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Association of Presence and Severity of Thrombocytopenia with Types and Severity of Malaria

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ABSTRACT

Malaria is a significant community health problem in affected areas such as Pakistan, the most prevalent causing parasitic species being Plasmodium vivax and Plasmodium falciparum. Very common hematological symptoms include thrombocytopenia, which is often seen in the two species. This cross-sectional research paper set out to establish the prevalence and degree of thrombocytopenia in malaria sufferers as well as evaluating the relationship with Plasmodium species. The study was completed in six months at Khyber Teaching Hospital, Peshawar and involved 85 microscopical-confirmed malaria cases. Platelet count (per microliter) was recorded and subdivided according to mild (50,001-150,000/ uL, moderate (20,000- 50,000/ uL) and severe (<20,000/uL) levels of thrombocytopenia. In general, thrombocytopenia was recorded in 70.6 percent of patients, and there were equal proportions of mild, moderate, and severe categories. The prevalence of P. vivax (60%) was much higher than P. falciparum (40%). The frequency of thrombocytopenia was higher in P. vivax (76.5 versus 61.8 per cent) but not significantly different ($p = 0.128$). P. falciparum cases had a higher frequency of severe thrombocytopenia (29.4%), which suggests that there may be a trend towards increased destruction of platelets during falciparum infections. Although the results did not show any significant association, the high prevalence of thrombocytopenia points to the potential of this lab marker as an early predictor of malaria in malaria-endemic areas, where delay of diagnosis is prevalent. These results justify the practice of assessing the platelet count among febrile individuals who live in endemic areas to develop malaria suspicion early and work on it aggressively. Molecular diagnostics and a larger sample size should be considered in further studies in order to shed more light on species-specific thrombocytopenia patterns.

INTRODUCTION

Malaria is one of the most urgent health concerns worldwide that is associated with considerable morbidity and mortality especially in tropical and sub-tropical areas. Even with constant control activities, the World Health Organization still registers millions of cases per year, emphasizing active transmission in endemic regions (Mace et al., 2021). The malaria health burden remains a severe challenge in Pakistan in tribal and under-resourced parts of the country where the development of healthcare infrastructure is weak and epidemiology is complicated (Karim et al., 2021; Braam et al., 2021).

The causative agents are protozoan parasites that belong to the genus Plasmodium, and four of its species (Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale and Plasmodium malariae) are currently the most clinically relevant (Daily et al., 2022; Sato, 2021). Where P. falciparum infection is commonly regarded as leading to severe morbidity and mortality such as cerebral malaria and multiorgan disorders, P. vivax also has been recognized to play a significant role in morbidity by relapses and haematolological derangements. Hematological abnormalities, especially thrombocytopenia, have been widely reported in both species among the different systemic presentations of malaria (Gopalakrishnan et al., 2021; Habtamu et al., 2022).

The decrease in the number of circulating platelets thrombocytopenia is a common manifestation in malaria, and it can be caused by different mechanisms such as immune-mediated destruction of platelets, sequestration of platelets in the spleen, suppression of bone marrow, as well as through changes in megakaryocyte function using cytokines (Mahittikorn et al., 2021). It is interesting to note that the occurrence of thrombocytopenia has also been suggested as an outcome of malaria as well as a possible diagnostic and prognostic indicator. Several studies have shown that the low platelet count in patients with fever is capable of increasing the clinical suspicion of malaria,

especially in endemic settings (Gebreweld et al., 2021; Mahittikorn et al., 2021).

Despite its extensive documentation occurring in the prevalence of thrombocytopenia in malaria, its relationship with parasites of varying Plasmodium species and the intense of the infection is an aspect of research that continues to be explored. There have been some suggestions that P. falciparum is more prevalently related to severe thrombocytopenia whereas the P. vivax is more to related to a mild to moderate drop in platelet count (Kumar et al., 2022; Mahittikorn et al., 2021). But the conclusions of all researchers are rather open, probably because of low geographic distribution, immunity, and diagnostic modality.

Pakistan is one country where malaria is endemic in rural as well as peri-urban contexts where the current data lacks local evidence to evaluate the hematological spectrum of malaria and its effectiveness in early diagnosis. Specifically, most studies have not addressed the relationship between the gravity of thrombocytopenia and the Plasmodium species infecting local people (Ahmad et al., 2023; Tiiba et al., 2023). It is important to plug this gap in order to increase the clinical suspicion and timely commencement of antimalarial therapy in resource-constrained settings where access to confirmatory diagnostics can be delayed.

The current research is expected to answer the question on the frequency and severity of thrombocytopenia among patients with malaria and understand whether this condition is associated with the type of Plasmodium infection. In explaining these relationships, we will be trying to aid the inclusion of hematological parameters in early diagnostic algorithms, which will allow to improve malaria management and diminish disease-related complications in endemic areas.

MATERIALS AND METHODS

It is a cross-sectional study done in the department of medicine, Khyber Teaching Hospital, Peshawar, after the permission received form the central ethical review committee of the institution between 22nd February to 22nd May 2025. The objective of the study was to assess the prevalence and severity of thrombocytopenia in patients with malaria as well as look into the relationship between the severity of thrombocytopenia and malaria species (Plasmodium falciparum and Plasmodium vivax).

The 85 patients were identified through a non-probability consecutive sampling method. The sample size was estimated on the WHO sample size calculator with the claims of 95 percent confidence level, 7 margin of error, and projected prevalence of severe thrombocytopenia in malaria patients as 12.3 percent. Participants were eligible in case they were 18 ye--65 years old, of either sex, with clinical characteristics of malaria, that is, fever (temperatures exceeding 101 degrees Fahrenheit), rigors, and chills with positive evidence of the presence of Plasmodium species on peripheral blood smear microscopy. Only patients who experienced the symptoms over 24 hours were taken into consideration.

Exclusion criteria included concomitant diseases which may confound the platelet counts such as pregnancy, severe liver disease, hepatitis B or C infection, autoimmune deficiency, malignancy, chronic renal failure (serum creatinine 3 mg/dL), and respiratory tract infection characterized by cough that was productive and longer than three weeks, fever or temperature greater than 100 o F lasting at least one week, and the presence of wheezing.

Demographic and clinical information such as age, gender, BMI, duration of complaints, monthly income, level of education and residence (rural/urban) will be collected under informed consent on a structured proforma. Venipuncture was done on each patient and 5 mL of venous blood was collected aseptically via trained phlebotomists to the laboratory where it was analyzed. Plasmodium species were microscopically identified and platelet counts were carried out to establish the occurrence and extent of thrombocytopenia. Platelet count 150,000/ 1/L was regarded as thrombocytopenia. The operational definitions of categories of severity were mild (50,001150,000/l), moderate (20,00050,000/l), and severe (<20,000/l).

The data were analyzed and fed into SPSS version 25.0. Shapiro-Wilk test has been used to examine the distribution of the continuous variables. Age, symptom duration, and platelet counts were denoted by mean plus standard deviation or median (interquartile range), as was appropriate. Frequencies and percentages were used to summarise categorical variables such as gender, residence, malaria type, presence and severity of thrombocytopenia. The interactions between thrombocytopenia severity and malaria species were assessed using the chi-square or Fisher exact test where possible. To represent statistical significance, a p-value <= 0.05 was chosen. The potential effect modifiers (age, gender, residence and symptom duration) were stratified and the post-stratification chi-square or Fisher exact test was performed to ensure the associations were robust.

RESULTS

Eighty-five patients were analyzed in the final outcome, having malaria as a diagnosis. The average age of study participants was 36.8/11.9 years. The study population consisted of 58.8 percent (n = 50) male and 41.2 percent (n = 35) female. Most of the participants (61.2%, n = 52) were living in the rural setting. Sixty percent (n = 51) had P. vivax identified whereas 40 percent (n = 34) had P. falciparum.

Platelet count was less than or equal to 150,000 /l in 70.6 percent (n = 60) of all patients (thrombocytopenia). Out of these 36.7% (n = 22) had mild, 31.7% (n = 19) moderate and 31.7% (n = 19) severe thrombocytopenia.

patients with P. vivax and P. falciparum had thrombocytopenia in 76.5 percent (n = 39) and 61.8 percent (n = 21) when stratified by malaria type, respectively. Mild thrombocytopenia, however, turned out to be more common in P. vivax (43.1%, n = 17), and moderate to severe thrombocytopenia was more common in P. falciparum (47.1%, n = 16). Nonetheless, there was no statistically significant correlation between species of malaria and occurrence or degree of thrombocytopenia (p = 0.128).

Table 1

Baseline Characteristics of Study Participants (n = 85)

Variable		Mean ± SD / n (%)
Age (years)		36.8 ± 11.9
Gender	Male	50 (58.8%)
	Female	35 (41.2%)
Residence	Urban	33 (38.8%)
	Rural	52 (61.2%)
Type of Malaria	*Plasmodium vivax*	51 (60.0%)
	Plasmodium falciparum	34 (40.0%)

Table 2

Frequency and Severity of Thrombocytopenia (n = 85)

Thrombocytopenia Status	n (%)
No thrombocytopenia	25 (29.4%)
Thrombocytopenia (Total)	60 (70.6%)
— Mild (50,001–150,000)	22 (36.7%)
— Moderate (20,000–50,000)	19 (31.7%)
— Severe (<20,000)	19 (31.7%)

Figure 1

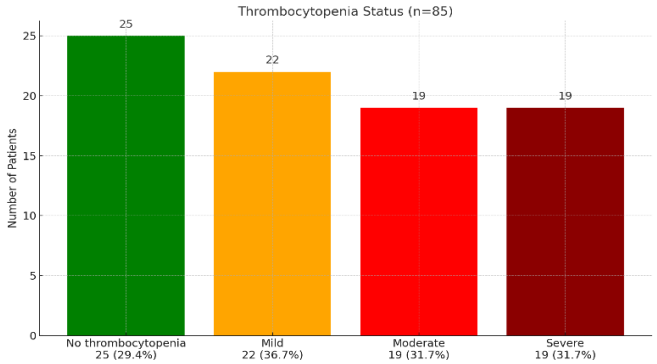

Table 3

Association of Thrombocytopenia with Type of Malaria

Malaria Type	No TP	Mild TP	Moderate TP	Severe TP	Total	p-value
P. vivax (n = 51)	12	17	13	9	51	
P. falciparum (n = 34)	13	5	6	10	34	0.128
Total (n = 85)	25	22	19	19	85	

Note: TP = Thrombocytopenia

Although a larger percentage of severe thrombocytopenia was found in P. falciparum-infected patients, the magnitude of the relationship between the severity of thrombocytopenia and the malaria species was not significant (X 2 = 5.684, d f = 3, p = 0.128). A stratified analysis based on age group, gender and residence did not significantly interact with all thrombocytopenia status.

DISCUSSION

The present research evaluated the relationship between the occurrence and the extent of thrombocytopenia and the kind of malaria infection developed by patients, who were admitted to a tertiary care hospital in Peshawar. Our results show that thrombocytopenia is a frequent type of hematological abnormalities in malaria, its total mass proportion among the participants was 70.6 percent. Our findings are in agreement with those of other authors, in whom thrombocytopenia has been mentioned in 7380 percent of patients infected by malaria, regardless of the infecting species (Kaur et al., 2010; Lathia & Joshi, 2004).

Plasmodium vivax was the most frequent, followed by Plasmodium falciparum in our cohort (60 per cent and 40 per cent respectively), in keeping with the prevailing local epidemiology in Pakistan that P. vivax persists infection proportionately compared with P. falciparum. The tendency to thrombocytopenia was a little bit higher in P. vivax (76.5%) than in P. falciparum (61.8%), but it was not statistically significant. Interestingly, mild thrombocytopenia has been seen more commonly in P. vivax infections but moderate and severe thrombocytopenia was more prevalent in P. falciparum. This is the result in the same direction as those studies reporting that P. falciparum can induce a more vigorous systemic inflammatory response, causing greater platelet lysis or sequestration (Gerardin et al., 2002).

The mechanisms of pathophysiology of thrombocytopenia during malaria are multi-factorial and they could include Immune-mediated destruction of platelets, platelet consumption, hypersplenism, and bone marrow suppression. High concentrations of inflammatory cytokines including TNF-a and IL-6, along with immune complexes may aid the lysis and clearance of platelets. Moreover, endothelial activation due to malaria can contribute to an even greater consumption of the platelets, especially in severe falciparum malaria.

This is notwithstanding the fact that nearly all the patients with malaria had thrombocytopenia; yet our results indicate that there is no reliable association between a platelet count and a malaria species. Nonetheless, thrombocytopenia especially of moderate to severe ranges should draw clinical attention to malaria among febrile individuals especially in endemic regions. By diagnosing and treating this hematological pattern early, a diagnosis and consequent treatment will be much easier, which is essential in limiting the risk of complications.

Our study is partially limited. The sample size, which is sufficient in estimating prevalence, might not be sufficient in identifying minor interspecies differences in the severity of thrombocytopenia. Besides, our species identification was based on microscopy that is potentially not as sensitive as PCR based ones especially with mixed infections. We equally failed to measure dynamic variations in platelet levels during treatment, but such considerations may provide additional information with regards to disease progression and response.

As a conclusion, this paper supports the intense prevalence of thrombocytopenia in individuals who have malaria and especially those infected by P. vivax, even though P. falciparum might be more likely related to severe cases. Due to its commonality, thrombocytopenia must be considered as significant early laboratory sign in the diagnosis of malaria and will help make early effective clinical decisions in the resource-limited area. To fully clarify species-specific hematological abnormalities and their prognostic significance, more studies with significantly larger sample size and molecular diagnosis should be conducted.

CONCLUSION

This paper has highlighted thrombocytopenia is very high in malaria patients with over 70 of the patients showing this, even in P. vivax infections the prevalence is large.

However, the thrombocytopenia was found to be more severe when P. falciparum was the causative agent though the difference was not significant. These results imply that, although thrombocytopenia is a very useful clinical sign in malaria, it is non-specific between Plasmodium species. Moderate to severe thrombocytopenia in febrile individuals nonetheless is a signal to be more clinically alert to malaria, especially in endemic and under-resourced settings. The inclusion of platelet count analysis in the early diagnostic schemes has the potential to make treatment faster and less prone to complications. Further researches using bigger sample sizes and molecular diagnostics will be important in confirming the role of thrombocytopenia in species differentiation and its prognostic value.

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