Journal of Research in Applied and Basic Medical Sciences 2024; 10(1): 54-64

Original Article

RABMS Journal of Research in Applied and Basic Medical Sciences

# Utility of newer WBC indices such as high fluorescent lymphocyte count in diagnosis and assessing the severity of dengue in the patients at a tertiary rural hospital

**Pappuri Swarna Latha[1], Swaroop Raj B V[2]***

[1] *Postgraduate Student, Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar, Karnataka, India*

[2] *Associate Professor Pathology, Yenepoya Medical College, Mangaluru, Karnataka, India*

***Corresponding author:** Swaroop Raj B V, **Address**: Yenepoya Medical College, Mangaluru, Karnataka, India
**Email**: dr.swaroop.raj@gmail.com, **Tel**: + 919844044473

## Abstract

***Background & Aims*:** In developing countries, lately dengue has become the most common cause of admission for fever with other infections such as malaria, enteric fever and leptospirosis on the decline. The differential diagnosis is usually sorted by serological investigation such as NS1 antigen; IgG and IgM for Dengue, though are confirmatory are expensive. The diagnosis of dengue is very important considering the sudden decline in the health of a patient due to thrombocytopenia and management of dengue which hinges on hydrating the patients and managing thrombocytopenia. The aim of this study was to study the correlation between newer parameter high fluorescent lymphocyte count (HFLC) with platelet count and dengue serology (NS1 antigen and IgM antibody).

***Materials & Methods:*** We conducted a study at R. L. Jalappa Hospital and Research Centre, a rural tertiary and academic teaching hospital attached to Sri Devaraj Urs Medical College with a prospective study period of twelve months and between June 2019 to May 2020. A total of 386 samples were analyzed for complete blood count, Dengue serology, and HFLC count and percentage. The data was entered in excel sheet and analyzed using SPSS 22 software.

***Results*:** The newer WBC index namely, HFLC Count correlated negatively with platelet count ($r = -0.28$, $p < 0.05$) and positively with lymphocyte percentage ($r = 0.506$, $p < 0.05$). The parameters that were statistically significant include WBC count, RBC count, hemoglobin, hematocrit, platelet count, RDW, PDW, MPV, PLCR, PCT, Neutrophil %, lymphocyte %, monocyte %, IgG%, HFLC count, HFLC % and Days in hospital including a difference in findings of these parameters between the dengue sero-positive and dengue sero-negative groups who came to the hospital with fever. Thus, highlighting that they can be used as a hint while starting prophylactic treatment until results are available when it is an emergency or when the results are delayed or in resource-limited settings in the periphery due to lack of availability of cost of serological tests.

***Conclusion*:** In resource-limited settings, HFLC percentage and count could be used as a low cost and reliable biomarker for diagnosis and assessing the severity of dengue infection in resource-limited settings.

***Keywords*:** Assessing the Severity, Count, Dengue, High Fluorescent Lymphocyte Diagnosis, Newer WBC Indices, Tertiary Rural Hospital

**Received 16 August 2023; accepted for publication 30 December 2023**



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

## Introduction

In developing countries, lately dengue has become the most common cause of hospital admission for fever with other infections such as malaria, enteric fever and leptospirosis on the decline (1). Dengue is one of the most common and deadly diseases in the world spread by mosquitoes. The World Health Organization estimated that between 100 and 400 million cases of dengue fever occur annually, putting nearly half of the world's population at risk (2). Serious complications and even death can result from dengue, particularly when additional infections with distinct virus serotypes occur. However, because many of dengue's symptoms overlap with those of other febrile infections, diagnosing the disease can be difficult. The diagnosis is usually confirmed by serological investigations as most of the diagnosis has similar clinical findings (3, 4). Serological tests such as NS1 antigen and IgM for Dengue, though are confirmatory, are expensive and hence not usually advised in developing countries like ours. The diagnosis of dengue is very important considering the sudden decline in the health of a patient due to thrombocytopenia and the management of dengue which hinges on hydrating the patients and managing thrombocytopenia (5). Furthermore, in situations with low resources, the usual serological tests for dengue are costly and not widely accessible. As a result, more economical and alternative techniques are required to identify dengue infections and determine their severity. Few studies have been done on similar parameters such as atypical lymphocyte count and have found a strong correlation with diagnosis of dengue infection (6).

Dengue is a mosquito-borne infection caused by Dengue viruses and commonly seen in tropical climates. It has been estimated that 3.9 billion dengue infections per year occur worldwide of which 96 million dengue manifesting clinically and a global burden with diseases like malaria and leptospirosis (1, 7).

Denv-2 was considered to be the predominant serotype in outbreaks before the year 2000, after that Denv-3 was found to be the predominant serotype for a period of almost 10 years, in the next decade i.e., after 2010, Denv-1 is still found to be the predominant serotype for outbreaks (8).

The primary infection of dengue is usually not severe but secondary infection with serotypes not encountered before may lead to severe infections as Dengue hemorrhagic fever or Dengue shock syndrome. Pathogenesis involves both humoral and cell-mediated immune responses. Infected macrophages release a variety of proteins which become responsible for the signs and symptoms of the disease.

Decreased intravascular volume also leads to hypalbuminemia and increased hematocrit which is a characteristic feature of Dengue hemorrhagic fever and Dengue shock syndrome.

ELISA and ICT test are used for detecting NS1 antigen serum. They are used in early detection of the infection. NS1 antigen is detectable on the first day of fever and will continue to do so until 18 days. The test is very specific and can differentiate between flaviviruses. It can also differentiate between the different dengue serotypes (9). In primary infection IgM is detected after 5 days of fever and disappears within 90 days. IgG is detectable at low titer in 14-21 days of illness and then it slowly increases. MAC-ELISA is the most recommended tool available currently for dengue infection. It has sensitivity and specificity of approximately 90% and 98% respectively (9). Platelets are produced from megakaryocytes in bone marrow. Site of megakaryopoiesis is bone marrow and platelets are produced from the progenitor cell as erythroid and myeloid lineages-(CMP/CFU-GEMM). Platelets are fragments of cytoplasm of mature megakaryocyte and the megakaryocyte is the platelet precursor cell (10, 11).

Platelets indices like MPV, PDW and P-LCR have been used as indicators of platelet activation (12). Platelet volume identified as mean platelet volume (MPV) is used as a platelet function surrogate by laboratories. When platelet production is decreased, platelets released become larger, giving rise to increased MPV levels. PDW and P-LCR is a useful marker to distinguish if thrombocytopenia was caused due to decreased production or increased destruction. An increased PDW indicates platelet anisocytosis and is an



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

estimate of variation in platelet size is a more sensitive marker for the estimation of platelet size variation. Increased PDW suggests large ranges of platelet size due to swelling, immaturity or increased platelet destruction (13). PDW may be useful in an early detection of pathological conditions as bacteremia, schistocytosis, platelet consumption and activation, which may take place in a condition like disseminated intravascular coagulation. A study done about platelet indices and methods for evaluating platelet function in thrombocytopenic patients concluded that MPV is a reliable marker for predicting bone marrow failure as a cause of thrombocytopenia. PDW gives no additional information regarding the bleeding risk in cases of thrombocytopenia (14).

Increased MPV indicates increased platelet diameter. MPV is an independent predictor of bleeding and an alternative marker of bone marrow activity. A raised MPV indicates increases in the megakaryocyte activity. A reduce in MPV indicates bone marrow suppression and a heightened risk of bleeding. Platelet activation leads to activation of the coagulation cascade and plays an important role in the pathogenesis of atherosclerosis (15). Larger platelets are more active enzymatically and have an increased prothrombotic potential than smaller platelets as they have lesser granules and hence the chance of bleeding is decreased when larger platelets are seen in the patent circulation. Increased MPV predicts the risk in certain conditions such as – Alzheimer's diseases, Familial Mediterranean fever and Bechet's diseases and MPV is found to be low in Endometriosis (15). MPV levels depend on thyroid hormone and thyroid hormones relates with platelet function. Lymphocytes constitute 20 to 40 % of the circulating white cells. The lymphocytes are subdivided into small and large depending on their size and B, T lymphocytes and NK cells depending on their origin. In the peripheral blood, the majority of them are small lymphocytes with few large lymphocytes. In tissue sections, it is usually not possible to distinguish T from B lymphocytes.

Activated lymphocytes are B and T lymphocytes when they are activated through antigen-specific receptors on their cell surface. This causes the cells to proliferative and differentiates into specialized effector lymphocytes.

Activated lymphocyte (AL) or reactive lymphocyte are responsible for the immune response and have been identified in many diseases including infection, drug hypersensitivity, immunological disorders, and lymph proliferative disorder (16, 17). Hence their identification is used to support the clinical diagnosis of viral infections. ALs differ morphologically from mature lymphocytes and they even differ from each other in the same blood smear. Downey type II, Downey type III, and plasmacytoid lymphocyte are all examples for activated lymphocytes (18).

Newer hematology analyzers not only provide standard parameters but also few research parameters such as high fluorescent lymphocyte count, immature granulocyte percentage, mean platelet volume and platelet large cell ratio. High fluorescent lymphocyte count is detected by their characteristically high fluorescence intensity reflecting a high RNA content. Haematology analyzers provide these research parameters with every hemogram and don't require any additional testing or sample. However, the reference ranges nor utility for the same hasn't yet been defined, they aren't routinely utilized for decision-making. This study intends to find the utility of high fluorescent lymphocyte count in in diagnosis and assessing the severity of dengue infection. The aim of this study was to study the correlation between newer parameter high fluorescent lymphocyte count (HFLC) with platelet count and dengue serology (NS1 antigen and IgM antibody).

## Materials & Methods

The study was carried out in R. L. Jalappa Hospital and Research Centre, a rural tertiary and academic teaching hospital attached to Sri Devaraj Urs Medical College with the study period of twelve months and between June 2019 to May 2020. After taking the ethical permission from the institutional ethical committee of the institution, an informed consent was taken from the patients for participating in the study.



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

**Sample Size:** Estimated using population prevalence of 50%, confidence interval of 95% and margin of error of 5% which was a total of 385. We included 386 patients with fever who had their samples tested for dengue serology (193 dengue-positive and 193 dengue-negative).

We collected the samples in EDTA vacutainer and processed within 4 hours in a Sysmex XN 550, 5-part differential hematology analyzer for complete blood count. Data was collected from patients and controls included in the study which included demographics of the patient, clinical diagnosis, complete blood count including routine RBC indices, high fluorescent lymphocyte cell count (HFLC), serum iron, serum ferritin and total iron binding capacity. RBC indices include mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration and red cell distribution width. HFLCs were analyzed in the WDF channel of the analyzer using polymethine fluorescent dye, with analysis based on the flow cytometry principle. HFLCs are present separately from lymphocytes and monocytes on the scattergram in an analyzer. The main characteristic of HFLCs is the high intensity of their fluorescent signal, which reflects an abundance of RNA content in HFLCs.

**Statistical analysis:** Data was entered into Microsoft Excel data sheet and was transferred to SPSS 22 version software for analysis. Categorical data was represented. Independent t test, significance test and Pearson's Correlation was used as a test of correlation. Continuous data was represented as mean and standard deviation. The p-value <0.05 was considered as statistically significant. R value would be interpreted accordingly identifying the degree of correlation.

## Results

193 seropositive and sero-negative patients each were included in the study with seropositive defined as being positive for NS1 Antigen or IgM positive for Dengue and sero-negative as negative for both NS1 Antigen and IgM positive for Dengue. The cut-off for NS1 Antigen and IgM was as per the literature which was 11 units.

The demographic data of the patients showed that in the dengue seropositive group that the male-to-female ratio was almost 1:1 was a slight predominance of female patients who were 98 out of the total 193 cases. In the dengue sero-negative group, there was a male predominance with 104 out of the 193 cases being males with a male-to-female ratio of 1.16:1.

Majority of the cases in the dengue seropositive group were aged between 11 and 20 years followed by 20-30 years whereas in the cases with fever but negative for dengue on serology most cases were aged between 20 and 30 years followed by 0-10 years.

**Demography of dengue seropositive cases:**

Table 1 and 2 demonstrates the Age and Sex Distribution of dengue seropositive and seronegative cases.

**Table 1.** Age and Sex Distribution of dengue seropositive cases

| Age Group (In years) | Male (No. of cases) | Male (%) | Female (No. of cases) | Female (%) | Total |
|---|---|---|---|---|---|
| <10 | 20 | 21 | 30 | 30.6 | 50 |
| 11-20 | 32 | 33.6 | 25 | 25.5 | 57 |
| 21-30 | 25 | 26.3 | 26 | 26.5 | 51 |
| 31-40 | 8 | 8.4 | 12 | 12.2 | 20 |
| 41-50 | 4 | 4.2 | 2 | 2 | 6 |
| 51-60 | 3 | 3.1 | 3 | 3 | 6 |
| >60 | 3 | 3.1 | 0 | 0 | 3 |
| Total | 95 | 100.00 | 98 | 100.00 | 193 |



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

**Table 2.** Age and Sex Distribution of dengue sero-negative cases

| Age Group (In years) | Male (No. of cases) | Male (%) | Female (No. of cases) | Female (%) | Total |
|---|---|---|---|---|---|
| <10 | 28 | 26.9 | 11 | 12.3 | 39 |
| 11-20 | 19 | 18.2 | 14 | 15.7 | 33 |
| 21-30 | 19 | 18.2 | 27 | 30.3 | 46 |
| 31-40 | 20 | 19.2 | 15 | 16.8 | 35 |
| 41-50 | 3 | 2.8 | 7 | 7.8 | 10 |
| 51-60 | 6 | 5.7 | 10 | 11.2 | 16 |
| >60 | 9 | 8.6 | 5 | 5.6 | 14 |
| Total | 104 | 100.00 | 89 | 100.00 | 193 |

**Table 3.** Mean and SD of CBC parameters between dengue seropositive and dengue sero-negative cases

| Sl No. | Parameter | Dengue Seropositive Cases | | Dengue Sero-negative Cases | | P value |
|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | (2 sample t test) |
| 1 | WBC Count | 6.5 | 4 | 8.3 | 4.5 | < 0.001 |
| 2 | RBC Count | 4.7 | 0.7 | 4.4 | 0.7 | < 0.001 |
| 3 | Hemoglobin | 12.8 | 2.3 | 12 | 2.3 | < 0.001 |
| 4 | Hematocrit | 37.9 | 6.3 | 35.3 | 6.1 | < 0.001 |
| 5 | MCV | 80.2 | 7.2 | 79.7 | 8.5 | 0.533 |
| 6 | MCH | 27.2 | 3 | 27.1 | 3.5 | 0.763 |
| 7 | MCHC | 33.7 | 1.3 | 33.9 | 1.5 | 0.162 |
| 8 | Platelet Count | 94.7 | 89.1 | 186.6 | 110.5 | < 0.001 |
| 9 | RDW CV | 13.6 | 1.6 | 14.4 | 2.8 | < 0.001 |
| 10 | PDW | 13.1 | 2.7 | 12.2 | 2.8 | 0.001 |
| 11 | MPV | 11 | 1 | 10.5 | 1.1 | < 0.001 |
| 12 | PLCR | 32.9 | 7.9 | 28.7 | 8.9 | < 0.001 |
| 13 | PCT | 0.1 | 0.08 | 0.2 | 0.09 | < 0.001 |
| 14 | Neutrophil % | 43.8 | 20.6 | 59.9 | 19.4 | < 0.001 |
| 15 | Lymphocyte % | 44.8 | 19.4 | 30.2 | 18.4 | < 0.001 |
| 16 | Monocyte % | 9.1 | 4.2 | 8 | 3.9 | 0.008 |
| 17 | IG % | 1.6 | 3.1 | 0.9 | 2.1 | 0.01 |
| 18 | HFLC Count | 0.5 | 0.6 | 0.1 | 0.3 | < 0.001 |
| 19 | HFLC % | 8.4 | 8.0 | 2.2 | 4 | < 0.001 |
| 20 | Days in hospital | 7.5 | 2.1 | 3.2 | 0.8 | < 0.001 |

In the present study with p-value of less than 0.05 indicating statistical significance. On using 2 sample t test of the mean and standard deviation of the two groups, the parameters that were statistically significant included WBC count, RBC count, Hemoglobin, Hematocrit, Platelet count, RDW, PDW, MPV, PLCR, PCT, Neutrophil %, Lymphocyte %, Monocyte %, IG%, HFLC Count, HFLC % and Days in hospital indicating a difference in findings of these parameters between the dengue sero-positive and dengue sero-negative groups who came to the hospital with fever. Thus, these can be used as a hint while starting prophylactic treatment until results are available when it is an emergency or when the results are delayed.



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

However, RBC indices such as MCV, MCH and MCHC were not statistically significant to distinguish between the dengue seropositive and sero-negative groups as expected as dengue infection does not affect the RBC morphology.

**Correlation between HFLC Count and Platelet Count in dengue seropositive cases:**

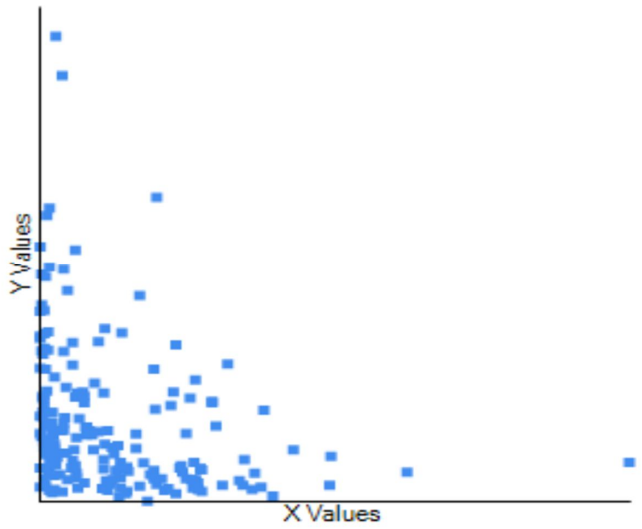


**Fig. 1.** Pearson's Correlation Scatter Plot of variables HFLC Count(x) and Platelet Count(y)

**r:** - 0.2839

In the present study, on using Pearson Correlation to identify the correlation between variables HFLC Count and Platelet Count, r (Pearson's Correlation Coefficient) of -0.2839 was obtained which indicated a low degree of correlation between the two variables.

**Correlation between HFLC Count and NS1 Antigen in dengue seropositive cases:**

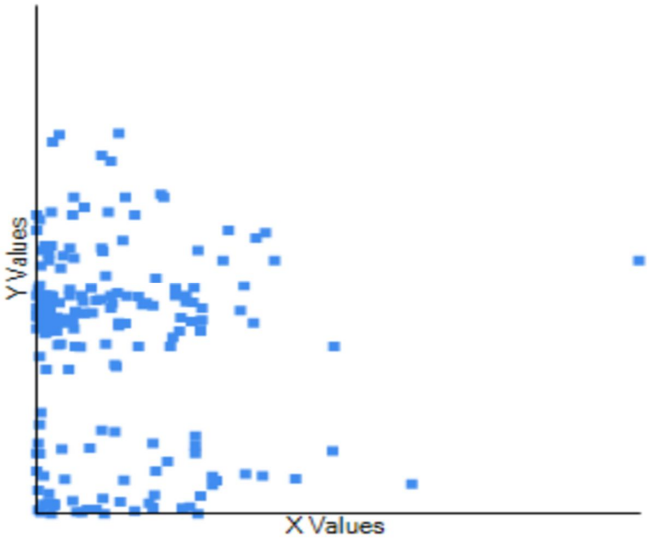


**Fig. 2.** Pearson's Correlation Scatter Plot of variables HFLC Count(x) and NS1 Antigen (y)

**r:** - 0.0841



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

In the present study, on using Pearson Correlation to identify the correlation between variables HFLC Count and NS1Ag, r (Pearson's Correlation Coefficient) of -0.0841 was obtained which indicated a low to no degree of correlation between the two variables.

**Correlation between HFLC Count and IgM in dengue seropositive cases:**

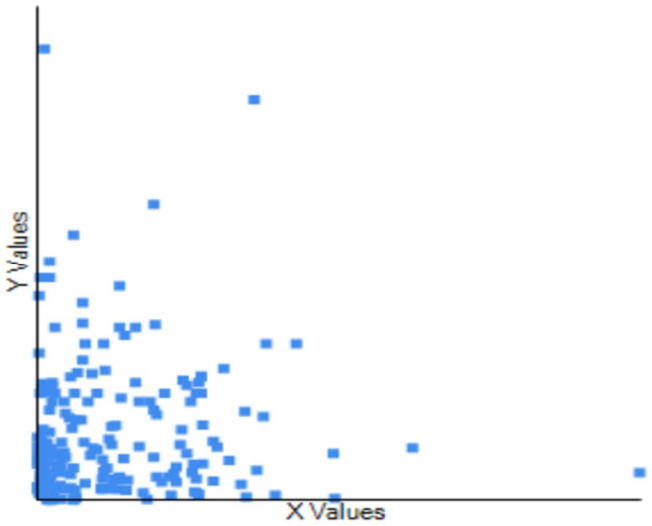


**Fig. 3.** Pearson's Correlation Scatter Plot of variables HFLC Count(x) and IgM (y)

**r:** 0.041

In the present study, on using Pearson Correlation to identify the correlation between variables HFLC Count and Dengue IgM, r (Pearson's Correlation Coefficient) of 0.041 was obtained which indicated a low to no degree of correlation between the two variables.

**Correlation between HFLC Count and Lymphocyte percentage in dengue seropositive cases:**

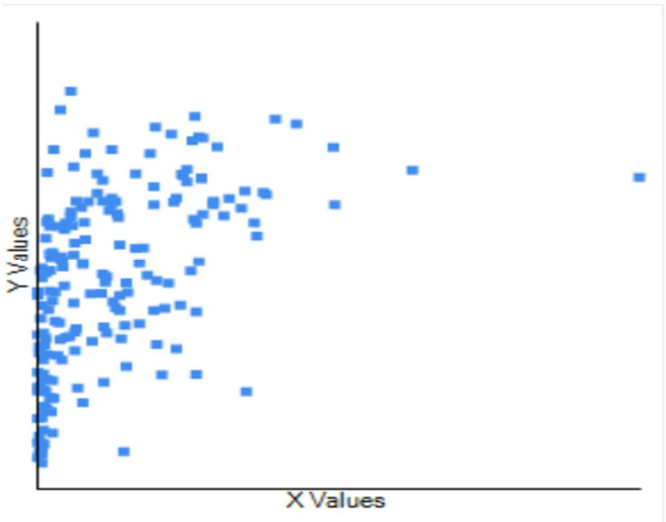


**Fig. 4.** Pearson's Correlation Scatter Plot of variables HFLC Count(x) and Lymphocyte percentage (y)

**r**: 0.506



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

In the present study, on using Pearson Correlation to identify the correlation between variables HFLC Count and Lymphocyte percentage, r (Pearson's Correlation Coefficient) of 0.506 was obtained which indicated a high degree of correlation between the two variables.

**Correlation between HFLC Count and days of admission in hospital in dengue seropositive cases:**


**Fig. 5.** Pearson's Correlation Scatter Plot of variables HFLC Count (x) and days of admission in hospital (y)

**r:** 0.305

In the present study, on using Pearson Correlation to identify the correlation between variables HFLC Count and Days of admission in the hospital, r (Pearson's Correlation Coefficient) of 0.305 was obtained which indicated a moderate degree of correlation between the two variables.

In the present study, on using Pearson Correlation to identify the correlation between variables HFLC percentage and Platelet Count, r (Pearson's Correlation Coefficient) of -0.34 was obtained which indicated a moderate degree of correlation between the two variables.

## Discussion

Our findings are similar to those of previous studies, such as Raharjo B et al. (2019), who reported a mean HFLC % of 11.6%, suggesting the increase in atypical lymphocytes seen in dengue which are identified in hematology analyzer as HFLCs (19). The presence of HFLC can be attributed to the virus activating the B Lymphocytes to produce interferons against antigens DEN 1 to 4 and it also activates the T Lymphocytes which in turn activate the complement system and produce cytokines. These activated lymphocytes can be seen in peripheral smear and detected in hematology analyzers as HFLC (20). Hence the increase in HFLCs indicate increase in activate B lymphocytes, T lymphocytes or monocytes and are seen in the infective phase and reduce as the person recovers (21). Study done by Clarice CSH et al. (2019) has suggested that the percentage of HFLCs in the blood may be proportional to the severity of dengue infection. Further research is needed to confirm this finding and determine whether HFLCs can be used to monitor dengue severity and guide clinical management (22).

Similar to our study, another study done by Oehadian A et al. (2015) have shown that increase HFLC Count and percentage along with Immature Granulocyte count on a hematology analyzers can be seen in dengue infection compared to other infections like malaria, leptospirosis and enteric fever which presents with fever (23).

Similar findings of platelet indices were seen in other studies to our study where the mean platelet count was just above 90,000/cumm at diagnosis. This highlights the finding that thrombocytopenia is the most common



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

finding on routine hematology studies in dengue infection. It is possible that the differences in platelet indices between our study and the study by Kanchana et al. (2019) are due to differences in the study populations or the methods used to measure platelet count and indices (24).

## Conclusion

In conclusion, in resource-limited settings and in developing countries, the diagnosis of dengue by ELISA may not be an option for everyone in resource-limited settings and peripheries, due to factors such as cost and the need for specialized equipment and training. Hence clinical features and platelet count are used routinely by clinicians in making a clinical diagnosis of dengue. This can be aided by newer parameters like high fluorescent lymphocyte count, immature granulocyte fraction, absolute counts, etc. that are available in hematology analyzers while running a hemogram and doesn't require any additional reagents and hence doesn't incur additional cost to the patient.

Newer WBC indices like high fluorescent lymphocyte counts represent activated / atypical lymphocytes which are elevated in viral infections including dengue and hence can deliver reliable results for predicting severity and diagnosis of viral infections like dengue (19, 22, 24). Further research is needed to confirm this finding and determine the optimal cut-off values for HFLC for predicting dengue severity.

The immunological response triggered in dengue can be reliably diagnosed with the study of high fluorescent lymphocyte count and is very helpful to start with the treatment in cases in need of immediate treatment before waiting for confirmatory diagnostic tests such as in cases where the patient's clinical presentation is severe or the patient is at high risk for complications.

In the present study statistical significance was noted in parameters such as WBC count, RBC count, Hemoglobin, Hematocrit, Platelet count, RDW, PDW, MPV, PLCR, PCT, Neutrophil %, Lymphocyte %, Monocyte %, IG%, HFLC count, HFLC %, and Days in hospital between the dengue sero-positive and dengue sero-negative groups who came to the hospital with fever. This indicates HFLC along with platelet count may be useful for differentiating dengue from other infections, such as malaria, leptospirosis, and enteric fever. However, more research is needed to determine the sensitivity and specificity of these parameters for this purpose.

Limitations: The study was carried out in a single center and analyzed patients for a considerably short period of time. Hence similar studies need to be done in other centers to validate the findings.

We plan to conduct a larger, multicenter study to validate our findings and determine the optimal cut-off values for HFLC for predicting dengue severity and differentiating dengue from other infections.

## Acknowledgments

The authors thank the colleagues and other helping hands that helped to make this work possible.

## Conflict of interests

The authors declare that they have no conflicts of interest.

## Funding/Support

No funding was required for the study.

## Data Availability

The raw data supporting the conclusions of this article are available from the authors upon reasonable request.

## Ethical Statement

The study was approved by the institutional ethical committee of the institution and conducted in accordance with the ethical standards. All the patients gave their informed consent before participating in the study.

## References

1. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, Drake JM, Brownstein JS, Hoen AG, Sankoh O, Myers MF, George DB, Jaenisch T, Wint



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

GR, Simmons CP, Scott TW, Farrar JJ, Hay SI. The global distribution and burden of dengue. Nature 2013;496(7446):504-7. https://doi.org/10.1038/nature12060

2. Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG, et al. Refining the Global Spatial Limits of Dengue Virus Transmission by Evidence-Based Consensus. PLoS Negl Trop Dis 2012;6(8):e1760. https://doi.org/10.1371/journal.pntd.0001760

3. Simmons CP, Farrar JJ, Nguyen V, Wills B. Dengue. New Eng J Med 2012;366(15):1423-32. https://doi.org/10.1056/NEJMra1110265

4. Libraty DH, Myint KS, Murray CK, Gibbons RV, Mammen MP, Endy TP, Li W, Vaughn DW, Nisalak A, Kalayanarooj S, Hospenthal DR, Green S, Rothman AL, Ennis FA. A comparative study of leptospirosis and dengue in Thai children. PLoS Negl Trop Dis 2007;1(3):e111. https://doi.org/10.1371/journal.pntd.0000111

5. Harris E, Perez L, Phares CR, Perez MdeL, Idiaquez W, Rocha J, Cuadra R, Hernandez E, Campos LA, Gonzales A, Amador JJ, Balmaseda A. Fluid intake and decreased risk for hospitalization for dengue fever Nicaragua. Emerg Infec Dis 2003;9(9):1003-6. https://doi.org/10.3201/eid0908.020456

6. Chaloemwong J, Tantiworawit A, Rattanathammethee T, et al. Useful clinical features and hematological parameters for the diagnosis of dengue infection in patients with acute febrile illness: a retrospective study. BMC Hematol 2018;18(1):20. https://doi.org/10.1186/s12878-018-0116-1

7. Murray CJ, Rosenfeld LC, Lim SS, Andrews KG, Foreman KJ, Haring D, Fullman N, Naghavi M, Lozano R, Lopez AD. Global malaria mortality between 1980 and 2010: a systematic analysis. Lancet 2012;379(9814):413-31. https://doi.org/10.1016/S0140-6736(12)60034-8

8. Wilder-Smith A, Gubler DJ. Geographic expansion of dengue: the impact of international travel. Med Clin N America 2008;92(6):1377-90. https://doi.org/10.1016/j.mcna.2008.07.002

9. Sastry AS, Bhat KS, Janagond A. Essentials of Medical Microbiology. 2nd ed. New Delhi: Jaypee Brothers Medical Publishers; 2017. https://doi.org/10.5005/jp/books/12637_53

10. Wang M, Zhang J, Ji Q, Yang Q, Zhao F, Li W, et al. Evaluation of platelet distribution width in chronic obstructive pulmonary disease patients with pulmonary embolism. BioMed Res Int 2015;10:587-96. https://doi.org/10.2217/bmm.15.112

11. Van den Bemt PM, Meyboom RH, Egberts AC. Drug-induced immune thrombocytopenia. Drug Safety 2004;27:1243-52. https://doi.org/10.2165/00002018-200427150-00007

12. Agdatli E, Gounari E, Lazaridou E, Katsibourlia E, Tsikopoulou F, Labrianou I. Platelet distribution width: a simple, practical, and specific marker of activation of coagulation. Hippokratia 2010;14(1):28-32.

13. Simsek E, Timur O, Carlioglu A, Durmaz A, Demirci M, Sevimli H. Mean platelet volume in hyperthyroid toxic adenoma patients after radioactive iodine treatment. Adv Endocrinol 2015;15:1-5. https://doi.org/10.1155/2015/436768

14. Vinholt PJ, Hvas AM, Nybo M. An overview of platelet indices and methods for evaluating platelet function in thrombocytopenic patients. Eur J Hematol 2013;92:367-76. https://doi.org/10.1111/ejh.12262

15. Polat H, Sarica MA, Bulut HT, Yucel MO, Gok A, Cift A, et al. The relationship between mean platelet volume and other platelet indices with testicular artery blood flow and fertility: a preliminary study. International J Clin Experi Med 2015;8:11554-8.

16. Shiftan TA, Mendelsohn J. The circulating "atypical" lymphocytes. Hum Pathol 1978;9(1):51-61. https://doi.org/10.1016/S0046-8177(78)80007-0

17. Bain BJ. Disorders of white cells. In: Hoffbrand AV, Moss PAH, editors. Blood Cells: A Practical Guide. 5th ed. West Sussex, UK: John Wiley and Sons; 2015. p. 416-481. https://doi.org/10.1002/9781118817322.ch9

18. Glassy EF, editor. Lymphocyte, reactive. In: Color Atlas of Haematology: An Illustrated Field Guide Based on Proficiency Testing. 1st ed. Northfield, IL: College of American Pathologists; 1998. p. 222-225.

19. Raharjo B, Hadi S. High fluorescent lymphocyte count examination in dengue hemorrhagic patients with Sysmex XN-1000 hematology analyzer. Indones J



[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]

Clinical Pathol Med Laboratory 2019;25(2):207-10. https://doi.org/10.24293/ijcpml.v25i2.1443

20. Tjahjono G, Nasronudin. Imunopatogenesis demam berdarah dengue. In: Nasronudin, editor. Penyakit infeksi di Indonesia. 2nd ed. Surabaya: Airlangga University Press; 2011. p. 117-122.
21. Linssen J, Jennissen V, Hildmann J, Reisinger E, Schindler J, et al. Identification and quantification of high-fluorescence-stained lymphocytes as antibody synthesizing/secreting cells using the automated routine hematology analyzer XE2100. Clin Cytometry Soc 2007;72B:157-66. https://doi.org/10.1002/cyto.b.20150
22. Clarice CSH, Abeysuriya V, de Mel S, Uvindu Thilakawardana B, de Mel P, de Mel C, et al. Atypical lymphocyte count correlates with the severity of dengue infection. PLoS ONE 2019;14(5):e0215061. https://doi.org/10.1371/journal.pone.0215061
23. Oehadian A, Michels M, de Mast Q, et al. New parameters available on Sysmex XE-5000 hematology analyzers contribute to differentiating dengue from leptospirosis and enteric fever. Int J Lab Hematol 2015;37(6):861-868. doi:10.1111/ijlh.12422. https://doi.org/10.1111/ijlh.12422
24. Kanchana PVN. Role of platelet indices in patients with dengue fever - a case-control study. IOSR J Dent Med Sci 2019;18(02):55-57.

This is an open-access article distributed under the terms of the Creative Commons Attribution-noncommercial 4.0 International License which permits copy and redistribute the material just in noncommercial usages, as long as the original work is properly cited.

[ Downloaded from ijrabms.umsu.ac.ir on 2024-05-19 ]

[ DOI: 10.61186/rabms.10.1.54 ]