EXAMINING THE RELATIONSHIP BETWEEN SEVERITY OF THROMBOCYTOPENIA AND THE PATTERN OF MALARIA: A HOSPITAL-BASED STUDY

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ABSTRACT

OBJECTIVES
To determine the association between the severity of thrombocytopenia and the pattern of malaria.

METHODOLOGY
This descriptive cross-sectional study included 194 patients who tested positive for malarial parasites on peripheral smear examination. The study comprised smear-positive malaria cases, both males and females, who were Pakistani nationals aged between 8 and 50. Exclusion criteria were individuals with dengue, typhoid, immunocompromised status, liver disease, and pregnancy. Data were recorded for age, gender, the pattern of malaria (Plasmodium (P). vivax, P. falciparum, or mixed), and type of thrombocytopenia (mild, moderate, and severe). The association between the severity of thrombocytopenia and the pattern of malaria was determined using a chi-square test, with the analysis stratified by gender.

RESULTS
The mean age of the participants was 28.58±11.70 years, with 114 (58.76%) being male. The lowest platelet count (64,627 ± 43,062) was found in cases of falciparum malaria, while the highest mean platelet count was found in cases of vivax malaria (130,919 ± 107,723), and this difference was statistically significant (p=0.004). The most common occurrence of severe thrombocytopenia was in falciparum malaria cases (n=11, 42.31%), and the difference was statistically significant (p=0.024).

CONCLUSION
Falciparum malaria has the lowest mean platelet count and more severe thrombocytopenia than vivax and mixed type.

KEYWORDS: Falciparum Malaria, Malaria, Platelet Count, Thrombocytopenia, Plasmodium Vivax

INTRODUCTION

Malaria ranks as the fifth major cause of death globally.3 Malaria poses a significant public health threat to individuals living in Asian countries, leading to substantial illness and economic consequences.2 Despite numerous control measures, around 40% of the population remains vulnerable to this infection. The primary cause of malaria is Plasmodium species, namely vivax, falciparum, malaria, and ovale.3 Despite being categorized as a country with moderate malaria prevalence, Pakistan still has an alarming number of around 177 million people who remain at risk of being infected with the disease. Around 60% of Pakistan's population reside in regions where malaria is endemic.2 Out of the total malaria burden in Pakistan, Plasmodium vivax accounts for 81.3%, P. falciparum for 14.7%, and mixed-species for 4%.4 Malaria is linked to haematological complications like anaemia and thrombocytopenia, caused by factors such as haemolysis, parasitic infections, antimalarial drugs, and deficiencies in essential vitamins and minerals like iron, folate, and vitamin B12.5,6 Despite widespread attention from the scientific community regarding anaemia associated with malaria and its associated mortality, thrombocytopenia has received less attention. However, the presence of thrombocytopenia can serve as a helpful indicator for primary care physicians in clinical diagnosis when other tests may not be accessible.7,8 While the exact mechanism responsible for thrombocytopenia in malaria is not yet fully comprehended, some researchers propose that the malarial parasite reduces the production of platelets from megakaryocytes as a means of survival, thereby evading platelet-mediated clearance.9 A previous study found that 80% of malaria cases had thrombocytopenia, which was observed in varying degrees of severity: 36.25% with mild thrombocytopenia, 40.0% with moderate thrombocytopenia, and 23.75% with severe thrombocytopenia.10 Understanding haematological parameters is essential for assessing the severity of malaria and avoiding invasive investigations. Thrombocytopenia is a common complication of malaria, and its severity has been observed to vary
Examining the Relationship between Severity of Thrombocytopenia

across affected individuals. Exploring the relationship between the severity of thrombocytopenia and the pattern of malaria could provide valuable insights into the pathophysiology of this condition. Specifically, understanding the role of malaria contributes to the degree of thrombocytopenia in malaria may aid in the early identification and treatment of severe cases, thereby reducing morbidity and mortality rates associated with this condition. Studying this relationship could also inform the development of new therapeutic approaches for malaria that specifically target the mechanisms underlying thrombocytopenia in the disease. This study aimed to determine the association between the severity of thrombocytopenia and the pattern of malaria.

METHODOLOGY

This descriptive cross-sectional study was conducted at the Department of Pathology, Saidu Group of Teaching Hospitals, Swat, from June 10, 2022, to February 28, 2023. Ethical approval was obtained from the hospital’s ethical committee. Ethical approval was not required separately, as it had already been secured through the informed consent process. All patients had consented to using their records for research purposes. A total of 194 patients who tested positive for malarial parasite on peripheral smear examination were included in the analysis. The sample size was calculated using the WHO sample size calculator at a 95% confidence level, with a 6% margin of error, and assuming a frequency of severe thrombocytopenia of 23.75% among malaria-positive patients. The study included smear-positive malaria cases, both male and female, Pakistani nationals between the ages of 8 and 50. Exclusion criteria consisted of individuals with dengue, typhoid, immunocompromised status, liver disease, and pregnancy (in all these cases, palate count can be affected). Cases recruited in the study underwent a detailed history-taking and complete general and systemic examination using a proforma. A medical specialist examined all patients, followed by routine and specific blood investigations to evaluate falciparum/vivax malaria. The platelet counts were obtained using a fully automated quantitative analyzer (Mandfredi, Italy 820-I) and were categorized into three subgroups - mild thrombocytopenia, moderate thrombocytopenia, and severe thrombocytopenia - based on the platelet count reference of previous study. Mild thrombocytopenia was characterized by platelet counts ranging from 100 to 150 x10^3/µl, moderate thrombocytopenia from 50 to 100 x10^3/µl, and severe thrombocytopenia by counts below 50 x10^3/µl. For patients with P. falciparum, P. vivax malaria, and mixed infections, treatment was administered according to the standard protocol, which varied depending on the clinical severity. The data analysis was performed using R programming version 4.1.2. Mean and standard deviation were computed for numerical data such as age and platelet count, while frequency and percentages were calculated for qualitative data such as gender, malaria pattern, and thrombocytopenia severity. The palatal count was compared among malaria types using an ANOVA test. The association between the severity of thrombocytopenia and the pattern of malaria was determined using a chi-square test, with the analysis stratified by gender. The level of significance was p<0.05.

RESULTS

The mean age of the participant was 28.58±11.70 years. Of total 194 participants, 114(58.76%) were males and 80(41.24%) were females. The participants were divided into three age groups: 8-20 (n=55, 28.35%), 21-35 (n=81, 41.75%), and 35-50 (n=58, 29.90%). Thrombocytopenia was absent in 39(20.10%). Most common type of thrombocytopenia was moderate, found in 63(32.47%), followed by mild (n=47, 24.23%) and the least was severe (n=45, 23.20%). Among the participants, 159(81.96%) had vivax malaria, 26 (13.40%) had falciparum malaria, and 9(4.64%) had mixed malaria. (Table 1). Fig 1 provides information on the mean platelet count and standard error for three categories of thrombocytopenia: mild, moderate, and severe. The mean platelet count(x10^3/µl) for mild thrombocytopenia was 12.44 with a standard deviation (SD) of 2.256. The mean platelet count for moderate thrombocytopenia was 12.4471, with an SD of 1.864. Finally, the mean platelet count for severe thrombocytopenia was 26.707, with an SD of 10.915. The lowest mean platelet count(x10^3/µl) was found for falciparum malaria, with a value of 64.627 ± 43.062, while the highest mean platelet count was found for vivax malaria, with a value of 130.919 ± 107.723. The mean platelet count(x10^3/µl) for mixed malaria was 79.143 ± 39.132. The ANOVA test showed a significant difference in mean platelet count(x10^3/µl) between the three types of malaria (p=0.004). Further analysis using multiple comparison tests revealed that the only statistically significant difference was found between falciparum and mixed type (p=0.002). (Table 2) Figure 2 shows the platelet count in different malaria patterns in both genders. The difference was statistically significant only in males. The data analysis revealed that the most common severe thrombocytopenia was found in falciparum malaria, with 11 cases representing 42.31% of the overall sample. The second most common was in mixed
malaria, with 3 cases representing 33.33%, and the least was found in vivax malaria (n=31, 19.5%). In contrast, moderate thrombocytopenia was most frequent in mixed malaria, with (n=4, 44.44%). The differences in severe and moderate thrombocytopenia incidence were statistically significant (p=0.024). Furthermore, the analysis showed significant differences between males (p=0.041) and females (p=0.034) in the incidence of severe and moderate thrombocytopenia with the type of malaria. (Table 3)

**Table 1: Distribution of Gender, Ages, Thrombocytopenia and Malarial Pattern**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Characteristic</th>
<th>N = 194¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female</td>
<td>80 (41.24)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>114 (58.76)</td>
</tr>
<tr>
<td>Age Group (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-20</td>
<td></td>
<td>55 (28.35)</td>
</tr>
<tr>
<td>21-35</td>
<td></td>
<td>81 (41.75)</td>
</tr>
<tr>
<td>35-50</td>
<td></td>
<td>58 (29.90)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nil</td>
<td></td>
<td>39 (20.10)</td>
</tr>
<tr>
<td>Mild</td>
<td></td>
<td>47 (24.23)</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td>63 (32.47)</td>
</tr>
<tr>
<td>Severe</td>
<td></td>
<td>45 (23.20)</td>
</tr>
<tr>
<td>Malaria</td>
<td>Falciparum</td>
<td>26 (13.40)</td>
</tr>
<tr>
<td></td>
<td>Mixed</td>
<td>09 (4.64)</td>
</tr>
<tr>
<td></td>
<td>Vivax</td>
<td>159 (81.96)</td>
</tr>
</tbody>
</table>

**DISCUSSION**

This study aimed to determine the association between the severity of thrombocytopenia and the pattern of malaria. Our findings showed that falciparum malaria had the lowest mean platelet count, while vivax malaria had the highest. There was a significant difference in mean platelet count between the three types of malaria, with only falciparum and mixed type showing a statistically significant difference. The Falciparum malaria has more severe thrombocytopenia than vivax and mixed-type malaria. The mechanism underlying the observed differences in mean platelet count among the three types of malaria is not fully understood.¹¹ However, it is thought that falciparum malaria may induce more severe thrombocytopenia compared to vivax and mixed-type malaria due to various factors.¹² These include the destruction of platelets by infected...
Thrombocytopenia is common in individuals with acute malaria, irrespective of whether they are infected with *P. falciparum* or *P. vivax*. Although thrombocytopenia may also be a characteristic of viral febrile illnesses, in areas where malaria is prevalent, its presence is considered a diagnostic indicator. Our study found that thrombocytopenia was present in 75% of patients diagnosed with malaria. This prevalence rate is consistent with previous studies conducted in India, which reported a range of 72.0% to 80.0%. Specifically, Jadhav et al. reported a prevalence of 78.4%, while Shetty et al. found a prevalence of 72.0%. These results suggest that thrombocytopenia is a common finding among patients with malaria in Asian countries and highlight the need for continued research to understand better the mechanisms underlying this phenomenon. Thrombocytopenia is a common complication of malaria. Researchers have conducted extensive studies to understand the relationship between thrombocytopenia and malaria. Our findings suggest that mild thrombocytopenia is more likely to occur in individuals with *P. vivax* malaria. In contrast, severe thrombocytopenia is more commonly linked to *P. falciparum* malaria, which is considered more severe than *P. vivax* malaria. Moreover, the severity of thrombocytopenia is significantly correlated with the presence of the M antigen. This antigen is a protein on the surface of malaria-infected red blood cells and is involved in binding infected cells to the blood vessel walls. Studies have shown that the presence of the M antigen is associated with the development of severe thrombocytopenia. Other studies, including Memon et al., have reported similar outcomes, showing that hospitalized malaria patients with *P. falciparum* are more likely to develop severe thrombocytopenia. However, Jadhav et al. reported that severe thrombocytopenia can occur in either type of malaria, and the presence of thrombocytopenia does not distinguish between them. In contrast, Kaur et al. found that patients with *P. vivax* malaria can also experience severe thrombocytopenia, contradicting the previous notion that severe thrombocytopenia is primarily associated with *P. falciparum* malaria. These findings suggest that the relationship between thrombocytopenia and malaria is complex and may depend on multiple factors, including the type of malaria, the severity of the infection, and the presence of specific antigens.

**LIMITATIONS**

This study has limitations that need to be considered when interpreting the findings. The descriptive and cross-sectional study cannot establish a temporal relationship between thrombocytopenia and malaria. There were fewer cases of *P. falciparum* malaria included in the analysis than *P. vivax* malaria cases, which could limit the comparability and generalizability of the results. Other factors, such as sex, genetics, and immune status, may play a role in thrombocytopenia development, were not examined. The study may have also been affected by selection bias as it may have only included individuals with more severe malaria cases, skewing the findings. Further research is needed to confirm the relationship between thrombocytopenia and malaria and address these limitations.

**CONCLUSIONS**

Our study suggests a significant difference in mean platelet count between the three types of malaria, with *falciparum* malaria having the lowest mean platelet count and more severe thrombocytopenia compared to *vivax* and mixed-type malaria. These findings highlight the importance of monitoring platelet count in individuals with malaria, especially those with *falciparum* malaria, as severe thrombocytopenia can lead to serious complications.

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CONTRIBUTORS

1. Javeria Rauf Saeed – Concept & Design; Data Acquisition; Data Analysis/Interpretation; Drafting Manuscript; Critical Revision; Supervision; Final Approval