# Monocytosis and Hypogranulation of Neutrophils as an early predictor of Dengue Infection

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## ABSTRACT

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Dengue infection is a major public health problem, affecting general population in the south East Asia region. The hematologic aberration including relative lymphocytosis, coagulopathy and predominant thrombocytopenia are common in patients with dengue infection .Complete blood count is an important part of the diagnostic work up of patients. Comparison of various findings in CBC which come with no extra cost can help the physician in an earlier diagnosis.

**Materials and Methods:** This observational study was carried out on a series of suspected dengue patients seen in the General Medicine unit of jubilee Mission Medical College in 2014. Based on the serology result, the patients with clinical suspicion of dengue was divided into dengue negative but febrile and dengue positive. A group of normal control was also simultaneously run which included samples of blood donors.

The various CBC parameters were studied in different groups. We used the VCS technology of the Beckmann counter automated analyzer to quantify the morphological characteristics of leukocytes like cell volume and granularity.

**Results:** There was marked Monocytosis in the dengue positive patients in comparison with the febrile control and normal control. Monocyte anisocytosis was seen in dengue positive cases reflected by Mean monocyte SD volume. We also found statistically significant changes in the neutrophil scatter for dengue positive cases like hypo granulation of neutrophils.

**Conclusion:** Leukopenia and thrombocytopenia are the usual indicators of dengue. But in their absence serological testing and diagnosis is delayed. In this study it is seen that monocyte volume and count is increased even in those dengue infected patients with unremarkable hematological profile which thus can be an early predictor of the disease.

**Keywords:**  Dengue infection, Monocytosis, Monocyticanisocytosis, No extra cost

*See End Note for complete author details

## INTRODUCTION

Monocytes are a type of white blood cells. They are part of the innate immune system of vertebrates including all mammals (humans  included), birds, reptiles, and fish. They are amoeboid in shape, having clear cytoplasm with bean-shaped nuclei that are unilobar, which makes them one of the types of mononuclear leucocytes (aranulocytes). Monocytes constitute 2% to 10% of all leucocytes in the human body. They play multiple roles in immune function. Such roles include: (1) replenishing resident macrophages under normal states, and (2) in response to inflammation signals, monocytes can move quickly (approx. 8–12 hours) to sites of infection in the tissues and divide/differentiate into macrophages and dendritic cells to elicit an immune response.[1]

Monocytosis  is the state of  excess monocytes in the peripheral blood. It may be indicative of various disease states. Examples of  processes that can increase a monocyte count include sarcoidosis, Subacute bacterial endocarditis, tuberculosis, malaria, Mumps and IMN. Studies have also demonstrated monocyticanisocytosis reflected by monocytic volume –standard deviation (moV-SD) in Dengue infection.[2]

Dengue is among the most important mosquito-borne viral diseases in the world. The highest burden of disease occurs in South-East Asia and the Western Pacific, where it is one of the 10 leading causes of hospitalisation  and  childhood mortality.[3] Well Known haematological aberration in dengue include relative lmphocytosis, thrombocytopenia and leucopenia. But little is known about other leucocyte characterisitics.[4]

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However, modern automated blood cell analyzers offer several parameters that may indicate dengue infection.[5] Automated hematology analyzers are critical tools known for their ability to perform fast and accurate analyses of human blood.

The current study focussed on the monocyte anisocytosis in dengue fever and it's detection using automated Beckman Coulter counter LH 750 series by analyzing the vcs parameter.

## MATERIALS AND METHODS

The present study was conducted on all dengue patients admitted at JMMC&RI between 1st of JAN to 31st of MAY 2013 who were confirmed by either Ig M or NS1 Ag testing.

Clinical data, reports of hematological and relevant serological investigations, and other data were collected using a questionnaire and were analyzed.

CBC and VCS parameters were simultaneously measured using automated hematology analyzers.

Based on the serology results (IgM & NS1Ag), the patients with clinical suspicion for dengue were divided into

1. Dengue negative,

2. Dengue positive &

3. A normal control group

All the parameters collected were compared between groups using different statistical methods.

**VCS Technology:** The volume conductivity scatter technology

**Volume:** Volume conductivity scatter utilizes the coulter principle of counting and sizing to measure the volume of the cell by using direct current (DC) across the two electrodes in a flow cell to physically measure the volume that the entire cell displaces in an isotonic diluent.

**Conductivity:** It reveals information about the internal structure of the Cell, including chemical composition and nuclear volume.

**Scatter:** The scattered light gives information about cell surface and granularity.

## RESULTS

The mean value of the Complete blood count

parameters are given below for three different groups.

The mean monocyte was significantly raised in the Dengue Positive group in comparison (Table 1).

**Table 1. Complete blood count parameters**

| Parameter | Dengue Positive | Dengue Negative | Normal |
|---|---|---|---|
| Total count | 4342 | 8032 | 10274 |
| Platelet count | 95,760 | 1,55,300 | 2,62,180 |
| Monocyte | 13.88 | 10.84 | 7.86 |

The other CBC Parameters were comparable between three groups (Table 2).

70 % of Dengue Positive groups showed Monocytosis in comparison with 48 % Dengue negative and 17 % of Normal controls.

**Table 2. Other CBC Parameters**

| Parameter | Dengue Positive | Dengue Negative | Normal control |
|---|---|---|---|
| Hb | 13.616 | 13.002 | 15.018 |
| HCT | 44.834 | 38.656 | 40.412 |
| Neutrophils | 51.44 | 58.28 | 53.9 |
| Lymphocytes | 33.32 | 28.3 | 33.6 |

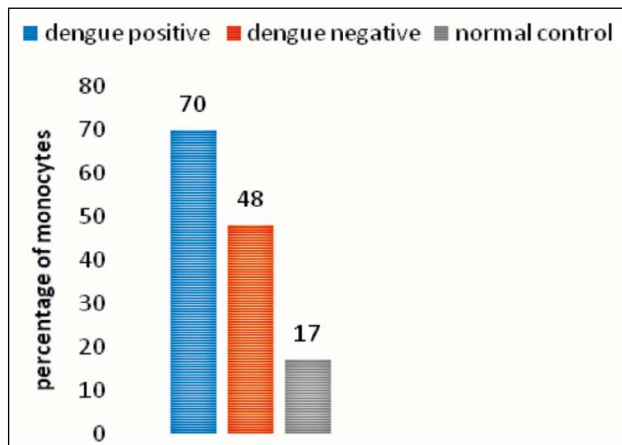The Monocyte Mean volume & SD were significantly increased in dengue positive patients



Figure 1: **Monosytosis among different groups**

Monocyticanisocytosis as reflected by Monocyte SD volume was raised in Dengue Positive Group (Table 3).

**Table 3. Mean monocyte volume**

| | Dengue Positive | Dengue Negative | Normal |
|---|---|---|---|
| Volume | 187.74 | 180.024 | 166.052 |
| conductance | 136.736 | 133.976 | 122.962 |
| Scatter | 84.631 | 85.308 | 89.046 |

We also did find statistically significant changes in the neutrophil scatter (Negative Corelation) for the Dengue positive cases (Table 4 & 5).

**Table 4. Paired T test for monocyte SD volume**

| Comparing | Sig 2 tailed |
|---|---|
| Dengue Positive and Dengue Negative group | .000 |
| Dengue Positive and Control group | .003 |

**Table 5. Hypogranulation of neutrophils in dengue positive cases**

| | | Dengue Positive | | Febrile Control | | Normal Control | |
|---|---|---|---|---|---|---|---|
| | | Mono-cyte | Neu-trophil | Mono-cyte | Neutro-phil | Mono-cyte | Neu-trophil |
| M E A N | Volume | 187.774 | 147.838 | 180.024 | 151.392 | 166.052 | 143.452 |
| | Conduct-ance | 136.736 | 160.512 | 133.976 | 189.896 | 122.962 | 148.26 |
| | Scatter | 84.631 | 137.828 | 85.308 | 139.738 | 89.046 | 141.542 |

## DISCUSSION

The Monocyte count, Mean volume & SD were significantly increased in dengue positive patients. We speculate that the strong immune stimulation caused by the virus leads to this monocyte anisocytosis. Since dengue fever is much less common than other viral diseases with similar symptoms, clinicians often rely on features such as thrombocytopenia and leukopenia as indicators of dengue. If these traditional findings are absent, serological testing and the correct diagnosis may be significantly delayed.

In this study, we have also demonstrated that the MoV-SD is increased even in those dengue infected patients with unremarkable hematological profiles, for whom the correct diagnosis could easily be overlooked. Since the MoV-SD is obtained automatically as part of any CBC with differential performed using VCS technology, it can greatly improve the detection of dengue fever in a timely and cost effective manner.

## END NOTE

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**Conflict of Interest:** None declared

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