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Prevalence of Malaria in Febrile Patients Presenting with Thrombocytopenia at LUMHS, Jamshoro

Zohaib Abbasi[1], Abdul Ghani Rahimoon[2], Kashif Shaikh[3], Muhammad Awais Qadri[4], Ghulam Rasool Rahimoon[5], Aakash Rai[6]

[1,4,5]Senior Resident of Medicine, [2]Associate Professor of Medicine, [6]House Officer of Medicine, [3]Associate Professor and Chairperson of cardiology, LUMHS, Jamshoro

Author`s Contribution

[1,2]Substantial contributions to the conception or design of the work; or the acquisition, [4,6]Active participation in active methodology, [2,3]analysis, or interpretation of data for the work, [5]Drafting the work or revising it critically for important intellectual content

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Address of Correspondent
Dr Zohaib Abbasi
Senior Resident of Medicine
LUMHS, Jamshoro
Abbasizohaib342@gmail.com

ABSTRACT

Objective: To determine the frequency of malaria in febrile patients presenting with thrombocytopenia at LUMHS, Jamshoro.

Methodology: A cross sectional study was conducted at Department of Medicine, LUMHS, Jamshoro, Hyderabad, during six months from 01-02-2023 till 31-7-2023. Febrile patients with thrombocytopenia, either gender aged 20-80 years were included. Blood sample was obtained from each cases and analyzed for complete blood count (CBC) and malaria diagnosis using Giemsa-stained thin and thick blood smears. Patients were assessed and labeled as malaria-positive based on the presence of malarial parasites under microscopy. After data collection the analysis was done by SPSS version 26.

Results: Overall mean age of the 153 patients was 39.65±14.30 years with male gender predominance 105 (68.6%). Overall, malaria was detected in 67.3% of 153 febrile patients with thrombocytopenia, with *Plasmodium vivax* being the most common species 60(39.2%), followed by Plasmodium falciparum 30 (19.6%) and mixed infections 13(8.5%). Among all patients, 37.3% had severe thrombocytopenia. Prevalence of malaria found statistically insignificant by gender, residence, or socioeconomic status, though it was slightly higher in rural areas and in patients with platelet counts <50,000/µL (p=>0.005), while there was a significant association between thrombocytopenia severity and parasite type (p= 0.001), as all mixed infections occurred in patients with platelet counts <50,000/µL.

Conclusion: Malarial detections was observed highly prevalent among febrile patients presenting with thrombocytopenia, with *Plasmodium vivax* being the predominant species, and with a significant association between thrombocytopenia severity and parasite type, as all mixed infections occurred in patients with severe thrombocytopenia.

Keywords: Febrile patients, Thrombocytopenia, Malaria, Vivax, Falciparum

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Introduction

Fever is one of the most common symptoms of infectious diseases, so it is not unexpected that clear and detailed descriptions of people suffering from fever can be found in some of the earliest written medical histories.[1] Most prolonged fevers are due to common illnesses presenting in unusual ways. Because temperature charts often show highly variable patterns that rarely point to a single diagnosis, thorough diagnostic evaluation is typically necessary so that appropriate treatment or supportive care can be initiated once the underlying cause is identified.[2] Low platelet count is a frequent finding in many infectious diseases, and when it occurs alongside fever, it can aid in narrowing the possible causes and guiding appropriate management. When thrombocytopenia occurs with fever, it often indicates serious underlying conditions that need targeted treatment.[3] While mild

cases are usually reversible and manageable, moderate to severe thrombocytopenia demands rapid diagnosis and intervention. Over the past decade, several regions in Asia have faced outbreaks of severe febrile illnesses with low platelet counts, associated with a significantly higher rate of mortality.[3,4]

Thrombocytopenia can result from a variety of causes, including idiopathic, infectious, and inflammatory conditions. Common infectious triggers of fever with low platelet counts include malaria, dengue, leptospirosis, typhoid, viral infections, and septicemia.[2,5] Such patients may initially present with only mild fever, but the condition can progress unpredictably, leading to complications like intra-cerebral bleeding, hemorrhage in vital organs, shock, and even death.[2]

In endemic regions, where fever is the most common symptom, malaria is considered a leading differential diagnosis in all patients presenting with acute febrile illness, as more than half of Pakistan's population resides in malaria-endemic areas,[6,7] and the country ranks sixth among nations with the highest malaria transmission in the Eastern Mediterranean region. Patients frequently present with high-grade fever accompanied by hematological abnormalities such as anemia, neutropenia and the thrombocytopenia.[6,8]

A reduced platelet count is commonly observed in severe cases of malaria, occurring with both *P. falciparum* and *P. vivax* infections, irrespective of disease severity. The exact cause of this reduction remains unclear, though proposed mechanisms include immune-driven platelet destruction, splenic sequestration, and impaired production in the bone marrow.[9] Malaria has also been linked to disruptions in platelet generation and consumption, and in rare cases, direct invasion of platelets by the parasite has been reported.

As the malaria is a major public health issue in endemic regions like Pakistan, where febrile thrombocytopenia is a common clinical presentation. Thrombocytopenia occurs in both *P. vivax* and *P. falciparum* infections and can lead to serious complications if not promptly recognized. Malarial differentiating from other causes of fever with low platelet counts is essential for timely diagnosis and effective treatment. Hence this study is important to better understand the prevalence and severity of thrombocytopenia in malaria, improve clinical decision-making, and reduce disease-related complications in high-risk population.

Methodology

A cross-sectional study was conducted in the Department of Medicine at Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro. The study duration spanned six months, from February 1, 2023, to July 31, 2023, following the approval of the study proposal. A total of 153 patients were enrolled, with the sample size calculated using WHO software based on a 17.3% frequency of malaria in febrile patients with thrombocytopenia, a 6% margin of error, and a 95% confidence level. Non-probability consecutive sampling was employed for participant selection. All the febrile patients (temperature ≥ 37.0°C) for more than 24 hours presenting with thrombocytopenia, aged between 20 and 80 years, of either gender were included. All the patients diagnosed with COVID-19, enteric fever, vasculitis, connective tissue disorders, immune thrombocytopenic purpura (ITP), leukemia, lymphoma, and those receiving anti-platelet therapy, patients with chronic conditions such as COPD, asthma, chronic renal failure, acute coronary syndrome, congestive heart failure, chronic liver disease, NAFLD, hepatitis B or C, and HIV were excluded. Informed consent was obtained and each participant was informed about the study's purpose, risks, and benefits. All the patients enrolled in the study were assessed for malaria. For this purpose, a sterile 5 ml venous blood sample was collected from each patient using standard aseptic techniques. The samples were immediately sent to the hospital's diagnostic laboratory for analysis. In the laboratory, the blood samples were examined using Giemsa-stained thin and thick smears to detect the presence of malarial parasites. The data collection was recorded using a predesigned proforma and analysis was done SPSS version 26.

Results

The overall mean age of the 153 patients was 39.65 ± 14.30 years. The mean duration of fever was 3.78 ± 1.55 days, while the mean BMI, height, and weight were 29.51 ± 2.93 kg/m², 161 ± 3.39 cm, and 81.5 ± 7.56 kg, respectively. Among the participants, 105 (68.6%) were male and 48 (31.4%) were female. Out of all 77 (50.3%) patients were from urban areas, while 76 (49.7%) were from rural areas. According to SES 33 patients (21.6%) had poor SES, 69 patients (45.1%) had middle SES and 51 patients (33.3%) had upper SES. Furthermore 50 patients (32.7%) were illiterate, 43 (28.1%) had primary education, 39 (25.5%) had secondary education, and 21 (13.7%) had higher education. Among 153 febrile

patients with thrombocytopenia, malaria was detected in 103 cases (67.3%), while 50 patients (32.7%) tested negative. Among the malaria-positive cases, *Plasmodium vivax* was the most common species, found in 60 patients (39.2%), followed by Plasmodium falciparum in 30 patients (19.6%) and mixed infections in 13 patients (8.5%). (Table I)

Table I: Prevalence of malaria and its severity among febrile patients with thrombocytopenia.

Variables		Frequency (%)
Malaria	Positive	103 (67.3%)
	Negative	50 (32.7%)
	Total	153(100%)
Types of malaria	Vivax	60(39.22%)
	Falciparum	30(19.61%)
	Mixed	13(8.50%)
	Negative	50 (32.7%)
	Total	153(100%)

Regarding platelet count distribution, 57 patients (37.3%) had counts <50,000/µL, 74 (48.4%) had counts between 50,000–100,000/µL, and 22 (14.3%) had counts between 100,000–150,000/µL, as presented in Figure 1.

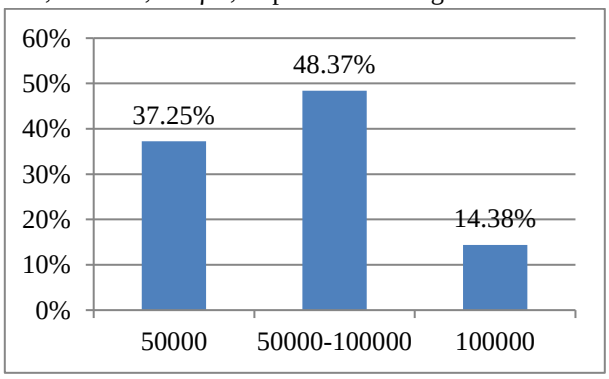

Figure 1: Severity of thrombocytopenia. (n=153)

There was no significant difference in the prevalence of malaria according to gender (66.7% in males vs. 68.8% in females, $p = 0.79$) or socioeconomic status ($p = 0.985$). Malaria was more frequent in rural residents (72.4%) compared to urban (62.3%), and stratification by platelet count showed higher prevalence in patients with lower platelet counts, particularly those with <50,000/µL, though these findings were not statistically significant ($p > 0.05$). However, a significant association was observed between the severity of thrombocytopenia and the type of malarial parasite ($p = 0.001$), with all mixed infections occurring in patients with platelet counts <50,000 as shown in Table II & III.

Discussion

Malaria, with high burden of incidences, and considerable morbidity and mortality rates, poses significant challenges to public health in Pakistan. This study assessed the frequency of malaria in febrile patients with thrombocytopenia, with an overall mean age of 39.65 ± 14.30 years, mean BMI of 29.51 ± 2.93 kg/m², and mean fever duration of 3.78 ± 1.55 days; the majority were males (68.6%), most were from urban areas (50.3%), 45.1% belonged to the middle socioeconomic group, and 32.7% were illiterate, findings comparable to the baseline demographics reported by Tareen et al[11] and Gebreweld et al.[12]

This study showed an overall prevalence of malaria of 67.3%, which, although high, aligns with the findings of Yasinzai MI et al[13], who reported a malaria incidence of 41.8%, considerably lower than our results. They further observed *P. vivax* as the predominant species (51.8%), followed by *P. falciparum* (48.1%), with March identified as the peak season for *P. vivax* infections (85.4%) and a predominance of male patients (75.7%) during this period. Similarly, a study by Tareen et al. [11] from Quetta district reported a malaria prevalence of 18.45%, markedly lower than that observed in our study.

Table II: Prevalence of malaria according to effect modifiers. (n=153)

VARIABLES		MALARIA		TOTAL	p-value
		YES	NO		
Gender	Male	70(66.7%)	35 (33.3%)	105(100%)	0.79
	Female	33 (68.8%)	15(31.2%)	48(100%)	
	Total	103 (67.3%)	50 (32.7%)	153(100%)	
Residence	Urban	48 (62.3%)	29 (37.7%)	77(100%)	0.186
	Rural	55 (72.4%)	21 (27.6%)	76(100%)	
	Total	103 (67.3%)	50 (32.7%)	153(100%)	
Severity of thrombocytopenia	< 50000	39 (68.4%)	18 (31.6%)	57(100%)	0.001
	50000-100000	46 (62.2%)	28 (37.8%)	74(100%)	
	>100000	18 (81.8%)	4 (18.2%)	22100%)	
SES	Poor	22 (66.7%)	11 (33.3%)	33(100%)	0.985
	Middle	47 (68.1%)	22 (31.9%)	69(100%)	
	Upper	34 (66.7%)	17 (33.3%)	51(100%)	

Table III: Severity of thrombocytopenia according to types of malaria. (n=153)

TYPES OF MALRIA	PLATELATES COUNT			TOTAL	p-value
	< 50000	50000-100000	>100000		
P. Vivax	12 (20%)	35 (58.3%)	23(21.7%)	60(100%)	0.001
P. Falciparum	14 (46.7%)	11 (36.7%)	5(16.7%)	30(100%)	
Mixed infection	13 (100%)	0 (0%)	0(0%)	13(100%)	
Not detected	18 (36%)	28 (56%)	4(8%)	50(100%)	
TOTAL	57(37.3%)	74(48.4%)	22(14.4%)	153 (100%)	

Another study by Yasinzai MI et al[14] from Musakhel and Loralai districts documented 28.8% malaria-positive cases, also substantially lower than our prevalence, with *P. falciparum* comprising the majority (71.7%) and *P. vivax* accounting for only 28.2% of cases. The differences in prevalence across the studies may be due to variations in study sample size, population characteristics, ecological factors, and diagnostic methodologies. Our hospital-based study specifically included febrile patients presenting with thrombocytopenia, a group inherently at higher risk for malaria. In contrast, the studies by Tareen et al[11] and Yasinzai and Kakarsulemankhel[13,14] were community-based studies involving broader populations. Additionally Geographic differences may also have contributed to these disparities, as our research was conducted in Sindh province, which has a distinct climate compared to Quetta and other regions.

In the present study, types of the malarial parasites revealed that *Plasmodium vivax* was the most common species (39.2%), followed by *Plasmodium falciparum* (19.6%) and mixed infections (8.5%). In aligns to these findings, a North Indian study by Kumar et al[15] reported *P. vivax* in 62.5% of malaria patients, *P. falciparum* in 33.18%, and co-infections in 3.7%. Consistently, Khan and Ally also documented a predominance of *P. vivax* in 92.21% of cases, with *P. falciparum* observed in only 7.79% of patients.[16] Idris et al[17] also found *P. vivax* as the most frequent species (72.4%), followed by *P. falciparum* (24.1%) and mixed infections (3.44%). However, contrasting findings were reported by Khan et al[18] where *P. falciparum* was identified in 61.74% of cases, followed by *P. vivax* in 35.29%, while 2.94% of cases involved unidentified species. These variations in parasite distribution across studies can likely be attributed to regional prevalence patterns, seasonal transmission dynamics affecting vector breeding, and disparities in community awareness and malaria control strategies.

In this study, most patients (48.4%) had platelet counts between 50,000–100,000/µL, followed by counts <50,000/µL (37.3%) and counts between 100,000–150,000/µL (14.3%). Platelet count stratification showed that malaria was more prevalent among patients with lower platelet counts, particularly those with <50,000/µL, ($p = 0.22$). However, a significant association was noted between platelet count and the type of malarial parasite ($p = 0.00$), as all mixed infections occurred in patients with platelet counts <50,000/µL. Supporting our findings, Mikre et al[19] reported a malaria prevalence of 36.1% among acute febrile patients, with thrombocytopenia present in 27.6% of suspected cases. Among confirmed malaria patients, 71.8% were thrombocytopenic, with a statistically significant association between thrombocytopenia and malaria ($p < 0.001$). Similar results were observed by Kotepui et al[20] who found significantly lower platelet counts in malaria cases, with a 31.8-fold higher likelihood of infection among individuals with platelet counts below 150,000/µL. They also documented thrombocytopenia in 84.9% of malaria-infected patients, independent of age, sex, or geographic region ($p < 0.0001$). Overall, the prevalence of malaria observed in this study was higher among febrile patients, highlighting the need for early screening and prompt diagnosis in this high-risk group. However, the study is limited by its relatively small sample size and other methodological constraints when compared with larger, community-based international studies. Hence, further large-scale, multicenter studies are recommended to validate these findings and better understand the burden and determinants of malaria.

Conclusion

Malarial prevalence was highly frequent (67.3%) among febrile patients presenting with thrombocytopenia, with *Plasmodium vivax* being the predominant species, and with a significant association between thrombocytopenia severity and parasite type, as all mixed infections occurred in patients with severe thrombocytopenia. Hence the findings underscore the importance of routine malaria screening and parasite differentiation in febrile thrombocytopenic patients, especially those with profound thrombocytopenia, to ensure the early diagnosis and management.

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