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Study on incidence and clinical profile in dengue fever-in tertiary health care center

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Abstract
Background: 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.
Aim & Objective: The study mainly focuses on the incidence and clinical profile of Dengue fever in Children's.
Methodology: A total number of 500 patients were studied. The study period was from March 2016 to Feb 2018. Sera collected from these patients were tested for the presence of Ig M antibodies and NS1 Ag against Dengue virus.
Results: Of the total 500 patients 250 were positive for Ig M antibody, 150 were positive for NS1 Ag against Dengue virus. The prevalence of dengue fever was more common among 3-6 years age group of children. A significant association was found between dengue serology (IgM Antibody & NS1 Ag detection) and complications that are DHF &DSS. A significant association was found between low platelet count and complications that are DHF &DSS. Of the clinical manifestations there was high incidence of pain abdomen, vomiting, arthralgia, body pains, poor intake, facial puffiness and abdominal distention
Conclusion: The detection of IgM Antibody & NS1 Ag were valuble in diagnosis of DHF &DSS. Early detection of cases helps in the appropriate control measures and early management of cases. Community participation with emphasis on control measures is very much essential for dengue control. Constant surveillance for dengue viral infection is required to take necessary action by health authorities.

Keywords: Dengue fever, IgM antibodies, plate late count, NSI Ag.

Introduction
Dengue fever is the most rapidly spreading 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.
Dengue virus belongs to the Arbovirus group, Family Flaviviridiae, Genus Flavivirus and Species Dengue virus. Dengue fever is characterized by fever, headache, myalgia, arthraligia, rash, nausea and vomiting affecting mainly younger age group, the presentation of dengue fever varies from asymptomatic to symptomatic. In symptomatic pateints it presents as classical dengue fever, dengue hemorrhagic fever or dengue shock syndrome [1].
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. Various factors responsible for resurgence of dengue epidemic are: (i) unprecedented human population growth; (ii) unplanned and uncontrolled urbanization; (iii) inadequate waste management; (iv) water supply mismanagement; (v) increased distribution and density of vector mosquitoes; (vi) lack of effective mosquito control has increased movement & spread of dengue viruses and development of hyper endemicity and (vii) deterioration in public health infrastructure [2].

Dengue in India
In India, dengue has seen resurgence in recent times. The first evidence of Dengue fever in India was reported during 1956 in Vellore district (Tamil Nadu). The first Dengue hemorrhagic fever outbreak occurred in calcutta (West Bengal) in 1963 with 30% of cases showing hemorrhagic manifestations. All of the four serotypes i.e. Dengue 1, 2, 3 and 4 have been isolated in India. Aedes aegypti breeds more commonly in urban areas.

However the trend is now changing due to socio economic and man made ecological changes; it has resulted in invasion of Aedes aegypti in to the rural areas, which has tremendously increased the chances of spread of the disease to rural areas.

Recurring outbreaks of DF & DHF have been reported from vaious states/union terriotories namely Andhra Pradesh, Delhi, Goa, Haryana, Gujarat, Karnataka, Kerala, Maharashtra, Rajasthan, Uttar Predesh, Pondicherry, Punjab, Tamil Nadu, West Bengal and Chandigarh.

During 1996, one of the most severe outbreaks of DF/DHF occurred in Delhi where 10.252 cases and 423 deaths occurred. In 2006 the country witnessed another outbreak, with a total cases of 12,317 cases and 184 deaths were reported in 21 states/ UTs. In 2007 only 5534 cases and 69 deaths reported from 18 states [4].

Hence the present study was under taken to investigate the incidence, clinical profile and outcome of Dengue fever in Tertiary health care centre

Material & Methods

Design: Prospective study.

Setting: Department of Pediatrics, Dr. V.R.K Womens Medical College and collaborate with Princess Durru Shevar Childrens Hospital, Hyderabad.

Period of study: Two years from March 2016 to Feb 2018.

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 for WHO protocol and will be fallowed for outcome.

All the children are subjected for following investigations

- Complete Blood Picture.
- IgM antibody detection. (SD Dengue IgM Capture Elisa kit)
- NS1 Antigen 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.

Test results

Cut-off value=mean absorbance of calibrator x calibrator factor (0.62)

(Calibrator factor is batch specific)

Index value=sample absorbance/ Cutoff value.

Pan bio units= Index value x 10

>11 Pan Bio units=Positive.

SD Dengue IgM Capture Elisa kit is used for qualitative detection of Ig M dengue antibodies specific to Dengue virus in human serum.

Test results

Absorbance value of sample < cut off value =Anti Dengue IgM Negative.

Absorbance value of sample ≥ cut off value =Anti Dengue IgM Positive.

Statistical analysis

Statistical analysis done by using MS EXCEL EPI INFO

Results

The present study was carried out in the department of pediatrics, Dr. V.R.K Womens Medical College during March 2016 to Feb 2018.The following observations were made in 500 cases with symptoms suggestive of Dengue fever

Gender distribution

Table 1: shows distribution of children according to gender

Sex	No. of patients	Percentage
Male	270	54
Female	230	46
Total	500	100.0

In this study occurrence of Dengue fever more in male children than in females

The distribution of dengue fever according to age is depicted in table no. 2

Table 2: Age group distribution of patients

Age group (Years)	No. of patients	Percentage
1 – 3	150	30
4 – 6	205	41
7 – 9	90	18
10 – 12	55	11
Total	500	100.0

Table 3: Geographic distribution rural Vs urban

Area	No. of patients	Percentage
Urban	150	30
Rural	350	70
Total	500	100

Out of 500 cases 350 belonged to rural areas 150 hailed from urban areas

Table 4: Clinical features

Clinical features	No. of patients	Percentage
Headache	250	50
Retro-orbital pain	175	35
Fatigue	265	53
Pain abdomen	380	76
Vomitings	370	74
Arthralgia	385	77
Body pains	385	77
Poor intake	385	77
Skin bleeds	250	50
Epistaxis	150	30
Haematemesis	100	20
Melaena	215	43
Convulsions	15	3
Conjunctival suffusion	391	78.2
Hepatomegaly	390	78
Splenomegaly	260	52
Tourniquet test	250	50
Facial puffiness	392	78.4
Ascites	395	73
Pedal edema	165	33
Pleural effusion	80	16

Major clinical features that were observed in most cases were pain abdomen, vomiting, arthralgia, body pain, poor intake, conjunctival suffusion & facial puffiness followed by hepatomegaly and ascites

Table 5: Investigative findings among patients

S. No	Investigative finding	No. of patients	Percentage
1.	Total leukocyte count		
	(A) >11000/cu mm	120	24
	(B) 4000-11000/cu mm	170	34
	(C) 4000/cu mm	225	45
2	AST > 45 IU/L	190	38
3	ALT > 45 IU/L	195	39
4	IgM Ab	250	50
5.	NSI Ag	150	30

In this study out of 500 cases leukopenia i.e., total leucucyte count <4000/cumm is seen in 45% of children, leukocytosis is seen in 24% of children, remaining 34% had normal counts 34 children showed raised serum AST and ALT levels i.e., >45 IU/L

Out of 500 cases 250 children had IgM antibody positive and 150 children had NS1Ag positive on serological diagnosis

Table 6: Complications among patients

S. No	Complication	No. of Patients	Percentage
1.	DHF	205	41
2.	DSS	206	41.2
3.	ARDS	35	7
4.	Encephalopathy	18	3.6

Major complication observed in this study was dengue shock syndrome (41.2%) followed by dengue hemorrhagic fever 41 %, ARDS was seen in 7 % children and encephalopathy was seen in 3.6% children

Table 7: Platelet count categorization of patients

Platelet category	No. of patients	Percentage
1 lakh-1.5 lakhs	40	8
0.5 lakh-1 lakh	220	44
<0.5 lakh	240	48
Total	500	100.0

In this study majority of children had low platelet count.i.e; less than 50,000 (48%)

Table 8: PCV categorization of patients

PCV category	No. of patients	Percentage
<35 %	75	15
35% -45 %	216	43.2
>45%	209	41.8
Total	500	100.0

In these studies haemoconcentration was observed in 41.8% of children

Table 9: Age group vs IgM category

Age group (Years)	IgM Categorization		Total (%)
	Positive (%)	Negative (%)	
1 – 3	68 (28.33)	80 (30.76)	148 (29.6)
4 – 6	100 (41.66)	105 (21)	205 (41)
7 – 9	45 (18.75)	45 (17.3)	90 (18)
10 – 12	27 (11.25)	30 (11.5)	57 (11.4)
Total	240 (48)	260 (52)	500 (100.0)

Most of the children in age group of 4-6 yrs had IgM antibody test positive

Table 10: Gender vs IgM category

Gender	IgM Categorization		Total (%)
	Positive (%)	Negative (%)	
Male	130 (54.16)	140 (53.84)	270 (54)
Female	110 (45.83)	120 (24)	230 (46)
Total	240 (48)	260 (52)	500 (100.0)

Study showed that most of the male children had IgM antibody test positive compared to female children

Table 11: DSS by IgM category

DSS	IgM Categorization		Total (%)
	Positive (%)	Negative (%)	
Positive	210 (87.5)	1 (0.38)	211 (42.2)
Negative	30 (12.5)	259 (99.61)	289 (57.8)
Total	240 (48)	260 (52)	500 (100.0)

Dengue shock syndrome more common in children with dengue IgM antibody test positive

Table 12: DHF by NS category

DHF	NS		Total (%)
	Positive (%)	Negative (%)	
Positive	110 (73.33)	100 (28.57)	210 (42)
Negative	40 (26.66)	250 (50)	290 (58)
Total	150 (30)	350(70)	500 (100.0)

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

Table 13: DSS by NS category

DSS	NS		Total (%)
	Positive (%)	Negative (%)	
Positive	110 (73.33)	99 (28.28)	209 (41.8)
Negative	40 (26.66)	251 (71.71)	291 (58.2)
Total	150 (30)	350 (70)	500 (100.0)

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

Table 14: Platelet count by DHF category

Platelet count	DHF Categorization		Total (%)
	Positive (%)	Negative (%)	
1 lakh-1.5 lakhs	6 (2.92)	40 (13.55)	46 (9.2)
0.5 lakh-1 lakh	2 (0.97)	220 (74.57)	222 (44.4)
<0.5 lakh	197 (96.09)	35 (11.86)	232 (46.4)
Total	205 (41)	295 (59)	500 (100.0)

Hemorrhagic manifestations are more common in children with platelet count < 50, 000. i.e., 96.09%

Table 15: Platelet count by DSS category

Platelet count	DSS Categorization		Total (%)
	Positive (%)	Negative (%)	
1 lakh-1.5 lakhs	5 (2.43)	40 (13.55)	45 (9)
0.5 lakh-1 lakh	4 (1.95)	218 (43.6)	222 (44)
<0.5 lakh	196 (95.06)	37 (7.4)	233 (46.6)
Total	205 (41)	295 (59)	500 (100.0)

Table 16: Symptoms among patients by DHF

S. No	Symptom	DHF		P value
		Yes	No	
1	Headache	109	149	0.51; NS
2	Retro-orbital pain	73	106	0.98; NS
3	Fatigue	110	154	0.49; NS
4	Pain abdomen	162	229	0.63; NS
5	Vomitings	162	229	0.63; NS
6	Arthralgia	162	229	0.63; NS
7	Body pains	162	229	0.63; NS
8	Poor intake	162	229	0.63; NS
9	Skin bleeds	210	46	<0.001; S
10	Epistaxis	155	0	<0.001; S
11	Haematemesis	102	0	<0.001; S
12	Melaena	210	0	<0.001; S
13	Convulsions	10	7	0.12; NS
14	Conjunctival suffusion	162	229	0.63; NS
15	Hepatomegaly	161	229	0.72; NS
16	Splenomegaly	110	150	0.49; NS
17	Tourniquet test	110	150	0.49; NS
18	Facial puffusion	162	229	0.63; NS
19	Ascites	162	228	0.57; NS
20	Pedal edema	65	100	0.64; NS
21	Pleural effusion	30	49	0.57; NS

More common bleeding manifestations in dengue hemorrhagic fever 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 17: Symptoms among patients by DSS

S. No	Symptom	DSS Categorization		P value
		Yes	No	
1	Headache	110	148	0.46; NS
2	Retro-orbital pain	73	106	0.98; NS
3	Fatigue	111	149	0.44; NS
4	Pain abdomen	163	228	0.60; NS
5	Vomitings	163	228	0.60; NS
6	Arthralgia	163	228	0.60; NS
7	Body pains	163	228	0.60; NS
8	Poor intake	163	228	0.60; NS
9	Skin bleeds	210	46	<0.001; S
10	Epistaxis	155	0	<0.001; S
11	Haematemesis	102	0	<0.001; S
12	Melaena	210	0	<0.001; S
13	Convulsions	10	7	0.12; NS
14	Conjunctival suffusion	163	228	0.60; NS
15	Hepatomegaly	162	228	0.69; NS
16	Splenomegaly	111	149	0.44; NS
17	Tourniquet test	111	149	0.44; NS
18	Facial puffusion	163	228	0.60; NS
19	Ascites	163	227	0.54; NS
20	Pedal edema	66	99	0.73; NS
21	Pleural effusion	66	99	0.73; NS

More common clinical features in dengue shock syndrome were skin bleeds and meleana

A study to know the incidence of dengue fever among patients presenting with clinical symptoms suggestive of dengue fever attended in department of paediatrics, Shadan Medical College & Princes Durru Shevar Childrens Hospital Hyderabad was undertaken.

Discussion

Dengue is an acute arboviral disease. It is probably one of the most important viral disease in terms of human morbidity and mortality. The WHO says some 2.5 billion people, i.e., two fifths of the world population are now at risk from dengue and estimates that there may be 50 million cases of dengue infection worldwide every year [3]. The spectrum ranges from self limiting dengue fever to more severe forms of dengue hemorrhagic fever or dengue shock syndrome. The problem of dengue has reached mammoth proportions in India since the first epidemic of clinical dengue like illness was recorded in madras in 1780. It is compounded by the huge population, poor medical and diagnostic facilities and inadequate mosquito control [3].

Vaccines or antiviral drugs are not available for dengue viruses. The only effective way to prevent epidemic dengue fever/ dengue hemorrhagic fever and dengue shock syndrome is to control the mosquito vector and prevent its bite.

The present study was conducted on 500 cases presenting with suspecting dengue fever admitted at Dr. V.R.K Womens Medical College, Princes Durru Shevar Childrens Hospital Hyderabad from March 2016 to Feb 2018. Among 500 cases tested 250 (50%) were found to be positive for IgM antibodies to dengue by IgM capture. ELISA method. Of 500 cases 130 (54.16%) were positive among 270 males, 110 (45.83) were positive among 230 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%) [4], S.L. Hoti *et al.,* (2004) (50.6%) [5], B. Mustafa MEH *et al.,* (36.9%) (2006) [6].

In this study Ns1Ag test was positive 30% cases. Similar observation seen in study by B. Mustafa MEH *et al.,* (31.2%) (2006) [6]. In our study there is strong correlation present between NS1Ag positivity and Dengue hemorrhagic fever and dengue shock syndrome complications.

In Shah G.S. *et al.,* (2006) [7] the mean age group was 8.3 yrs.in study conducted by Ira shah *et al.,* (2004) [14], the mean age group was 6.1yrs. In the present study also most of the reported cases were from the age group of 1-6 yr. these were the people who were active outdoors, whether schooling or playing outside their homes. Aedes aegypti is day biter with increased biting activity 2hrs after sunrise and early hours of evening.

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. M. and Lakshmi. V. *et al.,* (2006) [8].

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) [7] common bleeding manifestation was skin bleeds 59%.in study by Gurdeep. S. Dhooria *et al.,* (2008) [50] most common bleeding manifestation was petechiae in 85% followed by melena 6% echymosis 2.5% and epistaxis 2.5%. Gastro intestinal tract was reported as commonest site of bleeding in study by Ratageri *et al.,* 22% (2005) [9], ahmed *et al.,* 61% (2008) [10].

In our study dengue fever present in 58.9%, dengue hemorrhagic fever in 40.9%, dengue shock syndrome in 41.1% of cases. In study by Gurdeep. S. Dhooria *et al.,* (2008) [50] 92% of cases were dengue hemorrhagic fever, 7.4% cases presented in dengue shock syndrome.

In present study hematocrit more than 45% seen in 41.4% cases. Similar observation was seen in study of Gurdeep. S. Dhooria *et al.,* (2008) [11], that was hematocrit more than 40% in 27% cases.

In current study platelet count <50,000 seen in dengue hemorrhagic fever patients significantly in 48 %of cases. In

this study good correlation seen between thrombocytopenia and bleeding manifestation. In the study by Kamath *et al.*, (2006) [12] platelet count <50,000 were noted in 62.3% & same correlation seen as our study.

In study by Gurdeep. S. Dhooria *et al.*, (2008) [11], 59% cases had platelet count <50,000/cumm but poor correlation between thrombocytopenia and bleeding diathesis

In present study encephalopathy was known to occur in 3.6% of cases. Similar observations noted in studies done by Gurdeep. S. Dhooria *et al.*, (2008), (3.7%) [11].

In our study ARDS was seen in 7% of cases.in study by Gurdeep. S. Dhooria *et al.*, (2008) [11], ARDS was seen in 2.46% of cases.

The isolation of dengue viruses or demonstration of dengue viral genome sequences is useful for confirmation of dengue virus infection. These tests are only available in reference laboratories. The detection of IgM dengue antibodies by capture ELISA & 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.

Conclusion

We conclude that, the detection of IgM dengue antibodies by capture ELISA & NS1 Ag were helpful for diagnosis of acute dengue virus infection. Early detection 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. Community participation with emphasis on control measures is very much essential for dengue control. Constant surveillance for dengue viral infection throughout country is required to take necessary action by health authorities.

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Conflict of Interest

None

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Nil

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