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Clinical and laboratory profile of dengue fever in hospitalized children among South Indian population

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ABSTRACT

Background: Dengue fever is currently regarded globally as one of the most important mosquito-borne viral diseases. Children suffering from dengue fever shows a large variation in clinical features and laboratory parameters. This study was focused to evaluate the clinical presentation, associated laboratory and radiological profiles that may be useful to diagnose dengue fever.

Methods: Prospective observational study including 500 children with serological positive dengue fever admitted in a tertiary care hospital in South India.

Results: In this study mean age of presentation of children with dengue fever was 8.4 ± 1.2 years with male predominance. The incidence of children presenting with DF, DHF and DSS was 61%, 23% and 16% respectively. The most common symptom was fever in 100% patients followed by vomiting in 69%, abdominal pain in 64.2%, bleeding manifestations in 43% and periorbital pain in 28.8% of patients. The NS1 was positive in 39.2% cases, dengue IgM in 29% of cases and IgG positive in 30.4% cases. By ultrasonography it was observed that 34% of patients had ascites, 28% with pericholecystic edema, 12% with bilateral pleural effusion, 10% with right sided Pleural effusion and hepatomegaly and 5% with splenomegaly. The most common cause of death was cardiorespiratory arrest secondary to DIC.

Conclusions: Detection of Ns1 antigen to diagnose dengue is proposed to be superior when compared to antibodies detection. It is also concluded that diagnosis of dengue should be made comprehensively by clinical examination with supporting laboratory and radiological investigations.

Keywords: Dengue fever, Dengue hemorrhagic fever, Dengue shock syndrome

INTRODUCTION

Dengue fever is currently regarded globally as one of the most important mosquito-borne viral diseases which cause fever, rashes and muscle and joint aches. Dengue fever is caused by dengue virus belonging to family, flaviviridae, affecting many tropical and subtropical regions of the world. In the past 50 years, the prevalence of Dengue fever has increased 30-fold with increasing geographic expansion to new countries and in the present decade, from urban to rural setting. A history of

symptoms compatible with dengue can be traced back to the Chin Dynasty of 265-420 AD.³ The virus is distributed throughout tropical and subtropical regions of the world, particularly over the last half-century. Significant geographic expansion has been coupled with rapid increases in incident cases, epidemics, and hyperendemicity, leading to the more severe forms of dengue. Transmission of dengue is now present in every World Health Organization (WHO) region of the world and more than 125 countries are known to be dengue endemic.³ Around 2.5 to 3 billion individual's global

population at risk living mainly in urban areas in tropical and subtropical regions. There are at least 100 million cases of dengue fever annually and 500,000 of dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) and around 30,000 deaths, mostly amongst children, in that 90% are children under the age of 15 years. DHF mortality rates average 5%, with approximately 25,000 deaths each year Mortality averages 5% of DHF cases. Case fatality rates vary from 1 to 5% but can be <1% with appropriate treatment.²

Dengue case definition includes a suggestive clinical presentation (high fever, accompanied by two additional symptoms including severe headache, retro-orbital pain, muscle and joint pains, nausea, vomiting, swollen glands or rash, as defined by WHO, along with a positive rapid diagnostic test (RDT). RDT results obtained, describing the detection of NS1 antigen, anti-DENV IgM and IgG antibodies. NS1 Ag assay holds promise in early diagnosis of dengue infection. When used in combination with MAC-ELISA on a single sample it significantly improves the diagnostic algorithm without the requirement of paired sera.

Hemorrhagic manifestations observed with Dengue infection are petechiae, echymosis, purpurae, hematuria, hemoptysis, subconjunctival hemorrhages, epistaxis, hematemesis, skin bleeds, malena, gum bleeds, menorrhagia and positive tourniquet test. Laboratory investigations are often helpful in guiding to clinical diagnosis of Dengue fever and Dengue Hemorrhagic Fever include platelet count <1,00,000 /cumm, hematocrit >40%, abnormal coagulation profile with leucopenia or leukocytosis. In addition, abnormal liver function tests and a wide range of ultrasonographic findings will be observed in dengue fever.

Bleeding in dengue fever is multifactorial in etiology. Several factors like, thrombocytopenia, prolonged shock with capillary leak, derangements of coagulation profiles are known causes of bleeding. In this per view, an attempt has been made in this study to evaluate the association of clinical and laboratory profile with dengue fever in pediatric age group admitted in hospital diagnosed by antibody detection assays, the associated complications at the time of presentation, management strategies that have been applied and the predicted outcome in children with dengue fever.

This study was focused to evaluate the clinical presentation, associated laboratory and radiological profiles that may be useful to diagnose dengue fever in south Indian population admitted in a tertiary care hospital. The objectives are

- To evaluate the incidence of dengue fever in various age and sex groups of pediatric population
- To evaluate the various types of clinical presentation in children diagnosed with dengue fever

- To evaluate the incidence of various complications associated with dengue fever in children
- To evaluate the diagnostic significance of detection of NS1antigen, IgM and IgG antibodies in the diagnosis of dengue fever in pediatric population.
- To evaluate the various findings observed by ultrasonography in serologically positive dengue cases in pediatric age group.
- To evaluate the outcome of pediatric patients suffering from dengue fever.

METHODS

Present study was a prospective cross-sectional observational study. Patients attending Department of pediatrics and diagnosed with dengue fever from May 2012 to April 2014 were included.

A total of 500 pediatric patients presented to Department of Pediatrics, PES Medical College and Research Institute, Kuppam, Chittoor and diagnosed with Dengue fever based on Ns1antigen, IgM and IgG antibodies positive fever cases were included in the present study. All the cases were selected by simple random sampling method after taking well informed consent form from their parents.

Inclusion criteria

Age group between newborn to 17 years and cases presented with fever and diagnosed with Dengue fever based on Ns1antigen, IgM and IgG antibodies or all IgG/IgM/NS1 positive dengue cases.

Exclusion criteria

Age group >17 years. Study subjects presenting with fever with Ns1antigen, IgM and IgG antibodies negative cases. A detailed clinical examination was performed on all the patients as per the submitted proforma and clinical diagnosis was confirmed based on the above inclusion criteria.

Parameters studied under the present study

- Complete hemogram including Hb%, PCV, TLC, DC, platelet count
- Peripheral smear examination
- Smear for Hemoparasites
- Liver function tests
- X-ray Chest postero anterior view
- Abdominal ultrasound
- Dengue serology (Ns1antigen, IgM and IgG antibodies)

Statistical analysis

All the data was expressed as Mean±SD for continuous variables and as frequencies and contingency tables for

categorical variables. Comparison among variables will be performed by Chi-square test for categorical variables and by Independent sample 'T' test for continuous variables.

All the statistical analysis was performed using Microsoft excel spread sheets and SPSS for windows (Statistical presentation system software, SPSS Version 11.5). The present study was approved by Institutional ethical committee.

RESULTS

Total number of patients enrolled in our study was 500. The majority of patients diagnosed with dengue were between 4-8 years (37%) followed by 0-4 years 34.8%. Among these, majority of patients were diagnosed with DF (61%) followed by DHF (23%) followed by DSS 16% (Table 1).

Table 1: Variation in clinical features depending on age group.

Age (years)	No.	%	DF	DHF	DSS
0-4	174	34.8	106	42	26
4.1-8	185	37	117	34	34
8.1-12	91	18.2	53	28	10
12.1-16	46	9.2	27	9	10
16.1-18	4	0.8	2	2	0
Total	500		305 (61%)	115 (23%)	80 (16%)

Out of 500 patients, male children diagnosed with dengue were 58.6%, while female children comprised of 41.4%. The male to female ratio was 1.4:1.

Among both genders, DF was the most commonly diagnosed group (Table 2).

Table 2: Variation in clinical features depending on gender.

Gender	No.	DF	DHF	DSS	p-value
Male	293	172	68	53	0.01
Female	207	133	47	27	0.01
Total	500	305	115	80	0.05

Table 3: Analysis of symptoms at time of admission.

Symptoms	Total (500)	DF	DHF	DSS	P value
Fever	500	305	115	80	0.001
Vomiting	345	204	79	62	< 0.001
Bleeding manifest	215	20	115	80	< 0.001
Abdominal Pain	321	186	81	54	< 0.001
Periorbital Pain	144	84	33	27	0.03

The most common primary symptom at the presentation in patients with dengue was fever with 100% followed by vomiting 69%, abdominal pain 64.2%, bleeding manifestations 43%, and periorbital pain 28.8% (Table 3).

Table 4: Hematocrit levels at the time of admission.

нст	Total (n=500)	D F (n=305)	DHF (n=115)	DSS (n =80)	P Value
Mean	35.2	33.3	39.1	37.0	
SD	6.9	6.0	8.0	6.1	
<40	380	270 (88.5)	60 (52.1)	50 (62.5)	0. 001
≥40	120	35 (11.5)	55 (47.9)	30 (37.5)	

The mean hematocrit level in the present study was 35.2% (Table 4).

Table 5: Total leukocyte count at admission.

TLC	Total (n=500)	D F (n=305)	DHF (n=115)	DSS (n=80)	P* Value
Mean	7136	7117	7078	7291	
SD	2894	2916	2799	2972	
<4000	98	65	75	50	0.79
4000- 11000	342	204	27	19	0.79
>11000	60	36	13	11	

The mean total leukocyte count in the present study was 7136 cells/cumm. Among 500 children, 342 have TLC between 4000-11000/cumm and 60 have >11000/cumm. (Table 5).

Table 6: Platelet counts at admission.

Platelet count	Total (n=500)	D F (n=305)	DHF (n=115)	DSS (n=80)
<20,000	24	16	5	3
20,001- 50,000	98	56	30	12
50,001- 75,000	71	39	21	11
75,001- 100,000	22	10	6	6
100,01- 150,000	103	67	16	20
>150,000	182	117	37	28

The mean platelet count in the present study was 145,860/cumm with range of 12000 to 425,000/cumm. By taking the WHO definition of thrombocytopenia (platelet count <100000/cumm) 43% of children had thrombocytopenia (Table 6).

The mean SGOT, SGPT and ALP levels 126 ± 20 , 115 ± 18 and 259 ± 41 IU/L respectively. The mean serum albumin levels were found to be 2.7 ± 0.3 g/dL (Table 7).

Table 7: Liver function tests and their relation to dengue fever.

Liver function tests	Mean±SD	DF (n=305)	DHF (n=115)	DSS (n=80)	P value
SGOT (IU/l)	126±20	167	39	26	0.001
SGPT (IU/l)	115±18	60	59	31	0.45
ALP (IU/l)	259±41	78	72	40	0.69
S. albumin g/dL	2.7±0.3	257	81	58	0.001

Dengue NS1 positive was seen in 39.2% of patients, Dengue IgM was positive in 29% of cases, Dengue IgG was positive in 30.4% of cases, while PAN positive was observed in only 1.4% of cases (Table 8).

Table 8: Comparison of serologically positive cases in dengue.

IgM/ IgG/ NS1	Total	DF	DHF	DSS	P* Valu
IgM	145 (29%)	80	41	24	
IgG	152 (30.4%)	76	44	32	0.04
NS1	196 (39.2%)	110	50	36	0.04
IgM/IgG/ NS1	7 (1.4%)	3	2	2	

Table 9: Ultrasonographic findings in serologically diagnosed dengue.

Ultrasonographic findings	% of cases	DF (n=305)	DHF (n=115)	DSS (n=80)	P value
Hepatomegaly	10	32	10	08	0.001
Pericholecystic edema	28	88	35	19	0.001
Ascites	34	96	42	33	0.001
Rt Pleural effusion	10	32	11	08	0.05
Bilateral pleural effusion	12	41	10	08	0.04
Splenomegaly	5	16	07	04	0.001

Out of 500 patients diagnosed with serologically positive dengue fever, 34% of patients had ascites followed by 28% with pericholecystic edema,12% with bilateral Pleural effusion, 10% with right sided Pleural effusion and hepatomegaly followed by 5% cases with splenomegaly (Table 9).

Table 10: Clinical outcome of dengue cases during the course of admission.

Group	No. of cases	Recovered		Expired	
		No. of	%	No. of	%
		cases	70	cases	70
DF	305	305	100	0	0
DHF	115	110	95.6	5	4.4
DSS	80	78	97.5	2	2.5
Total	500	493	98.6	7	1.4

A total of 500 patients with serological positive dengue cases were included in our study. Out of which 305(61%) of cases were suffering from Dengue Fever and all of them recovered well. The number of patients suffering from Dengue hemorrhagic fever were 115 (23%) and out of 115 patients, 5 (4.4%) patients expired in this group. In our study 80 (16 %) patients were diagnosed with Dengue shock syndrome, out of which 2 (2.5%) patients expired in this group (Table 10).

DISCUSSION

Dengue is most frequent viral infection that affects a wide range of population globally and particularly pediatric population. Epidemiological studies have shown that dengue fever affects more than 100 million populations annually throughout the world with higher prevalence of morbidity manifested with complications including dengue hemorrhagic fever and dengue shock syndrome and higher incidence of mortality. It is hence prompting clinicians for early diagnosis of dengue by integrated approach of bed side clinical examination, supported and confirmed by laboratory and radiological diagnosis, prevention of dreadful complications and comprehensive management including the associated complications. Most of the studies have studied on the varied clinical presentation of dengue fever that range from nonspecific febrile illness to dengue hemorrhagic fever or DSS. It is the reticulo endothelial system that is affected due to virus infection leading to aberrant endothelial damage of vascular bed and finally presenting as bleeding manifestations from various sites. However, very few studies have showed the clinical and laboratory profile in pediatric population with reference to South Indian population and diagnostic importance of NS1, IgM and IgG antibodies testing in early detection of dengue fever and need for prompt management to prevent complications.

Age distribution

In the present study, it was observed that mean age at the time of presentation of child with dengue fever was 8.4±1.2 years. This is in agreement with earlier studies by Alam et al, Prakash O et al.^{6,7} It was observed that 4-12year age group children dominated in the present study accounting to 55% followed by 0-4 years age group. Lower incidence of dengue fever is observed in age group >12 years. In a study by Gomber S et al in New Delhi in 2001, it was observed that 78.9% patients belongs to the age group 4-12 years.8 In another study by Narayanan et al in Chennai in 2002, 45% patients belonged to the age group 4-12 years. Among the various types of presentation of dengue fever with or without complications as DHF or DSS, the present study has showed that higher incidences of dengue fever was observed with earlier age groups when compared to increasing age of the children. However, no significant difference was observed in relation to age group and dengue fever with associated complications.

Gender distribution

It was observed from the present study that male predominance with M:F = 1.4:1 was observed in overall group and also the predominance of male children across all the subgroups and are in accordance to previous studied by Wang CC et al, Ahmed M et al, Josi R et al. 10 -

Incidence of DF, DHF and DSS

The most serious complications associated with dengue fever and mortality includes DHF and DSS are serious clinical manifestation of the dengue infection. The relative incidence of children presenting with DF, DHF, and DSS in the present study was observed to be 61%, 23% and 16%. However, the incidence of DHF in the present study was observed slightly higher when compared to earlier study by Joshi R et al and Ng CF et al. ^{12,13}

Clinical features

Of the 500 children in the study, all children had fever as symptom at the time of admission. In the present study, the most important primary symptom at the presentation in patients with dengue fever was fever with 100% followed by vomiting 69%, abdominal pain 64.2%, bleeding manifestations 43% and the least incidence of clinical presentation in dengue fever observed was periorbital pain 28.8%.

The results of the present study have been comparable with earlier studies by Alam et al and Narayanan et al.^{6,9} In the present study bleeding manifestation were found in 43%. The incidence of bleeding in our study was lower when compared to Anuradha et al (52.6%) and Alam et al (54.3%) studies.^{3,6}

Investigations

The mean hemoglobin and hematocrit in the present study were 11.2 gm/dl and 35.2% respectively. There was a significant statistical correlation between hematocrit and severity of disease among the clinical subgroups of dengue. Narayanan et al reported the same to be 10.8 gm% and 33.2% respectively. The classical description of >20% rise in the hematocrit is difficult to establish, as the reference standards have not been established for children. Hence the rise in hematocrit was taken one of the diagnostic criteria in identifying dengue fever. Gomber et al had defined a cut off haematocrit value as 36.3% to be diagnostic of DHF in Indian population. Accounting of this value, children in present study came under the category of DHF, which correlated with clinical staging.

Although leucopenia has been reported in large number of studies, the present study had a mean total leukocyte count of 7136 cells/cumm. The highest and lowest TLC was 14523 and 1253/cumm respectively. One of the most important diagnostic clues in the diagnosis of dengue fever is abnormal low platelet count. On taking the WHO limit of <100000/cumm for low platelet count, 43% of children had in the present study. The mean platelet in the present study was 145,860/cumm with range of 12000, to 425,000/cumm. Only platelet count at admission was not taken as an indicator for bleeding tendencies. This suggests that other factors like platelet dysfunction or disseminated intravascular coagulation may have a role in bleeding in dengue fever cases. However, studies which include only DHF cases show correlation between low platelet count and bleeding manifestation. The studies by Gomber et al and Narayanan et al have documented the same.^{8,9} Platelet count provides a very useful means of diagnoses at the screening level. Hence platelet count was sensitive indicator for diagnosis. Bleeding manifestations are more frequent with low platelet count.

In the study of liver function test it was observed in the present study that SGOT, SGPT and ALP levels are elevated in dengue fever, DHF and DSS; however, there was a significant elevation was observed with respect to SGOT. A significant decrease in serum albumin was observed among the subgroup and it is observed the serum albumin concentrations were decreased in patients diagnosed with dengue fever and its association complications. The results of the present study are in agreement with earlier studies by Srivenu I et al.¹⁴

Dengue serology

The dengue IgM was tested positive in 29% of cases; IgG was tested positive in 30.4% and NS1 positive in 39.2% which show the importance of NS1 as an early antigen that can be useful in detection of dengue fever cases. However, combined use of all the antibodies in diagnosing dengue has been positive in only 1.4% cases.

Serology with clinical presentation and other investigations form the mainstay of diagnosis.

Ultrasonography

In the present study, it was observed that 34% of patients had ascites followed by 28% with pericholecystic edema, 12% with bilateral pleural effusion, 10% with right sided pleural effusion and hepatomegaly followed by 5% with splenomegaly. It is also observed that there was significant association between the mentioned ultrasonographic findings with various types of serologically diagnosed dengue suggesting ultrasonography may be helpful in guiding to diagnosis of dengue fever. The findings in the present study are not in agreement with the earlier studies by Chaterjee R et al.¹⁵

Outcome

Out of 500 children included in this study, 61% diagnosed as DF among which 100% recovered, 23% diagnosed as DHF out of which 95.6% recovered and 4.4% expired. Total 16% of cases belonged to DSS group, of which 97.5% recovered and 2.5% expired. The most common cause of death in patients is due to cardiorespiratory arrest secondary to DIC.

CONCLUSION

The present Prospective cross-sectional observational study was focused to evaluate the clinical presentation, associated laboratory and radiological profiles that may be useful to diagnose dengue fever in south Indian population admitted in a tertiary care hospital. The major strength of the present study is inclusion of Ns1 antigen and combined use of Ns1 antigen, IgM and IgG antibodies in the diagnosis of dengue cases. All the cases in the present study were selected based on the serology testing.

This signifies the importance of serological testing as diagnostic tool in the diagnosis of dengue. Another strength of the present study is comprehensive inclusion of liver function tests, radiological investigations including ultrasonography in arriving the diagnosis of dengue and its associated complications. The relative incidences of dengue and its complications, the various clinical presentations with associated mortality were assessed in the present study. The weakness of the present study is the non-selection of dengue cases which are serologically negative. The collection of blood in children to arrive at interpretation of various investigations is major difficulty faced in the present study. As bleeding manifestations and complications are more in patients with dengue requiring repeated blood collection.

Hence, it is concluded that dengue is one of the most common viral disease in the south Indian population affecting the children more commonly. It is inferred that detection of Ns1 antigen to diagnose dengue is proposed to be superior when compared to antibodies detection. It is also concluded that diagnosis of dengue should be made comprehensively by clinical examination with supporting laboratory and radiological investigations.

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Institutional Ethics Committee

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