Original Research Article

EVALUATION OF SOME HAEMATOLOGICAL BIOMARKERS OF INFLAMMATION IN CHILDREN WITH VARYING DEGREES OF MALARIA PARASITEMIA IN A TERTIARY HEALTH FACILITY IN JOS, NIGERIA.

Abstract:

Aim: This study aims to explore the correlation between specific hematological inflammatory markers (Neutrophil/Lymphocyte Ratio [NLR], Monocyte/Lymphocyte Ratio [MLR], Systemic Immune-inflammatory Index [SII]) and varying degrees of malaria in children, utilizing blood samples from children with malaria in Jos, Nigeria.

Study Design: A cross-sectional study involving 384 clinically symptomatic and laboratory-confirmed malaria-infected children with diverse parasitemia levels. Samples were obtained from both outpatient and hospitalized cases at Jos University Teaching Hospital.

Place and Duration of Study: The study was conducted in Jos University Teaching Hospital. Data collection spanned a specified duration of 14th September 2022 to 14th may, 2023.

Methodology: Malaria parasite density was determined through microscopic examination of peripheral blood films. Complete blood counts were analyzed, and predictive inflammatory biomarkers (NLR, MLR, SII) were computed.

Results: Significant correlations among hematological inflammatory markers were evident, with the following sequence of significance observed: NLR displayed the most pronounced positive correlation with malaria parasite density (r=0.683, p=0.001), followed by MLR (r=0.512, p=0.001), and SII (r=0.550, p=0.001). Eosinophil count exhibited marked significance, displaying a notably higher value in subjects with elevated malaria parasitemia compared to those exhibiting low, mild, and moderate levels (p=0.0154).

Conclusion: In conclusion, the investigation unveiled a robust relationship between malaria parasitemia and Hematological inflammatory markers (NLR, MLR, SII), The prominence of NLR in exhibiting the strongest correlation with malaria parasite density underscores its potential as a vital biomarker for assessing malaria severity. They all offer cost-effective means to gauge malaria severity and assess inflammation in resource-limited settings. These markers also hold promise for malaria prognosis and treatment monitoring.

Keywords: Hematological Inflammatory Markers, Malaria Parasite density, Resource-Limited Areas, Prognosis.

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1. INTRODUCTION

Malaria, a significant global health concern triggered by Plasmodium parasites and transmitted through female Anopheles mosquitoes, it has continued to impose a considerable burden on human populations (1). The World Health Organization (WHO) underscores that nearly 3.8 billion individuals spanning 91 countries, primarily in developing regions, are susceptible to malaria infection (2). Despite substantial strides in curbing malaria's worldwide ramifications, WHO report for 2019 documented 229 million malaria cases and 409,000 associated fatalities, with 94% of these instances concentrated in Africa (2). As the most severe global parasitic infection, approximately 40% of the global population remains vulnerable to contracting malaria (3).

Hematological biomarkers have surfaced as crucial indicators of immune responses and the severity of diseases linked to malaria parasitemia. Thrombocytopenia, characterized by a decreased platelet count, is commonly observed in malaria-infected individuals, rendering it a pivotal biomarker for assessing inflammation and disease intensity (4,5). Platelets play a diverse role in immune responses, engaging in both inflammation and modulation of the immune system (6). In the context of malaria, thrombocytopenia arises from various factors, such as platelet retention within the spleen, destruction due to immune responses, and utilization during coagulation processes (6). The significance of this biomarker stems from its correlation with unfavorable clinical outcomes, including the development of severe illness and heightened mortality rates (6). Monitoring platelet counts offers clinicians valuable insights into disease progression and the efficacy of therapeutic interventions. Alterations in leukocyte counts, encompassing monocytes, lymphocytes, and neutrophils, provide insightful perspectives into the immune response during malaria infection (8,9,10). The ratios of monocytes to lymphocytes and neutrophils to lymphocytes exhibit potential as indicators of both inflammation and disease severity in malaria (11,12Research has indicated that there is an elevation in eosinophil counts in reaction to Plasmodium infection (7). Higher levels of eosinophils are frequently noted among individuals afflicted with malaria, especially in areas where the ailment is prevalent. This increase in eosinophil concentration implies an intrinsic inflammatory mechanism, underscoring the active engagement of eosinophils within the immune response directed against the parasite.

Hematological biomarkers hold valuable potential for assessing risk and monitoring malaria patients. Integrating hematological analyses into routine clinical practices, alongside existing diagnostic tools, can facilitate early detection, personalized treatment strategies, and effective malaria management. However, acknowledging the complexities of these biomarkers is crucial, considering the variations in hematological responses across diverse Plasmodium species and host populations, necessitating further exploration. Furthermore, obtaining a comprehensive understanding of the precise mechanisms underpinning these hematological changes and their implications in disease pathogenesis demands thorough investigation. Future research endeavors should focus on standardizing the application of hematological biomarkers in clinical settings, unveiling their prognostic and predictive capabilities for malaria. Addressing these dimensions will contribute to advancing our comprehension of malaria's underlying pathogenesis, elevating patient care quality, and enhancing outcomes in regions profoundly affected by the disease.

2. Methodology

This study was conducted at the Jos University Teaching Hospital, Plateau State. It employed a cross-sectional research design to investigate the relationship between hematological inflammatory markers

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and malaria parasitemia in children. The study included 384 malaria-infected children aged zero (0) to seventeen (17) years, presenting with clinical symptoms and laboratory-confirmed malaria infection at the hospital's outpatient department or as hospitalized patients. Adults above seventeen (17) years and children with tumors and cardiovascular conditions were excluded. The systematic sampling technique was used to recruit subjects where venous blood samples were collected from each participant, and the microscopic method was utilized to determine malaria parasite density. Predictive inflammatory biomarkers such as NLR, MLR, and SII were calculated from complete blood count results summarized as thus; NLR was calculated as the ratio of the neutrophils count to Lymphocyte counts, and MLR was calculated as the ratio of the monocytes count to Lymphocyte counts. The SII was calculated as neutrophil x platelet/lymphocyte (13). Statistical analyses were performed using SPSS software, and results were presented in simple percentages, mean ± standard deviation. Ethical approval and informed consent were obtained from the Health Ethics and Research Committee of the University of Jos Teaching Hospital. The study's limitations include the lack of established reference ranges for inflammatory markers in the study area, the focus on children under eighteen (18) years of age, absence of evaluation on inflammatory markers in malaria co-infection, and the lack of comparison with non-malaria-infested patients.

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3. Results and Discussion

Malaria, a parasitic disease, triggers inflammation through intricate interactions involving the host, parasite, and environmental factors (14). The response to malaria infection in humans entails diverse activities mediated by cell-intrinsic and systemic pathways, with initial non-specific responses in naive hosts (9). Extensive research has been dedicated to identifying dependable predictors of malaria exposure, susceptibility, and severe complications. This study focuses on exploring the connection between specific surrogate inflammatory markers and children infected with Plasmodium falciparum.

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(Table 1) portrays the socio-demographic characteristics of 384 children affected by malaria. Of this cohort, 43.5% (167) were female, while 56.5% (217) were male. The distribution across age groups demonstrated that 16.7% (64) were infants, 20.8% (80) were toddlers, 29.4% (113) were in the school-age bracket, and the majority, accounting for 33.1% (127), were adolescents. In terms of education, 46.9% (180) had not yet commenced schooling, 31% (119) were in primary education, 18.8% (72) were pursuing secondary education, and only 3.4% (13) were engaged in tertiary education. In the realm of religion, 53.1% (204) identified as Muslims, while 46.9% (180) ascribed to Christianity. Ethnic diversity revealed that 12% (46) belonged to the Berom group, 10.7% (41) were Fulani, 29.7% (114) were Hausas, 4.9% (18) represented Igbos, 8.1% (31) identified as Angas, and 5.5% (21) were Yoruba, with other minority ethnicities comprising about 29.4% (113). Geographical distribution unveiled that 45.3% (174) were urban residents, 35.9% (138) inhabited rural areas, and 18.8% (72) resided in suburban locales. The density of malaria parasites was categorized as low (10.7%, 41 cases), mild (67.7%, 260 cases), moderate (7.8%, 30 cases), and high (13.8%, 53 cases). The investigation demonstrated that socio-demographic factors, namely age, educational level, ethnicity, and religion, significantly influenced parasitemia levels in malaria patients. Conversely, variables such as sex and place of residence did not exert a significant impact on parasitemia levels in subjects afflicted with malaria, all as shown in table 1 below. These findings underscore the intricate interplay between socio-demographic factors and the severity of parasitemia in children with malaria, underscoring the imperative of a comprehensive comprehension and targeted strategies in the management of this infectious disease.

Table 1: Showing Demographic Data of Subjects

Characteristics		Frequency (N)	Percentage (%)
Age (years)	Less than a year (infant)	64	16.7
	1-3 years (Toddler)	80	20.8
	4-9 years (School age)	113	29.4
	10-17 years (Adolescent)	127	33.1
Education	Yet to start	180	46.9
	Primary	119	31.0
	Secondary	72	18.8
	Tertiary	13	3.4
Sex	Female	167	43.5
	Male	217	56.5
Religion	Christian	180	46.9
	Islam	204	53.1
Ethnicity	Berom	46	12.0
	Fulani	41	10.7
	Hausa	114	29.7
	Igbo	18	4.9
	Angas	31	8.1

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	Yoruba	21	5.5
	Others	113	29.4
Residence	Rural	138	35.9
	Suburban	72	18.8
	Urban	174	45.3
Parasite density grade	Low	41	10.7
	Mild	260	67.7
	Moderate	30	7.8
	High	53	13.8

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The study found a significant increase in eosinophil count among subjects with high malaria parasitemia (P= 0.0154), aligning with prior research on acute Plasmodium falciparum infection (15), this suggests a cytotoxic role of eosinophils against parasitic infections, facilitated by T-helper cells and immune cytokines during the acute phase of malaria infection. While malaria parasitemia levels did not significantly impact the white blood cell count, there was a notable rise in eosinophil, neutrophil, and platelet counts, along with predictive inflammatory immune markers MLR, NLR, and SII (Table 2). These findings correspond to earlier reports on changes in white blood cell counts and inflammatory markers during acute Plasmodium falciparum infection (12). It is important to note that hematological alterations like anemia, thrombocytopenia, and leukocyte count changes can occur due to malaria infection, although this study did not assess confounding factors such as hemoglobinopathies, nutritional status, and malaria immunity as done in previous works (12).

Table 2: Showing Association Between the Parasite Density Grading and Some Hematological Inflammatory Biomarkers

Variables	Low	Mild	Moderate	High	p-values
WBC (10^3/µL)	8.1 ± 0.52	10.2 ± 0.57	8.9 ± 0.65	10.6 ± 1.58	0.426
Neutrophil (%)	43.5 ± 2.72	43.0 ± 1.18	52.0 ± 3.52	49.5 ± 2.54	0.016
Lymphocyte (%)	42.3 ± 2.80	43.6 ± 1.12	36.1 ± 3.09	37.9 ± 2.35	0.045
Monocyte (%)	11.5 ± 0.77	12.6 ± 0.40	11.3 ± 0.48	10.7 ± 0.30	0.129
Eosinophil (%)	3.70±0.11	3.16±0.22	3.26±0.21	3.74±0.42	0.0154
Platelet (10^3/µL)	280.4 ± 22.98	258.1 ± 9.00	165.7 ± 24.50	174.7 ± 20.61	0.001
NLR	1.6 ± 0.30	3.2 ± 0.70	2.2 ± 0.36	1.8 ± 0.19	0.001
MLR	0.43 ± 0.112	0.65 ± 0.142	0.36 ± 0.030	0.43 ± 0.109	0.001
SII	435.9 ± 74.87	849.9 ± 232.40	388.9 ± 133.27	246.3 ± 34.8	0.001
Parasite density (p/µL)	86.0 ± 2.05	417.1 ± 14.32	2426.3 ± 387.80	39837.8 ± 1939.85	0.001

Furthermore, the study demonstrated a positive correlation between NLR and malaria parasite density (Table 3), consistent with previous reports on imported malaria patients (16). Other studies also found higher NLR in severe falciparum malaria compared to uncomplicated cases (10,17). NLR is suggested as a marker for stress and inflammation, indicating that higher malaria parasitemia induces greater stress and inflammation (10,17). Similarly, the study established a strong positive correlation between MLR and malaria parasite density, (Table 3), corroborating previous research (10,18,19) reported that increased MLR was associated with higher parasitemia in children up to five years old, suggesting MLR as a valuable indicator of malaria severity and the immune response's efficacy against the infection. Additionally, the study identified a significant positive correlation between SII and different grades of malaria parasitemia (Table 3), supporting previous studies on its potential prognostic value in various cancers (20) and malaria patients (21), Only a few studies have explored this innovative inflammatory marker in individuals with malaria, and our research adds to the existing literature on hematological inflammatory biomarkers.

Table 3. Correlation of Immune-Inflammatory Markers of Malaria Patients to malaria parasite density.

Immune-Inflammatory Markers	Correlation co-efficient (r)	P-value
Neutrophil/Lymphocyte	0.683	0.001

Ratio		
Monocyte/Lymphocyte Ratio	0.512	0.001
Systemic Inflammatory Index (SII)	0.550	0.001

Hematological biomarkers play a crucial role in evaluating inflammation and immune activation during malaria infection. Integrating hematological analyses into routine clinical practice can enhance the assessment of risk, early detection, and management of malaria. Further research should focus on standardizing these biomarkers and exploring their prognostic and predictive capabilities across diverse settings and populations.

4. Conclusion

The study demonstrated a positive correlation between different levels of malaria parasite density and most inflammatory immune markers, including MLR, NLR, and SII. Demographic factors such as age, ethnicity, educational level, and religion significantly influenced the levels of parasitemia among malaria patients, highlighting the importance of considering these factors when evaluating inflammatory biomarkers in specific populations. These findings also suggest that selected inflammatory biomarkers can serve as valuable tools in resource-limited areas to assess malaria severity and tailor appropriate interventions. Monitoring hematological biomarkers provides insights into the inflammatory response, immune cell activation, and hematological changes during malaria infection. However, to enhance disease assessment and treatment monitoring, it is crucial to consider combining multiple biomarkers for a comprehensive understanding of the inflammatory state during malaria infection.

Consent

All authors unanimously declare that written informed consent was obtained from the participants for publication of this case study.

Ethical Approval

Ethical approval (ref; JUTH/DCS/IREG/127/XXXI/349) was obtained from Jos University Teaching Hospital Research and Ethics Committee before the commencement of the study.

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