0001), hepatitis (RR 18.57, 95% CI 11.99-28.76, P<0.0001) and ascites (RR 31.42, 95% CI 7.58 to 130.3, P<0.0001) while those associated with increased mortality were hypoalbuminemia (RR 36.8, 95% CI 18.92 to 71.2, P<0.0003), gastrointestinal bleed (RR 11.21, 95% CI 7.37 to 17.66, P<0.0001), major bleed (RR- 2.99, 95% CI 1.18 to 7.58, P=0.02) and platelet count <50,000/cu mm (RR-2.61, 95% CI 1.27 to 5.36, P=0.01).

Conclusion: Fever was the most common clinical presentation in our patients. The spectrum of the disease varied from self-limitd viral infection to life- threatening lethal disease. Clinicians should have a high index of suspicion for atypical manifestations. Vomiting, abdominal pain, absence of leucopenia, elevated transaminases; thrombocytopenia and ascites were associated with severe form of the disease and thus can be used as prognostic factors to alert clinician for the prevention of fatal evolution. The mortality can be brought down by high index of suspicion, effective fluid management and strict monitoring.

Keywords: Dengue fever; Dengue haemorrhagic fever (DHF); Dengue shock syndrome (DSS); Thrombocytopenia

Introduction

Dengue fever (DF) is caused by one of the four serotypes of the dengue virus (DENV; (DENV-1 to DENV-4), an enveloped, single stranded RNA virus of flaviviridae family [1]. Transmission to humans occurs by the bite of the female Aedes aegypti and Aedes albopictus mosquitoes infected by one of four serotypes of the virus.

It manifests with wide range of severity from asymptomatic mild febrile illness to life threatening disease including Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS). Classic dengue fever frequently presents with fever, headache, myalgias, arthalgias, nausea, and vomiting and maculopapular skin rash. According to the WHO report, the mortality in untreated cases of dengue fever was as high as 20% while in hospitalized patients the mortality rate was less than 1% [2]. Early diagnosis of dengue is important for provision of specific care which ensures marked reduction in the morbidity of the disease [2]. Dengue infection is a major health problem worldwide including our country. Globally the incidence of dengue has increased thirty folds in the last four decades [1]. The World Health Organization estimates that 50 to 100 million cases of dengue infection occur each year [1-3]. In India, the first evidence about the occurrence of dengue fever was reported during 1956 from Vellore district in Tamil Nadu. The first DHF outbreak occurred in Kolkata, West Bengal in 1963 with 30% of cases showing haemorrhagic manifestations [4]. Since then several outbreaks of dengue fever have been reported from India from time to time. All the four serotypes have been isolated in India.
Every year during the monsoon months and later, many parts of the country witness outbreaks of dengue infection. The year 2013 was no exception and we experienced an epidemic of this vector borne disease in Jamshedpur, Jharkhand, India. The present study was undertaken to evaluate the salient clinical features, laboratory findings, outcome and predictors of severity of serologically confirmed hospitalized cases of dengue fever during the period September to December 2013 in TMH, Jamshedpur.

**Aim**

This study was undertaken to evaluate the clinical profile and outcome of patients admitted with serologically confirmed dengue fever in TMH and assess haematological and biochemical parameters which were essentially associated with complications and contributed to adverse outcome, so as to be able to formulate strategies to combat this menace.

**Inclusion criteria**

Any acute febrile illness with some of the following symptoms: myalgia, arthralgia, headache, retro-orbital pain, bleeding, skin rash, altered sensorium, shock or low platelet count with positive NS1 antigen and/or IgM ELISA to dengue were included in the study. DHF and DSS were defined as per WHO criteria. DHF was characterized by 4 major manifestations: fever, hemorrhagic phenomena, and thrombocytopenia (platelets <100,000/cu mm) and increased vascular permeability as evidenced by increased haematocrit, pleural effusion, ascites or hypoalbuminemia [1]. DSS is defined as any case that meets the four criteria for DHF and has evidence of circulatory failure manifested by hypotension for age, restlessness, and cold, clammy skin [3].

**Exclusion Criteria**

These included patients with the identified bacterial focus, e.g.- typhoid or urinary tract infection with positive dengue tests, those with only IgG positive ELISA test for dengue and IgM negative and any other identified associated infections e.g. malaria with positive dengue IgM.

**Methodology**

An observational retrospective study of the case records of confirmed dengue fever cases admitted to the medical wards of TMH, Jamshedpur from September to December 2013 was done. The data analysed included demographic profile, clinical presentation, biochemical parameters, haematological profile, treatment strategy and clinical outcomes (length of hospital stay, mortality and complications).

**Biochemical profile**

Included liver function test serum bilirubin (direct and indirect fraction), Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline Phosphatase (ALP), serum proteins and renal function tests (blood urea and serum creatinine).

**Haematological profile**

Haematological parameters evaluated were complete blood count (CBC) and absolute platelet count in all patients, Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT) in presence of bleeding manifestations. CBC and platelet count were done by autoanlyser and also evaluated on peripheral smear simultaneously.

**Viral profile**

Dengue fever was confirmed by doing card test for nonstructural antigen NS1, IgM and IgG antibodies using commercial kits provided by Standard Diagnostics, Germany, in patients who had fever of less than one week duration. In those patients who had fever of more than a week, serological test for specific IgM antibodies to dengue in serum, with IgM antibody capture ELISA (with 99% specificity and sensitivity) was performed using kits supplied by PanBio (USA).

**Other evaluation**

Packed RBCs, fresh frozen plasma (FFP) and platelets transfused were recorded. Subsequent bleeding, platelet increment after transfusion and recovery were also noted. Chest X ray, abdominal ultrasound and echocardiography were done in those cases where there was an indication as decided by the treating clinician.

**Treatment**

All patients were treated symptomatically. Intravenous fluids were given based on the central venous pressure after establishing a central line in all patients with hypotension and shock. Antibiotics were given in few patients who were toxic as per the clinician's judgment. Those with bleeding manifestations and platelet count < 1 × 106/ cu mm were transfused platelets. In absence of bleeding manifestations, those with platelet count < 50,000/ cu mm and showing a falling trend were transfused prophyllactically.

**Statistical analysis**

Results were analysed and presented as mean ± standard deviation (SD) for continuous variables. Frequency and percentage were given for qualitative variables. Chi square test was used to compare categorical variables. A value of ≤ 0.05 was taken as significant. A univariate analysis was done to study the association of the risk factors with disease severity. To remove the effect of confounding factors, a multivariate analysis was done.

**Results**

Of the total of 431 admitted cases, 258 (59.6 %) were males and 174 (39.4%) were females. The male to female ratio was 1.48:1. Their age ranged from 4 months to 82 years with the average being 26.5 years (SD 14.53). While 242 patients (56.15%) were in the age range of 12 to 30 years, 57 patients (13.22%) were in the pediatric age group (≤ 12 yrs) and only 3 patients (0.7%) were beyond sixth decade of life. The age and sex distribution of cases is shown in Figures 1 and 2. The epidemiological distribution of cases in various localities of Jamshedpur is depicted in bar Table 1. Using the WHO criteria for classification of dengue severity, out of 431 cases, only 5 patients (1.2%) were classified as dengue shock syndrome (DSS), 16 patients (3.7%) as dengue haemorrhaghic fever (DHF), 357 patients (83.3%) had classical dengue fever while the remaining 53 (12.3%) were unclassifiable Figures 3 and 4. Of these, 6 patients (1.39%) had dengue fever with shock, 46 patients (10.67%) had dengue fever with haemorrhage and 1 patient (0.23%) had dengue fever with acute pancreatitis. The mean length of hospital stay in the survived group was 4.2 days (SD 1.1) Table 2.

Among the clinical manifestations fever was the most common presentation and was found in 350 (81%) of the patients. Mean duration of fever prior to admission was 3.3 days (SD 1.1). 100 patients (23%) had fever > 102°F during the hospital stay. Of these 20 patients (4.6%) had typical biphasic pattern of fever with afebrile period of 2 to 3 days between the episodes. 80 patients (18.5%) did not have documented fever. Fever was associated with diffuse headache in 160 patients (37%) and myalgias in 165 patients (38.8%). Macular, erythematous rash was noted in 58 patients (13.5%) during the 1st phase of the fever Figures 5 and 6. The rash was distributed all over the body in most cases but in 2
patients (3.44%), it was confined to the face and arms. It was associated with pruritus in 26 (44.8%) patients. Vomiting was the most common gastrointestinal symptom described by 201 patients (46.6%) followed by abdominal pain in 66 patients (15.3%), diarrhoea in 54 patients (12.5%), gastrointestinal bleed in 54 patients (12.5%) and abdominal distension in 5 patients (1.2%). Ascites was detected clinically in 3 (0.7%) patients and on ultrasound of abdomen in 11 (2.5%) patients. Pleural effusion (clinically, by chest radiograph and ultrasound) was detected in 12 patients (2.8%). Polyserositis was found in 15 (3.5%) patients. The atypical manifestations found were central nervous system involvement in form of seizures in 2 patients (0.5%), jaundice in 6 patients (1.4%), ARDS in 5 patients (1.2%), acute pancreatitis in 4 (0.9%) patients, myocarditis in 3 patients (0.7%) and acute kidney injury in 2 patients (0.5%) in absence of shock. Bradycardia was not observed in any patient. Average pulse rate noted was 90/minute. Sinus tachycardia of >120/minute was found in 15 patients (3.5%) Table 3. Abdominal pain (38.8% vs 11.8%), vomiting (52.7% vs 45.7%) and skin rash (29.8% vs 11%) were observed more commonly in children than in adults and this difference was found to be statistically significant (P<0.001). Bleeding manifestations were encountered in 60 (14%) patients, of which upper gastrointestinal bleed in the form of melaena was the commonest. It was seen in 42 patients (9.7%) followed by haematemesis in 15 (3.5%) patients. Other bleeding manifestations noted were petechial haemorrhages in 4 patients (0.9%), gum bleed in 3 (0.7%), epistaxis and
subconjunctival bleed in 1 patient (0.2%) each. DIC in form of bleeding from multiple sites with raised PT (INR), PTT-K and thrombocytopenia was found in 4 patients (0.9%), all of whom succumbed to their illness. Due to its low sensitivity and difficulties in performing, tourniquet test was not done in our patients. Shock, defined as SBP < 90 mm Hg was found in 10 patients (2.3%) while hypotension was found in 46 patients (10.7%). In 45 (10.4%) patients with hypotension and 6 (1.4%) patients with shock, BP improved with fluid resuscitation, while all 4 (0.9%) patients of DSS required inotropic support in form of noradrenaline with/without dopamine and succumbed to their illness Figures 7 and 8.

Laboratory parameters

Haemoglobin >16 g/dl was found in 6 patients (1.4%) while total WBC of < 4,000/cu mm was found in 102 patients (23.66%) of classic dengue fever. Average platelet count on admission noted was 94,640/cu mm (SD 70,000). Two ninety four (68%) out of 431 patients had thrombocytopenia (platelet counts less than 1 lakh (part of case definition of DHF). Thrombocytopenia was more common in young patients. One hundred twenty patients (42%) were transfused platelets. Average units transfused were 6.1 while the maximum units transfused were 19, in a patient with platelet count of 5,000/cumm. However, 30 patients out of 120 (25%), developed post transfusional thrombocytopenia. Mean duration required for normalization of platelet count was 3 to 5 days (4 days). The average platelet count at discharge was 1.44 lakhs/cu mm.

Hepatic involvement, described as elevation of transaminases (transaminitis) more than two times the upper limit of the normal (>2 ULN) was found in a total of 40 (9.28%) patients. The average ALT levels in survived group were 175.98 units/L (SD 84.14) and average AST levels were 117.85 units/L (SD35.3) while the average ALT levels and average AST levels in the non-survivor group were 455.28 (SD

<table>
<thead>
<tr>
<th>Platelet count Lakhs/ cumm (on admission)</th>
<th>Number of patients</th>
<th>Percentage (%)</th>
<th>Major bleed (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 20,000</td>
<td>15</td>
<td>3.48</td>
<td>5 (33.33)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>&gt;20,000-50,000</td>
<td>84</td>
<td>19.49</td>
<td>12 (14.28)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>&gt;50,000-1L</td>
<td>182</td>
<td>42.22</td>
<td>27 (14.83)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>&gt;1.0L</td>
<td>150</td>
<td>34.8</td>
<td>2 (1.33)</td>
<td>-</td>
</tr>
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</table>

Table 1: Shows the relationship between the severity of thrombocytopenia and major bleed.

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Relative risk (RR)</th>
<th>Confidence interval (CI 95%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>8.48</td>
<td>6.36 to 11.32</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.92</td>
<td>1.56 to 2.36</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>GI bleed</td>
<td>7.14</td>
<td>4.8 to 10.62</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Thrombocytopenia (&lt; 50,000/cu mm)</td>
<td>4.32</td>
<td>3.33 to 5.63</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Hepatitis (elevated transaminases)</td>
<td>18.57</td>
<td>11.9 to 28.76</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Ascites</td>
<td>31.42</td>
<td>7.58 to 130.3</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Table 2: Risk factors associated with severe Dengue infection.

<table>
<thead>
<tr>
<th>Symptomatology in children vs adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
</tr>
<tr>
<td>Myalgias</td>
</tr>
<tr>
<td>Rash</td>
</tr>
<tr>
<td>Loose motion</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Abdominal pain</td>
</tr>
</tbody>
</table>

Figure 5: Difference in symptomatology in children and adults.

<table>
<thead>
<tr>
<th>Bleeding manifestations (n = 65/431) - 15.08%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melaena</td>
</tr>
<tr>
<td>Haematemesis</td>
</tr>
<tr>
<td>Potechiae</td>
</tr>
<tr>
<td>Gumbledd</td>
</tr>
<tr>
<td>Epistaxis</td>
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<tr>
<td>SCH</td>
</tr>
</tbody>
</table>

Figure 6: Shows the details of the bleeding manifestations.
cholecystitis were noted in our series. 150 (35%) patients tested positive for NS1 ag. Analysis of the serological results showed that 261 (60.6%) patients tested positive for IgM ELISA while 10 (2%) patients tested positive for both IgM and IgG antibodies.

**Outcomes**

Most of the patients recovered completely without any complications. Eight patients of the series died, resulting in case-fatality rate of 1.8%. The male to female ratio was 1:1. 4 patients (50%) were from 10 to 20 years and 4 patients were in their 2nd to 6th decade of life. None of the patients >60 years died. Among these patients, 2 (25%) had DSS and 3 (37.5%) had DHF. Three (37.5%) patients did not fit into the WHO definition of severe dengue. Death in these patients was related to classical dengue fever with resistant shock, acute pancreatitis and severe hepatitis. Four (50%) patients who died had developed ARDS. Two (4.6%) patients had acute tubular necrosis in absence of hypotension.

**Discussion**

Dengue fever is an infectious disease which is difficult to distinguish from other viruses prevalent in our region as there are no specific markers that can diagnose the disease early. Because it is a disease that can evolve with serious consequences and even be fatal, this study aimed at analyzing clinical and laboratory data in order to try to identify the markers that are predictive of severity. This is the largest study from eastern India on Dengue patients. Our study showed the predominance of the classical (CD) form of the disease (96.7%). The cases occurred during the post-monsoon period (Sept- Dec). As in our study, outbreaks of DF and DHF have been reported during the post monsoon season and have continued till onset of winter (Aug-Nov).

The frequency of the cases was highest in the 2nd and 3rd decade of life with male preponderance. There was a tendency for DHS to present at an earlier age. The clinical features observed in this study in the order of frequency were fever (81%), vomiting (47%), myalgias (38%), headache (38%), abdominal pain (15%), haemorrhagic manifestations (14%), skin rash (13.5%), diarrhoea (12.5%), ascites (3%), polyserositis (3.5%), pleural effusion (2.8%) and hepatomegaly (1.9%). Similar clinical features were observed in other studies [4,5,6].

Exanthema is a prominent clinical sign and is reported from 3% to 53% in the series of severe dengue cases. Pervin et al. [7], reported occurrence of rash in 33% of patients. In our series, it was seen in 13.5% of the patients. Myalgia was observed in 38.3% of patients. Pervin et al. [8], reported myalgia in 84.5% of patients.

Gastrointestinal tract (GIT) was reported as the commonest site of bleeding (61%) in a study by Ahmed et al. [9] as well as Rachel et al. [10]. In our study, gastrointestinal bleeding in the form of melena and hematemesis was seen in 13% of cases and also was the most common haemorrhagic manifestation seen. This was also in comparison to other series reported by Sharma et al. from India [4] and Chairulfatah from Indonesia [7]. Gastrointestinal bleeding is secondary to microvascular damage leading to increased permeability (particularly when platelet function is decreased) or actual disruption and local hemorrhage [11]. In a study by Ratageri et al., common bleeding manifestations were GIT bleeding (22%) and petechiae (18%) [12]. Other sites of bleed noted in our study were skin, nose and subconjuntival space. The mechanisms underlying the bleeding in DHF are multiple including vasculopathy, thrombopathies (which include thrombocytopenia and platelet dysfunction [13] and disseminated intravascular coagulation (DIC).

The most consistent haematological abnormality noted in our study was thrombocytopenia as found in several other studies [11-18]. Two

**Table 3:** Risk factors associated with death in severe Dengue infection.

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Relative risk (RR)</th>
<th>Confidence interval (CI95%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis (elevated transaminases)</td>
<td>11.2</td>
<td>7.37 – 17.06</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hyponaibuimnemia</td>
<td>36.8</td>
<td>18.92 – 71.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thrombocytopenia (50,000/cu mm)</td>
<td>2.61</td>
<td>1.27 – 5.36</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>GI bleed</td>
<td>2.99</td>
<td>1.18 – 7.58</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>

521.63) and 265.56 units/L (SD 198.56) respectively. Most (38 out of 40) 95% patients had elevation of ALT. Of these 27 (67.5%) patients also had elevation of AST. One (2.5%) patient had elevation of AST only. Maximum serum levels of ALT and AST noted were 1,391 U/L and 649.3 U/L respectively. Only 2 patients (0.46%) had severe hepatitis (ALT ≥10 times ULN) while the rest had mild to moderate hepatitis. ALP was high in 1 (0.23%) patient. 6 (14.63%) patients had elevated transaminases (ALT ≥10 times ULN) while the rest had mild to moderate hepatitis.

**Figure 7:** Showing profile of platelet count on admission.

**Figure 8:** Age and sex distribution in thrombocytopenia.
hundred ninety three (68%) of our patients had thrombocytopenia with 15 (5%) patients having platelet count < 20,000/cu mm. This is thought to result from destruction of peripheral platelets or bone marrow megakaryocytes by virus which consequently reduce the platelet production or immune-mediated destruction of the platelets by the antibody. In our study, bleeding was significantly related to severe (platelet count ≤ 20,000/cu mm) (P<0.001) and moderate thrombocytopenia (< 50,000/cu mm) (P=0.05) while it was not associated with mild thrombocytopenia. Patients with severe thrombocytopenia not only developed mucocutaneous bleeding but also skin manifestations like bruises, petechiae and purpura. This was against the observation made by GS Dhooria et al. [19] in a study in children from North India in 2008 and by Sunil Goubier in 2001 who found poor association between thrombocytopenia and bleeding diathesis [16,18].

We noted 42 (14%) patients who had major bleeding manifestation with thrombocytopenia, had no signs of plasma leakage. Such manifestations have also been reported in other series and these cases are labeled as dengue fever with unusual bleeds [12]. Bleeding manifestations in absence of thrombocytopenia were reported in 5 (7.69%) out of 65 patients. It was also observed that prophyllactic platelet transfusion was not necessary for treating DHF Despite protocol, in some cases, platelet transfusions were given as prophylaxis in cases of thrombocytopenia may be due to pressure from relatives and fear of uncertainty about the outcome of the disease rather than on merit. The study from Kebra et al. and See Lun et al. [20] showed similar observation as found in our study.

A decrease in the total leukocyte count during the illness is mainly due to a decrease in granulocytes i.e. neutrophils and was seen in 100 (23%) of our patients. All patients who had DHF and DSS had leucocytosis rather than leucopenia. Absence of leucopenia may, therefore, be a sign of more severe dengue infection. This is in concordance with the results of a study from Thailand in 2008 [11]. Atypical lymphocytosis as reported by John Gawoski and Winnie Ooi was not seen in our patients.

The liver is one of the target organs for dengue virus. Dengue virus-induced damage to the hepatocytes, hypoxia, shock or associated liver disease have all been postulated to be the pathogenic mechanisms for the occurrence of transaminitis [4,9]. Hepatic manifestations are characterized by pain in right hypochondrium, hepatomegaly, and jaundice and raised aminotransferases [10]. In our study, hepatic dysfunction was seen in 40 (9.28%) patients who included all 16 (100%) patients of DHF and 4 (80%) patients of DSS. We noted higher values of ALT (mean 455.28, RR 6.85, 95% CI 4.5 to 10.44) and AST (mean 265.56, RR 7.59, 95% CI 4.91 to 11.7) in the non-survivor group when compared to the survived group and this difference was statistically significant (P=0.0001). Thus, elevated liver enzymes can be considered as bad prognostic indicator of outcome in dengue fever. Similar findings have been found in a number of other studies (Nimmannitya 1987; Kuo et al. 1992; Mohan et al. 2000) [14]. The series by Sharma et al. during the outbreak from Delhi in 1998, also reported elevated transaminases in 90% of patients with DHF [4]. Studies by De Souza et al. and Shukla et al. showed that there was a greater elevation in AST than ALT levels [10,15]. However, AST/ALT ratio >1 was found in only 11 (27.3%) of our patients with hepatic involvement. A study by Itha et al. also did not find preferential elevation of enzymes [9]. Vomiting was seen in 22 (57%) patients with elevated liver enzymes. Thus, presence of vomiting is a strong indicator of the hepatic involvement.

In a multivariate analysis, the risk factors that appeared predictive of the severity of dengue fever were abdominal pain (RR 8.48, P<0.0001), vomiting (RR 1.92, P<0.0001), gastrointestinal bleed (RR 7.14, P<0.0001), thrombocytopenia (RR 4.32, P<0.0001), hepatitis (RR 18.57, P<0.0001) and ascites (RR 31.42, P<0.0001). The present study not only proved the association of dengue fever with these features but also the correlation of these parameters with complications, hence they can be used to identify the patients who are prone to develop complications and thus contribute to the mortality. The study done in Jeddah by Ayub et al., showed similar kind of derangements in laboratory parameters [21]. Symptoms of abdominal pain, nausea and vomit were among the alarm signs that suggested the imminent evolution towards severity and these features were differentially seen in DHF cases compared to classical dengue fever cases.

Some of the unusual features noticed in this series were encephalitis, acute pancreatitis, acute renal failure and acute respiratory distress syndrome (ARDS). Encephalitis was observed in 2 patients (0.5%). Diagnosis was based on clinical symptoms, normal metabolic profile and CT scan of brain. CSF examination was not done, as there was no neck stiffness. Dengue infection can cause neurological manifestation ranging from nonspecific symptoms to encephalitis [8,20]. During the 2-year study period in a prospective case–control study carried out in a hospital in Vietnam, patients with dengue-associated encephalopathy accounted for 0.5% of all patients admitted with DHF (Camet al.2001). Any virus serotype may be involved but DEN2 and DEN3 are most frequently reported from India as the cause of neurological dysfunction [21].

Acute pancreatitis is an equally rare complication of dengue fever [22]. There are isolated case reports highlighting pancreatic involvement in dengue fever (Jusuf et al. and Chen et al.). Pancreas involvement might be due to the direct viral invasion or might be due to hypotension in DHF. We had 4 patients (1%) who had variable elevation of serum amylase and lipase with bulky pancreas on ultrasound.

Acute renal failure is rare in dengue fever and it mainly presents as shock induced acute tubular necrosis. Immune complex mediated glomerular damage and haemolytic uraemic syndrome have been implicated as other causes [23]. It has been observed as a complication of dengue fever in French Guiana (Hommel et al.) and was found to occur in 0.3% of cases in a series of 6154 patients with DHF (Wiwanitkit). In our series, 20 (0.5%) patients, who had normal serum creatinine on presentation showed rise in serum creatinine after admission in absence of shock and expired.

Dengue haemorrhagic fever can result in Adult Respiratory Distress Syndrome (ARDS) (Lum et al.; Thong; Sen et al.). Increased permeability of the alveolar-capillary membrane results in the edema of the alveoli and interstitial spaces which leads to pulmonary dysfunction (Lum et al.) [24]. Five patients (1.2%) in this series developed ARDS and needed mechanical ventilation in ICU, 4 (80%) of these expired while 1 survived.

All the admitted patients had sinus tachycardia with 15 patients (3.48%) having heart rate ≥ 120/min even in absence of fever. This could be due to viral myocarditis. The classical description of bradycardia in dengue fever was not found in any of our patients. 46 patients (10.35%) on admission had hypotension while 10 patients were in shock and majority of them (51 patients) improved with intravenous fluids. Hypotension in Dengue fever is due to increased vascular permeability leading to leakage of fluid from the vascular compartment into the interstitial space [25].

Majority of the patients had self-resolving course of illness. The
mortality in this series was low (1.9%) probably due to early diagnosis, strict monitoring and proper fluid management. In the study by Aneja et al. overall mortality seen was 6% [26], compared to 3% by Ahmed et al. [27]. This could be due to delay in recognition of epidemic in previous years or delay in seeking medical attention. India, Indonesia, Bhutan and Nepal still have case fatality rates (CFR) above 1% [28-30]. The factors which emerged as the strong predictors of mortality in our study were hypoalbuminemia (RR-3.68, 95% CI 1.89-71.2, P <0.0001), transaminitis (RR-11.21, 95% CI 7.37-17.06, P<0.0001), major bleed (RR-2.99, 95% CI 1.08-7.58, P=0.02) and platelet count <50,000/cu mm (RR-2.61, 95% CI 1.27-5.36, P = 0.01). Early diagnosis and improved case management of DHF/DSS is required to bring down CFR to below 1%. Lastly, WHO DHF/DSS classification may not be valid in more severe dengue disease associated with “unusual manifestations” such as encephalopathy, hepatic failure, cardiomyopathy and acute respiratory distress [31-35]. These presentations, which are not identified by the WHO case definition, are not rare in endemic regions such as India.

Limitations
Our study had following limitations:
1) This study has limited validity as it has not included patients who had visited outpatient department. It was conducted at a single hospital and the patient population may have been biased by the referral patterns.
2) Laboratory testing and imaging studies may have been biased by clinician selection based on personal recognition of clinical dengue severity.
3) The use of dengue IgM ELISA and card test for NS1Ag only for diagnosis due to non-availability of nucleic acid based tests in our hospital. 4) We did not determine the serotype of the virus.

Conclusion
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. The nonspecific presentation underscores the importance of laboratory testing and a high index of suspicion to reduce the morbidity and mortality due to the disease. Majority of the cases have self-resolving course of illness. The presence of vomiting, abdominal pain, absence of leucopenia, gastrointestinal bleed, elevated liver enzymes, thrombocytopenia and ascites are the signs of more severe dengue infection and can thus, be considered as bad prognostic indicators of the disease outcome. Bleeding manifestations correlate with the severity of thrombocytopenia when platelet count is <50,000/cu mm. Hypoalbuminemia and transaminitis are very strongly associated with increased mortality (P<0.0001). The mortality rate can be brought down by high index of suspicion, strict monitoring and proper fluid resuscitation.

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Reference


