Incidence of dengue fever and its clinical profile during an outbreak in a rural area in Tamil Nadu

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Received - 14 March 2019 Initial Review - 25 March 2019 Accepted - 18 April 2019

ABSTRACT

Background: In Southeast Asian countries, dengue is the major cause of pediatric morbidity and mortality and in that India reports the maximum number of cases. The annual incidence of dengue in India ranges from 8 to 33 million cases per year and an increased risk of dengue virus infection in children older than 5 years of age have been documented. **Aim:** The main objective of this study was to assess the incidence of dengue among the fever cases and to assess the clinical profile of various types of dengue fever and also to assess the predictive variables for the severity of dengue and their clinical outcomes. **Methodology:** A prospective longitudinal study was conducted at a pediatric hospital in a rural area of Tamil Nadu for a period of 6 months. A total of 325 patients were included in the study based on the study period and the inclusion criteria. For all the cases that were having a fever, basic blood investigations which includes hemoglobin, total count, and platelet count were performed along with peripheral smear study for malaria, dengue card test, and liver function test. Further, dengue positive patients were grouped into non-severe and severe dengue fever based on the operational definition formulated by the WHO. **Results:** The overall incidence of dengue among all the patients with fever was 71.3% among which 83.6% were non-severe dengue and the remaining 13.6% of the patients had severe dengue. Clinical signs such as palmar erythema, splenomegaly, and bleeding manifestations were more common in severe dengue patients than that of non-severe dengue, and this difference was found to be statistically significant. Hemoglobin and platelet count was found to be much lower among the patients with severe dengue along with raised liver enzymes (serum glutamic-oxaloacetic transaminase and serum glutamic pyruvic transaminase) than that of the non-severe dengue, and the difference was found to be statistically significant. Majority of the patients with severe dengue received crystalloid and few patients received blood products whereas only very few with non-severe dengue received crystalloids, and none of the patients in this group received blood products. **Conclusion:** Health-care personnel of all levels must be made aware of the clinical signs and symptoms of all dengue types. Early recognition, precise assessment and appropriate treatment with the help of the WHO revised classification and management guidelines would reduce the mortality due to dengue fever.

Key words: *Clinical manifestations, Management, Non-severe dengue, Severe dengue*

Dengue fever is a mosquito-borne disease caused by flavivirus with four distinct virus serotypes DEN-1, DEN- 2, DEN-3, and DEN-4 [1]. Approximately 400 million dengue cases occur worldwide every year in which, only 25% of the cases are detected by the public health surveillance system while the remaining 75% cases go unnoticed [2]. In Southeast Asian countries, dengue is the major cause of pediatric morbidity and mortality among which, India reports the maximum number of cases. The annual incidence of dengue in India ranges from 8 to 33 million cases per year [3].

The most common vector involved in dengue was *Aedes albopictus* which was found to be more abundant in the areas surveyed, followed by *Aedes aegypti*. Among the four serotypes, serot*ype* 2 was reported with more severe inflammatory response leading to severe dengue infection. According to the WHO reports, the case fatality rate for dengue was 5%, but studies had shown that the mortality ranged from <1% in classical dengue to 44% in untreated dengue hemorrhagic fever [4]. An increased risk of dengue virus infection in children older than 5 years has been documented, though there are case reports of neonatal dengue virus transmission [5,6].

Clinically, non-severe dengue is characterized by fever, headache, retro-ocular pain, myalgia and arthralgia, nausea and vomiting, lymphangitis, and exanthema. Some patients were presented with complications such as intense abdominal pain, persistent vomiting, tachypnea, petechiae, and other hemorrhagic manifestations, as well as neurological signs and a mild altered mental status, which are considered as warning signs [7,8]. Besides the signs and symptoms previously described, patients with severe dengue were reported with signs of plasma leakage or severe bleeding and severe end-organ damage [9,10]. In the pediatric population with dengue, high fevers, abdominal pain,

age older than 6 years, hepatomegaly and thrombocytopenia (<50,000/mm^3) have been described as strong predictors of the severity of the disease [11]. Measuring platelet counts may be unavailable in primary level health-care units. Dengue shock syndrome is a potentially lethal complication of severe dengue virus infection, especially in children; therefore, maintaining hemodynamic stability is the usual recommendation for inpatient management of dengue [12,13].

For a disease that is complex in its manifestations, management is relatively simple, inexpensive and very effective in saving lives if correct and timely interventions are administered. The key for a better prognosis in dengue is to understand and be alert to the clinical problems that arise during the different phases of the disease and about the rationality in case management [14]. Dengue mortality can be reduced by implementing early case detection and referral systems for patients. It also includes managing severe cases with appropriate treatment; reorienting health services to cope with dengue outbreaks, and training health-care personnel of all levels of the health-care system [15]. Although prior studies had been conducted on the clinical profile of dengue, only a few studies had been reported from a rural part of Tamil Nadu, India. Hence, the present study was undertaken in studying the clinical picture and the management outcome of dengue fever and to assess the predictive variables for the severity of dengue and their clinical outcomes.

METHODOLOGY

A prospective longitudinal study was conducted at a pediatric hospital in a rural area of Tamil Nadu, for a period of 6 months from June 2017 to November 2017. The study center is a secondary level care National Accreditation Board for Hospitals accredited pediatric hospital which was established 30 years back in Gobichettipalayam (Tamil Nadu). The study was started after getting the ethical clearance certificate. All patients in the age group of <16 years with complaints of fever and were willing to get admitted to the hospital, were included for the study. All those cases who were admitted with fever had initial screening done for enteric fever, malaria, and urinary tract infection along with blood counts. A total of 325 patients were included in the study based on the study period and the inclusion criteria. The informed consent was obtained from the parent or guardian accompanying the patient. For all the fever cases basic blood investigations which include hemoglobin, total count, and platelet count were performed along with peripheral smear study for malaria, dengue card test, and liver function test. Both card tests and ELISA were performed between the 3rd and 7th days of their illness.

Further, dengue positive patients were grouped into non-severe and severe dengue fever based on the operational definition formulated by the WHO. Patients with symptoms of headache, fever, retro-ocular pain, arthralgia, myalgia, exanthema, intense abdominal pain, persistent vomiting, tachypnea, and neurological disturbances or altered mental status were classified as non-severe dengue. Severe dengue is characterized by evident bleeding, with anemia, hematocrit changes, and hypovolemic shock. Patients were also observed for plasma leakage signs such as shock syndrome or tachycardia and cutaneous manifestations of peripheral vasoconstriction; fluid accumulation with acute respiratory distress syndrome, pleural effusion or ascites, and increased hematocrit (>20%). Patients with signs related to severe end-organ compromise such as liver damage (jaundice, acute liver failure, and encephalopathy) or gastrointestinal (persistent vomit, progressive, or intense abdominal pain), altered mental status and profound neurologic disturbances (lethargy, restlessness, coma, seizures or encephalitis), cardiac compromise (cardiomyopathy), and kidney injury (acute kidney injury) or other organs if occurred were recorded. In addition to, the patient's clinical profile all data related to the patients socio-demographic characteristics such as age, gender, residential address, date of hospital admission, date of first contact with health services due to the probable diagnosis of dengue virus infection, travelling to other locations in the previous 15 days, and the laboratory results, were noted.

All the data were entered and analyzed using SPSS version 21; mean and the standard deviation was derived for all the parametric variables. Chi-square test was used for analyzing the statistical inference considering $p<0.05$ as statistically significant.

RESULTS

The minimum age of the patient reported to our hospital was 3 months and the maximum age was 15 years. Males were found to be slightly more in number than the females with a male:female ratio of 1.3:1. In our study, we found that the majority of the patients with complaints of fever were in the age group of 12 and 15 years and the overall mean age was 10.3 years. Out of 325 patients who were presented with fever, 232 patients were ELISA dengue IgM antibody positive, with an incidence of 71.3%. This high incidence of dengue was due to the study carried out during the outbreak of dengue in the state (Tamil Nadu). Majority of the patients with dengue fever was found to be in the age group of more than 12 years (Table 1).

The dengue fever was classified as non-severe dengue and severe dengue based on the WHO classification. In our study subjects among the dengue fever case, we found that 294 (83.6%) of the patients had non-severe dengue and the remaining 38 (16.3%) had severe dengue. Almost all the patients presented with dengue had fever along with other common symptoms such as headache, coryza, abdominal pain, and retro-orbital pain. Conjunctiva congestion, vomiting, oliguria, and diarrhea were found to be more common among severe dengue patients than that of the non-severe dengue ($p<0.05$). In our study, seizures were also reported in two patients with severe dengue fever.

Among the various clinical signs elicited in dengue cases, we found hepatomegaly, lymphadenopathy, and epigastric tenderness were the most common signs seen in most of the patients with dengue fever, whereas particular signs such as palmar erythema, splenomegaly, and bleeding manifestations were more common in severe dengue patients than that of non-severe dengue and this difference was found to be statistically significant (Table 2). Ascites was seen in four patients with <1 year of age, and pleural effusion (11 patients) was found to be common in older children

Table 1: Age- and sex-wise distribution of dengue positive cases confirmed by dengue IgM ELISA test

Age group (years)	Male (n=129) n (%)	Female (n=103) n (%)	Total (n=232) n (%)	p
<3	15 (11.6)	5 (4.8)	20 (8.6)	0.638
3–6	12 (9.3)	6 (5.8)	18 (7.7)	
6–9	17 (13.1)	20 (19.4)	37 (15.9)	
9–12	32 (24.8)	30 (29.1)	62 (26.7)	
12–15	53 (41)	42 (40.7)	95 (40.9)	

Table 2: Distribution of the various clinical signs and symptoms presented among patients with dengue fever

Clinical manifestations	Non-severe dengue (n=194)	Severe dengue (n=38)	p
	Frequency (%)	Frequency (%)	
Fever	194 (100)	38 (100)	1.000
Conjuctiva congestion	63 (32.4)	34 (89.4)	<0.05
Coryza	162 (83.5)	30 (78.9)	0.712
Headache	155 (79.8)	26 (68.4)	0.681
Abdominal pain	138 (71.1)	26 (68.4)	0.818
Retro-orbital pain	146 (75.2)	24 (63.1)	0.549
Vomiting	54 (27.8)	22 (57.8)	<0.05
Oliguria	23 (11.8)	31 (81.5)	<0.05
Diarrhea	13 (6.7)	18 (47.3)	<0.05
Seizures	0 (0)	2 (5.2)	0.071
Palmar erythema	31 (15.9)	28 (73.6)	<0.05
Hepatomegaly	172 (88.6)	32 (84.2)	0.785
Splenomegaly	98 (50.5)	27 (71)	<0.05
Lymphadenopathy	166 (85.5)	30 (78.9)	0.889
Epigastric tenderness	174 (89.6)	33 (86.8)	0.815
Bleeding manifestations	0 (0)	38 (100)	<0.05
Ascites	0 (0)	4 (10.5)	<0.05
Pleural effusion	0 (0)	11 (28.9)	<0.05

and two children had encephalopathy and all these were seen in patients with severe dengue fever.

Laboratory investigations revealed that hemoglobin and platelet count was found to be significantly lower among the patients with severe dengue than that of non-severe dengue ($p<0.05$), whereas the total count did not show much variation between the two groups. Similarly in the liver function test the total protein and albumin did not show significant difference between the two groups, whereas the serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) levels showed a gross increase in patients with severe dengue than that of the non-severe dengue and the difference was found to be statistically significant ($p<0.05$) (Table 3).

Most of the cases in non-severe dengue were managed with symptomatic management with antipyretics such as paracetamol either given intramuscularly or orally. More than 50% of the patients in non-severe dengue group had received an antibiotic like doxycycline, while very few patients a crystalloid (13.4%) in this group compared to patients with severe dengue (63.1%). Similarly, none of the patients in the non-severe dengue group received blood

Table 3: Various laboratory investigations performed among patients with dengue fever

Laboratory investigations	Non-severe dengue (n=194) (mean±SD)	Severe dengue (n=38) (mean±SD)	p
Total blood count	8181±1898.6	7518±2018.5	0.818
Hemoglobin	11.6±2.8	9.8±3.2	<0.05
Platelet count	108,650±20,564.8	45,890±9,760.7	<0.05
Total protein	7.2±0.89	6.3±1.28	0.716
SGOT	78±18.8	127±31.6	<0.05
SGPT	49.3±16.4	74.6±21.4	<0.05
Albumin	4.3±1.18	3.8±1.71	0.616

SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, SD: Standard deviation

Table 4: Various types of management among patients with dengue fever

Type of intervention	Non-severe dengue (n=194) n (%)	Severe dengue (n=38) n (%)	p
Symptomatic/antipyretics	67 (34.5)	0	<0.05
Doxycycline tablets	101 (52)	6 (15.7)	<0.05
Crystalloids	26 (13.4)	24 (63.1)	<0.05
Blood products	0	8 (21)	<0.05

transfusion whereas, 21% of patients with severe dengue received a blood transfusion and this difference was found to be statistically significant (Table 4). No mortality was reported in our study subjects in both the severe and non-severe dengue patients.

DISCUSSION

The current study had shown the incidence of dengue, during an epidemic, was 71%. Among them, 84% had the non-severe type of dengue and the remaining 16% had severe dengue based on the WHO classification for dengue fever. A similar type of incidence was also reported in a study conducted by Jain [16]. In our study, children in the age group between 10 and 15 years were found to be more commonly infected with dengue followed by 6–10 years, and male to female ratio was 1.3:1 and similar pattern was seen in the retrospective analysis of the 2006 North Indian dengue outbreak [16]. A study done by Sahana and Sujatha had also quoted that boys are slightly more affected than girls, which might be due to outdoor activities of male children, where chances of getting bitten with mosquitoes are more [17].

In the current study, fever was the major presenting complaint in almost all patients. Headache, coryza, retro-orbital pain, and abdominal pain are the other most common symptoms reported in the present study which is on par with the previous studies [18,19]. Vomiting, oliguria, and diarrhea were found to be more common in severe dengue than that of non-severe dengue, andsimilar findings had been observed in a study conducted by Ahmed *et al*. [20]. Central nervous system (CNS) involvement was seen in two of the patients who were presented with drowsiness, altered sensorium, and later developed convulsions. Involvement of the CNS in dengue fever is recognized more frequently; dengue

encephalopathy should be considered as a possibility in any child presenting with neurological symptoms in endemic areas.

Overall hepatomegaly was seen in 88% in the present study which was similar to other previous studies where they found hepatomegaly was more common in severe dengue cases than non-severe dengue [19,21]. However, in our study, we did not find any significant difference in the occurrence of hepatomegaly between severe and non-severe dengue. Ascites (10.5%) and pleural effusion (28.5%) were significantly high in severe dengue as compared to non-severe dengue fever which is statistically significant ($p<0.001$). The presence of these signs helps in predicting the severity of the disease as noted in other studies also. In the current study, we found low hemoglobin levels and low platelet levels are more common in severe dengue cases than that of non-severe dengue, whereas the total count did not show any significant difference between the two groups and a similar report was also quoted in the studies done by Agarwal *et al*. and Srinivasa *et al*. [21,22]. Among the liver function test, we did not find any difference in the total proteins and albumin levels between the two groups whereas the SGOT and SGPT levels were significantly increased among severe dengue cases compared to non-severe cases, similar results were observed by Kalayanarooj *et al*. Mayosites involvements leads increase of aspartate transaminase and alanine aminotransferase [23].

In the present study, 76% of dengue affected children required crystalloids among which 63% were in severe dengue and 13% were non-severe dengue and a similar type of finding was also observed in the study done by Srinivasa *et al*. [22]. Colloids were not used in any patients as by adopting the revised the WHO classification. The WHO, in their recent guidelines on the management of dengue, has described stepwise approach to the management of dengue, where only isotonic solutions have been advised, followed by serial monitoring of clinical status, fluid balance, and hematocrit. For 21% of patients with severe dengue, blood products were used and it is almost similar to the study done by Sahana and Sujatha [17]. Judicious use of fluid was advised to maintain effective circulation during the leak period. Previous studies had shown that the mortality rate for dengue varies from 0 to 12%, similarly, in our study, no death due to dengue had occurred.

CONCLUSION

Dengue fever is becoming a major public health problem in India and the incidence of severe dengue is constantly increasing particularly in children in the age group between 5 and 15 years. All levels of health-care personnel must be made aware of the clinical signs and symptoms of all dengue types. Early recognition, precise assessment and appropriate treatment with the help of the WHO revised classification and management guidelines would reduce the mortality due to dengue fever.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Somasundaram D, Marimuthu S, Thiruselvam K, Radhakrishnan S. Incidence of dengue fever and its clinical profile during an outbreak in a rural area in Tamil Nadu. Indian J Child Health. 2019; 6(5):209-212.

Doi: 10.32677/IJCH.2019.v06.i05.004