

## Hematological Parameters and Its Utility in Dengue-A Prospective Study

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### **Abstract:**

**Background:** Dengue an endemic disease in subtropical and tropical regions of the world is causing severe epidemic in India and is endemic in many parts of India, especially the metropolitan cities and towns.

**Aim And Objectives:** To co-relate the haematological data during the evolution of dengue fever and to predict the severity of the disease, based on laboratory rapid screening tests for IgM and IgG antibodies and NS1 antigen and to study the seasonal variation. As dengue causes increased morbidity and mortality and requires prompt diagnosis and treatment for the proper management of these cases, the rapid screening test for IgM/IgG antibodies helps clinicians toward achieving this goal.

**Material And Method:** A prospective study of laboratory tests of positive dengue cases and its hematological profile over a period of one year between January 2013 to December 2013.

**Conclusion:** Awareness, early recognition and early diagnosis are important for favourable outcome. The study focuses the importance of complete hemogram and rapid screening tests for IgM and IgG antibodies and NS1 antigen for detection of dengue during the season. Thrombocytopenia may not always be a feature of dengue.

**Keywords:** Dengue, complete hemogram, Dengue Day-1 test.

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### **I. Introduction**

Dengue is the most important merging tropical viral disease in the world today. The WHO estimates 50 million dengue infections occur annually and almost half the world's population lives in countries where dengue infection is endemic [1](WHO,2008). Dengue is caused by one of the four serotypes of the dengue virus (DEN-1,DEN-2,DEN-3,DEN-4) also referred to as an arbovirus (arthropod-borne viruses) that belongs to the genus flavivirus of the family flaviviridae [1][2]. It is transmitted by mosquitoes of the genus *Aedes aegypti*. Dengue is a disease with wide clinical spectrum and a wide variety of presentations, ranging from asymptomatic to an undifferentiated fever (viral syndrome ) to the more severe forms such as severe dengue (SD) or dengue hemorrhagic fever(DHF)[3].

In 2005, the world health assembly, through WHA resolution 58.3, in a review of the international health regulation (IHR), included dengue fever as an emergent public health disease, with implications for health safety due to spread of the epidemic beyond national boundaries [4].

Dengue virus infection is known to exist in India for a long time [5].

The incidence of dengue fever (DF) has increased manifold in last four decades, in developing nations like India, unplanned urbanization and migration of population from rural to urban areas with complete lack of proper sanitation facilities are important factors resulting in this situation [6].

At present, information on adult dengue infections in south asia is quite limited, thus, the necessity of this study is to learn the prevalence of dengue infection based on laboratory screening rapid tests for IgM and IgG antibodies and the confirmatory IgM ELISA test, and to study the seasonal variation and the clinical profile in these cases.

### **II. Materials And Methods**

A prospective study was carried out in a tertiary care hospital over a period of one year (January 2013 to December 2013).

Complete hemogram including hemoglobin, hematocrit, total count, differential count, platelet count, mean platelet volume were noted of 209 patients.

Sera samples were collected from all individuals and tested for dengue by "dengue DAY 1 Test"- rapid visual test for the detection of dengue NS1 Ag & differential detection of IgM & IgG antibodies in human serum/plasma.

The sensitivity and specificity was reported to be almost 100 %.

Hemogram profile was done on ABX Micros 60 cell counter.

The suspected cases and the positive samples were studied monthwise to know the seasonal pattern of the disease.

### III. Results And Tables

A total of 209 cases were studied, based on positive dengue test. Complete haemogram of these patients were done and followed, till the patient is in hospital.

Platelet counts of the patients were grouped as follows:

< 20000/cumm, 20000 to 50000, 50000 to 75000 and >75000.

**Table 1: Platelet counts of patients**

Platelet count	No. Of patients	IgM positive	IgG positive	NS1 positive
<0.20	06	02	01	05
>0.20 and 0.50	32	04	04	27
>0.50 and 0.75	42	08	06	29
>0.75	129	44	23	81

Total leucocyte count were grouped as <4000/cmm, 4000-11000/cmm, >11000/cmm.

**Table 2: Total leucocyte count of patients**

Total leucocyte count (per cu mm)	No. of patients	IgM positive	Ig G positive	NS1 positive
<4000	81	13	03	71
4000 to 11000	111	39	26	63
>11000	17	06	05	08

#### Haemoglobin:

Range of hemoglobin percentage was lowest 3.6gm/dl and highest 16.7gm/dl with a mean of 11.95gm/dl. Hemoglobin percentage were grouped as 3.5-8.5gm/dl, 8.5-13.5gm/dl and 13.5-18.5gm/dl.

**Table 3 : Haemoglobin percentage of patients**

Hb %(gm/dl)	No. of patients	IgM positive	IgG positive	NS1 positive
3.5 to 8.5	25	06	05	15
8.5 to 13.5	169	50	28	114
13.5 to 18.5	15	02	01	13

Hematocrit were grouped as <30, 30 to 40, >40

**Table 4: Haematocrit of patients**

Haematocrit	No.of patients	IgM positive	IgG positive	NS1positive
< 30	64	20	11	39
30 to 40	129	37	21	89
>40	16	01	02	14

**Table 5: Monthwise of distribution of dengue cases**

MONTH	NO. OF CASES
JULY	05
AUGUST	33
SEPTEMBER	58
OCTOBER	47
NOV	51
DEC	13

Only one case each was found in the month of January and February.

There was three mortality due to the disease, one was IgM with classical dengue fever and two was NS1 positive with dengue hemorrhagic fever. Total leucocyte count was normal in all these patients and platelet were moderately decreased.

### IV. Discussion

Due to changing climate, urbanization, poor living conditions and inadequate waste management, vector born diseases like dengue fever are becoming more common. Although vector control programs are launched in endemic countries every year, yet dengue fever has become a serious problem worldwide. India being a tropical country provides suitable weather for aedes mosquito to grow and an increase in the disease burden has been noticed in recent years [6].

Dengue is caused by a virus belonging to the flaviviridae family (single stranded ,positive, nonsegmented RNA virus). It has four distinct serotypes DEN1, DEN2, DEN3 and DEN4 [7]. Infection with

one serotype confers immunity to only that serotype and hence a person may be infected four times[8]. Humans are the main reservoir of dengue virus[9]. Cross reactive anti dengue antibodies from the previous infection bind to the new infecting serotype and enhance viral uptake by monocytes and macrophages. This antibody dependant mechanism results in an amplified cascade of cytokines and complement activation causing endothelial dysfunction and consumption of coagulation factors leading to plasma leakage and hemorrhagic manifestations. The severity of the disease depends on the strain and serotype of the virus, age of the patient and degree of viremia.

It has been demonstrated that memory dengue T lymphocyte response after a primary infection includes both serotype-specific and serotype –cross reactive T lymphocytes [10]. NS3 protein seems to be the major target for CD4 + and CD 8+ T cells, although some Tcell epitopes have been recognized in other proteins such as envelope and capsid[11] [12]. The magnitude of proliferation to heterologous dengue serotype is variable depending on different factors such as the serotype causing the primary infection and the ethnicity of the individual [13]. These finding support the possibility that during a secondary infection T cells become activated due to interactions with infected monocytes. Recent observations suggest a massive T-cell activation during DHF, which could partly explain the mechanism of plasma leakage through cytokine production and infected cell lysis by CD4+ and CD8+ dengue –specific T lymphocyte .Cytokines could be released directly from monocytes/macrophages as a result of infection or after interactions between infected and immune cells or both[13][14]. Cytokines that may induce plasma leakage such as interferon  $\gamma$ , interleukin (IL) 2 and tumor necrosis factor TNF –  $\alpha$  are increased in DHF cases [14][15]. Interferon  $\gamma$  enhances uptake of dengue particles by target cells through increasing Fc cell receptors [15]. Other cytokines such as IL-6, IL-8 and IL-10 are also increased. A protein of 22-25 kDa responsible for increased capillary permeability has been detected in sera of DHF patients[16]. Besides secondary infection, chronic diseases such as bronchial asthma and diabetes predispose to a higher risk of developing DHF. Dengue 2 virus is known to replicate to higher concentration in the blood cells of whites [8]. The release of high levels of platelet-activating factor may induce platelet consumption and augment adhesiveness of vascular endothelial cells resulting in thrombocytopenia [17]. Primary infections are characterized by an increase in dengue – specific IgM antibodies four to five days after the onset of fever and by an increase in IgG antibodies only after the onset of fever and by an increase in IgG antibodies only after seven to ten days. IgM antibodies are detectable for three to six months, whereas IgG antibodies remain detectable for life. In secondary infections, the level of IgM antibodies is lower than in primary infections and the antibodies are sometimes absent, whereas levels of IgG antibodies rise rapidly in secondary infections, even during the acute phase, thus the presence of high titers of IgG early in the course of the disease is a criterion for secondary infection.

A total of 209 patients having serological positive dengue cases were studied. Of these 125 were males, 79 were females and 5 pediatric cases.

Of all the positive samples tested by tested by antigen –antibody reaction principle which is a rapid visual test for dengue.142 patients were positive for NS-1, out of these 12 patients were also positive for IgM and 4 for IgG. Only one patient was positive for all NS-1, IgM and IgG.

Out of 209 patients 58 patients were positive for IgM, out of these 12 were positive for NS-1 and 12 also for IgG. Out of 209 patients 34 patients were positive for IgG in which 12 were positive for IgM and 4 were positive for NS-1.

Other laboratory investigations revealed thrombocytopenia, platelet count <100000 in 112 patients.

Platelet counts results were grouped as counts <20000/cmm, >20000 to 50000, >50000 to 75000/cmm, and > 75000/cmm. Thrombocytopenia (platelet counts <100000/cmm ) were seen in in 112 cases. 6 cases had counts less than 20000/cmm, 32 cases had counts between >20000 and 50000/cmm, 42 cases had counts between >50000 and 75000/cmm and 129 cases had counts more than 75000/cmm.

Total leucocyte count results were grouped as counts <4000, 4000 to 11000, >11000/cmm.

Leucopenia (total leucocyte counts <4000/cmm) were seen in 81cases, normal count (count between 4000 to 11000/cmm) were seen in 111 cases.

Leucopenia with lymphocytosis were seen in 40 patients.

Normal haemoglobin count of 8.6 to 13.5 gm% were seen in 169 patients with anemia ( 3.5 to 8.5) were seen in 25 patients, haemoglobin count of 13.5 to 18.5 were seen in 15 patients. Increased hematocrit of > 40 were seen in only in 16 patients.

Most of the cases were found in post monsoon period in September to November.

Most of the patients were positive for NS1antigen.

## **V. Conclusion**

The study shows that most of the patients are within normal range of hematological profile in early course , which gives us enough time for treatment and management. Early and prompt diagnosis of any

symptom with complete hemogram and dengue test can save a life, rather than waiting for symptoms to progress and deteriorate.

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