Original Article

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Severe *Dengue* in Pediatric ICU: Experience from a Tertiary Care Referral Center

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Abstract

Background: Severe *Dengue* is associated with varied organ involvement and high mortality. *Aims and Objectives:* To study clinical profile and outcome of *Severe Dengue* in a tertiary care Pediatric ICU. *Materials and Methods:* Consecutive patients diagnosed as *Severe Dengue* were enrolled retrospectively over 6 months period (1st June 2015 to 30th November 2015). All patients were NS1 and/ or IgM positive for *Dengue* infection. The clinical presentation, laboratory parameters and patient outcomes were studied. *Results:* A total of 33 patients with Severe *Dengue* were included in the study (19 females, 57.5%). The common clinical presentations were with- fever (100%), vomiting (51.51%), abdominal pain (45.45%) and bleeding (45.45%). Central nervous system (CNS) features included - altered sensorium (33.33%) and seizures (24.24%). On admission, hypotension (96.96%), tachycardia (90.90%) and respiratory distress (63.63%) were seen. 63.63% cases had hepatomegaly, 48.48% had pleural effusion and 39.39% had ascites. Common laboratory findings included- thrombocytopenia (< 1 lakh/cumm) in 72.72%, hematocrit > 40 in 33.33% and SGPT > 150 IU/L in 44% of cases. Complications included- acute respiratory distress syndrome (ARDS- 18.18%) and disseminated intravascular coagulation (DIC- 21.21%). Colloids were used in 81.81% and ionotropes in 93.93% of patients. All the patients underwent mechanical ventilation. Packed red cells and platelets were given in 30.3% and 33.3% of cases. Case fatality was 42.42%. Altered sensorium (p = 0.024), seizures (p = 0.0473), DIC (p = 0.026) and ARDS (p = 0.0027) were significant predictors of mortality. *Conclusions:* Mortality in *Severe Dengue* was high in our study (probably due to late referrals and more severe illness). Altered sensorium, seizures, DIC and ARDS were predictors of mortality. CNS presentation was seen in about one third of cases. Hepatomegaly, raised liver enzymes and thrombocytopenia were seen in most of the cases.

Keywords: ARDS; Critical; Dengue; Intensive; Liver; Seizures; Shock; Ventilation.

Introduction

Dengue was initially reported by Benjamin Rush in 1780 as "break-bone fever" [1]. The first confirmed report of *Dengue* infection from India was in 1940s and different Indian states have reported this epidemic since then (with high morbidity and mortality) [2]. Among the various mosquito-borne viral diseases, *Dengue* is an important illness caused by any one of the 4 *Dengue* viruses, the agent being Aedes mosquito [3]. In the recent years, there has been a global rise in incidence of *Dengue* as shown by WHO estimates [4]. According to the World Health Organization (WHO) 2009 guidelines, *Dengue* has been classified into *Dengue* without warning signs, *Dengue* with warning signs and Severe *Dengue* for optimal triage and management [5]. Children presenting with severe bleeding, severe organ involvement and severe plasma leakage have been categorized into Severe *Dengue* (which is associated with increased mortality) [5]. Most *Dengue* deaths are associated with *Dengue* hemorrhagic fever (DHF) / *Dengue* shock syndrome (DSS) (WHO 1997 guidelines) and Severe *Dengue* (WHO 2009 guidelines) [5]. Hence, we conducted a retrospective study in our tertiary care urban Pediatric intensive care unit (PICU) (from Mumbai) to determine the clinical profile and outcome of Severe *Dengue* patients. Attempts were also made to determine the predictors of mortality in Severe *Dengue*.

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Materials and Methods

This was a retrospective (observational) study conducted in a Level III urban Pediatric (Medical) Intensive Care Unit (PICU) of a multi-speciality teaching (and referral tertiary care) hospital (in Mumbai, India), over a period of 6 months [from 1st June 2015 to 30th November 2015]. Our PICU has 9 beds and admits approximately 600 patients annually. All consecutive patients diagnosed as "Severe *Dengue*" were enrolled in the study. All these patients were NS1 and/ or IgM positive for *Dengue* infection. Paients with *Dengue*-like illnesses were excluded. Demographic data, clinical details, risk factors, laboratory and radiographic reports, treatment details and final outcome of all enrolled patients were recorded. All the patients were followed-up until discharge from PICU or till death. Outcome was measured in terms of survival and death. Statistical analysis- the clinical features and investigations were described as percentage of total patients with Severe *Dengue*. The risk factors for mortality were computed using Chi-square test and Fischer's Exact test. P value < 0.05 was considered to be significant.

Results

During the study period, 33 patients fulfilled the inclusion criteria and were enrolled in the study (N = 33). The clinical features, laboratory findings, complications and predictors of mortality are summarized in Table 1-5. The male to female ratio (14 males, 19 females) of our study population was 1:1.35. Most patients (n = 11) belonged to 6-9 years age-group followed by 9-12 years age group (n = 9). Seven cases were in 1 month to 3 years age-group while 6 patients were in 3 to 6 years age-group. The most common clinical presentation was fever (seen in all the 33 cases, 100%) followed by vomiting (17 cases, 51.51%), abdominal pain (15 cases, 45.45%), bleeding (15 cases, 45.45%) and decreased urine output (7 cases, 21.21%) as shown in Table 1. Central nervous system (CNS) features included- altered sensorium (11 cases, 33.33%) and seizures (8 cases, 24.24%). On admission, majority of the patients had hypotension (96.96%), tachycardia (90.90%) and respiratory distress (63.63%). On examination 63.63% (21 cases) had hepatomegaly, 48.48% (16 cases) had pleural effusion and 39.39% (13 cases) had ascites (as shown in Table 1). 81.81% (27 cases) were NS1 positive and 41.37% were *Dengue* IgM positive. Table 2 shows the common laboratory findings, which included thrombocytopenia (< 1 lakh/cumm) in 72.72%, hematocrit > 40 in 33.33%, SGPT > 150 IU/L in 44% and SGOT > 150 IU/L in 65.21% cases. Colloids were used in 81.81% (27 cases) and ionotropes in 93.93% (31 cases) patients. All the 33 patients underwent mechanical ventilation at some point during their PICU stay. Packed red cells and platelet transfusions were given in 30.3% (10 cases) and 33.3% (11 cases) respectively. Table 3 shows the complications seen in our study population and included acute respiratory distress syndrome (ARDS - 18.18%), disseminated intravascular coagulation (DIC - 21.21%) and multi-organ dysfunction syndrome (MODS - 15.15%). The overall morality in the study group was 42.42% (14 out of our 33 patients with Severe *Dengue* died). We admitted a total of 335 Pediatric patients diagnosed as *Dengue* infection during the 6 months study period. Of these, 14 patients of severe *Dengue* expired in the ICU (as given above) and 4 died in the Pediatric wards; resulting in an overall mortality of 5.37% (only). We also analyzed predictors of mortality (in our study population of 33 Severe *Dengue* cases) using the chi-square test. Altered sensorium (p value 0.024), seizures (p value 0.0473), DIC (p value 0.026) and ARDS (p value 0.0027) were significant predictors of mortality as delineated in Tables 4 & 5.

Table 1: Symptoms and Signs in 33 Patients with Severe *Dengue*

Symptom/ Sign	Number of Patients	Percentage
Fever	33	100%
Vomiting	17	51.51%
Abdominal Pain	15	45.45%
Bleeding	15	45.45%
Rash	9	27.27%
Seizures	8	24.24%
Decreased urine output	7	21.21%
Hypotension	32	96.96%
Tachycardia	30	90.90%
Respiratory Distress	21	63.63%
Pleural Effusion	16	48.48%
Ascites	13	39.39%
Hepatomegaly	21	63.63%
Altered Sensorium	11	33.33%

Table 2: Laboratory Parameters in study population (n=33)

Laboratory Parameters	Number of Patients	Percentage
Hematocrit > 40	11/33	33.33%
Thrombocytopenia	24/33	72.72%
Metabolic Acidosis	16/33	48.48%
SGPT > 150 IU/L	11/25	44%
SGOT > 150 IU/L	15/23	65.21%

Table 3: Complications in patients with Severe *Dengue* (n=33)

Complications	Number of Patients	Percentage
Disseminated intravascular coagulation (DIC)	7	21.21%
Pulmonary hemorrhage	4	12.12%
Acute respiratory distress syndrome (ARDS)	6	18.18%
Multiorgan dysfunction syndrome (MODS)	5	15.15%

Table 4: Predictors of mortality in severe *dengue* (symptoms & signs)

Parameter - Cases	**Survived (19 cases)**	**Expired (14 cases)**
Seizures (p=0.0473) - 8	2	6
Bleeding – 15	7	8
Vomiting – 17	10	7
Abdominal pain – 15	9	6
Decreased urine output - 7	2	5
Altered Sensorium (p=0.024) – 11	3	8
Respiratory distress – 21	9	12
Hepatomegaly – 21	11	10
Thrombocytopenia – 24	15	9

Table 5: Predictors of mortality in severe *dengue* (complications)

Parameter	Survived (19 cases)	Expired (14 cases)
DIC (P=0.026) – 7	1	6
Pulmonary hemorrhage – 4	1	3
ARDS (P=0.0027) – 6	0	6
MODS - 5	1	4

Discussion

The present study describes the clinical profile, laboratory features and outcome of Severe *Dengue* during the monsoon and post-monsoon season in an urban tertiary care referral hospital (in Mumbai). *Dengue,* an important emerging disease of the tropical and sub-tropical regions, has been reported from various parts of India in the last few decades. The identification of clinical cases is mainly by signs and symptoms, however, the patients can come with varied presentations [1,6,7].

In our study, the most common age group affected was more than 6 years, which is in accordance with Mittal H *et al.* [8] and Sahana KS *et al.* [9] With regards to the clinical features, fever was the most common presenting symptom seen in 100% of the cases (as expected). In various other studies like Sajid *et al.* [10] who studied 35 children with *Dengue* fever, found fever in all the 35 cases, so also Misra *et al.* [11] who reported fever in 100% cases. Vomiting was seen as a symptom in 51.51% cases in our study. Misra *et al.* [11] reported vomiting in 58% of cases and Narayanan M *et al.* [12] reported vomiting in 83% cases. Bleeding manifestations were seen in 45.45% of cases in our study population. Narayanan M *et al.* [12] reported hemorrhagic manifestations in 66.1% cases. Hepatomegaly (63.63%) was the most frequent finding noted by us and is similar to study done by Arunagirinathan A *et al.* [13] (who studied 50 cases and reported hepatomegaly in 70% cases). Similar observations have been made previously by Narayanan M *et al.* [12], Bethell DB *et al.* [14] and Joshi R *et al.* [15].

The CNS features in our study included altered sensorium (33.33%) and seizures (24.24%). This is comparable with study done by Joshi R *et al.* [15] (wherein out of 57 *Dengue* patients, altered sensorium and seizures were seen in 14% and 12.3% cases respectively). Pancharoen *et al.* [16] reported altered sensorium (83.3%) as the most common neurological finding followed by seizures (45.2%) in 42 cases with encephalitic presentation.

In our study, NS1 (non-structural protein-1) antigen was positive in 81.81% of cases indicating that it is a highly sensitive test for the detection of *Dengue* early as shown by Arunagirinathan A *et al.* [13] and

Kumarasamy V *et al.* [17]. Among the laboratory findings, a majority of the cases were found to have platelets <1,00,000/cumm (72.72%) which was similar to study done by Bansal N *et al.* [18] Raised liver enzymes SGPT > 150 IU/L in 44% and SGOT > 150 IU/L in 65.21% of our patients (with values ranging between 100 and 3500 IU/L) has also been noted in previous studies done by Sahana KS *et al.* [9] and Jagadishkumar K *et al.* [19].

In our study, packed red blood cell transfusions and platelet transfusions were given in 30.3% and 33.3% cases respectively. This was comparable to study done by Sahana *et al.* [9] where 24.7% required blood component therapy. While analyzing various complications we noted that 18.18% cases had ARDS. In another Indian study done by Kamath SR *et al.* [20], ARDS was seen in 10 of 109 patients with severe forms of the disease. *Dengue* associated ARDS has a high mortality [20]. Incidence of DIC (21.21%) reported in the present study was high as compared with 1.2-5.5% reported in previous studies done by Kamath SR *et al.* [20] and Dhooria GS *et al.* [21] In our study, altered sensorium, seizures, DIC and ARDS were significant predictors of mortality. Similar findings were noted by Kamath SR *et al.* [20] in their study population.

The major limitation of our study was its retrospective nature and a small sample size (n=33). Also, *Dengue* PCR/ viral studies could not be done.

Conclusions

Most of our patients with severe *Dengue* presented with hepatomegaly, raised liver enzymes and thrombocytopenia. These clinical features could be used to suspect *Dengue* fever during epidemics. Neurological manifestations were seen in about one third of our cases. Altered sensorium, seizures, ARDS and DIC were predictors of high mortality. Mortality was high in Severe *Dengue* in our study (probably due to late referrals and more severe illness). Further Pediatric studies need to be done on a larger scale so as to understand *Dengue* infection in depth which can help in designing effective interventions at community level for prevention and management of *Dengue* infection.

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