Look Out for Fever: Clinical Profile of Dengue in Young Adults in a Tertiary Care Center in North India

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Abstract

Background Dengue fever (DF) is a common viral disease, clinical manifestations of which vary from influenza-like illness (DF) to life-threatening dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS). The aim of this article was to study the clinical profile of DF in young adults.

Material and Methods This was an observational study conducted in the department of medicine over a period of 2 years (January 1, 2013—December 31, 2014). Patients aged between 18 and 30 years with serology proven (nonstructural protein 1 [NS1]/dengue immunoglobulin M [IgM]) DF were included in this study. The clinical and laboratory data was recorded and analyzed.

Results Out of 418 cases, the incidence of DF, DHF, and DSS was 87.32, 7.66, and 5.02%, respectively. The most common presentations were fever (99.76%) followed by vomiting (29.43%), pain abdomen (17.94%), myalgias (13.16%), petechial rash (12.92%), and bleeding (10.29%). Dengue NS1 and IgM antibodies were positive in 87.3% and 88.12% of the patients, respectively. Ascites, splenomegaly, hepatomegaly, pleural effusion, gall bladder wall edema, and pericardial effusion were present in 8.13, 6.94, 6.70, 5.98, 2.63, and 0.72% of the patients, respectively. Complications included bleeding (10.29%), acute respiratory distress syndrome (1.67%), myocarditis (1.44%), seizures (1.44%), hemarthrosis (0.24%), and encephalopathy (0.24%). The mortality rate was 3.35% with death of 14 patients. Shock, bleeding, and elevated serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase levels predicted adverse outcome.

Keywords
► dengue
► SGOT
► SGPT

Conclusion DF can present with a plethora of clinical manifestations in endemic areas. Adverse outcome is more likely if patients have elevated SGOT levels, shock, and bleeding. Continuous seroepidemiological surveillance is essential to control outbreak and minimize morbidity and mortality.

Introduction

Dengue fever (DF) is a common viral disease in tropical and subtropical regions, due to increased urbanization and population growth.[1–4] The seasonality of transmission of dengue is more in monsoon and post-monsoon.[5] In the last decade, major outbreaks and deaths have occurred in all parts of India.[6,7] Dengue infection can range in severity from an influenza-like illness (DF) to life-threatening dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS) that may turn fatal if left untreated.[8–10]

This study describes the salient clinical as well as laboratory findings of serologically confirmed hospitalized patients of DF during 2 years period from January 1, 2013 to December 31, 2014. The study group represented the adult population only and pediatric age group was not included in this study.

Materials and Methods

This observational study included young adults (aged 18–30 years) suffering from serology proven (nonstructural protein 1 [NS1] and/or immunoglobulin M [IgM]) DF, admitted in the department of medicine in our tertiary care institute over a period of 2 years from January 1, 2013, to December 31, 2014. The study design was approved by the institutional ethics committee. Informed consent was taken from all patients for using their data for academic purposes. The demographic data, clinical features, laboratory findings, and outcome were recorded in the proforma. The data of cases in the retrospective period of the study, that is, for the year 2013 (January 1, 2013—December 31, 2013), was collected from the files stored safely in medical records office. For the prospective study period (January1, 2014—December 31, 2014), detailed clinical history was taken, clinical examination was performed, laboratory and radiological findings noted, and clinical course in the hospital was followed up actively. Patients with thrombocytopenia because of other causes, for example, chronic liver disease, idiopathic thrombocytopenic purpura, leukemia as well as patients on antiplatelet drugs, were excluded from the study. The outcome of the study was in the form of an analysis of the varied clinical profile of DF and the result of treatment for the same resulting in either discharge on recovery, discharge on request, discharge against medical advice, or death of the patient. The statistical analysis was carried out using mean (range and standard deviation). Chi-squared test was applied and p-value of less than 0.05 was taken as statistically significant.

Results

Four-hundred eighteen patients were included in the study, with males comprising 319 (76.32%) of the patients and the rest 99 (23.68%) were females. Distribution of cases according to gender is tabulated in ►Table 1. The male to female ratio was 3.2:1.

Table 1 Distribution of cases according to gender in various age groups

Age group (years)	Females	Males	Total
18–20	18	57	75
20–25	45	146	191
25–30	36	116	152

Clinical Features

Three-hundred sixty-five (87.32%) patients had classical DF, 32 (7.66%) had DHF, and 21(5.02%) patients had DSS, respectively.

Out of 418 patients, fever was the commonest symptom followed by vomiting and abdominal pain. Other clinical features are summarized in ►Table 2.

Laboratory Findings

Biochemical and Microbiological Parameters
Increased levels of serum glutamic oxaloacetic transaminase and serum glutamic pyruvic transaminase (SGOT and SGPT) were noted in 55.8% cases. Rise of SGOT was more than SGPT. Dengue NS1 test was conducted in 198 patients, out of which it turned out to be positive in 173 (87.3%) patients. Similarly,

Table 2 Clinical presentation of dengue patients

Clinical presentation	No. of patients	Percentage (%)
Fever	417	99.76
Vomiting	123	29.43
Pain abdomen	75	17.94
Myalgias	55	13.16
Petechial rash	54	12.92
Bleeding	43	10.29
Headache	33	7.89
Diarrhea	20	4.78
Abdominal distension	20	4.78
Breathlessness	16	3.83
Melena	16	3.83
Cough	10	2.39
Retroorbital pain	7	1.67
Joint pains	7	1.67
Weakness	7	1.67
Jaundice	5	1.20
Urinary disturbance	3	0.72
Seizure	3	0.72
Loss of consciousness	2	0.48
Palpitations	1	0.24
Altered sensorium	1	0.24

dengue IgM test was conducted in 278 patients, out of which 245 (88.12%) patients turned out positive for the same.

Twenty-eight (6.7%) patients had coinfection with *Leptospira* (2.39%), scrub typhus (2.15%), enteric fever (0.96%), malaria (0.72%), *Salmonella* (0.24%), and *Staphylococcus aureus* (0.24%).

Hematological Parameters

Leucopenia with lymphocytosis was seen in 39% of patients. The minimum and mean platelet count at the time of admission were 2,000 and 36,798.54/μL, respectively; while the same on the day of discharge, the minimum and mean platelet count were 6,000 and 1,06,498.79/μL, respectively. One-hundred forty-seven (35.17%) patients had platelet count ranging from 1,000 to 20,000, while 125 (29.90%) patients had platelet count of 20,000 to 40,000/μL. The maximum and mean hematocrit at the day of admission were 56.2 and 42.2, respectively, while the same on the day of discharge, the maximum and mean hematocrit were 50.2 and 37.78, respectively.

Ultrasonographic and Echocardiographic Findings

Out of 418 patients, 34 (8.13%) had ascites, 29 (6.94%) had splenomegaly, and 28 (6.7%) had hepatomegaly. Pleural effusion, gall bladder wall edema, hepatomegaly, and pericardial effusion were seen in 25 (5.98%), 11 (2.63%), 8 (1.91%), and 3 (0.72%) patients, respectively.

Management and Outcome

The average duration of stay of the patients in the hospital was 5.42 days with a minimum stay of 1 day and maximum stay of 23 days.

Transfusions were needed in the form of random donor platelets and single-donor platelets in 33.25 and 27.51% patients, respectively, while packed cells were transfused in 2.39% patients.

Complications encountered were bleeding from various sites (10.29%), acute respiratory distress syndrome (ARDS) (1.67%), myocarditis (1.44%), seizures (1.44%), hemarthrosis (0.24%), and encephalopathy (0.24%). The most common site of bleeding was gum bleed. Out of 418 patients, 404 (96.64%) patients were discharged and 14 (3.35%) expired. Out of 404 patients who recovered from DF, shock was present in 45 (11.1%) patients that was managed conservatively. Out of 14 patients who expired, shock was present in 10 (71.4%) patients, *p*-value of which is statistically significant. Mean value of SGOT and SGPT in dengue patients who survived were 193.95 and 125.81 IU/L, respectively. The same values in patients who expired were 2,865.43 and 1,510.07, respectively (significantly high). Out of fourteen expired patients, bleeding was present in five patients (35.7%), out of which two (14.2%) patients had hematemesis, two (14.2%) patients had melena, and 1 (7.1%) patient had epistaxis. Shock, elevated SGOT and SGPT, and bleeding were significant risk factors for mortality.

Discussion

Dengue virus is a spherical, single-stranded enveloped RNA virus belonging to the Flaviviridae family, genus Flavivirus,

and is transmitted by Aedes aegypti (worldwide) and Aedes albopictus (United States, Asia, Latin America, and Caribbean) mosquitoes.[8] Dengue infection is caused by one of four related, but antigenically distinct, viral serotypes: dengue virus 1 (DENV-1), dengue virus 2 (DENV-2), dengue virus 3 (DENV-3), and dengue virus 4 (DENV-4). Infection with one serotype provides lifelong immunity to that serotype, but only partial and transient protection against subsequent infection by other three serotypes.[10] It is possible for a person to be infected as many as four times, once with each serotype. Sequential infection with different DENV serotypes increases the risk of developing DHF. Ninety percent of DHF infections occur in children less than 15 years of age. There is currently no specific treatment for DENV infection. Therefore, the only method of preventing DENV transmission is vector (mosquito) control.

In our study, there was a male predominance with male to female ratio of 3.2: 1. This is in agreement with other studies by Kashikunti et al, Avarebeel et al, Kauser et al, and Imam and Prashanth.[11–14] It can be attributed to increased outdoor activities, and hence increased exposure to mosquito bites and viruses. However, Tsai et al found equal incidence of dengue in males and females, while Fujimoto and Koifman reported increased incidence of dengue in females.[15,16] Our study group comprised of patients in 18 to 30 years of age with majority (45.69%) in 20 to 25 years age group. Kauser et al found maximum cases in age of 20 to 30 years, while Patil found majority of affected patients younger than 30 years.[13,17]

In this study, maximum number of patients were admitted in the rainy season (August to October) that is conducive for the growth of the vector Aedes aegypti. Transmission of dengue increases during monsoon. The correlation between occurrence of dengue and monsoon is clearly evident in this study and study conducted by Kauser et al and Imam and Prashanth.[13,14] The clinical profile of dengue revealed fever as the most common presenting symptom (99.76%), as also substantiated by Chan et al, Fujimoto and Koifman et al, Kauser et al, Mandal et al, Imam and Prashanth, Jayadas et al, and Padyana et al who have reported fever in 99.7, 79.8, 100, 100, 98.3, 100, and 94.8% of their patients, respectively.[13,14,17–21] Other presenting symptoms were vomiting and pain abdomen that can be due to liver injury caused by the dengue virus.[14] It is imperative to remember that other infections that cause fever and gastrointestinal symptoms such as typhoid, leptospirosis, enteroviral infections are common in India and may often lead to a delay in diagnosis of dengue. In DF, cutaneous manifestations can vary from maculopapular rash, petechiae, flushing to even desquamation. Petechial rash and myalgias were seen in 12.92 and 13.16% of our patients, respectively. Imam and Prashanth found rash in 20.7% and myalgia in 83.5% of their patients.[14] Jayadas et al found myalgia in 50% of their cases.[20] In a study of 62 patients in Japan by Itoda et al, rash was seen in 82% cases.[22] Karoli et al reported rash in 26% cases, while 16% had cutaneous hypersensitivity.[23] Rahim and Sikder also found rash in 78.5% in a Bangladesh-based study.[24] Bleeding was noted in 10.29%

of patients in the present study, with gums being the commonest site of bleeding (30.3%). Horvath from Australia and Sharma from India reported 63 and 69% of bleeding episodes, respectively.[25,26] Gastrointestinal tract was the predominant site of bleeding observed by Daniel et al, while Karoli et al found epistaxis (40%) as most common symptom.[23,27] Fujimoto and Koifman et al found petechiae (14.0%), gingival bleeding (13%), and epistaxis (10.9%) as common sites of bleeding.[15] Bleeding episodes were related to several factors including vasculopathy, thrombocytopenia, platelet dysfunction, and prothrombin-complex deficiency. Immune-mediated destruction of platelets and platelet consumption caused by release of high levels of platelet activating factor from monocytes have been implicated in causing thrombocytopenia during DENV infection.[14] Headache, diarrhea, abdominal distension, and breathlessness were not as frequent in our study as compared to other studies. Headache was found in 52.9, 79.14, and 80.7% patients in studies by Imam and Prashanth, Patil, and Jayadas et al.[14,16,20] Similarly, Itoda et al reported headache in 90% of their patients, while Seema et al found headache in only 9% of patients.[22,28] Retro-orbital pain that is generally considered a cardinal feature of DF was present in only 1.67% of our patients. Imam and Prashanth found retrobulbar pain in 28.9%, while Jayadas et al found retrobulbar pain in 17.9% of their cases.[14,20]

The causes of leucopenia with lymphocytosis and thrombocytopenia seen in dengue include bone marrow suppression, binding of dengue antigen to platelets, antibody-mediated immunological destruction of platelets.[29] In this study, leucopenia with lymphocytosis was observed in 39% of patients. Higher hematocrit is related to increased severity and is explained by the increased plasma permeability that is the basic pathophysiological alteration in dengue. In our study, higher hematocrit was related to severe dengue infection. DENV infection can cause inflammation of the liver with thickening of gall bladder wall, ascites, and pleural effusion. A rise in serum transaminases was observed in 55.8% of patients in this study. SGOT elevation was found to be more than SGPT, as also seen by Imam and Prashanth, Jayadas et al, and Bhushan and Kumar.[14,20,29] This finding can be explained by the fact that SGOT is also secreted by heart, muscles, and erythrocytes, while SGPT is only secreted by the hepatocytes.[29] Kauser et al found elevated SGOT and SGPT in 27.39 and 24.65% of patients, respectively.[13] Sharma and Sharma reported elevated transaminases in 90% of patients.[26] Mandal et al found raised SGOT in 83.78% and raised SGPT in 70.27% of their patients. In this study, mean SGOT and SGPT values in patients who survived were 193.95 and 125.81 IU/L, respectively, while same values in expired patients were 2,865.43 and 1,510.07 IU/L, respectively.[18] Similar observations were made by Imam and Prashanth, Daniel et al, and Bhushan and Kumar.[14,27,29] SGOT was elevated ($>$ 250 IU/L) in 84% of patients who died, thereby indicating association of abnormal SGOT with worse outcome, as also observed by Fujimoto and Koifman.[15] The detection of DENV antigens in hepatocytes and the recovery of DENV particles from liver biopsies support the view that

DENV is hepatotoxic.[30] Deranged liver function in dengue infection can be a result of the direct effect of the virus on the liver cells or the unregulated host immune response against the virus. Fulminant liver failure can occur because of the acute severe hepatitis and massive necrosis of the liver, causing hepatic encephalopathy and even death. In this study, NS1 antigen positivity was found in 87.3% of patients, while 88.12% had dengue IgM antibodies positivity. Manohar et al found 48.2% patients positive for IgM antibodies to dengue but only 29.2% of their cases were NS1 antigen positive.[31] In 28 patients (6.7%), coinfections with leptospirosis (2.39%), scrub typhus (2.15%), enteric fever (0.96%), malaria (0.72%), *Salmonella* (0.24%), and *Staphylococcus aureus* (0.24%) were seen. Bhaskar et al found coexistent serology proven leptospirosis in 6.2% and microscopy proven falciparum malaria in 4.6% of their cases.[32] On ultrasound examination, hepatomegaly, splenomegaly, gall bladder wall edema, ascites, pleural effusion, and pericardial effusion were seen in 6.70, 6.94, 2.63, 8.13, 5.98, and 0.72% cases, respectively. Similar findings have been observed by Lo et al.[17] Patil found pleural effusion in 7.36% cases and ascites in 6.13% of cases.[16] Padyana et al found gall bladder wall edema in 44% of their cases on ultrasonography.[21] The authors suggest that ultrasound features of thickened gall bladder wall, pleural effusion, and ascites in a febrile patient should strongly favor the diagnosis of DF.Complications encountered in our cases included bleeding in 44 (10.29%), ARDS in 7 (1.67%), myocarditis in 6 (1.44%), seizures in 6 (1.44%), hemarthrosis in 1 (0.24%), and encephalopathy in 1 (0.24%) patient. Patil has reported altered sensorium & convulsions as neurological complications.[17] The neurological involvement in dengue may occur because of neurotropism of the virus, immunologic mechanism, cerebral anoxia, intracranial hemorrhage, hyponatremia, and cerebral edema. Kamath and Ranjit (20%) and Méndez and González (25%) reported higher incidence of neurological manifestations in their study.[30,33] In study by Avarebeel et al, complications were seen in 6.71% of patients that included encephalitis, hepatitis, encephalitis, and ARDS.[12] In a study by Kumar et al, 14% patients developed complications that included pneumonia, renal failure, and multiple organ failure.[34] Kauser et al found pleural effusion in 13.69%, renal failure and encephalopathy in 1.36% each.[13] Kashinkunti et al have observed complications in form of hepatic dysfunction (34%), renal failure (26%), multiple organ failure (18%), encephalopathy (13%), and ARDS in (12%).[11] Out of 418 cases, 365 (87.32%) had classical DF, 32 (7.66%) had DHF, while 21 (5.02%) had DSS. Similar results were seen by Avarebeel et al with 80.59% patients of DF, 8.65% of DHF, and 0.74 of DSS. Manohar et al found DF in 58.9%, DHF in 40.9%, and DSS in 41.1% of patients.[12,31] Treatment of DF, DHF, DSS is supportive. In this study, all the patients received symptomatic treatment. In addition, transfusions were needed in the form of random donor platelets and single donor platelets in 139 (33.25%) and 115 (27.51%) patients, respectively. However, in 10 (2.39%) patients packed cells were transfused. Platelet transfusions have been used with different frequencies in different parts of the world. Avarebeel et al gave

platelet transfusion to 54 out of 134 patients.[12] Similar to our study, Fujimoto and Koifman gave platelet concentrates to 22.3% we, FFP to 21.2%, and packed red cells to only 2.6%.[15]

In our study of 418 patients, 14 (3.35%) patients expired, while 404 (96.65%) patients recovered and were discharged. Mortality rates reported by Jain et al, Bhushan and Kumar, Daniel et al, Avarbeel et al, Fujimoto and Koifman et al, and Kashinkunti et al are 1.7, 4.4, 3.2, 2,7.3, and 11%, respectively.[11,12,15,27,29,35] On the other hand, Kauser et al reported no mortality in their study.[13]

Conclusion

DF can have a plethora of clinical presentations with wide variation in serological and hematological features. In our study, we have highlighted the spectrum of findings in patients of tertiary center catering to population of North India. In this region, high mortality was seen in patients having bleeding tendency, shock, and/or markedly elevated transaminases. Continued surveillance of clinical and serological parameters is essential to devise an optimum management plan for dengue patients. Although vaccine candidates are being developed, further studies are required for a greater understanding of the humoral response to DENV infection and pathogenesis to control morbidity and mortality caused by dengue epidemics that ravage tropical countries every year.

Limitations

This is a hospital-based observational study based on hospitalized patients between 18 and 30 years of age group.

Conflict of Interest
None declared.

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