

ORIGINAL RESEARCH

CLINICAL PROFILES OF DENGUE FEVER IN A TEACHING HOSPITAL OF EASTERN INDIA

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ABSTRACT

Introduction: Dengue fever is one of the most common arbo virus mediated outbreaks, being reported from different parts of the world. Dengue fever (DF), Dengue hemorrhagic fever (DHF) and Dengue shock syndrome (DSS) are different modes of presentation of the disease. Now as the outbreaks are hitting different geographic locations, different clinical manifestations are more and more being reported recently. Our aim of this study is to document varied clinical manifestations of dengue patients in a tertiary care centre of eastern India.

Materials and Methods: Total 74 MAC ELISA positive dengue patients are included in this observational study and analyzed.

Results: Most common clinical feature was fever (100%) followed by headache (62.16%). Atypical features like transaminitis and different neurological manifestations were present in 83.83% and 11.11% cases respectively.

Conclusion: One should aware of different atypical presentations of dengue fever to diagnose and intervene timely.

Keywords- Dengue fever; Lateral rectus palsy; Transaminitis

INTRODUCTION

Dengue is the most rapidly spreading mosquito-borne viral disease in the world. In the last 50 years, incidence has increased 30-fold with increasing geographic expansion to new countries beyond national borders.¹ Currently, Dengue fever (DF) and Dengue hemorrhagic fever (DHF) are endemic to Southeast Asia, the Western Pacific and the Caribbean. So DF has become a major international public concern particularly in tropical and subtropical regions, affecting urban and suburban areas. Though several measures taken to prevent and control it, recurrent outbreaks have been reported in India, since the first recorded outbreak of DF in India in 1812.² During recent outbreaks in India, the clinical manifestations which were shown by the patients were slightly different from those in previous years.³ So in our study, we have tried to find out varied clinical manifestations of the Dengue patients who had been admitted in a tertiary teaching hospital in West Bengal.

MATERIALS AND METHODS

This was an observational study. The patients were selected from outpatient department and indoor of Medical College and Hospital, Kolkata, West Bengal, a tertiary care centre in the state. The study was approved by the ethics committee of the hospital and informed

consent was obtained from all the subjects. We included 74 patients suffering from dengue fever in the study period from March 2011 to December 2012. All the patients, who presented with fever and found positive Dengue IgM antibodies capture enzyme-linked immunosorbent assay (MAC-ELISA), were admitted in the indoor and included in the present study. But patients with other co infections like malaria, typhoid etc or with any other co morbid diseases are excluded from the study. A detailed history was taken and a careful clinical examination was performed. The laboratory investigations like haemoglobin (Hb), the total and the differential leucocyte counts (TLC and DLC), platelet count, haematocrit (Hct), liver function tests (LFT), Urea, Creatinine, Chest X-Ray and Ultrasonography of abdomen were done in all the patients. Other relevant investigations were performed according to the clinical conditions of the patients.

RESULTS

In this study, total 74 dengue MAC ELISA positive patients are included and analyzed. The different clinical features of these patients are shown in table 1. It was noted that fever was present in all patients. Next common symptom was headache followed by rash. Bleeding from different sites of the body was evident in 10 patients (13.51%).

Table 1: Clinical features of Dengue fever patients (n=74)

Clinical features	Patients (%)
Fever	74 (100)
Headache	40 (62.16)
Rash	28 (37.84)
Bleeding	10 (13.51)
Ascites	6 (8.1)
Pleural effusion	14 (18.91)
Neurological features	8 (11.11)

Among these 10 patients with bleeding manifestations, 2 patients had both gum bleeding and gastrointestinal bleeding in the form of melena, 4 patients had gum bleeding only and 4 patients had only melena. Among the 28 patients with rash, 12 patients had an erythematous hue of the skin and the rest had purpuric spots. 4 patients also had subconjunctival hemorrhage.

Out of 74 patients, 28 (37.84%) had platelet count below 50,000/cumm of blood and the rest 46 patients (62.16%) had more than 50,000/cumm of blood. And among these 28 patients with below 50,000 platelet count, 8 patients had both rash and bleeding, 6 had rash only and 2 had bleeding episode only without any rash in spite of having a low platelet count while other 12 had neither rash nor bleeding. Considering the rest 46 patients, only 14 patients had rash but none had bleeding episodes.

Table 2: Biochemical parameters of dengue Fever patients (n=74)

Parameters	Mean \pm SD
Hemoglobin(gm/dl)	12.5 \pm 2.49
Total count(/cmm)	4919 \pm 1612
Platelet count(/cmm)	99127 \pm 65836
PCV	40.9 \pm 5.4
Urea(mg/dl)	40.89 \pm 16.42
Creatinine(mg/dl)	1.15 \pm 0.43
Bil(Total)(mg/dl)	0.97 \pm 0.34
Bil(Direct)(mg/dl)	0.46 \pm 0.24
Bil(Indirect)(mg/dl)	0.50 \pm 0.19
AST(IU/ml)	152.8 \pm 121.2
ALT(IU/ml)	111.7 \pm 106.8
ALP(IU/ml)	206.1 \pm 101.7
Total Protein(gm/dl)	6.45 \pm 0.71
Albumin(gm/dl)	3.74 \pm 0.52
Globulin(gm/dl)	2.71 \pm 0.39

Eight patients (11.11%) had neurological manifestations. Out of these 2 had encephalopathy, 2 had Guillain-Barre' syndrome (GBS), 1 had unilateral UMN type facial nerve palsy and 3 had unilateral lateral rectus palsy. Both patients with encephalopathy presented with disorientation, confusion and rash with fever. MRI was done in both the patients and was normal. CSF Study in two patients revealed -cell-15/10, glucose-57/63mg/dl, protein-67/56gm/dl/, ADA - 5/4.6 respectively. Tests for Japanese encephalitis, Herpes simplex were negative. Test for dengue in CSF

by RT-PCR was not available in local laboratories. Serology was negative for HIV antibodies, ANA and ANCA. C3 and C4 complement levels were within normal limits.

NCV study was done in both the patients with GBS and showed features of demyelination. CSF study revealed albuminocytological dissociation in both. One patient develops weakness 6 days after admitted with fever with rash. Another patient admitted with weakness of both the lower limbs with a history of fever, rash 10 days back and positive MAC ELISA. Both the patients improved spontaneously with conservative management without requiring any plasmapheresis or immunoglobulin. One patient presented with fever with erythematous hue all over body. Two days after admission developed right sided UMN type facial palsy without any other neurological deficit. MRI of brain did not reveal any abnormality. Weakness improved completely within next 10 days.

Among the three lateral rectus palsy patients two were females and another was male. One female patient (32 years old) had papilloedema while others two had no other neurological features. MRI of the two female patients were absolutely normal. The male patient could not afford MRI, but C.T. Scan of brain with contrast did not reveal any abnormality. Others relevant investigations were performed to exclude any other etiologies of lateral rectus palsy.

Out of 74 patients, 58 patients (78.38%) had PCV less than 45 and 16 patients (21.62%) had more than 45. Among those 16 patients 10 (62.5%) had features of serositis; 4 patients had both ascites and pleural effusion and 6 patients only pleural effusion. Among those 58 patients, 6(10.34%) had serositis; 2 had ascites and 4 had pleural effusion.

Various biochemical parameters were depicted in table 2. One interesting finding in this table was transaminitis in these patients without elevation of bilirubin.

DISCUSSION

We have found that the varied spectrum of DF/DHF has ranged from some known clinical presentations of fever, rash, headache to some atypical presentations like lateral rectus palsy. Some features are increasing in the recent outbreaks like liver dysfunctions, 3rd space fluid loss in the form of ascites, pleural effusion and neurological manifestations, as evidenced by recent studies.

In DF, cutaneous manifestations can vary from maculopapular rash, petechiae, flushing to even desquamation. In our study we found rash in 37.84% cases, 16.26% had flushing and the rest having maculopapular. In a study of 300 patients by Nadia A et al⁴, flushing was present in 28.7% and 44.9% had maculopapular variety. In a study of 62 patients in Japan, by Itoda et al⁵, rash was more frequent in 82% cases. In a north Indian study by Karoli R et al⁶, rash

was present in 26% cases while 16% had cutaneous hypersensitivity. Rahim MA et al⁷, 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 14 patients out of 46 patients with platelet count more than 50000/cmm of blood, developed rash in our study. So, other mechanism like immunologic cause may be an explanation for developing these rashes. Dengue virus when interacts with host cells, there occurs release of cytokines and stimulation of immunologic mechanism by which vascular endothelial changes, infiltration of mono-nuclear cells and perivascular edema occurs⁴.

Bleeding diathesis is a known feature of DF because of low platelet count and leakage from blood vessels. Bone marrow suppression, Immune mediated clearance, spontaneous aggregation of platelets to virus infected endothelium-all may be responsible for such thrombocytopenia. In our study, we found 13.51% patients had bleeding episodes in the form of gum bleeding and melena while 37.84% patients had platelet count below 50,000/cmm. In a north Indian study by Seema A et al³, only 8% patients had bleeding episodes while 26% patients had platelet count below 20,000/cmm and 84% had <1 lakh/cmm. On the other hand, in a Delhi based study by Tripathy BK et al⁸, hematemesis, melena and epistaxis were found in 28.28%, 26.78% and 14.28% respectively but only 12.85% cases had platelet count < 70,000/cmm. But in a Hyderabad based study by Khan AH et al⁹, only 5% patients had bleeding while 40% had thrombocytopenia. A Study conducted on 84 cases in Sudan by Ageep AK et al¹⁰, bleeding was there in 93% cases and thrombocytopenia in 88% cases. In north Indian children, a study was done by Mittal H et al¹¹, which revealed thrombocytopenia in 92.6% while bleeding was there in 48.8% cases.

Low leukocyte count in DF, may be due to virus induced inhibition/destruction of myeloid progenitor cells. We found that only 29.73% cases had leukocyte count below 4000/cmm. But in study of Itoda et al⁵, leucopenia was detected in 71% cases, while Ageep AK et al⁸, reported leucopenia in 90%. Mittal H et al¹¹, found leucopenia in 19.2% cases and in Bangladesh based study by Rahim MA⁷ detected it in only 4.1% cases.

Headache and retro-orbital pain mostly from systemic inflammatory mediators, are well known features in dengue fever. In our study we found 62.16% patients presented with headache that is similar (61.6%) to the study by Singh NP et al². But in some studies like by Itoda I et al⁵, in Japan, headache was present in 90% cases. On the other hand the north Indian study by Seema A et al³ reported headache in only 9% of cases.

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 8.1% and 18.9% of cases and also in 21.62% of cases there was hemoconcentration from increase vascular permeability. In the study by Singh NP et al², ascites was in 1.08% and pleural effusion was also in 1.08% cases while haemoconcentration (Hct>20% of expected for age and sex) was found in much higher frequency of 52% of the cases. In a Bangladesh based study by Mia MW et al¹², 41% patients developed ascites and 42% had pleural effusion but hemoconcentration was there only in 27% of cases. But in a USG based study in Thail and, by Kalayanarooj S et al¹³, hemoconcentration and pleural effusion were in 18% and 16% of cases respectively, while Seema A et al³, in north India found these in only 0.3% of cases. On the other hand, in the study by Khan AH et al⁹, they did not found haemoconcentration or rise in hematocrit in any case, rather a fall in hematocrit was noticed during hospital stay once patients were afebrile and rehydrated adequately.

Dengue fever can cause hepatic injury and transaminase elevation similar to viral hepatitis. We found that in 70.27% patients, ALT was raised while AST raised in 83.78%. Among them 86.49% patients had more AST than ALT and only 13.51% patients had the reverse. In the study by Khan AH et al⁹, serum ALT was >40 U/L in 40% cases. In study by Kularatne SA et al¹⁴, 88% patients showed elevated ALT and AST, with 122 of them having a two-fold increase. Sedhain A et al¹⁵ have reported a case of fulminant hepatic failure from dengue fever in a young girl of Nepal. Kuo CH et al¹⁶, from Taiwan found raised AST and ALT in 93.3% and 82.2% cases. A nice study in Brazil by Silva EM et al¹⁷, C1q was found an interacting partner between NS1 protein and liver proteins in the causation of hepatic dysfunction in dengue fever.

We have noted some neurological manifestations which were not much enlightened in previous outbreaks. Neurological involvement in dengue may occur because of neurotropism of the virus, immunologic mechanism, cerebral anoxia, intracranial haemorrhage, hyponatremia, cerebral oedema, fulminant hepatic failure with portosystemic encephalopathy, renal failure or release of toxic products. Dengue fever can give rise to various neurological manifestations like GB syndrome, encephalopathy, ADEM, Lumbosacral plexopathy, polyradiculopathy, etc as evidenced by various studies. Like, in the study by Kamath SR et al¹⁸, neurological manifestations were noticed in 20% of the patients and Mendez A et al¹⁹ reported 25% patients with neurological manifestations. We found them in 11.11% of our patients in the form of encephalopathy (2.7%), GB syndrome (2.7%) and more interestingly facial nerve palsy (1.35%) and lateral rectus palsy (4.05%). Among those 2 patients developed GB Syndrome, 1 developed it after 6 days of fever and the other, after 10 days. Among 3 patients who developed lateral rectus palsy, only 1 had features suggesting raised intracranial tension like headache, papilloedema but they were absent in other 2 patients. In the 1st case, right LR palsy was present and in the other two, 1 had right and

the other had left LR palsy. Alternate etiologies were excluded by serology, imaging and electrophysiology. All these 3 cases were managed conservatively and there was spontaneous resolution of the palsy after 4-6 weeks. In the previous studies, Sanjay S et al²⁰, reported optic neuropathy, Donnio A et al²¹ found oculomotor paralysis in their studies in dengue patients. The rare association of isolated VI or VII cranial nerve palsy has been reported in very few cases. Peter S et al²² reported isolated LMN type VII cranial nerve palsy in dengue fever and Shivanthan MC et al²³ from Sri Lanka has also reported isolated VI cranial nerve palsy.

CONCLUSION

In the recent few years, the world has seen varied clinical presentation of the Dengue fever in different epidemics, even in the same regions and even with the period of time. 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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