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ATYPICAL MANIFESTATIONS OF DENGUE FEVER DURING AN OUTBREAK IN A TERTIARY CARE HOSPITAL OF WESTERN UTTAR PRADESH (NORTH INDIA)

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ABSTRACT

Introduction: Dengue is a rapidly emerging global health problem .It has variable clinical presentation with many atypical presentations, thus posing a diagnostic challenge for the physician.
Objective : To study the clinical profile of dengue infection during an outbreak in July-November, 2012 in a tertiary care teaching hospital of western UP.
Material and methods :A prospective, observational, single centre study was carried out on patients of dengue fever who were admitted to the medicine ward of Santosh Medical College Hospital, affiliated to Santosh University, Ghaziabad (UP).
Results :120 patients were diagnosed as dengue fever based on the presence of NS1 antigen and /or dengue IgM in blood samples .The common signs and symptoms were fever (100%), headache (81.6%), myalgia (55%), retro-orbital pain (51.6%) and abdominal pain (45%) .Among the a typical presentations, hepatitis (43.3%) was the most common followed byacalculous cholecystitis (32%), bradycardia (23.3%), febrile diarrhoea (15%), meningoencephalitis (1.6%) , pancreatitis (1.6%).
Conclusion: Dengue infection in India has evolved rapidly, and regular outbreaks have been observed with a changing epidemiology, as the disease is rapidly spreading from urban to rural areas with increasing atypical manifestations.

Key words: Dengue, acalculous cholecystitis

INTRODUCTION

Dengue is the most rapidly spreading arboviral disease in the tropical countries. Incidence of dengue fever has increased 30 fold in the last 50 years.[1] It is caused by one of the four serotypes called DENV 1,2,3 & 4.[2] The principal vector mosquito for the disease is *Aedes aegypti*. A majority of regions in India such as Delhi, Haryana, Rajasthan, Gujarat, Karnataka, Tamil Nadu & West Bengal are endemic for Dengue.[3] Dengue fever begins typically after an incubation period of 4-7 days.[4] The patients experience sudden onset fever, frontal headache, retro-orbital pain & severe myalgia – "break bone fever".[5] Additional signs & symptoms include anorexia, nausea or vomiting and marked cutaneous hypersensitivity.[5] Near the time of defervescence, a maculopapular rash begins on the trunk and spreads to the extremities and the face. Epistaxis and scattered petechiae are often noted in

uncomplicated dengue,[5] and preexisting lesions like peptic ulcers may bleed during the acute illness. Laboratory findings include leukopenia, thrombocytopenia, and in many cases, elevations of liver enzymes.

An increasing number of cases are being reported with atypical presentations. Rare manifestations of the disease are being reported as the awareness about the disease is increasing.

Table 1.

DF/DHF	Grade	Signs & Symptoms	Laboratory
DF	With or without hemorrhagic manifestations	Fever with two of the following: (i) Headache. (ii) Retro-orbital pain. (iii) Myalgia. (iv) Arthralgia/bone pain. (v) Rash. (vi) Hemorrhagic manifestations. (vii) No evidence of plasma leakage.	Leucopenia (WBC ≤5000cells/mm 3). (i) Thrombocytopenia (platelet count <150 000cells/mm 3). (ii) Rising hematocrit (5%–10%). (iii) No evidence of plasma loss.
DHF	I	Fever and hemorrhagic manifestation (positive tourniquet test) and evidence of plasma leakage.	Thrombocytopenia <100 000cells/mm 3 ; HCT rise ≥20%.
DHF	II	As in Grade I plus spontaneous bleeding.	Thrombocytopenia <100 000cells/mm 3 ; HCT rise ≥20%.
DHF	III	As in Grade I or II plus circulatory failure (weak pulse, narrow pulse pressure (≤20 mmHg), hypotension, restlessness).	Thrombocytopenia <100 000cells/mm 3 ; HCT rise ≥20%.
DHF	IV	As in Grade III plus profound shock with undetectable BP and pulse.	Thrombocytopenia < 100 000cells/mm 3 ; HCT rise ≥20%

Materials and methods

This study was conducted during a dengue outbreak in 2012 in a tertiary care hospital in western U.P to study the clinical profile and atypical presentations of the disease . All probable dengue cases were investigated initially. Out of them, 120 NS1Ag positive/ IgM-dengue sero-positive cases aged 18 years and above, satisfying WHO criteria were included in the study group after ruling out other causes of fever. A detailed clinical history, physical examination and baseline investigations were undertaken and followed-up till the patient got discharged from hospital. All clinical and laboratory details were carefully reviewed and data of atypical presentations were recorded.

Ethical Considerations

Departmental approval for the study and informed consent from the patients had been obtained.

Table2 : Distribution of the patients according to presenting symptoms

Symptoms	N	%
Fever	120	100.00
Headache	98	81.6
Myalgia	66	55.0
Retro – orbital Pain	62	51.6
Abdominal pain	54	45.0
Skin rash	48	40.0
Nausea/ Vomiting	42	35.0
Hemorrhagic manifestation	28	23.3
Breathlessness	18	15.0
Diarrhoea	18	.150
Itching	16	13.3

Table3 : Laboratory Parameters

Laboratory Parameters	N	%
Thrombocytopenia(>50000/cumm(	58	52.72
Leucopenia(>4000/cumm(	32	29.09
SGPT(<55IU/L)	48	40.0
SGOT(<45IU/L)	52	43.33
S. Total Billirubin(<2mg/dl)	4	3.63
Raised Hematocrit(<45(%	28	25.45
Malarial Antigen	1	0.09
Slide test for Malaria	1	0.09
Widal Test	3	2.72

Categorisation	Frequency	%
DF	81	67.5%
DHF	34	28.3%
DSS	5	4.1%

Result

The present study was done with the aim to describe the clinical manifestations, laboratory features and outcomes of dengue infection in adult patients with atypical presentations, if any. In our study the most common presenting symptom was fever (100%), headache (81.6%), myalgia (55%), retro-orbital pain (51.6%) and abdominal pain (45%).

More than half of our study group had one or the other atypical manifestations. Most common atypical manifestation was hepatitis (43.3%) followed byacalculous cholecystitis (32%), bradycardia (26%), febrile diarrhoea (12.5%), meningitis (3.3%), encephalitis (1.6%) , pancreatitis (1.6%).

Gastrointestinal symptoms were seen in 2/3rd of our patients (65%).Hepatitis manifested as hepatomegaly and raised aminotranferases. Of these jaundice was observed in only 10%. Most cases resolved within 5-8 days of supportive treatment.

On abdominal ultrasound 38 patients) 31.6(% with abdominal pain had edematous gall bladder without gall stones .These were diagnosed as acute acalculous cholecystitis. All patients responded well to supportive therapy and recovered completely without any sequelae.

15 patients presented with febrile diarrhoea. All these patients were treated with probiotics, intravenous fluid therapy and oral rehydration salt. All recovered completely.

Two patients with pain abdomen had raised serum lipase and serum amylase. A subsequent CECT abdomen revealed enlarged pancreas. Diagnosis of acute pancreatitis was made. Both cases were treated with IV fluids and broad spectrum antibiotics. Both the patients recovered completely without sequelae.

Most common conduction abnormality was sinus bradycardia observed in 23.3% patients. Pulse rate varied from 42-56 beats/minute. None of the patient had any history of cardiovascular disease and all recovered in 5-7 days.

Amongst the neurological manifestations, A 22-year-old female, with no comorbidities, presented to the emergency department with altered sensorium. There was a history of moderate to high grade, intermittent fever with associated chills and rigor of four days duration, along with a diffuse, continuous headache of two days' duration and three to four episodes of non-bilious vomiting prior to the presentation. There was an episode of seizure one day back. On examination, she was febrile (101°F) with a regular pulse rate of 104 beats/min, blood pressure 104/82 mmHg, Glasgow coma scale (GCS) 9/15 (eye-opening: 2/4, verbal response: 3/5, motor response: 4/6) and bilaterally reactive pupils. Meningeal signs were absent with bilateral flexor plantar response and no focal deficit. The rest of the systemic examination was within normal limits.

On investigations, non-contrast computed tomography (NCCT) of the brain, suggested diffuse cerebral edema. The patient also had thrombocytopenia, leucopenia and raised hepatic enzymes. Cerebrospinal fluid (CSF) analysis had raised protein (55mg/dl), mild lymphocytic pleocytosis (90 cells/cu mm) and normal glucose levels. On Gram staining and culture of the CSF, no organism was isolated and herpes simplex virus polymerase chain reaction (HSV PCR) was negative.
The patient was begun treatment with intravenous dexamethasone 4 mg 8 hourly, mannitol (0.5 mg/kg, 8 hourly) and ceftriaxone 2g 12 hourly.

On the second day she was subjected to contrast-enhanced magnetic resonance imaging (CEMRI) of the brain which revealed hyperintensities in bilateral frontotemporal lobes and cerebellar hemispheres and thalami. Susceptibility-weighted imaging suggested thalamic micro-hemorrhages. All these features were suggestive of acute hemorrhagic necrotizing encephalitis.
From day 4 onwards, she became afebrile with an improvement in GCS 14/15 (Eye-opening: 4/4, verbal response: 5/5, motor response: 5/6) and improving platelet count and liver enzymes. Her antibiotic was stopped and steroid was tapered.
On the sixth day, the patient was discharged with a GCS of 15/15, with no residual neurological deficit.

Discussion

Dengue infections in India impact all age demographics, with younger individuals particularly susceptible to Dengue Fever (DF) and children under 15 years at a higher risk for Dengue Hemorrhagic Fever (DHF)[6,7]. The current research indicates that the age group of 20 to 30 years is significantly affected. Historical data from epidemics in Delhi between 1999 and 2006, as well as in Chandigarh, Haryana, Maharashtra, Punjab, and Uttar Pradesh, supports the notion that young adults are predominantly impacted. Conversely, the highest incidence of cases among children aged 5 to 12 was recorded during the 1996 epidemic in Delhi, as well as in West Bengal in 1990 and 2005, Tamil Nadu in 1998 and 2003, Madhya Pradesh in 2001 and 2003, Uttar Pradesh from 2003 to 2006, and Puducherry from 2003 to 2004[7,8]. The elevated fatality rate among children may be attributed to their lack of immunity. However, existing literature does not distinctly categorize age groups for DF and DHF[6]. Determining which gender is more susceptible to dengue infection remains inconclusive. This study identified a male-to-female ratio of 2.7:1, consistent with most outbreaks in India[9]. In contrast,

another study found that females were more frequently infected than males[10]. Additionally, several studies reported no significant difference in the gender distribution of dengue cases[11]. The observed gender disparity may stem from social and cultural biases, given that India is a male-dominated society.

In tropical regions, dengue transmission occurs year-round, with a notable increase at the onset of the rainy season. This surge is attributed to a higher population of infected vector mosquitoes, as elevated humidity extends their lifespan and warmer temperatures reduce the extrinsic incubation period. Numerous studies have indicated that the majority of dengue cases in India arise during and after the monsoon months, with this study confirming that October marks the peak incidence, followed closely by November.

Recently, the clinical presentation of dengue has evolved, with atypical manifestations becoming more common. In this study, the most frequently observed laboratory abnormalities included leukopenia and thrombocytopenia, while liver function abnormalities were also noted, consistent with findings from previous research. Although pancytopenia and pancreatic dysfunction were less common, they were observed during the illness and resolved completely with recovery from dengue. Thrombocytopenia remains a characteristic and significant laboratory finding in dengue fever. Patients who receive multiple platelet transfusions or other blood products may develop alloimmunization to various human leukocyte antigens and platelet-specific antigens. Therefore, promoting single-donor apheresis platelet transfusions over random donor platelets is advisable to mitigate the risk of alloimmunization.

Conclusion

Dengue infection in India has evolved rapidly, and regular outbreaks have been observed with a changing epidemiology, as the disease is rapidly spreading from urban to rural areas with increasing atypical manifestations.

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Conflicts of interest

There are no conflicts of interest.

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