ORIGINAL ARTICLE

Dengue Fever Outbreak 2010: Clinical Experience in a Teaching Hospital of Lahore Pakistan

MUJEEB-UR-REHMAN ABID BUTT, MUZAMMIL SHAHZAD, AMIR IQBAL, *SEMAAB*

ABSTRACT

Objective: To study the clinical characteristics, laboratory findings and the outcome of patients presented to a teaching hospital in recent dengue outbreak in Lahore.
Study design: An observational study
Place and duration of study: Nawaz Sharif Social Security Teaching Hospital Lahore.
Patients and methods: All patients above 12 years of age presented to the hospital having typical features of Dengue Fever according to WHO criteria were included. They were either admitted or kept in outpatient clinic follow up. All underwent hematological investigations according to protocol. All the patients were divided into two groups; dengue proven and dengue probable depending upon the positivity of the dengue serology. Patients having features, both clinical or laboratory consistent with other febrile ailments were excluded from the study. Study spans between 1st September 2010 to 30th November 2010.
Results: Total 100 patients were included. Male to female ratio was 67:33. All patients either had fever on presentation or had recent history of fever. Majority of patients were in age bracket of 12-45 years (71%), while dengue serology was positive in 68% of patients. Overall myalgia, headache, and vomiting were the three most common symptoms present in 69%, 62% and 44% of patients respectively while encephalopathy was observed in 9% of patients. Thrombocytopenia, leucopenia and deranged liver function tests were present in 95%, 77% and 80.88% of patients. Concordance of clinical and laboratory features has been observed in dengue proven and dengue probable cases.
Conclusion: There is a variable manifestations of dengue fever but keen index of suspicion especially during the peak season of disease helps in reaching to the diagnosis irrespective of negative serological diagnosis.
Key words: Dengue fever, outbreak

INTRODUCTION

Benjamin Rush described a condition as 'Break Bone Disease' in 1780 which is now called as Dengue Fever. This is a rapidly emerging mosquito born viral infection manifesting as Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS)[1]**.** This disease has recently affected a huge population in the urban and suburban areas of Pakistan. Annual occurrence rate of DF and DHF worldwide is about 50-100 million and 50,000 cases respectively and out of these around 2000 die annually due to its complications[2]. There is a 1% mortality rate in patients with treated DHF/DSS but in untreated cases it escalates to 20%.[1] Its incidence world wide is expected to increase in future due to lack of antiviral medicines and vaccines[3,4]. Nearly 2.5 billion people worldwide are at risk of contracting this disease due to their habitat[5].

Department of Medicine Nawaz Sharif Social Security Teaching Hospital, The University of Lahore
Corresponding to Dr Mujeeb-ur-Rehman Abid Butt,
Email: mujeeb_b@yahoo.com

Dengue virus is a member of family flaviviridae and has got four closely related serotypes: DENV1,DENV2, DENV3 and DENV4. All are transmitted between humans by the mosquitoes of genus Aedes Aegypti. Due to significant increase in larval population of Aedes Aegyptii in rainy season, epidemics of DF generally coincide with this time period[6]. DF is characterized by high grade fever, musculoskeletal pains, retro bulbar pain and rash. Appearance of hemorrhagic manifestations in addition to above constitute DHF while DSS is characterized by shock, capillary leak and altered mental status[7]. In subcontinent first proven case of dengue was reported in 1940's and since then this disease is striking in more and more parts of subcontinent inflicting heavy morbidity and mortality[1]. Different outbreaks have been reported in Pakistan starting from 1994 till to date affecting Karachi, upper Punjab and parts of Khyber Pakhtoon Hua[4,8].

Purpose of this study is to observe the pattern of clinical manifestations of patients with serological proven DF and sero negative probable DF and their outcome.

MATERIAL METHODS

This observational study was carried out from 1st September 2010 to 30th November 2010 at Nawaz Sharif Social Security Teaching Hospital Lahore Pakistan. All patients with ages above 12 years, who were either hospitalized or treated in medical outdoor clinic due to acute febrile illness, were evaluated for clinical features of DF, DHF and DSS. All patients with typical clinical features of Dengue Fever as per WHO criteria[9] and associated thrombocytopenia or leucopenia were included in the study. Patients were divided into two groups. One group was labeled as dengue fever confirmed in which IgM was positive while the other group was labeled as dengue fever probable as their IgM was negative but their clinical features and other lab parameters were consistent with dengue fever/DHF/DSS. Bleeding manifestations were further split into two groups; one group was noted to have petechial hemorrhages while the second one were having other bleeding manifestations like bleeding from gums, malena, hematoma, hematemesis, hematuria and epistaxis.

All the patients underwent battery of investigations including complete blood count (CBC), thick and thin film for malarial parasite, liver function tests, typhidot, IgM for Dengue Fever, coagulation profile including Activated Partial Thromboplastin Time (APTT) and Prothrombin Time (PT). These tests were performed on the time of presentation and depending upon the state of patient and his/her previous blood profile reports samples were redrawn on day 3 and on the day of discharge either from the hospital or from the outdoor clinics. Patients having clinical as well as laboratory findings consistent with other febrile illnesses like malaria or typhoid etc were excluded from the study. Two milliliters of blood in EDTA anticoagulant, 2.8 ml blood in citrate anticoagulant and 3 ml blood in plain bottle was collected for blood counts, malarial parasite, dengue specific IgM, PT, APTT, Typhidot, and Liver function tests. Patients having positive serology for dengue fever were labeled as confirmed or proven cases while patients having negative serology for dengue fever but having clinical features and other laboratory reports consistent with dengue fever were considered as dengue probable cases. CBC was performed on Sysmax automated haematology analyzer, PT and APTT were performed by noticing clot formation visually and liver function tests were performed by standardized method as described by manufacturer using microlab 200 (Merck Marker). Dengue specific IgM were performed by standard enzyme linked immunosorbent assay (ELISA).[10] Blood counts were serially monitored till the platelet counts started showing a rising trend and were in the safe limits.

RESULTS

We selected 100 patients having clinical presentations and preliminary reports consistent with dengue fever. Serology was positive in 68 patients. Among the seronegative group other laboratory parameters were consistent with DF and therefore regarded as dengue probable cases. Out of all patients 67 were men while 33 were females. Age ranged from 12 to 77 years with mean of 31. There were 71 patients in the age range of 12 to 45, 21 patients in range between 46 to 60 and 8 patients were above 60 years of age. Number of male and female patients in the above three age ranges among dengue proven and dengue probable groups were 45& 22, 23 & 10, and 8 & 2 respectively. Details of gender and age distribution are shown in Table 1. All the patients in both the groups had either fever on presentation or had a very recent history of fever. Headache was present in 62 while petechial rash was seen in 19 patients. Beside these clinical manifestations other features are shown in Table 2. Fever lasted from 1 to 9 days. Day 1 temperature ranged from 98-104^{0}C(mean 101^{0}C), Day 3 temperature ranged from 99-102^{0}C(mean 99.6^{0}C), while day 5 and day 7 temperature ranged from 97-100^{0}C(mean 98.6^{0}C) and 98-99.6^{0}C(mean 98^{0}C) respectively. Three patients developed severe thrombocytopenia with platelet count less than 10,000/cmm while 9 patients in total from both groups developed hemorrhagic manifestations consistent with DHF.

Table 1: Age and Gender distribution of cases with DF n=100

	Male (n=67)		Female (n=33)		
Age	**Dengue Proven**	**Dengue Probable**	**Dengue Proven**	**Dengue Probable**	**Total**
12-45	30	15	17	9	71
46-60	10	5	5	1	21
>60	5	2	1	0	8
Total	45	22	23	10	100

Petechial hemorrhages were present in 14(20.58%) and 5(15.6%) patients of DF confirmed and probable groups respectively. Among the other bleeding manifestations 4 cases of bleeding from gums, 3 of hematoma and 2 of malena were recorded. While

none of the patient was noted to have epistaxis, hematemesis and hematuria. Among 9 patients distributed in the two groups who had encephalopathy dengue serology was positive in 7(10.29%) cases; all patients underwent lumbar puncture and had CSF examination including its culture for pyogenic infection. Details of all the laboratory findings are shown in Table 3.

Table 2: Clinical Features of Dengue Fever cases n=100

Clinical features	DEN Confirmed n=68	DEN Probable n=32
Fever	68(100%)	32(100%)
Vomiting	30(44.11%)	14 (43.7%)
Headache	42(61.76%)	20 (62.5%)
Abdominal pain	18(26.47)	9 (28.12%)
Diarrhea	14(20.58%)	7 (21.8%)
Retro-orbital pain	7(10.29%)	4 (6.25%)
Petechial rash	14(20.58%)	5 (15.6%)
Other bleeding manifestation	6(8.82%)	3(9.3%)
Myalgia	47(69.11%)	22(68.75%)
Skin rash	8(11.76%)	4(12.5%)
Encephalopathy	7(10.29%)	2 (6.25%)
Hepatomegaly	15(22.05%)	7(21.8%)
Splenomegaly	8(11.76%)	2(6.25%)

Mean total leukocyte count was lowest on day 2 of admission and started rising on day 8. Platelet count kept on falling and was lowest between day 2 and day 4 of admission and started improving at day 7. All cases improved and were either discharged from hospital or from outdoor clinics on by 10th day except 12, who were discharged in 2 to 3 weeks time.

Table 3: Laboratory findings of Dengue Fever n=100

Profile	Dengue Confirmed n=68	Dengue Probable n=32
White Cell Count<4000/cmm	52(76.47%)	25(78.12%)
Platelet Count<150,000/cmm	65(95.58%)	30(93.75%)
Raised ALT >40U/L	55(80.88%)	25(78.12%)
Raised AST >40U/L	55(80.88%)	25(78.12)
PT>3sec	1(1.47%)	1(3.12%)
APTT>5 sec	12(17.64%)	6(18.75%)

DISCUSSION

Dengue fever is an old disease; the first record of a clinically compatible disease being recorded in a Chinese medical encyclopedia in 992AD. Due to expansion of shipping industry in 18th and 19th century port cities grew in population and this created ideal situation for the growth and spread of vector mosquito aedes[11]. Dengue is an important emerging disease of the tropical and sub-tropical regions today. Since the first confirmed case of dengue in the subcontinent during the 1940s, intermittent reports of the infection and its sequelae have come from various parts of the region both from Pakistan and India[8,1214]. Research on dengue has grown exponentially, generating several specialized reviews.[1] Though DF is confused with number of bacterial, viral, rickettsial and parasitic infections, the identification of dengue cases is possible by distinct clinical features even though patients do present with varied manifestations[15]. Though it is difficult to diagnose mild dengue fever infection but definitive diagnosis is made by virus isolation and serology[10]. Multivariate analysis identified 3 laboratory features that together are highly predictive of a diagnosis of dengue and able to rule out the possibility of SARS: platelet count of <140x10^9 platelets/L, white blood cell count of <5x10^{9}cells/L, and aspartate aminotransferase level of >34 IU/L. A combination of these parameters has a sensitivity of 75% and a specificity of 100%[16]. Male to female ratio in this study was 2.03:1 respectively, and the majority of the patienst (71%) were in the age bracket of 12 to 45 years. Ashwini[1] observed that male to female ratio to be 1.8:1 and though they also have the maximum cases in the age group of 15-44 but out of 466 cases 57.3% cases fell in this age group. Latter study also incorporated the pediatric population and that can lead to disproportion in the findings. The clinical profile of dengue patients in this study revealed that fever was present in all the patients. Similar studies[1, 4, 8] in and around Pakistan have also substantiated fever as being the most common presenting symptom though Ashwini found 83.9% patients presenting with fever. Other common symptoms observed in this study were Myalgia(69%), headache(62%), vomiting(44%) and abdominal pain(27%), and it is consistent with many other studies done in recent past but Indians [1] recorded headache in 47.6% of patients. Retro-orbital pain is generally taken as a cardinal feature of dengue fever and it was present in 11% of patients in this study but among the huge number of patients studied in India this symptom was not recorded[1]. Shahid et[18] al also found strong congruence among Dengue confirmed and Dengue probable cases regarding different clinical features though he only had male patients, but in none of the dengue probable group he could find hepatomegaly and in dengue proven cases he could found hepatomegaly in only 1.5% of cases. In this study hepatomegaly was detected in 22.05% and 21.8% of patients among dengue confirmed and dengue probable cases respectively. An exclusive study on DSS, authors found hepatomegaly, aleterd

sensorium, diarrhea and rash in 97.4%, 58%, 50% and 42% respectively [17]. Similarly others have found these features in 53.2%, 10.3% and 13.9% and 21.7% respectively [1]. We found the last three features in 9%, 21% and 12% of patients respectively distributed in the two groups. In a study by Singh[19] fever was present in all the cases with an average duration of fever being 4.5 +/- 1.2 days with headache (61.6%), backache, (57.8%), vomiting (50.8%) and abdominal pain (21%) being the other major complaints. Hemorrhagic manifestations in the form of a positive tourniquet test (21%), gum bleeding and epistaxis (40%), hematemesis (22%), skin rashes (20%) and malena (14%) were also observed[19]. Most common bleeding manifestation in this study was petechiae seen in 21% of patients which is consistant with the findings of Ashwini[1] but Shahid[18] found petechial rash in his 8 patients (7.47%) out of 107, whereas during the 2006 outbreak of dengue in North India, malena (50%) and hematemesis (38%) were found to be the most common bleeding manifestations[20]. DHF was present in 9% of our patients which is consistent with other studies[1] while DSS was not observed in any of our patients. Other studies from Karachi have shown the occurrence of DHF to be between 1.86% to 2.75%.[18, 21] Occurrence of DHF and DSS was seen in 8.8% and 7.3% of patients respectively by Ashwini. [1]; while DHF was seen in 10% of the patients by HATI.[22] Reason of our patients having more DHF than those done earlier in Karachi could be that as there had been an outbreak of DF in Lahore in 2008 and now more patients are coming with seconday dengue virus infection involving different serotype but this could only be proved if one does the genotyping of the virus. We found 9% of our patienst to have encephalopathy manifesting as altered sensorium or seizures but in the study by Kamath[23], 20% of the patients had neurological manifestations. While in the study by Mendez[24] 25% patients presented with neurological manifestations. In this study liver enzymes were deranged in over 80% and 78% of patients respectively among dengue confirmed and dengue probable patients. Shahid[18] found raised ALT in 47% of dengue proven and 63% of dengue probable patients. Serology was positive in 68% of patients in our series; one reason of having negative serology among the remaining patients could be that the said test was done before the stipulated time period of 5 days. Studies have shown positive serology between 37-48.75% of patients.[12, 18] None of our patient died in this series but the mortality related to DF/DHF in other studies flutter between 1.32% to 8.5% [1, 22, 25]. In this study virus was not isolated either by cell culture or by polymerase chain reaction (RT-PCR), and due to this we cannot comment upon the genotype of dengue virus prevalent in this region and as paired sera were also not done in all the patients so we could have missed dengue confirmed patients who were rather considered under dengue probable. Further studies are required to detect the serotype more prevalent in our part of the world

CONCLUSION

The present study highlights the variable manifestations of DF including its complications and outcome of the disease. It further describes the more severe manifestations of this disease as compared to other studies done in the past in this region and recommends for effective vector control in order to prevent its subsequent epidemics.

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