Haematological Profile and its Clinical Implications in Dengue Viral Infections

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Abstract

Introduction: Dengue fever is the most common arboviral disease in the world. Transmission to humans of dengue virus initiates a spectrum of illness, from inapparent to severe and sometimes lethal infections. Complete blood count (CBC) is an important part of diagnostic workup of patients. Comparison of various findings in CBC and peripheral blood film can help the physician in diagnosis, management and assessment of prognosis of the patients.

Objective: To find out the pattern of haematological findings in dengue infection.

Methods: This cross sectional study was carried out on 62 dengue cases in CMH Savar from May to October 2019. Diagnosis of dengue was based on clinical features, haematological and biochemical findings and confirmed by serological tests. Haematological parameters analyzed include haemoglobin (Hb), haematocrit, total leucocyte count (TLC), differential leucocyte count (DLC), platelet count and peripheral blood film.

Results: Important findings in haematological profile were haemoconcentration, raised haematocrit, low WBC count, early neutrophilia and late lymphocytosis, reactive lymphocytes in peripheral blood and thrombocytopenia. Haemoglobin ranged from 10.0-18.5gm/dl. Haematocrit was raised in 13(20.96%) cases. Thrombocytopenia (platelet count <1.5 Lac/mm³) was observed in 59(95.16%) cases. Platelet count 1-1.5 Lac was seen in 4(6.45%) cases, 50,000-1 Lac in 25(40.32%) cases, 20,000-50,000 in 26(41.93%) cases and <20,000 in 4(6.45%) cases. Leucopenia (TLC<4000/mm³) was seen in 46(74.19%) cases and >11000mm³ in 2(3.22%) cases. On peripheral blood smear reactive lymphocytes including plasmacytoid lymphocytes were seen in almost all the cases.

Conclusion: CBC examination gives enough clue for early diagnosis of dengue infection which can be confirmed by dengue serology. Serial CBC examination is also important in disease monitoring, treatment of the patient and prediction of prognosis.

Key words: Dengue fever, Complete Blood Count (CBC), Haematological Profile, Dengue Viral Infections.

Introduction

Dengue viruses are a major cause of morbidity and mortality among tropical and subtropical areas of the world. It is a positive-stranded encapsulated ribonucleic acid (RNA) virus. The four serotypes of dengue virus, 1,2,3 and 4 form an antigenic subgroup of the flaviviruses (Group B arboviruses).[1] Transmission to humans of any of these serotypes initiates a spectrum of host responses, from inapparent to severe and sometimes lethal infections. In humans one serotype produces lifelong immunity against reinfection but only temporary and partial immunity against the other serotype.[2] Classic dengue fever is marked by rapid onset of high fever, headache, diffuse body pain (both muscle and bone), weakness, vomiting, sore throat, altered taste sensation and a centrifugal maculopapular rash.[3] The WHO 2009 classification divides dengue fever into two groups. Dengue with or without warning signs and severe dengue, though the 1997 WHO classification is still widely used. The 1997 classification divided dengue into 1) Undifferentiated fever 2) Dengue fever (DF) and 3) Dengue haemorrhagic fever (DHF). DHF is further subdivided into I to IV Grade; III and IV Grades are called as Dengue Shock Syndrome (DSS).[3,4]

Four main characteristic manifestations of dengue illness are (i) continuous high fever lasting 2-7 days (ii) haemorrhagic tendency as shown by a positive tourniquet test, petechiae or epistaxis (iii) thrombocytopenia (platelet count <100x10⁹/L and (iv) evidence of plasma leakage manifested by haemoconcentration (an increase in haematocrit 20% above from the baseline), pleural effusion and ascites etc.[4,5] Laboratory diagnosis of dengue is routinely done by demonstration of anti dengue immunoglobulin M (IgM) antibodies or by nonstructural protein 1 (NS1) antigen in patients' serum/plasma depending upon the day of illness using either enzyme–linked immunosorbent assay (ELISA) or immune chromatographic based rapid card test. Leucopenia is the most prominent haematological change, sometimes with

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counts of less than 2.0×10^9/L. At the onset of the disease there is short period of neutrophilia which is replaced later by neutropenia and lymphocytosis with the presence of atypical lymphocytes. The haematocrit should be monitored regularly. With the progression to DHF there will be a 20% increase in haematocrit from the patient's baseline[6,7], associated with thrombocytopenia ($<100 \times 10^9$/L). The Platelet count tends to fall over the course of the disease and have been found to predict the severity of the disease.[8]

Early diagnosis of dengue is important for provision of specific care which ensures marked reduction in the morbidity of the disease itself. This study focused on clinical presentation and haematological parameters serially during acute and convalescence phase. Thrombocytopenia, raised haematocrit, leucopenia, lymphocytosis with atypical lymphocytes are the consistent haematological findings in dengue infection.[9] The objective of this study was to find out the pattern of haematological findings in dengue infection.

Materials and Methods

The study was conducted in CMH Savar during the dengue outbreak from May 2019 to October 2019 in Bangladesh. A total of 62 cases diagnosed as dengue based on rapid immunological card tests (NS1 antigen and IgM antibodies) were studied. Their clinical features and haematological findings were noted. Complete blood count was carried out in auto analysers (Sysmex XN-500). Haematological parameters analysed include Hb, haematocrit, total leucocyte count (TLC), differential leucocyte count (DLC) and platelet count. Leishman stained peripheral blood smears were made of every patient to confirm the autoanalyzer values as well as to see the morphology of white blood cells like atypical/ reactive/ plasmacytoid lymphocytes. Haematocrit raised >20% of normal was considered as haemoconcentration. Leucopenia was taken as total leucocyte count <4000/mm³. Thrombocytopenia was taken as platelets count <1.5 lac/mm³.

Results

In this study, adult predominance was observed in age distribution of patients. The mean age of dengue patient was 37.68±14.11 years and the most belonged to 20-40 years age group which included 25 patients (40.32%). Regarding presenting symptoms fever was present in all the cases. The most frequent other symptoms were headache 50(80.0%) and body ache 45(72.58%) cases (Table-II). Total leucocyte count ranged from 2,000-12,500/mm³ and mean TLC was 4,177.74±1,880.65/mm³. Leucopenia was observed in 46(74.19%) cases. In normal adult total leucocyte count ranges from 4000-11000/mm³. Platelet count ranged from 10,000-2.2 Lac/mm³ and mean

platelet count was 64,979.03±37,486.18/mm³. Thrombocytopenia (platelet count <1.5 lac) was observed in 59(95.16%) cases. In normal adult platelet count ranges from 150-410×10⁹/L (Table-III). Haemoglobin ranged from 10-18 gm/dl and mean Hb was 11.34±2.01 gm/dl. Haematocrit ranged from 25%-55.3% and mean haematocrit was 38.33±6.69%. Normal value of Haemoglobin ranges from 13-17gm/dl in adult male and 11-16gm/dl in adult female. Normal value of haematocrit in adult male is 0.40-0.50L/L and in adult female is 0.36-0.46L/L. Neutrophil ranges from 21%-86% and lymphocytes from 08%-75% of total leucocyte count. Most of the patients show early neutrophilia followed by leocopenia and lymphocytosis. In normal adult neutrophils constitute 40-80% and lymphocytes constitute 20-40% of the total leucocyte count (Table-IV).

Table-I: Age distribution of patients studied (n=62)

Age in years	Frequency	Percentage
<20 years	10	16.12
20 - 40	25	40.32
41 - 60	23	37.09
61 - 70	04	06.45

Table-II: Clinical features of patients with dengue fever (n=62)

Signs and Symptoms	Frequency	Percentage
Fever	62	100.0
Headache	50	80.64
Body ache	45	72.58
Anorexia/ Nausea	22	35.48
Vomiting	18	29.03
Bleeding manifestations	04	06.45
Pleural effusion and ascites	05	08.06

Table-III: Total leucocyte and platelet count of patients with dengue fever (n=62)

Laboratory parameters		Frequency	Percentage
Leucocyte count/mm³	<4000	46	74.19
	4000-11000	14	22.58
	>11000	02	03.22
Platelet count/mm³	<20,000	04	06.45
	20000-50000	26	41.93
	50000-1.0 Lac	25	40.32
	1-1.5 Lac	04	06.45
	>1.5 Lac	03	04.83

Table-IV: Haemoglobin, haematocrit and differential leucocyte count of the patients.

Parameter	Range	Mean± SD
Haemoglobin (gm/dl)	10-18.5	11.34±2.01
Haematocrit (%)	25-55.3	38.33± 6.69
Neutrophils (%)	21-86	52.53±16.45
Lymphocytes (%)	08-75	31.18±11.68

Discussion

A total of 62 patients with fever and dengue IgM positive were studied. Out of 62 patients, 50(80.64%) patients were diagnosed to have DF. Seventeen (27.41%) patients were diagnosed to have DHF and 4(6.45%) patients were diagnosed to have DSS based on WHO criteria. Number of severe dengue patients (DHF and DSS) was high in the present study. This study comprised of 44(70.96%) males and 18(29.03%) females. The ages ranged from 7 to 70 years. Maximum patients 25(40.32%) fall in the age group of 20-40 years. Mean age was 37.68±14.11 years. Most of the patients were adults because they form the working age group and having more exposure to insect bites. In the study done by Ahmed AB et al, mean age of the cases was 29.39+SD 10.59 years (range 15 to 69) which was near to this study.[10] In this study, we found that fever was the commonest symptom in dengue infection, followed by headache 80.64% and body ache 72.58%. Other prominent symptoms were anorexia, nausea, vomiting and bleeding manifestation (skin haemorrhage, mucosal bleeding etc). These findings were comparable to those documented by others but the frequencies varied slightly.

For analysis of haematological profile blood samples were taken on the day of admission and then daily or intermittently till their discharge as per requirement of the individual patient. In this study haematocrit was raised in 13(20.96%) cases. Studies done by Gajera VV et al and Butt et al showed haematocrit values raised in 28% and 50% respectively.[11,12] While in this study we have found fewer cases with raised haematocrit. The fact was that due to fluid infusion to the patient actual haeamatocrit value could not be obtained in most of the cases. Rising haematocrit levels are a marker of the critical phase of dengue infection. The extent up to which haematocrit rises from the baseline can indicate the severity of plasma leakage and progression of disease from dengue fever to dengue haemorrhagic and shock state. Serial haematocrit examination also gives the guideline of fluid therapy.

In this study, TLC ranged from 1,500-14,440/mm³ and mean TLC was 4900/mm³. TLC less than 4000/mm³ was seen in 74.19% cases and >11000/mm³ was seen in 3.22% cases. In studies done by Yaseen et al and Gajera et al, TLC <4000/mm³ was seen in 50% and 39% respectively and >11000/mm³ was seen in 12% cases.[11,13] Leucopenia has been reported among dengue patients in many studies. In this study, percentage of leucopenic patient was high because CBC was examined daily in all the admitted patients and it was keenly observed that in most of the cases leucopenia (<4000/mm³) developes later i.e starting on 4th-5th day of fever which was counted in this study. In studies by Yaseen et al and

Gajera et al lower percentage of leucopenia may be due to random CBC examination. Leucopenia is the most prominent haematological change in dengue infection sometimes with counts of less than 2000/mm³. In this study, it is also observed that in most of the cases there is initial neutrophilia i.e higher percentage of neutrophil in differential count (upto 4-5 days from the onset of fever) developing leucopenia and lymphocytosis later on. Atypical lymphocytes were seen in almost all the cases of the studied population similar to other studies.[14] In some patients, atypical lymphocytes was the first finding. Atypical and plasmacytoid lymphocytes on the peripheral smear were representative of augmented immune response to control the spread of dengue virus infected cells.

In this study, thrombocytopenia (platelets <1.5 lac/mm³) was seen in 95.16% cases. In a study done by Shekar et al, thrombocytopenia was seen in 61% cases.[15] Reason for the high percentage of thrombocytopenia in our study was that we were dealing with more severe cases of dengue infection. In studies done by Gajera et al, Tahlan A et al and Ahmed AB et al, platelet count <1 lac/mm³ was seen in 81% , 67.37% and 54.7% cases respectively.[10,11,16] In this study, it was 55(88.70%) which corresponds with that of Gajera et al. Out of 62 cases, mild thrombocytopenia (50,000-1.5 lac/mm³) was seen in 29(46.77%), moderate thrombocytopenia (20,000-50,000/mm³) in 41.93% and severe thrombocytopenia (<20,000/mm³) in 6.45% cases. In study by Ahmed AB et al, moderate and severe thrombocytopenia were found in 16.98% and 3.77% of the patient's respectively.[10] Higher number of moderate and severe thrombocytopenia observed in this study was due to increased number of severe cases. Bone marrow suppression, immune mediated destruction and spontaneous aggregation of platelets to virus infected endothelium may be responsible for such thrombocytopenia. Platelet count starts falling from as early as 3rd day of the onset of symptoms and starts recovering by 7th to 9th day of illness.

Conclusion

Haemoconcentration, leucopenia, thrombocytopenia, neutrophilia at the onset and lymphocytosis later along with plasmacytoid lymphocytes in peripheral blood smear are the important haematological findings that gives enough clue to test for dengue serology so that dengue can be diagnosed in their initial stages. This facilitates early treatment and some guidelines about management so that fatality rates can be reduced.

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