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Clinical Study of Diagnosed Cases of Dengue Fever in Tertiary Care Hospital in North Maharashtra

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Abstract

Aims and Objective: To study the clinical presentations, laboratory profile, hematological complications and outcome of dengue fever. **Materials and Methods:** Descriptive study was carried which includes adult males and females who were serologically confirmed cases of dengue. These patients were assessed for their demographic features (age/sex etc.); clinical profile various signs and symptoms; labotrary profile; complications and outcome as mentioned in the proforma. **Results:** Total 56 patients studied. Out of 56 cases, the maximum number of cases, 22 (39.2%), belonged to the age group between 20 to 40 years. Thus the mean age of hospitalized patients was 31.2 ± 4.5 yrs. There were 33 (58.9%) males and 23 (41.1%) female patients. Majority were Dengue Hemorrhagic fever 20 (35.7%) and 8 (14.2%) were cases of severe dengue according to WHO guidelines. Fever was present in all patients. Two patients developed DIC and died. **Conclusion:** Patients with dengue syndrome showed varied clinical presentation. Symptoms and clinical signs are non specific. Most adults were positive for symptoms like fever, myalgia, arthralgia, and skin rash and bleeding.

Keywords: Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF), Disseminated Intravascular Coagulation (DIC), Dengue Shock Syndrome (DSS), Nonstructural Protein 1 (NS1)

1. Introduction

Dengue is present in almost all part of India and is a major public health concern[1], National Vector Borne Diseases Control Program have reported an annual average of 20,474 dengue cases and 132 deaths between 2006 and 2012. Regional comparisons suggest that these official numbers reflect only a small fraction of the full impact of the disease. Etiological agents for dengue include all four dengue serotypes, which belong to the genus flaviviruses of the family Flaviviridae. The principal vector is Aedes aegypti mosquito, which largely breeds indoors in clean artificial water containers. It bites humans during the daytime[2].

Dengue disease in humans causes a spectrum of illnesses ranging from in apparent febrile illness to severe and fatal hemorrhagic disease. The severity of DF manifestations increases with age. Infants and children with DF have symptoms ranging from an undifferentiated fever to mild febrile illness, sometimes associated with a rash. Older children and adults frequently suffer a more severe form with the triad of high fever, pain in various parts of the body, and a maculopapular rash. The infection is rarely fatal. DHF is considered a distinct disease characterized by increased vascular permeability leading to hemoconcentration and dengue shock syndrome (DSS)[3,4]caused by infection with dengue virus, is not a new disease, but recently because of its serious emerging health threats, coupled with possible dire consequences including death, it has aroused considerable medical and public health concerns worldwide. Today, dengue is considered one of the most important arthropod-borne viral diseases in humans in terms of morbidity and mortality. Globally, it is estimated that approximate

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50 to 100 million new dengue virus infections occur annually. Among these, there are 200,000 to 500,000 cases of potential life-threatening dengue hemorrhagic fever (DHF.

It is difficult to control dengue in India due to lack of awareness of Dengue in general population, with no vaccine available and no effective mosquito control technology. It is important to collect data for clinical manifestations, laboratory investigations, unusual complications and seasonal variability in the incidence. This data will help to control and prevent mortality due to dengue. This study was carried out to study the clinical presentations; laboratory profile and hematological complications and outcome of dengue fever.

2. Materials and Methods

Descriptive study was carried out at the Dept. of Medicine, Dr. Vasantrao Pawar Medical College Hospital, Nashik from Aug 2014 to December 2016. Study population includes adult male and female who were serologically confirmed cases of dengue. Patients having the clinical manifestations of dengue fever as mentioned in the clinical case definitions of dengue as per WHO guidelines of 2009, with serological evidence in the form of dengue NS1, IgM or both IgG and IgM by MAC ELISA and ready to participate were included in the study. Patients who were IgG positive but IgM negative, which is those who have not recent evidence of dengue infection were excluded from the study. Total 56 patients were included in the study.

Ethical clearance from college Institutional Ethics Committee was obtained. Informed verbal and written consent was obtained from patients to take part in the study. The patients were assured of confidentiality of the information. A structured assessment form was used to obtain the clinical history regarding febrile illness including clinical symptoms and signs. The patients were assessed for their demographic features (age/sex etc.) and clinical profile, various signs and symptoms as mentioned in the proforma.

Venous blood samples were collected aseptically from the study participants. The serological confirmations of dengue were done with the help of MAC-ELISA KIT (PAN-BIO), NS1, IgG and IgM were estimated. The patients were subjected to the routine laboratory tests like Complete Blood Count, Liver Function Tests, Renal Function Tests, urine routine and microscopy and peripheral smear for malaria parasite. Whenever indicated, patients underwent chest x-ray and ultrasound examination of abdomen to study the different radiological features of Dengue fever. Platelet count, Haemoglobin and Haematocrit were serially monitored. Patients with DHF and DSS were closely monitored for the progression of fever, blood pressure, level of consciousness, hydration, bleeding tendency and the complications occurring at any stage were studied. Patients who were seropositive for dengue were classified on the basis of WHO criteria as follows: Dengue Fever (DF); Dengue Fever with unusual Bleed (DFB); Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS)

The patients were treated with Oral Rehydration Solution/IV fluids depending on the level of hydration. Platelet concentrates were transfused in case of spontaneous bleeding or prophylactically if the platelet count is less than 10,000/cmm. Packed cells were given if there was severe blood loss. Descriptive and inferential statics were applied.

3. Results

There were total 56 patients. Out of these 56 patients, 2 patients expired during treatment.

The maximum number of cases, 22 (39.2%), belonged to the age group between 20 to 40 years. 16 (28.5%)cases belonged to the age group between 40 to 60 years. and only 12 (21.4%) patients were from 13 to 20 age group Thus the mean age of hospitalized patients was 31.2 ± 4.5 yrs. In our study, out of 56 patients, there were 33 (58.9%) males and 23 (41.1%) female patients and the Male Female ratio was found to be 1.42:1.

Among the total 56 diagnosed cases of Dengue, majority were Dengue Hemorrhagic fever 20 (35.7%) and 8 (14.2%) were cases of severe dengue according to WHO guidelines. There were 13 cases (23.2%) having dengue fever and 15 (26.7%) patients had dengue fever with unusual bleed (Table1).

Clinical symptoms and sign described in details. Serological markers were evaluated. NS1 was positive only in 24 (42.8%) cases, NS1 and IgM were positive in 7 (12.5%) together representing the incidence of new cases. The presence of IgM in 14 (25%) cases only without NS1 antigen could be due to early clearance of the antigen. NS1; IgM and IgG were positive in 10(17.8%) of cases.

Laboratory and radiological findings were described in Table 2 & 3.

All patients were treated and discharged only when

Table 1. Clinical Symptoms and signs in different groups of dengue infections

	DF (n:13)	DBS (n:15)	DHF (n:20)	DSS (n:8)	Total (n:56)
Symptoms					
Fever	13 (100%)	15 (100%)	20 (100%)	8 (100%)	56 (100%)
Myalgia	7 (53.8%)	10 (66.6%)	16 (80%)	3 (37.5%)	36 (64.2%)
Arthralgia	5 (38.4%)	8 (53.3%)	12 (60%)	1 (12.5%)	26 (46.4%)
Headache	3 (23.1%)	6 (40.0%)	10 (50%)	0	19 (33.9%)
Retro orbital Pain	2 (15.3%)	2 (13.3%)	3 (15%)	1 (12.5%)	8 (14.2%)
Vomiting	1 (7.6%)	9 (60.0%)	10 (50%)	3 (37.5%)	23 (41%)
Skin rashes	0	4 (26.6%)	8 (40%)	6 (75.0%)	18 (32.1%)
Bleeding Tendency	0	2 (13.3%)	3 (15%)	5 (62.5%)	10 (17.8%)
Abdominal Pain	0	1 (6.6%)	2 (10%)	3 (37.5%)	6 (10.7%)
Altered Mentation	0	0	0	1 (12.5%)	1 (1.7%)
Anorexia	0	3 (20.0%)	9 (45%)	2 (25%)	14 (25%)
Altered Taste	0	1 (6.6%)	0	0	1 (1.7%)
Cold clammy skin	0	0	2 (10%)	6 (75%)	8 (14.2%)
Decreased Urine Output	0	0	3 (15%)	7 (87.5%)	10 (17.8%)
Sign					
Shock	0	0	0	8 (100%)	8 (14.2%)
Bradycardia	6 (46.1%)	5 (33.3%)	8 (40%)	7 (87.5%)	26 (46.4%)
Petechiae	0	4 (26.6%)	9 (45%)	6 (75%)	19 (33.9%)
Pleural Effusion	0	0	3 (15%)	2 (25%)	5 (8.9%)
Hepatomegaly	1 (7.6%)	0	1 (5%)	5 (62.5%)	7 (12.5%)
Ascites	0	0	2 (10%)	2 (25%)	4 (7.1%)
Jaundice	0	0	2 (10%)	3 (37.5%)	5 (8.9%)
Neck stiffness/ altered sensorium	0	0	0	1 (12.5%)	1 (1.7%)
Tourniquet Test	0	1 (6.6%)	8 (40%)	2 (25%)	11 (19.7%)

Table 2. Laboratory profile among study participants

Parameters	**DF (n:13)**	**DBS (n:15)**	**DHF (n:20)**	**DSS (n:8)**	**Total (n:56)**
Hemoglobin (Hb %)					
Mean ± SD	9.5 ± 2.2	8.7 ± 1.9	7.8 ± 1.1	7.1 ± 1.8	7.3 ± 2.1
Haematocrit (%)					
< 40	10 (76.9%)	9 (60%)	11 (55%)	5 (62.5%)	35 (62.5%)
>or= 40	03 (23.1%)	6 (40%)	9 (45%)	3 (37.5%)	21 (37.5%)
Platelet count					
<20,000	0	0	1 (5%)	1 (12.5%)	2 (3.5%)
20,000 --50,000	1 (7.6%)	2 (13.3%)	3 (15%)	2 (25%)	8 (14.2%)
50,000 -- 1,00,000	4 (30.7%)	6 (40%)	7 (35%)	3 (37.5%)	20 (35.7%)
> 1 ,00,000	8 (61.5%)	7 (46.6%)	9 (45%)	2 (25%)	26 (46.4%)
Total leukocyte count					
Leukopenia (< 4000 cells/mm3)	7 (53.8%)	4 (26.6%)	6 (30%)	2 (25%)	19 (33.9%)
Leukocytosis (>11000 cells/mm3)	4 (30.7%)	3 (20%)	2 (10%)	1 (12.5%)	10 (17.8%)
Normal (4000-11000/mm3)	2 (15.3%)	8 (53.3%)	12 (60%)	5 (62.5%)	27 (48.2%)
Rise in SGPT (IU/L)					
< 50U	5 (38.4%)	7 (46.6%)	12 (60%)	5 (62.5%)	29 (51.7%)
50-200 U	3 (23%)	2 (13.3%)	6 (30%)	2 (25.5%)	13 (23.2%)
> 200U	0	1 (6.6%)	2 (10%)	1 (12.5%)	4 (7.1%)
Rise in SGOT (IU/L)					
< 50U	4 (30.7%)	6 (40%)	14 (70%)	4 (50%)	28 (50%)
50-200 U	3 (23.0%)	4 (26.6%)	5 (20%)	3 (37%)	15 (26.7%)
> 200U	1 (7.6%)	0	1 (5%)	1 (12.5%)	3 (5.35%)
Serum creatinine					
Raised (>1.5mg/dl)	0	0	4 (20%)	2 (25%)	6 (10.7%)
BUN					
Raised (> 20 mg/dl)	0	0	4(20%)	2 (25%)	6 (10.7%)

Table 3. Radiological findings among study participants

	DF (n:13)	DBS (n:15)	DHF (n:20)	DSS (n:8)	Total (n:56)
Chest X – ray					
Pleural effusion	0	1 (6.6%)	2 (10%)	3 (37.5%)	6 (10.7%)
Right sided effusion	0	2 (13.3%)	1 (5%)	2 (25%)	5 (8.9%)
Left sided effusion	0	0	0	1 (12.5%)	1 (1.78)
Right & left side effusion	0	0	2 (10%)	2 (25%)	4 (7.1%)
USG of abdomen					
Hepatomegaly	1 (7.6%)	1 (6.6%)	1 (5%)	3 (37.5%)	6 (10.7%)
Ascites	0	0	1 (5%)	2 (25%)	3 (5.3%)
Gall bladder wall edema	0	0	2 (10%)	1 (12.5%)	3 (5.3%)

they were afebrile, bleeding time normalized, and platelet counts were above 1, 50,000 per cu mm.

Four of our patients presented with ARDS and two patients presented with altered sensorium possibly due to dengue encephalopathy. Two patients had deranged creatinine, which later returned to normal. The patients had a creatinine of 4.0 which was attributed to shock and pre renal ARF. Pleural effusions and myocarditis were the complications seen amongst 3 (5.3%) and 4 (7.1%) patients.

Two of our patients developed DIC. The diagnosis was supported by elevated levels of fibrin degradation products in the blood. One of them recovered with platelet and FFP transfusions. The other patient had bleeding from multiplesites, required mechanical ventilation and ultimately died. Other death in the studywas also attributed to DIC, multiorgan failure and bleeding.

4. Discussion

In present study the majority of cases, 22 (39.2%), was seen in the group above 20 years of age. The mean age of hospitalized patients was 31.2 ± 4.5 yrs.Similar findings were also reported by other author Singh et al (2016)[5]so there is little evidence and awareness in this regard. A prospective observational study was carried out to determine the group of patients suffering from dengue syndrome; clinical parameters of the subjects for hospitalization and the pattern of presentation of dengue fever in a tertiary care centre of the state from September 2015 to November 2015. Method : Total 400 serologically positive cases were selected randomly and diagnosed clinically as dengue, and were classified into 3 groups, i.e. 260 cases of classical dengue fever, 120 cases of dengue hemorrhagic fever(DHF. The finding of involvement of all age groups and mainly adults was consistent with the epidemiological data obtained from other endemic areas. DHF/DSS are uncommon in individuals above 15 years and are more common in secondary infections but now the pattern seem to change with adult individuals being affected by DHF/DSS. Our findings are consistent with published literature[6].

In present study, majority patients suffered from Dengue Hemorrhagic fever with a number of 20 (35.7%) diagnosed cases according to WHO guidelines. Fever was present in all 56 (100%) cases; followed by myalgia in 36 (76.8%) and arthralgia in 26 (54.3%) cases. Skin rash and bleeding tendency were present in 18 (32.1%) and 10 (17.8%) respectively. Similar observation were observed by Singh et al (2016)[5]so there is little evidence and awareness in this regard. A prospective observational study was carried out to determine the group of patients suffering from dengue syndrome; clinical parameters of the subjects for hospitalization and the pattern of presentation of dengue fever in a tertiary care centre of the state from September 2015 to November 2015. Method : Total 400 serologically positive cases were selected randomly and diagnosed clinically as dengue, and were classified into 3 groups, i.e. 260 cases of classical dengue fever, 120 cases of dengue hemorrhagic fever(DHF in Haryana .Retro orbital pain was observed in 14.2 % of dengue confirmed patients. This is in accordance with other studies like Pervin et al., (2004)[7]. Even though, the proposed new WHO dengue case definition does not mention the system in its list of clinical features (WHO, 2009), omitting retro orbital pain from the dengue case definition may reduce clinical diagnostic accuracy[8].

One of the key clinical manifestations in dengue disease is thrombocytopenia (Halstead, 1997). It occurs due to decreased production and increased destruction of platelets. The degree of thrombocytopenia appears correlated with the clinical severity of DHF. However, a significant fraction of dengue fever patients also develop thrombocytopenia.The haematological analysis of the present study indicated that 57.1% % of dengue confirmed patients had thrombocytopenia which is in accordance with other studies like Kalayanarooj et al., (2002)[9] and Shah et al., (2005)[10] . The level of hemoglobin was also

analyzed in present study and it was found that there was a reduction in its level in confirmed dengue patients. Banerjee et al., (2008)[11] observed anemia in 11% of the patients. On the other hand, Kumar *et al* (2008)[12] did not observe anemia in the dengue patients. Reduction in hemoglobin content cannot be considered as a significant factor in the diagnosis of dengue infection. Yung *et al.,* (2015) reported a raised haematocrit dengue confirmed cases[13]. The haematological features of the dengue patients in the present study revealed that thrombocytopenia and leucopenia are the two important parameters in the early diagnosis of dengue infection and other parameters such as haematocrit and anaemia do not play any role in the diagnosis of dengue infection at an early stage.

In present study, the levels of SGOT and SGPT enzymes in the blood samples from serologically confirmed dengue patients were measured. It is important to emphasize that none of the patients included in the study had previous active liver disease. The results of present study revealed that there was an increase in the level of SGOT (46.4%) and SGPT (51.1%) in dengue confirmed patients.

The level of liver enzymes elevation seen in the present study was lower than those described in the patients with dengue belonged to other parts of India. A study carried out in Lucknow, India showed an elevation of ALT and AST in 96 % of the study population (Itha *et al.,* 2005)[14]. In many studies, elevation of AST was noticed from 73.5 to 96 % of patients and ALT elevation was noticed from 68% to 85%. The mechanism of liver injury in dengue infection remains unclear. Studies have proved the multiplication of virus in liver cells. The dengue virus has been isolated from liver of fatal cases. Dengue virus antigens and nucleic acid were detected in liver tissues by using immunochemistry hybridization and polymerase chain reaction.

Dengue induced acute kidney injury is a poorly studied complication. Renal insufficiency was defined as an increase in blood urea nitrogen and serum creatinine. In order to find out the degree of renal injury in classic dengue infection, an attempt was made to assess the level of serum creatinine, urea and uric acid. Raised serum creatinine and BUN in dengue patients were observed in 6 (10.7%) of cases. However, only a very low percentage DF patients showed increase in creatinine (35.35 %), urea (16.16 %) and uric acid (10.1 %) levels and hence, these parameters cannot be considered as early predictors of dengue infection .

In present study CXR showed pleural effusion in 6 patients i.e., 10.7% of total patients. Pleural effusion was seen in 3 (37.5%) patients among DSS group and is a sign of plasma leakage. Ultra sound examination of abdomen showed that the commonest finding was Hepatomegaly in 10.7% cases followed by ascites and thickening of GB wall in 5.3 % of patients. In a study by P. M. Venkata Sai et al.,[15] on the role of USG in dengue fever, 100% of the patients showed gall bladder wall thickening and pericholecystic fluid, 21% had hepatomegaly, 6.25% had spleenomegaly and minimal right pleural effusion. In a study done Thulkar S et al.,[16] Sonographic findings included pleural effusion in 21 patients (53%), thickening of the gallbladder wall in 17 (43%), and mild ascites in 6 (15%) patients Gallbladder wall thickening in dengue fever may be due to decrease in the intravascular osmotic pressure. It is also found in other viral infections, leptospirosis etc. and is a very nonspecific finding when considered in isolation.

Mortality rate in present study was 3.5%. Without proper treatment the fatality rate of DHF can approach 20% and early diagnosis and treatment can decrease the fatality rate to less than 1%. In a study of DHF in Mexico by Joel Navarette et al[17] the mortality rate was 1.98% similar to our study. The deaths were attributed to DIC and intracranial bleed due to dengue in this study.

In conclusion, patients with dengue syndrome showed varied clinical presentation. Symptoms and clinical signs are non specific. In adults, importance should be given to symptoms like fever, myalgia, arthralgia, skin rash and bleeding.

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