Original Research Article

Clinico-haematological profile of dengue virus infection at rural tertiary care centre in North India

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ABSTRACT

Background: In India, dengue epidemics are becoming more frequent. Dengue viral infections are among the most important mosquito-borne disease of the Indian subcontinent. The study aimed to compare the clinical and haematological profile of all patients diagnosed with dengue viral infection. Patient with confirmed infection with dengue virus were prospectively evaluated for disease progression and to determine their final clinical outcome. The objective of the study was to study the clinico-haematological profile of dengue infection at rural tertiary care centre.

Methods: This prospective study included 456 clinically suspected cases of dengue infection of ages more than 14 years of age. Dengue was confirmed by serological methods. Confirmed cases of dengue infection were analyzed according to age, sex and education. Clinical and hematological data were compared between dengue fever and dengue hemorrhagic fever.

Results: Serologic dengue infection was positive in 220 (48%) out of 456 clinically suspected cases of the dengue infection. 127 (57.73%) patients were males and 93 (42.27%) were females. 149 (67.72%) patient had dengue fever while 71 (32.27%) had dengue hemorrhagic fever. The proportion of dengue cases was highest among male aged 15 to 24 years-old. A gradual decrease occurred in the percentage of dengue cases in the population aged 44 years-old or more. Common clinical symptoms were fever, headache, abdominal pain, myalgia, joint pain and retro-orbital pain. Common haematological abnormalities were thrombocytopenia, leukopenia and elevated alanine aminotransferase (SGOT).

Conclusions: Differences in the clinical, biochemical and haematological profile of dengue virus infection, indicative of a variation in disease severity from DF to DHF. In this study, we present recent data on readily obtained clinical and laboratory data that can be used for early diagnosis and earlier appropriate treatment of dengue virus infection.

Keywords: Clinical profile, Dengue fever, Dengue hemorrhagic fever, Haematological profile, Rural area

INTRODUCTION

The dengue virus of the genus Flavivirus (family Flaviviridae) is represented by four serotypes (DENV1 to 4), which are transmitted to humans by infected female Aedes aegypti and A. albopictus mosquitoes, widely distributed throughout tropical and subtropical regions.[1] According to the World Health Organization, approximately 2.5 billion people i.e. two fifth of the world's population in tropical and subtropical countries are at risk of the disease. An estimated 50 million dengue infection occurs worldwide annually and about 500,000 people with DHF require hospitalization each year.[2]

Now it is endemic in more than 100 countries and the South-East Asia and the Western Pacific region are most

seriously affected.[3] In India, epidemics are becoming more frequent and the risk of dengue has shown an increase in recent years due to rapid urbanization, lifestyle changes and deficient water management including improper water storage practices in urban, peri-urban and rural areas.[4-6] Risk factors vary in populations world-wide.[7]

Disease manifestations in dengue virus (DENV) infected individuals range from absence or unspecified symptoms to classical dengue fever (DF), characterized by fever associated with muscle, joint and retro-orbital pain, photophobia and red body rash. The most severe and lethal forms of the disease are characterized by increased vascular permeability, plasma leakage, thrombocytopenia and hemorrhagic manifestations.[8-9]

Certain demographic characteristics such as age of the patients can be associated to distinct epidemiological patterns of DENV transmission.[10] Furthermore, early identification of the hematological profile during the fever period can differentiate DENV from other infectious diseases.[11]

Since, rural population is different from urban population and there are loco-regional and sociocultural variation of different population. Put them at different risk of dengue virus infection. Different population are shown to have different clinical presentation and severity. Therefore, this study was conducted to find out different clinical profile of dengue virus infection as seen in rural tertiary care hospital. Which, will enable to plan preventive and therapeutic investigation in these regions.[12-13]

We undertook this prospective study in the department of Medicine, Uttar Pradesh University of Medical Sciences (UPUMS), from July to December 2016 to assess the clinical profile of dengue infection and gender wide distribution in hospitalized patients as well as to observe rare manifestations of dengue fever in the current outbreak and compare them with the WHO dengue classification.[4]

METHODS

It was a prospective observational study. We included all suspected dengue patients of 14 years or older admitted to our hospital in medicine ward. All probable cases that had high grade fever with myalgia, headache, retro orbital pain, arthralgia, itching, abdominal pain, shock, bleeding, thrombocytopenia and rashes.

All cases with dengue virus infections confirmed by positive dengue test, either NS1 antigen, IgM, IgG antibody rapid serological test kit, or ELISA, were taken into the study group.

All cases were categorized as either dengue fever or dengue hemorrhagic fever or dengue shock syndrome according to the criteria of the WHO.[4] A detailed history and physical examination was recorded. All clinical and hematological profile and biochemical parameters were done from the time of admission to the time of discharge. A platelet count and hematocrit was done at the time of admission and repeated daily.

Average of TLC, DLC, Hb, hematocrit and other parameters were calculated for each patient and recorded. Daily vitals were monitored along with tourniquet test. Ultrasonography, chest X-ray and liver function test were done for assessment of plasma leakage. The frequency of various signs and symptoms and the biochemical and hematological parameter were compared between the non-severe and severe disease.

The whole number of patients which is suspected dengue fever included in our study was 456 (n = 456). In whom 220 (48%) were serologically confirmed to have dengue infection. 127 (57.73%) were males and 93 (42.27%) were females. The results were tabulated and correlated. The outcomes were recorded.

Differences in laboratory data between patients with dengue fever (DF) and dengue hemorrhagic fever (DHF) were analyzed using the Student's t-test for continuous variables. Differences in the demographic and clinical data between patients with DF and DHF were tested by the chi-square test and Fisher's exact test. An association was considered statistically significant when $p < 0.05$. Analysis were computed using statistical software SPSS (Statistical Package for Social Sciences) version 23.0

RESULTS

The total 456 patient was enrolled in our study, 236 were excluded during the first clinical evaluation. Overall, 220 patients had a dengue infection confirmed by ELISA; out of which 149 (67.7%) were cases of dengue fever and 71 (32.3%) were cases of dengue hemorrhagic fever according to WHO guidelines.[4] There were 127 (57.73%) males and 93 (42.27%) females in our study.

There was no significant difference in sex and duration of symptoms between patient with DF and those with DHF. Both the groups of DF and DHF males had high incidence. The male to female ratio was 1.36:1. There was significant difference in age wise distribution of dengue virus infection (p <0.05; Table 1). The maximum number of cases, 102 (46.4%), was seen in the age group of 15-25 years of age, out of whom male patient were 72 (70.6%) and female patient 30 (29.4%). The duration of the hospital stay was longer in those with DHF than in those with DF. The mean tenure of hospitalization was 5.9 days. In DF the mean stay was 5.46 days and in DHF the mean stay was 6.83 days.

The majority of the cases were admitted in the rainy and winter season between the months of July and December. The peak of admission was seen in the month of September.

In our study, the most common symptoms were fever (218, 99% Table 1), headache (97, 44%), abdominal pain (75, 34%), myalgia (69, 31.36%), rash (60, 27.27%), joint pain (58, 26.36), itching (45, 20.45%), vomiting (39, 17.72%), retro-orbital pain (35, 15.90%), epistaxis (14, 6.36%), melena (10, 4.54%), ecchymosis (6, 2.72%), hematemesis (1, 0.45%).

Table 1: Clinical profile

Parameter	DF (n = 149)	DHF (n = 71)	Total dengue positive (n = 220)	P value
Age				
15-24 years	72 (48.32%)	30 (42.25%)	102 (46.36%)	
25-34 years	24 (16.10%)	19 (26.76%)	43 (19.54%)	0.05*
35-44 years	13 (8.72%)	15 (21.12%)	28 (12.72%)	
>44 years	18 (12.08%)	29 (40.84%)	47 (21.36%)	
Sex				
Male	87 (58.38%)	40 (56.33%)	127 (57.73%)	0.773
Female	62 (41.61%)	31 (43.66%)	93 (42.27%)	
Duration of hospital stay (mean)	5.46 days	6.83 days	5.9 days	
Fever	148 (99.32%)	70 (98.59%)	218 (99.09%)	0.542+
Headache	69 (46.30%)	28 (39.43%)	97 (44.09%)	0.337
Abdominal pain	32 (21.47%)	43 (60.56%)	75 (34.09%)	0.018*
Myalgia	48 (32.21%)	21 (29.57%)	69 (31.36%)	0.693
Joint pain	36 (24.16%)	22 (30.98%)	58 (26.36%)	0.283
Rash	4 (2.68%)	56 (78.87%)	60 (27.27%)	<0.001*
Itching	25 (16.77%)	28 (39.43%)	45 (20.45%)	0.05*
Vomiting	22 (14.76%)	17 (23.94%)	39 (17.72%)	0.096
Retro-orbital pain	25 (16.77%)	10 (14.08%)	35 (15.90%)	0.610
Epistaxis	6 (4.02%)	8 (11.26%)	14 (6.36%)	0.04*
Melena	3 (2.01%)	7 (9.85%)	10 (4.54%)	0.014+
Echymosis	0	6 (8.4%)	6 (2.72%)	0.001+
Hematemesis	0	1 (1.40%)	1 (0.45%)	0.323+

*significant p values, +fisher exact test

A significant increase in the frequency of rash (p < 0.001), abdominal pain (p <0.018), itching (p <0.05), epistaxis (p < 0.04), ecchymosis (p < 0.001), melena (p < 0.014) were found in the DHF group before admission and at the time of admission, compared with the DF group.

Hemorrhagic manifestation was noted in 72 (32.72%) out of 220 dengue patients. Most common among these were rash 60 (27.27%), epistaxis 14 (6.36%) and melena 10 (4.54%). Hepatomegaly was found in 21 (9.54%) cases. 55% of the cases had normal or increase leukocyte count, while leucopenia was seen in 45% of the cases. The laboratory data also suggested that the platelet count was significantly lower (<100000/μL) in both DF and DHF group. Thrombocytopenia with platelet count below 100,000/μL was seen in 215 out of 220 (97.72%) patient, among these 144 out of 149 (96.64%) patient with DF and in 71 out of 71 (100%) patient with DHF; thus, the platelet count was not significantly associated with bleeding manifestation.

Per laboratory parameters, the liver enzymes, SGOT was significantly (p = 0.0009) elevated in a larger proportion 176 (80%) of patients when compared to SGPT which was 100 (45.45%). SGOT was very high (>1000 IU/L) in 5 patients whereas SGPT was very high (>1000 IU/L) in 3 patients. Levels of the albumin was significantly lower (p < 0.001 Table 2) in patients with DHF. Albumin levels greater than 4 g/dl were negatively associated with DHF. Tourniquet test was significantly positive in DHF (p < 0.001).

Pleural effusion was detected in 18.18% of the dengue cases by chest X-ray and USG. It was significantly associated with DHF (p < 0.001 Table 2). USG of the abdomen detected hepatomegaly in 9.54% of the cases and gall bladder wall edema in 19.09% of the cases. Ascites were detected in 33.36% of the cases and which was significant in DHF (p < 0.001).

Table 2: Investigation

Investigation	DF (n = 149)	DHF (n = 71)	Total (n = 220)	P values
Leucopenia	73 (48.99%)	26 (36.61%)	99 (45%)	0.085
Thrombocytopenia	144 (96.64%)	71 (100%)	215 (97.72%)	0.178[+]
Raised SGOT	110 (73.82%)	66 (92.95%)	176 (80%)	0.0009[*]
Raised SGPT	67 (44.96%)	33 (46.47%)	100 (45.45%)	0.8332
Chest X-ray				
Pleural effusion	11 (7.38%)	29 (40.84%)	40 (18.18%)	<0.001
USG				
Ascites	6 (4.02%)	68 (95.77%)	74 (33.63%)	<0.001[+]
Hepatomegaly	5 (3.35%)	16 (22.53%)	21 (9.54%)	<0.001[*]
Gall bladder wall edema	16 (10.73%)	26 (36.61%)	42 (19.09%)	<0.001[*]
Dengue serology				
NS1Ag	140 (93.95%)	56 (78.87%)	206 (93.63%)	0.776
IgM	39 (26.17%)	23 (32.39%)	62 (28.18%)	0.338
IgG	4 (2.68%)	0	4 (1.81%)	0.564
Hypoalbuminemia	76 (51%)	67 (94.36%)	143 (65%)	<0.001[*]
Tourniquet test	3 (2.01%)	48 (67.6%)	51 (23.18%)	<0.001[+]

In this study, the majority of the patients were positive for NS1 followed by IgM (Table 2). Eleven patients left the hospital against medical advice. In our study, all cases of dengue virus infection either DF or DHF recovered.

DISCUSSION

Dengue is an important arboviral infection in tropical countries. In recent decades, global incidence of dengue fever has dramatically increased. This study demonstrates the differences in clinical and laboratory feature between DF and DHF during admission under appropriate management according to WHO guidelines.

Elevation of the liver enzyme, a common feature of dengue infection was significantly observed in our study.[14] In this study, a rare manifestation of DHF, acute hepatic failure was reported in 8 (3.63%) of our patients, which is also reported in previous study.[15] Abdominal pain, itching, epistaxis, ecchymosis, melena and rash were more commonly associated with DHF.

A significant proportion of the patients with DHF had tourniquet test positive. The tourniquet test is an important diagnostic parameter for DHF, which is present in 67.6% of all DHF cases. Whereas other study also reported that tourniquet test positivity as the commonest bleeding manifestation.[16] It was found to be a sensitive test in this study. The test need to be re-evaluated on a larger population. Levels of SGOT and SGPT in dengue patient were higher than those in patient with non-dengue febrile conditions. Elevation of SGOT was significantly more compared to SGPT in our study, a finding that has also been reported in earlier study.[17]

The maximum number of cases were seen in the age group 15-24 years of age (46.36%). More involvement in these age group can be explained by more exposure and diurnal adaptation of Aedes mosquito in stored water. Male to female ratio in our study was 1.36:1 whereas In earlier study also suggested that there were no significant differences.[18] Plasma leakage, which indicates that dengue causes hypoalbuminemia, is an indicator of severity, which is also explained by another study.[19] In our study, albumin level lower than 4 g/dl was significantly associated with increased risk of DHF. Therefore, this parameter may be used as early indicator of plasma leakage and a useful prognostic marker.

The majority of the cases were admitted in the rainy and winter season, it can be explained by breeding season of mosquito. Duration of hospitalization was more in cases of DHF. DF also required a hospital stay longer than 3 days. In these study, thrombocytopenia was associated with both in DF and DHF and leukopenia was seen in 101 (45.9%) patients. The main hematological abnormalities were leucopenia and thrombocytopenia, which are in agreement with the findings of another study in Saudi Arabia.[20] A plain radiograph of the chest shows pleural effusion in 40 (18.18%) patients. Chest sonography have been proven to be highly efficient method to detect small amount of pleural effusion. Ascites was detected by ultrasonographic examination of the abdomen.[21] In our study fever was present in maximum cases. Headache, abdominal pain, myalgia, joint pain, retro-orbital pain was seen commonly. This is also suggested by earlier study.[22] There was no correlation between platelet count and bleeding manifestation in our study.

CONCLUSION

Dengue is a common disease in South Asian part of the world. Our data also show the differences in the frequency of clinical symptoms, such as abdominal pain, epistaxis, itching, melena, between patient with DF and DHF. Significantly ascites and pleural effusion were found in the DHF group, compared with the DF group. Lab parameter like raised SGOT is very significant for distinguishing DHF from DF.

REFERENCES

1. Lambrechts L, Scott TW, Gubler DJ. Consequences of the expanding global distribution of Aedes albopictus for dengue virus transmission. PLoS Negl Trop Dis. 2010;4(5):e646.
2. WHO. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever, Revised and expanded edition, Regional office of SEAR; 2011:1-6.
3. Dengue. Guidelines for diagnosis, treatment, prevention and control: new edition. Geneva: WHO Guidelines Approved by the Guidelines Review Committee; 2009:3-6.
4. World Health Organization, Geneva Dengue haemorrhagic fever: Diagnosis, treatment, prevention and control. 2nd edition; 1997:1-3.
5. Tripathi P, Kumar R, Tripathi S, Tambe JJ, Venkatesh V. Descriptive epidemiology of dengue transmission in Uttar Pradesh. Indian Pediatr. 2008;45:315-318.
6. Govt. of India, Annual Report 2011-2012, DGHS, Ministry of Health and Family Welfare,New Delhi; 2012:195-197.
7. Halstead SB. Dengue in the Americas and Southeast Asia: do they differ? Rev Panam Salud publica/Pan Am J Public Health. 2006;20:407-15.
8. Tang KF, Ooi EE. Diagnosis of dengue: an update. Expert Rev Anti Infect Ther. 2012;10(8):895-907.
9. Gubler DJ. Dengue and dengue hemorrhagic fever. Clin Microbiol Rev. 1998;11:480-96.
10. Cavalcanti LP, Coelho IC, Vilar DC, Holanda SG, Escossia KN, Souza-Santos R. Clinical and epidemiological characterization of dengue hemorrhagic fever cases in northeastern, Brazil. Rev Soc Bras Med Trop. 2010;43:355-8.
11. Daumas RP, Passos SR, Oliveira RV, Nogueira RM, Georg I, Marzochi KB, et al. Clinical and laboratory features that discriminate dengue from other febrile illnesses: a diagnostic accuracy study in Rio de Janeiro, Brazil. BMC Infect Dis. 2013;13(1):77.
12. Kumar A, Sharma SK, Padbidri VS, Thakrey JP, Jain DC, Dutta KK. An outbreak of dengue fever in rural areas of northern India. J Commun Dis. 2001;233:274-81.
13. Arunachalam N, Murty US, Kabilan L, Balasubramaniyam A, Thenmozhi V, Narhari D, et al. Studies on dengue in rural areas of Kurnool District, Andhra Pradesh, India. J Am Mosq Control Assoc. 2004;20:87-90.
14. Kuo CH, Tai DI, Chang-Chien CS, Lan CK, Chiou SS, Liaw YF. Liver biochemical tests and dengue fever. Am J Trop Med Hyg. 1992;47:265-70.
15. Kumar R, Tripathi P, Tripathi S, Kanodia A, Venkatesh V. Prevalence of dengue infection in north Indian children with acute hepatic failure. Ann Hepatol. 2004;7:59-62.
16. Krishnamurti CH, Kalayanarooj SI, Cutting MA, Peat RA, Rothwell SW, Reid TJ, et al. Mechanisms of hemorrhage in dengue without circulatory collapse. Am J Tropical Med Hyg. 2001;65(6):840-7.
17. Basuki PS, Puspitasari D, Husada D, Darmowandowo W, Soegijanto S, Yamanaka A. Application of revised dengue classification criteria as a severity marker of dengue viral infection in Indonesia. Southeast Asian J Tropical Med Public Health. 2010;41(5):1088.
18. De Souza LJ, Carneiro HG, Souto Filho JT, Ferreira de Souza T, Cortes VA, et al. Hepatitis in dengue shock syndrome. Braz J Infect Dis. 2006;6:322-7.
19. Rigau-Perez JG, Clark GG, Gubler DJ, Reiter P, Sanders EJ, Vorndam AV. Dengue and dengue hemorrhagic fever. Lancet. 1998;352:971-7.
20. Ayyub M, Khazindar AM, Lubbad EH, Barlas S, Alfi AY, Al-Ukayli S. Characteristics of dengue fever in a large public hospital, Jeddah, Saudi Arabia. J Ayub Med Coll Abbottabad. 2006;18:9-13.
21. Balasubramanian S, Janakiraman L, Kumar SS, Muralinath S, Shivbalan S. A reappraisal of the criteria to diagnose plasma leakage in dengue hemorrhagic fever. Indian Pediatr. 2006;43:334-9.
22. Khan NA, Azhar EI, EI-Fiky S, Madani HH, Abuljadial MA, Ashshi AM, et al. Clinical profile and outcome of hospitalized patients during first outbreak of dengue in Makkah, Saudi Arabia. Acta Trop. 2008;105:39-44.