Original Research Article

A Study on Clinical, Ultrasound and Laboratory Profile of Dengue Infection in Adults

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Abstract

Introduction: Dengue is one of the most rapidly spreading vector-borne viral diseases world wide and its incidence in India is also on the rise due to increasing urbanization. It has variable clinical presentation and can affect all age groups. The disease has a spectrum of dengue fever, dengue hemorrhagic fever and dengue shock syndrome. The laboratory values to be looked for include hematological and serological tests. **Aim of the study:** To determine the clinical, ultrasound and laboratory findings in adult patients with dengue infection. **Materials and Methods:** This was a Retrospective, hospital based study. Dengue patients were studied for clinical presentation, hemoglobin, total leucocyte count, platelet count, peripheral smear examination, NS1Ag, serum dengue IgM and IgG. Ultrasound was performed wherever required. The duration of hospital stay of patients was studied. **Observations and Results**: Total 53 cases of dengue were studied. There were 45 (84%) male patients and only 8 (15%) female patients and the male to female ratio was 5.6:1. Fever was universal and was noted in all 53 patients. Headache, myalgia and gastrointestinal symptoms were most commonly observed. NS1Ag was positive in 79.2% cases and 11 cases were positive for serum IgM. Leucopenia, elevated hematocrit and moderate thrombocytopenia were common findings. Mild hepatosplenomegaly was common on ultrasound. The average hospital stay was 3 to 4 days. **Conclusion:** Dengue fever can affect all age groups and has a varied clinical presentation with most common features of fever, headache, myalgia, and emesis. It commonly affects adult males. The laboratory results often show elevated hematocrit, low total leucocyte count, thrombocytopenia, and mildly elevated liver enzymes. Serological tests help to differentiate between a primary and secondary infection and have clinical implications.

Keywords: Dengue infection, NS1Ag, Thombocytopenia, Leucopenia, Elevated Hematocrit.

Introduction

Dengue is one of the most rapidly spreading vector-borne viral diseases world wide and its incidence in India is also on the rise due to increasing urbanization. [1]

Benjamin Rush reported for the first time Dengue fever in 1780 as "break bone fever." Aedes aegypti mosquitos are the vectors for this viral infection and it has four serotypes. It commonly presents as dengue without warning signs, dengue with warning signs and severe dengue. [2] Dengue infection is caused by infected mosquitoes of Aedes aegypti species which usually breed indoors in artificial water containers, and they are typically day time feeders. Dengue infection has clinical spectrum from totally asymptomatic presentation to dengue fever, or dengue hemorrhagic fever (DHF) or in the severest form it can present as dengue shock syndrome (DSS) which may be fatal. [3] WHO gave updated guideline in 2009 and classified dengue as probable dengue, dengue with warning signs, and severe dengue? [4] Severe dengue includes dengue fever (DF) which is an acute febrile disease which is characterized by sudden onset of fever of 3-5 days duration, severe headache, body aches, arthralgias, retro-orbital pain, and loss of appetite, gastrointestinal disturbances and rash. [5] It is frequently accompanied by rash and leucopenia. [6] And dengue hemorrhagic fever (DHF) which is characterized by four major clinical features: high grade pyrexia, hemorrhagic manifestations, and hepatomegaly and, sometimes with signs of circulatory failure. Severe plasma leakage in these patients can cause hypovolemic shock and circulatory failure leading to death and hence is called dengue shock syndrome (DSS).

There are four serotypes of dengue virus. In India, most commonly encountered serotype is the DENV-2 type in many states, though there are regional differences and diversity. [7]

Aim of the study

To determine the clinical, ultrasound and laboratory findings in adult patients with dengue infection.

Materials and Methods

Approval from the Institutional Ethics committee was taken and no ethical issues were involved in the study.

This was a retrospective, hospital based study, done in the department of General Medicine at Government medical College, Nizamabad over a duration of nearly fourteen months from August 2021 to September 2022. A total of 53 admitted and diagnosed cases of dengue infection in adult population were studied. The demographic details of patients, their clinical presentations, hematological and serological profile, limited biochemical tests, and abdominal ultrasound were done and the results were noted.

Inclusion criteria:

Patients willing to participate

Patient age above 18 years

Both genders

Patients with serologically confirmed IgM positive dengue fever admitted to General Medicine ward.

Exclusion criteria:

Patients not willing to participate

Age below 18 years

Admitted patients with non-dengue medical conditions

Patients of known chronic diseases

Critically ill patients in intensive care unit

Antenatal cases with confirmed dengue fever for cross consultation were excluded

Methodology: A predesigned profroma was prepared in which findings of demographic details, complete clinical examination with clinical history of presenting symptoms and local and systemic examination were noted.

The presenting clinical symptoms such as fever, headache, myalgia, rash, pain in abdomen, etc were noted. The duration of hospital stay was noted.

For hematological tests, blood samples were collected as routine phlebotomy, ie 2ml blood in EDTA vacutainer was collected. Complete blood picture (CBP) was tested for hemoglobin, packed cell volume/hematocrit, platelet count, total leucocyte count, and differential leucocyte count. Peripheral smear and blood group

were studied in some cases as per requisition form. Dengue IgM and IgG were tested by ELISA. In a few cases chest X-ray PA view, ECG, liver function tests, renal function tests, serum electrolytes, HIV test, Widal test and ultrasonography of abdomen were also done.

NS1-Ag (Nonstructural protein-1 antigen) was done in all cases. Serology for dengue IgM and IgG Enzyme Linked Immunosorbent Assay (ELISA) was done.

The above test results were noted as positive or negative for antigen and both antibodies.

The frequency and percentages were calculated for all parameters. Statistical analysis was done with STAT A software version 2.0

Observations and Results

Table 1 Age-wise distribution of the cases (n=53)

Age (in years)	No. of cases	Percent (%)
18-30	40	75.47%
31-40	5	9.4%
41-50	3	5.6%
51-60	2	3.7%
61-70	3	5.6%
Total	53	100%

Most commonly affected age group was of adolescents and young adults.

Gender-wise distribution: There were 45 (84%) male patients and only 8 (15%) female patients and the male to female ratio was 5.6:1

Table 2 Distribution of clinical features

Clinical features*	No. of cases	Percent (%)
Fever	53	100%
Fever with headache and myalgia	46	86.7%
Nausea and vomiting	28	52.8%
Chills and rigors	23	43.3%
Cough	8	15.0%
Mild pain in abdomen	5	9.4%
Diarrhea	2	3.7%
Skin rashes/petechiae	1	1.8%
Hematuria	1	1.8%
Pedal edema	1	1.8%
Melena	6	11.32%
Gum bleed	1	1.8%
Altered sensorium	0	-

*Symptoms were not mutually exclusive and many patients had more than one symptom.

Fever was universal and was noted in all 53 patients. Headache, myalgia and gastrointestinal symptoms were commonly observed.

NS1Ag test and serum IgM positive cases: There were 42 (79.2%) cases with positive NS1Ag test and 11 cases were positive for serum IgM test.

Table 3 Distribution of study population based on hemoglobin and hematocrit on admission

Hemoglobin level			Hematocrit		
Hb (gm/dl)	No. of cases	%	Hct (%)	No. of cases	%
6-9	2	3.77%	20-25	1	1.8%

9.1-12.0	14	26.41%	26-35	12	22.6%
12.1-15.0	29	54.71%	36-45	26	49.0%
15.1-18	8	15.0%	46-55	14	26.4%
Total	53	100%	Total	53	100%

Elevated hemoglobin was observed in 8 (15%) cases. Hemoconcentration was seen in 26.4% cases.

Table 4 Total leucocyte count and platelet count

Total leucocyte count			Platelet count		
TLC (cells/cumm)	No. of cases	%	Platelet (cells/cumm)	No. of cases	%
< 1500	-	-	<20,000	3	5.6%
1500-4,000	28	52.8%	20,000-50,000	17	32.07%
>4000-11,000	22	41.50%	>50,000-1.5 lakh	22	41.5%
>11,000	3	5.6%	>1 .5 lakhs	11	20.7%
Total	53	100%	Total	53	100%

Leucopenia was observed in 28 (52.8%) cases and very few patients had leucocytosis. Severe thrombocytopenia below 20000/cumm was noted in 3 (5.6%) cases. Most of the cases had moderate thrombocytopenia.

Peripheral smear examination: In the present study, peripheral smear (PS) was requested in 25 cases of which 15 (60%) showed reactive lymphocytes.

Biochemical tests: Serum was tested for liver enzymes like alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP), serum bilirubin, serum urea and creatinine and electrolytes. Serum AST and ALT were mildly elevated in 30 (56.6%) cases.

No significant changes were observed in renal tests and serum electrolytes.

Ultrasonography findings: Gall bladder wall edema was seen in 7 (13.2%) cases, ascites in 4 (7.5%) cases, pleural effusion and mild splenomegaly in 3 (5.6%) cases each and mild hepatomegaly in 1 (1.8%) cases.

Platelets transfusion: Single donor platelets (SDP) and random donor platelets (RDP) transfusion was administered to two and four patients respectively. SDP was given as single unit each to two patients and in RDP patients, three patients received two units each and one patient required four units of RDP.

There was no mortality case in our study.

Table 5 Duration of hospital stay (in days)

Duration of hospital stay (in days)	No. of cases	Percent (%)
1-2	3	5.6%
3-4	24	45.2%
5-6	21	39.6%
7-8	4	7.5%
9-10	1	1.8%

The duration of hospital stay ranged from 1 day to 9 days.

Discussion

Murhekar et al [8] conducted a nationally representative survey to determine the age specific seroprevalence of dengue infection.

They studied fifteen Indian states including rural and urban areas with a wide age range. They observed an overall seroprevalence of dengue infection as

48.7% in these areas which is quite high and alarming. Ganeshkumar et al [9] conducted a systemic review and meta-analysis of dengue infection in India and observed an overall prevalence of dengue infection that was confirmed by laboratory testing in clinically suspected patients to be 38.3%. They also estimated that in the general population the dengue seroprevalence and case fatality rate were 56.9% and 2.6% respectively. Dengue infection is on a rising trend in India and is a public health problem.

Age and gender-wise distribution: In the present study, age group 18 to 70 years was studied. We observed that most commonly affected age group was of adolescents and young adults with 40 (81.1%) cases in the 18 to 30 years age group. There were 45 (84%) male patients and only 8 (15%) female patients and the male to female ratio was 5.6:1. Murhekar et al [8] in their extensive epidemiological study found that dengue was more common in the pediatric and young adult age groups with 31.8% cases and 31.2% cases in age groups of 10 to 19 years and 20 to 29 years respectively.

Deshwal et al [10] in their study on dengue fever of 515 patients, observed that the most commonly affected age group was 21-40 year age group with 62.9% cases.

Gajera V et al [11] in their study of hundred patients of dengue fever, observed most commonly affected age group to be 15 to 25 year with 49% cases in this age. Meena et al [12] in a similar study found maximum cases (29%) in the 21-30 years age block.

In our study, males were more commonly affected. It could be due to the socio-cultural reasons. [13] Deshwal et al and Gajare V et al [10, 11] too reported dengue to be more common in males than in female

patients with a rate of 72.8% and 70% patients respectively.

In the study by Nagendra Prasad et al, [14] of the 120 dengue cases, (61.6%) were in the 18 to 30 years group with a male to female ratio of 3.2:1.

Sankhe P et al [15] studied 80 cases of dengue infection in Navi Mumbai area in India from 18 to 65 years age range and observed the mean age affected was 33±12 years, having male predominance as 66% were male patients.

Our findings compare well with the observations of the above authors.

Clinical features:

In the present study, all the patients (100%) had presented with fever of varying grades. In the study by Nagendra Prasad et al [14] also fever was the most common presentation and was observed in 27 cases (45%) cases, followed by fever and myalgia in 10 (6.6%) cases. Deshwal et al [10] also reported fever, headache and myalgia to be the most common complaints. Gajare V et al [11] observed fever in 95 (95%) of their cases, followed by myalgia, arthralgia and headache in 50% cases.

Sankhe P et al [15] in their study of 80 cases of dengue infection observed fever in 42% cases.

Nair KR et al [16] also observed fever as universal symptom (100%) in all of their 236 patients followed by myalgia in 53% cases and headache in 42% cases and vomiting in 22% cases.

Hematological parameters:

In the present study, hemoconcentration (>46%) was noted in 14 (26.4%) out of 53 patients. Khatroth S et al [17] in a similar study reported elevated hematocrit (>47%) in 16.6% of their patients at presentation. Deshwal et al [10] also reported increased hematocrit (>45%) in about 20.7% of their

dengue patients. Patel MK et al [18] in their study found elevated hematocrit in 17.5% cases.

The reason for this elevated hematocrit is said to be due to the capillary leak syndrome that is seen in dengue fever and dengue hemorrhagic fever.

Dengue fever commonly has leucopenia rather than leucocytosis at presentation.

In our study, we observed leucopenia at presentation in 52.8% cases with the TLC between 1500 to 4000 cells/cumm. This compares well with the findings of Meena KC et al [12] who reported leucopenia <4000/cumm in 51% of their cases. Sankhe P et al [15] observed leucopenia/borderline leucopenia in all of their 80 patients at presentation on day one. Deshwal et al [10] observed leucopenia in 20.19% patients. Butt N et al [19] and Gajera V et al [11] observed leucopenia of TLC <4,000/cumm in 50% and 39% cases respectively in their studies. They also observed leucocytosis of TLC more than 11,000/cumm in 12% cases, whereas in our study leucocytosis at presentation was seen in 5.6% cases.

In the present study, severe thrombocytopenia of less than 20000/cumm platelets count was seen in 5.6% cases and 6 (11.32%) out of 53 patients had bleeding manifestations as skin rashes, malena, hematuria and gum bleed. Most of the cases ie 41.5% cases had a platelet count of 50000 to 1.5 lakh/cumm at presentation.

In the study by Nagendra Prasad et al [14] of 120 cases of dengue fever, 38.3% had very severe thrombocytopenia. Meena KC et al [12] observed severe thrombocytopenia with bleeding in 14% cases. Deshwal et al [10] reported low platelet counts of < 50,000/cumm in 69.51% of their patients.

Patel MK [18] reported platelets <20000/cumm in 15% of their cases that were accompanied with bleeding manifestations. Platelet indices when studied from the hematology analyzer give valuable information [20] on whether the thrombocytopenia is hyperdestructive or hypodestructive type but was not part of our present study.

Suppression of the bone marrow suppression, immune-mediated clearance and spontaneous aggregation of platelets to virus infected endothelium are the proposed mechanisms for dengue related thrombocytopenia. [18]

Reactive lymphocytes were observed on PS examination in 60% of our cases. Similar findings of lymphocytosis with atypical and plasmacytoid lymphocytes on the smears were observed by Patel MK et al. [18] Direct PS examination also helps to confirm the low TLC and gives approximate estimate of platelet counts. Although megaloblastic anemia is the commonest cause for pancytopenia, [21] sometimes, dengue can give a picture of pancytopenia, wherein the reactive lymphocytes may give a clue for the viral etiology.

In the present study serum AST and ALT were mildly elevated in 30 (56.6%) cases Khatroth S et al [17] also observed mildly increased serum AST and ALT in 40 (66.6%) cases and Patel MK reported similar findings in 69% of their cases.

In our study, NS1 Ag test was positive in 42 (79.2%) cases and serum IgM test was positive in 11 (20.7%) cases. Some studies have reported 100% NS1Ag test positivity [14] whereas some other studies [22] have reported around 23% positivity for NS1Ag. In the study by Nagendra Prasad et al [14] 65% cases were primary infections and

35% were secondary infections. Changal et al [23] reported 66.7% to be secondary dengue. Reactive lymphocytes were observed on PS examination in 60% of our cases. Similar findings of lymphocytosis with atypical and plasmacytoid lymphocytes on the smears were observed by Patel MK et al. [18] Ultrasonography findings: In our study, hepatomegaly and splenomegaly were observed in 1.8% and 5.6% cases respectively and gall bladder wall edema was seen in 13.2% cases. Patel MK [18] noted hepatomegaly in 32 % and splenomegaly in 17% of their cases. Sankhe P et al [15] observed ascites in 19% of their patients and hepatomegaly in 18%. Nagendra Prasad et al [14] observed pleural effusion in 50% of the patients, hepatomegaly in 50% and splenomegaly in 66% of the cases. Duration of hospital stay: The duration of hospital stay ranged from 1 day to 9 days in our study with most of the cases (45.2%) requiring a 3 to 4 days indoor care and monitoring. Mishra S et al [24] studied 350 adult confirmed cases of dengue for duration of hospital stay and observed 44.3% required hospital stay of 4 to 6 days and 25% required less than 3 days stay. They observed that early arrival of patients to hospital and early intervention gives better recovery. Bringing awareness and education to the community about dengue infection is one of the ways to curb the menace of dengue. At present dengue vaccine is recommended in geographical settings with high burden of disease, ie where the seroprevalence is > 70% and higher by the age of 9 years. As India does not meet this criteria, dengue vaccine is not available in India at present. [25]

Conclusion

Dengue fever can affect all age groups and has a varied clinical presentation with most common features of fever with or without chills and rigors, headache, myalgia, and emesis. It commonly affects adult males. The laboratory results often show Elevated hematocrit, low total leucocyte count, thrombocytopenia, and reactive lymphocytes on the peripheral smear and mildly elevated liver enzymes. Serological tests help to differentiate between a primary and secondary infection and have clinical implications. The ultrasound findings often show mild hepatosplenomegaly.

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