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CLINICAL AND LABORATORY PROFILE OF DENGUE FEVER PATIENTS ADMITTED IN COMBINED MILITARY HOSPITAL RAWALPINDI IN YEAR 2015

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ABSTRACT

Objective: The purpose of this study was to determine the pattern of clinical presentations, haematological and biochemical abnormalities, and outcome of dengue fever patients admitted in Combined Military Hospital (CMH) Rawalpindi in year 2015.

Study Design: A descriptive cross sectional study.

Place and Duration of Study: Department of Medicine, CMH Rawalpindi, from January 2015 to December 2015.

Material and Methods: Patients meeting the inclusion criteria were admitted at CMH Rawalpindi and blood serology was done to confirm the diagnosis of dengue fever. Cases with positive dengue serology were included in the study. Clinical symptoms, signs, investigations and outcome of these patients were recorded on a pro forma. Blood samples were taken for analysis. Chest X-Ray and ultrasound abdomen were done on required basis.

Results: Out of forty confirmed cases of dengue fever, there were 25 (62.5%) males and 15 (37.5%) females. Mean age was 40 years. There were 39 cases (97.5%) of dengue fever and one case (2.5%) of dengue shock syndrome. There was no case of dengue haemorrhagic syndrome. Maximum cases were seen in the month of October 2015. The clinical features noted were: headache and myalgias 62.5%, chills and rigors 57.5%, retro-orbital pain 42.5%, vomiting 35.0%, pruritus 27%, skin rash 20%, abdominal pain 20%, diarrhoea 10%, bleeding 2.5%, ascites and pleural effusion 2.5%, and hepatomegaly 15%. The laboratory findings were: leucopenia 85% and thrombocytopenia 92.5%. Serum alanine transaminase (ALT), urea, and creatinine were raised in 30%, 2.5% and 7.5% cases respectively. Mortality was 2.5%.

Conclusion: This study showed that patients admitted to CMH hospital had a milder presentation of dengue fever in the year 2015.

Keywords: Dengue fever, Leucopenia, Thrombocytopenia.

INTRODUCTION

Dengue fever (DF) is a viral infection transmitted to the humans through the bites of infected Aedes mosquitoes which mainly breed on the surface of clean stagnant water. Once a patient is infected with dengue virus, the illness could range from minor symptoms to serious manifestations such as dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). However in 20% cases, the infected person remains asymptomatic[1].

Dengue virus has four serotypes referred as DEN-1 to 4. Primary infection induces lifelong protective immunity to the infecting serotype, but results only in partial and transient protection against subsequent infection by other serotypes. Subsequent infection with another serotype can cause life threatening illness[2]. All four serotypes of dengue virus have been isolated in different epidemics in Pakistan. DEN1 and DEN2 were confirmed in 1998, DEN2 and DEN3 in 2006 outbreak at Karachi, and DEN-2 was the predominant serotype in 2011 epidemic at Lahore[3-5]. There is a firm evidence that patients with DEN-2 infections have a worse outcome than patients with other serotypes[6].

There is a sharp increase in the number of dengue fever cases in recent years with an

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alarming impact on both human health and the global and national economies. The actual numbers of dengue cases are underreported and often misclassified. A recent estimate indicates 390 million dengue infections per year[7]. In Pakistan, 48,188 laboratory confirmed cases were reported during 2011-2014[8].

The toll that this disease is exacting on the economy and health makes it imperative to study it in greater depth. A review of the literature revealed that presentation of dengue fever had wide temporal and regional variations. A number of studies were done in Lahore, south Punjab and in Sind. However only limited studies were carried out in Rawalpindi region.

The purpose of this study was to determine the pattern of clinical presentations, haematological and biochemical abnormalities, and outcome of dengue fever cases admitted in CMH Rawalpindi in year 2015.

MATERIAL AND METHODS

This descriptive corss sectional study with prospective data collection were carried out at CMH Rawalpindi from January 2015 to December 2015. Forty patients were selected through non-probability purposive sampling technique. Inclusion criteria were: patients 12 years or older presenting with acute fever associated with two or more of the following; headache, retro-orbital pain, myalgias, arthralgia, rash, abdominal pain, haemorrhagic manifestations, leucopenia, thrombocytopenia or circulatory collapse in whom tests for dengue fever, NS1 antigen or IgM serology or both were positive.

Patients having haematological diseases such as idiopathic thrombocytopenia (ITP), haematological malignancy, myeloproliferative disorder, myelodysplasia, bone marrow infiltrative disorder, immune disorder, and patients taking steroids or cancer chemotherapy were excluded from the study.

A detailed history was obtained and thorough physical examination was done in all patients who were included in the study. Blood samples were obtained for blood complete picture (CBC), haematocrit (Hct), liver function tests (LFTs), serum urea, serum creatinine, serum electrolytes, and prothrombin time (PT). NS1

Table-I: Distribution of clinical manifestations of dengue fever (n=40).

Symptoms/signs	No. of patients	Percentage %
Headache	25	62.5
Myalgias	25	62.5
Chills and rigors	23	57.5
Retro-orbital pain	17	42.5
Vomiting	14	35.0
Weakness/fatigue	9	22.5
Pruritus	11	27.5
Skin Rash	8	20
Joint pain	7	17.5
Diarrhoea	4	10
Bleeding	1	2.5
Abdominal pain	8	20
Hepatomegaly	6	15
Ascites	1	2.5
Pleural Effusion	1	2.5
Splenomegaly	0	0
Lymphadenopathy	0	0

antigen was done in all patients and IgM serology was done if duration of illness was more than 5 days. Further tests like chest X-Ray, ultrasound abdomen, International normalized ratio (INR), D dimers and partial thromboplastin time (PTT) were carried out if required. CBC and Hct were done daily till defervescence. A rise in Hct from baseline is considered one of the indicators of plasma leak in DSS 1. As we didn't have patients' baseline haematocrit, we arbitrarily took a value above 45% in males and 40% in females to be of significance and followed these cases for plasma leak. Leucopenia was defined as total white cell count less than 4000 x 10^9/L and thrombocytopenia if platelet count was less than 150 x 10^9/L.

The dengue fever cases were further sub-classified in to DF, DHF and DSS according to World Health Organization (WHO) definition criteria of dengue infection[1].

Data were collected on a proforma, prepared on the basis of already reported signs, symptoms and laboratory parameters in the literature.

Statistical Analysis was performed by using SPSS version 19. Descriptive statistics were used to analyze the data. Mean and standard deviation were calculated for quantitative variables. Categorical variables were presented by frequency and percentage.

RESULTS

Forty serologically confirmed cases of dengue were included in our study. There were 25 males (62.5%) and 15 females (37.5%) with a male to female ratio of 1.7:1. Patients' mean age was 40 ± 15.95 years (range 15 to 85 years). Figure shows the distribution of cases according to the month in which they presented. There were 39 cases (97.5%) of DF while only one case (2.5%) met the criteria of DSS. There was no case of DHF. Patients were admitted to hospital after a mean 4 ± 1.7 days from onset of fever. Mean temperature during the course of illness was 101.3 ± 1.13 °F and duration of fever was 5.98 ± 1.51 days. Table-I presents clinical manifestations. None of the patient in the category of DF had bleeding manifestations, jaundice, lymphadenopathy, splenomegaly, pleural effusion or ascites; however 5 of them had hepatomegaly. There was only 1 patient of DSS. He had epistaxis, haematuria, ecchymosis, bleeding from gums and lower gastrointestinal bleed. He also had hepatomegaly, bilateral pleural effusion and ascites.

Table-II shows laboratory results. On admission the mean haemoglobin was 14.5 ± 1.45

Table-II: Laboratory parameters (n=40).

Laboratory values	No. of Patients	Percentage %
HCT >45% in males	4	10
HCT >40% in females	1	2.5
Leucopoenia on admission	25	62.5
Leucopoenia during hospital stay	34	85
Thrombocytopenia on admission	31	77.5
Thrombocytopenia during hospital stay	37	92.5
Serum bilirubin (>17 µmol/L)	1	2.5
ALT (>42 U/l)	12	30
Serum Urea (>7.1 mmol/l)	1	2.5
Serum Creatinine (>115 µmol/L)	3	7.5
Hyponatraemia (≤135 mmol/l)	3	7.5
Hypernatraemia (≥150 mmol/l)	1	2.5
Hyperkalemia (≥ 5.0 mmol/l)	3	7.5
DIC	1	2.5

grams/dl in males, and 12.8 ± 1.41 grams/dl in females, white cell count was 4.09 ± 1.83 x 10^9/L and mean platelet count was 115.9 ± 44.9 x 10^9/L. Four male patients and 1 female patient were having Hct above 45% and 40% respectively. Out of these patients, only 1 male patient later confirmed to have plasma leak.

One patient died in our study. This patient had DSS. All the rest 39 patients recovered uneventfully.

DISCUSSION

Our study describes the demographic pattern, clinical features, investigations and outcome of dengue fever in patients admitted in CMH Rawalpindi. Results of this study showed that patients admitted in CMH Rawalpindi had a milder presentation of disease. In our knowledge this was the first study in which clinical features and laboratory parameters were evaluated in the Rawalpindi region during the epidemic of 2015.

Our study showed male predominance among the patients. Most studies done In India, Pakistan, and Asia pacific region showed similar gender distribution[10-15]. The reasons for this could be that men are more likely to seek health care facilities; they dominate as workforce and are more exposed to mosquito bite because of work place environment. Another reason might be that women are less exposed to mosquito bite because of their clothing. However above quoted studies were hospital based, instead population based sero-epidemiologic studies are required to find out exact gender distribution among the population.

In our study maximum cases of dengue fever were seen in the post monsoon month of October. This is in accordance with results of Rawalpindi based study by Zafar et al[16] However Almas et al reported peak incidence of dengue fever in rainy season[17]. The monsoon months in Rawalpindi are July and August, sometime stretched up to mid September. We think that time lapse for peak incidence of dengue fever following monsoon can be due to time required by Aedes mosquitoes to breed in the pooled up water.

Our study showed that 57.5% patients had chills and rigors. Chills and rigors were not reported in most of the studies; however Ahmed et al and Khan et al reported these symptoms in 80% of cases[18,19]. In our study 20% patients had abdominal pain. Interestingly this was in sharp contrast to the results of most studies which reported this symptom in the range of 41-65%[9,14,16,20].

Headache and myalgias were seen in 62.5% cases in our study. These symptoms were reported similarly by other studies[16,18,19,21].

Vomiting occurred in 35% of our patients, comparable to many studies[11,12,16,20], however other studies reported this symptoms in 57.5%,

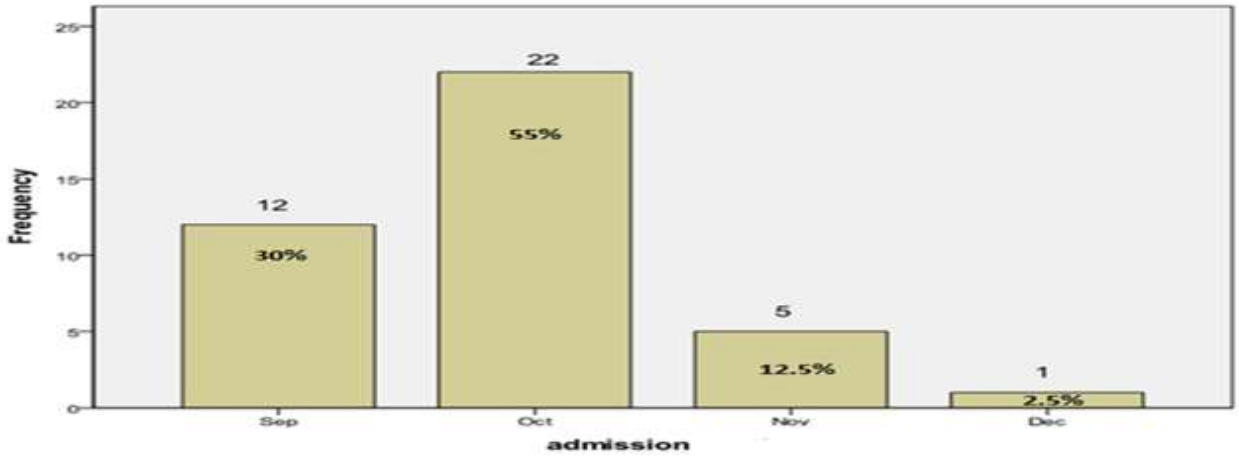

Figure: Monthly distribution of dengue fever cases (n=40).

85%, 60%, and 77.5% cases; these figure are considerably higher than ours[10,14,19,22].

In our study 27% patients had pruritus while Daniel et al and Fujimoto et al reported this symptom in 10.4%, and 8.8% cases respectively[9,20]. Skin rash in our study was 20%, comparable to other studies[18-20]. However Ahmed et al and Zafar et al documented this symptom in 56% and 41.3% cases respectively[14,16].

Retro-orbital pain was present in 42.5% of our patients. However in literature the reported incidence of retro-orbital pain had wide variations. Kauser et al, Ahmed et al and Fujimoto et al reported this symptom in 12.3%, 20%, and 16.1% cases respectively[10,14,20]. However Zafar et al reported this symptom in 65.3%[16].

Diarrhoea was reported in 10% of our cases. Similar figure have been reported by Daniel et al[9] however Zafar et al reported this symptom in 37.5%[16].

Reported incidence of bleeding manifestations had wide variations in literature. Vanamali et al and Fujimoto et al reported this feature in 32%, and 35% cases respectively[11,20]. In Rawalpindi population Zafar et al documented haematemesis in 28.8%, gum bleeding in 25%, melaena in 17.35, and haemoptysis in 12.5% cases[16]. However we noticed bleeding in only 2.5% of our cases.

In our study only one patient had pleural effusion and ascites. In other studies pleural effusion was found in 13.2% and 13.6%[9,10]. Daniel et al reported ascites in 12% of cases[9].

Thrombocytopenia and leucopenia were common findings in our study. Thrombocytopenia was seen in 92.5% and leucopenia in 85% cases. Other studies had similar pattern of cytopenias[12,14,18,19]. We found that leucopenia preceded development of thrombocytopenia. This is important as patients may present with leucopenia only. The analysis of liver functions in our study showed that biliriubin was raised in only 1 case while ALT was raised in 12 cases (30%). Other studies reported raised ALT in 80.8%, 62%, and 57% cases; these figure are higher than our study[12,14,18]. In our study only one patient had DIC highlighting the fact that patients in our series had a milder form of dengue fever.

The ratio of DF to DHF/DSS reported in literature had wide variation. In our series only one patient had DSS, comparable to other studies done in Pakistan[18,19,22]. However Riaz et al reported 39% cases of DHF/DSS in his study[23]. Wasay et al reported that combined cases of DHF and DSS rose from 12.5% in year 2000-2004 to 42% in year 2005[24]. Daniel et al from India also reported 33.6% cases of DHF/DSS in his study[9].

Mortality in our study was 2.5%. Mortality reported in literature varied from 0.68% to 7.3%[13,20].

The difference in clinical features, laboratory parameters, and mortality in our study as compared to rest of the studies could be explained by the fact that only one out of 40 patients in our series had DSS and rest of the cases were of DF. The reason for low incidence of DHF/DSS in our setup in year 2015 could be that the dengue virus was of a less virulent serotype. The other reasons could be that the population under study was relatively healthy, had better access to health facilities and most importantly probably naïve to the dengue virus. It is expected that in future we may encounter epidemics with higher morbidity and mortality.

We decided to do hospital based study with the view to better document and understand our patients but this was also the major limitation of our study. The other limitations of our study were that serotyping of dengue virus was not done and status of previous dengue exposure was not known. We suggest that sero-epidmiologic studies should be done in future to document previous exposure and to find out the serotype in upcoming epidemic. Moreover studies on the clinical presentation of dengue fever should be multicenter so that they can be better representative of dengue epidemics.

First DF vaccine, Dengvaxia (CYD-TDV) has been registered in Mexico in December 2015 and likely to be approved in 2016 by WHO[25]. This is likely to change dengue fever landscape all over the world; in future studies will be required to investigate the changing pattern of dengue fever.

CONCLUSION

This study showed that patients admitted to our hospital had a milder presentation of dengue fever in year 2015. This study further highlighted the temporal and regional variations in presentation and severity of dengue fever.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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