MALARIA AND PLATELETS: A WELL-KNOWN ASSOCIATION WITH NEW PERSPECTIVEGauri S. Metkar¹**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: INTRODUCTION: Malaria continues to be a great health problem in tropical and subtropical countries, causing significant morbidity and mortality worldwide. Most common hematological change associated with malaria is thrombocytopenia. Lot of research has been done in past to study changes in platelet count in malaria. Present study aims to evaluate changes in other platelet parameters like mean platelet volume, platelet distribution width and plateletcrit (PCT) in malaria caused by common species and its correlation with grade of malaria. **METHODOLOGY:** This observational study was conducted in central hospital laboratory of a tertiary health care centre in Mangalore, Karnataka. The laboratory confirmed cases of malaria from July 2013 to December 2013 were included in the study. Platelet indices in malaria caused by *P. vivax* as well as *P. falciparum* and its correlation with parasite density were studied. **RESULT:** Platelet count and PCT showed inverse relationship with increasing grades of malaria (both *P. falciparum* and *P. vivax*) which was found statically significant. Platelet distribution width showed increasing trends with increasing grades of malaria in both species. However, mean platelet volume showed no correlation with grades of malaria. **CONCLUSION:** Along with platelet count, other platelet indices like platelet distribution width and PCT can be utilized to assess the severity of malarial infection.

KEYWORDS: Malaria, platelet distribution width, PCT, mean platelet volume.

INTRODUCTION: Malaria is a widespread and well known disease mainly seen in Asia and Africa. Malaria is caused by protozoan plasmodium (P.) and transmitted by female anopheles mosquitoes. There are four species of malarial parasite namely *P. falciparum*, *P. vivax*, *P. malariae* and *P. ovale*. Out of these, *P. falciparum* and *P. vivax* commonly coexist in several parts of world including India.¹

As per world malaria report 2009, half of the world's population is at risk of malaria and an estimated 243 million cases led to nearly 8, 63, 000 deaths in 2008.² In India about 27% population lives in malaria high transmission area (more than 1 case per 1000 population) and 58% in low transmission area.³ In 2008 there were 1.52 million cases of malaria in India, out of which 0.76 million case of *P. falciparum*, comprising 50% of total malaria cases.

Association between malaria and thrombocytopenia is well known. Both non-immunological as well as immunological destruction of platelets have been implicated in causing thrombocytopenia. The mechanisms for platelet destruction are coagulation disturbances, sequestration in spleen, antibody mediated platelet destruction, oxidative stress, and the role of platelets as cofactors in triggering severe malaria.

Abnormalities in platelet structure and function have been described as a consequence of malaria, and in rare instances platelets can be invaded by malaria parasites.⁴⁻⁶ Present study aims at evaluating correlation between other platelet indices like PDW, MPV and PCT and grade of malaria.

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METHODOLOGY: This retrospective observational study was conducted in AJ Institute of Medical Sciences and Research Centre, Mangalore, Karnataka. A total of 1770 laboratory confirmed cases of malaria from January 2013 to December 2013 were included in this study.

Diagnosis and grade of malaria was confirmed by thin blood smears stained by Leishman stain as well as using HRP 2 (Histidine Release Protein 2) antigen card test. Platelet count and other platelet indices in all cases were determined using Lab-life D5 Supreme automated cell counter. All malaria positive smears were reviewed for confirmation, typing and grading of malaria and evaluation of platelets. The normal ranges for platelet indices provided for this equipment are as follow:

Platelet count: $1,50 - 4,50 \times 10^3 / \mu\text{l}$

Mean platelet volume (MPV): 7 - 11 fl

Platelet distribution width (PDW): 15.0 - 17.0

PCT (platelet-crit): 0.108 - 0.282 %.

Data was analyzed by Spearman's correlation coefficient and

Multivariate logistic regression. Statistical significance of p value was set at 0.05.

RESULT: Out of total 1770 cases of malaria, maximum 1410 (79.6%) were caused by *P. vivax*. In *P. vivax*, 604 (42.8%) cases were grade 1. Amongst *P. falciparum* cases, 62 (88.5%) out of 70 were grade 1. In mixed malaria patients, maximum 118 (40.6%) out of 290 had grade 2 malaria.

Malaria species	Grade 1	Grade 2	Grade 3	Total
Pl. vivax	604	407	399	1410 (79.6%)
Pl. fl	62 (88.5%)	2	6	70
Mixed	90	118	82	290

TABLE 1: Species and grade wise distribution in malaria cases

Distribution of species and grade of malaria

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In *P. vivax* infection no. cases showing thrombocytopenia increased with grade of infection. Out of 399 Grade 3 cases, 320(80.2%) showed thrombocytopenia as compared to 302(50%) out of 604 grade 1 cases.

Similar trend was seen in *P. falciparum* and mixed (*P. vivax* + *P. falciparum*) cases.

P. vivax Grade of infection	No. of cases (total - 1410)	Platelet count	
		Normal	Decreased
Grade I	604	302 (50%)	302(50%)
Grade II	407	200 (49.1%)	207 (50.8 %)
Grade III	399	79 (19.7%)	320 (80.2%)

Table 2: Correlation between grade of infection and thrombocytopenia

P. falciparum Grade of infection	No. of cases (total - 68)	Platelet count	
		Normal	Decreased
Grade I	62	60 (96.7%)	2 (0.3%)
Grade II	2	1 (50%)	1 (50%)
Grade III	6	1 (16.7%)	5 (83.3%)

Table 3: Correlation between grade and platelet count in *P. falciparum* malaria

Mixed (Pv +Pf) Grade of infection	No. of cases (total - 290)	Platelet count	
		Normal	Decreased
Grade I	90	86 (95.5%)	4 (5.5%)
Grade II	118	29 (24.5%)	89 (75.5%)
Grade III	82	2 (2.4%)	80 (97.6%)

Table 4: Correlation between grade of mixed malaria and platelet count

Table 5 shows that mean platelet volume was normal in most of the cases in *P. vivax* (100% cases of grade 1 and 98.7% of grade 3 infection).

p. vivax Grade of infection	No. of cases (total - 1410)	Mean platelet volume	
		Normal	Increased
Grade I	604	604 (100%)	0 (0%)
Grade II	407	404 (99.2%)	3 (0.8%)
Grade III	399	394 (98.7%)	5 (1.2%)

Table 5: *P. vivax* malaria and MPV

As seen in table 6 PDW showed increasing values with increasing grades of *P. vivax* infection. Only 28.6% grade 1 cases showed increased PDW as compared to 48. 4% grade 2 and 99.2% grade3 cases.

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P. vivax Grade of infection	No. of cases (total - 1410)	PDW	
		Normal	Increased
Grade I	604	431 (71.4%)	173 (28.6%)
Grade II	407	210 (51.6%)	197 (48.4%)
Grade III	399	3 (0.8%)	396 (99.2%)

Table 6: P. vivax and PDW

Table 7 shows that PCT showed decreasing values with increasing grades of P. vivax infection, with maximum, 79.9% cases of grade 3 infection showing decreased PCT.

P. vivax Grade of infection	No. of cases (total - 1410)	PCT	
		Normal	Decreased
Grade I	604	302 (50%)	302 (50%)
Grade II	407	163 (40.1%)	244 (59.9%)
Grade III	399	80 (20.1%)	319 (79.9%)

Table 7: P. vivax and PCT

Amongst P. fl cases, 90.3% of grade 1 cases and 83.3% of grade 3 cases showed normal MPV. There was no correlation between MPV and grade of malaria.

P. falciparum Grade of infection	No. of cases (total - 68)	Mean platelet volume	
		Normal	Decreased
Grade I	62	56 (90.3%)	6 (9.7%)
Grade II	2	2 (100%)	0 (0%)
Grade III	6	5 (83.3%)	1 (16.7%)

Table 8: Correlation between grade of P. falciparum and MPV

As seen in table 9 and 10 PDW and PCT in P. falciparum cases showed findings similar to P. vivax infection. All 6 cases (100%) of grade 3 P. falciparum cases showed increased PDW. 83.3% grade 3 cases showed decrease in PCT as compared to only 22.6% grade 1 cases.

Pl. falciparum Grade of infection	No. of cases (total - 68)	PDW	
		Normal	Increased
Grade I	62	34 (54.8%)	28 (45.2%)
Grade II	2	1 (50%)	1 (50%)
Grade III	6	0 (0%)	6 (100%)

Table 9: P. falciparum and PDW

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P. falciparum Grade of infection	No. of cases (total - 68)	PCT	
		Normal	Decreased
Grade I	62	48 (77.4%)	14 (22.6%)
Grade II	2	1 (50%)	1 (50%)
Grade III	6	1 (16.7%)	5 (83.3%)

Table 10: P. falciparum and PCT

Table 11 shows that 91.1% grade 1 cases of mixed malaria showed normal MPV whereas 87.8% cases of grade 3 infection showed normal MPV.

Mixed (P. vx + P. fl) Grade of infection	No. of cases (total - 290)	MPV	
		Normal	Increased
Grade I	90	82 (91.1%)	8 (8.9%)
Grade II	118	100 (84.7%)	18 (15.3%)
Grade III	82	72 (87.8%)	10 (12.2%)

Table 11: Mixed malaria and MPV

Table 12 and 13 show increased PDW and decreased PCT with increasing grade of mixed malaria.

Mixed (P. vx + P. fl) Grade of infection	No. of cases (total - 290)	PDW	
		Normal	Increased
Grade I	90	79 (87.7%)	11 (12.3%)
Grade II	118	30 (25.4%)	88 (74.6%)
Grade III	82	3 (3.7%)	79 (96.3%)

Table 12: Mixed malaria and PDW

Mixed (pv + pf) Grade of infection	No. of cases (total - 290)	PCT	
		Normal	Decreased
Grade I	90	75 (83.3%)	15 (16.7%)
Grade II	118	40 (33.8%)	78 (66.2%)
Grade III	82	12 (14.6%)	70 (85.4%)

Table 13: Mixed malaria and PCT

The data was analysed using Spearman's correlation coefficients to evaluate the relationships between platelet indices and severity of infection caused by P. vivax, P. falciparum and mixed malaria. Multivariate logistic regression models were constructed to compare and correlate severity and platelet indices. Platelet indices were divided into two groups, namely normal and decreased (platelet count, PCT) OR increased (MPV, PDW). This division was done because of the large range of the normal platelet indices.

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The backward stepwise method was used to include all the studied variables in the model. The level of significance was set at $p < 0.05$. It was found that in *P. vivax*, *P. falciparum* as well as in mixed infection, platelet count, PDW and PCT showed statistically significant correlation with grade of malaria. MPV did not show any correlation with grade and was within normal limits in most of the cases.

DISCUSSION: In the present study, the analysis of the platelet indices showed correlation with grade of malaria, except for MPV. However a study done by Bhaswari et al⁷ found increased MPV in *P. falciparum* cases. Franklin et al⁸ and Coelho et al⁹ also found similar results. Increasing number of cases with elevated PDW and its correlation with grade of malaria was seen in our study. Similar findings were also seen by Chandra S et al.¹⁰ Present study showed decreased PCT with increasing severity of malaria. Fábio A Leal-Santos et al¹¹ also found similar results.

CONCLUSION: Our study shows that platelet indices other than platelet count also show variations according to severity and grade of malaria. These indices like PDW, PCT AND MPV can be used to predict severity of malarial infection and prevent complications.

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