CLINICAL PROFILE OF CHILDREN WITH DENGUE AND FACTORS ASSOCIATED WITH SEVERE DENGUE AND DENGUE WITH WARNING SIGNS

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Abstract

Aim: To study the clinical profile of children with dengue and determine risk factors associated with severe dengue.

Methods: An observational prospective study was conducted in the pediatric ward and Pediatric Intensive Care Unit (PICU) in a Medical College in Mumbai, India over 2 years duration. Patients were classified for their severity based on World Health Organization (WHO) 2009 criteria for dengue. Factors associated with severe dengue and dengue with warning signs were determined.

Results: Out of 100 patients enrolled, mean age of presentation was 5.82 years. Forty-five children had dengue without warning signs, 44 had dengue with warning signs and 11 had severe dengue. Fifty-three children were in the age group of 6 to 12 years. Male: Female ratio was 1.43:1. Common clinical presentations were fever (100%), vomiting (57%), rash (50%), malaise (49%), hepatomegaly (46%), abdominal pain (44%), positive tourniquet test (45%), headache (45%), petechiae (37%) and bleeding manifestation (26%). Abdominal pain (79.5%) (p=0.0109), petechiae (62.2%) (p=0.0466), bleeding manifestations (65.4%) (p=0.0305), hepatomegaly (76.1%) (p=0.035) and splenomegaly (60%) (p=0.026) were more common with dengue with warning signs. Altered sensorium, convulsion, circulatory failure and hypotension were seen in children with severe dengue.

Conclusion: Most of the patients with dengue present in the age group of 6-12 years and have dengue with warning signs or severe dengue. There is a male preponderance mostly due to more outdoor activities. Abdominal pain, petechiae, bleeding manifestations and hepatosplenomegaly suggest dengue with warning signs and need more aggressive management.

Keywords
Dengue hemorrhagic fever, Dengue virus, Dengue.

Introduction

Dengue Fever is one of the arthropod borne diseases that are on the rise in India. (1) Dengue Fever (DF) and Dengue Hemorrhagic Fever (DHF) have emerged as a global public health problem. Infact dengue is hyper endemic in many urban, periurban and rural areas with frequent epidemics. (2) The south-east Asia region is one of the regions at highest risk of DF/DHF accounting for 52% of global risk. (3) Typically, people infected with dengue virus are asymptomatic or have mild symptoms (80%), others have more severe illness (5%), and in a small proportion it is life threatening. (4) Severe disease is more common in infants and young children and in contrast to many other infections, it is more common in well-nourished children. (5) According to World Health Organization (WHO) criteria 2009, patients are classified as severe dengue if they have manifestations of severe plasma leakage, severe hemorrhage or severe organ impairment. (6) Dengue may be diagnosed by microbiological laboratory testing for viral antigen detection or specific antibodies (serology), nucleic acid detection by PCR. (7) Early detection based on clinical suspicion and corroboratory laboratory evidence can help to limit number of cases that progress to developing complications with timely intervention. With there being an increasing number of cases detected, a study of the basic clinical and hematological aspect of the disease is important. Thus this study was undertaken to classify and study the clinical profile of the patients with dengue at a tertiary care centre in Mumbai.

Methods & Materials

An observational prospective study was conducted in the Pediatric ward and Pediatric Intensive Care Unit (PICU) in a medical college in Mumbai over a period of 2 years (Dec 2013 to Dec 2015). All the patients with laboratory confirmed dengue (either a positive Dengue NS1 antigen or a positive Dengue IgM or a positive Dengue PCR) hospitalized over a period of these 2 years in age group 1 month-12 years were included in study after approval of hospital ethics committee and written consent of the parents. Patients having other co-infections like malaria, typhoid or infective hepatitis, immunocompromised patients were excluded from the study. Detailed clinical manifestation, laboratory investigations and treatment details were recorded into a case proforma. Nutritional status was assessed by World Health Organization (WHO) guidelines into a case proforma. Nutritional status was assessed by World Health Organization (WHO) guidelines. (10) Patients were classified as severe malnutrition and moderate malnutrition. (8) Tourniquet test was considered as positive if there were more than 20 petechiae per 2.5cm square. (9) Tachycardia was defined as pulse rate more than normal for age and tachypnea was defined when respiratory rate was more than normal for the age as per American Heart Association (AHA) guidelines 2010. (10) Hypotension was defined when blood pressure (BP) was less than age as per AHA guidelines. (10). Circulatory failure was also defined as per AHA guidelines. (10). Patients were classified as dengue without warning signs, dengue with warning signs or severe dengue according to the WHO classification 2009. (6) Treatment was given according to severity based on WHO 2009 protocol. (6) Outcome in terms of mortality & morbidity was noted. Factors associated with severe dengue were determined.

Statistical Analysis

Qualitative data was represented as frequency and percentage. Association between qualitative variables were assessed by Chi-Square test or Fisher's Exact test. Analysis of Quantitative data was done using unpaired t-test, Mann-Whitney Test or One-way ANOVA. P value of <0.05 was taken as significant.

Results

Total 100 patients were enrolled in the study. Forty-five children had dengue without warning signs, 44 had dengue with warning signs and 11 had severe dengue. Fifty-three children were in the age group of 6 to 12 years, 36 were between 1-5 years of age and 11 were infants. Mean age of presentation was 5.8 years.
Table 1: Clinical Features of patients with dengue

| Clinical Features | No. of patients (n=100) |
|-------------------|-------------------------|
| Fever             | 100                     |
| Vomiting          | 57                      |
| Rash              | 50                      |
| Malaise           | 49                      |
| Hepatomegaly      | 46                      |
| Abdominal pain    | 44                      |
| Tourniquet test Positive | 45                |
| Headache          | 45                      |
| Petechiae         | 37                      |
| Bleeding manifestation | 26                  |
| Tachycardia       | 17                      |
| Splenomegaly      | 10                      |
| Signs of circulatory failure | 8          |
| Hypotension       | 7                       |
| Altered sensorium | 3                       |
| Convulsion        | 2                       |

Table 2: Factors associated with severe dengue and dengue with warning signs.

| Factors                         | Severe Dengue | Dengue with warning signs | Dengue without warning signs | Total | p-value |
|---------------------------------|---------------|---------------------------|-----------------------------|-------|---------|
| Age (years)                     |               |                           |                             |       |         |
| < 1 years                       | 0             | 3 (27.3%)                 | 8 (72.7%)                   | 11 (100%) | 0.29 |
| > 1 to 5 years                  | 4 (11.1%)     | 15 (41.7%)                | 17 (47.2%)                  | 36 (100%) |     |
| 6 to 12 years                   | 7 (13.2%)     | 26 (49.1%)                | 20 (37.7%)                  | 53 (100%) |     |
| Gender                          |               |                           |                             |       |         |
| Female                          | 6 (14.6%)     | 19 (46.3%)                | 16 (39.0%)                  | 41 (100%) | 0.479 |
| Male                            | 5 (8.5%)      | 25 (42.4%)                | 29 (49.2%)                  | 59 (100%) |     |
| Nutritional status              |               |                           |                             |       |         |
| Severe undernutrition           | 0             | 4 (50%)                   | 4 (50%)                     | 8 (100%) | 0.590 |
| Moderate undernutrition         | 2 (7.1%)      | 11 (39.3%)                | 15 (53.6%)                  | 28 (100%) |     |
| Normal nutrition                | 9 (14.1%)     | 29 (45.3%)                | 26 (40.6%)                  | 64 (100%) |     |
| Malaise                         | 7 (14.3%)     | 20 (40.8%)                | 22 (44.9%)                  | 49 (100%) | 0.559 |
| Abdominal Pain                  |               |                           |                             |       |         |
| Vomiting                        | 8 (14.0%)     | 28 (49.1%)                | 21 (36.8%)                  | 57 (100%) | 0.145 |
| Rash                            | 6 (12.0%)     | 21 (42.0%)                | 23 (46.0%)                  | 50 (100%) | 0.903 |
| Petechiae                       | 10 (27.0%)    | 23 (62.2%)                | 4 (10.8%)                   | 37 (100%) | 0.0466 |
| Bleeding Manifestation          | 9 (34.6%)     | 17 (65.4%)                | 0                           | 26 (100%) | 0.0305 |
| Headache                        | 6 (13.3%)     | 18 (40.0%)                | 21 (46.7%)                  | 37 (100%) | 0.686 |
| Tachycardia                     | 6 (35.3%)     | 10 (58.8%)                | 1 (5.9%)                    | 17 (100%) | 0.0024 |
| Hepatomegaly                    | 11 (23.9%)    | 35 (76.1%)                | 0                           | 46 (100%) | 0.035 |
| Splenomegaly                    | 3 (30%)       | 6 (60%)                   | 1 (10.0%)                   | 10 (100%) | 0.026 |
| Positive Tourniquet test        | 8 (17.8%)     | 26 (57.8%)                | 11 (24.4%)                  | 45 (100%) | 0.00067 |
Male: female ratio was 59:41. Sixty-four children had normal nutrition, 28 had moderate malnutrition and 8 had severe malnutrition. The common clinical features are depicted in Table 1. Factors associated with severe dengue and dengue with warning signs is depicted in Table 2. The mean duration of stay was 9.18 days for severe dengue, 6 days for dengue with warning signs and 3.96 days for dengue without warning signs respectively. The mortality rate in our study was 2%. Both patients died due to severe dengue.

Discussion
In our study, 44% of children had dengue with warning signs and 11% had severe dengue. This is in contrast with the study done by Kalanayarooj et al where 58.4% had dengue with warning signs and only 1.1% were severe dengue. (11) In a study by Prasad et al, 16% patients had dengue with warning signs and 82.1% as severe dengue. (12) In another study by Sahana et al, 27.2% had dengue with warning signs and 24.7% had severe dengue. (13) This variance in the subject distribution as per the classification of dengue may be attributable to the timing of admission, the awareness in the draining community and timely intervention.

Most of the patients in our study were in age group 6 to 12 years. Similarly most studies have reported the common age group of presentation to be between 4.9 -12 years. (2,14-16) More prevalence of dengue in this age group is probably due to more involvement in outdoor activities during the day time exposing them to a higher risk of mosquito bites. Though Shah et al (2) and Vincente et al (17) have shown that younger age is one of the predictive marker for DSS and DHF, in our study we found that severity of dengue was not related to age. Similarly, Maron et al showed no association between age and severity of dengue fever. (18) In a study by Pongpan et al, age more than 6 years is found to be a significant risk factor for severity. (19) However none of the above studies were based on WHO classification 2009.

Though we found a male preponderance in our study as seen in other studies (2), there was no association between gender and severity of dengue as seen in other 2 studies. (18,19) Male preponderance was seen in our study probably due to more involvement of boys in outdoor activities with increased risk of exposure to mosquitoes.

In our study we found that dengue affects most of the children with normal nutritional status but nutritional status is not a predictor of severity for dengue. Similarly, Kalayvanarooy et al reported in a review of over 4,000 cases that shock was more common in malformed children with dengue infection. (11) In another study by Maron et al, nutrition does not appear to be a risk factor for severe forms of dengue infection, nor does malnutrition appear to be predictive of good outcomes. (18)

Though vomiting is considered as one of the feature of severe dengue (20), we did not find the same in our study. Abdominal pain is reported as another prognostic factor for severe dengue. (20-22) We found the same in our study. It could be caused by gastrointestinal bleeding and/or hepatomegaly. Junia et al in their study proposed that during the shock or pre-shock state, blood supply to visceral organs was reduced causing tissue hypoxia followed by abdominal pain. (21) However, this has not been found in other studies. (19,22) Thus cause of abdominal pain remains undefined. In our study, we found that abdominal pain, petechiae, bleeding manifestations and hepatosplenomegaly were more common with dengue with warning signs whereas altered sensorium, convulsion, circulatory failure and hypotension were seen in children with severe dengue. Similarly, bleeding manifestations, hepatomegaly have been found to be predictive of severity. (19,23,24)

We found that patients with severe dengue had a longer stay in the hospital. Also mortality was 2% and both children had severe dengue. Similarly, case fatality rates for the world are approximately 1%, but in India, the focal outbreaks have reported case-fatality rates of 3-5 %. (16)

Conclusion
Most of the patients with dengue present in the age group of 6-12 years and have dengue with warning signs or severe dengue. There is a male preponderance mostly due to more outdoor activities. Most of patients present with fever, vomiting, rash, malaise, hepatomegaly, abdominal pain, positive tourniquet test, headache, petechiae and bleeding manifestation. Abdominal pain, petechiae, bleeding manifestations and hepatosplenomegaly were more common with dengue with warning signs whereas altered sensorium, convulsion, circulatory failure and hypotension were seen in children with severe dengue.

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