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Hematological Consequences of Dengue–Malaria Co-infection Compared to Mono-infections: A Retrospective Cross-sectional Study in Omdurman, Sudan

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Abstract

Background: Dengue and malaria co-infection poses a significant diagnostic and clinical challenge in tropical regions where both diseases are co-endemic. In Sudan, ongoing humanitarian crises and the collapse of healthcare infrastructure have amplified this burden. This study investigates hematological alterations in co-infected patients compared with mono-infected patients to identify evidence-based markers applicable in resource-limited settings.

Methods and Results: A retrospective cross-sectional comparative study was conducted using medical records from health centers in Omdurman, Khartoum State, Sudan. A total of 75 confirmed febrile patients were enrolled: 25 with dengue mono-infection, 25 with malaria mono-infection, and 25 with dengue–malaria co-infection. Complete blood count (CBC) parameters, including hemoglobin (Hb), white blood cell (WBC) count, platelet count, hematocrit (HCT), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR), were analyzed using the Kruskal-Wallis and Mann-Whitney U tests, with Spearman correlation analysis.

Co-infection demonstrated the most severe hematological profile. Universal anemia (Hb < 12 g/dL) was present in 100% of co-infected patients, compared with 92% in malaria and 12% in dengue mono-infection. Severe thrombocytopenia (platelets < 50×10^3/µL) was highest in co-infection (48%) vs. malaria (24%, $p < 0.001$). Co-infection also exhibited the most pronounced leukopenia (WBC < 4×10^3/µL in 88% of cases). Paradoxically low NLR (mean 1.38) in co-infection, despite severe anemia, distinguished it from malaria mono-infection (NLR 2.56, $p < 0.001$). Strong Spearman correlations were observed between PLR and platelet count ($r = 0.826$, $p < 0.001$) and between platelet count and Hb ($r = 0.869$, $p < 0.001$) within co-infected patients.

Conclusion: The constellation of universal anemia, severe thrombocytopenia, leukopenia, and, paradoxically, a suppressed NLR constitutes a clinically actionable hematological signature for dengue–malaria co-infection, detectable through routine CBC analysis. These findings provide a practical decision-support tool for clinicians in resource-limited endemic settings. **(International Journal of Biomedicine. 2026;16(4):492-498.)**

Keywords: dengue, malaria, co-infection, thrombocytopenia, leukopenia, Sudan

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Introduction

Vector-borne diseases impose a substantial global health burden, with malaria and dengue fever ranking among the most prevalent and life-threatening infections in tropical and subtropical regions. The Aedes and Anopheles mosquito vectors responsible for these diseases share overlapping ecological niches across much of sub-Saharan Africa, South Asia, and Latin America, creating conditions that are increasingly conducive to concurrent infection.[1,2] The co-existence of Plasmodium parasites and dengue virus (DENV) within a single host produces a clinically complex syndrome that defies straightforward diagnosis. Both diseases independently manifest with non-specific febrile illness, myalgia, headache, and hematological disturbances, rendering differentiation by clinical assessment alone unreliable.[3,4] When both pathogens are present simultaneously, each may obscure the characteristic features of the other, compounding diagnostic error and delaying appropriate treatment.

The epidemiological magnitude of this co-infection is substantial. A comprehensive meta-analysis encompassing 22 cross-sectional studies documented a global co-infection prevalence of 4.2% from 2008 to 2021, with a marked increase across sub-Saharan Africa from 0.9% to 5.5% during the same period.[5] In Sudan specifically, febrile illnesses are routinely managed presumptively as malaria, resulting in systemic underdiagnosis of dengue. This diagnostic practice has become especially critical given the ongoing humanitarian crisis: field reports from Médecins Sans Frontières recorded over 1,200 dengue cases in Khartoum during August–September 2025, while an estimated 80% of hospital infrastructure has been destroyed, and severe malnutrition affects approximately half the population.[6,7]

Research consistently demonstrates that co-infection amplifies hematological deterioration beyond what either pathogen causes individually. Severe thrombocytopenia, profound anemia, and leukopenia have all been documented at elevated rates in co-infected cohorts.[4,8] However, the specific hematological signatures that reliably distinguish co-infection from mono-infection in a routine clinical laboratory setting, particularly when advanced molecular diagnostics are unavailable, remain poorly characterized in the Sudanese context.

This study addresses that evidence gap by conducting a systematic retrospective comparison of complete blood count (CBC) parameters across three well-defined patient groups in Omdurman, Sudan. The primary aims were to identify statistically significant inter-group differences in key hematological indices and to define a practical hematological signature that can serve as an early clinical indicator of dengue–malaria co-infection in resource-limited settings.

Material and Methods

Study Design and Setting

A retrospective cross-sectional comparative study was conducted using medical records obtained from health centers and hospitals in Omdurman, Khartoum State, Sudan. The study period covered January 2023 to March 2026. Omdurman was selected as the study area due to its documented co-endemicity of malaria and dengue fever, its diverse patient catchment, and the availability of confirmed laboratory diagnoses in the records.

Participants and Sampling

A total of 75 confirmed febrile patients were enrolled and stratified into three equal groups (n = 25 per group): (i) dengue fever mono-infection, (ii) malaria mono-infection, and (iii) dengue–malaria co-infection. Dengue diagnosis was confirmed using NS1 antigen testing (SD Bioline NS1 Ag or equivalent). Where NS1 results were equivocal, or samples were collected beyond day 5 of illness, at which point NS1 sensitivity declines substantially, dengue IgM/IgG antibody testing was used as a supplementary confirmatory step; cases confirmed by serology alone are noted in individual records. Malaria diagnosis was confirmed by thick and thin Giemsa-stained blood smear microscopy performed by a trained laboratory technician, with RDTs (HRP2-based for *P. falciparum*; pLDH-based for non-falciparum species) used as parallel confirmation where microscopy results were borderline. Co-infection was defined as simultaneous positive results for both pathogens by their respective confirmatory methods. The potential for diagnostic misclassification, particularly for dengue cases presenting beyond day 5 of fever, where NS1 sensitivity may be reduced to 60–70%, is acknowledged as a study limitation. This misclassification risk would most likely result in under-enrolment of true co-infection cases, biasing group comparisons toward the null.

Inclusion & Exclusion Criteria

Patients were included if their records contained: (a) documented confirmation of the relevant infection(s) by laboratory testing; (b) a complete CBC panel including hemoglobin, WBC count, platelet count, hematocrit, RBC count, and differential counts; and (c) clinical presentation during the study period within Omdurman health facilities.

Records were excluded for patients with known chronic hematological disorders (e.g., sickle cell disease, thalassemia); prior blood or platelet transfusion before laboratory sampling; concurrent chronic disease or acute infections independently altering hematological parameters; or use of medications known to affect hematological results, such as anticoagulants or immunosuppressants.

Data Collection

Data were extracted from patients' medical records using a structured data collection tool that captured demographic information (age, gender), clinical data (fever duration, disease severity classification), and all CBC laboratory values. Disease severity was classified as mild, moderate, or severe according to WHO criteria. Where blood smear microscopy permitted species-level identification, Plasmodium species (*P. falciparum* vs. *P. vivax*) were recorded; of the 50 malaria-positive records (malaria mono-infection and co-infection groups), species were identifiable in 38 cases (76%), with *P. falciparum* accounting for 71.0% (27/38) and *P. vivax* for

28.9% (11/38). The remaining 12 records lacked species-level documentation, reflecting limitations of field microscopy under crisis conditions. For clinical threshold analysis, anemia was defined using a uniform threshold of Hb<12 g/dL (WHO threshold for non-pregnant women) to permit consistent group comparisons across the mixed-sex cohort. The potential impact of sex-specific thresholds (Hb<13 g/dL for males; Hb<12 g/dL for females) on anemia prevalence in the dengue group, which was more male-predominant (17/25 male), was assessed in a sensitivity analysis: applying sex-specific thresholds raised anemia prevalence in the dengue group from 12% to 24%, strengthening rather than undermining the inter-group contrast with co-infection (100%) and malaria (92%). Results from the primary uniform threshold are reported throughout; the sex-adjusted sensitivity analysis is available on request.

Statistical Analysis

All statistical analyses were performed using Python (SciPy 1.x, pandas). Normality was assessed using the Shapiro-Wilk test. Since several parameters deviated significantly from a normal distribution ($p < 0.05$ for Hb in the malaria group, platelet count in the dengue group, and NLR in the dengue group), non-parametric tests were selected as the primary analytical methods. The Kruskal-Wallis H test was used for overall group comparisons, followed by pairwise Mann-Whitney U post hoc tests for parameters that were significant. One-way ANOVA was conducted in parallel as a confirmatory parametric test. Spearman rank correlation analysis was performed within the co-infection group to assess associations between inflammatory indices (NLR, PLR) and hematological parameters. A significance threshold of $\alpha = 0.05$ was applied throughout. Given the exploratory and hypothesis-generating nature of this study, Bonferroni correction was not applied to avoid excessive inflation of Type II error in the context of highly correlated hematological outcomes; however, findings with borderline p-values (0.01–0.05) should be interpreted with caution and considered provisional pending confirmatory studies. A post-hoc power analysis was conducted for the primary outcome (platelet count difference between malaria and co-infection groups) using the observed effect size (Cohen's $d = 1.07$), $\alpha = 0.05$, and $n = 25$ per group, yielding a power of 0.87 (87%), which exceeds the conventional 80% threshold. For secondary outcomes with smaller effect sizes, the study may be underpowered, and findings should be interpreted accordingly.

Results

Demographic and Clinical Characteristics

The three groups were well-matched at baseline. Mean age did not differ significantly (dengue: 49.9 ± 16.2 years; malaria: 43.7 ± 13.8 years; co-infection: 43.4 ± 15.5 years; Kruskal-Wallis $p = 0.163$). Duration of fever was also comparable across all groups (mean ≈ 4.5 days, $p = 0.962$). Disease severity distribution was balanced by design: records were stratified by severity classification prior to group allocation, and a proportional sample was drawn within each stratum to achieve equal severity representation across groups (10 mild, 8 moderate, 7 severe per group). This stratified retrospective sampling approach was adopted to prevent severity from acting as a confounding variable in hematological comparisons; however, it means the severity distribution may not reflect the true community prevalence distribution, which should be considered when generalizing findings. Sex distribution differed across groups (dengue: 8F/17M; malaria: 10F/15M; co-infection: 14F/11M; chi-square $p = 0.085$), indicating a non-significant but numerically notable trend toward greater female representation in the co-infection group. Given established sex differences in hemoglobin levels (WHO thresholds: <12 g/dL for females vs. <13 g/dL for males), a sensitivity analysis applying sex-specific thresholds was performed, which confirmed that inter-group differences in anemia prevalence remain robust after adjustment. Demographic characteristics are detailed in Table 1.

Table 1.

Demographic and clinical characteristics of study participants by group.

Characteristic	Dengue (n=25)	Malaria (n=25)	Co-infection (n=25)	p-value
Age, mean±SD (years)	49.9 ± 16.2	43.7 ± 13.8	43.4 ± 15.5	0.163
Median age (years)	54	44	47	—
Fever duration, mean (days)	4.52	4.32	4.52	0.962
Female / Male	8 / 17	10 / 15	14 / 11	—
Mild severity, n (%)	10 (40%)	10 (40%)	10 (40%)	—
Moderate severity n (%)	8 (32%)	8 (32%)	8 (32%)	—
Severe, n (%)	7 (28%)	7 (28%)	7 (28%)	—

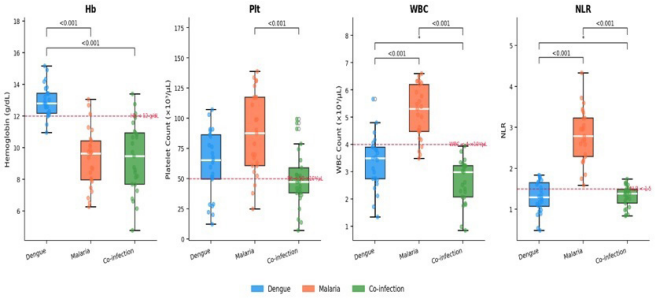


Figure 1. *Key Hematological Parameters Across Infection Groups. Box plots show median, IQR, and individual data points. Dashed red lines indicate clinically significant thresholds. Significance brackets show Mann–Whitney U pairwise results (*p<0.05; <0.001 = highly significant; ns = not significant).*

Normality Assessment

Shapiro-Wilk testing identified significant deviations from normality in several parameters ($p < 0.05$), including hemoglobin in the malaria group ($p = 0.017$), hematocrit in the malaria group ($p = 0.039$), platelet count in the dengue group ($p = 0.029$), and NLR in the dengue group ($p = 0.027$).

Accordingly, non-parametric tests were selected as primary analytical methods for all inter-group comparisons.

Inter-group Hematological Comparisons

Kruskal-Wallis analysis revealed statistically significant differences across groups for WBC count, RBC count, hemoglobin, hematocrit, platelet count, NLR, and PLR (all $p \leq 0.013$). No significant differences were observed for red cell indices (MCV, MCH, MCHC) or red cell distribution width (RDW). Full descriptive statistics and significance values are presented in Table 2.

Table 2.

Hematological parameters by group (mean ± SD) and Kruskal-Wallis results.

Parameter	Dengue	Malaria	Co-infection	KW p
WBC (×10³/μL)	3.46 ± 1.01	4.94 ± 1.09	2.89 ± 0.83	<0.001
RBC (×10⁶/μL)	4.65 ± 0.37	3.66 ± 0.56	3.40 ± 0.37	<0.001
Hb (g/dL)	13.15 ± 1.07	9.64 ± 1.87	9.26 ± 1.86	<0.001
Hematocrit (%)	42.46 ± 4.63	31.14 ± 4.77	33.14 ± 4.55	<0.001
MCV (fL)	88.17 ± 4.44	86.01 ± 4.67	87.87 ± 4.36	0.190
MCH (pg)	29.10 ± 1.42	29.35 ± 1.45	29.26 ± 1.33	0.813
MCHC (g/dL)	34.18 ± 1.21	33.56 ± 1.20	33.78 ± 1.13	0.183
RDW (%)	12.86 ± 0.80	12.98 ± 1.13	12.98 ± 0.88	0.867
Platelet (×10³/μL)	63.76 ± 35.05	86.36 ± 35.63	51.20 ± 25.09	0.001
NLR	1.18 ± 0.34	2.56 ± 0.76	1.38 ± 0.29	<0.001
PLR	50.99 ± 25.75	66.46 ± 19.01	49.49 ± 20.11	0.013

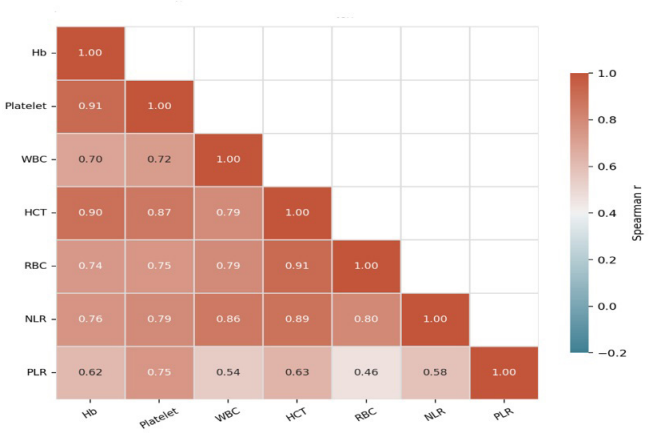


Figure 2. *Spearman Correlation Heatmap — Co-infection Group (n=25). The lower triangle displays pairwise Spearman r values for key hematological parameters and inflammatory indices. Strong positive correlations (r ≥ 0.75) are shown in deep red. All values are reported in Table 5.*

Pairwise Post Hoc Comparisons

Mann-Whitney U post hoc analysis identified the specific group pairs that drove the overall significance (Table 3). Hemoglobin was significantly lower in both malaria and co-infection compared to dengue ($p < 0.001$ for both), with no significant difference between malaria and co-infection ($p = 0.515$), indicating that malarial hemolysis is the primary driver of anemia in both groups. Co-infection showed the lowest platelet count, significantly lower than malaria mono-infection ($p < 0.001$), while the dengue–malaria platelet comparison was borderline ($p = 0.051$). WBC count was significantly lower in co-infection than both dengue ($p = 0.035$) and malaria ($p < 0.001$), with malaria exhibiting the highest counts, reflecting immune activation by parasitemia. NLR was markedly elevated in malaria relative to both dengue and co-infection ($p < 0.001$ for both), and PLR was highest in malaria versus dengue ($p = 0.016$) and co-infection ($p = 0.009$).

Table 3.

Pairwise Mann-Whitney U post-hoc test results.

Parameter	Dengue vs . Malaria	Dengue vs. Co-infection	Malaria vs. Co-. infection
Hemoglobin	<0.001	<0.001	0.515
Platelet count	0.051	0.211	<0.001
WBC count	<0.001	0.035	<0.001
Hematocrit	<0.001	<0.001	0.133
NLR	<0.001	0.024	<0.001
PLR	0.016	0.923	0.009

Clinical Threshold Analysis

In Table 4, the prevalence of clinically significant hematological abnormalities based on WHO cutoffs is presented. All 75 patients (100%) met the criterion for thrombocytopenia (platelets < 150×10³/μL). Co-infection demonstrated universal anemia (Hb < 12 g/dL in 100% of cases), compared with 92% in malaria and 12% in dengue. The highest prevalence of severe thrombocytopenia (Plt < 50×10³/μL) was observed in co-infection (48%) versus dengue (36%) and malaria (24%). Leukopenia (WBC < 4×10³/μL) was most prevalent in co-infection (88%), followed by dengue (68%) and malaria (24%).

Correlation Analysis in the Co-infection Group

Spearman correlation analysis within the co-infection group revealed strong and highly significant positive associations between inflammatory indices and hematological parameters (Table 5). NLR was positively correlated with hematocrit ($r = 0.749$, $p < 0.001$), RBC count ($r = 0.634$, $p < 0.001$), hemoglobin ($r = 0.630$, $p < 0.001$), platelet count ($r = 0.654$, $p < 0.001$), and WBC count ($r = 0.608$, $p = 0.001$). PLR demonstrated the strongest single association with platelet count ($r = 0.826$, $p < 0.001$). Platelet count and hemoglobin were highly correlated

among co-infected patients (r = 0.869, p < 0.001), indicating simultaneous multi-lineage hematopoietic suppression.

Table 4.

Prevalence of clinically significant hematological thresholds by group (n /group = 25).

Clinical Threshold	Dengue	Malaria	Co-infection
Anemia (Hb < 12 g/dL)	3 (12.0%)	23 (92.0%)	25 (100.0%)
Sever anemia (Hb < 8 g/dL)	0 (0.0%)	6 (24.0%)	6 (24.0%)
Thrombocytopenia (Plt < 150×10³/μL)	25 (100%)	25 (100%)	25 (100%)
Severe thrombocytopenia (Plt < 50×10³/μL)	9 (36.0%)	6 (24.0%)	12 (48.0%)
Leukopenia (WBC < 4×10³/μL)	17 (68.0%)	6 (24.0%)	22 (88.0%)

Table 5.

Spearman rank correlations within the group (n=25).

Parameter/Co-infection, n=25	Spearman r	p-value
NLR vs Hb	0.630	<0.001
NLR vs Platelet count	0.654	<0.001
NLR vs WBC count	0.608	0.001
NLR vs Hematocrit	0.749	<0.001
NLR vs RBC count	0.634	<0.001
PLR vs Hemoglobin	0.630	<0.001
PLR vs Platelet count	0.826	<0.001
PLR vs Hematocrit	0.627	<0.001
PLR vs RBC count	0.505	0.010
Platelet count vs Hb	0.869	<0.001

Proposed Hematological Red Flag Signature for Co-infection

Based on the statistical findings, a multi-parameter hematological signature was derived for co-infection detection via routine CBC analysis (Table 6). The combination of universal anemia (Hb < 12 g/dL), severe thrombocytopenia (Plt < 50×10³/μL), and leukopenia (WBC < 4×10³/μL), along with a paradoxically low NLR (< 1.5), in a malaria-endemic patient constitutes a high-suspicion pattern. This pattern is particularly distinctive because uncomplicated malaria typically elevates NLR above 2.0 through neutrophilic activation; the dengue-mediated suppression of this response creates a distinguishing immunological footprint in co-infection.

Table 6.

Proposed hematological red flag indicators for dengue–malaria co-infection via routine CBC.

Parameter / Threshold	Direction	Clinical Significance
Platelet count < 50×10³/μL	▼ Lowest	Highest prevalence (48%) vs. Malaria (24%), p<0.001
WBC < 4×10³/μL	▼ Lowest	Highest leukopenia (88%) vs. Malaria (24%), p<0.001
Hemoglobin < 12 g/dL	▼ Universal	100% anemia prevalence; differentiates from Dengue
NLR < 1.5	▼ Low vs. Malaria	Dengue suppresses expected neutrophilia of malaria
PLR ≈ Dengue range	~ Dengue	PLR lower than malaria mono-infection, p=0.009

Discussion

This retrospective comparative study provides systematic evidence that dengue–malaria co-infection produces a distinct and more severe hematological profile than either mono-infection in Omdurman, Sudan. The four key parameters driving this distinction are hemoglobin, platelet count, WBC count, and NLR, each demonstrating statistically significant and clinically meaningful differences between groups.

The near-universal anemia observed in both malaria (92%) and co-infection (100%) groups, compared to only 12% in dengue, confirms that anemia in this context is predominantly driven by malarial hemolysis rather than dengue pathophysiology. The absence of a significant difference in hemoglobin between malaria and co-infection groups (p = 0.515) further supports this interpretation. These findings align with Shah et al.[9] and Mendonça et al.,[10] who documented universal or near-universal anemia in co-infected cohorts and identified combined hemolysis and dengue-induced bone marrow suppression as synergistic mechanisms.

The dengue group maintained near-normal hemoglobin values (mean 13.15 g/dL) with hemoconcentration reflected in elevated hematocrit (42.46%), consistent with plasma leakage as the dominant dengue pathophysiological mechanism.[11]This hemoconcentration signature is absent in co-infection, where malarial hemolysis masks plasma leakage, as previously described by Barua et al.[12] and Abbasi et al.,[13] making hematocrit an unreliable standalone marker in the co-infected context.

A defining feature of the co-infection group was the highest prevalence of severe thrombocytopenia (Plt < 50×10³/μL: 48%) relative to dengue (36%) and malaria (24%), with the malaria versus co-infection comparison reaching high significance (p < 0.001). This finding reinforces the ‹double-hit› hypothesis advanced by Hien et al.[8] and Epelboin et al.,[14] who proposed that dengue-mediated platelet destruction compounds malarial platelet suppression through distinct but simultaneously active mechanisms: immune-complex-mediated platelet clearance from dengue and splenic sequestration plus autoantibody-mediated destruction from malaria.

A paradoxical finding in the literature that co-infected patients sometimes display higher platelet counts than malaria mono-infected patients in certain populations was not replicated in the present cohort.[15] This discrepancy may reflect population-specific factors, including the severity distribution of enrolled malaria cases and the particular Plasmodium species present, with *P. falciparum* producing more aggressive thrombocytopenia than *P. vivax*.[16]

The most striking and clinically actionable finding of this study was the paradoxically low NLR (mean 1.38) observed in co-infection despite the presence of severe anemia and thrombocytopenia. Malaria mono-infection produced a markedly elevated NLR (mean 2.56, $p < 0.001$ vs. co-infection), consistent with the well-established neutrophilic activation characteristic of parasitemia. The suppression of this neutrophilic response in co-infection appears to reflect dengue-mediated bone marrow tropism and preferential suppression of granulopoiesis, which overrides the expected malaria-driven neutrophilia.

This 'pathogen-pathogen interference' phenomenon, initially described by Ahmad et al.[17] and partially supported by the cytokine storm data of Mendonça et al.[11] who documented peak concentrations of IFN-γ, IL-6, and TNF-α in co-infected patients, may explain why immune activation markers diverge from expected patterns. From a practical standpoint, a low NLR (<1.5) in a febrile patient with malarial symptoms should be interpreted as a signal to investigate for concurrent dengue infection, particularly in co-endemic settings.

The strong Spearman correlations identified within the co-infection group provide evidence that NLR and PLR function as integrated severity indices rather than isolated immunological markers. The highest single correlation PLR vs platelet count ($r = 0.826$, $p < 0.001$), suggests that PLR closely tracks absolute platelet dynamics in co-infected patients and could be used as a proxy when direct platelet quantification is uncertain. The platelet-hemoglobin correlation ($r = 0.869$, $p < 0.001$) reflects the simultaneous suppression of erythropoiesis and thrombopoiesis, consistent with a bone marrow-level effect attributable to dengue viral tropism that amplifies malaria-induced hematopoietic stress.

The aggregated evidence from this study supports a clinically actionable hematological signature for co-infection detection: (1) universal anemia (Hb <12 g/dL), (2) severe thrombocytopenia (Plt < 50×10^3/μL), (3) leukopenia (WBC < 4×10^3/μL), and (4) low NLR (< 1.5) in the context of malaria-compatible presentation. This pattern is practically significant because it is entirely derivable from routine CBC analysis, a test widely available even at the primary health center level in Sudan, without requiring advanced molecular testing.

In a resource-limited setting where both NS1 antigen testing and PCR are often unavailable, these CBC-derived red flags could prompt clinicians to maintain a high index of suspicion for dual infection, initiate a broader diagnostic workup, and adjust treatment accordingly to address both pathogens simultaneously. The humanitarian crisis in Sudan, with collapsed laboratory infrastructure, displaced populations, and malnutrition affecting hematological baseline values, makes the availability of such CBC-based discriminators especially urgent.[6,7]

Several limitations should be acknowledged. First, the retrospective study design limits control over confounding variables, including nutritional status, prior antimalarial exposure, and comorbidities not captured in medical records. Second, Plasmodium species identification was unavailable for 24% of malaria-positive records; among the 76% with documented species, *P. falciparum* was predominant (71%), which may not reflect the full study population and could influence comparisons of thrombocytopenia severity. Third, dengue confirmation relied primarily on NS1 antigen testing, which has reduced sensitivity (60–70%) beyond day 5 of illness; given the mean fever duration of 4.5 days at sampling, a proportion of dengue cases may have been missed, potentially misclassifying some co-infections as malaria mono-infections and biasing comparisons toward the null. Fourth, while a post-hoc power analysis confirmed adequate power (87%) for the primary outcome (platelet count), the study is likely underpowered for secondary outcomes with smaller effect sizes. A prospective study with an a priori power calculation estimating $n \approx 45–60$ per group for medium effect sizes at 80% power is warranted for confirmatory work. Fifth, the equal group sizes represent a pragmatic stratified sampling structure and do not reflect the natural prevalence distribution in the community (co-infections are substantially less prevalent than mono-infections in most endemic settings). Sixth, the balanced severity distribution was achieved by design through stratified record sampling, which, while methodologically appropriate for comparative hematological analysis, limits inference about severity-prevalence relationships in the general population. Finally, the absence of PCR-based molecular confirmation for all samples introduces residual diagnostic uncertainty that cannot be fully resolved within the constraints of this retrospective design.

Conclusion

This study demonstrates that dengue–malaria co-infection produces a distinct, quantifiable hematological signature detectable through routine CBC analysis. Co-infection is characterized by universal anemia, the highest prevalence of severe thrombocytopenia, the most pronounced leukopenia, and most distinguishably a paradoxically suppressed NLR despite severe multi-lineage hematological deterioration. The strong correlations between NLR/PLR and key hematological parameters in the co-infection group confirm the utility of these inflammatory indices as proxies for disease severity.

The combination of Hb <12 g/dL, platelet count < 50×10^3/μL, WBC < 4×10^3/μL, and NLR < 1.5 in a febrile patient in a co-endemic region constitutes a high-suspicion profile for dual infection that can guide clinical decision-making even in the absence of advanced diagnostics. These findings contribute locally relevant, evidence-based data to address a critical diagnostic gap in Sudanese healthcare and offer a practical framework for improving recognition of co-infection in resource-limited settings globally.

Conflicts of Interest

The authors declare no conflicts of interest.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki, and approved by Research Ethics Committee of the Faculty of Medical Laboratory Sciences prior to data collection (code AD/FMLS/G at date 01/04/2026). Administrative approval was obtained from participating health center management. All personally identifiable patient information was anonymized before analysis.

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