

Original Research Article

A prospective study to analyze the clinical, biochemical and hematological parameters of dengue fever in Mahatma Gandhi Memorial Hospital, Warangal, Telangana, India

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ABSTRACT

Background: Dengue is the most common mosquito borne endemo-epidemic arboviral infection in many of the tropical and subtropical regions of the world. Dengue virus (DEN) is a small single-stranded RNA virus comprising of four distinct serotypes (DEN-1 to -4). Dengue virus infections were grouped into three categories: undifferentiated fever, dengue fever (DF) and dengue haemorrhagic fever (DHF). This study was done to analyze the clinical, biochemical and hematological parameters of dengue fever.

Methods: 100 patients admitted to AMC / IMC / WARDS of Mahatma Gandhi Memorial Hospital Warangal, Telangana, India during the period November 2012 - October 2013, presenting with acute febrile illness who are 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.

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. 10 (10%) patients were diagnosed to have dengue hemorrhagic fever (DHF) and 9 (9%) patients were diagnosed to have dengue shock syndrome (DSS) based on WHO criteria. The present study included 53 (53%) male patients and 47 (47%) female patients. Male to female ratio is 1.13:1.

Conclusions: In our study classical dengue fever was the most common clinical presentation followed by complicated forms such as dengue hemorrhagic fever and dengue shock syndrome. 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.

Keywords: Dengue virus, Dengue fever, Dengue haemorrhagic fever

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 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 Additionally, 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 and is

transmitted to humans by the bite of *Aedes aegypti* mosquito.

Dengue virus (DEN) is a small single-stranded RNA virus comprising of four distinct serotypes (DEN-1 to -4). These closely related serotypes of the dengue virus 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.^{4,5}

Intra-host 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 most patients recover following a self-limiting non-severe clinical course, a small proportion progress to severe disease, mostly characterized by plasma leakage with or without haemorrhage. Intravenous rehydration is the therapy of choice; this intervention can reduce the case fatality rate to less than 1% of severe cases.

The group progressing from non-severe 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 dengue virus infections were grouped into three categories: undifferentiated fever, dengue fever (DF) and dengue haemorrhagic fever (DHF). DHF was further classified into four severity grades, with grades III and IV being defined as dengue shock syndrome (DSS).⁶ This study was undertaken to analyze the clinical, biochemical and hematological parameters of dengue fever.

METHODS

100 patients collected from AMC / IMC / WARDS of Mahatma Gandhi Memorial Hospital Warangal, Telangana, India during the period November 2012 - October 2013, presenting with acute febrile illness who are 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 IgM to dengue fever were 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 included. Out of which 53(53%) were males and 47 (47%) females and male to female ratio was 1.13:1.

Out of 100 patients, 81(81%) patients were diagnosed to have dengue fever (DF), 10 (10%) patients were diagnosed to have dengue hemorrhagic fever (DHF) and 9 (9%) patients were diagnosed to have dengue shock syndrome (DSS) based on WHO criteria. Among males, 43 had DF, 5 DHF and 5 DSS. Among females 38 had 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%).

Majority of the cases of dengue fall in the age group between 13-40 years where in 21 cases (21%) belong to 13-20 years group and 24 cases (24%) belong to 21-30 years group and 23 cases (23%) belong to the age group of 31-40. The mean age in my study was 36.6 years±15.4 years. Youngest was 13 years and the eldest was 70 years. In the present study highest number of cases were found in the age group between 21-30 years with 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 31-40 years with 23 cases of which 17 (17%) cases of DF, 2 (20%) and 4 (44.44%) cases of DSS.

Fever is most common presenting symptom observed in 100 cases (100%) followed by myalgias seen in 71 cases (71%), headache in 61 cases (61%), joint pains in 65 cases (65%), vomitings 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 value of 0.00001. Shortness of breath 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 value of 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.

Bleeding manifestations were significantly high in patients with DHF and DSS than in patients with DF. Malena was seen in 15 (15%) cases of which 3 (3.70%) cases of DF all 10 (100%) cases of DHF and 2 (22.22%) cases of DSS.

Distribution of signs according to clinical spectrum

- Most common signs being Rash seen in 40 (40%) of cases
- Ascites is significantly high in patients with DHF seen in 4 (40%) cases and DSS in 4 (44.44%) cases compared to DF seen in 7 (8.64%) and is statistically significant with p value of 0.001
- Pedal edema is significantly higher in patients with DHF seen in 3 (30%) of cases and DSS in 2 (22.22%) than in DF in 3 (3.70%) cases and is statistically significant with p value of 0.003
- Pleural effusion was found to be higher in patients with DHF and DSS than in DF but is not statistically significant (p = 0.275)
- Hepatomegaly was higher in patients with DSS seen in 2 (22.22%) than in DF in 2 (2.46%) cases and is significant with p value of 0.012.

Tourniquet test

Tourniquet test was positive in 26 (26%) cases. It is a useful screening test in suspected patients with dengue fever. Is found in patients with platelet count < 1 lakh. None had positive test with platelet count of > 1 lakh.

Platelet count

Meeting the WHO criteria for Thrombocytopenia (i.e < 1 lakh) , thrombocytopenia was observed in 61(61%) cases. Severe thrombocytopenia i.e. platelet count <25000 cells/cu mm was seen in 13(16.04%) cases of DF, 4 (40%) cases of DHF and 4 (44.44%) cases of DSS

Mean platelet count according to clinical spectrum

Mean platelet count was 96,880 cells /cu mm. Mean count in patients with DHF was 30200 cells /cumm, in DSS was 38666.67 cells/cu mm and in patients with DF was 111580 cells/cu mm.

Mean count was low in patients with DHF and DSS than in DF and is statistically significant with p value of 0.000001.

Mean haemoglobin level

Haemoglobin level ranges from 8.3 % to 19.5% with a mean value of 13.1g/dl. Haemoglobin level is not significant in my study.

Mean hematocrit level

Heamatocrit ranged from 24.2% to 55% with mean value of 38.8%. Mean hematocrit was higher in DHF with 41.4 % and DSS with 40% compared to DF with mean hematocrit of 38.3%. Haematocrit values are not significant in this study.

Mean TLC

The range of leucocyte count varied from 1600 to 20,000 cells/ml with a mean count of 6,978 cells/ml. Leucopenia was observed in 13(16.05%) cases in DF, 3(30 %) cases in DHF and 2(22.22%) cases of DSS patients. Leucocytosis was observed in 8(9.88%) cases in DF, 1(10%) case in DHF and 1 (11.11%) in DSS patients. Leucocyte count is not significant in this study.

PT to clinical spectrum

Elevated prothrombin time was found in 2 (2.47%) cases in patients with DF 3(30%) cases in patients with DHF and 3(33.33%) cases in patients with DSS.

Mean PT according to clinical spectrum

PT ranged from 10 seconds to 32 seconds with a mean value of 12.5 seconds. Mean PT in patients with DF is 11.9 seconds, 15.3 seconds in patients with DHF and 15.3 seconds in patients with DSS. Mean PT is higher in patients with DHF and DSS and is statistically significant in my study with p value of 0.000 (F value 9.127).

APTT according to clinical spectrum

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

Mean APTT according to clinical spectrum

Activated partial thromboplastin time ranged from 27 second to 102 seconds with a mean value of 33.4 seconds. Mean APTT was 31.2 seconds in patients with DF, 39 seconds in patients with DHF and 47.2 seconds in patients with DSS. Mean APTT is higher in DSS patients compared to DF and DHF. APTT is significant in my study with p value of 0.000 (F value 9.274).

Blood urea according to clinical spectrum

Raised BUN was found in 5(6.17%) cases of DF, 3 (30%) cases of DHF and 5 (55.56%) cases of DSS.

Mean blood urea according to clinical spectrum

Blood urea values range from 14 mg/dl to 135 mg/dl with a mean value of 32.81mg/dl. Mean blood urea was 29.395 mg/dl in patients with DF, 46.4mg/dl in patients with DHF and 48.44 mg/dl in patients with DSS. DHF and 5 (6.17%) cases of DF and is found to be statistically significant with p value of 0.000 (F value 9.967).

Serum creatinine according to clinical spectrum

Raised serum creatinine was found in 3(3.70%) cases of DF, 2 (20%) cases of DHF and 2(22.22%) cases of DSS and is found to be statistically significant in my study.

Mean serum creatinine according to clinical spectrum

Serum creatinine ranged from 0.4 to 1.8 mg/dl with a mean of 0.799. Mean serum creatinine was 0.76 mg/dl in patients with DF, 0.9mg/dl in patients with DHF and 0.977 mg/dl in patients with DSS. Serum creatinine is statistically significant in my study.

Platelet count and bleeding

Bleeding is observed in 21 (34.43%) cases with platelet count below 1 lakh and is found to be statistically significant with p value of 3.7E-05 (χ^2 value - 16.9952).

Bleeding is observed in patients with platelet count below 75,000 cells/cu mm and is more common in cases with platelet count below 25,000 cells/cu mm.

Tourniquet test and platelet count

Tourniquet / Hess test is positive in 26(26%) case with dengue and is found in patients with platelet count < 1 lakh. None had positive test with platelet count of > 1 lakh. The association is statistically significant with p value of 2E-06.

Outcome of dengue

Of the 100 cases 99 (99%) cases were recovered. Mortality was noted in 1 (1%) case and is seen in patient with DSS.

DISCUSSION

Dengue fever is the one of the most important arboviral infections. It has become a major global public health problem with more than 100 million infections throughout the world 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 non-specific febrile illness to more serious forms of the disease dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS).

Bleeding involvement in dengue infection is usually mild and all stages of the disease can co-present 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.

Table 1: Comparison of clinical spectrum with other studies.

Author	Place	Clinical profile
Pancharoen et al ⁷	Thailand	DF:22.3% DHF:60.4% DSS:17.3%
Neerja M et al ⁸	Hyderabad	DF:85% DHF:5% DSS:10%
Present study	Warangal	DF:81% DHF:10% DSS:9%

In the present study, dengue fever 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 Neerja M et al the prevalence of DF, DHF, DSS was 85%, 5% and 10% respectively.⁸ In a study done by Pancharoen et al there was high incidence of DHF i.e. 60.4%.⁷ The results of the present study corresponds to a study by Neerja M et al.⁸ From these observations, we can conclude that the incidence of each clinical spectrum varies with geographical area.

The present 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 PK et al and Neerja M et al M:F ratio is 2.8:1, 2:1 respectively.^{8,9} In this study DSS is 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.

Analysis of various symptoms

Fever

Fever was the presenting complaints in all the cases in my study. In the study conducted by Aggarwal et al, Dash PK et al, Neerja et al and Khan et al, fever was present in 93%, 100%, 100% and 98.3% respectively.

Other symptoms

Myalgias and joint pains were seen in 71% and 65 % cases in my study respectively. In the study conducted by Dash PK et al, Neerja et al and Khan et al, myalgias was present in 70%, 53% and 23.8% respectively.⁸⁻¹⁰

Joint pains was found in 55% and 15% of patients in study done by Dash PK et Al and Neerja M et al respectively.^{8,9}

Headache was seen in 61% of patients in my study. Similar incidence was present in other studies too. In the study conducted by Dash PK et al, Neerja et al and Khan et al headache was present in 85%, 74% and 75%

respectively.⁸⁻¹⁰ Rash was one of the presenting complaint seen in 40% of patients. In the study conducted by Dash PK et al, Neerja M et al and Khan et al, rash was

found to be present in 56%, 41% and 37.8% respectively.⁸⁻¹⁰

Table 2: Comparison of various symptoms with other studies.

Study	Place	Fever	Myalgia	Joint pain	Headache	Rash	Bleeding
Dash PK et al ⁹	West bengal	100%	70%	55%	85%	56%	-
Neerja M et al ⁸	Hyderabad	100%	53%	15%	74%	41%	7%
Khan et al ¹⁰	Karachi	98.3%	23.8%	36%	75%	37.8%	-
Aggarwal et al ¹¹	Chennai	93%	-	-	-	-	-
Present study	Warangal	100%	71%	65%	61%	40%	21%

Table 3: Other studies have noted following pattern of bleeding.

Study	Place	Year	Bleeding	Type
Kumar et al ¹³	Lucknow	2000	31.2%	Haematemesis
Anuradha et al ¹⁴	New Delhi	1998	52.6%	Epistaxis
Rahman et al ¹⁵	Bangladesh	2002	46%	Malena
Present study	Warangal	2012-13	21%	Malena

Bleeding was a presenting complaint in 21 % of patients in my study. In study conducted by Neerja M et al bleeding was observed in 7% of the patients, the percentage of bleeding was found to be higher in my study.⁸

Vomiting and pain abdomen was found in 48% and 56% of patients in my study respectively. The incidence of this was not mentioned in other studies. The findings in the present study correlated with studies done by Dash PK et al, Neerja et al and Khan et al.⁸⁻¹⁰

Comparison of shock with other studies

Present study has shown features of shock in 9(9%) patients. Study conducted by Nimmanitya et al showed the incidence of shock in 35 % of patients.¹² From these observations we can conclude that incidence of each clinical complications varies with geographical area.

Clinical examination

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

Bleeding

In this study, bleeding manifestations were observed in 21 (21%) cases and the most common bleeding manifestation in my 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 haematemesis in 1 (1%) case. Bleeding manifestations were significantly high in patients with DHF and DSS than in patients with DF with p value of 0.00001. Haematemesis was the most common bleeding manifestation reported in other Indian studies.

Bleeding was observed in 21 (21%) cases in my study, studies done by Kumar et al, Anuradha et al and Rahman et al have noted bleeding in 31.2%, 52.6% and 46% respectively.¹³⁻¹⁵

Comparison of tourniquet test with other studies

Torniquet test was positive in 26(26%) cases in my 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 value of 2E-06. Other studies have noted varying results.

Systemic examination

The systemic examination revealed non specific findings like any other viral illness.

Comparison of hepatomegaly with other studies

The present study showed hepatomegaly in 4 % of patients. Study conducted by Neerja et al, Aggarwal et al, Nimmanitya et al and Mohan et al, showed incidence of hepatomegaly in 74%,90%,71% and 72% patients respectively.^{8,11,12,16}

Investigations

The mean haemoglobin and haematocrit in the present study were of 13.1g/dl and 38.8% respectively. The hematocrit ranged from 24.2% - 55%. In DHF and DSS, an increase in hematocrit levels was noted with mean hematocrit values of 41.4% and 40% respectively. Haemoglobin level ranges from 8.3 % to 19.5%.In DHF and DSS mean haemoglobin levels noted was with 14.3g/dl and 12.9 g/dl respectively. Haemoglobin and haematocrit values are not significant in my study. In a study done by Gurdeep SD et al, mean hematocrit value was 35.5%.¹⁷

Leucocyte count

The range of leucocyte count varied from 1600 to 20,000 cells/ml with a mean count of 6,978 cells/ml. Leucopenia 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. Leucocyte count is not significant in this study.

In Butt N et al study of 104 patients 55 (52.8%) had leucopenia.¹⁸ The mean total leucocyte count was 5200 cells/cu mm, which almost correlates with the present study.

Table 4: Comparison of thrombocytopenia with other studies.

Study	Place	Thrombocytopenia
Cherian et al ¹⁹	Hyderabad	94.7%
Singh et al ²⁰	Delhi	61.39%
Khan E et al ¹⁰	Thailand	81.4%
Present study	Warangal	61%

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

The association of thrombocytopenia with dengue virus infection has been proved to be significant (0.002). Studies done by Cherian T et al, Singh NP et al and Khan E et al showed the incidence of thrombocytopenia in 94.7%, 61.39 % and 81.4% respectively. This correlated with the above mentioned studies.^{10,19,20}

In the present 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-value 3.7E-05).

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. In this study Mean PT was significantly high in patients with DHF and DSS with p-value of 0.000 (F-value 9.127). Elevated PT was observed in 8 (8%) cases in this study. Elevated APTT was observed in 7 cases.

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 Neerja et al and Dash PK et al.^{8,10} As per WHO guidelines pedal edema, ascites and pleural effusion are the supporting evidence of plasma leakage, the distinguishing feature of DHF.

CONCLUSION

The present study had an objective of studying clinical manifestations, biochemical parameters and hematological profile associated with dengue fever. In our 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. Hypotension, hemorrhagic spots, jaundice, pedal edema, ascites, pleural effusion are the common findings on examination associated with complicated forms of the disease.

Bleeding, shock, hepatitis, 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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