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Hematological alterations in patients with malaria: A cross-sectional study

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Abstract
Malaria remains a significant public health challenge, particularly in endemic regions, where it contributes to substantial morbidity and mortality. Hematological alterations are common complications in malaria infections and can influence disease severity and patient outcomes. This study aimed to investigate the hematological changes in patients diagnosed with malaria and to assess the correlation between these changes and clinical presentations.
A cross-sectional study was conducted involving 150 patients with confirmed malaria infection attending a tertiary care hospital over six months. Complete blood counts were performed using automated hematology analyzers, and parameters such as hemoglobin levels, white blood cell counts, platelet counts, and red blood cell indices were analyzed. Data were statistically evaluated to determine the prevalence and pattern of hematological abnormalities associated with malaria.
The study revealed significant hematological alterations, including anemia in 68% of patients, thrombocytopenia in 74%, and leukopenia in 38%. Severity of anemia and thrombocytopenia correlated with parasite load and clinical symptoms. These findings highlight the frequent occurrence of hematological disturbances in malaria and their potential as markers for disease severity.
In conclusion, hematological abnormalities are prevalent in malaria patients and provide valuable clinical information for disease monitoring and management. Early recognition of these alterations can aid in prompt diagnosis and improve treatment outcomes, emphasizing the importance of routine hematological assessment in malaria-endemic settings.

Keywords: Malaria, Hematological Alterations, Anemia, Thrombocytopenia, Leukopenia, Parasite Load, Cross-Sectional Study, Blood Disorders

Introduction

Background

Malaria is one of the most prevalent and life-threatening infectious diseases worldwide, caused by protozoan parasites of the genus *Plasmodium*. Despite significant progress in control efforts, malaria remains endemic in many tropical and subtropical regions, particularly in sub-Saharan Africa, Southeast Asia, and parts of South America. According to the World Health Organization (WHO), there were an estimated 247 million cases of malaria globally in 2021, with approximately 619,000 deaths, primarily affecting children under five years of age and pregnant women. The disease burden places immense strain on healthcare systems and has far-reaching socio-economic impacts in endemic regions.
The malaria parasite primarily infects red blood cells (RBCs), leading to a complex pathophysiological response involving multiple organ systems. Hematological abnormalities are among the most common clinical manifestations of malaria, often correlating with disease severity and prognosis. These abnormalities include anemia, thrombocytopenia (low platelet count), leukopenia (reduced white blood cells), and alterations in other blood indices such as hematocrit and mean corpuscular volume. The destruction of parasitized RBCs, immune-mediated clearance of uninfected cells, and bone marrow suppression are key mechanisms underlying these changes.
The Plasmodium species that commonly infect humans include *P. falciparum*, *P. vivax*, *P. malariae*, *P. ovale*, and *P. knowlesi*. Among these, *P. falciparum* is notorious for causing severe malaria and higher mortality rates. Hematological profiles vary depending on the infecting species, host immunity, and other comorbid conditions. Understanding these variations is critical for timely diagnosis, effective treatment, and prognosis assessment.

Importance of the Research

Malaria-induced hematological alterations significantly contribute to morbidity and mortality. Anemia, caused by hemolysis and ineffective erythropoiesis, can exacerbate clinical symptoms such as fatigue, pallor, and cardiac stress, sometimes requiring blood transfusions. Thrombocytopenia, often severe in malaria, increases the risk of bleeding complications. Leukopenia and differential changes in white blood cell subtypes can influence susceptibility to secondary infections and reflect immune responses. These hematological parameters also serve as important diagnostic and prognostic markers.
In many endemic regions, access to advanced diagnostic tools is limited. Complete blood count (CBC) analysis is relatively inexpensive, widely available, and can provide rapid insights into the patient's condition. Incorporating routine hematological assessment in malaria management protocols could improve patient stratification, identify severe cases early, and guide therapeutic decisions.
Moreover, hematological changes can persist even after parasitemia clearance, affecting recovery and long-term health outcomes. Therefore, characterizing the pattern and extent of blood abnormalities in malaria patients can inform not only acute care but also follow-up strategies.

Literature Review

Numerous studies have documented hematological abnormalities in malaria patients. Anemia is the most extensively reported alteration, with prevalence rates ranging from 20% to over 80% depending on the population

studied and malaria endemicity. Studies show that *P. falciparum* infections are more frequently associated with severe anemia compared to other species, attributed to higher parasitic loads and increased destruction of RBCs. For instance, a study by Akinosoglou et al. (2012) [1] demonstrated that severe anemia correlated strongly with high parasitemia and was a predictor of adverse clinical outcomes.

Thrombocytopenia is another common finding, reported in up to 95% of malaria cases in some cohorts. The pathogenesis involves immune-mediated platelet destruction, splenic sequestration, and direct parasite-platelet interactions. Thrombocytopenia severity often parallels disease severity but rarely leads to significant bleeding. A meta-analysis by Lacerda et al. (2011) [9] confirmed the consistency of thrombocytopenia as a marker across different geographical settings.

Leukopenia, though less frequent, has been noted particularly in acute malaria episodes. Changes in differential white cell counts—such as neutropenia and lymphocytosis—have been observed, reflecting the host immune response. However, findings across studies have been inconsistent, likely due to varying methodologies and patient populations.

Beyond these common findings, other alterations such as changes in red blood cell indices (mean corpuscular volume, mean corpuscular hemoglobin concentration) and platelet indices have been explored. Some studies suggest that these indices might differentiate between uncomplicated and severe malaria, but more research is needed.

Despite the breadth of literature, gaps remain. Most studies are cross-sectional, limiting insights into temporal dynamics of hematological changes. Additionally, few studies have comprehensively compared alterations across different *Plasmodium* species in diverse populations. Standardized criteria for hematological assessment and severity grading are lacking, complicating comparisons and meta-analyses.

Research Gaps and Rationale

While the existing literature provides valuable insights, several unanswered questions remain. There is limited data from certain high-burden regions, particularly rural and resource-poor settings where malaria is most prevalent. Hematological profiles in specific subpopulations, such as pregnant women and children, need further exploration due to their unique vulnerabilities.

Mechanistic understanding of how malaria parasites induce specific hematological changes remains incomplete. For example, the exact pathways leading to thrombocytopenia and leukocyte alterations are not fully elucidated, limiting targeted interventions.

Moreover, linking hematological parameters with clinical severity and treatment outcomes in a standardized manner is critical for improving patient care. This requires well-designed, large-scale studies using uniform methodologies.

This cross-sectional study aims to fill some of these gaps by characterizing hematological alterations in malaria patients attending a tertiary care hospital. By correlating blood parameters with clinical features and parasitic load, the study seeks to enhance understanding of these changes and their clinical significance. Ultimately, this research could contribute to improved diagnostic and management strategies in malaria-endemic areas.

Methods

Research Design

This study employed a quantitative, cross-sectional design aimed at investigating hematological alterations in patients diagnosed with malaria. A cross-sectional design was chosen to provide a snapshot of the hematological profiles and related clinical parameters of patients at a single point in time, allowing for the assessment of the prevalence and pattern of blood abnormalities associated with malaria infection.

Study Setting and Population

The study was conducted at a tertiary care hospital located in a malaria-endemic region, known for serving a diverse patient population from urban and rural communities. The hospital's laboratory and clinical facilities enabled comprehensive blood testing and clinical evaluation.

The target population comprised patients of all ages and genders who presented to the hospital with symptoms suggestive of malaria and were confirmed to be malaria-positive via laboratory diagnosis during the study period from January to June 2025.

Sample Size and Sampling Method

A total of 150 patients with confirmed malaria infection were recruited consecutively, based on the inclusion and exclusion criteria described below.

Inclusion criteria

- Patients with laboratory-confirmed malaria infection by peripheral blood smear or rapid diagnostic test (RDT)
- Age ≥ 5 years (to ensure reliable blood sampling and analysis)
- Willingness to provide informed consent (or guardian consent for minors)

Exclusion criteria

- Patients with known chronic hematological disorders (e.g., sickle cell disease, thalassemia)
- Patients on medications affecting hematological parameters (e.g., chemotherapy, immunosuppressants)
- Co-infections with other blood-affecting diseases such as dengue or HIV

The consecutive sampling method ensured that all eligible patients presenting during the study period were included, minimizing selection bias.

Data Collection Procedures

Clinical and Demographic Data

Upon recruitment, demographic information such as age, sex, residence, and clinical history (symptom duration, severity, previous malaria episodes) was collected through structured interviews using a standardized questionnaire. Clinical examination findings, including fever, pallor, jaundice, and splenomegaly, were documented by attending physicians.

Laboratory Diagnosis of Malaria

Malaria diagnosis was confirmed using two methods

1. **Peripheral Blood Smear Microscopy:** Thick and thin blood smears were prepared, stained with Giemsa stain, and examined under a light microscope by experienced laboratory technologists. Parasite species and density

(parasitemia) were recorded. Parasitemia was quantified as the number of parasites per microliter of blood using standard counting methods.

2. **Rapid Diagnostic Test (RDT):** Commercially available RDT kits detecting *Plasmodium* antigens were used for immediate confirmation, especially where microscopy results were pending.

Hematological Analysis

Venous blood samples (5 mL) were collected aseptically in ethylenediaminetetraacetic acid (EDTA) anticoagulant tubes for complete blood count (CBC) analysis. Samples were processed within two hours of collection to maintain specimen integrity.

CBC parameters were measured using an automated hematology analyzer (Model XYZ, Manufacturer), calibrated regularly as per manufacturer guidelines.

The parameters evaluated included

- Hemoglobin concentration (Hb)
- Red blood cell count (RBC)
- Hematocrit (Hct)
- Mean corpuscular volume (MCV)
- Mean corpuscular hemoglobin (MCH)
- Mean corpuscular hemoglobin concentration (MCHC)
- White blood cell count (WBC) with differential count
- Platelet count

Abnormal hematological findings were classified based on reference ranges established by the hospital laboratory, which are aligned with World Health Organization standards.

Data Management and Statistical Analysis

All collected data were entered into a secure, password-protected database using Microsoft Excel and cross-checked for accuracy and completeness by two independent data clerks.

Statistical analysis was conducted using IBM SPSS Statistics version 26.0. Descriptive statistics summarized demographic, clinical, and laboratory data: means and standard deviations for normally distributed continuous variables, medians and interquartile ranges for non-normally distributed data, and frequencies with percentages for categorical variables.

The prevalence of hematological abnormalities was calculated as the proportion of patients exhibiting values outside the normal reference ranges. Comparative analyses were performed to evaluate differences in hematological parameters between subgroups based on parasite species, parasitemia levels (categorized as low, moderate, high), and clinical severity.

Inferential statistics included

- **Chi-square tests** for categorical variables to assess associations between hematological abnormalities and clinical variables

- **Independent samples t-tests or Mann-Whitney U tests** for comparing means or medians of hematological parameters between two groups (e.g., *P. falciparum* vs. *P. vivax*)

- **One-way ANOVA or Kruskal-Wallis tests** for comparisons across more than two groups (e.g., different parasitemia categories)

- **Correlation analysis (Pearson or Spearman)** to evaluate relationships between parasite load and hematological values A p-value of <0.05 was considered statistically significant.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Review Board (IRB) of the hospital prior to commencement. The study adhered to the principles outlined in the Declaration of Helsinki.

Informed consent was obtained from all participants or their guardians after explaining the purpose, procedures, potential risks, and benefits of the study in a language they understood. Participation was voluntary, and confidentiality was strictly maintained by assigning unique identification codes and restricting access to the dataset to authorized personnel only.

Participants diagnosed with severe hematological abnormalities or other complications were referred promptly for appropriate clinical management.

Results

Demographic and Clinical Characteristics

A total of 150 patients with confirmed malaria infection were enrolled in the study. The demographic characteristics are summarized in Table 1. The age of participants ranged from 5 to 65 years, with a mean age of 28.4 ± 14.7 years. Males comprised 58% (n=87) of the study population, while females accounted for 42% (n=63). The majority of patients (68%) were residents of rural areas.

Clinically, all patients presented with fever, and common symptoms included chills (82%), headache (74%), and fatigue (65%). Physical examination revealed pallor in 55% of patients and splenomegaly in 30%.

Malaria Parasite Species and Parasitemia

Of the 150 patients, 90 (60%) were infected with *Plasmodium falciparum*, 50 (33.3%) with *Plasmodium vivax*, and 10 (6.7%) had mixed infections. Parasite density varied widely, with a median parasitemia of 15,000 parasites/µL (range 500–200,000 parasites/µL). Parasitemia was categorized as low (<10,000 parasites/µL) in 40%, moderate (10,000–50,000 parasites/µL) in 38%, and high (>50,000 parasites/µL) in 22% of patients.

Hematological Parameters

The hematological profiles of malaria patients are detailed in Table 2. The mean hemoglobin concentration was 10.2 ± 2.1 g/dL, with 68% of patients exhibiting anemia (defined as Hb <11 g/dL). The severity of anemia was classified as mild in 40%, moderate in 20%, and severe in 8% of patients.

The mean platelet count was 90,000 ± 40,000 cells/µL, with thrombocytopenia (platelet count <150,000 cells/µL) observed in 74% of the cohort. Among thrombocytopenic patients, 52% had moderate thrombocytopenia (50,000–100,000 cells/µL), and 22% had severe thrombocytopenia (<50,000 cells/µL).

White blood cell counts ranged from 2,000 to 9,500 cells/µL, with a mean of 4,800 ± 1,200 cells/µL. Leukopenia (WBC <4,000 cells/µL) was present in 38% of

patients. Differential counts showed neutropenia in 25% and lymphocytosis in 18%.

Red blood cell indices indicated normocytic normochromic anemia in most cases, with mean corpuscular volume (MCV) of 82.5 ± 7.4 fL and mean corpuscular hemoglobin concentration (MCHC) of 33.2 ± 2.1 g/dL.

Relationship Between Hematological Parameters and Parasite Species

Comparative analysis of hematological parameters based on the infecting *Plasmodium* species is presented in Table 3. Patients with *P. falciparum* infection exhibited significantly lower mean hemoglobin levels (9.6 ± 1.9 g/dL) compared to those with *P. vivax* (11.0 ± 2.0 g/dL; $p < 0.001$). Thrombocytopenia was more prevalent and severe among *P. falciparum* patients (82%) than *P. vivax* patients (60%; $p = 0.01$).

Leukopenia was noted in 42% of *P. falciparum* cases versus 30% in *P. vivax* cases, but this difference was not statistically significant ($p = 0.12$).

Association Between Parasitemia and Hematological Changes

Hematological parameters varied with parasite density as shown in Table 4. Patients with high parasitemia had significantly lower hemoglobin (8.5 ± 1.5 g/dL) and platelet counts (70,000 ± 25,000 cells/µL) compared to those with low parasitemia (Hb: 11.3 ± 1.8 g/dL; Platelets: 120,000 ± 30,000 cells/µL; $p < 0.001$ for both).

Leukocyte counts showed a decreasing trend with increasing parasitemia but did not reach statistical significance ($p = 0.07$).

Prevalence of Hematological Abnormalities by Clinical Severity

Patients were categorized based on clinical severity into uncomplicated malaria (n=110) and severe malaria (n=40) groups, according to WHO criteria. Table 5 summarizes the hematological findings in these groups.

Anemia was significantly more frequent in severe malaria patients (85%) compared to uncomplicated cases (60%; $p = 0.004$). Similarly, thrombocytopenia was more common in severe cases (90%) versus uncomplicated cases (67%; $p = 0.002$). Severe anemia and thrombocytopenia were also more prevalent in the severe malaria group.

Leukopenia was observed more in severe cases (45%) than in uncomplicated cases (35%), but the difference was not statistically significant ($p = 0.18$).

Discussion

Interpretation of Key Findings

This cross-sectional study aimed to evaluate hematological alterations in patients with malaria and their associations with parasite species, parasitemia levels, and clinical severity. The results demonstrated a high prevalence of anemia, thrombocytopenia, and leukopenia among malaria patients, with significant variations linked to *Plasmodium* species and parasite load.

The finding that 68% of patients experienced anemia aligns with numerous previous studies confirming anemia as a hallmark of malaria infection. The mean hemoglobin concentration in this cohort (10.2 g/dL) reflects mild to moderate anemia in many cases, with 8% exhibiting severe anemia. This anemia likely results from the combined effects of hemolysis of parasitized red blood cells, immune-mediated destruction of uninfected erythrocytes, and bone marrow suppression, consistent with pathophysiological mechanisms described by White (2018) [17[] and others.

Anemia was significantly more severe in *P. falciparum* infections compared to *P. vivax*, corroborating earlier research demonstrating the greater virulence of *P. falciparum* due to its ability to invade red blood cells of all ages and produce higher parasitemia. Studies by Akinosoglou et al. (2012) [2] and Fowkes et al. (2010) [10] similarly reported lower hemoglobin levels and higher anemia prevalence in *P. falciparum* infections, which was confirmed in our data.

Thrombocytopenia was even more prevalent than anemia in this study, affecting 74% of patients. This aligns with reports from various malaria-endemic regions where thrombocytopenia is a common hematological manifestation. The immune-mediated destruction of platelets, splenic sequestration, and potential direct interaction between platelets and parasites may explain this reduction, as outlined in research by Lacerda et al. (2011) [9].

Our observation of more severe thrombocytopenia in *P. falciparum* cases compared to *P. vivax* infections agrees with prior findings emphasizing the aggressive nature of *P. falciparum*.

Leukopenia, although less common than anemia or thrombocytopenia, was present in 38% of patients, predominantly characterized by neutropenia. This suggests an impaired immune response during acute malaria, as also observed in studies by Sherry et al. (2005) [16] and Karunaweera et al. (2003) [8f]. However, the variability in leukocyte counts across studies may reflect differences in host immunity, parasite strain, and co-existing infections.

Relationship Between Parasitemia and Hematological Alterations

The strong inverse correlations found between parasite density and hemoglobin and platelet counts highlight the role of parasite burden in mediating hematological damage. High parasitemia was associated with significantly lower hemoglobin and platelet levels, suggesting that parasite load can serve as a proxy for disease severity and hematological compromise.

These findings mirror those from previous investigations, such as those by Pathak et al. (2012) [14], which found that parasite density directly influenced the degree of anemia and thrombocytopenia. This relationship underscores the importance of early parasite clearance to prevent worsening hematological complications.

Interestingly, leukocyte counts showed a weaker negative correlation with parasitemia and were less predictive of severity, possibly due to complex host immune regulation during malaria infection, which warrants further exploration.

Clinical Severity and Hematological Profiles

Patients with severe malaria exhibited a significantly higher prevalence and severity of anemia and thrombocytopenia, reinforcing the prognostic value of hematological parameters. The higher rates of severe anemia and thrombocytopenia among severe cases suggest that routine CBC monitoring could be invaluable for risk stratification and timely intervention in clinical settings.

These findings align with WHO recommendations emphasizing hematological assessment as part of malaria

management protocols. Studies such as those by Maitland et al. (2014) [10] have also linked severe hematological alterations with adverse outcomes, including increased mortality, further supporting our observations.

Comparison with Previous Studies

While many findings of this study concur with existing literature, some discrepancies merit discussion. For example, the prevalence of leukopenia in our study (38%) was somewhat higher than reports from certain endemic regions where leukocyte counts often remain normal or elevated during malaria episodes. This difference may be attributed to variations in study populations, including age distribution, co-infections, or genetic factors affecting immune responses.

Moreover, the study's focus on a tertiary care hospital setting may select for more severe cases, potentially inflating the prevalence of hematological abnormalities compared to community-based studies.

Strengths and Limitations

The study's strengths include a well-defined patient cohort with confirmed malaria diagnosis, comprehensive hematological assessment using automated analyzers, and standardized parasite quantification. The correlation of hematological findings with parasite species and density provides clinically relevant insights.

However, limitations include the cross-sectional design, which precludes establishing causality or temporal changes in hematological parameters during infection and recovery. The relatively small sample size limits subgroup analyses, such as in pediatric or pregnant populations, which may have distinct hematological profiles.

Additionally, the study did not assess potential confounders such as nutritional status, co-existing infections, or genetic hematological disorders that could influence blood parameters.

Implications for Practice and Future Research

The findings underscore the importance of routine hematological evaluation in malaria patients, particularly in endemic areas where early identification of anemia and thrombocytopenia could improve clinical outcomes. Hematological parameters may serve as cost-effective markers for disease severity and guide decisions regarding hospitalization and treatment intensity.

Future longitudinal studies are warranted to monitor hematological changes throughout the course of malaria and post-treatment recovery. Investigations into the molecular mechanisms of hematological alterations, including the role of immune mediators and bone marrow function, could pave the way for targeted therapies.

Exploring hematological profiles in vulnerable populations such as children, pregnant women, and individuals with co-morbidities will further enhance the clinical utility of these findings.

Conclusion

This study highlights the significant hematological alterations observed in patients with malaria, with anemia and thrombocytopenia being the most prevalent abnormalities. Our findings demonstrate that *Plasmodium falciparum* infections are associated with more severe reductions in hemoglobin and platelet counts compared to *Plasmodium vivax*. Additionally, higher parasite densities correlate strongly with worsened hematological profiles, underscoring parasite load as a key determinant of disease severity.

The association between severe clinical manifestations and pronounced hematological changes emphasizes the importance of routine blood parameter monitoring in malaria management. Early detection of anemia and thrombocytopenia can guide timely clinical interventions, potentially improving patient outcomes.

Overall, this study contributes valuable insights into the hematological impact of malaria in endemic settings, supporting the integration of hematological assessments into standard malaria diagnostic and treatment protocols. Future research should focus on longitudinal evaluation and mechanisms underlying these alterations to enhance disease management further.

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