

## STUDY OF CLINICAL AND LABORATORY PROFILE OF DENGUE FEVER PATIENTS

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**ABSTRACT**

**Objective:** Dengue fever is one of the most common arboviral mediated outbreaks reported with increased prevalence year after year with considerable morbidity and mortality. This study was designed to assess the clinical and biochemical parameters of dengue fever patients. **Methods:** Prospective observational study was undertaken among adult patients in a rural tertiary care hospital. One fifty-five patients were studied and analysed. All patients who were NS1 antigen/IgM dengue positive were included in the study. Clinical features, haematological and biochemical parameters were noted. **Results:** Of the 155 patients studied, Majority of the patients were in 18-40 age group (60.32%) and were predominantly males (70.97%). Fever was present in all patient, followed by myalgia (94.83%), headache (90.96%). Thrombocytopenia (<50,000/cumm) at presentation was seen in 78.06% of cases. Leucopenia was noticed in 34.19% of cases. Raised liver serum transaminases were noted in 61.93% of patients out of which SGOT was elevated in 72.67% and SGPT in 27.33% of patients. Raised haematocrit (>45%) was noted in 23.22% of patients at presentation. Mortality rate was 1.29%. **Conclusion:** We conclude that dengue infection, which possesses serious public health problem, can be diagnosed early with the help of clinical features like retro orbital pain, myalgia, bleeding manifestations, thrombocytopenia, SGOT greater than SGPT that is supported by detection of NS1 antigen, IgG and IgM antibodies. Platelet transfusions have little role in management of dengue patients.

**KEYWORDS:** Dengue fever, thrombocytopenia, serum transaminases.**INTRODUCTION**

Dengue is the most common arthropod-borne viral(arboviral) illness in humans. It is transmitted by mosquitoes of the genus *Aedes*.<sup>[1]</sup> Although initially reported from urban locales, dengue is now being reported from urban and rural backgrounds alike.<sup>[2]</sup> Based on the data of National Vector Borne Disease Control Programme(NVBDCP), the number of cases reported in India in 2013 was 74,454 for dengue with 167 deaths.<sup>[3]</sup> Dengue is caused by infection with one of the four serotypes of dengue virus, which is a Flavivirus. Infection with one dengue serotype confers lifelong homotypic immunity to that serotype and a very brief period of partial heterotypic immunity to other serotypes, but a person can eventually be infected by all 4 serotypes.<sup>[4]</sup> Several serotypes can be in circulation during an epidemic. Dengue is transmitted by mosquitoes of the genus *Aedes*, principally *Aedes aegypti*.<sup>[5]</sup> Initial dengue infection may be asymptomatic (50-90%),<sup>[6]</sup> may result in a nonspecific febrile illness, or may produce the symptom complex of classic dengue fever(DF). The disease presents with sudden onset fever, frontal headache, generalized myalgia, retro-bulbar pain and transient macular skin rash after an incubation period

of 4-7 days of infected mosquito bite. It is estimated that annually approximately 500,000 cases of severe dengue occur worldwide with case fatality to the tune of around 2.5%, which can be improved to <1% with good management.<sup>7</sup> Diagnosing dengue early is challenging because the initial symptoms of dengue infection are often non-specific and serological tests, which are the mainstay of current laboratory diagnosis, confirm dengue late in the course of illness.<sup>[8,9]</sup> there is a lacuna in diagnosing dengue virus infection early both in relation to clinical features and laboratory tests. Hence, this study was undertaken to address this issue and help clinicians to diagnose dengue fever early with help of clinical features and laboratory investigations.

**MATERIALS AND METHODS**

This prospective observational study was carried out between May 2015 and May 2016. All patients above 18 years with confirmed dengue fever, who were hospitalized with NS1 (non-structural protein) antigen and/ or IgM antibody positivity were included in the study. The patients with concomitant malaria, typhoid, leptospirosis were excluded from the study. Detailed history was recorded and careful clinical examination

was performed on each patient. Laboratory investigations such as haemoglobin, total and differential leucocyte counts, platelet count, haematocrit, liver function tests, blood urea and serum creatinine, chest radiograph and ultrasound scan of abdomen were done. Blood counts were monitored periodically as and when required till resolution. Other differential diagnosis were excluded by appropriate tests. The study was approved

by hospital ethics committee and informed consent was obtained from each patient.

## RESULTS

A total of 155 patients who reported between May 2015 and May 2016 were studied and analysed. Majority of these cases reported to our hospital coinciding with rainy season, showing the breeding of mosquitoes during the said period.

**Table 1: Age Distribution of patients.**

Age (years)	Male	Female	Total
21-40	74(67.27%)	23(51.11%)	97
41-60	21(19.09%)	14(31.11%)	35
>60	15(13.63%)	8(17.77%)	23

Majority of the patients were males (70.97%). Females formed 29.03% of the cohort. Maximum patients were in 18-40 age group (60.32%).

**Table 2: Clinical Features.**

S.No	Clinical features	Number of patients %
1	Fever	155 (100%)
2	Headache	141 (90.96%)
3	Myalgia	147 (94.83%)
4	Retro-orbital pain	24 (15.48%)
5	Abdominal pain	65 (41.93%)
6	Nausea/Vomiting	36 (23.22%)
7	Diarrhoea	34 (21.93%)
8	Conjunctival suffusion	47 (30.32%)
9	Skin Rashes	38 (24.51%)
10	Itching	14 (9.03%)
11	Bradycardia	43 (27.74%)
12	Bleeding	21 (13.54%)
13	Positive tourniquet test	30 (19.35%)
14	Pleural effusion	35 (22.58%)
15	Ascites	48 (30.96%)
16	Breathlessness	26 (16.77%)
17	Seizures	4 (2.5%)
18	Splenomegaly	24 (15.48%)
19	Hepatomegaly	23 (14.83%)

Fever was present in all patients followed by myalgia (94.83%), headache (90.96%), abdominal pain (41.93%), conjunctival injection (30.32%), morbilliform skin rash (24.51%), retro-orbital pain (15.48%), itching predominantly localized to palmar and plantar aspects of hands and feet (9.03%). Positive tourniquet test was found in 19.35% of patients, while bleeding in form of petechiae, ecchymosis and epistaxis was documented in 13.54% of cases. Pleural and ascitic fluid was documented in 22.58% and 30.96% of cases,

respectively. Hepatomegaly was noted in 14.83% and splenomegaly in 15.48% of all cases. The ECG findings revealed sinus bradycardia in 27.74% of patients. Platelet count at presentation was less than 50,000/cumm in 78.06% of cases, though it kept on falling further during hospitalization/observation. Minimum platelet count noted was 5,000/cumm. Leucopenia was noticed in 34.19% of cases. Raised liver serum transaminases were noted in 61.93% of patients. Raised haematocrit (>45%) was noted in 23.22% of patients at presentation.

**Table 3: Distribution of laboratory parameters**

S.No	Parameters	Number of patients %
1	Thrombocytopenia (<50,000/cumm)	121 (78.06%)
2	Leucopenia (<4,000/cumm)	53 (34.19%)
3	Raised AST, ALT >45 IU/L	96 (61.93%)
4	Raised haematocrit (>45%)	36 (23.22%)

All the patients were managed with careful monitoring of blood pressure, haematocrit, platelet counts on as and when required basis. Platelet transfusion was given in 13.54% of patients who presented with bleeding manifestation. Antipyretics (paracetamol) were used along with intravenous fluids (normal saline and ringer lactate) when required. Total mortality was 1.29% (02/155). All patients who expired have had evidence of preceding dengue infection (Ig G positive) in the preceding 2-3 months. Dengue shock syndrome was seen in two patients as cause of death. Platelet count in all patients who expired was above 50,000/cumm.

## DISCUSSION

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 increase in alertness among medical personnel following the epidemics and availability of diagnostic tools in the hospitals have contributed to the increased detection of cases.

Male to female ratio in our study was 2.44: 1. Slightly higher number of males is primarily because of the occupation. Fever was the most common presentation (100%), which is similar with other studies from India and South East Asia.<sup>[10-13]</sup> Headache and myalgia were seen in majority of cases. Retro-orbital pain was noticed in only 15.48% of cases. Conjunctival injection was documented in 30.32% of all cases and diffuse erythematous skin rash in 24.51%. Mandal et al in a similar study have documented headache in 62.16% and rash in 37.84% of cases.<sup>[14]</sup> Thrombocytopenia may not be the sole causative factor for development of these rashes as they developed in patients with platelet counts above 50,000/cumm. Dengue virus interacts with host cells, causing release of cytokines and stimulation of immunologic mechanism causing vascular endothelial changes, infiltration of mononuclear cells and perivascular edema.<sup>[15]</sup> Munde et al in their series of patients have shown myalgia in 50% and headache in 25% of all patients.<sup>[13]</sup> Muniraja et al documented conjunctival congestion in 2.6 to 7.3% of cases which is much less than our study patients.<sup>[16]</sup> Itching was noticed in 9.03% of our cases, this finding has not been noticed by most other studies except a few, Rachel et al from their study in Kollam, Kerala have documented pruritis in 10.4% of their patients.<sup>[12]</sup> Rajesh et al from their study in Agra have documented itching in 13.39%.<sup>[17]</sup> Positive tourniquet test was seen in 19.50% and bleeding in form of petechiae in around 13.54% of patients which was less than some other similar studies and in line with Shabid et al from Karachi.<sup>[18]</sup> Bleeding diathesis is a known feature of dengue fever because of low platelet count and leakage from blood vessels. The mechanism behind the platelet reduction is not yet clear till date due to lack of suitable animal model studies.<sup>[19]</sup>

There are two mechanisms causing thrombocytopenia. DENV induced bone marrow suppression decreases the platelet synthesis and leads to thrombocytopenia.<sup>[19]</sup> Immune mediated clearance of platelets also causes thrombocytopenia.<sup>[19,20]</sup> In this mechanism, anti-platelet antibodies clears the virus attached platelets via complement activation and also inhibits ADP-induced platelet aggregation.<sup>[19-23]</sup>

Raised liver transaminases were documented in 61.93% of cases which is much less compared to other studies. In study by Kularatne et al, 88% patients showed elevated ALT and AST, with 122 of them having a two-fold increase.<sup>[24]</sup> Mandal et al documented elevated transaminases in 83.78% of cases.<sup>[14]</sup> Patients with dengue fever are more prone to have liver enzyme derangement and preferentially high SGOT may serve as an early indicator of dengue infection. The SGOT levels in dengue infection have a tendency to be greater than SGPT levels.<sup>[25]</sup> This pattern is similar to that seen in alcoholic hepatitis but differs from the pattern in other viral hepatitis. The exact cause for this is unknown, but it is hypothesised that it may be due to excess release of SGOT from damaged liver cells during dengue infection. Another explanation is involvement of myocytes.<sup>[26]</sup> In our study we found elevation of liver enzymes with SGOT being higher than SGPT. The SGOT and SGPT found to be increased in 72.67% and 27.33% of patients respectively. This abnormal pattern may be used as an early indicator of dengue infection.

A study from Brazil by Silva et al, has found an interacting partner between NS1 protein and liver proteins in the causation of hepatic dysfunction in dengue fever.<sup>[27]</sup> Pleural effusion was documented in 22.58% on chest radiography and ascites seen in 30.96% of patients on ultrasound scan of abdomen was marginally higher from other similar studies.<sup>[28]</sup> The overall mortality in our study population was 1.29% which is correlating with fatality rates in South-East Asian countries.

## CONCLUSION

Dengue infection is increasing due to increased urbanization and compromised sanitation measures. Fever associated with headache, retro orbital pain, erythematous morbilliform rash, conjunctival suffusion and itching in palms and soles along with thrombocytopenia, Leucopenia, elevated liver transaminases should prompt a clinician on the possibility of dengue infection. Platelet transfusions have little role in management of dengue patients. Early diagnosis, careful monitoring and proper fluid management goes a long way in reducing the mortality due to dengue haemorrhagic fever and shock syndrome. Thus we conclude that dengue infection, which possesses serious public health problem, can be diagnosed early with the help of clinical features like retro orbital pain, myalgia, bleeding manifestations, thrombocytopenia,

SGOT greater than SGPT that is supported by detection of NS1 antigen, IgG and IgM antibodies.

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