ORIGINAL ARTICLE

Hematological Profile in Patients with Dengue Fever: Report of 47 Patients in 2010

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ABSTRACT
Background: Dengue fever is one of the major causes of morbidity and mortality in tropical and sub-tropical countries. The routine haematological examination is an important investigation for the diagnosis and proper management of such patients.
Objective: To evaluate haematological changes in patients with dengue fever.
Design: Prospective, follow-up study.
Place and duration of study: Department of Medicine, Shaikh Zayed Federal Postgraduate Medical Institute, Lahore from 3rd Oct 2010 to 20th Nov 2010.
Patients and Methods: Forty-seven serologically confirmed, admitted cases were evaluated for age, gender and haematological changes.
Results: Forty-seven out of 59 patients had positive serology for dengue fever. Male to female ratio was 1.09:1. Their ages ranged from 5 to 68 years with a mean of 31.3±15.39 years. Analysis of hematological data revealed normal levels of haematocrit, total leukocyte and platelet counts in 81 %, 36.2 % and 6.4 % patient respectively. Serial analysis of data over seven days showed marked improvement of platelet count after second day of admission.
Conclusion: Thrombocytopenia is a consistent finding in DF.

Key words: Dengue, thrombocytopenia, leucopenia, haemoconcentration

INTRODUCTION
Dengue fever (DF) is caused by a single stranded positive sense RNA virus belonging to flaviviridae family. Four serotypes of dengue virus are identified namely DENV 1-4. The virus is transmitted mainly by the bite of female *Aedes egypti* and also by *Aedes albopictus*.[1] The period of transmission from humans to mosquitoes begins one day before the start of fever up to the sixth day of illness corresponding to the viremia phase. After a female bites an individual in the viremia phase, viral replication (extrinsic incubation) begins in the vector in from 8 to 12 days. In humans, the incubation period ranges from 3 to 15 days (intrinsic incubation) with an average of 5 days. [2]

Most of dengue infections are asymptomatic. Those with symptoms can be classified into 3 patterns, based on their severity; undifferentiated fever DF, dengue haemorrhagic fever (DHF) and which if accompanied by shock, is called dengue shock syndrome (DSS).[3]

According to WHO, about 50 million cases of DF occur annually worldwide and 2.5 billion people live in risk areas.[4] In 2005, the World Health Assembly, through resolution 58.3, included dengue fever as an emergent public health disease, with implications for health safety due to the spread of the epidemic beyond national boundaries.[5]

Routine hematological examination is a part of diagnostic workup of the patients and sometimes one can predict the infection by the specific hematological changes observed in these diseases. Leukopenia is the most prominent hematological change, sometimes with counts of less than 2 x 10^9/L. Lymphocytosis is a common finding, with the presence of atypical lymphocytes. Values of hematocrit (Hct) concentration vary according to the duration of illness. There is a 20% increase in Hct from the patient's baseline, associated with thrombocytopenia (< 100 x 10^9/L).[6]

The present study was done to assess the hematological profile of patients with DF in order to

identify laboratory markers for diagnosis and better management of the disease.

MATERIAL AND METHODS

Fifty nine suspected cases of DF of all ages and both genders were included in the study. Those with underlying liver disease, known positive serology for viral hepatitis B and C or co-infections such as malaria, enteric fever, urinary tract infection or pneumonia were excluded. Sera of all cases were tested for anti dengue immunoglobulins (IgM and IgG) by enzyme linked immunoassay (ELISA). Forty seven cases were confirmed to have DF on the basis of Ig M alone or both IgM and IgG positivity. After written consent, detailed clinical evaluation and daily blood samples were taken for 7 days to see laboratory variables including Hct, total leucocyte count (TLC) and platelet count. All information was entered in SPSS 22.0. Demographic variables were reported as frequency and percentages. Numerical data was reported as Mean ± SD.

RESULTS

Out of 47 serologically diagnosed cases, 24 were males and 23 females (male to female ratio 1.09:1). 16 males and 21 females were found to have positive Ig M and while 8 males and 2 females had positive IgM and Ig G to dengue virus. Their ages ranged from 5 to 68 years with a mean of 31.32±15.39 years. The mean ages of males and female patients were 33.3±17.6 and 29.2±12.8 respectively. Maximum number of male and female patients belonged to second and fourth decades of life, respectively (Table 1).

Table 1: Age and gender distribution of patients with dengue fever (n=47)

Age group	Males	Females	Total	%
<10 yrs	1	1	2	4.5
11-20 yrs	6	6	12	25.5
21-30 yrs	5	6	11	23.4
31-40 yrs	3	7	10	21.3
41-50 yrs	3	2	5	10.6
51-60 yrs	4	0	4	8.5
61-70 yrs	2	1	3	6.3

Analysis of hematological data revealed (table 2 A, B, C) normal levels of Hct, total leukocyte and platelet counts present in 81 %, 36.2 % and 6.4 % patients respectively. No patient had ≥ 20% normal Hct levels. 29 (61.7 %) patient had leucopenia and 94% had thrombocytopenia at time of presentation.

Table 2: Haematological parameters in patients with DF (n=47)
Table 2A: Haematocrit Normal range (NR)= Males 40-52%, Females 36-47%

Gender	Range	Mean± SD	n(%) NR	n(%) <NR	n(%)>NR	n(%)≥20%NR
Male (n=24)	13.7-50.4	42.9± 6.9	20 (83.3%)	4 (16.7%)	0	0
Females (n=23)	20.4- 51.0	38.7±4.4	18 (78.3%)	4 (17.4%)	1 (4.3%)	0
Total (n=47)	13.7- 51.0	40.96±6.3	38 (81%)	8 (17%)	1 (2%)	0

Table 2 B: TLC NR= 4-11x10^9/l

Gender	Range	Mean± SD	n(%) NR	n(%)<NR	n(%)>NR
Male (n=24)	0.2-26	5.5± 3.4	11(45.8%)	12 (50%)	1 (4.2%)
Females (n=23)	0.9- 24.5	4.6±3.2	6 (26.1%)	17 (73.9%)	0
Total (n=47)	0.2- 26	5.1±3.4	17 (36.2%)	29 (61.7%)	1 (2.1%)

Table 2 C: Platelets NR= 150-450x10^9/l

Gender	Range	Mean± SD	n(%)NR	n(%)<50	n(%)50-100	n(%)100-150
Male (n=24)	4-501	107.9±81.4	1 (4.2%)	11(45.8%)	9(37.5%)	3(12.5%)
Females (n=23)	5-381	102.3±61.8	2(8.7%)	10 (43.5%)	3(13%)	8(34.8%)
Total (n=47)	4- 501	105.6±73.9	3(6.4%)	21(44.7%)	12(25.5%)	11(23.4%)

Serial analysis of data showed marked improvement of levels of platelets after second day of admission, almost constant values of TLC and slight worsening of Hct value on day 5 (figure 1).

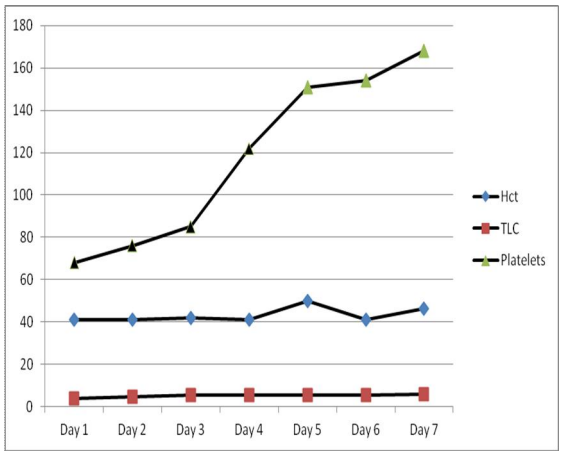

Figure 1: Mean Hct, TLC and platelets (n=47)

DISCUSSION

Dengue is one of the most important mosquito borne viral diseases affecting humans with over half of the world's population living in areas at risk. Recent years have seen many epidemics of dengue and presently it is endemic in 112 countries worldwide.[9] A range of haematological changes are observed in DF. Haemoconcentration and raised Hct are well known findings in patients of DHF[10]. Vasculopathy causes increased vascular permeability, leading to haemoconcentration and shock. [11] Haemoconcentration (Hct ≥20% of the initial value) is one of the WHO criteria to diagnose DHF. Only few studies reported no such association [12]. Development of leucopenia (TLC<4x10^9/L) and thrombocytopenia (platelets <100x10^9/L) are important investigations for measuring dengue severity. WHO also used platelets to categorize dengue infection into grade I-IV. [3] Low platelets were explained by bone marrow suppression and immune-response induced platelet destruction by liver and spleen. [13] A decrease in TLC during the illness is mainly due to a decrease in granulocytes, i.e., neutrophils. Presence of atypical lymphocytes and even plasma cells along with thrombocytopenia is reported consistently along with other laboratory findings.[14]

In present study thrombocytopenia was the most frequent abnormality observed in almost all (94%) patients at the time of presentation. The frequency of this finding varies from 19-97.7% in different studies. [1,7,8,15,16] It can be inferred that thrombocytopenia is a consistent finding in DF and it increases the risk of severity. In present study the platelet count improved from 2nd day onwards while Ahmed S et al., noticed such improvement at 7th day. [17] In another study thrombocytopenia in DF and DHF/DSS patients was observed on 4th and 1st days of the disease respectively.[18]

The normal range of Hct differs in males and females. Our 83.3% and 78.3% of males and females respectively had Hct in the normal range. In study by Kirtilaxmi[7] 25% patients under 12 years while 3% and 2% of male and female patients in that order above 12 years, showed increased Hct. In other studies [19,20] 8.5-10% of patients had Hct ≥20% of the expected age and gender. Singh et al.,[21] found Hct ≥20% in 52% of the cases while in our study no patient had such raised Hct**.** Ahmed S et al., [17]reported normal Hct in all cases which closely concurs with our findings. On 5th day of admission there was a slight increase in Hct which returned to normal over the next two days while another study reports fall in Hct during hospital stay once the fever settled and hydration status was improved.[17]

Leucopenia and neutropenia are well established features of DF which is due to the direct marrow suppression by the virus.[16] Some studies concluded that TLC more than 5x10^9/L is a prognostic factor for dengue severity [18] while others found leucopenia[12,22]. In the present study 61.7% patients had TLC< 4x10^9/L at the time of presentation and improvement in TLC was seen from 3rd day till 7th day when 95.83% of patients had TLC above 4x10^9/L. A number of other studies showed leucopenia in 62.5% children[7]and a variable percentage of adults (4.1%, 17%, 68%,71%, 90%).[7,10,15,21,23]

CONCLUSION

Haematological changes are good predictors of the severity of dengue infection. Thrombocytopenia is a consistent finding in most cases.

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