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A Study of Clinical and Laboratory Profile of Dengue Fever cases in a Tertiary Care Teaching Hospital

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ABSTRACT

The incidence of dengue has grown dramatically around the world in recent decades. The exact clinical and laboratory profile is crucial for diagnosis as well as successful management of the patients. This study is an attempt to assess the clinical and laboratory profile of serologically confirmed cases of dengue fever in a tertiary care hospital. This cross-sectional observational study was carried out including 45 dengue fever cases in a tertiary care teaching hospital. All patients above 18 years with confirmed dengue, who were either admitted in the medical wards of the hospital or managed as outdoor patients with NS1 (non-structural protein) antigen and/ or IgM dengue antibody positivity were included in the study. All the patients, who presented with fever and found positive Dengue IgM antibodies capture enzyme-linked immunosorbent assay (MAC-ELISA). The diagnosis of DF, DHF, and dengue shock syndrome (DSS) were based on the WHO criteria. Fever was documented in all 45 (100%) patients, the most common symptom followed by reduced appetite 41 (91.1%), myalgia 39 (86.7%), headache 36 (80%), abdominal pain 29 (64.4%), nausea/ vomiting 18 (40%), diarrhea 17 (37.8%) and pruritus 17 (37.8%). Bleeding manifestations occurred in 21 (46.7%) patients, of whom petechiae 17 (37.8%) was the most frequent followed by gum bleeding 5 (11.1%), gum bleeding 5 (11.1%). Ecchymosis 3 (6.7%), malena 3 (6.7%) and hematuria 2 (4.4%) were less common. Fever associated with headache, retroorbital pain, erythematous morbilliform rash and itching in palms and soles along with thrombocytopenia, leucopenia, and elevated liver transaminases should prompt a clinician on the possibility of dengue infection. Proper confirmation of diagnosis, early institution of therapy, public awareness, and vector control are important factors to be taken into consideration in the prevention and management of dengue.

Keywords

Dengue fever,
Dengue Shock
Syndrome,
Clinical features,
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Introduction

Dengue made its debut as early as 1780, when Benjamin Rush described the condition as "break bone fever". It is a systemic viral infection transmitted between humans by *Aedes* mosquitoes. This hitherto unfamiliar infection has now grown to demand the attention of all public health care providers especially in India. A mosquito borne fast emerging viral infection manifesting in four serotypes capable of causing dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS), poses an increasingly perilous situation due to lack of antiviral drugs or vaccine (Guzman *et al.*, 2002).

It has rapidly spread in all regions of WHO in recent years. Dengue virus is transmitted by female mosquitoes mainly of the species *Aedes aegypti* and, to a lesser extent, *Aedes albopictus*. This mosquito also transmits chikungunya, yellow fever and Zika infection. Dengue is widespread throughout the tropics, with local variations in risk influenced by rainfall, temperature and unplanned rapid urbanization (Dengue and severe dengue, 2016).

There are 4 distinct, but closely related, serotypes of the virus that cause dengue (DEN-1, DEN-2, DEN-3 and DEN-4). Recovery from infection by one provides lifelong immunity against that particular serotype. However, cross-immunity to the other serotypes after recovery is only partial and temporary. Subsequent infections by other serotypes increase the risk of developing severe dengue.

The infection causes flu-like illness, and occasionally develops into a potentially lethal complication called severe dengue. The global incidence of dengue has grown dramatically in recent decades. About half of the world's population is

now at risk. Dengue is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. Severe dengue is a leading cause of serious illness and death among children in some Asian and Latin American countries. There is no specific treatment for dengue/ severe dengue, but early detection and access to proper medical care lowers fatality rates below 1%. Dengue prevention and control depends on effective vector control measures.

Global burden of dengue

The incidence of dengue has grown dramatically around the world in recent decades. The actual numbers of dengue cases are underreported and many cases are misclassified. One recent estimate indicates 390 million dengue infections per year (95% credible interval 284–528 million), of which 96 million (67–136 million) manifest clinically (with any severity of disease) (Bhatt *et al.*, 2013).

Another study, of the prevalence of dengue, estimates that 3.9 billion people, in 128 countries, are at risk of infection with dengue viruses (Brady *et al.*, 2012). Member States in 3 WHO regions regularly report the annual number of cases. The number of cases reported increased from 2.2 million in 2010 to 3.2 million in 2015. India is one of the seven identified countries in the South-East Asia region regularly reporting incidence of DF/DHF outbreaks and may soon transform into a major niche for dengue infection in the near future. The first confirmed report of dengue infection in India dates back to 1940s, and since then more and more new states have been reporting the disease which mostly strikes in epidemic proportions often inflicting heavy morbidity and mortality, in both urban and rural environments.

Brazil alone reported over 1.5 million cases in 2015, approximately 3 times higher than in 2014. Also in 2015, Delhi, India, recorded its worst outbreak since 2006 with over 15 000 cases.

In India, dengue is endemic in 31 states/union territories, and all four serotypes have been isolated. Totally, 64,058 cases are reported, of which 135 cases died (till October 25, 2015). Highest number of cases was reported from Tamil Nadu, Punjab, Delhi, and Andhra Pradesh (Park *et al.*, 2013; Kumar *et al.*, 2010). Majority of infection occur affected. Mortality rate is only 1% in treated DHF/DSS cases; however, it increases to 20% when left untreated (Government of India. Annual Report 2014–15).

Clinical Characteristics

Dengue fever is a severe, flu-like illness that affects infants, young children and adults, but seldom causes death. Dengue should be suspected when a high fever (40°C/104°F) is accompanied by 2 of the following symptoms: severe headache, pain behind the eyes, muscle and joint pains, nausea, vomiting, swollen glands or rash. Symptoms usually last for 2–7 days, after an incubation period of 4–10 days after the bite from an infected mosquito.

Severe dengue is a potentially deadly complication due to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment. Warning signs occur 3–7 days after the first symptoms in conjunction with a decrease in temperature (below 38°C/100°F) and include: severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums, fatigue, restlessness and blood in vomit. The next 24–48 hours of the critical stage can be lethal; proper

medical care is needed to avoid complications and risk of death. Initial dengue infection may be asymptomatic (50-90%), may result in a nonspecific febrile illness, or may produce the symptom complex of classic dengue fever (DF). Classic dengue fever is marked by rapid onset of high fever, headache, retro-orbital pain, diffuse body pain (both muscle and bone), weakness, vomiting, sore throat, altered taste sensation, and a centrifugal maculopapular rash, among other manifestations. A small percentage of people who have previously been infected by one dengue serotype develop bleeding and endothelial leak upon infection with another dengue serotype. This syndrome is termed dengue hemorrhagic fever (DHF) (Deshwal *et al.*, 2015).

The exact clinical and laboratory profile is crucial for diagnosis as well as successful management of the patients. This study is an attempt to elucidate the clinical and laboratory profile of serologically confirmed cases of dengue fever in a tertiary care hospital

Materials and Methods

This cross-sectional observational study was carried out in a tertiary care teaching hospital in Dewas, MP from July 2015 to July 2016. All patients above 18 years with confirmed dengue, who were either admitted in the medical wards of the hospital or managed as outdoor patients with NS1 (non-structural protein) antigen and/ or IgM dengue antibody positivity were included in the study.

All the patients, who presented with fever and found positive Dengue IgM antibodies capture enzyme-linked immunosorbent

assay (MAC-ELISA). The diagnosis of DF, DHF, and dengue shock syndrome (DSS) were based on the WHO criteria (World Health Organization. Dengue and Dengue Hemorrhagic fever, 2016).

Inclusion criteria

1. Patients of both sexes of age more than or equal to 18 years, who were willing for admissions and who were positive for Dengue IgM antibody by ELISA.

Exclusion criteria

1. Patients of less than 18 years of age, tested negative for dengue IgM antibody by ELISA or who were not willing for admission.

2. Patient with concomitant malaria and typhoid.

Detailed history and careful clinical examination was performed on each patient. Laboratory investigations done were hemoglobin, total and differential leukocyte counts, platelet count, hematocrit, liver function tests, along with serum amylase and lipase, blood urea and serum creatinine, chest X-ray, ECG, and abdominal ultrasonography were carried out as indicated. Other relevant investigations were performed according to the clinical conditions of the patients. Other differential diagnoses were excluded by appropriate tests.

Case Definition of DF (World Health Organization, 2015)

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 DF [WHO].

Clinical Description

Dengue is defined by fever as reported by the patient or healthcare provider and the presence of one or more of the following signs and symptoms:

Nausea/vomiting

Rash

Aches and pains (e.g., headache, retro-orbital pain, joint pain, myalgia, arthralgia)

Tourniquet test positive

Leukopenia (a total white blood cell count of $<5,000/\text{mm}^3$), or

Any warning sign for severe dengue:

Abdominal pain or tenderness

Persistent vomiting

Extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites)

Mucosal bleeding at any site

Liver enlargement >2 centimeters

Increasing hematocrit concurrent with rapid decrease in platelet count

Dengue haemorrhagic fever (DHF) is defined as an acute febrile illness with minor, major bleeding, thrombocytopenia (platelet count $<1 \text{ lac}/\text{cmm}$), and evidence of plasma leakage documented by haemoconcentration (haematocrit increased by at least one-fifth or decreased by the same amount after intravenous fluid

therapy), plural or other effusions, or hypoalbuminaemia or hypoprotinaemia. Dengue Shock Syndrome (DSS) is defined as DHF with signs of circulatory failure, including narrow pulse pressure (20mm Hg), hypotension, or frank shock. The study was approved by institutional ethics committee and informed consent was obtained from each patient. Data were collected using a predesigned questionnaire and analyzed using Statistical Package for Social Sciences (SPSS version 17).

Results and Discussion

In this study, total 45 dengue MAC ELISA positive patients are included and analyzed [Table 1]. The different clinical features of these patients are shown in table 2. It was noted that fever was present in all patients. Next common symptom was headache followed by reduced appetite, myalgia and headache. Bleeding manifestations from different sites of the body was evident in 21 patients (46.7%), majority were non-serious category. Total number of the patients were 45, of whom 28 (62.2%) were male and 17 (37.8%) were female [Table 1]. Maximum number of patients belong to the age group 18-40 years, 22 (48.9%) followed by 41-60 years, 17 (37.8%) [Table.1]. Most of the dengue cases were admitted during the month of August to November indicating clustering of cases during monsoon and post-monsoon period.

The mean duration of the symptoms was 5 days. The average duration of stay of the patient in the hospital was 3-7 days. Fever was documented in all 45 (100%) patients, the most common symptom followed by reduced appetite 41 (91.1%), myalgia 39 (86.7%), headache 36 (80%), abdominal pain 29 (64.4%), nausea/ vomiting 18 (40%), diarrhea 17 (37.8%) and pruritus 17 (37.8%) [Table 2]. Bleeding manifestations

occurred in 21 (46.7%) patients, of whom petechiae 17 (37.8%) was the most frequent followed by gum bleeding 5 (11.1%), gum bleeding 5 (11.1%). Ecchymosis 3 (6.7%), malena 3 (6.7%) and hematuria 2 (4.4%) were less common [Table 2]. Bleeding manifestations were more likely with lower platelet counts, and 06 patients had more than one bleeding manifestations.

Skin rash mainly maculopapular and diffuse flushing were noted in 19 (42.2%), jaundice was observed in 5 (11.1%), hypotension 15 (33.3%), hyperacidity 13 (28.9%) and tachycardia was noted in 29 (64.4%) [Table 2]. Tourniquet test was positive in 11 (24.4%), commonly among young male patients. Isolated hepatomegaly and splenomegaly was found in 5 (11.1%) and 9 (20%) respectively while hepatosplenomegaly was found in 4 (8.8%). Ascites and Plural effusion was found in 2 (4.4%) and 3 (6.7%) patients respectively [Table 2, 4].

Among haematological parameters, raised haematocrit (>45%) was found in 35 (23.33%) and leukopenia (<4000/cmm) was found in 58 (38.66%) patients. Thrombocytopenia was observed in all the patients with varying severity, severe (<20000/ cmm) was observed in 23 (15.33%) patients while moderate (20000-50000/ cmm) in 62 (41.33) patients [Table 5]. Platelet count at presentation was <50000 in about 56.66% of the patients though it kept falling further during hospitalisation. Minimum platelet count noted was 9000/cmm.

Of the total 45 patients with DF the preexisting morbidities recorded were 7 (15.5%) with hypertension, 4 (8.8%) with type 2 diabetes mellitus, 3 (6.6%) with COPD/asthma, 1 (2.2%) with major bleeding tendency, 1 (2.2%) with chronic

kidney disease, 5 (11.1%) with cardiovascular accidents, and 2 (4.4%) with chronic liver disease-

The commonest complication observed was severe abdominal bloating in 16 (35.5%) patients, followed by hypotension 15 (33.3%), metabolic acidosis 11 (24.4%), major bleeding 5 (11.1%) and severe hepatitis 3 (6.67%) of the patients [Table 3]. Out of total of the 45 patients with DF, 6 (13.3%) required the ICU treatment, of the ICU admitted patients, who had multi organ failure, respiratory failure, major bleeding, severe hepatitis, shortness of breath due to pleural effusion as complications. Multi-organ failure and encephalopathy observed in 2 (4.4%) of the patients. About 5 (11.1%) had acute kidney injury [Table 3].

The median stay in ICU for the 6 (13.3%) was 4 days which ranged from 3 to 7 days. Briefly, 4 patients from ICU and all patients from the wards were discharged home after clinical cure with total of 43 out of 45 patients, 2 patients died with DF with major complications, both the patient died from multi-organ failure with associated diabetes mellitus as co-morbidity. After discharge from the hospital, none of the patients developed any residual organ injury or disability.

About 41 (91.1%) of the patients had thrombocytopenia (platelet count < 1.5 lakhs), followed by leucopenia in 29 (64.4%) of the patients [Table 5]. Minimum platelet count noted was 9000/cmm. Serological findings in the study subjects showed that in 39 (86.6%) patients NS1 was positive and IgM positives in 45 (100 %) of the patients.

All patients were managed conservatively with IV fluids, antibiotics and antipyretics. Platelet transfusion was reserved for patients

with active bleeding or prophylactically at a count of <10000/cmm based on clinical condition of the respective patients.

Dengue infection results in a wide spectrum of clinical severity, from self-limiting DF to severe dengue. DF was first referred as “water poison” associated with flying insects in a Chinese medical encyclopedia in 992 from the Jin Dynasty (265–420 AD). It is transmitted mainly by *Aedes aegypti* mosquito and also by *Aedes albopictus*. All four serotypes can cause the full spectrum of disease from a subclinical infection to a mild self-limiting disease, the DF and a severe disease that may be fatal, the DHF/DSS (Nivedita *et al.*, 2012).

Dengue is an important emerging problem of the tropical and sub-tropical regions today. The epidemics of dengue fever have been reported in the post-monsoon season, at every 2 - 3 year intervals. Majority of the patients in our study were diagnosed in the months of August and September which was in accordance with various other studies. These findings indicate that preventive measures against dengue virus infection should come into full action during water stagnation periods after the initial bouts of rainfall and at the end of monsoon. These findings indicate that preventive measures against dengue virus infection should come into full swing during water stagnation periods after the initial bouts of rainfall and at the end of monsoon. In this study, majority of the study subjects were males.

Various other Indian studies have also shown a male preponderance (Seema *et al.*, 2012; Karoli *et al.*, 2012; Jain *et al.*, 2002). In our study, male to female ratio was 1.49:1, similar pattern of male preponderance was found in previous studies conducted by Seema Avasthi *et al.*, (2012); Karolie *et al.*, Malavige *et al.*, Sri Lankaand Lepakshi *et al.* A recent study

from eastern India by Chatterjee *et al.*, however, found an equitable sex distribution. The majority of the patients in the present study were young individuals. Jain *et al.*, (2015) from Greater Noida, Patil *et al.*, from Maharashtra and Chaturvedi *et al.*, also reported a high incidence in young population.

Predominant presentations of fever, reduced appetite, myalgia polyarthralgia, gastrointestinal symptoms like abdominal pain and intractable vomiting observed is in concordance with many other studies (Nandini *et al.*, 2014; Mohamed *et al.*, 2014). Fever was the most common presentation (100%) which is in unison with most of the studies from India (Mohamed *et al.*, 2014; Mohan *et al.*, 2013) and South East Asia (Srikiathacorn *et al.*, 2010). Headache was found in 80% of the patients which is similar to the most of the previous studies. However study conducted by Munde *et al.*, showed lower incidence of 25%. Myalgia was noted in 86.7% of the patients which is comparable with previous studies conducted (Horvath *et al.*, 1999), however study conducted by Mohamed Murtuza Kauser *et al.*, showed lower incidence (32.87%). Abdominal pain was found in 63% of the patients which correlates with the previous studies, however Studies conducted by Ragini Singh *et al.*, and Munde *et al.*, showed slightly lower incidence of 3.6% and 15% respectively. In our study, 40% of the patients presented with nausea/vomiting comparable to 25% in study conducted by Munde *et al.*, however Rajesh Deshwal *et al.*, and Ragini Singh *et al.*, reported only 5.4% and 11.4% respectively.

Sore-throat was noted in 6.7% of the patients in our study comparable to the studies of Rachel Daniel *et al.*, 5.2%; however study done by Lepakshi *et al.*, has noticed in 50% and Ragini Singh *et al.*,

(18.6%) of the patient. Retro-orbital pain was noticed in 24.4% of the patients in present study comparable to Rajesh Deshwal *et al.*, (18.3%) and Lepakshi *et al.*, (14%); however study done by Nandini Chatterjee *et al.*, had 90%. Pruritus was noticed in 37.8% similar to the previous studies; however Mohamed Murtuza Kauser *et al.*, has noticed in 2.73% only.

Abdominal pain and vomiting were due to the liver injury caused by the dengue virus. Other infections that cause fever and gastrointestinal symptoms such as typhoid, leptospirosis, and enteroviral infections are common in India and may often lead to a delay in the diagnosis of dengue.

In a study of 62 patients in Japan, by Itoda *et al.*, rash was more frequent in 82% cases. In a north Indian study by Karoli *et al.*, rash was present in 26% cases, while 16% had cutaneous hypersensitivity. Rahim *et al.*, also found rash in high frequency of 78.5% in a Bangladesh based study. Thrombocytopenia is one of the important causes of developing petechial rash, but 12 patients out of 45 patients (26.7%) with platelet count more than 50,000/cumm of blood, developed rash in our study. So, other mechanism like immunologic cause may be an explanation for developing these rashes. Dengue virus, when it interacts with the host cells, causes a release of cytokines and stimulation of immunologic mechanism by which vascular endothelial changes, infiltration of mononuclear cells, and perivascular oedema occurs.

Ascites and pleural effusion from capillary leak syndrome are one of those features, more and more reported in recent years of outbreaks, by the help of technological advances like ultrasonography. We have detected 3rd space collection in the form of ascites and pleural effusion in 4.4% and 6.7% of cases.

Table.1 Age and sex characteristics of patients with dengue fever

Age group (in years)	Male	Female	Total (Percentage), n=45
18-40	15 (53.6)	7 (41.2)	22 (48.9)
41-60	9 (32.1)	8 (47.1)	17 (37.8)
Above 60	4 (14.3)	2 (11.8)	06 (13.3)
Total	28 (62.2)	17 (37.8)	45

Table.2 Clinical features in patients with dengue fever

Clinical Features	No of Patients (%)
Fever	45 (100%)
Reduced appetite	41 (91.1%)
Headache	36 (80%)
Myalgia	39 (86.7%)
Abdominal Pain	29 (64.4%)
Nausea/Vomiting	18 (40%)
Diarrhea	17 (37.8%)
Pruritus	17 (37.8%)
Arthralgia	15 (33.3%)
Retro-Orbital Pain	11 (24.4%)
Cough	8 (17.8%)
Breathlessness	5 (11.1%)
Insomnia/Lethargy	5 (11.1%)
Sore Throat	3 (6.7%)
Bleeding Manifestations:	21 (46.7%)
Gum bleeding	5 (11.1%)
Epistaxis	1 (2.2%)
Haemoptysis	0 (0)
Hematemesis	1 (6.89%)
Malena	3 (6.7%)
Haematuria	2(4.4%)
Venae puncture bleed	5 (11.1%)
Per Vaginal bleed	0 (0)
Petechiae	17 (37.8%)
Ecchymosis	3 (6.7%)
Skin Rash	19 (42.2%)
Jaundice	5 (11.1%)
Splenomegaly	9 (20%)
Ascites	2 (4.4%)
Pleural effusion	3 (6.7%)
Neurological features	5 (11.1%)
Altered sensorium	3 (6.7%)
Low blood pressure	15 (33.3%)
Low urine output	9 (20%)
Tachycardia	29 (64.4%)
Bradycardia	11 (24.4%)
Epigastric tenderness	6 (13.3%)
Hyperacidity	13 (28.9%)
Positive tourniquet test	11 (24.4%)

Table.3 Complications observed in patients with dengue fever (n=45)

Severe abdominal bloating	16 (35.5%)
Hypotension	15 (33.3%)
Metabolic acidosis	11 (24.4%)
Severe hepatitis	3 (6.67%)
Major bleeding	5 (11.1%)
Acute kidney injury	5 (11.1%)
Respiratory failure	7 (15.5%)
Shortness of breath due to pleural effusion	3 (6.7%)
Pneumonia	5 (11.1%)
Myocarditis with LV failure	0 (0)
Multi organ failure	2 (4.4%)
Encephalopathy	2 (4.4%)
CNS bleeding	1 (2.2%)
Total ICU admissions	6 (13.3%)

Table.4 Ultrasonography findings in patients with dengue fever (n=45)

Ultrasonography findings	N (%)
Hepatomegaly	5 (11.1%)
Splenomegaly	9 (20%)
Hepato-splenomegaly	4 (8.8%)
Pleural effusion	3 (6.7%)
Ascites	2 (4.4%)
Gallbladder edema	7 (15.5%)

Table.5 Biochemical and hematological parameters of dengue fever patients (n=45)

Biochemical and hematological parameters	Mean \pm SD, N (%)
Hemoglobin(gm/dl)	12.9 \pm 2.78
Total count(/cmm)	4987 \pm 1727
Leucopenia	29 (64.4%)
Platelet count(/cmm)	113,645 \pm 67,944
Thrombocytopenia	41 (91.1%)
PCV	40.8 \pm 7.6
Hematocrit change > 20%	11 (24.4%)
Urea(mg/dl)	42.78 \pm 19.23
Creatinine(mg/dl)	1.16 \pm 0.47
Bilirubin (total)(mg/dl)	0.96 \pm 0.52
Bilirubin (indirect)(mg/dl)	0.50 \pm 0.22
Elevated aspartate aminotransferase (AST) (IU/ml)	147.8 \pm 132.8
Alanine aminotransferase (ALT) (IU/ml)	129.7 \pm 111.8
ALP(IU/ml)	147.5 \pm 95.8
Total Protein(gm/dl)	7.12 \pm 0.89
Albumin(gm/dl)	3.98 \pm 0.69
Globulin(gm/dl)	3.14 \pm 0.57

In a Bangladesh based study by Mia *et al.*, 41% patients developed ascites and 42% had pleural effusion.

Hypotension recorded in 15 (33.3%) of the patients is consistent with studies in Kolkata and Bangalore. CNS features said to be very uncommon (Murthy, 2010). Bleeding manifestations 21 (46.7%) varied from minor in 7 (15.5%) to major bleeding tendency in 3 (6.6%) of patients while Kumar *et al.*, reported in 26.6% of the patients and Murtuza *et al.*, reported in 9.6% of the patients. The complication varied from severe abdominal bloating to all the major systemic manifestations is as similar to many other studies across different regions.

About 12% of the patients required the ICU referral. Dengue patients who were either between 50 and 59 years old or with pre-existing diabetes had higher risk of ICU requirement, compared with dengue patients who are less than 30 years old or without diabetes or any other co-morbidity, respectively. The 2.0% of the case fatality rate observed was in patients with associated co-morbidities,7 which demonstrates that prompt diagnosis and early institution of therapy creates significant changes in prognosis. Laboratory investigations reported, apart from thrombocytopenia gross leucopenia and transaminitis were significant derangements consistent with several studies across India (Prafulla *et al.*, 2012).

Raised haematocrit (>45%) was found in 24.4% comparable to previous studies. Leukopenia (<4000/cmm) was noticed in 29 (64.4%) higher than previous studies; however studies done by Munde *et al.*, and Karolis *et al.*, noticed in 50% and 89% respectively. NS1 antigen reactive patients found less in number when compared with

seropositive IgM antibody patients. Strength of this study is that it describes the acute clinical manifestations and role of laboratory investigations in DF patients which helps in early diagnosis, institution of therapy, and prevention of mortality. Limitations of this study are single centre based study, small sample size and extrapolation of the results into general population is poor.

In conclusion, a high index of suspicion is required to detect and timely manage the atypical manifestations of dengue fever as these are no more a rare occurrence. Proper confirmation of diagnosis, early institution of therapy, public awareness, and vector control are important factors to be taken into consideration in the prevention and management of dengue. The problem of dengue is enormous in our country. It is compounded by the huge population, poor medical and diagnostic facilities, inadequate mosquito control and all the ground conditions that favour multiplication of the vector. In view of the increase in the number of cases and the changing clinical spectrum of the disease, future studies should be designed to find predictive value of clinical and biochemical abnormalities that will help physicians in triaging patients in an outbreak situation. Where some known features are still manifesting, few atypical features are noted from several parts of the world. So a continuous sero-epidemiological surveillance and timely interventions are needed to indentify the cases, so that its complications, outbreak and mortality can be minimized.

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