

Diagnostic utility of platelet count and platelet indices in malaria among patients presenting with acute febrile illness

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ABSTRACT

Objective: To evaluate platelet count and platelet indices as adjunctive diagnostic markers for malaria in patients with acute febrile illness and compare these parameters in *Plasmodium vivax* and *Plasmodium falciparum* infections.

Methods: This cross-sectional analytic study was conducted from May 5 to December 20, 2025 at Karachi Institute of Medical Sciences and Diagnostic and Research Laboratory, LUMHS, Karachi. A total of 468 eligible patients were enrolled. Platelet count, plateletcrit (PCT), mean platelet volume (MPV), platelet distribution width (PDW), and platelet-large cell ratio (P-LCR) were compared between malaria-positive and malaria-negative patients and between *P. vivax* and *P. falciparum* infections. Receiver operating characteristic (ROC) curve analysis was performed to evaluate diagnostic performance.

Results: Malaria was confirmed in 295 (63.0%) patients, of whom 263 (89.2%) had *P. vivax* infection. Malaria-positive patients had significantly lower platelet count and PCT, and higher MPV, PDW, and P-LCR than malaria-negative patients (all $p < 0.05$). Moderate-to-severe thrombocytopenia occurred in 68.5% of malaria-positive patients compared with 2.9% of malaria-negative patients ($p < 0.001$). Platelet count and PCT demonstrated good diagnostic performance, with area under the curve (AUC) values of 0.971 and 0.970, respectively. MPV, PDW, and P-LCR showed poor diagnostic performance. No significant differences in platelet indices were observed between *P. vivax* and *P. falciparum* infections.

Conclusion: Platelet count and plateletcrit are inexpensive, readily available adjuncts to malaria microscopy in patients with acute febrile illness, whereas MPV, PDW, and P-LCR have limited diagnostic utility. Platelet alterations were not species-specific.

Keywords: Malaria, Platelet indices, Platelet count, Plateletcrit, Thrombocytopenia.

This article can be cited as: Adnan U, Harani M, Talib S, Abid SH, Kadir T, Saad M. Diagnostic utility of platelet count and platelet indices in malaria among patients presenting with acute febrile illness. Pak J Pathol. 2026; 37(3): 155-161. DOI: <https://doi.org/10.55629/pakjpathol.v37i3.1026>

INTRODUCTION

Malaria continues to pose a major global public health challenge despite advances in control efforts. The World Health Organization (WHO) estimated 282 million malaria cases and 610,000 deaths worldwide in 2024. The WHO Eastern Mediterranean Region accounted for an estimated 11.1 million cases and 22,100 deaths. Pakistan, reported approximately 1.8 million cases in 2025 despite a 10% reduction from 2024 levels, reflecting the persistent impact of climate-related surge in transmission. These figures highlight the continuing burden of malaria and the need for improved diagnostic tools and prognostic markers to support timely disease management [1,2].

In Pakistan, malaria is caused predominantly by two *Plasmodium* species. *Plasmodium vivax* (*P. vivax*) accounts for the majority of reported infections, *Plasmodium falciparum* (*P. falciparum*), although less prevalent, remains an important cause of severe malaria and its complications [3].

Malaria is an important differential diagnosis in patients presenting with acute febrile illness and should therefore be considered early during clinical evaluation [4]. The disease is frequently accompanied by several hematological abnormalities, particularly involving erythrocytes and platelets, that contribute significantly to disease morbidity and mortality [5]. Among these, thrombocytopenia has been shown to effectively distinguish between malaria-positive and malaria-negative patients with acute febrile illness [6]. Although the exact pathogenesis of thrombocytopenia in malaria remains unclear, it is thought to result from a combination of impaired platelet production and accelerated platelet destruction through immune-mediated processes,

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Receiving Date: 15 Jun 2026

Revision Date: 03 Aug 2026

Acceptance Date: 18 Sep 2026



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splenic sequestration, microvascular trapping, oxidative stress, and apoptosis [7,8].

Recent studies have demonstrated alterations in platelet indices in malaria, including mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR), and plateletcrit (PCT). These indices reflect platelet morphology and activation and may provide additional diagnostic and prognostic value beyond platelet count alone [9,10,11]. Although several studies have explored platelet indices in malaria, their diagnostic utility remains incompletely defined. While microscopic examination remains the gold standard for malaria diagnosis, its accuracy depends on parasite density, specimen quality, and the expertise of the microscopist. In contrast, platelet indices are routinely generated by automated hematology analyzers at minimal additional cost and may serve as readily available adjunct markers to support the early identification of malaria among patients presenting with acute febrile illness, particularly in resource-limited settings [9, 11].

Despite growing interest in platelet indices, evidence from Pakistan remains limited. It is important to generate data from our local population because demographic characteristics and distribution of *Plasmodium* species may influence hematological findings and their diagnostic utility. Therefore, this study aimed to:

- Evaluate platelet count and platelet indices in patients presenting with acute febrile illness;
- Assess their diagnostic utility in distinguishing malaria-positive from malaria-negative cases; and

Compare platelet indices between *P. vivax* and *P. falciparum* infections.

MATERIAL AND METHODS

This cross-sectional analytic study was conducted from May 5 to December 20, 2025 at Karachi Institute of Medical Sciences and the Diagnostic and Research Laboratory, Liaquat University of Medical and Health Sciences (LUMHS), Karachi, after institutional review board approval (Letter No. LUMHS/REC/-1926).

Patients of all ages and both sexes presenting with acute febrile illness who underwent both malaria microscopy and complete blood count (CBC) testing, were included. Patients who had received antimalarial treatment within the preceding two weeks, had an established alternative cause of fever, known hematological disorders, or other conditions likely to affect platelet parameters were excluded.

The sample size was calculated using the single population proportion formula with a 95% confidence level and a 5% margin of error [12]. An expected malaria prevalence of 23.3%, derived from a recent systematic review and meta-analysis by Khan et al., was used to calculate a minimum required sample size of 275 participants [3]. A total of 468 participants were ultimately enrolled using consecutive non-probability sampling. Written informed consents were obtained from all participants or their guardians. Demographic and clinical data (age, sex, prior antimalarial use, and fever duration) were recorded using a standardized proforma.

A 5 mL venous blood sample was collected in EDTA tubes. Complete blood count (CBC), including platelet count and platelet indices [mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and platelet-large cell ratio (P-LCR)], was performed using a Sysmex XN-1000 automated hematology analyzer (Sysmex Corporation, Kobe, Japan).

Malaria diagnosis was established by microscopic examination of Leishman-stained thick and thin peripheral blood smears. Thick smears were used for parasite detection and thin smears for species identification. A smear was considered positive if one or more malaria parasites were identified. All slides were independently examined by two experienced microscopists, and discrepant findings were resolved by consensus.

Thrombocytopenia was defined as a platelet count $<150 \times 10^9/L$ and classified as mild ($100\text{--}149 \times 10^9/L$), moderate ($50\text{--}99 \times 10^9/L$), and severe ($<50 \times 10^9/L$). Standard internal quality control procedures were followed throughout specimen collection and analysis.

Statistical analysis was performed using IBM SPSS version 26. Age was expressed as mean $\pm$ standard deviation (SD), while gender, malaria status, *Plasmodium* species, and thrombocytopenia severity were expressed as frequencies and percentages. Platelet count, PDW, MPV, P-LCR, and PCT were not normally distributed, and therefore, summarized as medians and interquartile ranges (IQR). Comparisons of platelet indices between malaria-positive and malaria-negative patients and between *Plasmodium* species were performed using the Mann–Whitney U test. Associations between categorical variables such as, thrombocytopenia severity, and malaria status were assessed using the Chi-square test or Fisher's exact test. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of

platelet count and platelet indices. The area under the curve (AUC) with 95% confidence intervals (CI) was calculated, and optimal cut-off values were determined using the Youden index. A P -value <0.05 was considered statistically significant.

RESULTS

A total of 468 patients meeting the inclusion criteria were included. The mean age was 30.5 years (SD = 18.0), and most patients 169(36.1%) were aged 16-30 years. Males were more frequently represented than females, 285(60.9%) vs 183(39.1%). Malaria was confirmed microscopically in 295(63.0%) patients. Among positive cases, *P. vivax* was the predominant species 263(89.2%), whereas *P. falciparum* and mixed infections accounted for 26(8.8%) and 6(2.0%) cases, respectively, as shown in Table-I.

Malaria-positive cases had significantly lower platelet counts and PCT, but higher PDW, MPV, and P-LCR values than malaria-negative patients (all $P<0.05$). The distribution of thrombocytopenia severity differed significantly between the two groups ($\chi^2=298.9$, $P<0.001$). Among malaria-positive patients, moderate and severe thrombocytopenia were observed in 34.6% and 33.9% of cases, respectively, whereas

91.3% of malaria-negative patients had platelet counts within the normal range (Table-II).

ROC analysis demonstrated that platelet count and plateletcrit (PCT) had superior discriminatory performance for predicting malaria compared with PDW, MPV, and P-LCR (Figure-I).

As shown in Table III, platelet count and PCT demonstrated excellent diagnostic accuracy, with AUCs of 0.971 and 0.970, respectively. Platelet count $\leq 148.5 \times 10^9/L$ yielded 88.1% sensitivity and 97.1% specificity, whereas PCT $\leq 0.195\%$ yielded 94.6% sensitivity and 91.3% specificity. In contrast, PDW, MPV, and P-LCR showed poor diagnostic performance, with AUCs ranging from 0.572 to 0.633. Although these indices showed relatively high specificities (85.0-87.9%), their sensitivities were considerably lower (35.9-43.4).

Among the 295 malaria-positive patients, 263 (89.2%) had *P. vivax* infection, 26 (8.8%) had *P. falciparum* infection, and 6 (2.03%) had mixed infections. Mixed infections were excluded from species-wise comparison. No statistically significant differences were observed in platelet count, and platelet indices between *P. vivax* and *P. falciparum* malaria (all $p>0.05$), as shown in Table-IV.

Table- I: Baseline characteristics of study participants (n=468).

Characteristics	n (%)	
Age, mean $\pm$ SD (years)	30.5 (SD=18.0)	
Age group (years)	1-15	102(21.8%)
	16-30	169(36.1%)
	31-45	99(21.2%)
	46-60	68(14.5%)
	>61	30(6.4%)
Gender	Male	285(60.9%)
	Female	183(39.1%)
Microscopy results	Positive	295(63.0%)
	Negative	173(37.0%)
Plasmodium species (n=295)	<i>p. vivax</i>	263(89.2%)
	<i>P. falciparum</i>	26(8.8%)
	Mixed infection	6(2.0%)

Table- II: Comparison of platelet indices and thrombocytopenia between malaria-positive and malaria-negative patients.

2A: Platelet indices			
Parameter	Malaria Negative (n=173) Median (IQR)	Malaria Positive (n=295) Median (IQR)	P value
Platelet count ($\times 10^9/L$)	261(87.5)	71(72.0)	<0.001
PDW (%)	11.7(2.05)	12.8(5.50)	<0.001
MPV (fL)	10.3(1.3)	10.5(1.7)	0.009
P-LCR (%)	27.2(10.25)	30.8(14.60)	<0.001
PCT (%)	0.27(0.09)	0.08(0.08)	<0.001
2B: Severity of Thrombocytopenia			
Severity	Malaria Negative n (%)	Malaria Positive n (%)	P value
Normal	158(91.3)	31(10.5)	<0.001
Mild	10(5.8)	62(21.0)	
Moderate	3(1.7)	102(34.6)	
Severe	2(1.2)	100(33.9)	

Continuous variables: median (IQR); Mann-Whitney U test, Categorical variables: n (%); Pearson Chi-square test.

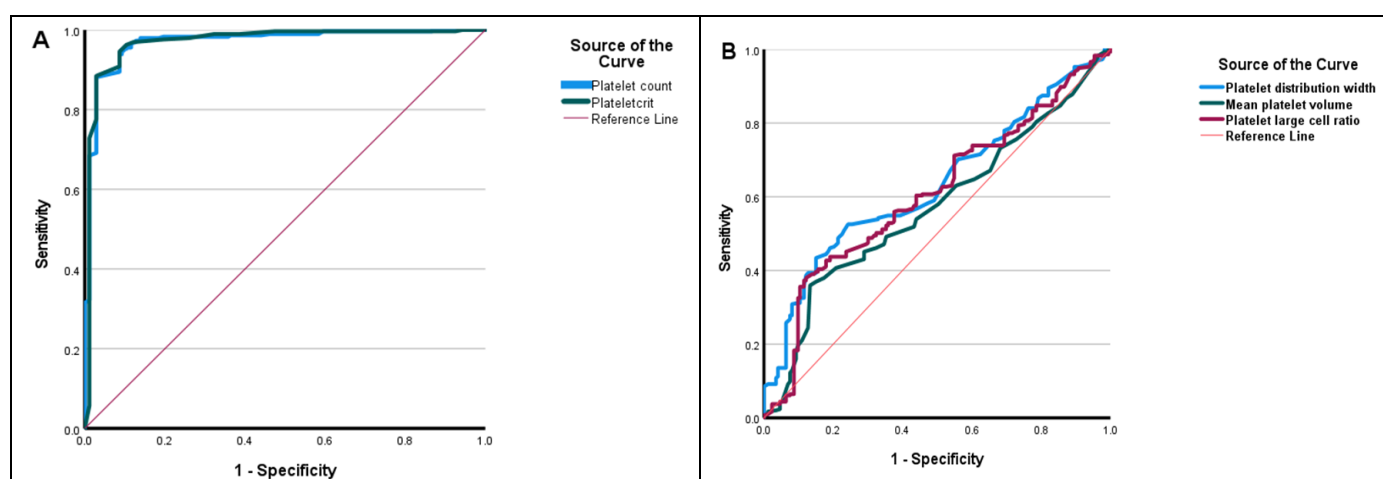
Table- III: Diagnostic Performance of Platelet Indices for Predicting Malaria

Parameter	AUC (95% CI)	p-value	Optimal Cutoff	Sensitivity (%)	Specificity (%)
Platelet Count ($\times 10^9/L$)	0.971 (0.955-0.986)	<0.001	≤ 148.5	88.1	97.1
Plateletcrit (%)	0.970 (0.952-0.988)	<0.001	≤ 0.195	94.6	91.3
Platelet distribution width (fL)	0.633 (0.582-0.683)	<0.001	≥ 13.55	43.4	85.0
Mean platelet volume (fL)	0.572 (0.519-0.624)	0.009	≥ 11.45	35.9	86.7
Platelet large cell ratio (%)	0.609 (0.557-0.661)	<0.001	≥ 36.4	38.0	87.9

Table- IV: Comparison of Platelet Indices Between *P. vivax* and *P. falciparum* Malaria

Parameter	<i>P. vivax</i> n=263 (89.2%) Median (IQR)	<i>P. falciparum</i> n=26 (8.8%) Median (IQR)	P value
Platelet count ($\times 10^9/L$)	74.0(72.0)	67.0(83.25)	0.971
PDW (%)	12.9(5.8)	12.3(5.23)	0.858
MPV (fL)	10.5(1.8)	10.6(1.6)	0.840
P-LCR (%)	30.5(14.9)	31.05(13.7)	0.968
PCT (%)	0.08(0.08)	0.065(0.08)	0.845

Continuous variables: median (IQR); Mann–Whitney U test.

**Figure-I: Receiver operating characteristic (ROC) curves showing the diagnostic performance of platelet indices for predicting malaria**

A: ROC curves for platelet count and plateletcrit (PCT), B: ROC curves for platelet distribution width (PDW), mean platelet volume (MPV), and platelet-large cell ratio (P-LCR).

DISCUSSION

In this study, the majority of patients were young adults aged less than 30 years, and males constituted 60.9% of the study population. Similar demographic patterns have been reported by Khan et al in Pakistan, reflecting comparable transmission dynamics and exposure patterns within malaria-endemic areas of the country. *P. vivax* was the leading malaria species consistent with its recognized predominance in Pakistan [3].

Significant alterations in platelet indices were observed among malaria-positive patients in our series. Platelet count and PCT were markedly lower whereas PDW, MPV, and P-LCR were significantly higher in malaria-positive compared with malaria-negative individuals. Similar findings have been reported by Tangvarasittichai et al in Thailand [13]. The observed elevation in MPV, PDW, and P-LCR may represent a compensatory bone marrow

response to peripheral platelet destruction in malarial infection, resulting in the release of larger and more heterogeneous platelets into circulation. This explanation is supported by a Brazilian study of uncomplicated *P. vivax* malaria, suggesting that platelet activation and immune mediated mechanisms may contribute to thrombocytopenia and alterations in platelet indices [14]. Similarly, a study from Sudan proposed that increasing MPV with higher parasitemia reflects reactive thrombopoiesis in response to malaria-associated platelet destruction [10].

Comparable changes in platelet indices have also been described in symptomatic pediatric malaria patients from Nigeria, supporting the association between malaria infection and platelet activation across different age groups [15]. Asmerom et al observed significantly lower platelet count and PCT values together with higher PDW and P-LCR levels

among malaria-infected patients compared with healthy controls, however, they reported lower MPV values in contrast to our findings [16]. The elevated MPV observed in our study is supported by a study from Turkey that reported similar findings among pregnant women with malaria [17]. This variation in MPV highlights the inconsistent behavior of this parameter across different populations and study settings.

Thrombocytopenia was strongly associated with malaria infection, with nearly 90% of malaria-positive cases exhibiting some degree of thrombocytopenia. More than two-thirds of our malaria-positive cases exhibited moderate to severe thrombocytopenia, whereas the majority of malaria-negative patients had normal platelet counts. Similar findings were reported by Gebreweld et al. from Ethiopia and Ahmad et al. and Khalid et al. from Pakistan, who observed thrombocytopenia in 79.5%, 73%, and 90% of malaria-positive patients respectively, highlighting thrombocytopenia as one of the most consistent hematological manifestations of malaria [6,18,19].

ROC curve analysis demonstrated that platelet count and PCT were the most accurate platelet parameters for identifying malaria, both achieving AUC values of approximately 0.97. These findings indicate excellent discriminatory ability and suggest that both parameters may serve as useful adjunctive markers for the early recognition of malaria in patients presenting with acute febrile illness.

Our findings are consistent with the findings of an Ethiopian study, who reported an AUC of 0.893 for thrombocytopenia as a diagnostic marker of malaria among febrile patients [6]. The higher AUC observed in our study may be due to the differences in genetic makeover of the study population, and the platelet count cutoff employed.

In contrast to our findings, a Nigerian study found significant differences in MPV and P-LCR but not platelet count or PCT between malaria-positive and malaria-negative patients [20]. Our ROC analysis, however, showed limited discriminatory ability of these two indices. These differences may be due to variations in malaria-species distribution, and analytical methods. Whereas Nigerian study compared mean values between groups, we evaluated diagnostic performance using ROC analysis, providing clinically relevant measures of discrimination. Also, Algin et al. found that platelet parameters performed poorly as markers of malaria severity, indicating that diagnostic and prognostic utility may differ substantially [5].

Conversely, MPV, PDW, and P-LCR exhibited relatively low AUC values, despite relatively high specificity, indicating limited ability to discriminate between malaria-positive and malaria-negative patients when used individually, and hence have considerably lower diagnostic value. Santos et al. demonstrated altered platelet indices in patients with *P. vivax* malaria and suggested their potential role in assessing disease severity [11]. Our findings extend this evidence by demonstrating the excellent diagnostic utility of plateletcrit for distinguishing malaria-positive from malaria-negative patients.

In the present study, we did not observe significant differences in platelet count or platelet indices between patients infected with *P. vivax* or *P. falciparum*, although the small *P. falciparum* sample limited statistical power. In contrast, Gupta et al. reported more pronounced thrombocytopenia, while Ajmal et al. observed a higher frequency of thrombocytopenia among patients with *P. vivax* malaria than among *P. falciparum* [21,22]. In another study, Asare et al. reported lower MPV and PDW values among children infected with *P. falciparum* malaria, in contrast to the higher values observed in our predominantly *P. vivax* cohort [23]. These discrepancies may reflect variations in the clinical and demographic profiles of study populations, as well differences in the infecting species.

Conclusion:

Platelet count and plateletcrit demonstrated good diagnostic utility as adjuncts to malaria microscopy in patients presenting with acute febrile illness, whereas MPV, PDW, and P-LCR have limited discriminatory value. Thrombocytopenia is a common hematological finding in malaria, with no significant differences in platelet alterations between *P. vivax* and *P. falciparum* infections. In patients with persistent clinical suspicion, low platelet counts and plateletcrit may support consideration of repeat malaria smear examination, while microscopy remains the diagnostic standard.

LIMITATIONS / RECOMMENDATIONS

Although samples were obtained through 13 collection centers across the city, all analyses were performed at a central diagnostic laboratory, which may limit the generalizability of the findings beyond the study setting. In addition, the relatively small number of *P. falciparum* infections limited the ability to detect species-specific differences in platelet indices.

Future multicenter studies involving larger sample size are warranted to validate these findings across different *Plasmodium* species and clinical presentations.

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHORS CONTRIBUTION

Umbur Adnan: Conceptualization, data acquisition, analysis and interpretation of data, manuscript writing, final approval, responsible for every aspect of the research

Mahadev Harani: Research supervision, critical review, final approval, responsible for every aspect of the research

Sadia Talib: Substantial contribution in data recording, manuscript writing, final approval, responsible for every aspect of the research

Syeda Hira Abid: Substantial contribution to data analysis and interpretation, final approval, responsible for every aspect of the research

Tahira Kadir: Substantial contribution to study design and concept, critical review, final approval, responsible for every aspect of the research

Maliha Saad: Substantial contribution to analysis and interpretation, final approval, responsible for every aspect of the research

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