Original Research Article

Hematological parameters in dengue fever: A study in tertiary care hospital

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A R T I C L E   I N F O

A B S T R A C T

Introduction: Dengue fever has been known for more than a century in the tropical countries. Dengue fever is now the most common cause of arboviral disease in the world, with an estimated annual occurrence of 100 million cases of dengue fever and 250,000 cases of dengue hemorrhagic fever and a mortality rate of 25,000 per year. Most cases of dengue hemorrhagic fever are reported from Asia, where it is a leading cause of hospitalization and death among children. Dengue fever presents with confusing clinical profile and has to be differentiated from other febrile illnesses like malaria, typhoid, leptospirosis etc. Dengue is diagnosed by reverse transcription polymerase chain reaction (RT-PCR) and detection of NS1 antigen with corresponding IgM, IgG antibodies by Enzyme immunoassay & Immunochromatographic test. These tests may not be available in the periphery. So the hematological parameters like platelet count, hematocrit, lecocyte count and peripheral smear findings will aid in the diagnosis of Dengue Fever.
Materials and Methods: 100 cases with proven diagnosis of dengue by serology were taken. Detailed history, physical examination and investigations including Complete blood count, coagulation profile, Liver function tests were done. Their stay in hospital and outcome were observed.
Results: Dengue infection was more common in adult age group with slight male preponderance. It presented commonly as dengue fever with other constitutional symtoms. Petechial ecchymosis was the most common sign elicited clinically. Hematological findings like raised hemotocrit, platelet count and atypical lymphocytes were seen in majority of the cases. Supportive treatment was the mainstay mode of management. Overall mortality was seen in 2% of the cases.
Conclusion: Raised hematocrit, thrombocytopenia, leucopenia and atypical lymphocytes in the peripheral smear will aid in early diagnosis of Dengue infection. Early recognition and prevention rather than treatment of complications is most important for favourable outcome of the disease.

1. Introduction

Dengue epidemics are known to have occurred regularly over the last three centuries in tropical, subtropical and temperate areas around the world. The first epidemic of dengue was recorded in 1635[1] in the French West Indies, although a disease outbreak compatible with dengue had been reported in China as early as 992 AD.[1] The first dengue fever in India was reported during 1956 from Vellore and the first dengue haemorrhagic fever occurred in Calcutta in 1963.[2] In India the annual incidence is estimated to be 7.5 to 32.5 million.[3] All the four serotypes i.e. Dengue 1, 2, 3 and 4 have been isolated in India. The Dengue virus infection may be asymptomatic or may cause may cause undifferentiated febrile illness (viral syndrome), dengue fever (DF), or dengue haemorrhagic fever (DHF) including dengue shock syndrome (DSS). Though Dengue infection is self limiting disease, it can prove lethal if not diagnosed and treated at the early stage. Diagnosis of Dengue is by viral isolation, detection of viral genomic sequence

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by reverse transcription polymerase chain reaction (RT-PCR) and detection of NS1 antigen.[4–7] The haematological parameter of upmost importance for Dengue diagnosis is the platelet count.[5,7,8] Many studies and literature have proven the importance of decrease in platelet count and rise in hematocrit as a predictive and recovery parameter of DHF/DSS.[9] The other hematology parameters like total white cell count and atypical lymphocyte count aid in diagnosis and prognosis in dengue.[9–11]

In the present study, we have emphasised the importance of platelet count, rise in hematocrit, total leucocyte count and atypical lymphocytes on peripheral smear and total leucocyte count in diagnosing Dengue infection even in peripheral areas with very little resources where viral isolation and genomic sequencing may not be possible. This will help in alerting the clinicians in preventing complications and mortalities.

2. Materials and Methods

It was a prospective study done from August 2016 to August 2018. All the patients of both sexes aged >15years admitted at medicine wards with proven case of Dengue fever using IgM/IgG ELISA Test were included in this study. All adult patients who were negative for dengue IgM/IgG ELISA Test were excluded from the study. Demographic data like age, gender, address and occupation was recorded on predesigned and pretested proforma. All baseline investigations like complete blood count, coagulation profile, liver function test, kidney function test, X-ray chest, ultrasound abdomen were done at admission. The level at which the hematocrit and hemodynamic status stabilized during recovery was used as an index of each patient baseline (normal) hematocrit. The ratio was calculated to evaluate the degree of hemoconcentration in patients as follows.[12]

[(Highest HCT – Recovery HCT) / Recovery HCT] X 100

A value of 20% or more was considered as evidence of significant hemoconcentration. The patients who bleed enough to lower his hematocrit were excluded from these calculations. Blood sample for serological testing were centrifuged for detection of IgM antibodies by MAC ELISA test. All cases were graded according to severity criteria based on the technical guidelines from the WHO.[13–15]

2.1. Statistical methods

Descriptives, Frequencies, Crosstabs, Chi-Square Test were used.

The Statistical software namely SPSS (version 16.0) and Minitab (version 11.0) were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

3. Results

The male:female ratio was 3:2, majority (32%) of the patients were in the age group of 15 to 25 years and the least patients were more than 55 years of age. Fever was the most common presenting symptom followed by vomiting, backache and myalgia. 54% of the patients with dengue virus infection at the time of admission had dengue fever, 17 (17%) were DHF Grade I, 12(12%) were DHF Grade II, 17(17%) were in DSS that is DHF Grade III + Grade IV. The mean temperature among the dengue patients during the hospital stay had decreasing trend. Out of 100 patients, 15 (15%) had hematocrit levels > 20%, 57 (57%) had < 20% and 28 (28%) had normal hematocrit and the results were statistically significant. Thrombocytopenia in 97% of patients as seen in Table 1. Leucocyte count was normal in majority of the cases as seen in Table 2. Peripheral smears showed atypical lymphocytes in 97% of the cases. LFT in the present study, out of 100 patients, 53(53%) patients had normal liver function test and 47 (47%) had deranged liver function. Activated partial thromboplastin time in 64(64%) patients was normal and in 36 (36%) patients aPTT was raised and the findings were statistically significant (P<0.005). Bleeding manifestations were seen commonly when the platelet dropped below 10,000/cu.mm as depicted in Table 3. Classical Dengue fever showed no positive IgG antibodies while DHF 1, 2, 3 and 4 showed positivity. The mean Platelet count among the dengue patients during the hospital stay had increasing trend (Table 4). In present study there was no mortality in dengue fever and grade-I, II and III dengue hemorrhagic fever. Two (2%) patients with dengue hemorrhagic fever Grade IV succumbed to death.

Majority 18% of the patients received platelet transfusion followed by 10% received vitamin K, 5% received fresh frozen plasma and least being 3% received steroid.

Table 1: Platelet count on day

Platelet count (/mm3)	No. of patients	Percentage
<10,000	12	12%
10,000-20,000	29	29%
20,000-50,000	42	42%
50,000-1,00,000	14	14%
>1,00,000	3	3%
Total	100	100%

Table 2: Leucocyte count

Leucocyte count (/mm3)	No. of patients	Percentage
<4000	22	22%
4,000-11,000	62	62%
>11,000	16	16%
$X2 = 37.520$, DF = 2, P = 0.000		

Table 3: Correlation between thrombocytopenia and bleeding

Platelet count	Bleeding manifestations		Without bleeding manifestations		Total	
	Number	%	Number	%	Number	%
<10,000	10	10%	2	2%	12	12%
10,000 –20,000	11	11%	18	18%	29	29%
20,000 –50,000	18	18%	24	24%	42	42%
50,000 –1,00,000	5	5%	9	9%	14	14%
>1,00,000	2	2%	1	1%	3	3%
Total	46	46%	54	54%	100	100%
P = 0.000						

Table 4: Platelet trend during the hospital stay

Duration	Platelet count (/mm3)	
	Mean	SD
Day 1	36892.7835	28659.01272
Day 2	61333.3333	29993.87693
Day 3	89437.8947	38918.92604
Day 4	105242.4242	44510.34819
Day 5	120447.3684	54025.36810
Day 6	127687.5000	56757.63532
Day 7	179666.6667	65178.72864

4. Discussion

In the present study, the sex ratio was comparable to the studies done by Agarwal et al[16] and Sharma et al[17] with males being affected the most. Fever was the most common mode of presentation as was also seen in studies done by Sharma et al,[17] Rachel Daniel et al,[18] SK Agarwal et al[19] and Eva Harris et al.[20] Petechial/ecchymosis was the most common sign seen in our study as well as study done by Sharma S et al[17] while the studies done by Rachel Daniel et al[18] and Krishnamurthy K et al[21] showed hepatomegaly as the most common sign of presentation. Dengue viral infection presents most commonly as dengue fever as seen in our study as well as studies done by Eva Harris et al[20] and Kalayanarooj S et al.[22]

Hemoconcentration with an increase in the hematocrit of 20% or more is considered to be definitive evidence of increased vascular permeability and plasma leakage.[23] In the present study, Hct> 20% was present in 15 (15%) of cases and <20% in 57 (57%). Sharma S et al[17] showed an epidemic of DHF in adults in Delhi during 1996 that raised Hct> 48% were present in 6 (6.12%) cases and Hct> 20% were present in 14 (14.28%) cases. Hematocrit was raised in more than half of the patients in a study done by Nazis et al[24] and Joshi AA et al.[25] In one of the study, a raised hematocrit of more than 20% was seen in only 1 (2.17%) patient[26] while in another, an increase in hematocrit levels was above 45% in DHF AND DSS.[27] In the present study a low Hct value is probably due to high prevalence of anemia in this region.

Thrombocytopenia ($<1, 00,000/mm^3$) is one of the defining criteria for dengue haemorrhagic fever and was seen in 97% of the cases in the present study, study done by Sharma S. et al,[17] Joshi AA et al,[25] Tahlan A et al[26] and Surendra Nath Singh Yadav.[28]

Dengue infection had no much impact on the total leucocyte count. The leucocyte count was normal in majority of the cases as seen by in the present study,and studies done by Krishnamurthy K. et al[21] and Joshi AA et al.[25] While the studies done byNazish Butt et al,[24] Shamsunder Khatroth,[27] Surendra Nath Singh Yadav[28] and Meena KC et al[29] observed leucopeniain more than 50% of the cases.94% of the cases showed leucopenia in a study done by Fu-Xi Qiu et al.[30] Peripheral smear showed atypical lymphocytes, few showing dark basophilic cytoplasm and large nucleus while few had plasmacytoid morphology. Similar observations were seen in studies done by Singh Yadav[28] and Choudhary et al.[31]

Liver function tests were normal in 53% of cases while was deranged in 47% of the cases. Sharma S et al[17] observed elevation of SGOT in 88.4% of cases and SGPT in 76.7% of the cases. Raised liver transaminases of more than 80% were seen in studies done by Mohan et al,[32] Deshwal et al,[33] Kularatneet al[34] and Mandal et al.[35]

In our study out of 100 patients, 64(64%) had normal PT/APTT and 36 (36%) patients had raised PT/APTT. Prolonged APTT was seen in 26% cases,20% and 10% of the cases in studies done by Irfan Arshad, Choudhary et al and Ayub et al[31,36,37] respectively. Bleeding manifestation was seen in majority of the patients whose platelet count dropped below $20,000/mm^3$. But was also seen in patients whose platelet count was more than 1 lakh/mm^{3}. So bleeding manifestation is independent of the platelet count.

Similar observations were made by a study conducted in Indonesia.[38] Average time taken for the rise of the platelet count to near normal was six to seven days.

In the present study out of 100 patients 54 (54%) were only IgM positive out of which 2 (2%) had dengue hemorrhagic fever. Remaining 44 (44%) patients had both IgM and IgG positive dengue serology in which all had dengue hemorrhagic fever. A study conducted in Thailand[39] in 2000 recorded 32 IgM positive patients out of which 23 had dengue hemorrhagic fever and 133 patients with both IgM and IgG positive out of which 53 had dengue hemorrhagic fever.

There is no specific treatment indicated for dengue fever. Despite majority (41%) of the patients with the platelet count being less than $20,000/mm^3$ only 18 patients received platelet transfusion in combination with Vitamin K, fresh frozen plasma and fluid therapy. Even though steroids are not indicated in dengue fever some of the patients (3%) responded to steroid therapy in the form of rapid recovery and stabilizing bloodpressure.

In the present study, overall out of 100 patients of DF, DHF/DSS, 2 (2%) patients died.

There was no mortality in DF and DHF Grade I and Grade II.

In DSS, one patient died, due to hypovolemic shock and respiratory failure. Another due to acute kidney injury and disseminated intravascular coagulation (DIC).

Hence, early recognition of the disease and prevention rather than treatment of complications are most important for the favorable outcome of the disease.

5. Conclusion

Hematological parameters like reduced platelet count, raised hemotocrit, coagulation profile and atypical lympho-cytes in peripheral smear supported by liver function tests and serology aid in early detection of Dengue infection and thus help in preventing complication and mortality.

6. Source of Funding

None.

7. Conflict of Interest

None.

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