



EVALUATION OF PLATELET INDICES IN DENGUE FEVER WITH THROMBOCYTOPENIA.

Pathology

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ABSTRACT

Introduction: Dengue fever is an acute viral illness caused by an arthropode-borne dengue virus which occurs mainly in monsoons. The platelet indices are of great value in determining the severity of the disease and prognosis. MPV is a surrogate marker of bone marrow activity; a high MPV indicates increased megakaryocyte activity. PLCR is inversely related to platelet count & is significantly increased in thrombocytopenia. PLCR is directly associated with PDW and MPV. IPF is a novel platelet parameter that measures reticulated platelets in peripheral blood reflecting the status of thrombopoiesis. **Methods:** A retrospective study where secondary data obtained from previous laboratory records of NS1/ ELISA positive dengue cases admitted during July 2022- October 2022 at a tertiary care hospital in Delhi were analyzed. The study also includes healthy adults (25-30 years) from July 2022 - October 2022 to constitute the control group. All blood samples were analyzed on Mindray BC 6200 five-part differential fully automated analyzer. **Results:** The total number of confirmed dengue cases was 129. A total of 109 individuals were selected as a control group. Thrombocytopenia was seen in 124 cases (96.1%). High MPV was seen in 122 (94.5%) cases. High PDW was seen in 125 (96.8%) cases. High plateletcrit was seen in only 1 case (0.7%) case and high P-LCR in 112 (86.8%) of cases respectively. IPF was high in 109 cases (84.8%). **Conclusion:** Mean platelet count and plateletcrit were significantly low and mean MPV, PDW, P-LCR and IPF were significantly high in dengue cases indicating the pathogenesis of thrombocytopenia in dengue cases as peripheral destruction or consumption of platelets rather than bone marrow suppression.

KEYWORDS

Dengue, IPF, platelet indices, thrombocytopenia

INTRODUCTION

Dengue fever (DF) is a mosquito-borne acute viral illness occurring chiefly during the monsoon season. An estimated 50 million infections occur per year worldwide affecting approximately 100 countries. The dengue virus is caused by four different serotypes DEN-1, DEN-2, DEN-3, and DEN-4, and is transmitted by *Aedes aegypti* mosquitoes.[1] DF can cause a range of manifestations from mild dengue fever to dengue hemorrhagic fever which may progress to dengue shock syndrome and death. DF is characterized by fever, myalgia, headache, rash, leukopenia, and variable thrombocytopenia. Severe thrombocytopenia and increased vascular permeability are life-threatening vascular complications of dengue. [2]

The immunopathogenesis of thrombocytopenia in dengue fever is complex. Possible mechanisms of thrombocytopenia in DF may be due to direct bone marrow suppression by the virus, anti-dengue antibody-mediated platelet destruction, peripheral consumption of platelets, or isolated viral replication in the platelets.[3]

The most common laboratory finding in dengue is thrombocytopenia. The decreasing platelet count has been found to predict the severity of the disease. In addition to platelet count, other platelet indices such as Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), plateletcrit (PCT), Platelet Large Cell Ratio (PLCR) and Immature platelet fraction (IPF) are of great value in determining the prognosis in dengue patients.

MPV is a surrogate marker of bone marrow activity; a high MPV indicates increased megakaryocyte activity. A low MPV indicates marrow suppression. PLCR is inversely related to platelet count and directly related to PDW and MPV. IPF is a novel platelet parameter that measures reticulated platelets in the peripheral blood, reflecting thrombopoiesis.[3] IPF is an important parameter as its level rises with

increased bone marrow production of platelets & remains low with suppressed megakaryopoiesis.[4]

Therefore, platelet indices play a pivotal role in predicting the intensity of the disease and immunopathogenesis of thrombocytopenia. It also gives vital information to the clinicians in determining the need to hospitalize the patient and the need for platelet transfusion.

AIMS AND OBJECTIVES

1. To investigate the effect of dengue virus on platelet count and other platelet indices like MPV, PDW, Plateletcrit, PLCR, and IPF and to compare with those of the healthy control group.
2. To determine the clinical importance of the novel parameter IPF.

MATERIALS AND METHOD

1. A retrospective case-control study where secondary data obtained from previous laboratory records of Dengue cases admitted during July 2022-October 2022 at a tertiary care hospital in Delhi were analyzed.
2. The study also includes previous records of apparently healthy adults aged between 25- 30 years from July 2022 to October 2022 to constitute the control group.
3. All venous blood samples included in the study were analyzed for platelet parameters on MINDRAY BC 6200 five-part differential fully automated analyzer.

Inclusion And Exclusion Criteria:

Inclusion Criteria:

1. Patients with a positive dengue serology Non-Structural protein 1 antigen-NS1 and ELISA.
2. Platelet count <1 lakh/cumm.

Exclusion Criteria:

1. All disorders related to thrombocytopenia other than dengue.

Sample Size:

The sample size is calculated by the standard formula. It is assumed that the prevalence rate of dengue is 28.4% based on previous studies. With these assumptions, the sample size works out as 96. Since the number of patients fulfilling the inclusion criteria in the given period was 129, we have taken 129 cases and 109 controls.

RESULTS

The total number of confirmed dengue cases was 129. The age distribution was between 6 months- 70 years with mean age of 30.36 ± 15.5 . A total of 109 individuals were selected as a control group. Age distribution in the control group was between 25-35 years with a mean age of 27.07 ± 3.58 (Table1).

Table 1: Mean Age Comparison Between Both Groups

	Cases (n=129)	Controls (n=109)
Mean age in years	30.36 ± 15.51	27.07 ± 3.58

Of the 129 cases, 72 (55.8%) were males and 57 (44.2%) were female having M: F of 1.2:1.

Of the 109 controls, 57 (52.3%) were males and 52 (47.7%) were female having M: F of 1.09:1 (Table2).

Table 2: Gender Wise Distribution Between Both Groups

	Cases (n=129)	Controls (n=109)
Male	72 (55.8%)	57 (52.3%)
Female	57 (44.2%)	52 (47.7%)

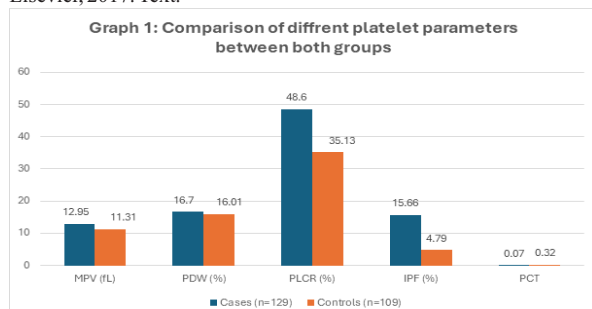
All 129 cases and 109 controls were analyzed for platelet count, MPV, PDW, PCT, PLCR, and IPF. Thrombocytopenia was seen in 124 cases (96.1%). Low MPV was seen in 4 (3.1%) cases and high MPV in 122 (94.5%) normal range of MPV was seen in 3 (2.4%) cases. Low PDW was seen in 4 (3.2%) and high PDW in 125 (96.8%) of cases. Low plateletcrit was seen in 124 (95.4%) and high plateletcrit in 1 (0.7%) of cases and 4 cases (3.9%) were within the normal range. Low P-LCR was seen in 4 (3.1%) and high P-LCR in 112 (86.8%) cases and 13 (10.1%) cases had a normal range of P-LCR. Low IPF seen in 5 (3.7%) and high IPF in 109 (84.8%) cases and 15 (11.5%) cases were within the normal range.

Mean MPV, PDW, P-LCR, and IPF were high in cases as compared to the control group, and mean plateletcrit was found to be low in cases. P values for MPV, PDW, P-LCR, IPF, and plateletcrit in cases was <0.001 which shows that there is a significant difference in cases and control group platelet indices (Table 3 and Graph 1).

Table 3: Comparison Of Different Platelet Parameters Between Both Groups

	Normal reference range (*)	Cases (n=129)	Controls (n=109)	p value
Platelet count (per mm ³)	1.5- 4.5 lakh	36,000 (20-64,000)	2.82 lakh (2.32-3.21)	<0.001
MPV (fL)	7.2-11.7	12.95 ± 1.83	11.31 ± 1.70	<0.001
PDW (%)	8.3-56.6	16.70 ± 1.12	16.01 ± 0.30	<0.001
PCT (%)	0.22-0.24	0.070 ± 0.071	0.329 ± 0.081	<0.001
PLCR (%)	15-35	48.60 ± 11.97	35.13 ± 12.23	<0.001
IPF (%)	1.5-7	15.66 ± 7.89	4.79 ± 3.90	<0.001

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The literature when reviewed showed very few studies where all the platelet indices were included in the study. Our study encompassed all the platelet indices along with platelet count and it was found to be significant when compared with the healthy control group.

DISCUSSION

Very few studies have been conducted on the effect of the dengue virus on IPF. Therefore, in the present study, core emphasis is given to evaluate the pathogenesis of thrombocytopenia in dengue patients through the study of all platelet parameters including IPF.

The present study showed thrombocytopenia in 124 (96.1%) cases. Corresponding to the study done by Kritika Sharma et al. [2] in which 98% of dengue cases had thrombocytopenia. A study was done by Wayez A et al. [4] also showed that 98.11% of patients had thrombocytopenia.

MPV is inversely related to platelet count. Our study showed statistically significant ($P < 0.001$) high MPV. It can be used as a marker of platelet production rate and platelet activation. MPV was significantly higher in cases of dengue fever when compared to controls due to the activation of platelets causing a rise in MPV. This is in accordance with the study done by Kumar N et al. [3] and Afsar N et al. [5] where they found that MPV values increased with decreased platelet count. This was not in correlation with a study done by Wiwanitkit et al. [6] and Dewi et al. [7] probably due to a small sample size.

In the current study, 96.8% of cases had high PDW and it was statistically significant ($P < 0.001$) in dengue cases. Study done by Muddapu L et al. [8], Vijay Kumar Meena et al. [9], Navya et al. [10] showed high PDW in 59.19%, 62%, 92% cases respectively. This is not in accordance as per the study done by Asha, et al. [11] who found higher values of PDW in only those patients who required platelet transfusion.

The present study shows statistically significant ($P < 0.001$) low plateletcrit in 124 cases (96.1%). The study by Asha et al. [11] also found that 98% of patients have low PCT. Vijay Kumar Meena et al. [9] observed a low PCT (<0.1) value in 64.3% of cases. Rai A et al. [12] also found reduced plateletcrit in 65.6% of cases. However, conflicting results were shown by Shradha Khatri et al. [13] who found plateletcrit to be within the normal range as they included dengue patients with normal platelet count in their study done in a tertiary care center from a small geographic area.

Our study showed high PLCR in 112 (86.8%) of cases. The study by Asha, et al. [11] shows 36.3% of the patients having high PLCR. These were those patients who had severe thrombocytopenia and required platelet transfusion. Babu E et al. [14] also showed that P-LCR was increased in destructive thrombocytopenia than those with hypoproliferative thrombocytopenia. [14]

Our study found raised IPF in 109 (84.8%) of cases. An increased IPF suggests increased thrombopoiesis and predictor for recovery of platelet count in dengue patients. This is the same as the study done by Asha, et al. [11] where 68.4% of patients had high IPF. Ahmad Wayez et al. [4] also observed 84.91% of patients had an IPF of more than 8% (high IPF) and only 15.09% of patients had IPF below 8%. Dadu et al. [15] found that IPF had a strong correlation with the recovery of platelet counts in patients with dengue. Kantharaj A. [16] and Lavanya N et al. [17] stated that increased IPF is suggestive of responsive marrow and a reliable parameter in guiding decisions related with platelet transfusion in thrombocytopenia.

IPF as quoted by Ahmad Wayez et al. [4], Asha, et al. [11], Dadu et al. [15], Kantharaj A. [16] and Lavanya N et al. [17] establishes that it is a consistent marker of platelet recovery even in cases of low platelet count and should be in routine in the evaluation and monitoring of patients with thrombocytopenia.

The present study as well as all above-mentioned studies have shown significantly increased IPF indicating a responsive marrow activity. Therefore, it can be used as the perfect tool to help the clinicians to decide for the need of platelet transfusion.

Limitation Of The Study

A limitation of the study is that it could not be ascertained that at which day of fever, the blood sample was collected for evaluation of platelet parameters.

CONCLUSION

In our study, platelet count and plateletcrit were significantly low and

Mean MPV, PDW, P-LCR and IPF were significantly high in dengue cases compared to the control group. High MPV, PDW, PLCR, and IPF in dengue cases with thrombocytopenia indicate increased thrombogenic activity of bone marrow.

Thus, indicating the pathogenesis of thrombocytopenia in dengue cases as peripheral destruction or consumption of platelets rather than bone marrow suppression.

Conflict Of Interest: None.

Acknowledgements: NIL

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