



Analysis of Platelet Indices and its correlation with platelet count In Dengue

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ABSTRACT

Dengue is a global arboviral disease of growing public health concern. Several parameters have been used to detect the infection and severity of dengue. Recent evidence suggests that platelet indices can be used to assess the severity and prognosis of dengue infection. This retrospective study aims at assessing the role of the platelet indices – Mean Platelet Volume (MPV), Platelet Distribution Width, (PDW), P-LCR (Platelet Large Cell Ratio) and Plateletcrit (PCT) and its correlation with the platelet count in 50 Dengue NS1 antigen positive cases and to find the sex ratio and the age-wise distribution of the dengue cases. The indices were obtained using an Automated Hematology analyzer and were compared with the platelet count, considering p-value <0.05 as statistically significant. Thrombocytopenia was found in a majority of the cases and PDW and PLCR were found to be inversely proportional to the platelet count. MPV was found to have no correlation with the platelet count. Hence, we conclude that Platelet count, PDW, and P-LCR can be used as predictors of Dengue infection and severity, whereas MPV cannot be used as a predictor of Dengue infection or severity.



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INTRODUCTION

Dengue is the most rapidly spreading mosquito-borne viral disease in the world caused by one of the four serotypes (DEN1, DEN2, DEN3, DEN4) of the dengue virus. This arbovirus belongs to the genus flavivirus, which belongs to the family Flaviviridae and is transmitted by mosquitoes of the genus *Aedes aegypti*. Dengue infection can progress from uncomplicated Dengue fever to Dengue Hemorrhagic Fever or Dengue Shock Syndrome which

makes it a public health disease of global concern. An estimation of the annual incidence of dengue is 50 million, with an increase in geographic expansion to new countries (Dengue, 2009). About 1,29,166 cases of dengue were reported in the year 2016, with the maximum cases from West Bengal and the southern state of Karnataka accounting for about 4.7% of the disease burden (NVBDPC, 2017). According to a study done in 2017, there has been a near doubling of cases from the year 2012 to 2016 and a steady rise in the trends of mortality in India has been observed from the year 2014 to 2016 (Sahaana et al., 2017). Thrombocytopenia is the most common laboratory finding in dengue fever that can be used as a predictor of the severity of this disease. Although the exact mechanism of thrombocytopenia in dengue is unclear, the probable causes are direct bone marrow suppression by the dengue virus, anti-dengue antibody-mediated platelet destruction, peripheral consumption of platelets and isolated viral replication in the platelet (Mukker and Kiran, 2018). With the advent of automated hematology analyzers, there has been an increase in the number of

studies regarding the role of platelet indices namely plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) and Platelet Large cell ratio (P-LCR) in several diseases as they provide details about the morphology and maturity of the platelets and could be used as prospective platelet activation markers (Budak *et al.*, 2016). With the help of these indices, it has become possible to assess the functional state of the bone marrow. An increase in MPV and platelet large cell ratio indicates that the bone marrow is active and is releasing the immature larger platelets at a higher rate than usual. In thrombocytopenia due to hypo functional bone marrow, these indices remain unchanged (Krishnamurthy *et al.*, 2016). With the advent of these indices, we can infer the predominant mechanism of thrombocytopenia in dengue patients without a bone marrow examination. As thrombocytopenia has been proven to have a significant association with dengue infection and severity (Jayashree *et al.*, 2011), a correlation of these indices with the platelet count will help in determining the usage of these indices as predictive parameters of dengue infection and severity. However, platelet indices are not specific for any particular pathological condition and large randomized control studies are required to signify and establish the utility of these parameters in dengue beyond doubt.

MATERIALS AND METHODS

The present study was conducted as a retrospective study of 50 patients admitted within August 2019 to November 2019 with clinical features of dengue fever in a tertiary care centre in Chennai. The Complete blood count values of all the patients were obtained using a fully automated six-part hematology analyzer- SYSMEX XN 1000 model within one hour of venepuncture. The subjects were divided into 7 groups according to their platelet count (<10000/ μL , 10001 - 50000/ μL , 50001 - 100000/ μL , 100001 - 200000/ μL , 200001-300000/ μL , 300001 - 400000/ μL , > 400000/ μL). The platelet indices - PDW, MPV, PLCR, Plateletcrit and hematocrit, were obtained from the CBC values. The values were entered into Microsoft Excel and were compared with the platelet counts. Statistical analysis was done using the Statistical Package for Social Sciences - SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA). The descriptive statistics were reported using mean with the Standard Deviation (SD). A p-value of < 0.05 was considered as statistically significant.

Inclusion criteria

1. Patients with the clinical features of Dengue

according to the WHO criteria

2. Patients with serological positivity (NS1 antigen positivity).

Exclusion criteria

1. Serologically negative patients
2. IGM positive but NS1 antigen-negative patients
3. Patients whose peripheral smears had platelet clumps present, which would largely differ from the original values.
4. Patients with CBC values where the platelet indices showed blank values.

RESULTS AND DISCUSSION

The study included a total of 50 patients who had the clinical features of Dengue and were NS1 positive. Out of the total patients, 34 of them were males and 16 were females (Figure 1). The age-wise demographic details showed that 2 (4%) patients belonged to the age group 5 -14 years, 17 (34%) patients to the group 15 -24 years, 11 (22%) patients to the group 25 - 34 years, 9 (18%) patients to the group 35 - 44 years, 6 (12%) patients to the group 45 - 54 and 5 (10%) patients to the group > 55 years (Figure 2).

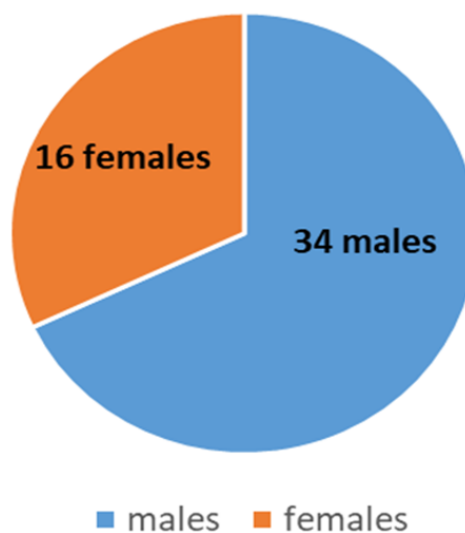


Figure 1: Sex ratio of affected patients

Thrombocytopenia was noted in 35 cases. The platelet count distribution among the affected patients and its correlation with the MPV has been depicted in Table 1. The haematocrit values and their distribution among the patients have been depicted in Table 2. The relationship between the

Table 1: Platelet distribution among affected patients and relationship with the MPV values

Platelet count (μL)	N	MPV (fL) (Mean) p=0.05
<10000	1	13.9
10001-50000	7	12.04
50001-100000	15	12.10
100001-200000	15	10.92
200001-300000	7	9.85
300001-400000	4	10.8
>400000	1	9.6

Table 2: Hematocrit distribution

Hematocrit (%)	N
<20	1
21-30	4
31-40	29
41-50	14
>50	2

Table 3: Relationship between Hematocrit levels and Platelet count levels

Platelet count (μL)	N	Hematocrit (%) (Mean) p = 0.004
<10000	1	23
10001-50000	7	41.7
50001-100000	15	42.14
100001-200000	15	37.27
200001-300000	7	37.7
300001-400000	4	30.5
>400000	1	37

Table 4: Relationship of PDW with Platelet count levels

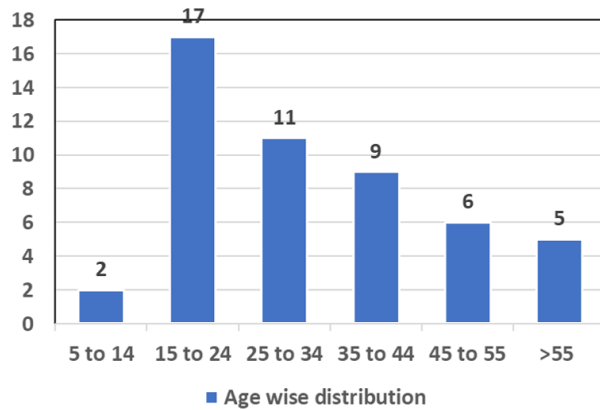
Platelet count(μL)	N	PDW (fL)(Mean) p = 0.0003
<10000	1	26
10001-50000	7	16.04
50001-100000	15	16.6
100001-200000	15	13.76
200001-300000	7	11.08
300001-400000	4	11.27
>400000	1	10.8

Table 5: Relationship between PLCR and platelet counts

Platelet count(μL)	N	PLCR(%) (Mean)P=0.000007
<10000	1	52
10001-50000	7	41.04
50001-100000	15	41.26
100001-200000	15	32.63
200001-300000	7	23.3
300001-400000	4	25.62
>400000	1	21.8

Table 6: Relationship between PCT and platelet counts

Platelet count ($/\mu\text{L}$)	N	PCT (%) (Mean) p <0.00001
<10000	1	0.01
10001-50000	7	0.04
50001-100000	15	0.08
100001-200000	15	0.13
200001-300000	7	0.24
300001-400000	4	0.35
>400000	1	0.49

**Figure 2: Age-wise distribution (years)**

haematocrit and the platelet counts have been depicted in Table 3. The relationship between PDW, P-LCR and PCT with platelet count is shown in Tables 4 and 5 and Table 6, respectively.

Dengue is a growing cause of international health concern and the incidence and geographical distribution of dengue infections have significantly increased in the past few decades and a large number of cases remain undiagnosed and underreported. Platelet indices have been used as a diagnostic value in inflammatory diseases, such as inflammatory bowel diseases, rheumatoid arthritis, ankylosing spondylitis, ulcerative colitis, and atherosclerosis (Budak *et al.*, 2016).

Thrombocytopenia in dengue is thought to be due to direct bone-marrow suppression of thrombopoiesis modulation of an endothelial cell by dengue virus or destruction of platelets by Anti-NS1 antibodies directed against the virus cross-reacting with the platelets (Khatri *et al.*, 2018; Kantharaj, 2018). In the present study out of the total 50 subjects, 68 % were males and 32 % similar to the study done by Sharma and Yadav (2015), where the proportion of males was 63.5% and females 36.5%. The most number of cases were found to belong to the age group of 15 to 24, which was similar to the study done by Ukey *et al.* (2010) in which the maximum

cases were noted in 15 to 30 years of age group. The mean age of the affected patients was 30.3 years (SD = 13.07). The average haematocrit obtained in our study was 38.592 %, with the averages in males and females being 40.25% and 34.7%, respectively. The maximum subjects had a haematocrit between 31 to 40% and only one patient had a high haematocrit of 60%. The haematocrit was found to be maximum in the platelet range 50001 to 100000/ μL . An increase in HCT 20 % above the baseline signifies hemoconcentration and possibly impending shock. This is caused due to the fluid leakage from capillaries, which is seen in dengue cases. Such patients are more likely to develop Dengue Shock Syndrome and require immediate and aggressive management with IV fluids. The release of high levels of platelet-activating factor may cause the consumption of platelets and amplifies the adhesiveness of vascular endothelial cells leading to thrombocytopenia (Navya *et al.*, 2016). The maximum thrombocytopenia was noted in 70% of the cases which corresponded to the study done by Anuradha and Dandekar (2014), where there were 89% of patients with thrombocytopenia. The maximum number of patients belonged to the platelet groups 50001 to 100000/ μL and 100001 to 200000/ μL which was 15 each. The average platelet count in our study was 1.395 Lakh / μL and the range was 0.08 to 5.12 Lakh / μL . An increase in MPV with falling platelets implies the destruction of platelet and signals need for platelet transfusion while a reduction in MPV with low platelets signifies underproduction or bone marrow suppression. The average MPV value in our study was 11.22fL (SD = 1.53) and 13 cases had MPV values that fell towards the higher range (Normal MPV - 7.5 - 12fL) (Korniluk *et al.*, 2019). However, there was no significant correlation between the Mean Platelet Volume and the Platelet count in our study which was corresponding to the study done by Sharma and Yadav (2015) and Dewi (2013). This finding can be explained by the fact that there could be bone marrow suppression even in patients with peripheral platelet

destruction (Krishnamurthy *et al.*, 2016). A possible cause for the differences in the mean MPV values of various studies could be explained because of differences in the machines used and their working principles. Plateletcrit is the volume of platelets as a percentage of the total blood volume and was found to be consistent with the platelet count in our study as expected. A reduction of platelet count and PCT signifies that platelets have been excessively consumed. The normal range for PCT is 0.22–0.24% (Chandrashekar, 2013). The mean PCT of the patients in our study was 0.144%. During platelet activation, platelets with increased number and size of pseudopodia differ in size, thus affecting the platelet distribution width (PDW) and P-LCR (Mohamed *et al.*, 2015). P-LCR is used as an indicator of the circulating larger platelets which are more than 12 fL, represented as a percentage. The normal range of P-LCR is 15–35% and has also been used to monitor the platelet activity. The mean P-LCR in our study was 34.3% (SD = 11.4). PDW is a marker of variation in volume in the platelet size and is elevated in the presence of platelet anisocytosis (Mukker and Kiran, 2018). The mean PDW in our study was 14.54fL (SD = 4.665). In our study, there was an inverse proportionality of PDW and P-LCR with platelet count signifying increased activation in low platelet patients corresponding to the study done by Mukker and Kiran (2018). Platelet counts do not have an important role in determining the need for a transfusion in dengue fever. However, Platelet indices can give the clinician information on whether the platelet destruction is ongoing (which would require a platelet transfusion) or whether the bone marrow is responsive and platelet transfusions can be delayed or put on hold. These indices are often calculated and given by the automated cell counters, but often these values are not reported. This is possibly due to the under-recognition of the importance and utility of these platelet parameters by the clinicians, pathologists as well as laboratory technicians. Another reason could be a lack of standardization.

CONCLUSION

The present study that included a total of 50 patients admitted with clinical features of dengue fever (according to WHO criteria) and NS1 Antigen positivity had an objective of studying the role and trend of platelet indices Mean Platelet Volume, Platelet Distribution Width, Platelet – Large Cell Ratio and Plateletcrit in association with thrombocytopenia to assess its prognostic utility. PDW and P-LCR were found to be inversely proportional to platelet count and PCT was directly proportional, whereas MPV

showed no significant correlation with thrombocytopenia or serology, thus excluding the role of MPV in detecting dengue cases or using it as a prognostic index.

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Conflict of Interest

None.

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