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C-REACTIVE PROTEIN AS AN EARLY DIAGNOSTIC BIOMARKER FOR MALARIAL AND DENGUE INFECTION IN LAHORE, PAKISTAN

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Abstract

Background: *Malaria and dengue are major causes of acute febrile illness in Pakistan and often present with overlapping clinical features, making early diagnosis challenging in resource-limited settings. C-reactive protein (CRP), an acute-phase inflammatory biomarker, may provide a rapid and cost-effective tool for differentiating these infections and assessing disease severity.*

Objective: *To evaluate the diagnostic utility of serum CRP levels in patients with malaria and dengue infection and to determine its association with disease severity. A cross-sectional study was conducted among 100 participants. Non-parametric statistical analyses, correlation testing, logistic regression, and receiver operating characteristic (ROC) curve analysis were performed.*

Results: *Mean CRP levels were significantly elevated in malaria patients (126.71 ± 54.75 mg/L) compared with dengue patients (88.45 ± 41.38 mg/L) and healthy controls (3.77 ± 1.50 mg/L) ($p < .001$). CRP demonstrated significant negative correlations with platelet count ($r_s = -0.477$, $p < .01$) and WBC count ($r_s = -0.251$, $p < .05$), indicating an association with disease severity. Logistic regression identified CRP as an independent predictor of infection status ($p = .010$). ROC analysis showed acceptable diagnostic performance for malaria detection (AUC = 0.720).*

Conclusion: *CRP is a valuable and affordable biomarker for the early diagnosis and severity assessment of malaria and dengue infections. Elevated CRP levels, particularly in malaria, may aid clinicians in differentiating these infections and improving patient management in resource-constrained settings.*

INTRODUCTION

Malaria and dengue remain major public health concerns in tropical and subtropical regions, including Pakistan, where recurrent outbreaks contribute substantially to morbidity and mortality (Islam et al., 2023; Kularatne & Dalugama, 2022). Both diseases commonly present as acute febrile illnesses with overlapping clinical manifestations such as fever, thrombocytopenia, leukopenia, and generalized weakness, making early differential diagnosis challenging in resource-limited healthcare settings (Valdivia-Conroy et al., 2023).

Malaria is a parasitic disease caused by *Plasmodium* species and transmitted through the bite of infected *Anopheles* mosquitoes. In Pakistan,

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Plasmodium vivax accounts for most cases, whereas *P. falciparum* is associated with severe disease and mortality (Islam et al., 2023). C-reactive protein (CRP) is an acute-phase reactant synthesized predominantly by hepatocytes in response to inflammatory cytokines, particularly interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin-1β (IL-1β) (Orsolini et al., 2023). Under normal physiological conditions, CRP concentrations are typically below 1 mg/L; however, levels may increase up to 1,000-fold during acute inflammatory responses (Fazal, 2021). Owing to its rapid response to infection and tissue injury, CRP has emerged as a useful biomarker in infectious disease diagnosis and severity assessment. Given the overlapping clinical presentation of these infections and the need for affordable diagnostic tools, this study aimed to evaluate CRP as an early diagnostic biomarker for malaria and dengue infection in Lahore, Pakistan. Specifically, the study assessed serum CRP levels among malaria and dengue patients, compared CRP concentrations with healthy controls, evaluated its diagnostic utility, and explored its association with disease severity.

C-reactive protein has been extensively investigated as an inflammatory biomarker in infectious diseases. A systematic review by Wilairatana et al. (2021) reported significantly elevated CRP levels among malaria patients, particularly those with severe disease manifestations. Similarly, Bhardwaj et al. (2019) observed higher CRP concentrations in severe malaria compared with uncomplicated malaria, suggesting a potential role for CRP in disease severity assessment.

In dengue infection, elevated CRP levels during the early febrile phase have been associated with adverse clinical outcomes. Recent evidence suggests that CRP may also assist in differentiating among causes of acute febrile illness. Elevated CRP concentrations have been observed in malaria, dengue, bacterial infections, and other inflammatory conditions, although malaria generally produces higher CRP responses than dengue (Hashmi et al., 2023; Bruhn et al., 2025).

Methodology

Study Design & Study Setting

A hospital-based cross-sectional study was conducted to evaluate C-reactive protein (CRP) as an early diagnostic biomarker for malaria and dengue infections. The study was carried out in a tertiary care hospital in Lahore, Pakistan, equipped with diagnostic and laboratory facilities for the management of infectious diseases.

Study Population & Sample Size

The study included patients presenting with clinical features suggestive of malaria or dengue infection during the study period. Healthy individuals served as controls. Based on a 95% confidence level, 10% margin of error, and an estimated prevalence of 60%, the minimum required sample size was calculated as 92 participants. To compensate for incomplete data and potential exclusions, a final sample of approximately 100 participants was included.

RESULTS

4.1 Demographic Characteristics of Participants

Table 4.1

Participant Characteristics and Biomarker Profiles by Diagnostic Group (N = 100)

Variable	Healthy Control (n = 23)	Dengue (n = 35)	Malaria (n = 42)
Male, n (%)	11 (47.8)	20 (57.1)	22 (52.4)
Female, n (%)	12 (52.2)	15 (42.9)	20 (47.6)
CRP (mg/L), M ± SD	3.77 ± 1.50	88.45 ± 41.38	126.71 ± 54.75
Platelets (×10³/µL), M ± SD	247.52 ± 56.79	64.03 ± 26.53	106.74 ± 33.92
WBC (×10³/µL), M ± SD	7.90 ± 1.49	3.57 ± 1.13	6.42 ± 1.84

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Variable	Healthy Control (n = 23)	Dengue (n = 35)	Malaria (n = 42)
Hemoglobin (g/dL), M ± SD	14.12 ± 1.07	11.73 ± 1.01	10.51 ± 1.65

Note. *CRP = C-reactive protein; WBC = White Blood Cell count. Malaria patients exhibited the highest CRP levels, whereas dengue patients showed the lowest platelet counts.*

CRP levels showed a clear stepwise increase from Healthy Control (Mean = 3.765 mg/L) to Dengue (Mean = 88.451 mg/L) to Malaria (Mean = 126.710 mg/L), consistent with a stronger acute-phase inflammatory response in malaria. Platelet count was lowest in Dengue (Mean = 64.03 × 10^3/μL), reflecting characteristic thrombocytopenia. Hemoglobin was progressively reduced across groups, lowest in Malaria patients.

Tests of Normality

Table 4.2

Normality Test Results (Kolmogorov-Smirnov & Shapiro-Wilk)

Variable	Healthy Control	Dengue	Malaria
CRP	.454	.111	.032*
Platelets	.089	.008**	.136
WBC	.043*	.029*	.081
Hemoglobin	.169	.104	.076

Note. *Values represent Shapiro–Wilk p-values. p < .05 indicates non-normal distribution. Because several variables violated normality assumptions, non-parametric analyses were applied.*

Several groups showed non-normal distributions, particularly Platelets in Dengue (S-W p = .008) and WBC in Healthy Control and Dengue groups. Non-parametric tests were therefore used for all between-group comparisons.

Table 4.3

Spearman Rank Correlations

Pairwise Comparisons of CRP Levels between Diagnostic Groups**.** Spearman Correlations Among CRP, Platelets, and WBC

Analysis	Test Statistic	p
Gender × Diagnosis	$\chi^2(2) = 0.50$	.781
CRP: Malaria vs Dengue	U = 412.00	.001**
CRP: Malaria vs Healthy Control	U = 44.00	< .001***
CRP: Dengue vs Healthy Control	U = 0.00	< .001***
CRP–Platelets Correlation	rs = −.477	< .01**
CRP–WBC Correlation	rs = −.251	< .05*

Note. **p < .05, **p < .01.*

CRP was significantly negatively correlated with platelet count (rs = -.477, p < .01) and WBC count (rs = -.251, p < .05). Elevated CRP levels were associated with worsening hematological abnormalities, suggesting that CRP may reflect disease severity in dengue and malaria infections.

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Variables in the Equation

Table4.4

Binary Logistic Regression Analysis Predicting Diagnostic Status From CRP, WBC Count, and Platelet Count

Predictor	B	SE	Wald χ^2	Df	*p*	Odds Ratio, Exp(B)
CRP (mg/L)	-0.028	0.011	6.55	1	.010*	0.972
WBC Count (×10³/µL)	-1.277	0.395	10.45	1	.001**	0.279
Platelet Count (×10³/µL)	-0.051	0.019	7.19	1	.007**	0.950
Constant	13.146	3.244	16.42	1	< .001***	512,170.50

Note. *B = regression coefficient; SE = standard error; Exp(B) = odds ratio. p < .05. ** p < .01. *** p < .001.*

CRP was a significant predictor of diagnostic status, $B = -0.028$, Wald $\chi^2(1) = 6.55$, $p = .010$, OR = 0.972. The odds ratio indicates that for each one-unit increase in CRP level, the odds of the outcome category decreased by approximately 2.8%, while controlling for the other predictors. WBC count was also a significant predictor, $B = -1.277$, Wald $\chi^2(1) = 10.45$, $p = .001$, OR = 0.279. This finding suggests that higher WBC counts were associated with substantially lower odds of the outcome category, with each unit increase in WBC count reducing the odds by approximately 72.1%.

Discussion

The present study evaluated the diagnostic utility of C-reactive protein (CRP) as an early biomarker for malaria and dengue infections among patients presenting with acute febrile illness in Lahore, Pakistan. The findings demonstrate that CRP levels were significantly elevated in both malaria and dengue patients compared with healthy controls, with malaria patients exhibiting substantially higher CRP concentrations than dengue patients. These results support the role of CRP as a useful inflammatory biomarker for differentiating tropical infections and assessing disease severity. Gender distribution did not differ significantly among the study groups, indicating that gender was not associated with disease status. This finding is consistent with previous studies reporting no meaningful gender-related differences in CRP-based diagnostic assessment among dengue and malaria patients (Suma & Keerti, 2025).

A key finding of this study was the markedly elevated CRP levels in malaria patients (M = 126.71 mg/L) compared with dengue patients (M = 88.45 mg/L) and healthy controls (M = 3.77 mg/L). These results are consistent with the meta-analysis by Wilairatana et al. (2021), which reported significantly higher CRP concentrations in malaria patients than in healthy individuals and demonstrated a positive association between CRP levels and malaria severity. Similarly, Bhardwaj et al. (2019) reported significantly elevated CRP levels among severe malaria cases, supporting the current findings that malaria elicits a stronger acute-phase inflammatory response than dengue infection.

The ROC analysis in the present study demonstrated acceptable diagnostic performance of CRP for malaria (AUC = .720), supporting its potential application as a screening biomarker in resource-limited settings. Overall, the findings suggest that CRP is a practical, inexpensive, and clinically valuable biomarker for the early identification of malaria and dengue infections. Its ability to differentiate malaria from dengue, predict disease severity, and complement routine laboratory investigations supports its incorporation into the initial evaluation of patients presenting with acute febrile illness, particularly in resource-constrained healthcare settings.

Conclusion

This study demonstrates that C-reactive protein (CRP) is a significant biomarker for the early diagnosis and clinical assessment of malaria and dengue infections. CRP levels were significantly

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higher in infected patients than in healthy controls and were markedly elevated in malaria compared with dengue infection. CRP also showed significant associations with platelet and white blood cell counts, indicating its relationship with disease severity and inflammatory burden. The acceptable diagnostic accuracy of CRP for malaria (AUC = .720) and its independent predictive value in logistic regression analysis highlight its usefulness as a supplementary diagnostic tool.

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