RESEARCH ARTICLE

ASSESSMENT OF CLINICAL & LABORATORY PARAMETERS OF PATIENTS PRESENTED WITH DENGUE FEVER AT SECONDARY HEALTH CARE CENTRE

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ARTICLE INFO	ABSTRACT
	Introduction: Dengue is the most extensively spread mosquito-borne disease, transmitted through the bite of infected mosquitoes of Aedes species. It is caused by the dengue virus (DENV, 1–4 serotypes). This viral infection has a wide clinical spectrum ranging from asymptomatic disease to undifferentiated fever (or viral syndromes).High dengue disease burden and frequent outbreaks result in a serious drain on country's economy and stress on the health systems. The present study was conducted at secondary health care hospital in Nanded, highlighting the various clinical, epidemiological and laboratory presentations of dengue fever patients. *Materials and Methods:* This was an observational study conducted on the patients admitted at Secondary health care hospital, Nanded, Maharashtra, India.120 patients suffering from dengue fever during an outbreak of the disease were enrolled. Data related to their clinical presentation and important laboratory parameters were collected and studied analytically. *Results:* 120 subjects confirmed dengue fever with either NS1 Antigen or IgM antibody positive with age more than 18 years were included in the study. In present study we found that 80% of patients had headache , 75% had body ache and 40% had typical retro-orbital pain. 60 patients (50%) had abdominal pain. 24 patients (20%) had associated hepatosplenomegaly and six patients (5%) had ascites associated with hepatosplenomegaly.. 18 patients (15%) had breathlessness, out of which 12 patients (10%) had pleural effusion. Twenty seven patients were diagnosed with DHF and three with DSS. . Six patients (5%) had expanded dengue syndrome (EDS). *Conclusion:* Therefore detailed analytical study of clinical presentations and laboratory parameters of this disease for early recognition, correct diagnosis, prompt intervention, and appropriate treatment is best method to solve this complex health issue.

INTRODUCTION

Dengue is a vector-borne disease that is a major public health threat globally. It is caused by the dengue virus (DENV, 1–4 serotypes), which is one of the most important arboviruses in tropical and subtropical regions.[1,2] Dengue is the most extensively spread mosquito-borne disease, transmitted through the bite of infected mosquitoes of *Aedes* species. Dengue virus, the causative agent of dengue fever belongs to the Flavivirus genus and has four serotypes (DEN-1, DEN-2, DEN-3, and DEN-4).[3] Each serotype has several subtypes or genotypes. In humans, one serotype produces lifelong immunity against re-infection but only temporary and partial immunity against the other serotypes.[4] Incubation period is 4 to 7 days (range 3–14 days) [5].

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Once the symptoms start, person can remain infectious for next six to seven days. In addition to mosquito bite, dengue has been reported to be transmitted by transfusion of blood from an infected donor, injuries by infected sharps to health care workers, transplantation of organs and tissues from infected donors, and from infected pregnant mother to her foetus by vertical transmission [6-8]. This viral infection has a wide clinical spectrum ranging from asymptomatic disease to undifferentiated fever (or viral syndromes), classical dengue fever (DF), dengue hemorrhagic fever (DHF), or dengue shock syndrome (DSS) and expanded dengue syndrome (EDS) [5]. The revised WHO classification of 2009 categorizes dengue patients according to different levels of severity as dengue without warning signs, dengue with warning signs (abdominal pain, persistent vomiting, fluid accumulation, mucosal bleeding, lethargy, liver enlargement, increasing haematocrit with decreasing platelets) and severe dengue [5,9]. Dengue fever is endemic in more than 100 countries with most cases reported from the Americas, South-East Asia and Western Pacific

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regions of WHO [5]. In India, dengue is endemic in almost all states and is the leading cause of hospitalization. Dengue fever had a predominant urban distribution a few decades earlier, but is now also reported from peri-urban as well as rural areas [10,11]. High dengue disease burden and frequent outbreaks result in a serious drain on country's economy and stress on the health systems. In India, case detection, case management, and vector control are the main strategies for prevention and control of dengue virus transmission [12]. Information about dengue disease burden, its prevalence, incidence and geographic distribution is necessary in decisions on appropriate utilization of existing and emerging prevention and control strategies. The present study was conducted at secondary health care hospital in Nanded, highlighting the various clinical, epidemiological and laboratory presentations of dengue fever patients.

MATERIALS AND METHODS

This was an observational study conducted on the patients admitted at Secondary health care hospital, Nanded, Maharashtra , India, during the period from June 2018 to January 2019. 120 patients suffering from dengue fever during an outbreak of the disease were enrolled. All patients who were admitted with complaint of fever and were found positive for either NS1 antigen or dengue IgM antibodies were enrolled in the present study. A detailed history was taken and careful clinical examination was performed. Besides routine biochemical and hematological investigations [hemoglobin, total leucocyte count (TLC) , platelet count, hematocrit (HCT), liver function tests (LFT), blood urea, and serum creatinine], malarial antigen, Slide test for malarial parasite, IgM antibodies and Widal test for typhoid, and X-ray chest and ultrasonography (USG) of abdomen were also done in all patients. Other investigations were performed according to the clinical conditions of the patients. All subjects were classified according to WHO guidelines as shown in Table 1 [5]. Patients having neurological, cardiac, gastrointestinal, musculoskeletal, renal, ocular, and other nonspecific manifestations were grouped in expanded dengue syndrome (EDS) category. Thrombocytopenia was taken as platelet count less than 1 lac/mm^3 and leucopenia as wbc $\leq$ 5000 cells/mm^3

RESULTS

200 subjects with fever and clinical suspicion of dengue were tested for NS1 antigen and dengue IgM antibody and 120 subjects (60 %) of confirmed dengue fever with age more than 18 years were included in the study. Age distribution of patients is as shown in Table 2. We had 66 (55%) males and 54 (45%) females enrolled in our study. As far as clinical spectrum was concerned, all patients had come with fever along with varied clinical manifestations as shown in Table 3.Besides fever, headache (80%) and Body ache (75%) revealed as most common symptoms. 90 patients (75%) had thrombocytopenia with platelet count less than one lakh. There was significant difference in the platelet count among the four groups, with DHF and DSS having significantly low values .78 patients (65%) had leucopoenia with relatively decreased lymphocyte count. 60 patients (50%) had abdominal pain, out of which 30 had right upper quadrant pain with fever. Nine patients had positive Murphy's sign. All the 30 patients with pain had oedematous gall bladder without gallstones. Diagnosis of acalculous cholecystitis was made and all patients responded well to supportive therapy. 24 patients (20%) had associated Hepatosplenomegaly and six patients (5%) had ascites

associated with hepatosplenomegaly.. 18 patients (15%) had breathlessness, out of which 12 patients (10%) had pleural effusion on chest X-ray as shown in Table 5. Out of 120 patients 3 (2.5%) patients got expired despite of aggressive treatment due complications like dengue shock syndrome (1 patient) and Respiratory failure from ARDS (2 patients). Clinical categorisation of subjects was done as shown in Table 6. Twenty seven patients were diagnosed with DHF and three with DSS. 27 patients (22.5%) had hemorrhagic manifestations in form of epistaxis, hematemesis, hemoptysis, melena, subconjunctival haemorrhage, and menorrhagia. Twelve patients required both blood and platelet transfusion and six required only platelet transfusion. A total of thirty 32 units of platelets were transfused. Intravenous fluid therapy was given according to WHO guidelines. Six patients (5%) had expanded dengue syndrome (EDS) affecting nervous system (encephalopathy) in three, cardiovascular system (myocarditis) in two, and gastrointestinal system in one (jaundice). Out of 120 patients, seven had co-infections with malaria in five (confirmed by Slide test and malarial antigen test) and typhoid in six were confirmed with Widal test as shown in Table 5.

DISCUSSION

This was a hospital based, observational study, where we tried to find out the clinical and laboratory spectrum of dengue patients presenting to our hospital (Secondary care centre). We tried to find out the features more common in dengue with warning signs and predictors of complications in dengue patients as well. We have found that age group affected by dengue in the present study is lower than in other Indian studies.(13) Fever, Headache, body ache, abdominal pain, Retro Orbital pain, vomiting hepatosplenomegaly, thrombocytopenia, raised liver enzymes, and pleural effusion were the predominant clinical and laboratory findings in our patients and the same have also been reported in previous studies.[13] The present study highlighted the varied spectrum of dengue fever ranging from some known clinical presentations of fever, rash, headache to some atypical presentations like acalculous cholecystitis, encephalopathy and myocarditis. Headache, Body ache and retro-orbital pain are well-known features of dengue fever. In present study we found that 80% of patients had headache , 75% had body ache as chief complaint and 40% had typical retro-orbital pain.

In study by Mandal et al. [14], 62.16% patients presented with headache. In some studies like Itoda et al. [15], 90% of patients presented with headache. Ultrasonography was helpful in the present study to detect ascites and pleural effusion in 6 and 12 patients, respectively. Ultrasonography has already been reported to have the highest sensitivity in detecting plasma leakage in dengue.[16] Bleeding Manifestations were seen in 24 (20%) patients in present study in the form of epistaxis, haematuria, haematemesis,menorrhagia, subconjunctival hemorrhag and malena. The most common bleeding manifestation in our patients was epistaxis, However, Agarwal et al have reported hemetemesis as the most common manifestation.[13]. In the present study, the mean platelet count was 54.50 ± 36.42 .and 90 patients (75%) had thrombocytopenia with platelet count less than one lakh.. Thrombocytopenia may be because of spontaneous aggregation of platelets to virus-infected endothelium, bone marrow suppression, or immune mediated clearance A platelet count <50,000/mm3 in dengue has a six-fold higher mortality.[17]

Table 1. WHO Grading severity of dengue haemorrhagic fever

DF/DHF	Grade	Signs and symptoms	Laboratory
DF	1	Fever and haemorrhagic manifestation (positive tourniquet test) and evidence of plasma leakage.	Thrombocytopenia <100 000 cells/mm^3; HCT rise $\geq$ 20%.
DHF	II	As in Grade I plus spontaneous bleeding.	Thrombocytopenia <100000 cells/mm^3; HCT rise $\geq$ 20%.
DHF	III	As in Grade I or II plus circulatory failure (weak pulse, narrow pulse pressure ($\leq$ 20 mmHg), hypotension, restlessness).	Thrombocytopenia <100 000 cells/mm^3; HCT rise $\geq$ 20%.
DHF	IV	As in Grade III plus profound shok with undetectable BP and pulse.	Thrombocytopenia <100 000 cells/mm^3; HCT rise $\geq$ 20%.

Table 2. Frequncy distribution of cases as per age group

Age groups	Frequency	%
18–20 years	22	18.33%
21–30 years	52	43.3%
31–40 years	24	20%
41–50 years	12	10%
>50 years	10	8.3%
Total	120	100%
Mean ± SD	32.36 ± 14.26	
Median	31	

Table 3. Obsereved Clinical symptoms and signs

Symptoms	Number of patients	Percentage%
Fever	120	100
Headache	96	80
Body ache	90	75
Backache	66	55
Retro-orbital pain	48	40
Bleed (any hemorrhagic manifestation)	24	20
Rashes	25	21
Vomiting	77	64
Weakness	84	70
Pain abdomen	60	50
Breathlessness	18	15
Vertigo	12	10
Sweating	29	24
Syncope	13	11
Diarrhoea	35	29
Sore throat	24	20
Neurological manifestations	4	3
Itching	28	23
Others	12	10

Table 4. Laboratory Parameters

	Mean ± SD
PL count (K)	54.50 ± 36.42
Total Leucocyte Count	3824.38 ± 2411
HCT	36.82 ± 6.42
UREA	22.84 ± 8.22
Creatine	1.14 ± 1.20
Serum bilirubin	1.46 ± 0.48
AST	66.50 ± 54.52
ALT	58.10 ± 34.55

Table 5. Complications Observed and Associated Tests Results

Finding	Positive cases	Total	Percentage%
Pleural effusion (PE)	12	120	10
Gall bladder edema (GBE)	30	120	25
Hepatosplenomegaly (HS)	24	120	20
Hepatosplenomegaly + ascites (HS + A)	6	120	5
Malarial antigen (R-MAT)	2	120	1.66
Slide test for malaria	3	120	2.5
Widal test	6	120	5

Table 6. Obsereved Clinical Spectrums Of Dengue Fever

Categorisation	Frequency	%
DF	84	73%
DHF	27	22.5%
DSS	3	2.5%
EDS	6	5%
Total	120	100%

In our study, there was no correlation between platelet counts and bleeding manifestations. Previous studies have reported similar findings,[17] and this finding points towards the fact that bleeding in dengue is multifactorial. Various factors leading to bleeding in dengue, include thrombocytopenia, abnormal platelet function, prolongation of prothrombin time, fibrinogen consumption, etc.[18]. Low leucocyte count may be due to virus-induced inhibition of myeloid progenitor cells or due to destruction. We found that in our study 78 patients (65%) had leucocyte count <5000 almost similar to a study by Itoda *et al.*[15]. 50% of patients presented with pain abdomen along with fever. 25% had acalculous cholecystitis with right upper quadrant abdominal pain, positive Murphy's sign, abnormal liver function tests, and thickened gall bladder wall without stones on ultrasonography. The exact mechanism of acalculous cholecystitis in dengue is not known. It could be due to viral invasion of gall bladder wall causing microangiopathic injury and increased vascular permeability leading to protein rich plasma leakage. This could be the cause of thickening of gall bladder wall [19]. Elevation in liver enzymes is a common finding in dengue infection[20] and it was also noted in the current study. We found that, AST levels were equal to or greater than ALT levels. This feature has already been reported in previous studies.[21]. The overall mortality was 2.5%, which is comparable with other previous studies conducted in India.[13].

Conclusion

Over the past few years, dengue has emerged as a serious public health concern especially in India. The emergence of dengue in India has gone into epidemic proportions and dengue outbreaks are frequently engulfing different parts of the country in both urban and rural populations. Dengue infections may vary from flu-like self-limiting illness to life-threatening dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) which can be fatal, if left untreated. Multi-systemic involvement, varied, atypical, and sometimes life-threatening clinical and laboratory presentations makes dengue a very complex heath problem for the society. Therefore detailed analytical study of clinical presentations and laboratory parameters of this disease for early recognition, correct diagnosis, prompt intervention, and appropriate treatment is best method to solve this complex health issue.

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