

ORIGINAL ARTICLE

## ROLE OF PLATELET PARAMETERS IN DENGUE FEVER IN CHILDREN

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### ABSTRACT

**Aim:** To evaluate the role of platelet parameters in dengue fever and also to determine relationship of platelet parameters with platelet count and the severity of the disease.

**Materials and methods:** The platelet parameters [platelet count, plateletcrit, mean platelet volume (MPV), platelet distribution width (PDW)] of 50 dengue infected children were calculated using BC 3000 plus Mindray Automated Hematology Analyzer. Normal range of MPV is 7.5-11.5 fl. Plateletcrit cut off value in thrombocytopenia is 0.2-0.36%. The PDW reported varies with reference intervals ranging from 8.3 to 56.6%. Subjects were divided into four groups according to their platelet count on day 3 of illness (<20,000 cells/cumm, 20,000 to 50,000 cells/cumm, 50,000 to 100,000 cells/cumm and >100,000 cells/cumm). Platelet indices were studied among these groups and also the indices were evaluated with respect to the severity of disease as group A (dengue without warning signs), group B (dengue with warning signs and group C (severe dengue).

**Results:** Male: female ratio was 28:22. Mean age of presentation was  $7.8 \pm 2.2$  years. Thirty-five patients belonged to Group A, 26 to group B and 2 belonged to group C. PLT (cells/cumm) on Day 3 and Day 7 was  $91,828 \pm 33,532$  vs  $195,371 \pm 70,586$  in Group A patients ( $p < 0.0001$ ),  $69,076 \pm 45,904$  vs  $163,230 \pm 85,053$  in Group B patients ( $p = 0.0018$ )  $38,500 \pm 38,890$  vs  $86,000 \pm 28,284$  in Group C patients ( $p = 0.29$ ). PCT (%) on Day 3 and Day 7 was  $0.09 \pm 0.04$  vs  $0.18 \pm 0.06$  in Group A patients ( $p < 0.0001$ ),  $0.07 \pm 0.04$  vs  $0.15 \pm 0.07$  in Group B patients ( $p = 0.0009$ ) and  $0.04 \pm 0.04$  vs  $0.08 \pm 0.28$  in Group C patients ( $p = 0.84$ ). MPV (fl) on Day 3 and Day 7 was  $10.73 \pm 1.07$  vs  $11.34 \pm 1.09$  in Group A patients ( $p = 0.0212$ ),  $10.41 \pm 1.39$  vs  $10.87 \pm 0.99$  in Group B patients ( $p = 0.3389$ ),  $9.35 \pm 1.62$  vs  $10.3 \pm 1.41$  in Group C patients ( $p = 0.59$ ). PDW (fl) on Day 3 and Day 7 was  $14.46 \pm 1.35$  vs  $13.22 \pm 1.10$  in Group A patients ( $p = 0.0001$ ),  $14.61 \pm 1.36$  vs  $13.0 \pm 0.76$  in Group B patients ( $p = 0.0011$ ) and  $14.5 \pm 1.84$  vs  $13.5 \pm 0.71$  in Group C ( $p = 0.54$ ). Though MPV was lower in patients with platelet count <20,000 cells/cumm ( $8.57 \pm 0.5$  fl) as compared to other groups, it was not statistically significant ( $p = 0.325$ ). PCT increases with increase in platelet count on Day 3 and Day 7 ( $p = 0.000$ ). Though PDW was lower on Day 3 in patients with platelet count <20,000 cells/cumm as compared to the other 3 groups, it was not statistically significant ( $p = 0.0740$ ).

**Conclusion:** Lower platelet count and low PCT are seen with severe dengue, increasing platelet count and PCT suggest recovery phase of dengue. MPV had no correlation with severity of dengue or level of thrombocytopenia suggestive that there is no role to predict severity of dengue. PDW does not fluctuate with severity of dengue or level of thrombocytopenia.

### Introduction

Dengue fever (DF) is an acute febrile disease characterized by sudden onset of fever of 3-5 days, intense headache, myalgia, joint pain, retro-orbital

pain, anorexia, gastrointestinal disturbances and rash.<sup>1</sup> Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) are life threatening reversible vascular complications of DF and are associated with severe thrombocytopenia, bleeding and increased vascular permeability.<sup>2</sup> Decreasing platelet counts have found to predict the severity of the disease.<sup>3</sup> Platelet indices like mean platelet volume (MPV), platelet distribution width (PDW) have been investigated as prospective platelet activation indicators.<sup>4</sup> The combined interpretation of platelet (PLT) count, plateletcrit (PCT), MPV, PDW can be very useful in various inflammatory disorders.<sup>5</sup> MPV is average size

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of the platelets in blood. Normal range of MPV is 7.5-11.5 fl.<sup>6</sup> Usually MPV >13 occurs in hyperdestruction & MPV <8 in hypoproduction of platelet.<sup>7</sup> Correlation of parameters like platelet count and MPV with bleeding and severity of the disease can be a predictor of disease outcome.<sup>8</sup> Plateletcrit is a measure of total platelet mass. The cut off value in thrombocytopenia is 0.2-0.36%.<sup>9</sup> Plateletcrit is an effective screening tool for detecting platelet quantitative abnormalities. PCT is the volume occupied by platelets in the blood as a percentage and calculated by the formula  $PCT = \text{platelet count} \times MPV/10,000$ .<sup>9</sup> PDW is a marker of volume variability in platelet size and is elevated in the presence of platelet anisocytosis. The PDW reported varies with reference intervals ranging from 8.3 to 56.6%.<sup>10</sup> PDW directly measures variability in platelet size, changes occurring with platelet activation, and suggests the heterogeneity in platelet morphology.<sup>10</sup> The aim of our study was to investigate the platelet parameters and to assess their relationship between the platelet count and the severity of the dengue disease in children.

### Methods & Materials

This was a prospective observational study carried out in a tertiary care hospital on all dengue infected children during the outbreak of dengue infection over a period of 3 months from June 2018 to September 2018 in the Department of Paediatrics, SDM Medical College and Hospital, Dharwad. The platelet parameters of 50 dengue infected children like PLT, MPV, PDW, PCT were noted. Subjects were divided into four groups according to their platelet count on day 3 of illness (<20,000 cells/cumm, 20,000 to 50,000 cells/cumm, 50,000 to 100,000 cells/cumm and >100,000 cells/cumm). Platelet indices were studied among these groups and also the indices were evaluated with respect to the severity of disease as group A (dengue without warning signs), group B (dengue with warning signs and group C (severe dengue) based on WHO 2009 guidelines on dengue (11). Dengue was diagnosed on the basis of clinical features and positive dengue serology (NS1 antigen, IgM/IgG antibody to the dengue virus). **Statistical analysis:** Data was entered in Microsoft Office Excel 2007 and analysis done using SPSS (version 16) windows. Categorical data was calculated as mean  $\pm$  standard deviation (SD). Platelet parameters were compared with severity of illness and platelet count on Day 3 and Day 7 by student t test and anova 1 test. P value <0.05 was taken as significant.

### Results

Male: female ratio was 28:22. Mean age of presentation was  $7.8 \pm 2.2$  years. Thirty-five patients belonged to Group A, 26 to group B and 2 belonged to group C. On day 3 of illness, 4 (8%) had PLT below 20,000 cells/cumm, 9 (18%) patients had PLT between 20,000 to 50,000 cells/cumm, 12 (24%) had PLT between 50,000 to 1,00,000 cells/cumm and 25 (50%) patients had PLT above 100,000 cells/cumm. On day 7 of illness, none of them had PLT below 20,000 cells/cumm, 1 (2%) had PLT between 20,000 to 50,000 cells/cumm, 9 (18%) had PLT between 50,000 to 1,00,000 cells/cumm and 40 (80%) had PLT above 1,00,000 cells/cumm. The mean PLT on day 3 was  $83,000 \pm 39,000$  cells/cumm and on day 7 was  $1,83,000 \pm 77,000$  cells/

cumm. The mean PCT on day 3 was  $0.07 \pm 0.04$  % and on day 7 was  $0.16 \pm 0.07$  %. Mean MPV on day 3 was  $10.6 \pm 1.2$  fl and on day 7 was  $11.18 \pm 1.1$  fl. Mean PDW on day 3 was  $15.5 \pm 1.3$  fl and on day 7 was  $13.2 \pm 1$  fl. The average hospital stay in these patients was  $9 \pm 5.6$  days. Table 1 shows comparison of platelet indices among the four groups based on platelet count on day 3 and day 7 of illness. Table 2 shows comparison of platelet parameters with severity of dengue on day 3 and day 7 of illness. Though MPV was lower in patients with platelet count <20,000 cells/cumm ( $8.57 \pm 0.5$  fl) as compared to those with higher platelet count on Day 3, it was not statistically significant ( $p=0.325$ ). Similarly, on recovery, MPV did not vary with the platelet counts on Day 7 ( $p=0.07$ ). PCT increases with increase in platelet count on Day 3 and Day 7 ( $p=0.000$ ). Though PDW was lower on Day 3 in patients with platelet count <20,000 cells/cumm as compared to the other 3 groups, it was not statistically significant ( $p=0.0740$ ).

### Discussion

Low platelet count in dengue is either due to decreased production of platelets in the bone marrow or increased destruction and clearance of platelets from peripheral blood.<sup>12</sup> Low PCT and low platelet count could be used as a significant predictor of severity of dengue illness<sup>8</sup> which was also seen in our study. Shah et al and Borkatakya et al, found a higher PDW in hyper destructive thrombocytopenia when compared to hypoproduative thrombocytopenia.<sup>12,13</sup> In our study, the severity of dengue did not correlate with PDW nor did the PDW fluctuate with recovery suggestive that thrombocytopenia in dengue could be multifactorial and not due to isolated hyperdestruction or hypoproduction though PDW was lower in patients with platelet count <20,000 cells/cumm suggestive of bone marrow involvement with lower platelet counts. A low MPV implies marrow suppression as a cause of thrombocytopenia and a rising MPV heralds the improvement in platelet count.<sup>8</sup> Our study revealed a low MPV in patients with platelet counts below 20,000 compared to higher platelet count groups. However, it was not statistically significant. Similar result was seen in a case control study by Bashir et al. They found MPV was decreased in dengue positive cases and was normal in control group.<sup>14</sup> Sharma et al studied 200 dengue fever cases. MPV showed no significant correlation with severity, serology and treatment outcome, thus excluding its role in dengue cases.<sup>15</sup> Similarly, in our study MPV had no correlation with severity of dengue suggestive that there is no role to predict severity of dengue. In the study, done by Dewi et al, there was no significant difference in MPV between DF, DHF and DSS ( $9.18 \pm 1.5$  fL vs.  $8.94 \pm 1.94$  fL vs.  $8.57 \pm 1.03$  fL,  $p=0.761$ ).<sup>16</sup> Wiwanitkit et al, found that MPV for patients with DHF is not decreased and appears to be similar to that for the general healthy population.<sup>17</sup>

### Conclusion

Lower platelet count and low PCT are seen with severe dengue, increasing platelet count and PCT suggest recovery phase of dengue. MPV had no correlation with severity of dengue or level of thrombocytopenia suggestive that there is no role to predict severity of dengue. PDW does not fluctuate with severity of dengue or level of thrombocytopenia.

**TABLE 1.** Comparison of severity of thrombocytopenia with platelet parameters on day 3 and day 7 of illness

PLT (cells/cumm) (N)	PLT (cells/cumm) Day 3	PLT (cells/cumm) Day 7	P value	PCT (%) Day 3	PCT (%) Day 7	P value	MPV (FL) Day 3	MPV (FL) Day 7	P value	PDW (FL) Day 3	PDW (FL) Day 7	P value
<20,000 (n=4)	15,500 ± 3,109	77,250 ± 28,535	0.0051	0.02 ± 0.01	0.07 ± 0.03	0.0096	8.57 ± 0.5	9.6 ± 0.5	0.023	13.67 ± 1.02	12.9 ± 0.58	0.238
20,000-50,000 (n=9)	36,222 ± 9,614	122,888 ± 38,653	<0.0001	0.04 ± 0.01	0.12 ± 0.04	<0.0001	10.43 ± 1.10	11.16 ± 0.72	0.12	15.47 ± 0.73	13.4 ± 1.02	0.0001
50,000-100,000 (n=12)	75,750 ± 11,810	129,833 ± 3,819	<0.0001	0.08 ± 0.02	0.12 ± 0.04	0.0007	11.22 ± 1.2	11.64 ± 1.21	0.41	14.78 ± 1.46	12.8 ± 1.09	0.0011
>100,000 (n=25)	11,7120 ± 12,336	246,360 ± 42,960	<0.0001	0.12 ± 0.03	0.22 ± 0.04	<0.0001	10.67 ± 0.9	11.21 ± 1.01	0.05	14.16 ± 1.31	13.28 ± 1.02	0.0107

**Note:** PLT - platelet counts, PCT - Plateletcrit, MPV - mean platelet volume, PDW - platelet distribution width

**TABLE 2.** Comparison of platelet parameters with severity of dengue on day 3 and day 7 of illness.

Severity of Dengue	PLT (cells/cumm) Day 3	PLT (cells/cumm) Day 7	P value	PCT (%) Day 3	PCT (%) Day 7	P value	MPV (FL) Day 3	MPV (FL) Day 7	P value	PDW (FL) Day 3	PDW (FL) Day 7	P value
GROUP A (35)	91,828 ± 33,532	195,371 ± 70,586	<0.0001	0.1 ± 0.04	0.18 ± 0.06	<0.0001	10.73 ± 1.07	11.34 ± 1.09	0.0212	14.46 ± 1.35	13.22 ± 1.1	0.0001
GROUP B (13)	69,076 ± 45,904	163,230 ± 85,053	0.0018	0.07 ± 0.04	0.15 ± 0.07	0.0009	10.41 ± 1.39	10.87 ± 0.99	0.3389	14.61 ± 1.36	13.0 ± 0.76	0.0011
GROUP C (2)	38,500 ± 38,890	86,000 ± 28,284	0.29	0.04 ± 0.04	0.08 ± 0.08	0.84	9.35 ± 1.62	10.3 ± 1.4	0.59	14.5 ± 1.84	13.5 ± 0.71	0.54

**Note:** PLT - platelet counts, PCT - Plateletcrit, MPV - mean platelet volume, PDW - platelet distribution width

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