

**HEMATOLOGICAL MANIFESTATIONS IN DENGUE FEVER – AN OBSERVATIONAL STUDY**M. K. Malathesha<sup>1</sup>, Ashwini H. N<sup>2</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: BACKGROUND:** Dengue is a major preventable and treatable cause of morbidity and mortality among children and adults that occurs mainly in tropical and subtropical regions. Early diagnosis of dengue is important for provision of specific care which ensures marked reduction in the morbidity of the disease itself. **OBJECTIVE:** To evaluate hematological changes in serologically proven patients with clinical manifestations of Dengue in Bapuji & Chigateri Hospital, Davangere. **METHODS:** Clinical, hematological and serological information from Patients diagnosed with dengue infection in Bapuji & Chigateri hospital Davangere from April 2013 -June 2013. **RESULTS:** 221 cases of classic dengue predominated (90.2%), with mild clinical manifestations lacking complications. The main hematological findings were raised hematocrit (79.6%), lymphocytosis (66%) monocytosis (84.6%), basophilia (52.9%), thrombocytopenia (100%) and atypical lymphocytes (87%). In dengue hemorrhagic fever, thrombocytopenia was more prolonged and the number of atypical lymphocytes was higher, while the other hematological abnormalities presented daily evolution similar to those in classic dengue. The hematological changes observed in dengue presented according to the clinical course of the disease and its severity.

**KEYWORDS:** dengue hemorrhagic fever, thrombocytopenia.

**INTRODUCTION:** Dengue Fever is the most common arboviral disease in the world, and presents cyclically in tropical and subtropical regions of the world. The four serotypes of dengue virus, 1, 2, 3, and 4, form an antigenic subgroup of the flavi viruses (Group B arboviruses).<sup>1,2</sup>

The geographic distribution of dengue virus has greatly expanded and the number of cases has dramatically and increased during the past three decades.<sup>3</sup>

Transmission to humans of any of these serotypes initiates a spectrum of host responses, from in apparent to severe and sometimes lethal infections. Complete Blood count (CBC) is an important part of the diagnostic workup of patients.

Comparison of various finding in CBC including peripheral smear can help the physician in better management of the patient.

The present communication documents the observations on hematological parameters with intent to evaluate: (i) the utility of certain hematological parameters as diagnostic markers of dengue fever namely, (i) Increased hematocrit & "cut off" value of hematocrit diagnostic of DHF in Indian population. (DHF) (ii) Lymphocytosis with atypical forms, Monocytosis, Basophilia; and (iv) decreased platelet count.

**MATERIALS AND METHODS:** This was an observational study. 221 patients, who presented with fever and found positive for Dengue IgM antibodies via capture enzyme-linked immunosorbent assay (MAC-ELISA). The patients were selected from outpatient department and inpatient of Bapuji Medical

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College and Hospital, Chigateri government hospital, Davangere, a tertiary care center in the state during the period April 2013 to June 2013.

The study was approved by the ethics committee of the hospital.

**Exclusion criteria:** Patients with serologically negative dengue and other co infections like malaria, Typhoid with positive Dengue Ig M/ IgG were excluded from the study.

A detailed history was taken and a careful clinical examination was performed. The laboratory investigations like hemoglobin (Hb), the total and the differential leucocyte counts (TLC and DLC), platelet count, hematocrit (Hct), Peripheral smear examination was done in all the patients. Other relevant investigations were performed.

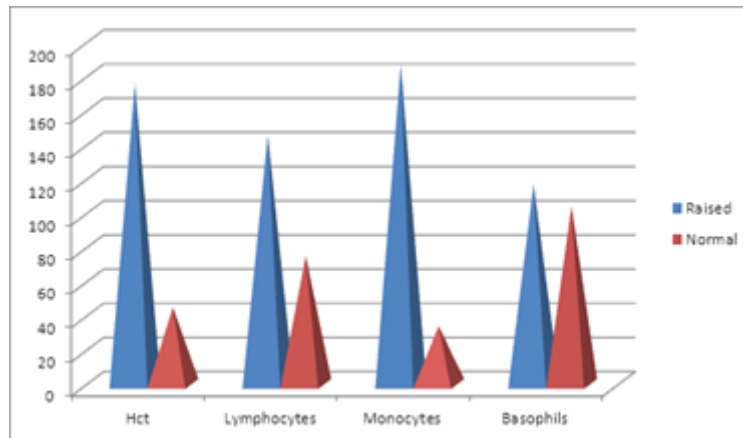
**RESULTS:** In this study, total 221 dengue MAC ELISA positive patients are included and analyzed.

The patients were both males and females ranging from 4months -76 years with mean age of 38 years. It was noted that fever was present in all patients. Next common symptom was headache followed by rash.

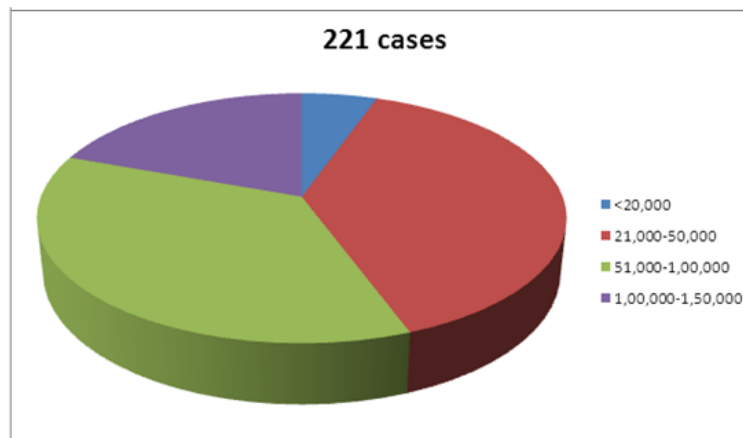
Out of 221 patients, 39 (17.6%) had Hemoglobin (Hb) <10 g/dl & 33 (14.9%) had Hb>15 g/dl. Hematocrit (Hct) >35 was seen in 176 (79.6%) cases. Leucopenia was seen in 61(27.6%) cases. Lymphocytes >45% was seen in 146 (66%) cases. Monocytes >10% was seen in 187 (84.6%) cases. Basophils>2% was seen in 117(52.9%).98 (44.4%) had platelet count below 50, 000/cumm of blood and the rest 123 patients (55.6%) had more than 50, 000/cumm of blood.

Age group:	4 months-76 yrs.	Mean-38 yrs.	P value
M:F	130: 91		
Hb-<10 g/dl	39/221 cases	17.6%	
Hb>15 g/dl	33/221 cases	14.9%	
Hct>35	176/221 cases	79.6%	P<0.05
WBC-<4, 000(leucopenia)	61/221 cases	27.6%	P>0.05
>11, 500(age group >6years), >16, 000 (age group <6 years)	17/221 cases	7.6%	P>0.05
Lymphocytes (>45%)	146/221 cases	66%	P<0.05
Atypical Lymphocytes (plasmacytoid forms)	192/221 cases	87%	P<0.05
Monocytes (>10%)	187/221 cases	84.6%	P<0.05
Eosinophils (>5%)	17/221 cases	7.6%	P>0.05
Basophilia (>2%)	117/221 cases	52.9%	P<0.05
Platelet			
<20, 000	12 cases	5.4%	P<0.05
21, 000-50, 000	86 cases	38.9%	
51, 000-1, 00, 000	80 cases	36.19%	
1, 00, 000-1, 50, 000	43 cases	19.4%	

Table 1: Hematological parameters in Dengue Fever



**Fig-1: Graphic representation of various lab. parameters in this study**



**Fig 2: Graphic representation of varying degrees of thrombocytopenia**

**STATISTICAL ANALYSIS:** The data were analyzed by using Percentages & mean values.

**DISCUSSION:** A range of findings in peripheral blood is seen mostly during dengue viral infections. Hemoconcentration and raised hematocrit are well known findings in patient of Dengue hemorrhagic fever.<sup>4</sup>

A total decrease in the leukocyte count during the illness is mainly due to a decrease in granulocytes, i.e., neutrophils. Presence of atypical lymphocytes with activated lymphocytes and even plasma cells along with thrombocytopenia is reported consistently along with other laboratory findings.<sup>5</sup>

A number of studies have shown that early in the course of illness, patients with either primary or secondary dengue infections exhibit a fall in the leukocyte count associated with a rise in the percentage of lymphocytes and this finding is in parallel to marrow suppression during acute phase.<sup>6,7</sup>

Most prominently increase in the percentage and total number of lymphocytes and an increase in the percentage and number of atypical lymphocytes.<sup>8</sup>

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Atypical lymphocytes are frequently seen in a variety of viral illnesses, including infectious mononucleosis, herpes, rubella, influenza and viral hepatitis. The exact function of atypical lymphocytes is unclear, they incorporate increased amounts of [3H] thymidine into deoxyribonucleic acid and are similar in appearance to lymphocytes which undergo blast transformation after stimulation with mitogens (such as phytohemagglutinin).<sup>9</sup> Thus, it is possible that atypical lymphocytes represent a response to non-specific viral stimulation or to specific viral antigens due to recognition followed by transformation.<sup>8</sup>

The potential importance of this in DHF stems from studies which have demonstrated that the dengue virus in vitro invades and replicates poorly in resting lymphocytes but well in stimulated transformed B lymphoblast cells.<sup>10</sup>

We observed a marked increase in concentration of Plasmacytoid Lymphocytes. Similar findings have been reported by John Gawoski and Winnie Ooi and it mainly represents that serum immune globulin production is enhanced during dengue viral infection, these are mostly against the specific serotype and obviously not protective to the infections caused by other serotypes.<sup>11</sup>

It has been suggested that the atypical lymphocytes in secondary dengue infection can be representative of augmented immune response in an attempt to control the spread of dengue virus-infected cells.<sup>12</sup>

Differences between the samples at the time of admission and collected later during convalescence were also found in the concentrations of eosinophils.

Similar findings have been reported for other viral infections, where, in response to inflammation during the acute phase, eosinophil concentrations fell. During convalescence, the eosinophil concentrations rise to normal or even more.<sup>13</sup>

Eosinophilia during the convalescent phase of dengue fever has been reported consistently in a number of studies.<sup>14, 15</sup>

An increase in the total number of basophils is also seen in the convalescent period. The increase in basophils may be due to element of recovery from the bone marrow suppression during convalescence.<sup>6</sup>

The most significant laboratory abnormality seen in our patients was thrombocytopenia, as observed in other studies.<sup>16</sup> This is thought to be due to depression of bone marrow observed in acute stage of dengue virus infection.<sup>6</sup>

Other explanations are direct infection of the megakaryocytes by virus leading to increased destruction of the platelets or the presence of antibodies directed against the platelets.<sup>17</sup> Thrombocytopenia may result from by destruction of peripheral platelet or bone marrow megakaryocytes by viruses which consequently reduce the platelet production.<sup>18</sup>

Hemorrhagic manifestations are very common with severe thrombocytopenia and severity of hemorrhagic tendency correlates with the platelet counts.

**CONCLUSION:** Peripheral blood parameters are very helpful for disease monitoring and can be useful in prediction of prognosis. Most of the cases in our study had raised hematocrit, lymphocytosis with atypical forms (plasmacytoid forms), monocytosis, Basophilia & thrombocytopenia. These indicators, if rightly and timely assessed can be of value for better care of complicated cases.

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**AUTHORS:**

1. M. K. Malathesha
2. Ashwini H. N.

**PARTICULARS OF CONTRIBUTORS:**

1. Assistant Professor, Department of General Medicine, JJMMC, Davanagere.
2. Assistant Professor, Department of Pathology, JJMMC, Davanagere.

**NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:**

Dr. M. K. Malathesha,  
#1839/16, 5<sup>th</sup> Cross, Taralabalu Badavane,  
Davanagere – 577005, Karnataka.  
E-mail: malthesh\_mk@yahoo.co.in

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