International Journal Dental and Medical Sciences Research
Volume 4, Issue 6, Nov-Dec 2022 pp 779-783 www.ijdmsrjournal.com ISSN: 2582-6018

Hematological Parameters in Dengue Positive Cases: A Study in Tertiary Care Teaching Hospital

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Submitted: 15-12-2022 Accepted: 26-12-2022

ABSTRACT
Introduction:Dengue fever has been known for more than a century in tropical countries. Dengue fever is now the world's most common cause of arboviral disease. Over the past two decades, there has been a global increase in the frequency of DF, DHF, and its epidemics, with a concomitant increase in disease incidence. Dengue fever presents with a 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,and IgG antibodies by Enzyme immunoassay &Immunochromatographic test. The serology of definite diagnosis is costly and inaccessible in many hospitals.So the hematological parameters like platelet count, hematocrit, leucocyte count, and peripheral smear findings will aid in the diagnosis of Dengue Fever.**Materials and Methods:** This is a study conducted in the pathology department over a period of 5months from April 2022 to August 2022. Patients with documented NS1 positivity were included in the study.Hematological analysis was obtained from an automated hematology analyzer - Horiba Pentra XLRand subsequent peripheral smearswere screened for estimation of platelets and differential counts.**Results:**Dengue infection was more common in the adult age group with slight male preponderance.Hematological findings like raisedhematocrit, decreased platelet count and atypical lymphocytes were seen in the majority of the cases.**Conclusion:** Raised hematocrit, thrombocytopenia, leucopenia, and atypical lymphocytes on the peripheral smear will aid in the early diagnosis of Dengue infection. Early recognition and prevention rather than treatment of complications are most important for a favorable outcome of the disease.

KEYWORDS: Dengue fever, Hematocrit, Thrombocytopenia,Leucopenia,Atypical lymphocytes.

I. INTRODUCTION

Dengue is a major preventable and treatable cause of morbidity and mortality among children and adults, mainly in tropical and subtropical regions.[1]According to the estimates of the WHO, about 50 million cases of dengue fever occur annually worldwide and 2.5 billion people live in the risk areas.[1,2,3,4]In 2005, the International Health Regulation (IHR)included dengue fever as an emergent public health disease, with implications for health safety due to the spread of the disease beyond national boundaries.[1,2,4]The incidence of dengue fever (DF) has increased manifold in the last four decades. In developing nations like India, unplanned urbanization and migration of the population from rural to urban areas with a lack of proper sanitation facilities are important factors resulting in this situation.[4]The disease is mainly found in tropical and subtropical regions around the world.[5]The first dengue fever in India was reported in 1956 from Vellore and the first dengue haemorrhagic fever occurred in Calcutta in 1963.[6]In India the annual incidence is estimated to be 7.5 to 32.5 million.[7]Dengue fever is caused by four closely related but serologically distinct dengue virusstrains called DEN-1,DEN-2, DEN-3, and DEN-4, also referred to as an arbovirus (arthropod-bornevirus) that belongs to the genus flavivirus of the family Flaviviridae.[1,2,4]All 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 undifferentiated febrile illness (viral syndrome), dengue fever (DF), or Dengue Haemorrhagic Fever (DHF) including Dengue Shock Syndrome (DSS). Though Dengue infection is a self-limiting disease, it can prove lethal if not diagnosed and treated atan early stage. Diagnosis of dengue is by viral isolation, detection of the viral genomic sequence by Reverse Transcription Polymerase Chain Reaction(RTPCR), and detection of NS1 antigen.[8] The hematological parameter of utmost importance

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for dengue diagnosis is the platelet count.[9,11,12] Manystudies and literature have proven the importance of a decrease in platelet count and a rise in hematocrit as a predictive and recovery parameter of DHF/DSS.[13]The other hematology parameters like total white cell count and atypical lymphocyte count aid in the diagnosis and prognosis of dengue.[13-15]In the present study, we have emphasized 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 few resources where viral isolation and genomic sequencing may not be possible. This will help in alerting the clinicians in preventing complications and mortalities.

II. AIMS AND OBJECTIVES

To study hematological parameters in dengue-positive cases.In the present study, we have emphasized the importance of hematocrit, platelet count, total leucocyte count, and atypical lymphocytes on peripheral smear in diagnosing dengue infection even in peripheral areas with very few resources where viral isolation and genomic sequencing may not be possible.The objective is to help in alerting clinicians to prevent complications and mortalities.

III. MATERIALS AND METHODS

This study is conducted in the Department of Pathology, B.J. Medical College,Ahmedabad for a period of 5 months from April 2022 to August 2022. All the patients of both gendersadmitted to medicine wards with a proven case of Dengue fever using the NS-1 Antigen Test were included in this study. All patients who did not havea fever and who had a feverand tested negative for dengue NS-1 Antigen were excluded from the study. Results of the NS-1 Antigen Test were obtained from LIS.Hematological analysis was carried out usingan automated hematology analyzer (Horiba Pentra XLR) and subsequently,Leishman stainedperipheral smearwas examined for estimation of platelet count and differential counts.

IV. RESULTS

A total of 100 NS-1 Antigen positive dengue cases were seen during the study period. Out of these, 64(64%) were males and 36(36%) were females with an M:F ratio of 1.77:1 and tested positive for dengue(Table 1).A maximum number of cases were seen in August (54%).

Table 1: Gender-wise distribution of cases

Month	Number of Cases	Male	Female
April	8	4	4
May	12	9	3
June	8	5	3
July	18	11	7
August	54	35	19
Total	100	64	36
Percentage		64 %	36 %

Cases ranged from 0-70 years of age with a maximum number of patients in the third decade.

Table 2:Age-wise distribution of cases

Age Group	Number of cases(%)
0-10	17(17%)
11-20	27(27%)
21-30	31(31%)
31-40	6(6%)
41-50	10(10%)
51-60	7(7%)
61-70	2(2%)

Hemoglobin was ranging from 4.5 g/dl to 17.7 g/dl and Hb-wise distribution is given in Table 3. 57% of the patients had decreasedHb while 4% had increased Hb.

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Table 3: Hemoglobin percentage of patients

Hb (g/dl)	No. of cases(%)
<8	7(7%)
8-10	15(15%)
10-12	35(35%)
12-14	27(27%)
14-16	12(12%)
>16	4(4%)

Hematocrit distribution is givenin the Table 4showing 22% of the cases had raised hematocrit suggesting hemoconcentration.

Table 4: Hematocrit of patients

Hematocrit	No.of cases (%)
<30	25(25%)
30 to 35	27(27%)
35-45	26(26%)
>45	22(22%)

Platelet counts of the patients were grouped asmild,moderate, and severe thrombocytopenia (Table 5).In this study, 74% of patients had thrombocytopenia, and out of them,23% of the patients had severe thrombocytopenia.

Table 5: Platelet count of patients

Platelet count	No. of cases(%)
<50000(severe)	23(23%)
50-100000(moderate)	22(22%)
100-150000(mild)	29(29%)
>150000	26(26%)

Total leucocyte counts were grouped asleucopenia, leukocytosis, and normal WBC count.Among them 40% of the patients had lymphocytosis and 25% of patients were having atypical lymphocytes. 21% of the cases showed leukocytosis withneutrophiliain a few cases.

Table 6: Total leucocyte count of patients

Total leucocyte count /cu mm	No. of cases(%)
<4000	23(23%)
4000-11000	56(56%)
>11000	21(21%)

V. DISCUSSION

Being a tropical country,India provides suitable weather for Aedes to grow and an increase in the disease burden has been noticed in recent years. Dengue fever is a self-limiting disease. Dengue hemorrhagic fever causes morbidity and mortality. No antiviral treatment is available hence fluid and electrolyte replacement with supportive therapy are the available modalities of treatment. Since no vaccine is available for the disease, vector control is the only way to check the transmission of thedisease.[1]

The clinical manifestations of Dengue include fever, headache, muscle& joint pain, nausea, vomiting, and rash. Dengue fever presents with a confusing clinical profile and has to be differentiated from other febrile illnesses like malaria, typhoid, leptospirosis, etc.

It is diagnosed by Reverse Transcription Polymerase Chain Reaction(RT-PCR),detection of NS1 Antigen with corresponding IgM, and IgG antibodies by ELISA &Immunochromatographic test. These tests may not be available in the periphery. So the hematological parameters like

platelet count, hematocrit, leucocyte count, and peripheral smear findings will aid in the diagnosis of Dengue Fever.

Most of the patients are within the normal range of hematological profile in the early course.

A totalof 100 NS-1 Antigen positive dengue cases were seen during our study period. Studies by Patel et al and Meena et al and Deshwal et al were showing male preponderancein dengue positive cases. Similar results were seen in our study in which theM:F ratio was 1.77:1.[1,16,17] This may be due to the increased risk of exposure of male gender to mosquito bites during outdoor occupational activities.

The rise in hematocrit was seen in the study by Patel et al and Meena et al, and Deshwal et al which was due to hemoconcentration attributed to plasma leakage as a result of increased capillary permeability occurring in the critical period.[1,16,17]It aids in the prognostication and management of dengue.In the present study 22% dengue positive cases showed a rise in hematocrit.

Thrombocytopenia was a frequent finding in a study by Patel et al,Meena et al, and Deshwal et al.[1,16,17]Similar results were found in our study having severe thrombocytopenia in 23% of the dengue-positive cases.They required immediate prophylactic platelet transfusion to prevent any hemorrhagic complications.Thrombocytopenia is due to the direct and antibody-mediated destruction of the platelets and megakaryocytes and also due to the suppression of the bone marrow by the virus.[1]Otherexplanation for thrombocytopenia includes the presence of antibodies directed against the platelets.[5]

A study by Patel et al showed leucopenia in nearly half the patients while in the study by Deshwal et al, leucopenia was seen in only 4% of cases with leukocytosis being a more prominent finding.[1,17] In our study 23% of patients were having leucopenia and21% had leukocytosis.Leukocytosis along with neutrophiliais usually observed in patients with Classical Dengue in the first few days of the disease, followed by leucopenia.[2] Leucopenia is due to the direct suppression of bone marrow by the virus.[1]

Dengue causes leucopenia with lymphocytosis and thrombocytopenia.[18]The causes include bone marrow suppression and binding of dengue antigens to platelets and antibody-mediated immunological destruction of platelets.[18] WBC changes are poor indicators of the severity of the disease. The changes in WBC count are useful in differentiating dengue fever from other febrile illnesses.[18]

The atypical lymphocytes may represent the anamnestic antibody response to the dengue virus since the anti-dengue IgG antibody has been found to rise rapidly to high titers early in the course of secondary dengue infection.[19]Atypical lymphocytes are seen in a large percentage of patients; however, atypical lymphocytes are also seen as a non-specific response to any viral infection.[20]

VI. CONCLUSION

Dengue infection is now endemic in India and no longer seasonal though the peak incidence remains during the rains.This can be attributed to improper sanitation and unplanned urbanization. Stagnant water is the commonest breeding ground.Measures to maintain proper sanitation and to create awareness for the same are required.Any patient with fever and other clinical symptoms suspicious of dengue should be subjected to a complete hematological profile as well as specific tests for dengue. Early and prompt diagnosis with aggressive measures for proper sanitation can greatly limit dengue-afflicted mortality.

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