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Frequency of Thrombocytopenia in malaria and its prognostic significance

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ABSTRACT

BACKGROUND & OBJECTIVE: Thrombocytopenia is a common hematological manifestation of malaria, but locally there is limited data on the association of thrombocytopenia degree and malarial species in Pakistan. Therefore, the present study aims to assess the frequency of thrombocytopenia and its severity among patients with malaria.
METHODOLOGY: In this prospective cross-sectional study, a total of 120 patients with smear-positive for malaria on microscopy were included. The patient's complete blood count (CBC) was assessed daily to monitor the platelet counts, and thrombocytopenia was divided into four categories, i.e., mild, moderate, severe, and very severe thrombocytopenia.
RESULTS: Out of the total 120 malaria-positive cases, 78(65%) were positive for P. vivax, 32(26.7%) were affected by P. falciparum, and 10(8.3%) patients had mixed infection. Thrombocytopenia developed among 73% of the total patients with malaria; of these, 35.23% developed mild thrombocytopenia, while 31.82%, 23.86%, and 9.09% developed moderate, severe, and very severe thrombocytopenia, respectively. Among those 30(34.0%) infected with P. falciparum, 8(26.7%) developed mild thrombocytopenia, while 8(26.7%) and 14(46.7%) developed moderate to very severe thrombocytopenia. Similarly, most patients with P. vivax 23(39.7%) had mild to moderate 20(34.5%) thrombocytopenia, 15(25.9%) had severe, and only 5.19% had very severe thrombocytopenia p-value=0.141 shows non-significant association. Furthermore, P. vivax group developed complications, while two of the four patients of the P. falciparum group developed cerebral malaria, one developed renal failure, and the last one had pancytopenia.
CONCLUSION: In conclusion, thrombocytopenia is frequent among patients with malaria. Moreover, the severity of thrombocytopenia and complications are more evident among those infected with P. falciparum than those with P. vivax.
KEYWORDS: Thrombocytopenia, Malaria, P. falciparum, P. vivax.

INTRODUCTION

Malaria is a disease of serious concern and a significant cause of morbidity and mortality in various parts across the globe [1,2]. Based on the World Health Organization (WHO) report (2019), around 229 million people were affected by malaria, attributing 409,000 deaths worldwide. The infection rate is highest in WHO African Region, i.e., 94% of the overall malarial incidence and deaths were documented from the region mentioned above in 2019 [3].

Locally, more than 50% of the Pakistani population live under the critical zone, i.e., the malaria-endemic regions [4,5]. Pakistan is recognized as the sixth country with the highest malarial transmission in the Eastern Mediterranean region [6,7]. However, the endemicity varies across the provinces; till now, Khyber Pakhtunkhwa shares the highest disease burden in Pakistan [8]. Among its species, P. vivax is more prevalent in the Pakistani population than P. falciparumm[5,9,10]. In contraction, a study from Sindh reported a higher prevalence of P. falciparum (64.56%) than P. vivax (35.44%) [11]. As per the Pakistan Malaria Annual Report of 2019, out of 374,513 malarial cases, P. vivax accounted for 84.0%, followed by P. falciparum 14.9%, and 1.1% cases were of mixed infection [1].

Malaria presents with episodes of high-grade fever typically along with various hematological abnormalities on blood complete picture as anemia, thrombocytopenia, and neutropenia. To date, thrombocytopenia is recognized as

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the best-known indicator of malaria by a number of studies [12-14]. In malarial hematopathy, thrombocytopenia occurs in response to platelets pooling, reduced platelet life span, and elevated serum concentration of both pro-and anti-inflammatory cytokines [15]. In addition to thrombocytopenia, malaria can even lead to disseminated intravascular coagulation (DIC). However, thrombocytopenia is an early manifestation, and more than 80% of the P. vivax and P. falciparum present with thrombocytopenia [16-18].

The local data from Pakistan, specifically from KPK on thrombocytopenia in malaria and its prognostic role, is limited. Therefore, the present study aims to assess the frequency of thrombocytopenia among patients with malaria and the association of its severity with malarial species.

METHODOLOGY

The hospital ethical review committee granted the ethical approval for the study [R.No.7312 dated 25/03/2019]. Written informed consent was taken from all the study participants, and all patients were fully briefed regarding the study objectives.

This prospective cross-sectional study was conducted at the Department of Medicine, District Head Quarter (DHQ) Hospital, Timergara Dir Lower. Patients presented with high-grade fever, rigors, and chills were investigated for malaria. Patients positive for malarial parasite both on thick and thin blood smears and aged between 15-75 years were considered eligible for inclusion in the study. While known patients with platelets disorder, like ITP etc., were excluded from the study sample. The study continued for 6 months, from April to October 2019, and the data of 120 malarial patients were analyzed.

Patient's complete blood count (CBC) was assessed daily to monitor the platelet counts. A fully automated quantitative analyzer (SYSMEX-XP 100) was used for estimating the platelet counts. As per the operational definitions, Thrombocytopenia was divided into four categories i.e., platelets count 100,000 cells/µl -150,000 cells/µl (mild thrombocytopenia), 50,000 cells/µl -100,000 cells/µl (moderate thrombocytopenia), <50,000 cells/µl but > 20,000 cells/µl (severe thrombocytopenia) and <20,000 cells/µl (very severe thrombocytopenia). The patients were strictly monitored for any complications like cerebral malaria or renal failure. All the patients infected with P. vivax, P. falciparum and mixed infections were treated with oral antimalarial, i.e., Artemether and Lumefantrine combination or IV Artesunate.

Data were analyzed using SPSS version 22.0. Percentages and frequency were calculated for categorical variables like gender and thrombocytopenia. While mean and standard deviation was used to present the continuous variable, i.e., age. The chi-square test was used to evaluate the association of thrombocytopenia with malaria species, where a p-value < 0.05 was considered significant.

RESULTS

Among the enrolled cases, more than 50% were males. The mean age was 40.85 ± 15.6 years, and most of them were ≤ 45 years of age, as shown in table-I.

Table-I: Baseline characteristics (n=120).

Variables		
Age (years); Mean±SD		40.85 ± 15.6
Gender n(%)	Male	68(56.6)
	Female	52(43.3)
Age Group n(%)	≤45 years	76(63.3)
	>45 years	44(36.6)

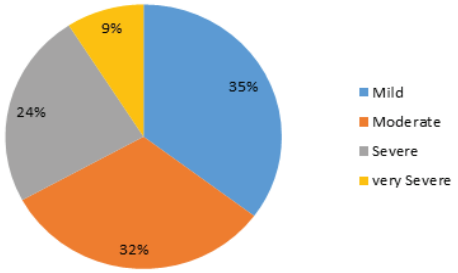

Figure-I: Degree of thrombocytopenia in the study population.

Out of the total, 88(73.3%) patients developed thrombocytopenia. Among them, 31(35.23%) had mild thrombocytopenia, 28(31.82%) had moderate, 21(23.86%) were severe cases, and 8(9.09%) had very severe thrombocytopenia, as shown in figure-I.

There were 58(66%) patients infected by P. vivax, 30(34%) by P. falciparum. Among those infected with P. falciparum, 8(26.7%) developed mild thrombocytopenia, while 8(26.7%) and 14(46.7%) developed moderate to severe thrombocytopenia. Similarly, most patients with P. vivax had mild thrombocytopenia i.e., 23(39.7%), 20(34.5%) moderate, and 15(25.9%) severe thrombocytopenia (Table-II).

Table-II: Association of thrombocytopenia with malaria species.

Variables		Malaria		Total	p-value
		p.vivax	p.falciparum		
Category	Mild	23 (39.7)	8(26.7)	31(35.2)	0.141
	Moderate	20 (34.5)	8(26.7)	28(31.8)	
	Sever	15(25.9)	14(46.7)	29(33.0)	
Total		58 (100.0%)	30 (100.0%)	88 (100.0%)	

*p-value<0.05 is considered significant.
Values are given as n(%)

None of the patients from P. vivax group developed complications, while two of the four patients of the P. falciparum group developed cerebral malaria, renal failure (n=1), and pancytopenia (n=1).

DISCUSSION

This present study was conducted at District Head Quarter (DHQ) Hospital, Timergara, Lower Dir. Around 73% of the enrolled malaria patients had co-existing thrombocytopenia. A similar local study conducted by Arif et al. observed thrombocytopenia in 79% of patients with Malaria [19]. Likewise, Shaikh and his colleagues reported 80.6% of malaria-positive patients with thrombocytopenia [13].

There were eight patients with platelet counts below 20,000 Cells/µl in the current study, which is also consistent with the study[20]. The possible mechanism for the low platelets may be oxidative stress, immune mechanism, variation in splenic functions due to organomegaly, and direct interaction between plasmodium and platelets. In the present study, we had a patient presented with pancytopenia, usually due to bone marrow aplasia and was found to be positive for P. falciparum. A similar case of bone marrow aplasia was also reported[21].

It is evident that patients infected with P. falciparum were more prone to severe thrombocytopenia and developed complications of malaria as compared to P. vivax. Studies have found similar results, which further strengthens our statement regarding the severity of P. falciparum malaria [22,23]. In our study, P. vivax infection was more common than P. falciparum and mixed. Moreover, the incidence of thrombocytopenia was also highest among those infected with P. vivax (65.9%). Our results are consistent with a few studies; while contradictory to others, a similar Indian study reported a higher incidence rate of thrombocytopenia among patients with P. falciparum (83.80%) than those with P. vivax (74%). A study by Kochar et al. reported more P. vivax cases with thrombocytopenia than P. falciparum, which is consistent with our findings [22].

Although the present study determined a high frequency of thrombocytopenia of various grades among the studied malaria-positive cases, a few limitations must be considered. We had a small sample size, and there was no specific appropriate assessment for the causes of thrombocytopenia other than malaria.

CONCLUSION

Based on the study outcomes, thrombocytopenia is a common occurrence in patients with malaria. Early diagnosis and treatment of complications reduce the global burden of malaria. Thus, platelet count could serve as an important screening tool among patients with acute febrile illness.

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Author's Contribution:

Saleh Ahmad: Substantial contributions to the conception or design of the work
Saeed-ur-Rehman: cquisition, analysis, or interpretation of data for the work
Qazi Ikramullah: Drafting the work or revising it critically for important intellectual content
Iqbal Ahmad: Final approval of the version to be published

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