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Variations in haematological and inflammatory biomarkers and their association with *Plasmodium falciparum* malaria: a cross-sectional comparative study at a clinic in Ghana

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Abstract

Background Malaria remains a significant public health challenge in Ghana, with haematological alterations being a common feature of infection. Understanding these changes is crucial for improving disease management, particularly in endemic regions where resource limitations may affect diagnostic capabilities. This study aimed to evaluate variations in haematological and inflammatory biomarkers and their association with *Plasmodium falciparum* malaria in a Ghanaian setting.

Methods A cross-sectional comparative study was conducted at the Ghana Ports and Harbours Authority Clinic from January to May 2018, involving 200 participants (100 *P. falciparum*-infected and 100 malaria-negative participants). Full blood count parameters and derived inflammatory indices were analysed. Kruskal–Wallis and Mann–Whitney U tests were used to determine the variations in haematological and inflammatory biomarkers across malaria and non-malaria groups. Logistic regression was also used to find the haematological and inflammatory biomarkers associated with malaria. A *p-value* less than 0.05 was considered statistically significant.

Results Significant differences were observed in several haematological parameters between *P. falciparum* malaria and non-malaria groups. *Plasmodium falciparum* malaria patients showed markedly lower white blood cell counts (4.88 vs. 5.84×10^9/L, $p < 0.001$), lymphocyte counts (0.91 vs. 2.10×10^9/L, $p < 0.001$), and platelet counts (117.50 vs. 224.50×10^9/L, $p < 0.001$). Inflammatory indices revealed elevated neutrophil-to-lymphocyte ratio (3.49 vs. 1.43, $p < 0.001$) and systemic inflammatory response index (1.83 vs. 0.73, $p < 0.001$) in *P. falciparum* malaria patients. Notably, the platelet-monocyte ratio was significantly reduced in malaria patients (207.45 vs. 457.78, $p < 0.001$). Haemoglobin levels showed significant variation across parasite densities, particularly between moderate and low parasitaemia groups ($p = 0.026$). The logistic regression also revealed that the odds of malaria decreased with increasing haematocrit (aOR: 0.77,95% CI 0.60–0.97, $p = 0.032$), platelets (aOR:0.96, 95% CI 0.94–0.99, $p = 0.013$) and platelets-monocyte ratio (aOR:0.98, 95% CI 0.97–0.99, $p = 0.004$), and increased with increased platelets-lymphocyte ratio (aOR:1.04, 95% CI 1.00–1.07, $p = 0.031$).

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Conclusion This study demonstrated significant alterations in haematological and inflammatory biomarkers during *P. falciparum* malaria infection. These findings reveal the importance of haematological parameters in malaria diagnosis and severity assessment, with potential implications for improving early detection, risk stratification, and clinical management of *P. falciparum* malaria patients.

Keywords *Plasmodium falciparum*, Malaria, Variations, Haematological, Inflammatory, Biomarkers

Background

Malaria, most often caused by *Plasmodium falciparum*, remains endemic in 85 tropical countries and was responsible for an estimated 247 million cases and 619,000 deaths in 2021 [1]. In Ghana, *P. falciparum* drives year-round transmission with marked seasonal peaks in the north, despite sustained national control efforts [1]. The parasite is transmitted mainly via the bite of an infected female *Anopheles* mosquito, although congenital and transfusion-associated infections also occur [2]. Globally, Africa and Asia bear the highest *P. falciparum* burden [3], accounting for more than 95% of cases and 96% of deaths in the World Health Organization (WHO) African Region in 2021 [4]. Children under 5 years suffer over 65% of malaria mortality, reflecting the gradual acquisition of anti-parasite immunity with repeated exposures [5]. In Ghana, malaria accounts for roughly 40% of outpatient visits [5], and point-prevalence surveys, such as one in the Shai Osudoku district reporting 20.9% infection, reflect ongoing transmission [6]. Despite new rapid diagnostic tests, microscopy remains the gold standard for detecting *P. falciparum* in many endemic settings [7].

Haematological changes in malaria are anticipated since the parasites inhabit and affect the blood throughout most of their complex life cycle [8]. Malaria-related haematological changes are influenced by factors such as immunity, baseline haemoglobinopathies, endemicity levels, and demographic characteristics [8]. Understanding these haematological and inflammatory changes could improve malaria diagnosis, severity assessment, and disease management [9].

Several studies have documented notable alterations in haematological parameters, including white blood cell count, platelet count, haemoglobin levels, and inflammatory indices in malaria patients, with variations depending on parasite density [10, 11]. The effect of malaria parasitaemia on laboratory biomarkers is of clinical significance, as these changes can aid in the early detection and management of the disease [12].

Thrombocytopenia, for instance, has been widely associated with malaria infection and is often used as a supportive diagnostic indicator [9]. Furthermore, emerging inflammatory markers like the neutrophil-to-lymphocyte ratio (NLR) and lymphocyte-to-monocyte ratio (LMR) are elevated in both complicated and uncomplicated malaria cases [13]. It is against this background that this study sought to evaluate the association and variations of haematological and inflammatory biomarkers with malaria at the Ghana Ports and Harbours Authority clinic in Ghana.

Methods

Study design

This study was an analytical cross-sectional comparative study which recruited *P. falciparum* malaria and non-malaria participants from January 2018 to May 2018 at the Ghana Ports and Harbours Authority (G.P.H.A) Clinic.

Study site

This study took place at the medical laboratory of the G.P.H.A Clinic. The clinic is a ten-minute drive from the G.P.H.A, Port of Tema and a 5-minute drive from the staff quarters at community 5, Tema. The study area is in the coastal zone located at the heart of Community 2, Tema, Greater Accra Region.

Study participants

The study participants were patients infected with malaria (*P. falciparum* species*)* and non-malaria-infected subjects.

Sample size

The malaria patient population in Ghana, according to the WHO World Malaria Statistics 2016, was estimated to be 8,453,557 as of 2014, including children and adults [14].

The sample size required for the study was calculated based on Solvin's formula [15] below:

$$n = \frac{N}{1 + N(e^2)}$$

[15] where n = sample size.
e = allowable error (10%).
N = estimated malaria patient population (8,453,557).

$n = 8{,}453{,}557/(1 + 8{,}453{,}557 \times 10\%^2)$.

$n = 100$.

100 participants each were therefore recruited for the study making a total of 200.

Inclusion and exclusion criteria

Participants aged 70 years or younger with a confirmed malaria diagnosis based on microscopy, as well as those without malaria confirmed by microscopy, were included in the study. Participants who received anti-malarial treatment in the past 2 weeks, had co-infections (e.g., typhoid, dengue, HIV, tuberculosis), were pregnant, had haematological disorders (e.g., sickle cell disease, leukaemia), or had a blood transfusion in the past 3 months were excluded.

Blood sample collection and laboratory analysis

Blood sample collection

Peripheral venous blood samples obtained from participants enrolled on the malaria study were collected into 5 mL ethylene-diaminetetracetic acid (EDTA) tubes. The ideal vein was located, and the appropriate site was disinfected with 70% alcohol before samples were collected. The samples were labelled with the participant's identification numbers.

Blood smear preparation and staining

Two blood smears (thick and thin films) were prepared on the same slide using 6µL and 2µL of blood, respectively. The thin film was spread at a 30° angle to form a 40 mm-long smear, while the thick film was spread concentrically over a 15 × 15 mm area. After labelling, slides were air-dried before staining. A 1:10 dilution of Giemsa in phosphate buffer (pH 7.2) was applied for 10 min. Thin smears were fixed in methanol, whereas thick smears remained unfixed to allow red blood cell lysis for malaria parasite detection. Stained slides were rinsed with buffer, air-dried, and examined microscopically. The standard WHO procedure for Giemsa staining and reading of blood smears was strictly followed [16].

Examination of blood smears

Each slide was initially screened at 10X and 40X to identify appropriate fields for detailed examination, then examined under 100X oil immersion following a standardized pattern (starting at the top left) to detect malaria parasites, species, and pigments. At least 100 high-power fields were inspected; if no parasites were observed after this initial screening, the thick smear was declared "no malaria parasite seen." For parasite detection, a multiple tally counter was used to simultaneously count asexual parasites (gametocytes were excluded) and white blood cells. Counting stopped once either ≥ 100 parasites were found in 200 WBCs or ≤ 99 parasites were observed in 500 WBCs, with results recorded accordingly. The thin film was subsequently examined to confirm species identification, and a slide was declared positive only when two independent microscopists concurred.

Haematological biomarkers analysis

The full blood counts (FBC) analysis was performed to measure biomarkers such as red blood cell (RBC), white blood cell (WBC), haemoglobin (Hb), platelets (PLT), haematocrit (HCT), monocytes, lymphocytes, eosinophils, basophils, mean platelets value (MPV), mean cell volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC), using the Sysmex XS-1000*i* Automated Haematological Analyzer for each participant's sample. Internal quality controls (QA) and the scheduled external quality assessment plans were adhered to as a quality measure.

Malaria parasite grading

The parasite density was calculated using the WHO parasite density formula [16].

$$\text{Parasites/uL of blood} = \frac{Number\ of\ parasites\ counted}{No.of\ white\ cells\ counted} \times actual\ white\ blood\ cells/\mu L$$

Using standard microscopy techniques, parasite density was initially quantified as the number of parasites per microlitre (p/µL) of blood. These continuous counts were subsequently grouped into an ordinal scoring system to simplify interpretation and reduce variability due to extreme values based on a study by Saksabre et al. [17]. The categorization was as follows:

Low parasitaemia: < 1,000 p/µL.

Moderate parasitaemia: 1,000–9,999 p/µL.

High parasitaemia: 10,000–99,999 p/µL.

Severe parasitaemia: > 100,000 p/µL.

Definition of operational terms

Leucopenia is defined as a decrease in the total number of white blood cells (WBCs) in the blood, typically below 4000 cells per microlitre [18]. Lymphopenia refers to a reduction in the absolute lymphocyte count, usually defined as fewer than 1000 lymphocytes per microlitre [19]. Thrombocytopenia is defined as a platelet count of less than 150,000 per microlitre of blood [20].

Platelet-lymphocyte ratio was calculated as absolute platelet value divided by absolute lymphocyte value [21], neutrophil–lymphocyte ratio was calculated as absolute neutrophil count divided by absolute lymphocyte count [22]. Lymphocyte-monocyte ratio was calculated as absolute lymphocyte count divided by absolute monocyte

value [23]. Platelet-monocyte ratio was calculated as absolute platelet count divided by absolute monocyte value [24]. Neutrophil-monocyte ratio was calculated as absolute neutrophil count divided by absolute monocyte count [25]. Systemic inflammatory response index was calculated as the product of the absolute neutrophil count and monocyte count/lymphocyte count [26]. Systemic Immune-Inflammatory Index was calculated as platelet count × neutrophil/lymphocyte ratio [27]. Aggregated index of systemic inflammation was calculated as the product of neutrophil count, platelet count and monocyte/lymphocyte [22].

Data analysis

All data were entered, cleaned, and coded in Microsoft Excel 2021, then imported into STATA 15.0 and R version 4.4.2 for analysis. Categorical variables are presented as percentages, while continuous variables that violated normality assumptions based on the Shapiro–Wilk test are summarized as medians with interquartile ranges (25th–75th percentiles). The Mann–Whitney U test was used to assess differences between two groups, while the Kruskal–Wallis's test, followed by Bonferroni-adjusted post hoc comparisons, was used for comparisons across three or more groups. To determine the factors independently associated with *P. falciparum* infection, two adjusted logistic regression models were developed. Model 1 included sex as a covariate based on its established biological relevance and observed variation in infection rates between males and females [28]. Model 2 introduced age group as an additional covariate to evaluate its potential confounding effect, given age's known influence on both malaria susceptibility and haematological indices [29]. All measured haematological and inflammatory biomarkers were retained in both models to capture the full spectrum of host response and to account for their potentially overlapping and interrelated effects, thereby minimizing omitted-variable bias and allowing the independent contribution of each biomarker to be assessed. Adjusted odds ratios with 95% confidence intervals are reported for all models. Statistical significance was set at $p < 0.05$. The discriminative ability of the full model was evaluated using receiver operating characteristic (ROC) analysis in R, with the area under the curve (AUC), sensitivity, and specificity reported.

Ethical consideration

Ethical approval was obtained from the Ethics and Protocol Review Committee of the School of Biomedical and Allied Health Sciences, University of Ghana, with reference number [SBAHS-MLS/10516299/SA/2017–2018]. Written informed consents were obtained from participants above 18 years for the studies. Assent forms for minors were also obtained from guardians and parents. The nature, aims, objectives and significance of the study were explained to the participants. Informed permission was sought form the Laboratory Manager of G.P.H.A. Clinic before the study was carried out.

Results

Sociodemographic characteristics of *P. falciparum* malaria and non-malaria groups

The median age of participants was 34 years, ranging from 4 to 69 years. The most represented age group was 26–35 years (25.5%), followed by 36–45 years (24.5%). Males formed the majority of the study population (61.5%). *Plasmodium falciparum* malaria infection was more common among males (61.8%) than females (31.2%). Across age groups, the highest proportion of malaria was observed among participants aged ≤ 15 years (69.6%), followed by those aged 16–25 years (54.8%) and 46–55 years (50.0%). There was a significant association between sex and *P. falciparum* malaria infection ($\chi^2 = 17.67$, $p < 0.001$) (Table 1).

Variations in haematological biomarkers across the *P. falciparum* malaria and non-malaria groups

Table 2 presents the variations in haematological biomarkers between *P. falciparum* malaria and non-malaria groups. Significant differences were observed in several biomarkers, with malaria patients showing lower median white blood cell counts (4.88×10^9/L vs. 5.84×10^9/L, $p < 0.001$) and platelet counts (117.50×10^9/L vs. 224.50×10^9/L, $p < 0.001$) compared to non-malaria individuals. Lymphocyte counts were significantly lower in malaria patients (0.91×10^9/L vs. 2.10×10^9/L, $p < 0.001$), whereas neutrophil-to-lymphocyte ratio (NLR) (3.49 vs. 1.43, $p < 0.001$) and systemic inflammatory response index (SIRI) (1.83 vs. 0.73, $p < 0.001$) were significantly higher. Additionally, platelet-monocyte ratio (PMR) was markedly reduced in malaria patients (207.45 vs. 457.78, $p < 0.001$). Eosinophil and basophil counts were also significantly lower in the malaria group ($p < 0.001$).

Variations in haematological biomarkers across various densities of *P. falciparum* malaria parasite

Table 3 below shows variations in haematological biomarkers across different *P. falciparum* malaria parasite densities. Although most biomarkers did not show statistically significant differences, haemoglobin levels were notably lower in participants who had moderate parasitaemia compared to patients who had low parasitaemia ($p = 0.026$). Additionally, the lymphocyte-monocyte ratio was significantly higher in patients who had severe parasitaemia than in low and moderate parasitaemia patients ($p = 0.003$). Other inflammatory and immune indices,

Table 1 demographic characteristics of study participants, stratified by *Plasmodium falciparum* malaria infection status

Variable	Total n (%)	*P. falciparum* malaria n (%)	Non-malaria n (%)	X^2 (p-value)
Overall	200	100	100	
Age group (years)				
Median (minimum–maximum)	34 [4–69]	33 [4–69]	37 [6–62]	
≤ 15	23 (11.5)	16 (69.6)	7 (30.4)	5.14 (0.399)
16–25	31 (15.5)	17 (54.8)	14 (45.2)	
26–35	51 (25.5)	22 (43.1)	29 (56.9)	
36–45	49 (24.5)	23 (46.9)	26 (53.0)	
46–55	24 (12.0)	12 (50.0)	12 (50.0)	
55–70	22 (11.0)	10 (45.5)	12 (54.5)	
Sex				
Female	77 (38.5)	24 (31.2)	53 (68.8)	17.67 (< 0.001)
Male	123 (61.5)	76 (61.8)	47 (32.2)	

Table 2 Variations in haematological biomarkers across the *P. falciparum* malaria and non-malaria groups

Laboratory biomarkers	Total median[25th–75th]	*P. falciparum* malaria median[25th–75th]	Non-malaria median[25th–75th]	P-value
Total	200	100	100	
Haematological biomarkers				
White blood cell (10^9/L)	5.52 [4.24–6.56]	4.88 [3.88–6.11]	5.84 [5.15–7.13]	< 0.001
Red blood cell (10^{12}/L)	4.64 [4.24–5.05]	4.55 [4.23–4.55]	4.64 [4.22–5.03]	0.392
Haemoglobin (g/dL)	13.34 [12.41–14.95]	13.10 [11.73–13	13.45 [12.22–14.60]	0.156
Haematocrit (%)	38.04 [34.93–40.70]	37.50 [34.08–40.30]	38.60 [35.40–41.20]	0.076
Mean cell volume (fL)	82.44 [78.54–85.88]	81.50 [76.78–85.38]	83.15 [79.90–85.97]	0.019
Mean corpuscular haemoglobin (pg)	28.85 [27.42–29.92]	28.60 [26.75–30.03]	29.00 [27.75–29.98]	0.081
Mean corpuscular haemoglobin concentration (g/dL)	34.91 [34.20–35.84]	34.90 [34.23–35.95]	35.00 [34.20–35.70]	0.396
Platelets (10^9/L)	189.02 [117.0–232.0]	117.50 [91.0–171.00]	224.50 [199.25–279.00]	< 0.001
Neutrophil (#)	3.02 [2.31–44.34]	3.01 [2.13–4.21]	2.98 [2.33–4.29]	0.725
Lymphocytes (#)	1.41 [0.82–2.32]	0.91 [0.58–1.41]	2.10 [1.52–2.53]	< 0.001
Monocytes (#)	0.52 [0.41–0.72]	0.59 [0.39–0.87]	0.53 [0.42–0.65]	0.121
Eosinophils (#)	0.05 [0.01–0.12]	0.02 [0.01–0.05]	0.09 [0.05–0.16]	< 0.001
Basophils (#)	0.02 [0.01–0.03]	0.01 [0.01–0.02]	0.02 [0.01–0.03]	< 0.001
Mean platelets volume (fL)	10.20 [9.60–10.20]	10.10 [9.50–10.70]	10.30 [9.60–11.00]	0.403
Inflammatory biomarkers				
Platelet-lymphocyte ratio	126.21 [91.07–174.87]	136.29 [90.49–192.85]	116.07 [91.65–116.07]	0.061
Neutrophil–lymphocyte ratio	2.12 [1.20–4.20]	3.49 [1.97–5.74]	1.43 [1.07–2.43]	< 0.001
Lymphocyte-monocyte ratio	2.52 [1.43–2.52]	1.58 [1.11–2.48]	3.88 [2.78–4.90]	< 0.001
Platelet-monocyte ratio	354.34 [192.40–504.27]	207.45 [124.29–355.90]	457.78 [344.62–571.12)	< 0.001
Neutrophil-monocyte ratio	5.16 [4.00–7.79]	4.95 [3.21–8.39]	5.80 [4.60–7.40]	0.056
Systemic immune-inflammatory Index	387.43 [227.93–636.46]	403.23 [234.08–629.39]	356.31 [200.84–663.99]	0.325
Systemic inflammatory response index	1.17 [0.65–2.37]	1.83 [1.10–3.51]	0.73 [0.52–1.58]	< 0.001
Aggregated index of systemic inflammation	190.92 [123.60–332.01]	225.50 [125.22–381.85]	174.68 [112.40–317.00]	0.349

P-value is significant at $P < 0.05$

such as the systemic immune-inflammatory index and neutrophil–lymphocyte ratio, showed trends across parasite densities but did not reach statistical significance.

Binary logistic regression of sociodemographic factors and haematological biomarkers associated with *P. falciparum* malaria

Table 3 Variations in haematological biomarkers across various densities of *P. falciparum* malaria parasite

***P. falciparum* Malaria parasitaemia**						
	Low (A)	**Moderate (B)**	**High (C)**	**Severe (D)**	**P-value**	**Post-Hoc**
Laboratory biomarkers	Median [25th–75th]	Median [25th–75th]	Median [25th–75th]	Median [25th–75th]		
Total	39	33	20	8		
Haematological biomarkers						
White blood cell (10^9/L)	5.14 [4.18–6.37]	4.28 [3.65–5.94]	4.47 [3.88–6.22]	4.69 [4.47–5.37]	0.666	–
Red blood cell (10^{12}/L)	4.75 [4.40–5.05]	4.37 [4.08–4.89]	4.43 [4.08–4.83]	4.43 [4.08–4.83]	0.116	–
Haemoglobin (g/dL)	13.80 [12.60–14.9]	12.80 [11.15–13.80]	12.5 [11.23–13.70]	13.35 [12.18–14.88]	0.026	A&B
Haematocrit (%)	38.50 [35.60–41.5]	36.80 [31.80–39.40]	36.10 [31.90–38.53]	38.10 [34.50–41.45]	0.069	–
Mean cell volume (fL)	82.00 [75.90–85.30]	79.50 [76.90–85.45]	81.40 [76.60–85.63]	81.30 [77.28–89.18]	0.839	–
Mean corpuscular haemoglobin (pg)	28.80 [27.40–30.40]	27.90 [26.40–29.35]	28.60 [26.33–30.33]	28.10 [25.63–32.35]	0.786	–
Mean corpuscular haemoglobin concentration (g/dL)	35.10 [34.40–36.50]	34.70 [33.85–35.25]	34.90 [34.20–35.90]	34.55 [34.40–36.08]	0.251	–
Platelets (10^9/L)	120 [88.00–171.00]	113.00 [87.50–183.50]	117.50 [92.75–186.25]	124.50 [112.00–148.75]	0.966	–
Neutrophil (#)	3.36 [2.47–4.75]	2.64 [2.05–4.03]	2.93 [1.76–4.51]	3.72 [2.88–4.24]	0.364	–
Lymphocytes (#)	0.89 [0.54–1.29]	0..76 [0.59–1.39]	1.32 [0.70–1.73]	1.81 [0.58–1.53]	0.466	–
Monocytes (#)	0.64 [0.50–0.87]	0.59 [0.37–1.01]	0.54 [0.33–0.81]	0.32 [0.23–0.54]	0.225	–
Eosinophils (#)	0.20 [0.01–0.01]	0.20 [0.01–0.04]	0.03 [0.01–0.08]	0.01 [0.00–0.01]	0.178	–
Basophils (#)	0.01 [0.01–0.02]	0.01 [0.01–0.02]	0.02 [0.01–0.02]	0.01 [0.01–0.02]	0.213	–
Mean platelets volume (fL)	10.00 [9.50–10.80]	10.10 [9.75–10.60]	10.20 [9.50–11.00]	9.90 [9.50–11.25]	0.718	–
Inflammatory biomarkers						
Platelet-lymphocyte ratio	141.94 [101.80–195.38]	134.78 [71.44–218.82]	121.51 [90.60–184.39]	165.41 [100.57–223.77]	0.593	–
Neutrophil–lymphocyte ratio	4.80 [2.41–6.50]	3.29 [1.76–4.53]	2.96 [1.31–5.61]	3.44 [2.53–5.41]	0.353	–
Lymphocyte-monocyte ratio	1.43 [1.00–1.94]	1.46 [1.13–2.55]	2.00 [1.21–2.50]	2.60 [1.30–3.71]	0.003	A&D, B&D
Platelet-monocyte ratio	176.25 [117.19–320.69]	224.39 [88.02–355.54]	218.61 [161.25–336.48]	408.62 [297.77–495.65]	0.296	–
Neutrophil-monocyte ratio	4.94 [3.86–7.79]	4.46 [2.69–8.35]	5.06 [2.82–9.55]	10.73 [5.11–16.71]	0.451	–
Systemic immune-inflammatory index	426.67 [289.30–602.90]	309.09 [204.89–579.38]	392.65 [233.41–656.37]	477.21 [358.21–904.21]	0.507	–
Systemic inflammatory response index	2.40 [1.32–4.36]	1.85 [0.95–2.89]	1.46 [1.09–2.32]	1.24 [1.09–2.99]	0.099	–
Aggregated index of systemic inflammation	311.64 [142.33–430.55]	182.49 [103.31–312.02]	186.96 [82.27–282.33]	176.40 [126.24–391.42]	0.323	–

P-value is significant at $P < 0.05$, Bonferroni was used as post hoc test to perform multiple comparison test

Table 4 below identified significant sociodemographic and haematological predictors of *P. falciparum* malaria. Age and sex were not significantly associated with malaria, but haematocrit ($p = 0.032$), platelet count ($p = 0.013$), mean platelet volume ($p = 0.003$), platelet-lymphocyte ratio ($p = 0.031$), and platelet-monocyte ratio ($p = 0.004$) were significant predictors in Model 2. Neutrophil count showed borderline significance in Model 1 ($p = 0.033$) but lost significance in Model 2 ($p = 0.061$). Model 1 had a lower Akaike Information Criterion (AIC = 116.46) compared to Model 2 (AIC = 122.04), suggesting that Model 1 provides a better fit. However, both models demonstrated high predictive accuracy, with Area Under Curve (AUC) values of 0.9744 and 0.9769, respectively. Given the lower AIC, Model 1 is preferred as it balances model complexity and goodness of fit.

Performance of binary logistic models by ROCs

In Fig. 1, both Model 1 and Model 2 demonstrated strong diagnostic accuracy, as indicated by their high AUC values (97.4% and 98.0%, respectively). Model 1 exhibits slightly higher specificity (93.9% vs. 91.9%), suggesting better ability to correctly identify true negatives. However, Model 2 has a marginally higher AUC, indicating slightly improved overall performance. Sensitivity remains the same for both models (89.0%), meaning they are equally effective at identifying true positives. Positive and Negative Predictive Values are also comparable, with Model 1 showing slightly better predictive reliability.

Table 4 Binary logistic regression of sociodemographic factors and haematological biomarkers associated with *P. falciparum* malaria

Variables	Model 1				Model 2			
	aOR	CI lower	CI upper	p-value	aOR	CI lower	CI upper	p-value
Age (years)								
≤15					1			
16–25					0.25	0.01	4.02	0.328
26–35					3.17	0.28	35.89	0.351
36–45					1.12	0.08	16.19	0.936
46–55					0.86	0.05	15.62	0.917
>55–70					2.14	0.11	40.49	0.612
Sex								
Female	1				1			
Male	1.41	0.24	8.28	0.701	1.56	0.22	11.21	0.656
Haematological biomarkers								
White blood cell (10^9/L)	1.95	0.50	7.71	0.339	1.48	0.29	7.67	0.638
Haematocrit (%)	0.80	0.64	0.99	0.038	0.77	0.60	0.97	0.032
Mean cell volume (fL)	1.06	0.86	1.31	0.597	1.11	0.89	1.39	0.353
Mean corpuscular haemoglobin (pg)	0.65	0.37	1.16	0.145	0.49	0.24	1.00	0.050
Platelets (10^9/L)	0.96	0.94	0.99	0.014	0.96	0.94	0.99	0.013
Neutrophil (#)	0.15	0.03	0.86	0.033	0.16	0.02	1.09	0.061
Eosinophils (#)	0.15	0.00	91.65	0.565	0.15	0.00	164.56	0.594
Mean platelets volume (fL)	0.33	0.16	0.69	0.003	0.30	0.14	0.67	0.003
Inflammatory biomarkers								
Platelet-lymphocyte ratio	1.03	1.00	1.06	0.038	1.04	1.00	1.07	0.031
Neutrophil–lymphocyte ratio	1.66	0.50	5.53	0.406	1.48	0.44	4.94	0.523
Lymphocyte-monocyte ratio	1.30	0.94	1.78	0.108	1.26	0.89	1.77	0.188
Platelet-monocyte ratio	0.99	0.98	0.99	0.007	0.98	0.97	0.99	0.004
Neutrophil-monocyte ratio	1.17	0.73	1.89	0.509	1.34	0.78	2.29	0.287
Systemic immune-inflammatory index	1.00	0.99	1.00	0.433	1.00	0.99	1.00	0.497
Aggregated index of systemic inflammation	0.99	0.99	1.00	0.652	0.99	0.99	1.00	0.548
Akaike information criteria (AIC)	116.4568				122.0411			
Model significance	<0.001				<0.001			

aOR;Adjusted Odds Ratio, CI Confidence interval-value was statistically significant at P < 0.005

Overall, while Model 2 has a higher AUC, Model 1 offers better specificity.

Discussion

This study revealed significant haematological alterations in *P. falciparum* malaria patients, with pronounced changes in leukocyte and platelet parameters. The significant leucopenia observed in these patients (4.88 vs. 5.84×10^9/L, $p < 0.001$) contrasts notably with findings from Antwi-Baffour et al. [30], who reported a positive correlation between parasite density and total WBC count ($r = 0.300$, $p = 0.004$). This divergence may reflect variations in infection stage or immune response phases. Our findings align more closely with Ogbonna et al. [31], who reported decreased WBC counts in *P. falciparum*-infected children, suggesting bone marrow suppression and peripheral sequestration of leukocytes. Additionally, Sakzabre and colleagues [17] similarly, documented reduced total WBC counts among *P. falciparum*–infected adults in the Volta Region of Ghana. While Adamu & Jigam [32] also observed decreased white blood cell counts in *P. falciparum* malaria patients; their results did not reach statistical significance, highlighting the variability in host responses to infection.

The marked lymphopenia in this study (0.91 vs. 2.10×10^9/L, $p < 0.001$) presents an interesting contrast with Adamu & Jigam [32] report of increased lymphocytes in malaria patients. However, findings from this study strongly correlate with a study by Ayyadevara [33], who documented significant lymphocyte reduction ($27.05 \pm 10.1\%$ vs. $38.1 \pm 0.87\%$, $p < 0.001$) in comparable cases. This observation is further supported by Elkhalifa et al. [34], who reported significantly lower lymphocyte percentages in malaria patients. Roy *et al*

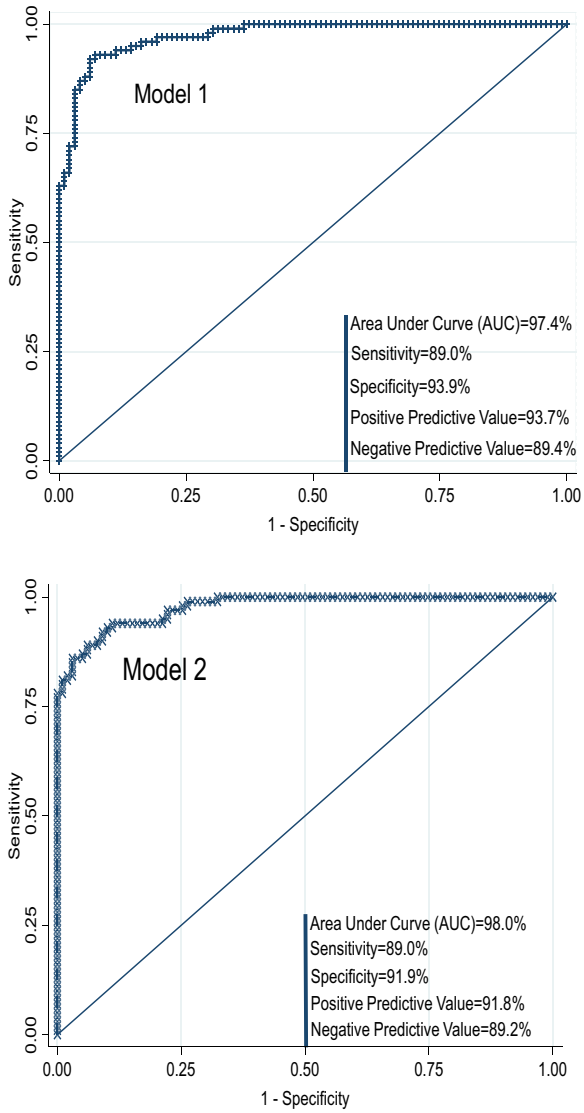

Fig. 1 Performance of binary logistic models by ROCs

[8]. also reported significant lymphocyte depletion in an Indian hospital–based cohort of acute *P. falciparum* malaria, underscoring a consistent global pattern of lymphopenia in *P. falciparum* infection. The consistency of lymphopenia across these studies suggests that lymphocyte redistribution to peripheral tissues, sequestration, and potential apoptosis may be key features of acute infection. The significant reduction in eosinophils and basophils ($p < 0.001$ for both) in this study partially aligns with Adamu & Jigam [32], who observed decreased eosinophils but reported increased basophils. These variations may reflect the complex, time-dependent nature of leukocyte responses to malarial infection.

While this study did not demonstrate significant differences in overall haemoglobin levels between groups (13.10 g/dL vs. 13.45 g/dL, $p = 0.156$), this study observed significant variations across parasite densities, particularly lower haemoglobin in moderate versus low parasitaemia ($p = 0.026$). This finding aligns with Punnath et al. [35], who reported lower haemoglobin levels with increasing parasitaemia in *P. falciparum* infections. The absence of overall significant haemoglobin differences contrasts with findings from both Ayyadevara [33] and Hyder et al. [36], who reported significant reductions in malaria patients, as well as more recent work by Alanzi et al. [37]. These variations may reflect differences in study populations or pre-existing anaemia prevalence.

The most striking finding in this study was the significant thrombocytopenia in *P. falciparum* malaria patients (117.50 vs. 224.50×10^9/L, $p < 0.001$). This observation is remarkably consistent with existing literature. Ayyadevara [33] reported significantly reduced platelets in akin cases (1.37 ± 0.42 vs. $3.13 \pm 0.52 \times 10^9$/L, $p < 0.001$), while Alanzi et al. [37] reported substantially lower platelet counts in similar patients ($140.5 \pm 108.2 \times 10^9$/L vs. $282.76 \pm 68.16 \times 10^9$/L), and Hussain et al. [38] found thrombocytopenia in 71% of malaria patients ($p = 0.0002$). Gebreweld *et al* [9]. found that platelet counts $< 150 \times 10^9$/L had 85% sensitivity and 90% specificity for malaria in a similar acute-febrile-illness cohort, further supporting the diagnostic utility of thrombocytopenia. The relationship between platelet count and parasite burden was further elucidated by Khan et al. [39], who demonstrated an inverse relationship between platelet count and parasite index ($127.44 \pm 90.81 \times 10^9$/L in low PI vs. $61.20 \pm 31.09 \times 10^9$/L in high PI, $p = 0.000$). Given the consistent pattern of thrombocytopenia in *P. falciparum* infections, this parameter may serve as a rapid, low-cost adjunctive marker in malaria-endemic regions, especially where microscopy or rapid diagnostic tests are limited, thus aiding early suspicion, triaging, and timely intervention.

The analysis of inflammatory indices in this current study revealed significantly elevated neutrophil-to-lymphocyte ratio (NLR) (3.49 vs. 1.43, $p < 0.001$) and systemic inflammatory response index (SIRI) (1.83 vs. 0.73, $p < 0.001$). Ayyadevara [33] similarly documented elevated neutrophils (65.02 ± 8.98 vs. $54.7 \pm 3.1\%$, $p < 0.001$) with concurrent lymphopenia. These support the potential use of these indices in characterizing acute inflammatory responses in malaria.

Meanwhile, the significantly reduced platelet-monocyte ratio (PMR) in the malaria patients included in this study (207.45 vs. 457.78, $p < 0.001$) represents a novel finding. This parameter emerged as a significant predictor in the regression models (aOR = 0.98, 95% CI 0.97–0.99,

p = 0.004), suggesting potential utility in malaria diagnosis or prediction. Additionally, the observed association between the lymphocyte-monocyte ratio and severe parasitaemia (p = 0.003) may indicate a threshold effect, whereby increasing parasite density triggers distinct immunological responses.

The regression analysis identified multiple significant predictors of malaria, including haematocrit (aOR = 0.77, 95% CI 0.60–0.97, p = 0.032), platelet count (p = 0.013), and various platelet-related ratios (p < 0.031). This multi-parameter approach builds upon work by Mutala et al. [40], who identified haemoglobin and plateletcrit as significant predictors, and advances beyond Ullah et al. [41], who reported thrombocytopenia in 54.4% of malaria patients without quantifying diagnostic accuracy. The exceptional predictive accuracy of our models (AUC > 0.97) suggests that combining these parameters may enhance diagnostic efficiency, particularly in resource-limited settings where microscopy expertise may be limited, as proposed by Elkhalifa et al. [34].

These findings collectively suggest that readily available haematological parameters, particularly platelet-related indices and inflammatory markers, may serve as valuable adjunctive tools for *P. falciparum* malaria diagnosis. The association between these parameters and malaria, coupled with their widespread availability, indicates their potential utility in resource-limited settings.

This study had certain limitations. As this research focused exclusively on *P. falciparum*, which is endemic to Ghana, the findings may have limited applicability to regions with different *Plasmodium* species distributions. Although careful screening protocols were implemented to exclude participants with comorbidities, the possibility of asymptomatic conditions influencing haematological parameters cannot be eliminated. Additionally, the recruitment from a single clinical setting in Ghana may affect generalizability to other geographical regions with different malaria transmission intensities, seasonal patterns, and population genetics. These considerations, however, do not diminish the clinical significance of the findings in this current study, particularly regarding the potential integration of routine haematological parameters into malaria diagnostic algorithms within similar endemic settings.

Conclusion

This study demonstrates significant variations in haematological and inflammatory biomarkers between *P. falciparum* malaria and non-malaria patients. The findings of this study reveal distinct patterns of alterations, particularly in white blood cell parameters and platelet indices. The significantly lower lymphocyte counts and marked thrombocytopenia in *P. falciparum* malaria patients reflect the profound impact of malarial infection on these cellular components. The elevated inflammatory markers, notably the neutrophil-to-lymphocyte ratio and systemic inflammatory response index, indicate a robust inflammatory response to infection. These alterations showed varying relationships with parasite density, particularly evident in the significant differences in haemoglobin levels between moderate and low parasitaemia groups. The consistent pattern of reduced platelet-monocyte ratio adds to our understanding of cellular interactions during *P. falciparum* malaria infection.

Recommendations

Based on these findings, it is recommended that platelet count and inflammatory indices should be incorporated into routine malaria screening protocols, particularly in resource-limited settings where microscopy expertise may be scarce. Healthcare facilities should consider implementing standardized cut-off values for thrombocytopenia and NLR as supplementary diagnostic indicators. Further research should investigate the temporal dynamics of the platelet-monocyte ratio during different stages of infection and its potential role in monitoring treatment response.

Abbreviations

NLR	Neutrophil-monocyte ratio
PLR	Platelets-lymphocytes ratio
PNR	Platelets-monocytes ratio
MCV	Mean corpuscular volume
MCH	Mean corpuscular haemoglobin
SIRI	Systemic immune-inflammatory index
SIII	Systemic immune-inflammatory index
AISI	Aggregated index of systemic inflammation
LMR	Lymphocyte-monocyte ratio
NMR	Neutrophil-monocyte ratio
WHO	World Health Organization
EDTA	Ethylene-diaminetetracetic acid

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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