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Original Research Article

Clinical spectrum of dengue at a tertiary care hospital in Eastern India

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ABSTRACT

Background: Dengue is a vector borne disease by four different serotypes of dengue virus transmitted by bite of female Aedes mosquito. It is an acute febrile illness characterised by myalgia, joint pain, gastrointestinal manifestations. Complications like dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) , Extended Dengue Syndrome(EDS) may be fatal for patients. Authors analyse different clinical spectrum of of manifestations, complications and correlation bleeding to platelet level.
Methods: This study conducted from July 2017 to December 2018 comprising of 100 dengue patients of age more than 15 years in IMS & SUM Hospital.
Result: Out of 100 dengue patients' males 73% and females 27%. From the patients 57% were NS1 Antigen positive, 29% IgM positive, 9% NS1 and IgM positive, 4% IgM and IgG positive and 2 % with all NS1, IgM, IgG positive. In our series in clinical manifestations, all cases (100%) presented with fever, myalgia (78%), headache (53%), rashes (14%), nausea, pain abdomen (21%) loose motion (17%), and Retro-orbital pain (6%). Bleeding manifestations in any form was seen in 39% cases like Purpura or Petechie (23%), malena (18%), hematemesis (2%), epixtasis (6%), Gum bleeding (2%), Hematuria (1%), and Ophthalmic bleeding like sub conjunctival hemorrhage, intra-vitreal hemorrhage in 8% cases. Complications detected e.g. hepatopathy in 53%, nephropathy. 4%, ascites 8%, pneumonia 7%, DSS (4%), Multi Organ Dysfunction (MODS) (4%), DHF (8%) and EDS in 2% cases. It was observed that 95.8% of patients with platelet counts between 20,000-50,000/cu.mm and 61% of patients less than 25000 had bleeding manifestations.
Conclusion: Wide clinical spectrum of manifestations and complications makes it common differential diagnosis of acute febrile illnesses and bleeding manifestation does not always corelate with lower platelet count.

Keywords: Dengue hemorrhagic fever, Dengue shock syndrome, NS1 Antigen, Petechie, Platelet Count

INTRODUCTION

Dengue is a vector borne disease. Its virus is a member of the genus *Flavivirus* of the family Flaviviridae, that includes four different serotypes (DEN-1, DEN-2, DEN-3, and DEN-4).[1,2] Dengue is a major global public health problem in the tropical county and subtropics nations. Worldwide there is an increase prevalence of dengue infection between 1960 and 2010, due to increased population growth rate, global warming, unplanned urbanization, inefficient mosquito control, frequent air travel, and lack of health care facilities.[3-5] Nearly 3.97 billion people from 128 countries are at risk of infection.[6-7] WHO region of western Pacific and Southern

Asia (SEA) represent approximately 75% of global burden of dengue.[8] The first reported case of dengue like illness in India was in Madras in 1780, the first virologically proved epidemic of Dengue fever(DF) in India occurred in Calcutta and Eastern Coast of India in 1963-1964.[9] Since mid-1990s,epidemics of dengue in India have become frequent, especially in urban zones, and have quickly spread to regions, such as Arunachal Pradesh, Mizoram and Odisha.[10] In early 2000s,dengue was endemic in a few southern and northern states, recently it had spread to a number of new states and union territories.[10] It has also spread from urban to rural regions.[11]

Dengue is transmitted by bite of female. Aedes mosquito, Adesaegypti and Aedes albopictus main vectors in India.[12] Trasmission usually occurs in rainy season. Etiology for dengue viral infections are viral replication, primarily in macrophages and immunological and chemical-mediated mechanism induced by host–viral interaction.[13] Humoral, cellular, and innate immunity of host are implicated in the progression of the illness. Dengue is clinically characterized by acute onset of biphasic, high-grade fever lasting for 3 days to 1 week, associated with symptoms of malaise, vomiting, cough, headache (retro-orbital),muscle ache, joint pain, vomiting and stomach-ache.[14,15] Of patients with DF, 50-82% report with a peculiar cutaneous rash.[16,17] Severe clinical presentation during the infection course does not correlate with a high viral load.[13] Dengue infection is diagnosed clinically but confirmed by laboratory test. Virus segregation in cell cultures, nucleic acid demonstration by polymerase chain reaction (PCR), and serological detection of viral antigens (such as NS1) or particular antibodies are the preferred microbiological assays.[5] During early phase of infections (febrile period), dengue PCR is performed. After febrile illness dengue IgG and Ig M is preferred tests.

Dengue is a self-limiting infection mostly. Oral facial features are less frequently seen in dengue virus infection but are slightly more commonly associated with dengue haemorragic fever (DHF).

METHODS

This study was a prospective, observational study conducted in department of Medicine comprising of 100 patients suffering from dengue selected from Indoor of Department of Medicine of IMS and SUM Hospital, a tertiary care hospital, Bhubaneswar, during the period from July 2017-December 2018.

Inclusion Criteria

Patients of more than 15 years of age who had fever and who were found to be positive for NS1 antigen (Micro ELISA, J. Mitra) and dengue IgM (antibody) with or without IgG positive for Dengue were included in study.

Exclusion criteria

Any patient with concomitant existing bleeding disorders, hemoglobinopathies, and infections like malaria, scrub typhus, enteric fever, tuberculosis and other viral illness were excluded from our study.

Total of 100 patients(age>15years) were enrolled during the outbreak of disease. A detail clinical history, systemic examination routine haematological examination i.e. haemoglobin (Hb), total leukocyte count(TLC),platelet count(PC), Liver Function Test(LFT), Renal Function Test(Serum Urea, Creatinine),Fasting Blood Sugar(FBS), PT, INR, Stool for Ocult Blood, Urine Routine and Microscopy, malarial antigen Test(MP ICT), slide test for malaria parasite, IgM antibodies for typhoid and Widal test for typhoid ,Chest X ray PA View , Ultrasonography of Abdomen and Pelvis was performed. Patients who were suffering from diabetes, hypertension and other correlated disease were excluded from our study. All subjects were classified according to WHO guidelines. Thrombocypopenia was taken as platelet count less than 1 lakh/mm^3 and leuopenia as white blood cells (WBC) <5000 cells/mm^3.

Data were entered and analysed in SPSS version 12 statistical software.

RESULTS

A total of 100 hospitalised patients (Age >15 years) diagnosed as dengue were enrolled in our study out of which 73 patients were males (73%) and 27 patients were females (27%) (Table 1). Mean age of presentation was 38.53 years (18-65years). Maximum number of cases was found in age group 30-40 years. Mean time of presentation was 7 days (4-14 days). Median duration of stay in hospital was 7 days. Patient mainly belong to low socioeconomic status. Out of 100 cases with distribution in antigenic presentation, 57% patients were NS1 positive, IgM positive in 29% of cases, NS1 & IgM positive in 9% patients ,IgM and IgG positive in 4 % of case which indicated secondary cases and 2 cases with all NS1,IgM,IgG for Dengue positive (Table 2).

Age distribution of 100 patients is depicted in Table 1. Out of which.73 males and 27were females.

Table 1: Age at presentation.

Age at presentation	Number of patients	Percentage(%)
15-20	6	6
20-30	21	21
30-40	33	33
40-50	25	25
50-60	9	9
>60	6	6

Table 2: Antigenic/ Antibody presentations of dengue cases.

Antigen/ Antibody detected	No of patients (Out of 100)
NS1 Antigen	56
IgM Antibody	29
NS1 Antigen +IgM Antibody	9
IgM Antibody+IgG Antibody	4
NS1 Antigen +IgM Antibody+IgG antibody	2

Table 3: Clinical manifestations.

Symptoms	Number of cases	Percentage (%)
Fever	100	100
Myalgia and backache	78	78
Headache	53	53
Loose Motion	17	17
Abdominal Pain	21	21
Retro orbital pain	6	6
Rashes	14	14
Bleeding manifestation	39	39

In our series in clinical manifestations, all cases (100%) presented with fever, myalgia(78%), headache(53%), rashes in 14% cases others clinical features are nausea, pain abdomen(21%) loose motion(17%), puritus etc. None of our patient have visual complains. Retro-orbital pain was noted in 6 patients (6%). Bleeding manifestations in any form was seen in 39% cases (Table 3).

In spectrum of bleeding manifestations bleeding in skin manifestatins like Purpura or Petechie predominates(23%). Gasto-intestinal bleeding like malena(18%) and hematemesis in 2% cases and other bleeding features like epixtasis in 6% cases ,Gum bleeding in 2%, Hematuria in1%, and Ophthalmic bleeding like sub conjuctival hemorrhage, intra-vitreal hemorrhage in 8% cases (Table4). Complications and organ involvements are found, and commonest organ involvement is Liver(hepatopathy) in 53% cases. Other complications like nephropathy in 4% cases, ascites 8%, pneumonia in 7%. Dengue shock syndrome (DSS)in 4%,MultiOrgan Dysfunction (MODS) in 4%,Dengue Hemorrhagic fever in18% and Extended Dengue Syndrome in 2% cases were observed (Table 5). Out of 100 cases 39 cases were having any form of bleeding manifestation. Correlation to bleeding manifestation was done according to platelet count and observed that lower the platelet count more no of patients were having bleeding manifestation. It was observed that 61% Patients with less than 25000 platelet, 40% patients with platelet count 25000-50000, 29% of patient with platelet count 50000-100000,18% of patients with platelet count 100000 to 150000 and no patients with platelet count more than 150000 were found to be having any bleeding manifestations (Table 6).

Table 4: Spectrum of bleeding manifestation.

Spectrum of Bleed Manifestation	Number of cases	Percentage
Purpura /Petechie	23	23
Malena	18	18
Hematemesis	2	2
Epistaxis	6	6
Gum Bleeding	2	2
Hematuria	1	1
Ophthalmic bleed	8	8

Table 5: Complications.

Complications	Number of cases	Percentage(%)
Hepatopathy	53	53
Nephropathy	4	4
Ascites	8	8
Pneumonia	7	7
DSS	4	4
MODS	4	4
DHF	18	18
EDS	2	2

Table 6: Correlation of bleeding to platelet count.

TPC	Number of cases	Cases with bleeding manifestation	Percentage (%)
<25000	26	16	61
>25000-50000	32	13	40
>50000-100000	24	7	29
>100000-150000	16	3	18
>150000	2	0	0
Total	100	39	39

DISCUSSION

The incidence, and geographical distribution of dengue have increased due to increase in global temperature and increased population, unplanned urbanization, inefficient mosquito control, and lack of health care facilities.[3-5]

Dengue affects humans of all age groups. In our series the mean age of presentation is 34 years which is similar to other studies with a male preponderance which is a common observation.[18-20] In our study 56% were NS1 positive and 29% had IgM positive for Dengue. NS1 and IgM positive in 9% patients , IgM and IgG positive in 4 % of case which indicated secondary cases and 2 cases with all NS1,IgM,IgG for Dengue positive. Mehta et al,

found NS1 antigen was positive in 88% of cases, dengue IgM antibodies in 21% of cases, and IgG in 20% of cases also by Chakravarti and Kumaria's study in Delhi where 57.36% were confirmed as serologically positive, out of which 22.28% cases were positive for dengue-specific IgM antibodies indicating primary infection, and IgG antibodies alone were also detected in 35.05% cases.[21,22]

Dengue has diverse of clinical manifestations starting from simple fever to life threatening complications and severe encephalopathy too. In our series all patient presented with fever (100%), followed by myalgia(78%). Headache is also one of common presentation 53% but retro-orbital pain which is a classical feature of dengue was seen only in 6% of cases which is much less than other studies but similar to Kapoor at al,[19,22,23] Our clinical findings were similar to that of other previous studies.[8-12] These were GI manifestations like loose stools (17%) and abdominal pain (21%). Rash, mostly of maculo-papular variety, rarely pruritic, seen in extremities and trunk was found in 14 cases (14%). Gupta et al, reported a similar results with 100% presenting with fever, but a higher incidence of rash (36%) and retro-orbital pain(40%).[13] Ashwin kumar on the other hand reported 98% presentation with fever, a similar incidence of rash (19.1%) but a lower incidence of headache.(31%).[24]

There were 39 cases (39%) who presented with any form of bleeding manifestations. Purpura and petechiae, a common manifestations of dengue was found 23% of cases. However, Melena was found in 18% cases. Bleeding from other sites like Epistasis 6%, Gum bleeding 2%, Ophthalmic Bleeding like subconjuctival hemorrhage was observed only in a few cases. Sreenivas et al, found that 26% of cases had melaena, 20% had petechiae, 8% had haematemesis, 4% had epistaxis and 2% had gum bleeding.[25] Hematuria was the least common finding among our patients , accounting for about 1%, it was reported the same in the earlier studies of Sreenivasan et al, Narayanan et al, that bleeding by the urogenital tract is less common among the bleeding manifestations.[14,25]

Various types of complications were seen during course of disease. These were hepatopathy, acute renal failure (nephropathy), ascites, Pneumonia, dengue hemorrhagic fever(DHF), Dengue complicated with shock (DSS), multi-organ dysfunction syndrome and extended dengue syndrome. Hepatopathy was the most common seen in cases 53% patients. This was mostly witnessed as jaundice and/or transaminitis. It has been reported by Ashwin Kumar that pleural effusion was their most common complication.[24] While nephropathy, DSS (Dengue shock syndrome), MODS(Multi organ dysfunction syndrome) shared an incidence of 4% of the complications each in our patients, the least common complication in our study was EDS(extended dengue syndrome).

With regard to the platelet counts, TPC was done at least twice every day in patients with ongoing bleeding. Mostly the haematocrit was initially low, but in patients of DHF or DSS had high hematocrit values; although the lower values of hematocrit can be attributed to Iron deficiency anemia and malaria, which is vastly prevalent in this part of the India. While 39% of all patients had bleeding, 61% of patients with platelet count less than 25000 had bleeding manifestations. and no bleeding was seen in patients with platelet counts of more than 1,50,000. It was observed that 95.8% of patients with platelet counts between 20,000-50,000/cu.mm developed haemorrhage according to Sreenivasa et al, While Joshi et al, Sunil Gomber et al, and Dhooria et al, reported poor correlation between thrombocytopenia and bleeding manifestations.[25-28] Authors found that the percentage of patients that develop bleeding decrease with rising platelet levels.

The pathophysiology of dengue infections is complex and not completely understood. Various manifestations of dengue is due to direct virus invasion or complex immune mechanism comprise of complement system pathway and NK cells. Complements activation due to immune activation and cytokine production are involved in mechanism of plasma leakage. Various cytokines that may induces plasma leakage are interleukin (IL)-2, interferon g, tumor necrosis factor (TNF)α, IL-6,IL-8 and IL10[29,30]

CONCLUSION

With the rise in incidence in dengue fever, there is necessity to understand dengue fever, now more than ever, and this study brings out the intricacies of symptomatology, platelet counts relation with bleeding, complications and antigen antibody variation with regard to dengue. Dengue needs to be suspected in any patient presenting with a short duration of fever and myalgia. NS1 antigen is most commonly detected and while the pathophysiology of dengue is yet to be clearly understood, bleeding manifestations relate to platelet count, which should aid in diagnosis and treatment.

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