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Clinical Profile and Outcome of Dengue Infections in Children

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Abstract:
Introduction: *In India, there is increased proportion of Dengue cases with severe disease and all forms of serotypes are circulating in the community. Of those with DHF, 90% are children less than 15 years of age. Early recognition and prompt initiation of appropriate treatment are vital to reduce disease related morbidity and mortality. Additional data about the disease leads to implementation or alteration in public health programs. An attempt is made to study the clinical profile and outcome during August to November of 2011 in hospitalized Dengue fever cases.*
Materials and Methods: *This is an observational study done at NilouferHospital Hyderabad. A total of 141 children tested positive for Dengue with Clinical features of Dengue fever during August to November 2011 were included in the study. All patients were tested for dengue by Dengue IgM/IgG rapid test (immunnochromatographic test) after 5-6 days of fever. Other relevant laboratory investigations were done.Cases tested positive were classified as per revised WHO classification as Dengue fever without warning signs, Dengue fever with warning signs and severe Dengue. The data was analyzed, using chi-square test. The statistical package used was IBM SPSS version 19.0.*
Observations and Results: *141 seropositive dengue cases reported in our hospital during the study period. 51.1% were from urban areas and 48.9% from rural areas. 19 (13.5%) were Dengue fever without warning signs, 89 (63.1%)were Dengue fever with warning signs and Severe Dengue were 33 (23.4)Out of 33 cases of severe Dengue, 21 cases were Dengue shock syndrome, 10 cases were with CNS involvement and 1 case was with severe liver function impairment (ALT >1000IU/L). One case was noted to have Dengue shock syndrome with seizures and liver function impairment.*
Conclusions: *Dengue fever is becoming more prevalent in India. Incidence of severe Dengue is increasing.*
Keywords: *Dengue fever, Dengue hemorrhagic fever, Dengue shock syndrome, Dengue fever without warning signs, Dengue fever with warning signs, Severe Dengue, platelet count, hematocrit, SGOT,SGPT*

I. Introduction

Dengue viral infections are one of the most important mosquito borne diseases in the world. Annually 100 million cases of dengue fever and half a million cases of dengue haemorrhagic fever (DHF) occur in the world with a case fatality in Asian countries of 0.5%–3.5% [1]. Of those with DHF, 90% are children less than 15 years of age. At present, dengue is endemic in 112 countries in the world [2, 3]. In India, there is increased proportion of Dengue cases with severe disease. The dengue epidemics in India are cyclical and are more frequent, expanding geographically into the rural areas and all forms of serotypes are circulating in the community. Uncontrolled population growth, urbanization, inadequate wastewater management, and lack of effective mosquito control have been implicated in the increased distribution and density of the vector and also the increased spread of the virus [4]. However, microevolution of the dengue virus may have also contributed to the spread of more virulent strains around the world. In fact there is evidence that the more virulent genotypes of the virus are replacing the less virulent genotypes, which may explain the global emergence of dengue infections[5]. Hospital-based studies on the risk of shock and death in severe dengue in tropical Asian countries showed that the percentage of admitted cases developing shock, ranged from 9 to 60% with in-hospital case fatality rates ranging from 0.2 to over 9%. Early recognition and prompt initiation of appropriate treatment are vital to reduce disease related morbidity and mortality. Additional data about the disease leads to implementation or alteration in public health programs. Hence an attempt was made to study the clinical profile and outcome of hospitalized dengue fever cases during August to November of 2011.

II. Aims & Objectives

To study the clinical profile and outcome of dengue infections in children.

III. Material And Methods

This is an observational study done at Niloufer hospital, Hyderabad from August to November 2011. A total of 141 children tested positive for dengue with clinical features of dengue were included in study.

Inclusion Criteria

Serologically confirmed (Ig M positive alone or both Ig M and Ig G) case up to 14 yrs were included in the study.

Exclusion Criteria

All children with negative dengue IgM antibody were excluded from study.

IV. Methodology

The study was done after obtaining approval from the ethics committee of Osmania medical college. Informed consent was taken from parents/guardian. A detailed history and physical examination was done. All patients were tested for dengue by Dengue IgM/IgG rapid test (immunno-chromatographic test) after 5-6 days of fever. The comparison results of SD BIOLINE Dengue IgM/ IgG test with haem-agglutination inhibition test showed that SD BIOLINE Dengue IgM/ IgG test had good correlation with haem-agglutination inhibition test. The sensitivity of the test is 91.2% with a specificity of 90% [6]. Platelet count was done by manual method using light microscope. Dengue virus isolation, PCR analysis could not be done due to non availability of facility. Other laboratory investigations included hemoglobin, total and differential count, hematocrit, PT, APTT, liver transaminases, renal function tests, chest X ray, ultrasound abdomen. Cases tested positive were classified as per revised WHO classification as, Dengue fever without warning signs, Dengue fever with warning signs, and Severe Dengue[7].The data collected was analyzed, using chi-square test. The statistical package used was IBM SPSS version 19.0. The results were compared with other studies. After analysis conclusions were arrived.

V. Observations And Results

141 seropositive dengue cases reported in our hospital during the study period.51.1% from urban areas and 48.9% from rural areas. These cases were classified according to revised WHO classification as Dengue fever without warning signs 19 (13.5%) Dengue fever with warning signs 89 (63.1%),and Severe Dengue 33 (23.4%).Out of 33 cases of severe Dengue, 21 cases were of Dengue shock syndrome, 10 cases were with CNS involvement and 1 case was with severe liver function impairment (ALT>1000IU/L). One case was noted to have Dengue shock syndrome with seizures and liver function impairment.

The age group of the affected children was between 3 months to 12 years. (Mean 5.16 year, standard deviation 3.67). Infants comprised 20(14.2%) in the total study group. 48(34%) children were between 1 and 5 years of age. 61(43.3%) children were between 6 and 10 years. 12(8.5%) children were with age more than10years.

Table 1 AGE WISE CLASSIFICATION OF CASES

NO	FEATURE	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	Mean age (yr) (SD)	5.16(3.67)	5.77(3.23)	4.71(3.71)	6.15(3.60)	.219
2	Age < 1 yr	20(14.2%)	5(26.3%)	7(7.9%)	8(24.2%)	.148
3	Age 1-5 yr	48(34%)	7(36.8%)	33(37.1%)	8(24.2%)	-
4	Age 6-10 yr	61(43.3%)	6(31.6%)	40(44.9%)	15(45.5%)	-
5	Age >10 yr	12(8.5%)	1(5.3%)	9(10.1%)	2(6.1%)	-

CAT 1 = DENGUE WITHOUT WARNING SIGNS.
CAT 2 = DENGUE WITH WARNING SIGNS.
CAT 3 = SEVERE DENGUE.

Total males affected were 83(58.9%) and females affected were 58(41.1%). It was not significant (P=0.479). In severe Dengue group, male and female cases were 51.5% and 48.5% respectively. Most common manifestations were fever (100%), vomiting (63.8%), bleeding manifestations (57.4%), conjunctival congestion (42.6%), abdominal pain (40.4%), rash (37.6%), facial puffiness (29.1%), flushing (25.5%) and myalgia (16.3%). Head ache, myalgia, vomiting, altered sensorium were more common in severe dengue. Abdominal pain, conjunctival congestion and facial puffiness were more common in Dengue with warning signs group.

Table 2 Clinical Features

NO	FEATURE	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	FEVER	141(100%)	19(100%)	89(100%)	33(100%)	-
2	HEAD ACHE	40(28.4%)	4(21.1%)	25(28.1%)	11(33.3%)	.050
3	MYALGIA	23(16.3%)	1(5.3%)	16(18%)	6(18.2%)	.050
4	VOMITING	90(63.8%)	10(52.6%)	56(62.9%)	24(72.7%)	.334
5	ABDOMINAL PAIN	57(40.4%)	0	44(49.4%)	13(39.4%)	.000
6	FACIAL PUFFINESS	41(29.1%)	0	30(33.75%)	11(33.3%)	.011
7	ALTERED SENSORIUM	4(2.8%)	0	0	4(12.1%)	.001
8	HEPATOMEGALY	69(48.9%)	1(5.3%)	45(50.6%)	23(69.7%)	.000

12.1% (4 cases) of severe dengue presented with altered sensorium and it is statistically significant (P=.001). Various factors contribute for altered sensorium in Dengue like electrolyte abnormality, cerebral anoxia, hepatic encephalopathy, cerebral edema, renal failure. Out of 4 cases of altered sensorium one child had signs of meningitis, hypoglycemia, hyponatremia, elevated aPTT and normal CT scan of brain. In two cases, there was Dengue shock syndrome leading to decreased cerebral perfusion and altered sensorium. Out of these two cases, one case died because of multi organ dysfunction in fourth case the reason for altered sensorium was hepatic encephalopathy.

Table 3 CLINICAL FEATURES

NO	FEATURE	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	HEPATOMEGALY	69(48.9%)	1(5.3%)	45(50.6%)	23(69.7%)	.000
2	LOW BP	18(12.8%)	0	1(1.1%)	17(51.5%)	.000
3	RASH	53(37.6%)	2(10.5%)	37(41.6%)	14(42.4%)	.032
4	CONVULSIONS	9(6.4%)	0	0	9(27.3%)	.000

Hepatomegaly was present in 69.7% in severe group and 50.6% in Dengue with warning signs group. It was statistically significant when compared with non severe Dengue group (P=0.000). Convulsions were present in 27.3% cases in severe dengue group and it is statistically significant (P=0.000). In 4 children there was previous history of febrile seizures. In one case there was associated altered behaviour due to Dengue encephalopathy, CSF analysis was normal in this case. In one case there was multi organ dysfunction with Dengue shock syndrome. In three cases course was uneventful and cause could not be evaluated. Lymphadenopathy (2.8%), relative bradycardia (1.4%) was less common manifestations. Rashes were seen in 37.6% of children and it is statistically significant (P=.032). In most of the cases it was maculopapular. Among bleeding manifestations, malena was more common and it is statistically significant (P=.001). Among 141 cases, 9 presented with hematemesis, 7 with epistaxis, 3 with petechiae, 2 with gum bleeds and 1 case with hematuria.

Table 4 BLEEDING **MANIFESTATIONS**

NO	FEATURE	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	MALENA	51(36.2%)	0	35(39.3%)	16(48.5%)	.001
2	HEMATEMESIS	9(6.3%)	0	4(4.5%)	5(15.2%)	.048
3	EPISTAXIS	7(4.9%)	0	5(5.6%)	2(6.1%)	.561
4	HEMATURIA	1(.7%)	0	1(1.1%)	0	.745
5	GUM BLEED	2(1.4%)	0	0	2(1.4%)	.036
6	PETECHIAE	3(2.1%)	0	2(2.2%)	1(3%)	.760

Mean Hb was 11.236g%. It was 11.55, 11.21, and 11.23 in Dengue without warning signs, with warning signs and severe dengue respectively.

Table 5 HEMOGLOBIN AND HEMATOCRIT

NO	FEATURE	TOTAL	CAT 1	CAT 2	CAT 3
1	HEMOGLOBIN MEAN (SD)	11.236(1.32)	11.55(1.18)	11.21(1.29)	11.23(1.3)
2	HEMATOCRIT (SD)	36.46(3.63)	36.04(2.34)	36.59(3.715)	36.35(4.077)

Mean hematocrit was 36.46. Hematocrit in Dengue with warning signs and severe Dengue was higher than Dengue without warning signs group. Platelet count below 40,000 were found in more percentage of Dengue cases with warning signs and severe Dengue but statistically it is not significant (P=.167).

Table 6 PLATECOUNT PER CUBIC MM

NO	PLATELET COUNT	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	>1,00,000	33(23.4%)	7(36.8%)	23(25.8%)	3(9.1%)	.167
2	>40,000-1,00,000	62(44%)	9(47.4%)	39(43.85%)	14(42.4%)	-
3	20,000-40,000	43(30.5%)	3(15.8%)	25(28.1%)	15(45.5%)	-
4	<20,000	3(2.1%)	0	2(2.2%)	1(3%)	-

Prothrombin time was elevated in 7 cases. 4(12.1%) cases belonged to severe dengue group but it is statistically not significant (P=.080). Activated partial thromboplastin time was elevated in 17 cases .Out of them 8 cases belonged to category 2 and 9 cases to category 3.This value is statistically significant (P=.005).

Table 7 SGOT AND SGPT(>50U/L)

NO	FEATURE	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	SGPT	11(7.8%)	0	4(4.5%)	7(21.2%)	.004
2	SGOT	5(3.5%)	0	3(3.4%)	2(6.1%)	.518

SGOT and SGPT levels were elevated in Dengue with warning signs and severe dengue. Elevation of SGPT is statistically significant (P=.004)

Table 8 CHEST X RAY

NO	CHEST X RAY FINDINGS	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	EFFUSION	35(24.8%)	2(10.5%)	18(20.2%)	15(45.5%)	.005
2	PNEUMONIA	8(5.7%)	0	7(7.9%)	1(3%)	.305
3	NORMAL	99(70.2%)	17(89.5%)	65(73%)	17(51.5%)	-

Pleural effusion was high in severe dengue and it is statistically significant (P=.005). Pneumonia was high in Dengue with warning signs but it is statistically not significant (P=.305).

Table 9 ULTRASOUND ABDOMEN

NO	ULTRASOUND ABDOMEN FINDINGS	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	HEPATOMEGALY	35(24.8%)	1(5.3%)	22(24.7%)	12(36.4%)	.044
2	GB EDEMA	30(21.3%)	1(5.3%)	16(18%)	13(39.4%)	.007
3	SPLENOMEGALY	17(12.1%)	1(5.3%)	11(12.4%)	5(15.2%)	.568
4	POLYSEROSITIS	43(30.5%)	1(5.3%)	25(28.1%)	17(51.5%)	.002
5	NORMAL STUDY	80(56.7%)	16(84.2%)	52(58.4%)	12(36.3%)	-

In ultrasound abdomen, hepatomegaly was found in higher percentage in dengue with warning signs and severe dengue. It is statistically significant when compared with dengue with out warning signs (P=0.044). Gall bladder wall edema and polyserositis were also significantly more in cat 2 and 3 with p value .007 and .002 respectively. 80 children had no abnormalities in ultrasound abdomen. Children in CAT 1 had more reports of normal ultrasound abdomen when compared to other two groups.

Table 10 MANAGEMENT

NO	MODE OF MANAGEMENT	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	CONSERVATIVE	94(66.7%)	19(100%)	61(68.5%)	14(42.4%)	.000
2	PRP	38(27%)	0	22(24.7%)	16(48.5%)	.001
3	FFP	16(11.3%)	0	7(7.9%)	9(27.3%)	.003
4	IONOTROPES	6(4.3%)	0	0	6(18.2%)	.000
5	WHOLE BLOOD	3(2.1%)	0	1(1.1%)	2(6.1%)	.193

66.7% cases were managed conservatively. All cases without warning signs were managed conservatively (P=.000). 42.4% cases in severe dengue were managed conservatively. Platelet transfusion was given only in 27% cases. In patients with bleeding manifestations and platelet count <50,000. even without bleeding manifestations with low platelet count(<30,000) Fresh frozen plasma was given in patients with DIC and in patients in whom hematocrit not improving inspite of fluids. Whole blood was given in patients with anemia and in cases where there was rapid rise in hematocrit.

Table 11 DURATION OF STAY IN HOSPITAL

NO	DURATION OF STAY (DAYS)	TOTAL	CAT 1	CAT 2	CAT 3
1	<2	9(6.4%)	3(15.8%)	5(5.6%)	1(3%)
2	3-5	85(60.3%)	12(63.2%)	61(68.5%)	12(36.4%)
3	6-8	37(26.2%)	4(21.1%)	22(24.7%)	11(33.3%)
4	9-11	7(5%)	0	0	7(21.2%)
5	>11	3(2.1%)	0	1(1.1%)	2(6.1%)

Majority of cases stayed in hospital for 3 to 5 days. Duration of stay in cat 1 was significantly less than cat 2 and 3 (P=.000).

Table 12 OUTCOMES

NO	OUTCOME	TOTAL	CAT 1	CAT 2	CAT 3	P VALUE
1	RECOVERY	139(98.6%)	19(100%)	89(100%)	31(93.9%)	.036
2	DEATH	2(1.4%)	0	0	2(6.1%)	-

Out of 141 children, 139 were recovered from the illness. Two children from severe dengue group died.

VI. Discussion

Total of 141 cases of sero-positive dengue children presented were analyzed. According to revised Dengue classification system proposed by Dengue control DENCO, cases were classified as Dengue fever without warning signs (13.5%), Dengue fever with warning signs (63.1%) and severe Dengue (23.4%). Siripen Kalyanarooj et al (Thailand 2011), reported 31% Dengue fever without warning signs, 58.4% Dengue fever with warning signs and 10.6% severe Dengue cases.

In this study, infants (14.2%), 1-5 years (34%), 6-10 years (43.3%), >10years (8.5%) were observed. Kabilan et al [8] reported 20% for infants and 28.7% and 1-5 years group. 6-15 years formed 51%. In our study, <5years were 48.2%. More than 5 years were 51.8%. Aggarwal et al [9] reported 45% & 55% for the same groups. Infants are lesser in present study when compared with Kabilan et al.

Table 13 SEX

NO	STUDY	MALE%	FEMALE%
1	Narayana et al	52.4	47.6
2	Gomber et al	56	44
3	Aggarwal et al	60	40
4	Present study	58.9	41.1

It is comparable with other studies. Males are more affected than females, this could be due to the fact that in these social regions, males spend more time outdoors than females, thereby have increased risk of mosquito bites.

Mean duration of fever was 5.09 days. Narayanan et al[10] reported 4.9 days.

Table 14 VOMITINGS

NO	STUDY	PERCENTAGE
1	Kalyanarooj (Indonesia)	66
2	Ratageri (Hubli)	82
3	Narayanan (Chennai)	83
4	Present study	63.8

Malena was most common bleeding manifestation in this study. Hematemesis was most common in other studies. It was significantly more common in severe Dengue group. Headache was seen in 28.8% (Narayanan), 77% (Kalyanarooj)[11,12], 22% (Ratageri) [13]. It is 28.4% in the present study. Younger kids may not complain this symptom. High percentage in Kalyanarooj's study may be due to different age composition. Abdominal pain was present in 40.4% in present study and 34.5% in Kalyanarooj. Aggarwal reported 49%. He studied only DHF and DSS and may be the reason for high percentage. Hepatomegaly was seen in (72%) in Aggarwal, (52.5%) in Narayanan and (48.9%) in present study. Hepatomegaly was significantly more common in DHF and DSS.In all studies. Coryza is reported to be a common manifestation in young children (28). However, in our series it was exceedingly uncommon compared to other clinical features.

Table 15 SHOCK

NO	STUDY	PERCENTAGE
1	Aggarwal et al	33
2	Gomber et al	20
3	Narayanan et al	8.4
4	Kabilan et al	23.8
5	Ratageri et al	22
6	Present study	15.6

DSS was low in Narayanan et al. Due to increasing endemicity and changing epidemiology, DSS is in increasing trend. Polyserositis was noted in 51.5% cases of severe dengue. Kalyanarooj reported 84% in DHF. Narayanan et al reported low percentage as there was low DHF and DSS Lymphadenopathy is 2.8% in present study and 10.2% in Narayanan et al study. Mean haemoglobin is 11.5g% in present study. Narayanan et al reported 10.8g%.Mean hematocrit in present study is 36.04%, 33.2% in Narayanan et al study. Gomber et al[14] reported 38.34%. Mean hematocrit value was significantly higher in Dengue with warning signs and severe dengue group. Platelet count in this study was >1 lakh (23.4%), >40000-1 lakh (44%), 20000-40000 (30.5%), <20000 (2.1%). Aggarwal et al reported, >50000 (31%), 25000-50000 (47%), <25000 (22%). In severe dengue (DHF & DSS), ascites, gall bladder wall edema and hepatomegaly on ultrasound were significantly more common in present study ($P<0.05$). Other studies also reveal the same. Gall bladder wall edema more than 5 mm in clinically suspected dengue cases signifies 91.7% specificity towards DHF and DSS.

According to Halstead et al [15] mortality due to dengue in Asian countries is 0.5%-3.5% (if early recognition and appropriate treatment was instituted). Mortality in this study is 1.4%. Kabra et al[16] and Srivastava et al[17]reported 12% to 13% mortality.

Table 16 MORTALITY

NO	STUDY	MORTALITY(%)
1	Kabra et al(1992)	12-13
2	Srivastava et al (1990)	12-13
3	Aggarwal et al (1996)	6
4	Gomber et al (2001)	4.8
5	Narayanan et al(2001)	3.3
6	Kabilan et al(2001)	No mortality
7	Ratageri et al (2003)	No mortality
8	Present study	1.4

Mortality rate is drastically reduced by early recognition, precise assessment and appropriate fluid management as per WHO protocol. This study was undertaken to define the natural history of this disease in terms of clinical presentation and outcome in children. The epidemic started in August 2011, the post-monsoon season. This timing can be explained by increased mosquito breeding[18] due to ambient temperature and humidity [19]present in the preceding months. As regards the clinical presentation, experience from numerous outbreaks of confirmed Dengue fever show similar presentation with few exceptions. Fever has been the main finding in all epidemics including ours. Average duration of fever was 5 days and biphasic pattern was seen in 40% cases. Similar findings were observed in Dengue epidemics in Bangladesh and Chennai. Serological diagnosis of dengue viral infection was done but viral isolation and PCR was not done due to non availability of facility. Serotypes were not identified. So the predominant serotype was not determined.

Present study shows slight difference in the presentation and course of patients with Dengue infection compared to epidemics in other parts of the world, thus indicating the need for continuous sero epidemiological surveillance in India for identification of clinical features of Dengue infection in our region and for timely implementation of an effective control programme to prevent such outbreaks in future.

VII. Conclusions

1. Dengue fever is becoming more prevalent in India. Incidence of severe Dengue is increasing.
2.Vomiting, hematemesis, skin bleeds, altered sensorium, hepatomegaly, elevated SGOT & SGPT, gall bladder wall thickening, ascites, pleural effusion following the period of fever defervescence strongly indicate severe Dengue (Dengue hemorrhagic fever and dengue shock syndrome).
3. The bleeding in dengue is not purely due to thrombocytopenia. It is due to multiple etiologies including vascular changes. There is no role for prophylactic platelet transfusion.
4. Early recognition, precise assessment with WHO revised classification and appropriate treatment have reduced the mortality.
5. Parental health education about the fever defervescence, warning signs and early referral may prevent deaths due to dengue.

6. Vector control by avoiding stagnant water sources can decrease incidence of Dengue.

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