

ORIGINAL ARTICLE

Clinical and Laboratory Profile of Dengue Fever in a North Indian Tertiary Hospital

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Abstract

Objectives: The present study was done to ascertain the presentations of dengue fever in a North Indian tertiary care Hospital, and to compare the clinical and laboratory features among patients with and without warning signs in dengue fever.

Methods: A total of 600 patients of dengue admitted to medical wards were included in the study. A detailed history as well as a general and systemic clinical examination were carried out. Haematological profiles and biochemical investigations were done at the time of admission and were followed daily or at times twice a day. Signs of plasma leakage were assessed by chest radiograph and abdominal ultrasonography, serum albumin etc. Patients were classified as dengue fever without warning signs and with warning signs and laboratory diagnosis of dengue was established by demonstration of NS1 antigen and specific antibodies to dengue in serum.

Results: Of the 600 dengue positive patients, 421 (70.2%) were males and 179 (29.8%) were females. Mean age of the patients was 27.35 ± 11.43 years. Among all patients of dengue, 21 (3.5%) presented with bleeding from any site. Out of these, only 7 of those presenting without warning signs had bleeding episodes whereas, 22 (34.3%) of patients presenting with warning signs had bleeding and this difference was statistically significant ($p=0.01$). Haematocrit was an important factor to predict severity of dengue. Whereas the mean haematocrit among all patients was $39.79 \pm 3.23\%$, it was $39.49 \pm 4.25\%$ among those without warning signs and $42.22 \pm 3.54\%$ among those with warning signs of dengue, and this was significant statistically, with a p-value of 0.002.

Conclusion: Early diagnosis, monitoring and prompt supportive management can reduce mortality in dengue. In the present study, it was found that newer signs and symptoms are emerging and may cause delay in the diagnosis. It was found that the mortality rate was significantly higher in patients of dengue with warning signs.

Introduction

Over the past few years, dengue has emerged as a serious public health concern especially in India. It is estimated that around 2.5 billion people, in urban areas of tropical countries, are at a risk of developing dengue infection.¹ Most of the cases of Dengue Fever are being reported from Southeast Asian and the western Pacific regions.² 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.³⁻⁸ 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. The mortality rates with dengue have been reported to be as high as 20%.² In recent years some new presentations of dengue have been reported. Many atypical presentations have led to delayed suspicion and diagnosis of dengue. Some presentations have been completely different from any of the features of dengue described until now in literature.^{9,10} We conducted this study in the Department of Medicine, J N Medical College, AMU, Aligarh,

from June to October 2013 to assess the clinical profile of patients diagnosed to have dengue fever as well as to compare the differences in clinical and laboratory parameters among patients of dengue with and without warning signs admitted in medicine wards.

Materials and Methods

A total of 600 patients of dengue admitted to medical wards were included in the study. An informed consent was taken from all the patients. A detailed history as well as a general and systemic clinical examination (including the tourniquet test) was recorded. Haematological profiles and biochemical investigations were done at the time of admission and were followed daily or at times twice a day. Signs of plasma leakage were assessed by chest radiograph and abdominal ultrasonography, serum albumin etc. Specific investigations were performed in patients who presented with neurological involvement (cerebrospinal fluid analysis, neuroimaging, electrodiagnostic studies or muscle biopsy) or hepatic failure (viral markers, peripheral smear and serology for plasmodium falciparum, typhoid fever and leptospirosis).

Patients were classified as dengue fever without warning signs and with warning signs and laboratory diagnosis of dengue was established by demonstration of NS1 antigen and specific antibodies to dengue in serum. The study enrolled patients of acute febrile illness confirmed to have dengue infection.

Statistical analysis

All data are described as means with standard deviations or numbers with percentages. Statistical analysis was

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Received: 17.03.2015; Accepted: 20.05.2017

performed by Chi Square test done by using the Statistical Package for Social Sciences (SPSS 21) with $p < 0.05$ taken as statistically significant. Wilcoxon's signed rank test and ANOVA were also applied wherever applicable.

Results

It was a hospital based observational study conducted in a tertiary care hospital. A total of six hundred patients were included in the study. Of the 600 dengue positive patients, 421 (70.2%) were males and 179 (29.8%) were females. Mean age of the patients was 27.35 ± 11.43 years. Of the total 600 patients 536 (89.33%) presented without warning signs and 64 (10.66%) presented with warning signs. Among the patients presenting with warning signs the mean age was 31.04 ± 11.8 years which was slightly more than the mean age of patients presenting without warning signs (27.01 ± 11.38 years), however this difference was not statistically significant ($P=0.09$). Out of all patients of dengue fever, 129 (21.5%) had vomiting, 46 (7.7 %) had pain abdomen and 20 (3.3%) had a rash. 28 (4.7%) patients had a history of travel to endemic areas. 8 (1.3%) had a history of past dengue infection.

Among all patients of dengue, 21 (3.5%) presented with bleeding from any site. Out of these, only 7 of those presenting without warning signs had bleeding episodes whereas, 22 (34.3%) of patients presenting with warning signs had bleeding and this difference was statistically significant ($p=0.01$). 36 (6%) patients presented with shock or developed shock during the hospital stay, however as many as 26 (40.64%) of those with warning signs had shock ($p=0.01$). A total of 3 (0.5%) patients had pleural effusion, of which one had presented with warning signs. 21 (3.5%) patients had presented with ascites, of which, 6 (9.36%) had presented with warning signs (Table 1).

Of the total dengue patients, 159 (26.5%) had hepatitis. Among those without warning signs 126 (23.5%) had hepatitis, whereas among those with warning signs 33 (51.56%) had hepatitis. This difference was also statistically significant ($p < 0.001$). Whereas, the mean duration of hospital stay was 5.13 ± 1.45 days among all patients of dengue, it was 4.93 ± 1.34 days among those without warning signs and 6.76 ± 1.2 days among those

with warning signs. This difference was also statistically significant ($p=0.002$). Mortality was significantly increased among patients presenting with warning signs.

Among all the 600 patients of dengue, the mortality was 2.7% (Total 16 patients died during hospital stay), however only one (0.2%) of those presenting without warning signs died during treatment. However, of all the 64 patients presenting with warning signs, 15 (23.43%) died during hospital stay, and this was statistically significant ($p=0.001$).

Of all the 600 patients of dengue, 553 (92.2%) patients had NS1Ag positive. However, among the patients without warning signs of dengue, 499 (93.1%) had positive NS1Ag, while, among the patients with warning signs 54 (84.37%) had positive NS1Ag.

Among all the 600 patients suffering from dengue, IgM antibody was raised in 116 (19.3%) patients ($p=0.012$). However, it was raised in 95 (17.7%) and 21 (32.81%) patients with warning and without warning signs of dengue fever respectively.

Out of all the 600 patients of dengue, 95 (15.8%) patients had raised IgG antibody level ($p=0.013$), of which 79 (14.7%) and 16 (25%) patients had raised levels with and without warning signs respectively.

Mean lowest platelet count of all the patients was 46273.33 ± 12432.55 ($p=0.042$). However among the patients with warning signs, it was 34221 ± 17112 and among the patients without warning signs, it was 23656 ± 14123 .

Mean AST of all the 600 patients, was 28.68 ± 11.11 U/L ($p=0.011$). It was 26.94 ± 10.1 U/L in patients with warning signs while it was 51.17 ± 14.3 U/L in patients without warning signs.

Of all the patients of dengue, mean ALT was 31.53 ± 12.34 ($p=0.021$). It was found to be 26.94 ± 10.1 and 568 ± 23.4 in the patients with and without warning signs of dengue.

Mean alkaline phosphatase of all the patients of dengue was 9.73 ± 2.11 U/L. However, in patients with warning signs of dengue, mean alkaline phosphatase was 9.37 ± 1.22 U/L and in patients without warning signs, it was 9.4 ± 3.6 U/L.

Mean serum bilirubin of all the patients suffering from dengue was

1.71 ± 0.66 mg/dl. It was 1.01 ± 0.22 mg/dl and 0.99 ± 0.34 mg/dl in patients with and without warning signs of dengue respectively.

Mean serum albumin of all the 600 patients was found to be 3.82 ± 0.74 mg/dl. However, among the patients with warning signs of dengue, it was 3.95 ± 0.71 mg/dl and among the patients without warning sign signs, it was 3.41 ± 0.83 mg/dl. Mean Prothrombin time was 14.33 ± 1.55 seconds among all patients, whereas it was 13.65 ± 3.33 seconds among patients without warning signs and 16.93 ± 5.5 seconds among patients with warning signs, and this data was statistically significant with a p value of 0.01.

Haematocrit was an important factor to predict severity of dengue. Whereas the mean haematocrit among all patients was $39.79 \pm 3.23\%$, it was $39.49 \pm 4.25\%$ among those without warning signs and $42.22 \pm 3.54\%$ among those with warning signs of dengue, and this was significant statistically, with a p-value of 0.002 (Table 2).

Discussion

This was a hospital based, observational study, where we tried to find out the clinical spectrum of dengue patients presenting to our hospital. 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.¹¹ Fever, vomiting, hepatomegaly bleeding, thrombocytopenia, raised liver enzymes, deranged PT, hyponatremia, hypoalbuminemia, ascites and pleural effusion were the predominant clinical and laboratory findings in our patients and the same have also been reported in previous studies.¹¹ The most common bleeding manifestation in our patients was epistaxis, which was in concert with that reported by Kulkarni et al.¹² However, Agarwal et al have reported hemetemesis as the most common manifestation.¹¹

Average duration of fever in our patients was 4.63 ± 2.01 days, similar to the study by Manjith et al. (4.9 days)¹³ and Ratageri et al. (5.4 days).¹⁴ Altered sensorium was present in nine patients and convulsions were present in five of these patients. Pancharoen has earlier reported altered sensorium (83.3%) as the most common neurological finding, followed by seizures (45.2%).¹⁵

Table 1: Comparison of clinical parameters between dengue fever and dengue hemorrhagic fever

	Total dengue (n=600)	Without warning signs (n=536)	With warning signs (n= 64)	P value
Males	421 (70.2%)	378 (70.5%)	43 (67.18%)	0.346
Females	179 (29.8%)	158 (29.5)	21 (32.81%)	0.442
Mean age (yrs)	27.35±11.43	27.01±11.38	31.04±11.8	0.09
Days of illness	4.63±2.01	4.64±2.07	4.5±1.4	0.66
Vomiting	129 (21.5%)	116 (21.6%)	13 (20.31%)	0.15
Pain abdomen	46 (7.7%)	40 (7.5%)	6 (9.37%)	0.78
Past history of dengue	8 (1.3%)	7 (1.3%)	1 (1.56%)	0.09
Travel to endemic area	28 (4.7%)	22 (4.1%)	6 (9.37%)	0.13
Rash	20 (3.3%)	18 (3.4%)	2 (3.12%)	0.78
Bleeding	21 (3.5%)	7 (1.3%)	22 (34.37%)	0.01
Shock	36 (6%)	10 (1.9%)	26 (40.64%)	0.01
Pleural effusion	3 (0.5%)	2 (0.4%)	1 (1.56%)	0.05
Ascites	21 (3.5%)	15 (2.8%)	6 (9.36%)	0.003
Hepatitis	159 (26.5%)	126 (23.5%)	33 (51.56%)	<0.001
Length of hospital stay	5.13±1.45	4.93±1.34	6.76±1.2	0.002
Mortality	16 (2.7%)	1 (0.2%)	15 (23.43%)	0.001

Dengue causes cerebral hypoperfusion due to shock, and there may also be encephalitis/encephalopathy, hepatic dysfunction, metabolic derangements or acute disseminated encephalomyelitis which may lead to the neurological manifestations. Rarely, Guillain-Barré Syndrome (GBS) may also be a manifestation following dengue fever.¹⁶ Ultrasonography was helpful in the present study to detect ascites and pleural effusion in 21 and 3 patients, respectively. Ultrasonography has already been reported to have the highest sensitivity in detecting plasma leakage in dengue.¹⁷

A platelet count $<50,000/\text{mm}^3$ in dengue has a six-fold higher mortality.¹⁸ In our study, there was no correlation between platelet counts and bleeding manifestations. Previous studies have reported similar findings,¹⁸ 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.¹⁹ The average duration of hospital stay was longer in patients with warning signs. Patients with warning signs required more supportive therapy (blood products and inotropes), compared to those without warning signs.

Elevation in liver enzymes is a common finding in dengue infection²⁰ 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 Acute hepatic failure, is a rare manifestation of severe dengue.²² It was found in four of our patients. Derangement in

liver function may be found in dengue due to the direct effect of the virus on liver cells. Fulminant hepatic failure may occur secondary to acute severe hepatitis and massive necrosis of the liver, causing hepatic encephalopathy and even death.

The overall mortality was 2.7%, which is comparable with other previous studies conducted in India.¹¹ Joshi et al have reported a mortality rate of 3.5%.²³

Conclusion

Dengue is taking epidemic form in India. It is one of the common acute febrile illnesses seen in India like enteric fever, malaria, leptospirosis, and viral hepatitis. Symptoms like fever, vomiting, headache, and musculoskeletal pain, hemorrhagic tendencies, hepatomegaly, macular rash, pleural effusion and ascites are commonly the presenting features of dengue fever. Laboratory findings may reveal hemoconcentration, elevated liver enzymes and thrombocytopenia. Early diagnosis, monitoring and prompt supportive management can reduce mortality in dengue. In the present study, it was found that newer signs and symptoms are emerging and may cause delay in the diagnosis. It was found that the mortality rate was significantly higher in patients of dengue with warning signs.

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Table 2: Comparison of laboratory parameters between dengue fever and dengue hemorrhagic fever

	Total dengue (n=600)	Without warning signs (n=536)	With warning signs (n= 64)	P value
NS1Ag	553 (92.2%)	499 (93.1%)	54 (84.37%)	0.43
IgM	116 (19.3%)	95 (17.7%)	21 (32.81%)	0.012
IgG	95 (15.8%)	79 (14.7%)	16 (25%)	0.013
Lowest platelet count	46273±12432	34221±17112	23656±14123	0.042
AST (U/L)	28.68±11.11	26.94±10.1	51.17±14.3	0.011
ALT (U/L)	31.53±12.34	28.51±11.66	56.8±23.4	0.021
Alk. phosphatase (U/L)	9.73±2.11	9.37±1.22	9.4±3.6	0.76
Sr. bilirubin (mg/dl)	1.71±0.66	1.01±0.22	0.99±0.34	0.23
Sr. albumin (mg/dl)	3.82±0.74	3.95±0.71	3.41±0.83	0.79
Prothrombin time (Sec)	14.33±1.55	13.65±3.33	16.93±5.5	0.01
Mean Hb (g/dl)	12.43±1.44	12.45±1.82	12.63±1.8	0.77
Mean WBC count	4857±1124	4904±1022	4468±1917	0.48
Mean haematocrit (%)	39.79±3.28	39.49±4.25	42.22±3.54	0.002
Blood sugar (mg/dl)	97.23±27.22	97.05±23.52	96.93±21.85	0.26
Blood urea (mg/dl)	31.09±15.01	30.98±15.1	31.51±14.6	0.71
Sr. creatinine (mg/dl)	0.921±0.232	0.91±0.12	0.96±0.43	0.22

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