

# Haematological Predictors of Recovery in Dengue Cases

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## ABSTRACT

**Introduction:** Dengue fever is associated with relative increase in haemoglobin, haematocrit and monocyte counts and reduction in platelet counts, eosinophil percentage and absolute eosinophil count. Recovery is marked by decrease in haemoglobin, haematocrit and monocyte percentage and increase in platelet count, eosinophil percentage and absolute eosinophil count.

**Aim:** To assess the haematological parameters like haemoglobin, haematocrit, monocyte counts, eosinophil counts and absolute eosinophil counts which may be used as a surrogate marker for recovery.

**Materials and Methods:** This retrospective study was conducted at Chettinad Hospital and Research Institute for a

period of three months. Hundred consecutive cases of dengue fever were included in the study. All haematological parameters including haemoglobin, haematocrit, total WBC count, differential count with neutrophils, lymphocytes, monocytes, eosinophils, basophils, platelet counts and absolute eosinophil counts were noted on hospital admission and on recovery.

**Results:** The different haematological parameters which change statistically significantly during dengue infection and recovery are the haemoglobin, haematocrit, monocytes, eosinophil, absolute eosinophil count and platelet count (p-value<0.001).

**Conclusion:** These changes in haemoglobin, haematocrit, monocyte percentage and the platelet count, eosinophil percentages and absolute eosinophil count could be used to monitor recovery in dengue cases.

**Keywords:** Absolute eosinophil count, Eosinophil percentage, Haemoglobin, Platelet count

## INTRODUCTION

Dengue fever cause changes in the peripheral blood counts including relative increase in haemoglobin, haematocrit and monocyte counts and reduction in platelet counts, eosinophil percentage and absolute eosinophil count. Haematologically, recovery is marked by decrease in haemoglobin, haematocrit and monocyte percentage and increase in platelet counts, eosinophil percentage and absolute eosinophil counts. Haematological recovery coincides with clinical recovery in all cases [1,2].

In low resource and rural setting, where the automated haematology analysers and skilled technicians may not be available and hence accurate platelet counts may not be possible, a combination of other haematological parameters like haemoglobin, haematocrit, monocyte counts, eosinophil counts and absolute eosinophil counts may be used as a surrogate marker for recovery. This was a feasibility study to assess the same.

Other studies have not highlighted the rebound eosinophilia that occurs with recovery in dengue. Thus, the aim of the study was to assess the haematological parameters like haemoglobin, haematocrit, monocyte counts, eosinophil counts and absolute eosinophil counts which may be used as a surrogate marker for recovery.

## MATERIALS AND METHODS

This retrospective study was conducted at Chettinad Hospital and Research Institute, Chennai, Tamil Nadu, India, for a period of three months. Hundred consecutive cases of dengue fever were included in the study after obtaining Institutional Ethics Committee approval (245 IHEC/5-17) and informed consent of the patient. Since nine parameters were being evaluated a sample size of 90-100 was taken.

Ratio estimate=Benchmark population\*Linear estimate/Linear estimate of total population. Ratio estimate=20\*2000/10,000. Ratio estimate=100.

**Inclusion criteria:** Confirmed cases of dengue fever having positive antibody to dengue specific IgM with detection of Dengue NS1Ag

(the method of detection is through enzyme-linked immunosorbent assay) and IgG IgM Test by ELISA.

**Exclusion criteria:** Any case of fever with thrombocytopenia negative for dengue tests (Dengue NS1Ag and IgG IgM Test).

All haematological parameters including haemoglobin, haematocrit, total WBC count, differential count with neutrophils, lymphocytes, monocytes, eosinophils, platelet counts and absolute eosinophil counts were noted on hospital admission and on recovery. The counts were done using automated analyser Beckman Coulter LH-780. Recovery was defined as the day platelet counts showed an upward trend and correlated with clinical recovery in all cases. The platelet count was done daily for first few days. In some cases, the platelet count was done three times a day in those with marked thrombocytopenia. The pattern of haematological changes during the recovery phase was studied. The Complete Blood Count findings were confirmed by peripheral smear examination by a pathologist.

## STATISTICAL ANALYSIS

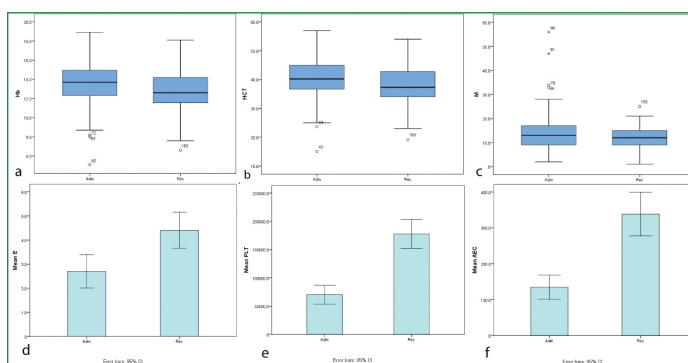
The evaluated parameters were represented as box plots and bar diagrams. The mean and standard deviation are tabulated with p-value obtained using paired t-test (Mann Whitney U-test). The area under the Receiver Operator Characteristic (ROC) curve is used to measure the predicting power of test variables and for determining the efficacy of tests in correctly classifying diseased and non-diseased individuals. In general, the ROC analysis shows the curve fit between the true positive rate (TPR or sensitivity) against the false-positive rate (FPR or 1-specificity). True Positive Rate=probability of positive test result /diseased and False Positive Rate =probability of positive test result /not diseased.

## RESULTS

In this study, paired t-tests showed a statistical decrease in haemoglobin, haematocrit and monocyte and a statistical increase in eosinophil, platelets and absolute eosinophil count with recovery (p-value<0.001) [Table/Fig-1,2].

Variables	At the time of admission (Mean±SD)	On recovery (Mean±SD)	Paired t-test p-value	Remarks/Description
Hb (gm/dL)	13.4±2.2	12.8±2.0	<0.001	Significantly reduced on recovery
HCT (%)	40.2±6.6	38.2±6.1	<0.001	Significantly reduced on recovery
TC (cells/cu mm)	7875±15153	8736±8368	0.486	No significant change
N (%)	39.9±18.7	38.4±15.7	0.404	No significant change
L (%)	42.5±17.2	44.6±14.7	0.233	No significant change
M (%)	14.1±8.3	12.1±4.3	0.016	Significantly reduced on recovery
E (%)	2.7±3.5	4.4±3.8	<0.001	Significantly increased on recovery
B (%)	0.5±0.7	0.4±0.5	0.416	No significant change
PLT (cells/cu mm)	70115±83858	177725±127913	<0.001	Significantly increased on recovery
AEC (cells/cu mm)	134.7±169.7	338±305	<0.001	Significantly increased on recovery

**[Table/Fig-1]:** Mean and standard deviation (SD) values of the evaluated parameters.

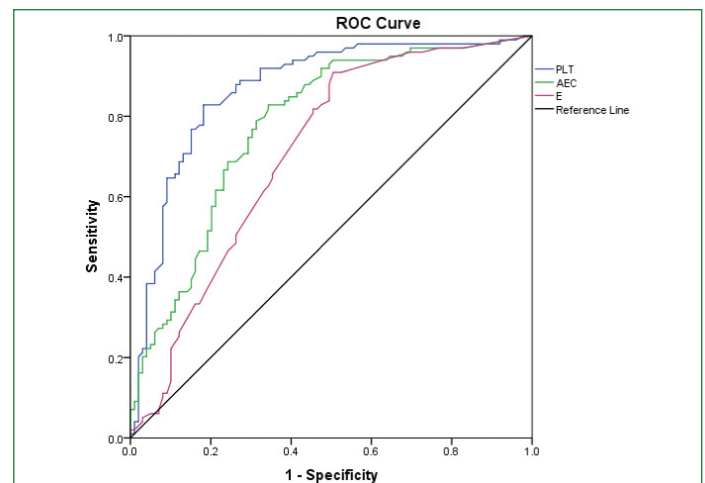


**[Table/Fig-2]:** a) Hb (haemoglobin in gms/dL) on adm(admission) and rec (recovery); b) HCT (haematocrit in %) on adm (admission) and rec (recovery); c) M (monocyte in %) on adm (admission) and rec (recovery); d) E (eosinophil in %) on adm(admission) and rec (recovery); e) PLT (platelet count in cells/cu mm) on adm (admission) and rec(recovery); e) PLT (platelet count in cells/cu mm) on adm (admission) and rec (recovery); f) AEC (absolute eosinophil count in cells/cu mm) on adm (admission) and rec (recovery).

In this study, the area under the curve (AUC) is significantly higher for the parameters haemoglobin, haematocrit, monocyte, eosinophil, platelet count and absolute eosinophil count [Table/Fig-2,3]. The sensitivity and specificity for PLT: 82% and 88%; for AEC: 82% and 65% for E: 90% and 50% for Hb 78% and 48%; for HCT: 77% and 48% respectively [Table/Fig-3].

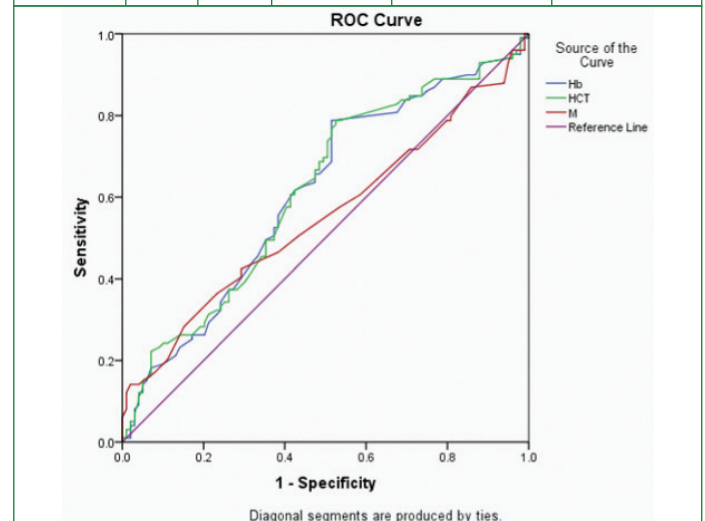
The different haematological parameters which change statistically significantly during dengue infection and recovery are the haemoglobin, haematocrit, monocytes, eosinophil, absolute eosinophil count and platelet count. The total WBC count, neutrophils, lymphocytes and basophils did not change to a statistically significant level in present study. Clinical recovery from dengue infection is marked by a rising platelet count and the haematological parameters paralleled the rising platelet count.

Most cases presented with fever which was high grade and intermittent with chills and rigors for 1-4 days. Few cases had low grade fever. Headache was seen in 28% of cases. Abdominal pain was seen in 16% cases, loss of appetite in 10% of cases, mostly in paediatric cases. Loose stools and rashes in 9% and 8% cases respectively. A total of 96 patients had Dengue fever, 4 patients had Dengue Haemorrhagic Fever and none had Dengue Shock Syndrome in this study. Bleeding mostly in the form of haematuria was seen in 4% cases and rashes were also seen in 4% cases. Hepatomegaly with right hypochondrial tenderness was seen in 13% cases. Activated partial thromboplastin time and Prothrombin time was elevated in 8% cases. An elevation in liver enzymes was seen in 15% cases. One patient had associated pregnancy with eclampsia,



**Area under the curve**

Test result variable(s)	Area	Std. error	Asymptotic sig.	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
PLT	0.869	0.027	0.000	0.816	0.921
AEC	0.780	0.033	0.000	0.715	0.845
E	0.708	0.037	0.000	0.635	0.781



**Area Under the Curve**

Test result variable(s)	Area	Std. error <sup>a</sup>	Asymptotic sig. <sup>b</sup>	Asymptotic 95% confidence interval	
				Lower bound	Upper bound
Hb	0.611	0.040	0.007	0.532	0.689
HCT	0.616	0.040	0.005	0.537	0.694
M	0.552	0.041	0.208	0.471	0.632

**[Table/Fig-3]:** The ROC curve analysis for platelet count (PLT), absolute eosinophil count (AEC), and Eosinophil percentage (E); The ROC curve analysis for haemoglobin (Hb), haematocrit (HCT), and Monocyte percentage (M).

who recovered. One patient had associated diabetes mellitus and one paediatric patient with mesenteric adenitis which resolved on treatment. Four patients had platelet transfusion and one patient had fresh frozen plasma transfusion and one patient had packed cell transfusion. All patients recovered and patients with Dengue Haemorrhagic Syndrome had a stormy course and were treated with adequate hydration, platelet transfusions and fresh frozen plasma transfusion. Three Patients with Dengue Haemorrhagic Syndrome recovered while one was discharged against medical advice.

All cases presented with thrombocytopenia which lasted for 3-4 days and for 6-7 days in a few cases. Clinical recovery was marked by a significant rise in platelet count.

## DISCUSSION

The haemoglobin and haematocrit showed an increase in count [1-8]. In a study, there was no significant changes in haematocrit values,

except for a few patients who had severe bleeding [2]. In another study, the haemoglobin levels remained elevated on discharge in 2.1% of cases [9]. In another study, the haematocrit increased by 20% above the levels seen in the convalescent period in 91.5% patients, in another 8.4% patients, the haematocrit increased by 10%-19% [4]. This is in accordance with our study where the haemoglobin and haematocrit increased during the acute phase. It was more marked in patients with Dengue Haemorrhagic fever. Co-existent anaemia has also been reported. Thrombocytopenia was seen consistently in all studies and an increase heralding recovery [1,2,4-10].

Leucopenia (defined as total WBC count <4,000 cells/cu mm) was seen in most studies [1-3,5,10,11]. In present study, the total WBC count did not show any statistical difference between the acute phase and convalescent phase of the disease.

Granulocytopenia was seen in one case study [2] and increase in granulocytes during convalescence in another study [8]. Neutropenia was seen [3,11]. Lymphocytosis and atypical forms were seen in 93% patients. Plasmacytoid forms were seen [3,8]. An increase in absolute monocyte counts during convalescence were also seen as was noted in this study [11]. An increase in basophils has also been seen in convalescence possibly due to recovery from bone marrow suppression.

Eosinopenia was seen in the acute phase of the disease [2] and a rebound increase in eosinophils was seen with an increase in absolute eosinophil count [7,8,12]. A similar finding has been seen with viral infections. In some cases, the eosinophil counts rose more than in the non-infected state [13]. A similar phenomenon has been seen following treatment of filarial infections, where there is rise in eosinophil counts (4 days) after an initial drop in eosinophil counts [14].

## LIMITATION

The reason for the rise of different parameters could not be assessed.

## CONCLUSION

The haemoglobin, haematocrit and monocyte counts rise during the acute phase of the illness and fall during the convalescent phase

of the disease. There is a rebound eosinophilia in recovery phase of the disease. As such, these parameters could be used as surrogate markers of recovery in low resource settings and rural areas where an automated haematology analyser may not be available to obtain accurate platelet counts.

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Date of Submission: **May 24, 2019**

Date of Peer Review: **Jun 21, 2019**

Date of Acceptance: **Aug 03, 2019**

Date of Publishing: **Oct 01, 2019**

FINANCIAL OR OTHER COMPETING INTERESTS: None.