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Original article

Clinical and microbiological profile of Acute Dengue infection in teaching hospital

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Abstract:

Over the past two decades, there has been global increase in the frequency of dengue fever, dengue hemorrhagic fever and its epidemics, with a concomitant increase in disease incidence. Objective: To study the clinical and microbiological profile of Dengue infection and correlating clinical and microbiological profile in children in S.V.R.R.G.G.H, Tirupati.Hospital based Prospective study included Children age group of 1-12 years presenting with fever assessed clinically, serologically and managed as for WHO protocol and will be followed for outcome. Of the 514 children tested 248(48.2%) were found to be positive for IgM antibodies to dengue by IgM capture.

Key Words: Denguefever; dengue hemorrhagic fever

Introduction:

Dengue fever is an important arthropod (mosquito) borne viral disease of tropics and subtropics affecting urban and periurban areas. It is a self limiting disease transmitted by bite of an infected female Aedes mosquito [1].Dengue virus belongs to Arbovirus group, Family Flaviviridiae, Genus Flavivirus and Species Dengue virus. Dengue fever is characterized by fever, headache, myalgia, arthralgia, rash, nausea and vomiting affecting mainly younger age group. The presentation of dengue fever varies from asymptomatic to symptomatic. In symptomatic patients it presents as classical dengue fever, dengue hemorrhagic fever or dengue shock syndrome [2]. It is estimated that each year, 50 million infections occur with five lakh cases of dengue hemorrhagic fever and at least 12,000 deaths mainly among children, although facilities could be twice as high [3]. Currently the disease is endemic in all continents except Europe [4].

In 2008, for SEAR as a whole, there is a about 18% increase in the number of reported cases and about 15% increase in the number of reported dengue deaths as compared to the same period in the previous year. The case fatality rates are high in major endemic countries (about 3.5%) [4].

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Viral antigen detection

The NS1 gene product is a glycoprotein produced by all flaviviruses and is essential for Replication and viability of the virus. The protein is secreted by mammalian cells but not by Insect cells. NS1 antigen appears as early as Day 1 after the onset of the fever and declines to undetectable levels by 5–6 days. Hence, tests based on this antigen can be used for early diagnosis. ELISA and dot blot assays directed against the envelop/membrane (EM) antigens and non-structural protein 1 (NS1) demonstrated that this antigen is present in high concentrations in the sera of the dengue virus-infected patients during the early clinical phase of the disease and can be detectedin both patients with primary and secondary dengue infections for up to six days after the onset ofthe illness. Besides providing an early diagnostic marker for clinical management, it may also facilitate the improvement of epidemiological surveys of dengue infection [5].

Serologic diagnosis:

Five basic serologic tests have been routinely used for diagnosis of denuge infection. They are hemagglutination inhibition test(HI), complement fixation test (CF), neutralization test(NT), immunoglobulin M (IgM) capture ELISA and indirect immunoglobulin G (IgG)ELISA [5].

MAC-ELISA has become the most widely used serologic test for dengue diagnosis in the past few years. It is a simple, rapid test that requires very little sohphisticated equipment. Anti-dengue IgM antibody develops a little faster than IgG antibody. Nearly all patients develop detectable IgM antibody 6 to 10 days after onset of illness. The IgM antibody is produced by patients with both primary and secondary dengue infections IgM antibody titres in primary infections are significantly higher than in secondary infections.

MAC-ELISA has become an invaluable tool for surveillance of dengue, DHF and DSS. In areas where dengue is not endemic, it can be used in clinical surveillance for viral illness or for random, population-based sero surveys, with the certain that any positive results detected indicate recent infections(within the last 2 to 3 months).

But this test is very non-specific and exhibits the same broad cross reactivity among Flaviviruses as the HI test does; therefore it cannot be used to identify the infecting dengue virus serotype [5].

Aims & objective: To study the clinical and microbiological profile of Dengue fever in children in S.V.R.R.G.G.H, Tirupati.To study the outcome of Dengue fever correlating the microbiological profile.

Material & methods

- **DESIGN:** Prospective study.
- **SETTING:** Department of Pediatrics, Sri VenkateswaraRamnarainRuia Government General Hospital, Tirupati
- **PERIOD OF STUDY:**Two years from September 2010 to August 2012.
- **METHOD:** Children age group of 1-12 years presenting with fever and other features suggestive of Dengue fever according to WHO guidelines will be assessed clinically, serologically and managed as per WHO protocol and will be followed for outcome.

All the children are subjected for following investigations

- Complete Blood Picture.
- IgM antibody detection.(SD Dengue IgM Capture Elisa kit)

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- NS1Antigen detection(Panbio Dengue Early ELISA kit)
- Other relevant investigations for renal, liver and other functions.

Inclusion criteria

- ❖ Children age group 1 - 12 years.
- ❖ Children's with fever and other features suggestive Dengue fever according to WHO guidelines { headache, retro orbital pain, myalgia / arthralgia, rash, haemorrhagic manifestations, thrombocytopenia and leukopenia } .

Exclusion Criteria

- Those with other viral fevers with thrombocytopenia.
- Those with positive for Malaria parasite (All species).
- Those with acute and chronic liver disease.
- Those with blood dyscrasias.

The Panbio Dengue Early ELISA is a dengue NS1 antigen capture Elisa. It is for qualitative detection of NS1 Ag in human serum. SD Dengue IgM Capture Elisa kit is used for qualitative detection of Ig M dengue antibodies specific to Dengue virus in human serum.

Results

The following observations were made in 514 cases with symptoms suggestive of Dengue fever

Statistical analysis done by using MS EXCEL and EPI INFO

Table 1: Age group vs IgM category

Age group (Years)	IgM Categorization		Total (%)
	Positive (%)	Negative (%)	
1 – 3	72 (47.1)	81 (52.9)	153 (100.0)
4 – 6	100 (48.1)	108 (51.9)	208 (100.0)
7 – 9	47 (51.1)	45 (48.9)	92 (100.0)
10 – 12	29 (47.5)	32 (52.5)	61 (100.0)
Total	**248 (48.2)**	**266 (51.8)**	**514 (100.0)**

χ^2=0.40; P=0.93; NS

Table 2: DHF and DSS by IgM Category

DHF	IgM categorization		Total	DSS	IgM Categorization		Total
	Positive (%)	Neagtive (%)			Positive (%)	Neagtive (%)	
Positive	209 (99.5)	1 (0.5)	210 (100.0)	**Positive**	210 (99.5)	1 (0.5)	211 (100.0)
Negative	39 (12.8)	265 (87.2)	304 (100.0)	**Negative**	38 (12.5)	265 (87.7)	303 (100.0)
Total	**248 (48.2)**	**266 (51.8)**	**514 (100.0)**	**Total**	**248 (48.2)**	**266 (51.8)**	**514 (100.0)**

χ^2=373.8; P<0.001; S *χ^2=376.9; P<0.001; S*

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Table 3 :DHF and DSS by NS1 category

DHF	NS1		Total (%)	DSS	NS1		Total (%)
	Positive (%)	Negative (%)			Positive (%)	Negative (%)	
Positive	110 (52.4)	100 (41.6)	210 (100.0)		110 (52.1)	101 (47.9)	211 (100.0)
Negative	40 (13.2)	264 (86.8)	304 (100.0)		40 (13.2)	263 (86.8)	303 (100.0)
Total	**150 (29.2)**	**364 (70.8)**	**514 (100.0)**		**150 (29.2)**	**364 (70.8)**	**514 (100.0)**

χ^2=92.4; P<0.001; S *χ^2=91.2; P<0.001; S*

Dengue hemorrhagic fever and Dengue shock syndrome more common in children with NS1 Ag test positive

Table 4: Platelet count by DHF and DSS category

Platelet count	DHF Categorization			DSS Categorization		Total
	Positive (%)	Negative (%)	Total	Positive (%)	Negative (%)	
1 lakh-1.5 lakhs	5 (11.1)	40 (88.9)	45 (100.0)	5 (11.1)	40 (88.9)	45 (100.0)
0.5 lakh-1 lakh	3 (6.7)	222 (93.3)	225 (100.0)	4 (1.8)	222 (98.2)	225 (100.0)
<0.5 lakh	203 (83.2)	41 (16.9)	244 (100.0)	203 (83.2)	41 (16.9)	244 (100.0)
Total	**211 (41.1)**	**303 (58.9)**	**514 (100.0)**	**211 (41.1)**	**303 (58.9)**	**514 (100.0)**

χ^2=342.3; P<0.001; S *χ^2=338.5; P<0.001; S*

Hemorrhagic manifestations and shock are more common in children with platelet count < 50,000 .i.e., 83.2%

Table 5: Symptoms among patients by DHF and DSS

S.No	Symptom	DHF		P value	DSS		P value
		Yes (%)	No (%)		Yes (%)	No (%)	
1	Headache	109 (51.9)	149 (49.0)	0.51; NS	110 (52.1)	148 (48.8)	0.46; NS
2	Retro-orbital pain	73 (34.8)	106 (34.9)	0.98; NS	73 (34.8)	106 (34.9)	0.98; NS
3	Fatigue	110 (52.4)	154 (50.7)	0.49; NS	111 (52.6)	149 (49.2)	0.44; NS

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4	Pain abdomen	162 (77.1)	229 (75.3)	0.63; NS	163 (77.3)	228 (75.2)	0.60; NS
5	Vomitings	162 (77.1)	229 (75.3)	0.63; NS	163 (77.3)	228 (75.2)	0.60; NS
6	Arthralgia	162 (77.1)	229 (75.3)	0.63; NS	163 (77.3)	228 (75.2)	0.60; NS
7	Body pains	162 (77.1)	229 (75.3)	0.63; NS	163 (77.3)	228 (75.2)	0.60; NS
8	Poor intake	162 (77.1)	229 (75.3)	0.63; NS	163 (77.3)	228 (75.2)	0.60; NS
9	Skin bleeds	210 (100.0)	46 (15.1)	<0.001; S	210 (100.0)	46 (15.1)	<0.001; S
10	Epistaxis	155 (73.8)	0 (0.0)	<0.001; S	155 (73.8)	0 (0.0)	<0.001; S
11	Haematemesis	102 (48.6)	0 (0.0)	<0.001; S	102 (48.3)	0 (0.0)	<0.001; S
12	Melaena	210 (100.0)	0 (0.0)	<0.001; S	210 (100.0)	0 (0.0)	<0.001; S
13	Convulsions	10 (4.8)	7 (2.3)	0.12; NS	10 (4.8)	7 (2.3)	0.12; NS
14	Conjunctival suffusion	162 (77.1)	229 (75.3)	0.63; NS	163 (77.3)	228 (75.2)	0.60; NS
15	Hepatomegaly	161 (76.7)	229 (75.3)	0.72; NS	162 (76.8)	228 (75.2)	0.69; NS
16	Splenomegaly	110 (47.6)	150 (49.3)	0.49; NS	111 (52.6)	149 (49.2)	0.44; NS
17	Tourniquet test	110 (47.6)	150 (49.3)	0.49; NS	111 (52.6)	149 (49.2)	0.44; NS
18	Facial puffusion	162 (77.1)	229 (75.3)	0.63; NS	163 (77.3)	228 (75.2)	0.60; NS
19	Ascites	162 (77.1)	228 (75.0)	0.57; NS	163 (77.3)	227 (74.9)	0.54; NS
20	Pedal edema	65 (31.0)	100 (32.9)	0.64; NS	66 (31.3)	99 (32.7)	0.73; NS

21	Pleural effusion	30 (14.3)	49 (16.1)	0.57; NS	66 (31.3)	99 (32.7)	0.73; NS

[More common bleeding manifestations in dengue hemorrhagicfever and dengue shock syndrome were skin bleeds and meleana followed by epistaxis . Most common non bleeding manifestations in dengue hemorrhagic fever were pain abdomen , vomiting, arthralgia , body pains]

Table 6 : Outcome:

S.No	Complication	No.of Patients	Percentage
1.	DHF	210	40.9
2.	DSS	211	41.1
3.	ARDS	40	7.8
4.	Encephalopathy	17	3.3

Major complication observed in this study was dengue shock syndrome (41.1%) followed by dengue hemorrhagic fever 40.9 % , ARDS was seen in 7.8% children and encephalopathy was seen in 3.3% children

Discussion

Among 514 cases tested 248(48.2%) were found to be positive for IgM antibodies to dengue by IgM capture. ELISA method .Of 514 cases 137 (48.9%) were positive among 280 males, 111(47.4) were positive among 234 females. In present study the ratio of positive cases among the males and females was 1.23:1. Similar results were found in studies conducted by Ira shah et al (2004) (48.44%) [6] ,S.L.Hoti et al (2004) (50.6%) [7],B.Mustafa MEH et al (36.9%)(2006)[8].

In this study Ns1Ag test was positive 29.2% cases,similar observation were seen in study by B.Mustafa MEH et al (31.2%)(2006) [8]. In our study there is strong correlation present between NS1Ag positivity and Dengue hemorrhagic fever and dengue shock syndrome complications.Mean ge of presentation reported by different author's are as follows- IraSha et al - 6.1 years [6], Hoti et al 1-15 years [7], Raju BJ and Rajaram G -0-10 age group [9].In the present study also most of the reported cases were from the age group of 1-6 yr.

In the present study the most common clinical presentation along with fever was pain abdomen, vomiting, arthralgia, bodypains, poor intake facial puffiness and abdominal distention. Similar observations were made in study conducted by Neeraja et al(2006) [10]Gurdeep et al(2008)[11],Manjith Narayana et al(2002) [12],Agarwal et al(1998)[13].In present study most common bleeding manifestation in dengue hemorrhagic fever patients were skin bleeds(100%) and melena (100%) followed by epistaxis 73.8% and hematemesis 48.6%.in study by Shah G.S. et al (2006) [14] common bleeding manifestation was skin bleeds 59% .in study by Gurdeep.S.Dhooria et al(2008) [11] most common bleeding manifestation was petechiae in 85% followed by melena 6% echymosis 2.5% and epistaxis 2.5%. In our study dengue fever present in 58.9%, dengue hemorrhagic fever in 40.9%, dengue shock syndrome in 41.1% of

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cases. In study by Gurdeep.S.Dhooria et al(2008) [11].92% of cases were dengue hemorrhagicfever , 7.4% cases presented in dengue shock syndrome.In current study platelet count <50,000 seen in dengue hemorrhagic fever patients significantly in 83.2%of cases.In this study good correlation seen between thrombocytopenia and bleeding manifestation.A study by Kamath et al(2006)[15] reported that platelet count <50,000 were 62.3% and same correlation seen as our study.In present study encephalopathy was known to occur in 3.3% of cases. Similar observations noted in studies done by Gurdeep.S.Dhooria et al(2008), (3.7%) [11].

Limitations of the study: Sample size is small.MAC ELISA test is very non-specific and exhibits the same broad cross reactivity among Flaviviruses

Conclusion

The isolation of dengue viruses or demonstration of dengue viral genome sequences is useful for confirmation of dengue virus infection.The detection of IgM dengue antibodies by capture ELISA and NS1 Ag were helpful for diagnosis of acute dengue virus infection. The serological diagnosis of dengue fever has a role in categorizing primary and secondary infection and it also serves as a predictor of disease progression and mortality especially in severe forms.i.e. dengue hemorrhagic fever/ dengue shock syndrome.

What's new: Early detection especially in endemic areas by rapid screening of cases helps the public health authorities to take appropriate control measures to prevent the spread of the disease and also helps in early management of cases.

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