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A Hospital-Based Observational Study on Hematological Alterations in Patients with Malaria Infection

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Abstract: ***This pilot study sheds light on the critical role that hematological analysis can play in the timely diagnosis and management of malaria, especially in resource-constrained, endemic regions. By comparing malaria-infected patients with healthy controls, it is evident that malaria profoundly disrupts several blood parameters, with notable reductions in hemoglobin, hematocrit, and platelet counts, alongside shifts in leukocyte populations. What stands out is the consistent presence of anemia and thrombocytopenia in malaria cases, which, in many ways, can serve as early indicators when other diagnostic tools are unavailable. The observed microcytic, hypochromic anemia and increased red cell distribution width suggest that the disease's impact on red blood cell morphology is both acute and multifactorial, involving destruction and impaired production. Interestingly, while leukopenia was a common finding, the relative rise in neutrophils and monocytes hints at a complex immune response that warrants deeper exploration. This suggests that, beyond the well-documented fever and chills, malaria leaves a recognizable signature in the blood that, if properly interpreted, could guide quicker, more effective clinical decisions. Although the study's scope is limited by its sample size and lack of species-specific data, it highlights a meaningful starting point for larger investigations that could refine hematological markers as reliable diagnostic and prognostic tools in malaria care.***

Keywords: malaria, hematological changes, anemia, thrombocytopenia, diagnosis

1. Introduction

Malaria remains a major global health concern, particularly in endemic regions across Africa, Asia, and parts of South America. As per the World Health Organization (WHO) Fact Sheet dated 11 December 2024, an estimated **263 million malaria cases** and **597,000 deaths** occurred worldwide in 2023, spanning 83 countries. The WHO African Region bears the greatest burden, accounting for **94% of global malaria cases (246 million)** and **95% of deaths (569,000)**, with **children under the age of five** representing **76% of all fatalities**. These alarming statistics highlight not only the prevalence but also the deadly potential of this parasitic disease, especially in vulnerable populations [1]. Malaria is caused by protozoan parasites of the genus *Plasmodium*, with *P. falciparum* and *P. vivax* being the most clinically significant [2]. After transmission via the bite of an infected *Anopheles* mosquito, the parasite undergoes hepatic and erythrocytic stages, with the latter responsible for most clinical manifestations [3]. Once inside the bloodstream, the parasites invade red blood cells (RBCs), multiply, and eventually cause cell lysis, leading to a cascade of hematological changes . The pathophysiological alterations in hematological parameters in malaria are multifactorial. Anemia results from hemolysis of both parasitized and non-parasitized erythrocytes, dyserythropoiesis, and increased clearance of RBCs by the spleen [4]. Thrombocytopenia is frequently observed and may be attributed to peripheral destruction, splenic pooling, immune-mediated lysis, and bone marrow suppression. Leukopenia or a relative lymphocytosis is also commonly noted, and shifts in leukocyte subpopulations may reflect both the immune response and disease severity [5]. Moreover, alterations in mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red cell distribution width (RDW) can provide insights into the chronicity and type of anemia involved [6]. Recognition of these hematological abnormalities is crucial in clinical settings, particularly in endemic regions where malaria presents with non-specific symptoms similar to other febrile illnesses. Routine hematological investigations, therefore, not only support early diagnosis but may also provide prognostic value in assessing the severity of infection [7]. This hospital-based observational study aims to evaluate and characterize the spectrum of hematological alterations in patients diagnosed with malaria, with the goal of enhancing clinical interpretation, early diagnosis, and informed treatment decisions in affected populations.

2. Material and Methodology

Study Site and Design

This pilot hospital-based observational study was conducted at NIMS Hospital, a tertiary care center with diagnostic and treatment facilities for infectious diseases, enrolling patients of all age groups and both sexes diagnosed with malaria through inpatient or outpatient services.

Study Population

The study population was divided into two groups: a malaria-infected group consisting of patients of all age groups and both sexes with confirmed malaria infection (Group 1), and a control group comprising healthy individuals without any clinical signs of infection and with normal hematological parameters (Group 2). All participants were selected from patients attending or admitted to NIMS Hospital, based on the inclusion and exclusion criteria.

Inclusion Criteria

- Patients with confirmed diagnosis of malaria based on peripheral blood smear and/or rapid diagnostic tests RDTs for *Plasmodium* species.
- Patients who provided informed consent.
- Both inpatients and outpatients presenting with clinical symptoms consistent with malaria.

Exclusion Criteria

- Patients with acute and chronic hematological and infectious diseases.
- Pregnant women (due to physiological hematological variations).
- Patients who did not provided informed consent.

Data Collection

Blood samples were collected aseptically from the median cubital vein using sterile techniques and transferred into EDTA vials for hematological analysis after obtaining informed consent forms and based on the inclusion and exclusion criteria. The samples were processed using a Sysmex 6-part automated hematology analyzer to evaluate various hematological parameters.

Statistical Analysis

Data were compiled using Microsoft Excel and analyzed using **SPSS software 26**. Descriptive statistics such as mean, standard deviation, and frequency were used to summarize the data. Comparative analysis of hematological parameters between different subgroups (e.g., *P. falciparum* vs. *P. vivax*) was performed using appropriate statistical tests such as the t-test and chi-square test, with a **p-value < 0.05** considered statistically significant.

3. Result

Demographic Characteristics

The present study included a total of 30 participants, divided equally into two groups: Group 1 (malaria-infected individuals) and Group 2 (healthy controls). The mean age of participants in Group 1 was 39.93 ± 11.46 years, while in Group 2 it was 39.80 ± 11.97 years, indicating a comparable age distribution between the groups (Table 1).

Table 1: Mean Age with Standard Deviation by Group

Group	Mean Age (years)
Group 1	39.93 ± 11.46
Group 2	39.80 ± 11.97

All values were Mean and SD.

When analyzed according to gender, females in Group 1 had a mean age of 42.22 ± 8.26 years, while males had a mean age of 36.50 ± 15.33 years. In Group 2, the mean age of females was 34.67 ± 6.89 years, and males had a mean age of 43.22 ± 13.71 years, as shown in Table 2.

Table 2: Age by Gender within Each Group

Group	Gender	Mean Age (years)
Group 1	Female	42.22 ± 8.26
Group 1	Male	36.50 ± 15.33
Group 2	Female	34.67 ± 6.89
Group 2	Male	43.22 ± 13.71

All values were Mean and SD.

In terms of gender distribution, Group 1 comprised 9 females and 6 males, whereas Group 2 included 6 females and 9 males. The gender frequency within each group is presented in Table 3.

Table 3: Gender Frequency by Group

Group	Female	Male
Group 1	9	6
Group 2	6	9

All values were frequency of gender by group

Regarding residential location, Group 1 had a predominance of urban participants (13 urban vs. 2 rural), whereas Group 2 had a relatively balanced distribution (9 urban vs. 6 rural), as shown in Table 4.

Table 4: Location Frequency by Group

Group	Rural	Urban
Group 1	2	13
Group 2	6	9

All values were frequency

Hematological Findings

A comparative analysis of hematological parameters between the malaria-infected group (Group 1) and healthy controls (Group 2) is presented in Table 5. Statistically significant differences were observed in most parameters. The mean hemoglobin level was significantly lower in Group 1 (10.48 ± 1.05 g/dL) compared to Group 2 (13.22 ± 0.91 g/dL) ($p < 0.001$). Similarly, hematocrit values were markedly reduced in malaria patients (32.65 ± 3.01%) relative to controls (40.18 ± 2.50%) ($p < 0.001$). The total leukocyte count (TLC) was significantly decreased in the malaria group (5.09 ± 0.90 ×10³/µL) compared to the control group (6.95 ± 0.70 ×10³/µL) ($p < 0.001$). However, neutrophil percentage was significantly elevated in Group 1 (60.3 ± 5.2%) versus Group 2 (55.1 ± 4.1%) ($p = 0.041$), while lymphocyte percentages were significantly lower in Group 1 (28.4 ± 4.4%) than in Group 2 (34.9 ± 3.9%) ($p = 0.002$). Monocyte count was also elevated in the malaria group ($p = 0.024$), whereas eosinophils and basophils showed no statistically significant difference between groups ($p > 0.05$). Among red cell indices, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) were significantly reduced in the malaria group ($p < 0.05$). Red cell distribution width (RDW) was significantly increased in malaria patients (17.6 ± 1.4%) compared to controls (15.1 ± 1.1%) ($p < 0.001$), indicating anisocytosis. Notably, platelet counts were markedly decreased in Group 1 (122.5 ± 24.8 ×10³/µL) compared to Group 2 (247.2 ± 29.5 ×10³/µL), with a highly significant p-value < 0.001, indicating thrombocytopenia as a prominent hematological abnormality in malaria.

Table 5: Comparison of Hematological Parameters Between Malaria and Control Groups

Parameter	Group 1 (Mean ± SD)	Group 2 (Mean ± SD)	t-value	p-value
Hemoglobin (g/dL)	10.48 ± 1.05	13.22 ± 0.91	-7.89	<0.001**
Hematocrit (%)	32.65 ± 3.01	40.18 ± 2.50	-8.23	<0.001**
Total Leukocyte Count	5.09 ± 0.90	6.95 ± 0.70	-6.45	<0.001**
Neutrophils (%)	60.3 ± 5.2	55.1 ± 4.1	3.15	0.041*
Lymphocytes (%)	28.4 ± 4.4	34.9 ± 3.9	-4.44	0.002*
Monocytes (%)	6.1 ± 1.3	5.0 ± 1.1	2.39	0.024*
Eosinophils (%)	2.0 ± 0.7	1.9 ± 0.5	0.51	0.615
Basophils (%)	0.5 ± 0.2	0.4 ± 0.1	1.23	0.228
MCV (fL)	78.4 ± 3.9	82.6 ± 3.6	-2.92	0.007*
MCH (pg)	25.0 ± 1.7	27.9 ± 1.4	-5.38	<0.001**
MCHC (g/dL)	31.2 ± 1.3	33.0 ± 1.0	-4.56	<0.001**
RDW (%)	17.6 ± 1.4	15.1 ± 1.1	5.66	<0.001**
Platelet Count (×10³/µL)	122.5 ± 24.8	247.2 ± 29.5	-13.52	<0.001**

Group 1 – Malaria-infected patients (n = 15); Group 2 – Healthy controls (n = 15).
Values are presented as Mean ± Standard Deviation (SD). $p < 0.05$ indicates statistical significance (*); $p < 0.001$ indicates high statistical significance (**).
t-test was applied for comparison between groups.

4. Discussion

This pilot study evaluated the hematological profile of malaria-infected patients (Group 1) in comparison to healthy controls (Group 2) at a tertiary care center. Alongside laboratory data, demographic characteristics including age, gender, and residence were also analyzed.

Demographic Characteristics

The mean age of participants was comparable between the two groups, with Group 1 (malaria) having a mean age of **39.93 ± 11.46 years** and Group 2 (controls) showing **39.80 ± 11.97 years** (Table 1), indicating no significant age disparity. Gender distribution was nearly equal but inverse, with more females in Group 1 (9 females, 6 males) and more males in Group 2 (6 females, 9 males) (Table 3). Regarding residence, Group 1 had a higher urban representation (13 urban vs. 2 rural), while Group 2 was more balanced (9 urban vs. 6 rural) (Table 4). Within-group gender-based age analysis showed slightly higher mean age in Group 1 females (**42.22 ± 8.26 years**) compared to males (**36.50 ± 15.33 years**), while in Group 2, males were older (**43.22 ± 13.71 years**) than females (**34.67 ± 6.89 years**) (Table 2). Significant hematological alterations were found in malaria-infected individuals when compared with healthy controls (Table 5). Hemoglobin levels were significantly reduced in Group 1 (**10.48 ± 1.05 g/dL**) compared to Group 2 (**13.22 ± 0.91 g/dL**), with a **p-value < 0.001**, consistent with the anemia commonly associated with malaria[8], [9]. Similarly, hematocrit levels were lower in Group 1 (**32.65 ± 3.01%**) vs. Group 2 (**40.18 ± 2.50%**) (**p < 0.001**), confirming the anemia was also characterized by reduced packed cell volume. Red cell indices revealed a microcytic, hypochromic picture: Group 1 had significantly lower mean corpuscular volume (MCV: **78.4 ± 3.9 fL**), mean corpuscular hemoglobin (MCH: **25.0 ± 1.7 pg**), and mean corpuscular hemoglobin concentration (MCHC: **31.2 ± 1.3 g/dL**) compared to controls (MCV: **82.6 ± 3.6 fL**, MCH: **27.9 ± 1.4 pg**, MCHC: **33.0 ± 1.0 g/dL**) (**all p < 0.01**). Red cell distribution width (RDW), a marker of anisocytosis, was significantly higher in malaria patients (**17.6 ± 1.4%**) compared to controls (**15.1 ± 1.1%**, **p < 0.001**), indicating increased variability in red blood cell size—often due to ineffective erythropoiesis or hemolysis [10]. Total leukocyte count (TLC) was significantly reduced in the malaria group (**5.09 ± 0.90 x10³/µL**) compared to controls (**6.95 ± 0.70 x10³/µL**, **p < 0.001**), in line with previous studies reporting leukopenia as a typical feature of malaria [11]. However, the differential count showed neutrophilia (**60.3 ± 5.2%** in Group 1 vs. **55.1 ± 4.1%** in Group 2, **p = 0.041**) and monocytosis (**6.1 ± 1.3%** vs. **5.0 ± 1.1%**, **p = 0.024**), which are markers of acute inflammation and immune response. Conversely, lymphocyte percentage was significantly lower in malaria cases (**28.4 ± 4.4%**) than controls (**34.9 ± 3.9%**, **p = 0.002**), reflecting immunosuppression as noted in other studies [12]. Thrombocytopenia was a prominent finding, with the platelet count significantly decreased in Group 1 (**122.5 ± 24.8 x10³/µL**) versus Group 2 (**247.2 ± 29.5 x10³/µL**, **p < 0.001**). Thrombocytopenia in malaria is attributed to peripheral destruction, immune complex-mediated clearance, or splenic sequestration [13]. This finding has been well-documented and suggested as a reliable diagnostic marker in endemic regions [14]. Although eosinophils and basophils showed minor differences, these were statistically insignificant ($p > 0.05$), aligning with the literature indicating they are not central players in malaria pathophysiology [15]. This study affirms that malaria infection results in substantial hematological changes, particularly anemia, thrombocytopenia, and leukocyte alterations. These findings agree with the works of **Kotepui et al.** [10]**, Erhart et al.** [11]**,** and **Jadhav et al.** [14], highlighting their diagnostic and prognostic potential in malaria-endemic settings. Early recognition of these changes can facilitate rapid diagnosis and appropriate management, especially when microscopy or antigen testing is unavailable.

5. Limitations

Being a pilot study, limitations include a small sample size and lack of *Plasmodium* species identification. A larger, multicentric study including parasitaemia grading and longitudinal follow-up could offer more robust insights.

6. Conclusion

The present study demonstrates that malaria infection is associated with significant hematological alterations, including anemia, thrombocytopenia, leukopenia, neutrophilia, lymphocytopenia, and elevated red cell distribution width. These changes reflect the pathophysiological impact of malaria on erythropoiesis, immune modulation, and platelet dynamics. The statistically significant differences in hemoglobin, hematocrit, red cell indices, and platelet counts between malaria patients and healthy controls suggest that routine hematological profiling can serve as a valuable adjunct in the early diagnosis and management of malaria, particularly in endemic regions with limited diagnostic facilities. Future studies with larger sample sizes and species-specific analysis are warranted to further validate these findings and enhance their clinical utility.

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