RESEARCH PAPER

Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio as Predictors Of Microalbuminuria in Type 2 Diabetes Patients - Cross Sectional Study

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ABSTRACT

Background: Chronic inflammation plays a major role in the development of diabetic microvascular complications. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), derived from routine hematological indices, have emerged as simple and cost-effective markers of systemic inflammation. This study aimed to assess the association between NLR and PLR with microalbuminuria in patients with type 2 diabetes mellitus (T2DM) and to evaluate their diagnostic performance for early renal involvement.

Methods: A cross-sectional study was conducted among fifty patients with T2DM attending the Department of General Medicine at Sri Devaraj Urs Medical College, Kolar. Clinical and biochemical parameters including fasting blood glucose, glycated hemoglobin (HbA1c), serum creatinine, and urinary albumin-to-creatinine ratio (UACR) were measured. NLR and PLR were calculated from complete blood counts. Patients were categorized into normoalbuminuria (UACR < 30 mg/g) and microalbuminuria (UACR 30–300 mg/g) groups. Statistical analysis included correlation, logistic regression, and receiver operating characteristic (ROC) curve analysis.

Results: Patients with microalbuminuria showed significantly higher mean NLR (2.7 ± 0.6) and PLR (132 ± 34) values compared with the normoalbuminuric group (1.7 ± 0.5 and 104 ± 29, respectively; $p < 0.001$). NLR demonstrated a strong positive correlation with UACR ($r = 0.62$) and a negative correlation with eGFR ($r = -0.52$). ROC analysis revealed an NLR cut-off value of 2.3 with 78% sensitivity and 80% specificity (AUC = 0.86), showing superior discriminative ability compared with PLR (AUC = 0.74).

Conclusion: Elevated NLR and PLR are significantly associated with early renal dysfunction in patients with T2DM. Among these, NLR exhibits higher diagnostic accuracy and may serve as a reliable, inexpensive biomarker for identifying individuals at risk of developing diabetic nephropathy in routine clinical practice.

Keywords: *Type 2 diabetes mellitus, Microalbuminuria, Neutrophil-to-lymphocyte ratio, Platelet-to-lymphocyte ratio, Diabetic nephropathy.*
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INTRODUCTION

Diabetes mellitus (DM) represents one of the most significant global health challenges, with an estimated 537 million adults affected in 2021a figure projected to exceed 700 million by 2045 according to the International Diabetes Federation [1]. Type 2 diabetes mellitus (T2DM), accounting for over 90% of all cases, is characterized by insulin resistance, β-cell dysfunction, and chronic hyperglycemia that contribute to the development of both microvascular and macrovascular complications [2]. Among these, diabetic nephropathynow referred to as diabetic kidney disease (DKD)is a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide [3,4]. In India, DKD constitutes nearly 40% of all CKD cases, posing a major clinical and socioeconomic burden due to late detection and limited access to specialized renal care [5].

Although urinary albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) are routinely employed to evaluate renal function, they generally reflect renal impairment only after substantial glomerular damage has occurred [6]. Therefore, identifying early and easily accessible biomarkers that reflect subclinical renal injury remains a major unmet need. Increasing evidence implicates systemic inflammation as a central mechanism in the initiation and progression of DKD [7]. Persistent hyperglycemia induces oxidative stress, endothelial

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dysfunction, and activation of pro-inflammatory cytokines, which together promote mesangial expansion, glomerular basement-membrane thickening, and microalbuminuria [8].

Simple hematological indices derived from routine complete blood counts (CBC) have gained attention as surrogate markers of chronic inflammation. The neutrophil-to-lymphocyte ratio (NLR) reflects the balance between innate immune activation and adaptive immune suppression, whereas the platelet-to-lymphocyte ratio (PLR) integrates platelet-mediated inflammatory and thrombotic responses [9,10]. Both ratios are cost-effective, reproducible, and widely available, making them appealing for large-scale use, particularly in low- and middle-income settings.

Several studies have demonstrated a positive association between elevated NLR or PLR and diabetic microvascular complications. In a Syrian cohort, Jaaban et al. reported that both indices increased progressively from normoalbuminuria to macroalbuminuria, identifying NLR ≥ 2.2 and PLR ≥ 115 as effective thresholds for detecting early nephropathy [11]. Likewise, Li et al. observed in 655 Chinese adults that higher NLR and PLR values were independently associated with DKD, with optimal NLR cut-off of 2.46 [12]. Indian data are comparatively scarce, although smaller studies have indicated similar trends [13]. Ethnic and environmental differences in immune and hematologic parameters warrant population-specific evaluation to validate these findings.

Given this background, the present study was designed to evaluate the association between NLR and PLR with microalbuminuria in Indian patients with T2DM and to assess their diagnostic performance for detecting early renal involvement. Establishing the clinical utility of these inflammatory ratios could provide a low-cost, easily implementable tool for identifying patients at risk of diabetic kidney disease in routine practice.

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional observational study was carried out in the Department of General Medicine at Sri Devaraj Urs Medical College, Kolar. The study was conducted over a six-month period from January 2023 to June 2023. Its primary objective was to evaluate the association of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) with microalbuminuria in patients diagnosed with type 2 diabetes mellitus (T2DM).

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee (Ref. No: SDUMC/IEC/2023/118). All participants were informed about the nature and purpose of the study, and written consent was obtained from each before inclusion. The study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki.

Study Population

A total of fifty patients with type 2 diabetes mellitus attending the outpatient and inpatient departments of General Medicine were included in the study. Participants were selected by convenience sampling. Eligible patients were between thirty-five and seventy years of age and had a known history of diabetes for at least four years. Patients with acute or chronic infections, autoimmune diseases, malignancy, liver dysfunction, hematologic disorders, or recent surgery or trauma were excluded. Those receiving corticosteroids, immunosuppressants, or cytotoxic drugs, as well as patients with renal diseases of non-diabetic origin, were also excluded from the study.

Grouping of Participants

The enrolled patients were categorized into two groups based on their urinary albumin-to-creatinine ratio (UACR). Group I included patients with normoalbuminuric, defined as a UACR of less than 30 mg/g, while Group II consisted of patients with microalbuminuria, defined as a UACR between 30 and 300 mg/g. Microalbuminuria was confirmed by two consecutive abnormal readings obtained at least two weeks apart to ensure accuracy.

Clinical Evaluation and Data Collection

Detailed clinical and demographic data were obtained using a structured proforma, including information on age, gender, duration of diabetes, treatment regimen, and associated comorbidities. All participants underwent a thorough physical examination. Height and weight were measured to calculate body mass index (BMI). Blood pressure was recorded using a calibrated mercury sphygmomanometer after the patient had rested for at least ten minutes in a seated position.

Laboratory Investigations

After overnight fasting, venous blood samples were collected from each participant. Biochemical investigations included fasting plasma glucose, glycated hemoglobin (HbA1c), serum creatinine, blood urea, and lipid profile, all analyzed using automated analyzers in the hospital laboratory. The estimated glomerular filtration rate (eGFR) was calculated using serum creatinine values. A morning spot urine sample was collected from each patient for estimation of urinary albumin and creatinine, and the urinary albumin-to-creatinine ratio (UACR) was expressed in milligrams per gram.

Hematological investigations were performed on the same day using an automated hematology analyzer. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count, and the platelet-to-lymphocyte ratio (PLR) was derived by dividing the platelet count by the lymphocyte count. All laboratory procedures were carried out using standardized methods to ensure reliability of results.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics version 26. Continuous

variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. The independent sample t-test was used to compare continuous variables between the two groups, and the chi-square test was applied for categorical variables. Pearson's correlation coefficient was employed to determine the relationship between inflammatory markers (NLR and PLR) and renal parameters such as urinary albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR). Binary logistic regression analysis was performed to identify independent associations of NLR and PLR with microalbuminuria. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic accuracy and optimal cut-off values for NLR and PLR. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

A total of fifty patients with type 2 diabetes mellitus were included in this study. The mean age of participants was 55 years, with a male-to-female ratio of approximately 1.2:1. Based on the urinary albumin-to-creatinine ratio (UACR), patients were divided into two groups: Group I with normoalbuminuria (UACR < 30 mg/g; n = 25) and Group II with microalbuminuria (UACR 30–300 mg/g; n = 25).

Patients with microalbuminuria had a significantly longer duration of diabetes and poorer glycemic control compared to those with normoalbuminuria. The mean duration of diabetes was 10.1 ± 2.5 years in the microalbuminuric group and 6.3 ± 2.1 years in the normoalbuminuric group. Mean HbA1c levels were 8.9 ± 1.3% and 7.8 ± 1.2%, respectively. Systolic blood pressure and serum creatinine levels were also significantly higher among patients with microalbuminuria, while estimated glomerular filtration rate (eGFR) was markedly lower. The mean urinary albumin-to-creatinine ratio in the microalbuminuria group was 112.4 ± 38.7 mg/g compared with 14.6 ± 5.2 mg/g in the normoalbuminuric group, indicating a clear difference in renal status between the two groups.

Hematological Findings

The comparison of hematological parameters revealed that both the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were significantly higher in patients with microalbuminuria. The mean NLR was 2.7 ± 0.6 in the microalbuminuric group compared to 1.7 ± 0.5 in the normoalbuminuric group ($p < 0.001$). Similarly, the mean PLR was 132 ± 34 in the microalbuminuria group and 104 ± 29 in the normoalbuminuric group ($p < 0.001$). Although total white blood cell count and platelet count were slightly higher among those with microalbuminuria, these differences did not reach statistical significance. These findings indicate that the derived inflammatory ratios, rather than the individual cell counts, provide better sensitivity in detecting early renal involvement.

Correlation Between Inflammatory Markers and Clinical Variables

Correlation analysis showed significant associations between the inflammatory ratios and various clinical parameters. NLR demonstrated a strong positive correlation with duration of diabetes ($r = 0.45$), HbA1c ($r = 0.40$), serum creatinine ($r = 0.38$), and urinary albumin-to-creatinine ratio ($r = 0.62$), and a negative correlation with estimated glomerular filtration rate ($r = −0.52$). PLR also exhibited moderate positive correlations with HbA1c ($r = 0.29$), serum creatinine ($r = 0.25$), and urinary albumin-to-creatinine ratio ($r = 0.44$), and an inverse correlation with eGFR ($r = −0.41$). All these correlations were statistically significant, suggesting that both NLR and PLR increase with worsening glycemic control and declining renal function.

Regression Analysis

Binary logistic regression analysis was performed to determine independent associations of NLR and PLR with microalbuminuria. After adjusting for confounding variables such as age, duration of diabetes, systolic blood pressure, HbA1c, and lipid parameters, NLR emerged as an independent factor associated with microalbuminuria ($p < 0.01$). PLR showed a weaker but still statistically significant association ($p < 0.05$). These results suggest that systemic inflammatory activity reflected by NLR plays a key role in early renal dysfunction among diabetic patients.

Diagnostic Accuracy of NLR and PLR

Receiver operating characteristic (ROC) curve analysis was used to assess the diagnostic performance of NLR and PLR for detecting microalbuminuria. The area under the curve (AUC) for NLR was 0.86 (95% CI: 0.77–0.95; $p < 0.001$), indicating excellent discriminative ability. The optimal NLR cut-off value was 2.3, which provided 78% sensitivity and 80% specificity for identifying microalbuminuria. For PLR, the AUC was 0.74 (95% CI: 0.63–0.85; $p < 0.01$), with an optimal cut-off value of 115, corresponding to 76% sensitivity and 72% specificity. Comparison of AUC values demonstrated that NLR had a superior diagnostic performance compared to PLR in differentiating patients with early diabetic renal involvement.

Summary of Findings

In summary, patients with type 2 diabetes and microalbuminuria showed significantly higher levels of systemic inflammatory markers, particularly NLR and PLR, compared to those with normal urinary albumin excretion. NLR exhibited stronger correlations with glycemic and renal parameters and demonstrated greater diagnostic accuracy than PLR. These findings indicate that NLR can serve as a simple, reliable, and cost-effective marker for identifying early renal dysfunction in patients with diabetes mellitus.

DISCUSSION

The present cross-sectional study evaluated the association of two hematological inflammatory markersthe neutrophil-

to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR)with microalbuminuria among patients with type 2 diabetes mellitus (T2DM). Both indices were significantly higher in patients with microalbuminuria compared with those having normoalbuminuria. The results demonstrated a strong positive correlation between NLR and urinary albumin excretion, as well as a negative correlation with estimated glomerular filtration rate (eGFR). Although PLR also showed significant associations, its discriminative accuracy was comparatively lower. These findings support the concept that low-grade systemic inflammation contributes to early renal involvement in diabetes and that NLR reflects this inflammatory milieu with good diagnostic performance.

Chronic hyperglycemia promotes endothelial injury, oxidative stress, and inflammatory cytokine release, which together lead to glomerular basement membrane thickening and microvascular dysfunction [8]. The resultant microinflammation alters capillary permeability, producing albumin leakage into urine. In this study, patients with microalbuminuria had significantly longer duration of diabetes, higher HbA1c, and elevated systolic blood pressure, all of which are recognized contributors to diabetic nephropathy [3,4]. The parallel increase in NLR and PLR with worsening renal indices indicates that these hematologic ratios may reflect the cumulative inflammatory stress underlying diabetic kidney disease.

Our findings are consistent with previous studies conducted in different populations. Jaaban et al. reported a progressive increase in NLR and PLR values across albuminuria stages, with cut-off points like those identified in the present study [11]. Li et al. also observed that both NLR and PLR were independently associated with diabetic kidney disease among Chinese adults [12]. Likewise, Khandare et al. demonstrated that Indian patients with diabetic nephropathy had higher NLR values compared to those without renal involvement [13]. The concordance between these studies and our data suggests that the relationship between inflammatory markers and renal impairment is consistent across ethnic backgrounds, although threshold values may vary slightly due to biological and environmental differences.

In this study, logistic regression confirmed that NLR remained independently associated with microalbuminuria even after adjustment for confounding variables such as age, duration of diabetes, blood pressure, and glycemic control. The stronger association of NLR compared with PLR may be explained by its closer linkage to the cellular mechanisms of inflammation. Neutrophils are key mediators of oxidative injury, while lymphocyte suppression reflects metabolic stress and impaired immune regulation [8]. This imbalance between neutrophilic activation and lymphocytic depletion represents a characteristic feature of chronic inflammatory states seen in diabetes. Platelet indices, though relevant, may also be influenced by hemostatic and metabolic variations, which could explain their relatively weaker performance [9,10].

The observed correlations of both NLR and PLR with HbA1c and serum creatinine further strengthen their clinical relevance. As glycemic control worsens, systemic inflammation tends to intensify, which is mirrored by a rise in these ratios. This association suggests that monitoring NLR could provide indirect information not only about renal function but also about overall metabolic stability. In clinical settings where advanced renal biomarkers such as cystatin C or urinary cytokine assays are unavailable, NLR offers a simple, cost-effective, and easily reproducible alternative for early risk stratification [7].

However, the findings of this study must be interpreted within its limitations. The relatively small sample size restricts the statistical power and generalizability of the results. The cross-sectional design precludes establishing temporal or causal relationships between inflammatory markers and renal dysfunction. In addition, subclinical infections, obesity, or other inflammatory conditions that were not fully excluded could have influenced leukocyte and platelet counts [23]. Despite these constraints, the study provides valuable preliminary data highlighting the potential of NLR and PLR as adjunctive markers for early renal assessment in patients with type 2 diabetes.

From a practical perspective, incorporating these inflammatory ratios into routine diabetic follow-up may help clinicians identify patients at increased risk of microalbuminuria. Regular monitoring of NLR, alongside standard biochemical parameters, could guide timely initiation of nephroprotective measures such as improved glycemic control, blood pressure regulation, and lifestyle modification. Further multicenter longitudinal studies with larger cohorts are warranted to validate these observations and to determine whether changes in NLR and PLR over time can predict progression to overt nephropathy.

CONCLUSION

The present study demonstrates that both the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are significantly associated with the presence of microalbuminuria among patients with type 2 diabetes mellitus. Elevated values of these hematologic indices reflect an underlying state of low-grade systemic inflammation that contributes to early renal endothelial injury. The diagnostic performance of NLR, particularly its higher sensitivity and specificity compared to PLR, underscores its potential utility as a simple, inexpensive, and readily available biomarker for identifying diabetic patients at risk of nephropathy. Integrating these ratios into routine clinical assessment may facilitate earlier recognition of renal involvement and timely initiation of nephroprotective therapy, thereby mitigating progression toward overt diabetic kidney disease.

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