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Original Research Article

A study to determine the severity based outcome of pediatric patients with dengue spectrum disorders in a tertiary care hospital

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ABSTRACT

Background: Dengue Fever (DF) has become a major global public health problem. The majority of dengue viral infections are self-limiting, but complications may cause high morbidity and mortality. Dengue infection ranges from mild illness to a severe form of haemorrhagic fever and shock syndrome which may prove fatal. Objective of the study was to determine severity-based outcome in children with dengue spectrum disorder in a tertiary care centre in Mumbai.
Methods: It was a prospective, non-interventional, observational, surveillance study conducted over 14 months (from September 2016 till October 2017). Children aged <18 years admitted to Nanavati Super Specialty Hospital, Mumbai diagnosed with dengue spectrum disorders according to WHO 2009 classification with clinical features and laboratory investigation confirming dengue were enrolled as study participants.
Results: Out of 127 patients, 57(44.9%) were females and 70(55.1%) were males. 81(63.8%) were ward patients, 46(36.2%) required PICU admission. 17(13.4%) patients had dengue with warning signs, 100(78.7%) had dengue without warning signs and 10(7.9%) had severe dengue according to WHO 2009 case classification of dengue. 122(96.1%) were discharged home, 4(3.1%) died of dengue and dengue related complications all four deaths occurred in children with severe dengue.
Conclusions: This study showed that commonest inpatient admission category among children with dengue according to WHO 2009 classification was dengue without warning signs Overall mortality in patients with dengue fever without warning sign as well those with warning sign remains very low. Children presenting with severe dengue associated with either organ failure or refractory shock are at increased risk of mortality.

Keywords: Children, Dengue, Fever, Mortality, Outcome, World health organization

INTRODUCTION

Dengue fever is caused by arthropod borne viruses and is characterized by biphasic fever, myalgia or arthralgia, rash, and lymphadenopathy. Infection can be caused by any of four dengue virus serotypes (DENV1 to 4), transmitted by Aedes mosquitoes. Over half the world's population is thought to live in areas at risk for transmission of dengue and recent estimates suggest that around 400 million infections occur annually, of which 100 million are clinically apparent.[1]

The clinical phenotype varies from a mild self-limiting febrile illness through to severe and occasionally life-threatening disease. Symptomatic disease typically follows three phases: an initial febrile phase lasting 3 to 7 days; a critical phase around effervescence, during which complications appear in a small proportion of patients;

and a spontaneous recovery phase. Complications primarily affect the vascular system and include an unusual plasma leakage syndrome that may result in hypovolemic shock - the potentially fatal Dengue Shock Syndrome (DSS); a coagulopathy sometimes accompanied by bleeding; and organ impairment.[2]

No specific treatments are available except for symptomatic.[3] In patients with severe infection, shock and hemorrhage usually follow.[4,5] If not treated, death may be a consequence. Early detection may avoid such severe complications.[5,6] However, with good supportive care (primarily judicious use of parenteral fluid therapy to offset plasma volume losses due to leakage) mortality rates of less than 1% are possible even among DSS cases.[7,8]

Dengue transmission has followed a seasonal pattern punctuated by the co-circulation of several serotypes and increasingly frequent epidemics.[9] However, despite the reinforcement of surveillance systems, published studies about comprehensive description of the epidemiology of dengue fever in terms of clinical characteristics, severity and trends over time have been lacking.[10] The available literature especially in pediatric population is scanty. The current study was planned to fill this lacuna by conducting an epidemiological study about clinical presentation of dengue with its variable presentations and outcomes with respect to severity of dengue spectrum disorders.

Objective of the study was to determine severity-based outcome in children with dengue spectrum disorder in a tertiary care centre in Mumbai.

METHODS

A Prospective non-interventional observation study was carried out in the Department of Pediatrics at Nanavati Super Speciality Hospital, Mumbai from September 2016 to October 2017.

Based on previous similar studies at 95% confidence interval 10% margin of error, the sample size estimate to be 100 prospectively enrolled children.

Children aged <18 years admitted to Nanavati Super Specialty Hospital, Mumbai diagnosed with dengue spectrum disorders according to WHO 2009 classification with clinical features and laboratory investigation confirming dengue were enrolled as study participants.

Inclusion criteria

- Patients from 1 day to 18 years old diagnosed with dengue on clinical features and lab investigations (either NS1 antigen or IgM antibody positive) and admitted either to ward or Pediatric Intensive Care Unit (PICU).

Exclusion criteria

- Children diagnosed with other co-existent illnesses such as malaria, leptospirosis, influenza, enteric fever, congenital heart disease.
- Outpatient cases diagnosed with dengue were excluded.

Patient details were collected in prescribed preform. It included demographic data, clinical parameters, laboratory investigations (platelets and blood counts, liver function tests, coagulation profile and dengue IgM, IgG and NS1 antigen). Patient outcomes were recorded that included mortality and morbidity (interventions needed, duration of stay).

Microbiological confirmation was done using (1) NS-1 antigen and dengue serum immunoglobulin M (Alera BIO LINE Dengue Duo SD Dengue NS1 + Ab Combo and Panbio Dengue IgM capture ELISA). Patients were classified into dengue with warning signs, dengue without warning signs and severe dengue according WHO dengue case classification 2009.[11] Demographic and clinical details were recorded at admission in a predesigned proforma, whereas laboratory findings were recorded daily until discharge or death.

The frequency of various signs and symptoms and the laboratory tests were compared between the non-severe and severe disease. The results were tabulated and correlated. The outcomes were recorded. The clinical manifestations and laboratory findings such as hemoglobin estimation, total platelet count, hematocrit estimation, NS1 antigen, and IgM antibody of each group of illness were compared using Pearson Chi-square test for proportions. SPSS software was used for data entry and analysis, p value below 0.05 was considered significant.

RESULTS

A total of 127 study subjects were enrolled during the study period.

A total of 127 patients were included in this study, maximum number of children i.e. 47(37%) were aged more than 10 years of age, followed by 6 to 10-year age group having 42 children (33%) and 1 to 5-year age group had 31 children (24.4%). The least number of patients belonged to those age less than one-year i.e. 7(5.5%). Out of 127 patients, 46(36.2%) were admitted to PICU whereas 81(63.8%) were admitted only in wards. In this study, predominant patient population constituted of male gender 70(55.1%); females constituted 57(44.9%) of the study population. In this study, 127 patients were classified according to new WHO guidelines, 100(78.7%) patients had dengue without warning signs, 17(13.4) had dengue with warning signs, 10(7.9%) had severe dengue (Table 1).

Table 1: Social profile of the study subjects.

Social profile		Frequency	%
Age group	Less than 1 year	7	5.5
	1 to 5 years	31	24.4
	6 to 10 years	42	33.1
	More than 10 years	47	37.0
Gender	Female	57	44.9
	Male	70	55.1
Admission	PICU	46	36.2
	Ward	81	63.8
Final diagnosis acc WHO classification	With warning signs	17	13.4
	Without warning signs	100	78.7
	Severe dengue	10	7.9

In this study it was observed that 53.5% of patients had lowest platelet count on 5th day, 22.8% of patients had lowest counts on 6th day, and 15.7% of patients had lowest counts on 4th day. 5.5% of patients had lowest counts on 7th day.

In this study, out of 127 patients, 109(85.8%) patients showed dengue NS1 positive, 13(10.2%) patients showed IgM positive, 2(1.5%) showed IgG positive, 2(1.6%) showed both NS1 and IgM positive (Table 2).

Table 2: Distribution of the diagnostic test results of dengue fever.

Diagnostic test	Frequency	Percentage
Ig G	2	1.57
Ig M	13	10.24
IgM/Ig G	1	0.8
NS 1	109	85.8
NS1 and Ig M	2	1.6

Table 3: Distribution of the outcome and complication of dengue syndrome.

Outcome of the condition		Frequency	Percentage
Pleural Effusion	Yes	23	18.1
	No	104	81.9
Platelet Transfusion	Yes	6	4.7
	No	121	95.3
Inotropes required	Yes	8	6.3
	No	119	93.7
Maximum IV Fluid Rate Required	3	36	28.3
	4	38	29.9
	5	42	33.1
	6	6	4.7
	7	5	3.9
Outcome	DAMA	1	0.8
	Death	4	3.1
	Discharge	122	96.1

In this study, 23(18.1%) patients with dengue developed pleural effusion whereas 104(81.9%) had no pleural effusion. out of 127 patients, only 6(4.7%) patients received platelet transfusion, rest did not require platelet transfusion. In this study 9 patients had platelet counts <10000, 15 patients had platelet counts between 10000 to 20000 and 24 patients had platelet counts between 20000 to 50000. However only six patients were administered platelets. None of the remaining patients with low platelet count had bleeding. The outcome in this group excellent even without platelet transfusion. In this study, 42(33.1%) patients required iv fluids at the rate of 5ml/kg/hr, 38(29.9%) patients required at the rate of 4ml/kg/hr, 36(28.3%) patients required at the rate of 3ml/kg/hr, 6(4.7%) patients required at the rate of 6ml/kg/hr and 5(3.9%) required IV fluids at 7 ml/kg/hr. out of 127 patients, 8(6.3%) required inotropes for hypotension and shock and rest did not require it. In this study, out of 127 patients, 122(96.1%) patients were discharged home without any morbidity, 4(3.1%) patients died of dengue and 1(0.8%) patient was discharged against medical advice (Table 3).

Table 4: Association of high prism score in predictor of severity of disease.

PRISM score	Final diagnosis according to WHO classification		
	With warning signs	Without warning signs	Severe dengue
High	1(5.9%)	1(1%)	3(30%)
Low	16(94.1%)	99(99%)	7(70%)

Chi square = 20.41 p=0.0001

Out of 127 patients, 23 patients developed pleural effusion. Pleural effusion was seen in 6 patients with severe dengue. Association of pleural effusion as predictor of severity of dengue was statistically significant (p value=0.000) (Table 4).

Association of age groups and gender in predictor of severity of dengue was not statistically significant (p value=0.762 and 0.904 respectively). Association of patients admitted in PICU as a predictor in severity of disease was statistically significant (p value=0.000). Children admitted in PICU were more likely to be suffering from severe dengue. Association of low platelet counts in predictor of severity of dengue is statistically significant (p value=0.000). Association of duration of hospital stay in predictor of severity of disease is statistically significant (p value=0.000). Children with severe dengue were likely to have longer duration of hospital stay than those with non-severe forms of dengue. Association of platelet transfusion as predictor of severity of dengue was statistically significant (p value=0.000). Association of pleural effusion as predictor of severity of dengue was statistically significant (p value=0.000). Association of use of inotropes as a predictor of severity of dengue was statistically significant (p value=0.000). (Table 4).

DISCUSSION

Dengue is an important arbovirus infection in tropical countries. Global incidence of dengue fever has increased dramatically in the recent decades.[11] There are very few studies evaluating dengue severity and epidemiology in Indian children, based on the revised WHO dengue classification. In this study total numbers of male patients were 70(55.1%) and female patients were 57(44.9%), male: female ratio in this study was (1.2:1). There was no significant difference in this study p-value of 0.904 in other studies also there were no such significant difference. S. Ahmed, F et al, studied dengue fever outbreak in Karachi and shown significance difference among males and females. Covered dress used by females may be a cause for fewer incidences.[12]

In this study thrombocytopenia was seen more on 5th day of the illness. 53.5% of the patients had thrombocytopenia on 5th day of the dengue illness, which was also explained in similar studies conducted in the past.[13] In this study low platelet counts were statistically significant predictor of severity (p value=0.001), which was also explained in the similar studies conducted in the past such as a study by Karoli R et al.[14] They studied clinical profile of dengue infection at a teaching hospital in North India in 2010.

Mishra S et al, studied clinical profile of dengue fever in Children in Southern Odisha. They observed that 27.83% presented with thrombocytopenia (platelet <100000) in 69(23%) of severe dengue cases had thrombocytopenia whereas only 21.42% of non-severe dengue cases had thrombocytopenia. Thrombocytopenia was seen to be more relevant in those with severe dengue.[15]

Jain S et al, studied dengue-related mortality and disease severity in a tertiary care centre in north India in 2017 observed fifteen patients (10%) had bleeding manifestations without thrombocytopenia (defined as platelet counts <100000/mm^3). In contrast, 15 patients had no bleeding even with platelet counts below 10000/mm^3 (median = 5000/mm^3).[13]

Sanjaya Kulasinghe et al, found statistically significant associations between abnormal coagulation results and DHF/bleeding when compared with DF. Ninety-five percent had a raised APTT and 12% had a raised INR before leaking. One hundred patients had raised APTT and 46% had raised INR before bleeding. APTT had a good sensitivity and specificity as a predictor while INR was low in sensitivity and high in specificity.[16]

Isarangkura P et al, described the behavior of transfused platelets as platelet response and platelet increment in DHF patients with and without shock.

Fresh human platelet concentrate was transfused to 5 non-shock cases and 10 shock cases with different dosages as the low dose (0.15-0.23 U/kg) and high dose (0.28-0.46 U/kg). The cessation of active bleeding was noted by clinical observation or hematocrit determination. The degree of elevation of the circulating platelets tended to vary inversely to the degree of shock and directly to the amounts of platelets infused.[17]

CONCLUSION

This epidemiological study about clinical profile of dengue in children presenting at a tertiary referral centre showed that commonest inpatient admission category according to WHO 2009 classification is- dengue without warning signs. Following WHO guidelines for fluid administration can result in good outcome in children with dengue spectrum disorders. Overall mortality in patients with dengue fever without warning sing as well those with warning sign remains very low. The current study had no case fatality from this class. Children presenting with severe dengue associated with either organ failure or refractory shock are at increased risk of mortality. Children with dengue with severe thrombocytopenia (platelets count <20000) can be managed conservatively without platelet transfusion as long as there is no bleeding. Transfusing platelets and/or colloids may not alter the course of severe dengue with refractory shock or organ failure, unless there is bleeding.

Recommendations

Judicious use of intravenous fluids according to WHO guidelines should be followed so as to improve outcome in management of children with dengue spectrum disorders. Transfusion of blood products especially platelets can be safely withheld unless there are signs of bleeding in patients with dengue. Severe thrombocytopenia (platelets count less than 20000) alone shall not be indication for transfusing platelets as long as there is no bleeding or organ failure. Sever dengue with shock should be managed in PICU under regular monitoring of vitals and laboratory parameters and an institutional protocol for refractory shock. Parents of pediatric patients should be counselled about the better outcome of dengue fever even without transfusion of platelets and blood products.

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