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Comparative Analysis of Platelet-to-Lymphocyte Ratio and Neutrophil-to-Platelet Ratio as Diagnostic Markers in Dengue and Malaria

Shereen Naz[1*], Ikram Din Ujjan[1], Sadia Majeed[1], Abdul Ghani[1], Sughand Khaksheli[1] and Asma Rajput[1]

[1]Department of Pathology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan

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***Corresponding Author:**
Shereen Naz
Department of Pathology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
drshereensmbbmu@gmail.com

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ABSTRACT

Dengue fever and malaria are endemic febrile illnesses in South Asia that often present with overlapping clinical features. Accurate differentiation is essential for timely and appropriate treatment. Inflammatory biomarkers such as the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Platelet Ratio (NPR) may aid diagnostic decision-making. **Objectives:** To evaluate the role of PLR and NPR as diagnostic markers in distinguishing dengue fever from malaria in patients presenting with acute febrile illness. **Methods:** A cross-sectional comparative study was conducted at LUMHS, Hyderabad, over 5 months. A total of 116 patients (58 each with confirmed dengue and malaria) were enrolled using non-probability consecutive sampling. Clinical data and complete blood counts were collected. PLR and NPR were calculated and analyzed for diagnostic accuracy using SPSS version 21.0. ROC curve analysis determined optimal cutoffs, sensitivity, and specificity. **Results:** The mean PLR was significantly lower in dengue (109.7 ± 58.2) compared to malaria (131.6 ± 69.3) (p=0.034). NPR did not show a significant intergroup difference (p=0.321). At a cutoff of 73.89, PLR demonstrated moderate sensitivity (65.52%) and low specificity (36.21%). NPR showed high specificity (100%) but no sensitivity (0%) at a cutoff of 0.0500. **Conclusions:** PLR can be considered a modestly useful marker in differentiating dengue from malaria, while NPR lacks diagnostic sensitivity. These findings suggest that PLR, in conjunction with clinical evaluation, may support early differentiation between the two diseases.

INTRODUCTION

Dengue and malaria are among the most prevalent vector-borne febrile illnesses in tropical and subtropical regions, particularly affecting South Asian countries such as Pakistan. These diseases present with overlapping clinical features such as fever, malaise, and thrombocytopenia, posing significant challenges to differential diagnosis, especially in resource-limited settings [1, 2]. According to the World Health Organization (WHO), dengue cases have increased dramatically worldwide in the last two decades. In 2022 alone, more than 2.8 million dengue cases and over 1,200 deaths were reported from 70 countries, including South Asia [3]. Similarly, the WHO's World Malaria Report 2023 states that there were an estimated 249 million malaria cases globally in 2022, with Pakistan contributing to over 900,000 confirmed cases, primarily caused by *Plasmodium vivax* and *Plasmodium falciparum* [4]. In Pakistan, both dengue and malaria remain endemic, with seasonal outbreaks peaking during the post-monsoon period. Sindh, Punjab, and Khyber Pakhtunkhwa are the most affected provinces. According to the National Institute of Health (NIH), Islamabad, over 75,000 confirmed dengue cases and 185 deaths were reported nationwide in 2022 [5]. Concurrently, malaria cases surged following the 2022 floods, with Sindh alone recording over 400,000 confirmed infections [6]. Given the clinical similarities and co-circulation of these diseases, there is a pressing need

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for rapid, accurate, and cost-effective diagnostic tools, especially in rural and district-level healthcare centers lacking molecular diagnostics. Hematological indices derived from complete blood counts (CBC) have recently gained attention as adjunct markers for the early differentiation of infectious diseases. Among these, the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Platelet Ratio (NPR) have been proposed as accessible and inexpensive inflammatory biomarkers [7, 8]. PLR, calculated as the ratio of platelet count to lymphocyte count, reflects systemic inflammation and immune response. Elevated PLR has been reported in bacterial infections and some parasitic diseases, while decreased PLR is frequently observed in viral infections such as dengue due to profound thrombocytopenia and reactive lymphocytosis [9]. Conversely, NPR, a ratio of neutrophil count to platelet count, has been studied less extensively but may have potential in differentiating etiologies with varying neutrophil responses [10]. Despite growing international literature on PLR and NPR, evidence from Pakistan remains scarce and inconclusive. Few local studies have explored their utility in differentiating dengue from malaria, and none have established population-specific thresholds. Moreover, routine clinical reliance on NS1 antigen, IgM/IgG serology, or malarial smears may not be feasible in peripheral settings with limited lab support. Therefore, evaluating the diagnostic performance of PLR and NPR in a Pakistani cohort is not only timely but crucial for strengthening clinical decision-making and outbreak response strategies [11].

Although dengue and malaria are highly prevalent in Pakistan and share overlapping clinical features, there is limited local evidence on the use of simple hematological markers such as Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Platelet Ratio (NPR) for their early differentiation, particularly in resource-limited settings. This gap restricts timely diagnosis and appropriate management where advanced diagnostic tools are not readily available. This study aims to evaluate the role of PLR and NPR as diagnostic markers in distinguishing dengue fever from malaria in patients presenting with acute febrile illness.

METHODS

This cross-sectional comparative study was conducted at the Diagnostic and Research Laboratory of Liaquat University of Medical and Health Sciences, Hyderabad, in collaboration with the Department of Medicine at Liaquat University Hospital. The study was conducted over a 5-month duration from January 2025 to May 2025. The study was approved by the Ethical Review Committee of Liaquat University of Medical and Health Sciences, Jamshoro (Ref. No. LUMHS/REC/-563). A total of 116 adult patients (58 with confirmed dengue fever and 58 with confirmed malaria) presenting with acute febrile illness were enrolled through non-probability consecutive sampling. The sample size was calculated using the WHO OpenEpi sample size calculator, based on an estimated odds ratio of 3.26 for the platelet-to-lymphocyte ratio (PLR) when comparing dengue to malaria [12]. Margin of error was 5%, confidence interval was at 90%, and a statistical power of 80% was used to calculate sample size. Patients aged 18 years or older with acute febrile illness of less than seven days and confirmed diagnosis of either dengue (NS1 antigen/IgM/IgG positive) or malaria (peripheral smear or rapid diagnostic test) were included, while those with co-infections, chronic hematologic or autoimmune disorders, or pregnancy were excluded. On arrival, overlapping symptoms commonly noted in both groups were fever, headache, myalgia, nausea, vomiting, and fatigue, with some also presenting with rash, retro-orbital pain, chills, and sweating, making initial differentiation difficult. Dengue was diagnosed based on clinical signs and confirmed by NS1 antigen or IgM/IgG serology, while malaria diagnosis was established using peripheral blood smear or rapid diagnostic test. After obtaining informed consent, demographic and clinical data were collected using a structured questionnaire. Blood samples were collected for complete blood count (CBC), from which the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Platelet Ratio (NPR) were calculated. PLR was determined by dividing platelet count by lymphocyte count and categorized as normal (100–200) or raised (>200). NPR was calculated by dividing neutrophil count by platelet count, with values <10 considered normal and >10 considered raised. Data were analyzed using SPSS version 21.0. Normality of continuous variables (WBC, PLR, and NPR) was assessed using the Shapiro-Wilk test before applying parametric tests. The data was normally distributed. Independent t-tests were used to compare the means of PLR and NPR between the dengue and malaria groups. Chi-square tests were applied to assess differences in proportions for categorical outcomes such as normal vs. raised PLR and NPR. Diagnostic accuracy of PLR and NPR was evaluated using Receiver Operating Characteristic (ROC) curve analysis, and the area under the curve (AUC) was calculated. Optimal cutoff thresholds were derived to determine sensitivity and specificity. A p-value of <0.050 was considered statistically significant.

RESULTS

The mean age of participants in both groups was comparable, with 38.8 ± 11.2 years in the dengue group and 39.1 ± 10.7 years in the malaria group. Gender distribution was nearly equal across both groups. Most participants resided in urban areas, with 62.1% in the dengue group and 58.6% in the malaria group. The mean duration of

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symptoms was slightly shorter in dengue patients (3.2 ± 1.6 days) compared to malaria patients (3.4 ± 1.8 days). Similarly, the mean hospital stay was marginally shorter in dengue cases (5.6 ± 2.1 days) versus malaria (6.1 ± 2.4 days) (Table 1).

Table 1: Descriptive Demographics and Clinical Features

Variables	Dengue (N=58)	Malaria (N=58)
Mean Age (years)	38.8 ± 11.2	39.1 ± 10.7
Gender		
Male	30 (51.7%)	31 (53.4%)
Female	28 (48.3%)	27 (46.6%)
Residence		
Urban	36 (62.1%)	34 (58.6%)
Rural	22 (37.9%)	24 (41.4%)
Mean Duration of Symptoms (days)	3.2 ± 1.6	3.4 ± 1.8
Mean Hospital Stay (days)	5.6 ± 2.1	6.1 ± 2.4

The mean WBC, neutrophil, lymphocyte, and platelet counts were similar between groups. However, the mean PLR was lower in dengue patients (109.7 ± 58.2) than in malaria patients (131.6 ± 69.3). A raised PLR (>200) was seen in 22.4% of dengue cases and 32.8% of malaria cases. NPR values remained low in both groups, with very few cases crossing the revised cutoff (>0.050), suggesting limited diagnostic utility for this marker (Table 2).

Table 2: Hematological Parameters and Ratios

Parameters	Dengue (N=58)	Malaria (N=58)
Mean WBC (cells/µL)	5408 ± 1472	5523 ± 1521
Mean Neutrophils	2950 ± 802	2983 ± 789
Mean Lymphocytes	1775 ± 491	1810 ± 502
Mean Platelet Count	148200 ± 29650	151800 ± 31000
Mean PLR	109.7 ± 58.2	131.6 ± 69.3
PLR Status		
Normal (100–200)	45 (77.6%)	39 (67.2%)
Raised (>200)	13 (22.4%)	19 (32.8%)
Mean NPR	0.020 ± 0.006	0.021 ± 0.007
NPR Status		
Normal (≤ 0.0500)	56 (96.6%)	57 (98.3%)
Raised (> 0.0500)	2 (3.4%)	1 (1.7%)

Statistical analysis revealed a significant difference in PLR between dengue and malaria groups (p=0.034), whereas the difference in NPR was not statistically significant (p=0.321), indicating PLR as a potentially useful discriminative marker (Table 3).

Table 3: Inferential Statistics for PLR and NPR

Parameters	Mean ± SD (Dengue)	Mean ± SD (Malaria)	p-Value
PLR	109.7 ± 58.2	131.6 ± 69.3	0.034
NPR	0.020 ± 0.006	0.021 ± 0.007	0.321

PLR at a cutoff of 73.89 yielded a sensitivity of 65.52% and specificity of 36.21%, indicating moderate diagnostic performance. NPR demonstrated 100% specificity but 0% sensitivity, limiting its clinical applicability (Table 4).

Table 4: Diagnostic Accuracy of PLR and NPR

Markers	Optimal Cutoff	Sensitivity	Specificity
PLR	73.89	65.52%	36.21%
NPR	0.0500	0.00%	100.00%

DISCUSSION

The findings demonstrate that PLR was significantly lower in dengue patients compared to those with malaria (p=0.034), whereas NPR showed no statistically significant difference between the two groups. ROC analysis revealed that PLR demonstrated modest diagnostic accuracy, with a sensitivity of 65.52% and specificity of 36.21%. Although NPR demonstrated 100% specificity, its sensitivity was 0%, which limits its practical diagnostic utility. Our findings are consistent with studies from other endemic regions. Alsedig *et al.* reported significantly lower PLR values in dengue compared to malaria and endorsed its potential as a cost-effective diagnostic marker [13]. Iqbal et al. also observed reduced PLR values in dengue patients and suggested its usefulness in early diagnosis in resource-limited settings [14]. Similarly, Previous studies highlighted the utility of PLR in distinguishing viral from bacterial infections, including dengue and malaria, though with only moderate performance, similar to our results. One aspect not explored in our study is whether combining PLR with other hematological indices, such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), or red cell indices, could enhance diagnostic accuracy. Recent studies have proposed such integrated approaches to improve the reliability of differentiating febrile illnesses, and future research may benefit from evaluating multi-marker strategies. A multicenter study by Karunaratna *et al.* [15] suggested that variations in lymphocyte responses, despite similar thrombocytopenia patterns, may explain differences in PLR between dengue and malaria. In contrast, our study did not find significant variation in NPR between the groups, consistent with the findings of Iqbal *et al.* [16], who also reported poor diagnostic accuracy for NPR in distinguishing viral and parasitic infections. The potential for PLR and NLR to vary with disease severity has been acknowledged in earlier literature. Obeagu [17] highlighted how the diagnostic performance of these markers fluctuates depending on malaria severity and host immune response. However, our study did not assess the relationship of PLR or NPR with clinical severity, which is a limitation. Incorporating this dimension in future studies may provide deeper insights into their prognostic value. Our findings also support the conclusion by Kabir *et al.* [18], who emphasized that PLR should be integrated with clinical assessment and rapid

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diagnostic tests due to its limited specificity. The pathophysiological basis of PLR differences likely relates to dengue's characteristic lymphocytosis and marked thrombocytopenia, whereas malaria typically induces neutrophilia with relatively stable platelet counts [19, 20]. This mechanism explains the PLR shift observed in dengue and the relatively unchanged NPR across both conditions. This study has several limitations. The relatively small sample size and exclusion of pediatric patients may reduce generalizability, especially in endemic regions where children are disproportionately affected. The use of non-probability consecutive sampling further limits the representativeness of the findings. Additionally, reliance on single-time-point blood samples may have reduced diagnostic accuracy, whereas serial PLR measurements could provide greater insight, as suggested by Hossain *et al.* [21]. Finally, the sensitivity and specificity values of both PLR and NPR were relatively low, which reduces their standalone clinical utility.

This study was limited by a relatively small sample size and the exclusion of pediatric patients, which may affect the generalizability of the findings. Additionally, reliance on single time-point measurements and not assessing disease severity may have reduced the diagnostic accuracy of PLR and NPR. Future studies should include larger, multicenter populations with severity stratification and combined hematological markers to improve diagnostic performance.

CONCLUSIONS

In conclusion, PLR appears to be a useful supplementary marker in differentiating dengue from malaria, particularly in resource-limited settings. However, it should not be used in isolation; PLR must be interpreted alongside clinical presentation and serological findings to enhance diagnostic accuracy. NPR, due to its poor sensitivity, showed limited clinical utility. Further large-scale prospective studies are necessary to validate these findings and establish more robust cutoff values for broader clinical application.

Authors' Contribution

Conceptualization: SN
Methodology: SN, IDU, SM, AG, AR
Formal analysis: SN, SK, AR
Writing and Drafting: SN, IDU, SM, AG, SK
Review and Editing: SN, IDU, SM, AG, SK

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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