

Clinical Manifestations and Bio-Chemical Profile of Dengue Fever in A Tertiary Care Centre

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ABSTRACT

Introduction: Dengue fever is an acute infectious disease caused by an arbovirus in the Flavivirus genus. The disease manifestations range from a flu like illness known as dengue fever (DF) to a severe dengue haemorrhagic fever, dengue shock syndrome. Early diagnosis helps in the proper monitoring of the disease, admission to hospital, management of complications and reducing the case fatality rate. We designed a descriptive study of adult dengue infection to describe the clinical and biochemical parameters and their role in identifying severe disease.

Material and methods: Our study includes 150 dengue positive patients. A detailed history, clinical examination, relevant laboratory and radiological investigations were recorded. Patients were divided into three groups DF, DHF, DSS. Clinical features and laboratory investigations were compared between the groups.

Results: Among 150 patients fever was the major symptom in 90% followed by Arthralgia (40%), Myalgia (35.6%), Rashes (26%), bleeding symptoms (50.6%), Retro-orbital pain (6%). Myalgia, abdominal pain, icterus, tachycardia, bradycardia, hepatomegaly, Splenomegaly, leucopenia, elevated liver enzymes, deranged coagulation profile, raised serum creatinine had a significant difference between dengue fever group and DHF/DSS group. Mortality was observed to be 4%.

Conclusion: Leucopenia, elevated liver enzymes, thrombocytopenia, elevated serum creatinine may help in differentiating patients with DHF/DSS. Early diagnosis, prompt observation and strategic approach in segregating patients into different grades, aggressive treatment can help decrease the mortality rate.

Keywords: Dengue fever, Clinical features, Bio-chemical profile, Mortality

INTRODUCTION

Over the last few years dengue has become a major international health problem affecting tropical and subtropical regions around the world, especially in urban and peri-urban areas. It is the most common Arbovirosis in the world and also the most important one in terms of morbidity and mortality.¹ The World Health Organization (WHO) estimates that more than 2.5 billion people are at risk of dengue infection.² Dengue fever is an acute infectious disease caused by an Arbovirus in the Flavivirus genus. The disease manifestations range from a flu like illness known as dengue fever (DF) to a severe and at times fatal disease characterized by haemorrhage and/or shock, known as dengue haemorrhagic fever/dengue shock syndrome (DHF/DSS). There are four viral serotypes (DEN-1, DEN-2, DEN-3, and DEN-4). The virus transmits from viraemic to susceptible humans mainly by bites of the *Aedes aegypti* and *Aedes albopictus* mosquito species.³ Epidemiological evidence shows that DHF and

DSS, the more serious manifestations of the disease, occur more frequently on re-infection with a second serotype. The co-circulation of multiple serotypes has also been reported from many countries.² The situation in India is reflected by the occurrence of major disease outbreaks in India from time to time over the last few decades.^{4,5}

In India, there is increased proportion of Dengue cases with severe disease. The dengue epidemics in India are cyclical and are more frequent, expanding geographically into the rural areas and all forms of serotypes are circulating in the community. The diagnosis of dengue infection early in the course of illness, before development of severe manifestations of the disease, can be challenging. Serologic tests, the mainstay of laboratory diagnosis, are unreliable early in infection (during the first 3 days after symptom onset) and usually require collection of paired acute- and convalescent-phase samples. Polymerase chain reaction (PCR) testing, which is more sensitive early in dengue infection⁶, is usually unavailable in the countries with the highest burden of disease, and no rapid diagnostic test is in widespread clinical use. Diagnosis, therefore, typically relies on identification of clinical features consistent with the World Health Organization (WHO) case definitions. Early diagnosis helps in the proper monitoring of the disease, admission to hospital, management of complications and reducing the case fatality rate.⁷

We designed a descriptive study of adult dengue infection to describe the clinical and biochemical parameters and their role in identifying severe disease.

MATERIAL AND METHODS

Study population included suspected dengue cases aged above 18 yrs admitted in wards and ICU of M.S.Ramaiah group of hospitals, Bangalore from February 2009 to August 2011. Patients with the following complaints – fever, myalgia, arthralgia, headache, retro orbital pain, rashes whose serology showed evidence of dengue disease were included in the study.

A detailed history and physical examination was done at the time of admission. Informed consent was taken. Routine baseline laboratory investigations like complete blood count,

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liver function tests, renal function tests, coagulation profile, blood and urine cultures, chest X ray in lateral decubitus position for evidence of pleural effusion, ultrasonography of abdomen and pelvis at the time of admission were done. A tourniquet test was done at admission and in patients with features of shock.

Blood samples for serological evidence of dengue were collected at the time of admission, repeated after 3 or 5 days after admission in high degree of suspicion. Dengue antibodies were demonstrated by a rapid test-Immunochromatographic assay for the rapid qualitative detection of IgM and IgG antibodies to dengue virus in human serum, plasma, or whole blood. This test device has 3 pre coated lines G(dengue IgG line), M(dengue IgM), C(Control line). All the 3 lines are not visible before applying the blood sample. If the C and M line is visible then the test is positive for IgM antibodies to dengue virus. If the C and G line are visible then the test is positive for IgG antibodies. If the C, G, and M line are visible then the test is positive for both IgG and IgM antibodies. Platelet counts and hematocrit values were recorded at the time of admission and repeated at intervals depending on the clinical course. Patients were followed up through the entire course of hospitalization until discharge or death.

Case definition of dengue fever

Acute febrile illness with two or more of the following manifestations:

- Headache
- Myalgia
- Arthralgia
- Retro- orbital pain
- Rashes
- Hemorrhagic manifestations
- Leucopenia

And supportive serology or occurrence at the same location and time as other confirmed cases of dengue fever.

Case definition for dengue haemorrhagic fever

The following must all be present

- Fever lasting for 2-7 days
- Hemorrhagic tendencies, evidenced by atleast one of the following
 - Positive tourniquet test
 - Petechiae, ecchymoses, or purpura
 - Bleeding from mucosa, gastrointestinal system, injection sites
 - Haematemesis or melena
- Thrombocytopenia (100000 cells per mm³ or less)
- Evidence of plasma leakage due to increased vascular permeability manifested by atleast one of the following:
 - A rise in the haematocrit equal to or greater than 20% above average for age, sex and population
 - A drop in the haematocrit equal to or greater than 20% of baseline following volume replacement therapy
 - signs of plasma leakage like pleural effusion, ascites and hypoproteinemia

Case Definition of Dengue Shock Syndrome

All the above criteria for DHF should be present, plus the evidence of circulatory failure manifested by-

- Rapid and weak pulse
- Narrow pulse pressure (<20mmHg)
- Hypotension for age (Sys Press<80mmHg for <5yrs, <90mmHg for>5yrs)
- Cold, clammy skin, restlessness

Patients were divided in to four grades of DHF

- GRADE 1- fever accompanied by constitutional symptoms and presence of positive tourniquet test, thrombocytopenia and no evidence of plasma leakage
- GRADE 2- spontaneous bleeding with thrombocytopenia and evidence of plasma leakage
- GRADE 3- circulatory failure manifested by a rapid weak pulse, narrow pulse pressure, with the presence of cold clammy skin and restlessness
- GRADE 4- profound shock with no pulse or recordable blood pressure.

STATISTICAL ANALYSIS

The data collected was tabulated in excel sheet. All quantitative variables were expressed as mean and standard deviation. Comparisons of continuous variables were performed using the Student *t* test. The χ^2 test was used to evaluate statistical differences in categorical variables between groups. All statistical analyses were performed using the SPSS statistical package, version 16.0.0 (SPSS).

RESULTS

A total of 3,500 patients with symptoms consistent with dengue were screened, out of which 150 patients were found to be positive for dengue fever.

In the study population, Age ranged from 18 years to 75 years, Mean age = 35+/-12.8. Males constituted 60% of the study population, remaining 40% were Females. Among 150 patients fever was the major symptom in 90% followed by Arthralgia in 40%, Myalgia in 35.6%, Rashes in 26%, bleeding symptoms in 50.6%, Retro-orbital pain was seen in 6%. Gastrointestinal symptoms, abdominal pain was seen in 10%, vomiting in 8% and Diarrhea in 4%. Altered sensorium was present in 3 patients, 1 patient had encephalitis and 2 had acute liver failure.

CLINICAL FEATURES

Majority of patients had high grade fever with temperature recordings ranging from 101°F-104°F. Conjunctival congestion was seen in 9.8% of patients. Icterus was clinically identified in 10.2% of patients. Rashes were seen in 26% of patients, majority of patients had generalized erythematous flush which blanches on applying pressure. Around 3% of patients had petechial rashes noticed in the tibial aspect of lower limbs and flexor aspect of arm and forearm. Majority of patients had tachycardia, only 9% had bradycardia which was thought to be secondary to myocarditis. Clinically hepatomegaly was identified in 28% of patients, clinical Splenomegaly in 20% and ascites in 5%. Positive tourniquet test was seen in 48% patients.

LABORATORY INVESTIGATIONS

40% of patients had leucopenia with WBC count as low as

2200. The fall in WBC count was noticed 3-5 days after the onset of illness.

Majority of patients had thrombocytopenia less than 50,000. Patients were divided into 4 groups according to their platelet count. It was found that majority of patients with bleeding manifestations had platelet count less than 50,000. Drop in platelet count was maximal 5 days after the onset of illness.

Bleeding manifestations was seen 76 patients, 30 had petechiae, 10 had bleeding gums, 8 had epistaxis, 10 had hematemesis, 9 had melena, 14 had conjunctival haemorrhage. None of the patients had haematuria or intracranial haemorrhage. Elevated liver enzymes, serum alanine transaminase (ALT) and serum aspartate transaminase (AST) were seen 118 patients. Majority of patients had 3 fold increase in liver enzymes. Predominant elevation was seen in AST compared to ALT. Mean ALT elevation was 216+/-184 and AST elevation was 516+/-264. Deranged prothrombin time was seen in 30 patients and deranged APTT was seen in 31 patients. Serum creatinine more than 1.5 was seen in 32 patients. 28.4% of patients were IgM positive, 71.6% were IgM and IgG positive. Chest radiography – 60% of patients had evidence of pleural effusion, 10% had bronchopneumonia. Ultrasonography of abdomen showed features of gall bladder wall thickening in 55% of patients, hepatomegaly in 40%, Splenomegaly in 34%, ascites in 60%, nephropathy chang-

es in 6%. Mortality rate was observed to be 4%. Out of 6 patients, 3 had sepsis with multi-organ dysfunction, 2 had ARDS and 1 had acute liver failure. All patients received symptomatic and supportive treatment including IV fluids, anti-pyretics, anti-emetics, and anti-biotics. Blood products like platelet transfusions were given to 50% of patients with bleeding manifestations and those with platelet count less than 50,000. 12 patients required inotropic/vasopressors support and 10 patients required ventilator support. Out of 150 patients, 40 had classical dengue fever and the remaining 110 met the criteria of DHF/DSS. Out of these 98/150 (65.3%) patients of dengue virus infection met the criteria for DHF and 12/150 (8%) qualified for DSS.

Further patients were divided in to different grades of DHF according to WHO GRADING system. Majority of patients met the criteria of grade 2 DHF.

Management of patients in different grades of DHF/DSS

We found that 15% of patients in grade 1, 78.5% in grade 2, all patients with grade 3 and grade 4 DSS needed ICU

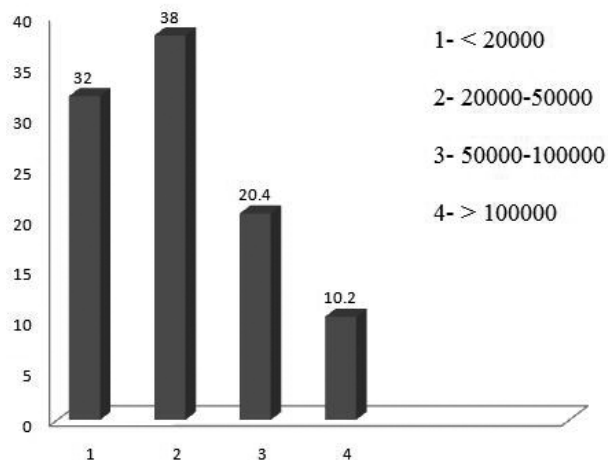


Figure-1: Bar diagram showing percentage of patients with different platelet count ranges

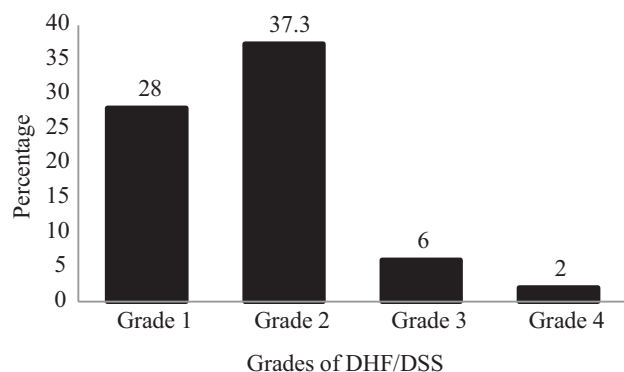


Figure-2: Bar diagram showing percentage of patients in different grades of DHF/DSS.

Clinical symptoms/signs	DF(40/150)	DHF/DSS(110/150)
Fever	35(23%)	100(66.6%)
Myalgia*	15(10%)	38(25.3%)
Arthralgia	28(18.6%)	32(21.3%)
Rashes	18(12%)	21(14%)
Retro-orbital Pain	3(2%)	6(4%)
Headache	15(10%)	21(14%)
Abdominal pain*	5(3%)	10(6.6%)
Nausea/vomiting	3(2%)	9(6%)
Diarrhoea	2(1.3%)	4(2.6%)
Altered sensorium	0	3(2%)
Conjunctival congestion	4(2.6%)	11(7.3%)
Icterus*	1(0.6%)	14(9.3%)
Tachycardia*	35(23.3%)	63(42.2%)
Bradycardia*	0	13(9%)
Hepatomegaly*	12(8%)	30(20%)
Splenomegaly*	8(5.3%)	22(14.6%)

Laboratory parameters	DF	DHF/DSS
Leucopenia*	10(6.6%)	50(33.3%)
Raised AST*	20(13.3%)	88(58.6%)
Raised ALT*	18(12%)	78(52%)
Raised PT*	0	30(20%)
Raised PTT*	0	30(20%)
Raised serum creatinine* (more than 1.5)	2(1.3%)	30(20%)

* These parameters had a significant difference between DHF/DSS and DF group of patients with a significant p value (less than 0.05).

	Observation	ICU CARE, Blood tranfusion	Death
Grade 1	36(85%)	6(15%)	0
Grade 2	12(21.4%)	44(78.5%)	1(1.7%)
Grade 3	0	7(77.7%)	2(22.2%)
Grade 4	0	0	3(100%)

Table-1: Showing management and mortality rates in different grades of DHF.

care and blood transfusion. Mortality rate was higher in DSS group.

DISCUSSION

Dengue is an important emerging disease of the tropical and sub-tropical regions. Since the first confirmed case in India in 1940, intermittent reports of the epidemic infections have been reported. Steady increase in the number of dengue cases over the past few years has been attributed to rapid unplanned urbanization with unchecked construction activities and poor sanitation facilities contributing fertile breeding areas for mosquitoes, it is also seen that an increase in alertness among medical personnel following the epidemics and availability of diagnostic tools in the hospital have contributed to the increased detection of cases.⁸

The male to female ratio in this study is 1.5:1. The clinical profile revealed that fever was the most common presenting symptom (90%). Similar studies in and around India also substantiated fever as the common presenting symptom.^{9,10} Majority of patients had arthralgia, myalgia followed by rashes. Reported frequency of rash in dengue ranges from 50 to 66%.¹¹ Recently premantra et al demonstrated a rash in 95% of the patients.¹² In our study it was noticed in 26% of patients, and majority had generalized erythematous flush. In view of this it is suggested that evaluation of rash in patients presenting with fever may also help in diagnosis of dengue fever.

Abdominal pain, vomiting was noticed in 20% of patients which was less compared to other studies. Retro-orbital pain which is cardinal feature of dengue fever was not seen significantly in our patients. The most common bleeding symptom was petechiae which was similar to other studies in India.

Leucopenia was noted in 40% of patients out of which 33.3% was noted in DHF/DSS group. AST and ALT liver enzymes were elevated to 3 times the normal in DHF/DSS group of patients when compared to DF. Liver injury from dengue virus is mediated by its direct infection of hepatocytes and kupffer cells.^{13,14} Recently Luiz et al suggested the use of markers such as AST and ALT as parameters to evaluate severity in patients with dengue fever. Thus grossly elevated liver enzymes are the early predictors for estimating the severity of dengue infection.^{13,22}

Pleural effusion in chest radiography and ascites in ultrasonography of abdomen served as markers of increased vascular permeability when compared to rise in haematocrit. The same was also seen in other studies.^{15,16,21}

The overall case fatality rate in south-east Asian countries is less than 1%.¹⁷ In our study mortality rate was 4% comparable to the following studies.^{18,19} High mortality in our study could be due to re-infection, infection with virulent serotype, late presentation to hospital.

Early diagnosis, appropriate investigations, strict monitoring and prompt management can help in reducing mortality in dengue haemorrhagic fever.²¹

CONCLUSION

The results of this study describe the clinical features and laboratory investigations in dengue. Leucopenia elevated liver enzymes, thrombocytopenia, elevated serum creatinine

may help in differentiating patients with DHF/DSS. Markers of plasma leakage like pleural effusion in chest radiography and ascites in ultrasonography of abdomen helps to differentiate patients with DHF/DSS. Early diagnosis, prompt observation and strategical approach in segregating patients into different grades, aggressive treatment can help decrease the mortality rate.

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