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Original Article

Clinical, Biochemical and Hematological Profile in Dengue Fever

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Abstract

Introduction: Dengue is the most common mosquito borne endemo-epidemic arboviral infection in many of the tropical and subtropical regions of the world. In the last 50 years, an incidence has increased 30-fold with increasing geographic expansion to new countries and in the present decade from urban to rural settings. About 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries.

Objectives: To analyze the clinical, biochemical and hematological parameters of dengue fever.

Materials and Methods: A total of 100 patients collected from AMC/IMC/WARDS of Mahatma Gandhi Memorial Hospital Warangal, during the period November 2012-October 2013.

Results: A total of 100 patients admitted to our hospital with fever and immunoglobulin M dengue positive were studied. Out of 100 patients, 81 (81%) patients were diagnosed to have dengue fever.

Conclusion: To conclude, in this study classical dengue fever was the most common clinical presentation followed by complicated forms such as dengue hemorrhagic fever and dengue shock syndrome. Most of the patients presented with classical features such as fever myalgias, arthralgias, pain abdomen, vomiting, headache, rash, and bleeding manifestations. The treatment of dengue is mainly supportive. However, appropriate fluid management plays a major role in outcome of the disease.

Key words: Dengue, Dengue hemorrhagic fever, Dengue shock syndrome, Thrombocytopenia

INTRODUCTION

Dengue is the most common mosquito borne endemo-epidemic arboviral infection in many of the tropical and subtropical regions of the world. In the last 50 years, an incidence has increased 30-fold with increasing geographic expansion to new countries and in the present decade from urban to rural settings. About 50 million dengue infections occur annually and approximately 2.5 billion people live in dengue endemic countries.[1]

In addition, the impact of dengue illness on the health sector leads to considerable global economic burden in endemic countries, most of which are developing nation.[2,3] Dengue is caused by dengue virus (DEN) and is transmitted to humans by the bite of *Aedes aegypti* mosquito.

DEN is a small single-stranded RNA virus comprising four distinct serotypes (DEN-1 to -4). These closely related serotypes of the DEN belong to the genus Flavivirus and family Flaviviridae. "Asian" genotypes of DEN-2 and DEN-3 are frequently associated with severe disease accompanying secondary dengue infections.[4-6]

Intrahost viral diversity (quasi species) has also been described in human hosts. Dengue has a wide spectrum of clinical presentations, often with unpredictable clinical evolution, and outcome. While the most patients recover following a self-limiting nonsevere clinical course, a small proportion progress to severe disease, mostly characterized by plasma leakage with or without hemorrhage. Intravenous rehydration is the therapy of choice; this intervention can reduce the case fatality rate to <1% of severe cases.

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The group progressing from nonsevere to severe disease is difficult to define, but this is an important concern since appropriate treatment may prevent these patients from developing more severe clinical conditions. Symptomatic DEN 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).[7,8]

Objectives

To analyze the clinical, biochemical and hematological parameters of dengue fever.

MATERIALS AND METHODS

A total of 100 patients collected from AMC/IMC/WARDS of Mahatma Gandhi Memorial Hospital Warangal, during the period November 2012-October 2013, presenting with acute febrile illness, who are immunoglobulin M (IgM) seropositive for dengue and satisfying inclusion and exclusion criteria.

Patients belonging to the age group of above 12 years, belonging to both sexes were selected and included in the study group.

Inclusion Criteria

- Any acute febrile illness with positive lgM to DF was included in the study.

Exclusion Criteria

- Patients with age group below 12 years of age
- Patient with identified bacterial focus (e.g.,: Typhoid fever with positive dengue IgM)
- Any other identified specific infections (e.g., malaria with positive dengue IgM and patients with inadequate data, lab parameters)
- Patients with only IgG but not IgM.

RESULTS

A total of 100 patients admitted to our hospital with fever and IgM dengue positive were studied. Out of 100 patients, 81 (81%) patients were diagnosed to have DF.

Ten (10%) patients were diagnosed to have DHF and 9 (9%) patients were diagnosed to have DSS based on WHO criteria (Table 1).

This study included 53 (53%) male patients and 47 (47%) female patients. Male to female ratio is 1.13:1 (Table 2).

Among males 43 were DF, 5 DHF and 5 DSS.

Among females 38 DF, 5 DHF and 4 DSS.

DF cases were more among males, i.e., 43 (53%) than in females, i.e., 38 (47%).

DHF cases among males were 5 (50%) and females 5 (50%).

DSS cases were more among males, i.e., 5 (55.5%) and females 4 (44.5%) (Table 3).

Age-wise Distribution of Dengue Cases

The majority of the cases of dengue fall in the age group between 13 and 40 years where in 21 cases (21%) belong to 13-20 years group, 24 cases (24%) belong to 21-30 years group, and 23 cases (23%) belong to the age group of 31-40 years. The mean age, in our study, was 36.6 ± 15.4 years. Youngest was 13 years and the eldest was 70 years.

Age Distribution According to Clinical Spectrum

In this study, the highest number of cases were found in the age group between 21 and 30 years with a total of 24 cases of with 20 (20%) cases of dengue fever, 2 (20%) cases of DHF, and 2 (22.22%) cases of DSS, followed by age group between 31 and 40 years with 23 cases of which 17 (17%) cases of DF, 2 (20%), and 4 (44.44%) cases of DSS. Fever is the most common presenting symptom observed in 100 cases (100%) followed by myalgias seen in

Table 1: Clinical spectrum of dengue cases

Diagnosis	*n* (%)
DF	81 (81)
DHF	10 (10)
DSS	9 (9)
Total	100 (100)

DF: Dengue fever, DHF: Dengue hemorrhagic fever, DSS: Dengue shock syndrome

Table 2: Gender wise distribution

Sex	*n* (%)
Male	53 (53)
Female	47 (47)
Total	100 (100)

Table 3: Sex distribution of dengue cases according to clinical spectrum

Sex	*n* (%)		
	DF	DHF	DSS
Male (53)	43 (81.13)	5 (9.43)	5 (9.43)
Female (47)	38 (80.85)	5 (10.64)	4 (8.51)
Total (100)	81 (81)	10 (10)	9 (9)

DF: Dengue fever, DHF: Dengue hemorrhagic fever, DSS: Dengue shock syndrome

71 cases (71%), headache in 61 cases (61%), joint pains in 65 cases (65%), vomiting in 48 cases (48%), pain abdomen in 56 cases (56%), and bleeding in 21 cases (21%).

- Bleeding manifestations were significantly high in patients with DHF, i.e., in 10 (100%) and DSS in 3 (33.3%) patients than in DF seen in 8 (9.8%) patients. The difference was statistically significant with $P = 0.00001$.
- SOB was significantly high in patients with DSS seen in 3 (33.3%) of patients and in 4 (4.94%) patients with DF. The difference is statistically significant with $P = 0.004$.
- Bleeding was noted in 21 (21%) patients.
- Malena was the most common manifestation seen in 15 (15%) cases followed by gum bleeding seen in 4 (4%) cases, epistaxis in 3 (3%) cases, skin bleeding in 3 (3%) cases, hematuria in 2(2%) cases, and hematemesis in 1 (1%) case.

DISCUSSION

DF is the one of the most important arboviral infections. It has become a major global public health problem with more than 100 million infections worldwide annually, including 2,50,000-5,00,000 cases of DHF and 24,000 deaths annually. In the last 50 years, incidence has increased 30-fold with increasing geographic expansion to new countries.

Dengue inflicts a significant health, economic, and social burden on the population endemic for the disease. In India, epidemics are becoming more frequent. Involvement of younger age group and increasing in the frequency of epidemics are indicators of higher incidence of infection. The presentation of dengue infection varies from nonspecific febrile illness to more serious forms of the disease DHF or DSS.

Bleeding involvement in dengue infection is usually mild and all stages of the disease can copresent with bleeding manifestations, significant bleeding can occur in patients with DHF and DSS. Early recognition and meticulous management are very important to save precious lives from this disease.

A total of 100 patients admitted to our hospital with fever of >101°F and IgM dengue positive were studied.

Comparison of Clinical Spectrum with other Studies

In this study, DF was seen in 81% of the study population and the incidence of DHF and DSS was 10% and 9%, respectively. In a study done by Neeraja *et al*.,[8] the prevalence of DF, DHF, DSS was 85%, 5% and 10%, respectively. In a study done by Pancharoen *et al*.,[8] there was high incidence of DHF, i.e., 60.4%. The results of this study corresponds to a study by Neeraja *et al*.[8] (Table 4).

From these observations, we can conclude that the incidence of each clinical spectrum varies with geographical area.

Comparison of Sex Distribution with other Studies

This study included 53 (53%) male patients and 47 (47%) females, out of which 43 (43%) males and 38 (38%) females were diagnosed to have DF. Male to female ratio was 1.13:1. In studies done by Dash *et al*.[11] and Neeraja *et al*.,[8] Male: Female ratio is 2.8:1, 2:1, respectively (Table 5).

In our study, DSS is a more common in males than females. 5 (5%) males and 5 (5%) females were diagnosed to have DHF. 5 (5%) males and 4 (5%) females were diagnosed to have DSS.

Fever was the presenting complaints in all the cases in our study. In the study conducted by Aggarwal *et al*.,[12] Dash *et al*.,[11] Neeraja *et al*.[8] and Khan *et al*.[2] fever was present in 93%, 100%, 100% and 98.3%, respectively (Table 6).

Comparison of Various Symptoms with other Studies

Other symptoms

Myalgias and joint pains were seen in 71% and 65% cases in our study, respectively. In the study conducted by Dash *et al*.,[11] Neeraja *et al*.[8] and Khan *et al*.,[2] myalgias was present in 70%, 53% and 23.8%, respectively. Joint pain was found in 55% and 15% of patients in study done by Dash *et al*.[11] and Neeraja *et al*.,[8] respectively.

Table 4: Clinical profile of the disease

Author	Year	Place	Clinical profile
Pancharoen *et al*.[9]	1995	Thailand	DF: 22.3% DHF: 60.4% DSS: 17.3%
Neeraja *et al*.[8]	2004	Hyderabad	DF: 85% DHF: 5% DSS: 10%
Present study	2012-13	Warangal	DF: 81% DHF: 10% DSS: 9%

DF: Dengue fever, DHF: Dengue hemorrhagic fever, DSS: Dengue shock syndrome

Table 5: Sex distribution

Author	Year	Place	Male: Female ratio
Kamal *et al*.[10]	2002	Warangal	0.72:1
Dash *et al*.[11]	2003	Gwalior	1.28:1
Neeraja *et al*.[8]	2004	Hyderabad	2:1
Present study	2012-13	Warangal	1.13:1

Table 6: Analysis of various symptoms fever

Study	Year	Place	Fever (%)	Myalgia (%)	Joint pain (%)	Headache (%)	Rash (%)	Bleeding (%)
Dash *et al*[11]	2003	West Bengal	100	70	55	85	56	-
Neeraja *et al*[8]	2004	Hyderabad	100	53	15	74	41	7
Khan *et al*[2]	2006	Karachi	98.3	23.8	36	75	37.8	-
Aggarwal *et al*[12]	1996	Chennai	93%	-	-	-	-	-
Present study	2012-13	Warangal	100	71	65	61	40	21

Headache was seen in 61% of patients in our study. Similar incidence was present in other studies too. In the study conducted by Dash *et al*.,[11] Neeraja *et al*.[8] and Khan *et al*.,[13] headache was present in 85%, 74% and 75%, respectively. Rash was one of the presenting complaint seen in 40 % of patients. In the study conducted by Dash *et al*.,[11] Neeraja *et al*.[8] and Khan *et al*.,[2] rash was found to be present in 56%, 41% and 37.8%, respectively.

Bleeding was a presenting complaint in 21% of patients in our study. In study conducted by Neeraja *et al*.,[8] bleeding was observed in 7% of the patients, the percentage of bleeding was found to be higher in our study.

Vomiting and pain abdomen was found in 48% and 56% of patients in our study, respectively. The incidence of this was not mentioned in other studies. The findings in this study correlated with studies done by Dash *et al*.,[11] Neeraja *et al*.,[8] and Khan *et al*.[2]

Comparison of Shock with other Studies

This study has shown features of shock in 9 (9%) patients. The study conducted by Nimmanitya *et al*.[4] showed the incidence of shock in 35% of patients (Table 7).

From these observations, we can conclude that incidence of each clinical complications varies with geographical area.

Table 7: Shock

Study	Place	Shock (%)
Nimmanitya *et al*[14]	Sear	35%
Present study	Warangal	9%

Clinical Examination

Out of 100 patients in our study all had fever, i.e., 100%.

Bleeding

In our study, bleeding manifestations were observed in 21 (21%) cases and the most common bleeding manifestation in our study was malena noted in 15 (15%) cases followed by followed by gum bleeding in 4 (4%) cases, epistaxis in 3 (3%) cases, skin bleeding in 3 (3%) cases, hematuria in 2 (2%) cases, and hematemesis in 1 (1%) case.

Bleeding manifestations were significantly high in patients with DHF and DSS than in patients with DF with $P = 0.00001$.

Hematemesis was the most common bleeding manifestation reported in other Indian studies.

Comparison of Bleeding with other Studies

Bleeding was observed in 21 (21%) cases in our study, studies done by Kumar *et al*.[15] Anuradha *et al*.[16] and Rahman *et al*.[17] have noted bleeding in 31.2%, 52.6% and 46%, respectively (Table 8).

Comparison of Tourniquet Test with other Studies

Tourniquet test was positive in 26 (26%) cases in our study and is found in patients with platelet count <1 lakh.

None had positive Hess test with platelet count of >1 lakh. The association is statistically significant with $P = 2E-06$. Other studies have noted varying results (Table 9).

Systemic examination

The systemic examination revealed nonspecific findings like any other viral illness.

Hepatomegaly

This study showed hepatomegaly in 4% of patients. Study conducted by Aggarwal *et al*.[12] Neeraja *et al*.[8] Halstead *et al*.[20] and Mohan *et al*.[21] showed incidence of hepatomegaly in 90%, 74%, 71% and 72% patients, respectively (Table 10).

Comparison of Hepatomegaly with other Studies

Investigations

The mean hemoglobin and hematocrit in this study were of 13.1 g/dl and 38.8%, respectively.

The hematocrit ranged from 24.2% to 55%. In DHF and DSS, an increase in hematocrit levels was noted with mean hematocrit values of 41.4% and 40%, respectively.

Hemoglobin level ranges from 8.3% to 19.5%. In DHF and DSS mean hemoglobin levels noted was with 14.3 g/dl and 12.9 g/dl, respectively. Hemoglobin and hematocrit values are not significant in our study.

Table 8: Other studies have noted following pattern of bleeding

Study	Place	Year	Bleeding	Type
Kumar *et al*[15]	Lucknow	2000	31.2%	Haemat-Emesis
Anuradha *et al*[16]	New Delhi	1998	52.6%	Epistaxis
Rahman *et al*[17]	Bangladesh	2002	46%	Malena
Present study	Warangal	2012-13	21%	Malena

Table 9: Tourniquet/Hess test

Study	Place	Test
Nimmanitya *et al*.[4]	Sear	83.9%
Kabra *et al*[18]	Delhi	40%
Gomber *et al*[19]	Delhi	25%
Present study	Warangal	26%

Leukocyte count

The range of leukocyte count varied from 1600 to 20,000 cells/ml with a mean count of 6,978 cells/ml. Leukopenia was observed in 18 (18%) cases with 13 (16.05%) cases in DF, 3 (30%) cases in DHF, and 2 (22.22%) cases of DSS patients.

Leukocyte count is not significant in our study.

In Butt *et al*., study of 104 patients 55 (52.8%) had leukopenia.[22] The mean total leukocyte count was 5200 cells/cu mm, which almost correlates with this study.

Comparison of Thrombocytopenia with other Studies

In this study, 61 (61%) patients had thrombocytopenia meeting the WHO criteria, i.e., <1 lakh cells/cu mm. The mean platelet count in our study is 96,880 cells/cu mm.

The association of thrombocytopenia with DEN infection has been proved to be significant (0.002). Studies done by Cherian *et al*.,[23] Singh *et al*.[24] and Khan *et al*.[2] showed the incidence of thrombocytopenia in 94.7%, 61.39% and 81.4%, respectively. This correlated with the above mentioned studies.

In this study, a comparison was done between the platelet count and the presence of bleeding. Bleeding manifestations were seen more in patients with thrombocytopenia than with patients of normal platelet count. The association between thrombocytopenia and bleeding manifestations has been proved to be statistically significant (P = 3.7E-05) (Table 11).

Prothrombin Time and Activated Partial Thromboplastin Time

Few studies have documented utility of PTT as a diagnostic indicator. PT is a sensitive indicator of synthetic function of liver. The prolonged APTT in the acute phase may be due to hepatic injury and a low grade disseminated intravascular coagulation.

Table 10: Hepatomegaly

Study	Year	Place	Hepatomegaly (%)
Mohan *et al*.[21]	2000	Delhi	74%
Aggarwal *et al*[12]	1996	Chennai	90%
Present study	2012-13	Warangal	4%

Table 11: Thrombocytopenia

Study	Year	Place	Thrombocytopenia (%)
Cherian *et al*[23]	1990	Hyderabd	94.7%
Singh *et al*[24]	2003	Delhi	61.39%
Khan *et al*[2]	2006	Thailand	81.4%
Present study	2012-13	Warangal	61%

Mean PT in our study is 12.5 s and is 11.9 s in patients with DF, 15.3 s in patients with DHF and DSS. Mean PT is significantly high in patients with DHF and DSS with P = 0.000 (F value 9.15).

Elevated PT was observed in 8 (8%) cases in our study with 2 (2.47%) cases in DF, 3 (30%) cases in DHF and 3 (33.33%) cases of DSS.

Mean APTT in our study was 33.4 s and is 31.2 s in patients with DF, 39 s in patients with DHF and 47.2 s in patients with DSS.

Elevated APTT was observed in 7 cases in our study with 2 (2.47%) cases of DF, 2 (20%) cases of DHF and 3 (33.33%) cases of DSS.

Features of Fluid Leakage

Out of 100 patients in the study, 15 (15%) patients showed evidence of pleural effusion, 8 (8%) patients were found to have pedal edema, 15 (15%) patients were found to have ascites. This correlated with the studies done by Neeraja *et al*.[8] and Dash *et al*.[11] As per WHO guidelines pedal edema, ascites and pleural effusion are the supporting evidence of plasma leakage, the distinguishing feature of DHF.

Final Diagnosis

This study had DF 81 (81%), DHF 10 (10%), and DSS 9(9%) cases among total of 100 cases.

CONCLUSION

To conclude, in this study, classical DF was the most common clinical presentation followed by complicated forms such as DHF and DSS. Most of the patients presented with classical features such as fever myalgias, arthralgias, pain abdomen, vomiting, headache, rash, and bleeding manifestations. Hypotension, hemorrhagic spots, jaundice, pedal edema, ascites, and pleural effusion

are the common findings on examination associated with complicated forms of the disease. Bleeding, shock, hepatitis, and polyserositis are the complications seen in severe forms. On investigation deranged liver function tests, renal function tests, ascites, hepatosplenomegaly on ultrasonography and pleural effusion on chest radiography are more commonly seen in patients with DHF and DSS. Platelet count does not correlate with the severity of the disease. Positive Hess test needs close observation and early hospital referral. Blood pressure should be monitored for evaluating the progress of the disease. Bleeding tendencies should be closely watched. The treatment of dengue is mainly supportive. However, appropriate fluid management plays a major role in outcome of the disease.

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