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Original Research Article

Clinical and laboratory profile and outcome of dengue cases among children attending a tertiary care hospital of South India

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ABSTRACT

Background: Dengue fever is an arboviral disease which is endemic in tropical countries and is of major concern with its morbidity and mortality. WHO classified dengue into three categories: undifferentiated fever, dengue fever (DF) and dengue haemorrhagic fever (DHF). Severe dengue is also regularly observed during primary infection of infants born to dengue-immune mothers. The objective of present study was to assess the clinical profile, laboratory profile and associated risk factors related to outcome of children less than 15 years of age. The outcome of the children and their management protocols were also assessed in the study.
Methods: A prospective cross sectional study with 174 confirmed cases of dengue in children <15 years were enrolled and classified as per WHO guidelines. The demographic data, clinical history, laboratory parameters were noted in a separate questionnaire form. Hematological parameters were noted, chest x-ray, ultra-sonogram in required cases was done and observations noted. Cases were managed as per WHO protocol and risk factors were observed. The outcomes of the cases were noted as discharge or death of the case.
Results: A total of 174 children with 149 non-severe dengue and 25 severe dengue cases with 95 males and 79 females were enrolled in the study. 6-10 years was the most common age group. The mean age of children admitted with severe dengue fever was 5.81yrs.and without severe dengue fever was 7yrs.The mean duration of hospitalization was 5.21 days in severe dengue and 3.4 days in non-severe dengue cases. Fever was the most common presenting symptom and hepatomegaly was the common clinical finding in the study. Bleeding manifestations were seen in cases of severe dengue with raised haematocrit levels, raised SGOT levels and severe thrombocytopenia. Pleural effusion and gall bladder wall thickening with ascites was seen in severe dengue cases. Management was by administration of colloids and crystalloids.
Conclusions: Dengue is a dreadful fever among pediatric age group which needs to be considered with great caution in management. Understanding the risk factors helps in predicting the mortality which helps in management and better outcome of the fever.

Keywords: Dengue fever, Dengue Hemorrhagic fever, Haematocrit, Hepatomegaly

INTRODUCTION

Dengue is a mosquito borne febrile viral illness. Dengue virus belongs to the family Flaviviridae (single stranded non segmental RNA viruses) and has four distinct serotypes: DEN-1, DEN-2, DEN-3 and DEN-4. Humans are the main reservoir for the dengue virus. Urbanization, substandard living conditions, lack of vector control and climatic changes are some of the important causes for dengue infection. Once considered an urban problem, it

has now penetrated into rural areas also due to high population density and other factors**.** An estimated 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries.[1] Globally 50 million dengue infections are reported annually with annual incidence of 7.5 to 32.5 million cases in India.[2]

Changes in the epidemiology of dengue, lead to problems with the use of the existing WHO classification. Symptomatic dengue virus infections were grouped into three categories: undifferentiated fever, dengue fever (DF) and dengue hemorrhagic fever (DHF). DHF was further classified into four severity grades, with grades III and IV being defined as dengue shock syndrome (DSS).[3,4] Individual risk factors determine the severity of disease and include secondary infection, age, ethnicity and possibly chronic diseases.

Sero-epidemiological studies consistently support the role of secondary heterotypic infection as a risk factor for severe dengue, although there are a few reports of severe cases associated with primary infection.[5-8] Severe dengue is also regularly observed during primary infection of infants born to dengue-immune mothers. The present study was conducted to assess the clinical profile, laboratory profile and associated risk factors related to outcome of children less than 15 years of age. The outcome of the children and their management protocols were also assessed in the study.

METHODS

An observational, prospective cross sectional study was done in department of Pediatrics of Narayana Medical College, a tertiary care hospital of Andhra Pradesh. The study period was 12 months from August 2015 to July 2016. All the children from 1 month to 15 years of age were included in the study and all were confirmed Dengue cases, and classified as per WHO guidelines 2009. The cases were confirmed based on presence of NS1 antigen and Ig M and Ig G antibodies demonstration serological test by rapid ICT (J Mithra & Co Ltd). Informed and written consent was obtained from all the mothers and attendants of the cases enrolled in the study. The study was approved by the institutional ethical committee.

Exclusion criteria

All other confirmed cases of malaria, chickungunya, typhoid. rickettsial fevers and other fevers co-infected with dengue were excluded from the study.

The demographic data and clinical history of all the cases which met the inclusion criteria were entered in a separate structured questionnaire sheet. Clinical history included duration fever, presence of vomiting, abdominal pain, myalgia, rash etc. Clinical examination includes pulse rate and volume, respiratory rate, blood pressure, presence of hepato-spleenomegaly, rash, bleeding manifestations. Haematological parameters like Hb%, total leukocyte count (TLC), haematocrit, total platelet count, coagulation profile (PT, APTT), liver enzymes were estimated regularly until discharge. Chest X ray, ultra-sonogram was done in cases when required.

Children were managed in the ward or PICU depending upon the status at the time of presentation. Management includes oral fluids in hemodynamically stable children, IV fluid boluses followed by maintenance with introduction of oral fluids as early as possible in cases of shock. Crystalloids, blood products for resuscitation were used depending on the need. Platelet concentrates given to patients with thrombocytopenia who has significant bleeding. Ventilation (non-invasive and invasive) was required in some children managed in PICU. Co-infections if noted were treated appropriately. Outcome of the children was also included in the study.

Statistical analysis

All the data was entered in Microsoft excel sheet and analyzed. P value <0.005 was considered significant.

RESULTS

In the present study, 174 confirmed cases were included with 95 (54.6%) males and 79 (45.4%) females. Among males, 87 were diagnosed with non-severe dengue, 8 were severe dengue cases and 62 among female were non-severe cases and 17 were of severe cases. In present study, non-severe dengue cases were more among males and severe dengue cases were more in females. Male to female ratio in our study was 1.2:1.

The most common age group affected in the study was 6-10years (52.9%), 92 cases with 84 non-severe and 8 severe dengue cases. The mean age of children admitted with severe dengue fever was 5.81 years and without severe dengue fever was 7yrs.

The mean duration of hospitalization was 5.21 days in severe dengue and 3.4 days in non-severe dengue cases. Out of 174 cases in the study, 133 (76.4%) were classified as dengue with warning signs, 16 (9.2%) without warning signs and 25 (14.4%) severe dengue cases (Table 1). Incidence of cases were high in the 2nd half of the year from August 2105 to January 2016 with 124 cases and 50 cases in 1st half from February 2016 to July 2016. Peak of admissions were observed in the month of August, 52 cases (29.88%) followed by 39 in September (22.41%).

Among the clinical features, fever (100%) was the most common presenting feature, followed by vomiting in 115 (66%) and abdominal pain in 73 (41.9%). Rash was observed in 43 (24.7%), significant bleeding was seen in 9 (5.2%). Usual forms of bleeding were malena, hematuria, epistaxis, and excessive menstrual bleeding in

adolescent girls. Other common symptoms were myalgia, loose stools. Hepatomegaly was present in 140(80%), spleenomegaly in 21 (12%), and 80 children (45.9%) had hypotension either at the time of admission or during hospital stay. Petechiae were observed in 69(39.6%) children (Table 2).

Table 1: Epidemiological parameters.

Parameters	Variables	Numbers	%	Severe dengue	Non severe dengue
Age	1month-5yr	53	30.4	14	39
	6-10yr	92	52.9	8	84
	11-<15yr	29	16.6	3	26
Gender	Male	95	54.6	8	87
	Female	79	45.4	17	62
Classification	Dengue with warning signs	133	76.4	-	-
	Dengue without warning signs	16	9.2	-	-
	Severe dengue	25	14.4	-	-

Table 2: Clinical profile of patients.

Signs and symptoms	Severe dengue (n=25) (%)	Non severe dengue (n=149) %	Total (n=174) %
Fever	25 (100)	149 (100)	174 (100)
Vomiting	25 (100)	90 (60.4)	115 (66.09)
Abdominal pain	24 (96)	49 (32.8)	73(41.95)
Rash	9 (36)	34 (22.8)	43 (24.71)
Significant bleeding	6 (24)	3 (1.7)	9 (5.17)
Hepatomegaly	25 (100)	115 (77)	140 (80.46)
splenomegaly	4 (16)	17 (11)	21 (12.07)
Hypotension	22 (88)	90 (60)	112 (64.37)
Petechiae	16 (64)	52 (35)	68 (39.08)

Leukopenia (<4000/mm^3) was observed in 96 (55.17%) cases of study with 3 severe dengue cases and 93 non-severe dengue cases, while 26 cases (14.94%) had leukocytosis (>11,000/mm^3). In the recovery phase, it normalized earlier than platelet count. In children with persistent leukocytosis co-infections may be considered. Normal leukocyte counts were observed in 52 (29.89%) cases with counts between 4000-11000cells/mm^3 with 10 cases of severe dengue and 42 cases of non-severe dengue. Serial hematocrit values were measured during the hospital stay to modify the treatment. Initial hematocrit values were found <30% in 10 children (5.7%), 30-40% in 118 children (67.8%) and >40% in 46 children (26.4%).

Platelet count <10,000 was seen in 22 (7.3%) cases, 10,000-20,000 in 40 (13.2), 20,000-50,000 in 99 (32.7%), 50,000-1,00,000 in 66 (21.8%) and >1 lakh in 66 (21.8%). Statistical significance was associated with raised haematocrit (P value <0.001) and severe thrombocytopenia (<50,000cells/mm^3) (P value <0.005) and more associated with severe dengue cases than non-severe dengue cases. Liver enzymatic profile was classified as Normal, mildly elevated, moderately elevated and severely elevated cases of SGOT and SGPT. SGOT levels were normal in 42.53% of cases and mild elevation was noted in 72 cases with 63 in non-severe dengue cases and 9 in severe dengue cases. SGOT was severely elevated in 3 cases all are of severe dengue. SGPT was normal in 12.64% of cases, mildly elevated in 84 cases in total with 81 among non-severe dengue cases and 3 in severe cases, and severely elevated in 3.45% of cases all of which were of severe dengue cases.

Statistical association (p valve<0.05) was associated with both raised SGOT and SGPT values which was observed in severe cases of dengue than in non-severe dengue cases. PT was prolonged in 12.64% of cases with32% in severe dengue cases and 9.4% in non-severe dengue cases. APTT was abnormal in 74.71% of total cases with 73.83% in non-severe cases and 80% among severe dengue cases.

Pleural effusion was seen in 47 cases (27%) in total with right sided effusion in 29 cases (16.67%), 14 (8.05%) on left side and Bilateral effusion in 4 cases (2.3%). 21 cases of non-severe dengue had pleural effusion and 22 among severe dengue cases. 3 cases of severe dengue had bilateral pleural effusion which is statistically significant. In our study gall bladder wall thickening and ascites was a significant finding by USG abdomen. 64 cases (36.78%) had GB wall thickening and 39 cases (26.17%) among non-severe cases and 25 cases (100%) of severe dengue cases. Spleenomegaly was observed in 40 cases in total (23%) with 23 cases of non-severe dengue and 17 cases of severe dengue. Hepatomegaly was observed in

41 cases (23.56%) in total with 23 among non-severe and 18 among severe dengue cases. However considerable significance was not associated with these findings in our study (Table 3).

Table 3: Investigation profile of patients.

Investigations	Variations	Non severe dengue (n= 149) %	severe dengue (n= 25) %	Total (n=174) %
Leukocyte count	<4000	93(62)	3(12)	96 (55.17)
	4000-11000	42(28)	10(40)	52 (29.89)
	>11000	14(9)	12(48)	26 (14.94)
Hematocrit	<30	5(3)	5(20)	10 (5.75)
	30-40	109(73)	9(36)	118 (67.82)
	>40	35(23)	11(44)	46 (26.44)
Platelet count	<10,000	6(4)	6(24)	12 (6.90)
	>10,000-<20,000	14(9.4)	8(32)	22 (12.64)
	>20,000-<50,000	49(32.88)	10(40)	59 (33.91)
	>50,000-<1 lakh	43(28.85)	1(4)	44 (25.29)
	>1 lakh	37(24.83)	0(0)	37 (21.26)
Liver enzymes	**Level of SGOT (IU/L)**			
	Normal	74(50)	0(0)	74 (42.53)
	Mild elevation	63(41.89)	9(36)	72 (41.38)
	Moderate elevation	12(8.1)	13(52)	25 (14.37)
	Severe elevation	0(0)	3(12)	3 (1.72)
	Levels of SGPT (IU/L)			
	Normal	22 (14.66)	0	22 (12.64)
	Mild elevation	81 (54.66)	3 (12)	84 (48.28)
	Moderate elevation	46 (30.66)	16 (64)	62 (35.63)
	Severe elevation	0	6 (24)	6 (3.45)
Coagulation profile				
APTT	Normal	39 (26.17)	5 (20)	44 (25.29)
	Abnormal	110 (73.83)	20 (80)	130 (74.71)
PT	Normal	135 (90.6)	17 (68)	152 (87.36)
	Abnormal	14 (9.4)	8 (32)	22 (12.64)
Chest X-ray	Normal	127 (85.23)	0	127 (72.99)
	Right pleural effusion	14 (9.40)	15 (60)	29 (16.67)
	Left Pleural effusion	7 (4.70)	7 (28)	14 (8.05)
	Bilateral Pleural effusion	1 (0.677)	3 (12)	4 (2.3)
Ultrasound	Normal	42 (28.19)	0	42 (24.14)
	Pleural effusion	22 (14.77)	25 (100)	47 (27.01)
	Hepatomegaly	23 (15.44)	18 (72)	41 (23.56)
	Spleenomegaly	23 (15.44)	17 (68)	40 (22.99)
	Gall bladder wall thickening and Ascites	39 (26.17)	25 (100)	64 (36.78)

Among the 174 children 129 (74.1%) were managed in the ward and 45 children (25.8%) required PICU admission or transfer. Admission into PICU was based on the criteria for admission or transfer to HDU. In our study 80(45.9%) children presented with hypotension. All these children received crystalloids. These were normal saline or ringer lactate. Colloids were used in whom shock was not correctable with crystalloids. Colloids needed in 8(4.6%), mainly Gelofusine. Most of the children (43.2%) started orally on 2nd day of admission. 39 cases (22.4%) in our study required blood products, PRBC used in 10 children (5.7%), platelets used in 20 (11.5%) and FFP in 9 (5.2%). 15 cases (8.6%)were ventilated, Noninvasive ventilation in 11 (6.3%) and invasive ventilation in 4 (2.3%) (Table 4).

DISCUSSION

Trending changes in the epidemiology of dengue has leads to problems with the use of the existing WHO classification. According to new WHO guidelines on Dengue by using a set of clinical and/or laboratory

parameters, one sees a clear-cut difference between patients with severe dengue and those with non-severe dengue. Those in the non-severe dengue are split into two subgroups patients with warning signs and those without them. In our study the cases were categorized based on WHO guidelines 2009 into non-severe which included undifferentiated fever and dengue fever with or without warning signs and severe dengue which included dengue hemorrhagic fever (DHF) and dengue shock Syndrome (DSS).[3]

Table 4: Management and outcome of dengue cases in the study.

Outcome	Non severe dengue (n= 149)%	severe dengue (n= 25)%	Total (n=174)
Discharged	120 (80.54)	18 (72)	138 (79.31)
Discharged against medical advise	23 (15.44)	4 (16)	27 (15.52)
Death	6 (4.03)	3 (12)	9 (5.17)
Management of Cases in the study			
Antipyretics	149 (100)	25 (100)	174 (100)
Crystalloids	72 (48.32%)	8 (32%)	80 (46%)
Colloids	0	8 (32%)	8 (4.6%)
PRBC	0	10 (40%)	10 (5.74%)
Platelets	0	20 (80%)	20 (11.5%)
FFP	0	9 (36%)	9 (5.17)

The present study demonstrates the peak incidence of cases in the months, between August-October in contrast to a study done by Kabilan et al who found more cases in September-January.[9] The predominant age group in our study was between 6-10 years (52.9%) followed in order by 1month 5year (30.4%) and 11<15 years (16.6%) which is contrary with findings of Gurudeep et al who reported 59% of cases in children between 10-15 years but on par with findings of Sharma NL et al.[10,11] Male were predominant than female (54.6%) in our study as similar to many studies. In our study 76.4% presented with dengue fever with warning signs, 9.2% without warning signs and 14.4% with severe dengue. Our findings were on par with findings of Kabilan et al who reported 75.9% of children with warning signs and 6.6% of severe dengue cases in his study.[9] The duration of stay of hospitalization was almost similar in both non-severe and severe cases in contrast to few studies which mentions duration of stay more in severe dengue cases.[12]

Fever was the common presenting feature in all children (100%) followed by vomiting in 115 children 66%, abdominal pain in 41.9%, and rash in 24.71% and significant bleeding manifestations in 5.17%. In children with severe dengue the most common presentation was with shock/ hypotension (88%) followed by severe organ dysfunction (45%) and bleeding (24%). Findings of our study were similar to findings in the study of Anju et al.[13] Clinically Hepatomagaly was observed in 80% of cases and spleenomegaly in 12% of cases in our study which doesn't match with findings of Anju et al who reported 79% of hepatomegaly and 19% of spleenomegaly in their study. Petechiae were observed in 39.08% of cases with 64% in severe dengue and 35% of cases with non-severe dengue. Rash was observed in 24.71% with 36% among severe dengue cases and 22.8% in non-severe dengue cases. These findings were on par with findings of Guzmán MG et al.[14] In the present study, leucopenia was observed in 55% of children while 31% of children had normal leukocyte count which is similar to findings of Sunil Gomber et al.[15] Haematocrit was raised (>40) in 26.4% of cases , 30-40 in 67.8% and <30 in 5.7% of cases, mean and standard deviation was 36.48±5.89 which is almost similar to that of observations by Sunil Gomber et al but contrast to findings of Agarwal et al.[16] In severe dengue children Haematocrit value of more than 40 was found in 44%. Thrombocytopenia was found in all cases of Dengue). Severe thrombocytopenia (platelet count <20,000) in 34 (19.5%) children, and platelet count >1 lakh was found in 37 cases of non-severe cases only. In this study, there was no correlation between bleeding manifestations and platelet counts as similar to finding of Sharma NL et al. GI bleed and bleed at venipuncture sites occurred in 7 children whose platelet counts were between 20,000 to 50,000. Rise in AST was observed more than ALT in our study which coincides with the findings of Manjith et al but in our study elevated AST was observed in 87% and ALT in 57.5% in contrary to Manjith et al where only 42% of cases showed rise in AST.[17] Elevated liver enzyme levels correlated well with the severity of dengue fever and are an indicator of organ dysfunction as all children with severe dengue had elevated liver enzymes. Chest x-ray was abnormal in 47 (27.1%) of the cases, children with severe dengue had abnormal x-ray showing pleural effusion. Vinod et al observed 70% cases to have pleural effusion and more so, on right side (52%).[18] USG findings were abnormal in 26.17% of children without severe dengue and normal in 43.1%. Abnormal USG findings observed were pleural effusion, hepatomegaly, spleenomegaly, free fluid in abdomen. However, significance was not associated with abnormal USG findings in our study which is in contrary to findings of Sharma NL et al who reported significant association of hepatomegaly in his study.

Though coagulation profiles were abnormal in 25.3%, significant bleeding was seen only in 5.2%. In a study conducted by Mairuhu et al coagulation abnormalities are found in >75% of children with severe dengue fever.[19] In our study, 92% of severe dengue fever had abnormal coagulation profile while bleeding was observed in only 24%.

In present study, crystalloids were used in 80 (45.9%) children who presented with shock or developed shock during the hospital stay and Colloids in 8 (4.6%) children who had persistent shock after crystalloid boluses. Most of the children (43.2%) were started on oral feeds on 2nd day of hospitalization. In our study blood products were

required in 39 (22.4%) children, platelets required in 20 (11.5%), PRBC in 10 (5.7%), FFP in 9 (5.2%). These findings are in contrary to study of Kumar et al where twenty eight children (13.4%), received a transfusion of fresh whole blood, platelets in 26%, FFP in 9%.[20]

Respiratory distress was present in 15 (5.6%) children of whom 11 children required non-invasive ventilation and 4 required invasive ventilation. Persistent shock, presence of bleeding, high elevation of liver enzymes (more than 1000 U/L), and respiratory distress were identified as risk factors for mortality in severe dengue children in our study as observed in many other studies. However, some studies reported the presence of spontaneous bleeding, hepatomegaly, signs of capillary leakage like ascites and pleural effusion, leucopenia <4000 mm^3 and age >5 years to be significant risk factors of mortality for severe dengue.[21] Mortality in the present study was 1.7% compared to 12-13% in previous studies. Reduced mortality in the present study could have been due to the basic fact that all the children with dengue were classified according to the newer classification given by WHO.[22,23] Of the children with warning signs 33% needed PICU care and all were discharged well. The above-mentioned fact reiterates once again that those who present with severe dengue should be treated with utmost care in PICU so as to reduce mortality due to this dreaded but treatable condition.

CONCLUSION

To conclude, Dengue is a dreadful fever among pediatric age group which needs to be considered with great caution in management. Understanding the risk factors helps in predicting the mortality which helps in management and better outcome of the fever. In the present study, we listed the risk factors and are persistent shock, presence of bleeding, high elevation of liver enzymes (more than 1000 U/L), and respiratory distress. Rise in AST levels, pleural effusion, hepatomegaly are significant findings in distinguishing severe from non-severe cases of dengue fever.

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