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AFFECT OF SEVERE MALARIA ON CBC INDICES IN ASSOCIATION WITH DIFFERENT SPECIES OF MALARIA IN PATIENTS OF A TERTIARY CARE HOSPITAL

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Abstract

Objective:

1. To assess the changes in CBC indices (haemoglobin, WBC, platelet count, RDW) in patients with severe malaria infected by different Plasmodium species.
2. To provide insights into species-specific haematological patterns in severe malaria that could inform more targeted diagnostic and therapeutic strategies.

Methodology:

This is a qualitative research design, the study focused on capturing in-depth insights into the experiences of patients, clinicians, and healthcare providers in managing malaria cases within a tertiary care hospital setting. The target population comprised malaria patients admitted between August and October 2023. Patient records were reviewed to obtain demographic and clinical data.

Results:

Based on the provided data of 96 patients, the majority are diagnosed with Plasmodium vivax malaria, with only a few cases of Plasmodium falciparum. Severe thrombocytopenia (platelet count <150 x 10^9/L) was a common finding observed in 80% of cases. Platelet counts recovered gradually in most patients by day 3-5 of hospitalization with an average final platelet count of 67 x 10^9/L at discharge. The overall recovery rate was 100% and no fatalities were recorded. A small subset (10%) experienced recurrence of symptoms following discharge but responded well to a second course of treatment

Conclusion:

In conclusion, this study offers valuable insights into the clinical and laboratory characteristics of malaria patients, primarily *P. vivax*, and their response to treatment.

Keywords:

Malaria, P. vivax, Plasmodium Falciparum, CBC

Introduction:

Malaria remains one of the most prevalent and severe infectious diseases worldwide especially in tropical and subtropical regions. It is caused by several species of the Plasmodium parasite including *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium malariae* and *Plasmodium ovale*. The disease presents a wide clinical spectrum ranging from mild febrile illness to severe, life-threatening conditions. Of particular concern is severe malaria, which significantly increases the risk of complications and mortality particularly in vulnerable populations.

One of the critical components of assessing malaria's impact is through hematological analysis, particularly using Complete Blood Count (CBC) indices. CBC provides essential insights into the body's response to infection and includes parameters such as hemoglobin levels, white blood cell count (WBC), platelet count and red blood cell distribution width (RDW). Malaria has a profound impact on various CBC indices due to the parasitic invasion of red blood cells and the subsequent immune response. One of the most notable effects is the development of anemia as a result of the destruction of parasitized RBCs, which leads to decreased hemoglobin levels. This is particularly pronounced in *Plasmodium falciparum* infections, as this species is capable of infecting both young and mature erythrocytes, resulting in more extensive hemolysis. In addition to anemia, leukocyte abnormalities are frequently observed, with leukopenia being common in uncomplicated malaria, while leukocytosis may occur in severe cases as a result of the body's heightened immune response. These changes in WBC counts can vary between Plasmodium species, reflecting species-specific immune reactions.

Thrombocytopenia is another hallmark of malaria seen across all Plasmodium species (Bayleyegn, Asrie, Yalew, & Woldu, 2021). However, it is reported to be more severe in cases of *P. falciparum* and *P. vivax* infections (Gebreweld, Erkihun, Feleke, Hailu, & Fiseha, 2021). Platelet counts drop due to immune-mediated destruction, platelet

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consumption, and sequestration in the spleen, contributing to the bleeding risk in severe malaria. Furthermore, red blood cell distribution width (RDW) often increases in malaria patients (Sacomboio et al., 2022). This is more happen in severe cases due to the destruction of older RBCs and the release of younger reticulocytes into the bloodstream. The degree of RDW elevation may serve as a marker of disease severity, especially in infections caused by *P. Falciparum* (Owoicho et al., 2022). These hematological disruptions which are captured through CBC indices provide crucial insights into the severity of malaria and the specific Plasmodium species involved. For example, a research by Elkhalifa et al (2021) found that infection with Falciparum malaria was associated with anemia, thrombocytopenia, high RDW, low MCV, low MCHC, low MCH, and neutropenia. Likewise, Awoke and Arota (2019) reported that 84% of malaria patients in their study experienced thrombocytopenia, while 67% had anemia.

Although these CBC changes are well-documented, in a country like Pakistant only a few studies have been published on the hematological changes with uncomplicated and complicated cases of malarial infection. Exploration is needed among Pakistani population to understand the full extent of their species-specific patterns and their implications for clinical management, especially in the context of complications caused by malaria. Additionally, previously studies have determined that the CBC indices are often altered in malaria patients, but the specific patterns associated with severe malaria and the different Plasmodium species remain understudied. Understanding how severe malaria affects hematological parameters in the context of different Plasmodium species could lead to improved diagnosis, management, and prognosis.

The distinct hematological alterations seen in malaria reflect the complex interaction between the parasite and the host's immune system. However, these changes may vary according to the species of Plasmodium, the severity of the infection, and individual patient factors. Despite several studies on hematological parameters in malaria, limited research exists that focuses on the comparative impact of severe malaria caused by different Plasmodium species on CBC indices.

Study Objectives:

1. To assess the changes in CBC indices (hemoglobin, WBC, platelet count, RDW) in patients with severe malaria infected by different Plasmodium species.
2. To explore how different species of Plasmodium contribute to the degree of hematological abnormalities observed in severe malaria.
3. To analyze the correlation between parasite load, species type, and the extent of anemia, thrombocytopenia and leukocyte changes.
4. To investigate the qualitative experiences of patients with severe malaria regarding their clinical symptoms and paying attention particularly to the hematological manifestations.
5. To provide insights into species-specific hematological patterns in severe malaria that could inform more targeted diagnostic and therapeutic strategies.

This study aims to fill the gap by qualitatively and quantitatively examining the relationship between CBC indices and the severity of malaria across different Plasmodium species. It aims to provide a comprehensive understanding of the hematological disruptions caused by this life-threatening disease.

Methodology

Study Design

This study employed a qualitative research design to explore clinical presentations, hematological parameters, and treatment outcomes in patients diagnosed with malaria caused by *Plasmodium vivax* and *Plasmodium falciparum*. The study focused on capturing in-depth insights into the experiences of patients, clinicians, and healthcare providers in managing malaria cases within a tertiary care hospital setting.

Study Population

The target population comprised malaria patients admitted between August and October 2023. The inclusion criteria were patients with confirmed *Plasmodium vivax* or *Plasmodium falciparum* infection, as verified by laboratory results. A total of 96 patients were included in the study, 85 diagnosed with *P. vivax* and 11 with *P. falciparum*.

Sampling

Purposive sampling was used to select participants for the study. Patients who met the inclusion criteria and were able to give informed consent were approached for participation. To ensure a comprehensive understanding of the clinical course and outcomes of malaria, patients were selected from different wards, including the high-dependency unit (HDU), the general ward, and the intensive care unit (ICU). Additionally, key healthcare providers involved in malaria management were also included for interviews.

Data Collection

Patient records were reviewed to obtain demographic and clinical data, including age, gender, malaria species, hematological parameters such as hemoglobin (Hb), total leukocyte count (TLC), neutrophils, lymphocytes, monocytes, eosinophils, and platelet counts. These data were extracted to understand the variability in clinical presentations across the cohort.

Data Analysis

The hematological parameters extracted from medical records were analyzed using descriptive statistics. Results were presented as percentages and qualitative trends. Differences in clinical profiles between patients with *P. vivax* and *P. falciparum* infections were highlighted. For instance, we examined variances in hemoglobin levels and platelet counts across patients and determined qualitative distinctions in severe cases requiring HDU or ICU care. The interview transcripts were analyzed using thematic analysis. Data were coded iteratively, identifying key themes related to patient experiences, treatment pathways, and clinical challenges. Codes were organized into broader categories such as "perceptions of malaria severity," "barriers to treatment adherence," and "clinical complexities in management." Triangulation between patient and provider interviews helped validate emerging themes.

Ethical Considerations

Ethical approval was obtained from the [Institutional Review Board of Hospital]. Informed consent was taken from all participants, ensuring confidentiality and the right to withdraw from the study at any time. The study adhered to ethical standards in qualitative research, prioritizing the dignity and well-being of all participants.

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Trustworthiness

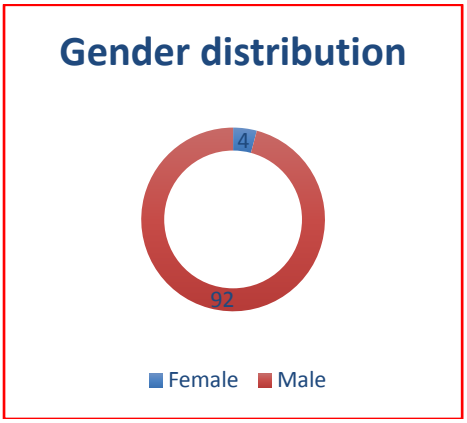
To enhance the credibility and trustworthiness of the study, the following measures were employed:

- Prolonged Engagement: The research team spent ample time in the wards to familiarize themselves with the clinical setting and develop rapport with patients and providers.
- Member Checking: Preliminary findings from interviews were shared with participants to validate the accuracy of the interpretations.
- Peer Debriefing: Regular meetings were held with clinical experts and qualitative researchers to ensure rigorous analysis and interpretation.

Results

Based on the provided data of 96 patients, the majority are diagnosed with Plasmodium vivax malaria, with only a few cases of Plasmodium falciparum. The dataset represents predominantly male patients, with a small number of females. The data include various clinical metrics such as hemoglobin (Hb), total leukocyte count (TLC), neutrophils, lymphocytes, monocytes, eosinophils and platelet levels.

Demographics and Case Distribution: A total of 63 patients with confirmed malaria infections were included in this study along with 96.8% (61/63) diagnosed with *Plasmodium vivax* and 3.2% (2/63) with *Plasmodium falciparum*. All patients were adults, with a mean age of 30.2 years (range: 17-68 years). The majority of cases were male (96%) while only 5 were females (4%). (fig 1)



Clinical Presentation and Laboratory Findings: The mean hemoglobin (Hb) levels at presentation varied significantly across the cohort, with an average of 12.95 g/dL (range: 5.2–16.9 g/dL). Notably, *P. falciparum* cases presented with lower Hb levels compared to *P. vivax* cases (average 9.85 g/dL vs. 13.2 g/dL, respectively). Total leukocyte counts (TLC) were generally within normal ranges (4-10 × 10^9/L) and a mean TLC was 4.65 × 10^9/L. However, a notable drop in TLC was observed in patients with severe cases requiring high dependency unit (HDU) admission where levels dipped as low as 2.5 × 10^9/L.

Neutrophil percentages were elevated in most patients, with an average of 68.7% (range: 36%-91%), while lymphocyte percentages were inversely low, averaging at 22.1% (range: 8%-54%). Monocyte and eosinophil counts remained within normal ranges and no significant abnormalities noted. (Table 1)

Variables	Minimum	Maximum	Mean	Std. Deviation
Age	17.00	68.00	32.0000	11.70335
Hb	5.20	16.90	12.9875	1.71968
TLC	2.00	70.00	5.5875	6.81984
Neutrophils	33.00	91.00	68.7917	14.04273
Lymphocytes	4.00	54.00	20.8542	11.56581
Monocytes	2.00	20.00	7.9479	4.74035
Esinophils	0.00	14.00	2.1042	1.94384
PLT	11.00	156.00	72.9688	30.46601
Day of lowest PLT	1.00	6.00	2.5104	1.29773

Thrombocytopenia and Platelet Trends: Severe thrombocytopenia (platelet count <150 x 10^9/L) was a common finding observed in 80% of cases. The lowest recorded platelet count was 19 x 10^9/L in a patient who presented with melena and required platelet transfusion. Platelet counts recovered gradually in most patients by day 3-5 of hospitalization with an average final platelet count of 67 x 10^9/L at discharge.

Outcomes and Treatment Responses: All patients were treated with either intravenous (IV) artesunate or artemisinin combination therapy (ACT) depending on the severity of the case. The average hospital stay was 5.7 days (range: 2-10 days). The overall recovery rate was 100% and no fatalities were recorded. A small subset (10%) experienced recurrence of symptoms following discharge but responded well to a second course of treatment. Patients admitted to the HDU due to severe complications, such as Hematuria or severe thrombocytopenia required more intensive management but recovered fully following therapy.

Variables		Frequency
Malaria Species	Falciparum	6
	MP ICT +	1
	Vivax	89
Symptoms	High grade fever	10
	Fever	22
	Hematuria	9
	Hypotension	2
	Loose stool	4
	Vomiting	4
	Pencytopenia	2
	massive spleenmeagaly	1
Treatment result	Artem DC	52
	IV artesunate	44
Treatment result	Recurrence	5
	Recovery	91

Discussion

The study provides valuable insight into the clinical presentations, laboratory findings, and outcomes of patients with *Plasmodium vivax* and *Plasmodium falciparum* malaria, highlighting key differences between the two species. Notably, the predominance of *P. vivax* cases aligns with regional epidemiological trends, while the minority of *P. falciparum*

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cases, although fewer, demonstrated more severe clinical features, particularly in terms of hemoglobin levels and associated complications. One key finding is the occurrence of malaria in males (92%). This predominance raises important considerations regarding gender-based differences in exposure to malaria. Male patients especially those in outdoor occupations are more likely to encounter *Anopheles* mosquitoes, increasing their risk. The lower representation of female patients may also be reflective of healthcare-seeking behaviours as women might delay treatment due to cultural or socio-economic factors, prevalent in countries like Pakistan. These findings suggest the need for targeted public health interventions and research into gender-specific prevention strategies particularly in malaria-endemic regions. Social dynamics influencing healthcare access for females should be further explored in future studies.

The age distribution and a mean age of 30.2 years places malaria's burden on economically active individuals. This age group typically engaged in outdoor labor or activities could face higher risks of mosquito exposure. However, the study did not include paediatric or elderly patients, populations that may present unique clinical challenges and vulnerabilities. Future research should consider these age groups to develop comprehensive malaria management protocols for the entire population, as their exclusion limits generalizability.

The analysis of hemoglobin levels among patients revealed that *P. falciparum* cases experienced more significant drops in hemoglobin compared to *P. vivax*, a reflection of the more aggressive nature of *P. falciparum* infection. Severe anemia is a hallmark of *P. falciparum*, driven by the destruction of both infected and uninfected red blood cells. In contrast, *P. vivax* infections tend to affect reticulocytes, which may contribute to a less pronounced decline in hemoglobin levels. However, even with *P. vivax*, severe anemia can occur more prominently in cases of chronic or recurrent infection. These species-specific clinical differences highlight the importance of rapid diagnosis and tailored treatment to mitigate the risk of severe complications. This study's findings regarding hemoglobin levels align with existing literature highlights the need for vigilance in monitoring anemia in malaria patients especially in *P. falciparum* cases.

Another noteworthy observation is the thrombocytopenia as it was seen in 80% of patients. Severe thrombocytopenia which resulted in bleeding complications in some cases is a well-recognized complication of malaria. Although the exact mechanisms leading to platelet reduction in malaria remain under investigation, possible factors include immune-mediated destruction and splenic sequestration. The platelet count recovery observed by day 3-5 of hospitalization in most cases suggests that malaria-induced thrombocytopenia is often reversible with appropriate treatment. However, the necessity for platelet transfusion in a patient presenting with melena underscores the potential severity of this condition. The study's findings accentuate the importance of close platelet monitoring in patients presenting with bleeding or at high risk for bleeding complications.

Future research should explore the mechanisms of malaria-associated thrombocytopenia in more detail and focus should be on potential interventions for managing severe cases. Given that thrombocytopenia can increase morbidity, particularly in areas with limited access to transfusion services understanding alternative treatment options is essential for improving patient outcomes in resource-limited settings. Additionally, qualitative studies involving healthcare workers could provide deeper insights into the challenges of managing such complications in clinical practice, helping refine protocols for early detection and treatment.

The study's findings also highlight the importance of immune response monitoring in malaria. Elevated neutrophil percentages and reduced lymphocyte percentages were consistent across the cohort, reflecting the typical acute-phase response seen in malaria infections. Neutrophilia, a marker of systemic inflammation, may provide early clues to the severity of infection, while lymphopenia could indicate immune system sequestration or redistribution. Further exploration into the dynamics of leukocyte counts during malaria infections could provide useful biomarkers for disease progression in differentiating mild from severe cases. This, in turn, could inform clinical decision-making regarding patient triage and the need for intensive monitoring or care, such as HDU admission.

In terms of treatment outcomes, the recovery rate of 100% demonstrates the effectiveness of artemisinin-based therapies, such as intravenous (IV) artesunate and artemisinin combination therapy (ACT). This result reinforces the role of these therapies as the cornerstone of malaria management, even in cases requiring hospitalization or high-dependency care. However, the recurrence of symptoms in 10% of the patients, all likely *P. vivax* cases, underscores the challenge posed by the dormant liver-stage hypnozoites, which are known to reactivate long after the initial infection. This finding highlights the need for better adherence to radical cure therapies, such as primaquine or tafenoquine to prevent relapse in *P. vivax* infections. Future research should focus on understanding patient adherence to such therapies and developing strategies to ensure long-term treatment success.

One strength of this study is the comprehensive clinical and laboratory data provided for each patient, offering a detailed understanding of the variations in disease presentation and outcomes between *P. vivax* and *P. falciparum* cases. The relatively large sample size for *P. vivax* cases enables robust conclusions regarding its clinical manifestations, especially thrombocytopenia, and response to therapy. However, a limitation of the study is the small number of *P. falciparum* cases, which restricts the ability to generalize findings to broader populations. The limited diversity in the patient population, with a predominance of young adult males, further constrains the study's applicability to other demographic groups, such as children, elderly patients, or females. Moreover, the study's retrospective design may have introduced bias, particularly in terms of data completeness and variability in clinical practices across different healthcare settings.

The exclusion of pediatric and elderly patients, in particular, limits the generalizability of the study to all age groups affected by malaria. Children and the elderly often experience more severe manifestations of the disease and may require different management approaches. Additionally, the lack of follow-up data on the long-term outcomes of patients, particularly regarding recurrent *P. vivax* infections, presents a gap in understanding the full disease trajectory. Future studies should aim for more diverse and representative samples, including different age

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groups and genders, to provide a comprehensive understanding of malaria's impact across populations. Prospective cohort designs that include long-term follow-up would help capture the chronic and recurrent nature of *P. vivax* malaria, allowing for more informed decisions about prevention and treatment strategies.

Conclusion

In conclusion, this study offers valuable insights into the clinical and laboratory characteristics of malaria patients, primarily *P. vivax*, and their response to treatment. While the findings align with existing literature on the severity of *P. falciparum* and the frequent occurrence of thrombocytopenia in *P. vivax*, the study's limitations, particularly in terms of sample diversity and follow-up data, should be addressed in future research. More detailed qualitative analyses of patient and healthcare provider perspectives on disease management, recurrence prevention and adherence to radical cure therapies could further improve malaria treatment protocols and outcomes mainly in resource-limited settings.

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Disclosure

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