

## Original Research Article

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# Correlation of Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio with Grades of Urine Albumin Creatinine Ratio in Type-2 Diabetes Mellitus

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### HIGHLIGHTS

1. Neutrophil-Lymphocyte ratio increases with UACR grades.
2. Platelet-Lymphocyte ratio correlates with albuminuria levels.
3. Higher UACR indicates elevated inflammatory markers.
4. NLR and PLR reflect diabetic kidney damage.
5. Increased NLR, PLR suggest worsening UACR

### ABSTRACT

This study aimed to explore the correlation between Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) with varying levels of Urine Albumin-Creatinine Ratio (UACR) in patients diagnosed with Type-2 Diabetes Mellitus, with the goal of determining the effectiveness of NLR and PLR as biomarkers for assessing the severity of diabetic nephropathy. A cohort of 200 patients with type-2 diabetes was included in the study, and they were divided into three distinct groups based on their UACR values: A1 (0-30 mg/g), A2 (30-300 mg/g), and A3 ( $\geq 300$  mg/g). The analysis revealed a significant increase in both NLR and PLR values as the severity of albuminuria worsened (NLR:  $p < 0.001$ ; PLR:  $p < 0.001$ ), indicating a strong association between higher UACR grades and elevated levels of inflammatory markers. Specifically, the study found that mean NLR and PLR values escalated markedly with increasing albuminuria; group A1 exhibited mean values of  $2.44 \pm 1.42$  for NLR and  $86.61 \pm 34.46$  for PLR, while group A3 showed substantially higher mean values of  $5.76 \pm 3.61$  for NLR and  $151.42 \pm 106.76$  for PLR. The Receiver Operating Characteristic (ROC) curve analysis further supported these findings, demonstrating that NLR had an Area Under the Curve (AUC) of 0.793, reflecting good diagnostic accuracy. At a cutoff value of 3.1, NLR achieved a sensitivity of 69.1% and a specificity of 68.4%. Similarly, PLR also showed promise as a diagnostic tool, with a sensitivity of 43.6% and a high specificity of 94.7% at a cutoff value of 123.1. These findings suggest that NLR and PLR are practical and cost-effective biomarkers for monitoring the progression of diabetic nephropathy, particularly in resource-limited settings where advanced diagnostic tools may not be readily available.

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## INTRODUCTION

Diabetes mellitus is a group of diseases characterized by high blood glucose levels, commonly referred to as blood sugar. Type 2 diabetes, is the most prevalent form of diabetes, is a condition characterized by elevated blood glucose levels, or blood sugar. Blood glucose is main source of the body energy and is derived mainly from the food we consume. Insulin, a hormone produced by the pancreas, facilitates the entry of glucose into cells, where it is used for energy. In individuals with type 2 diabetes, the body either doesn't produce sufficient insulin or is unable to use it effectively[1]. In type 2 diabetes, the body either doesn't produce enough insulin or doesn't use it effectively. As a result, excess glucose remains in the bloodstream and insufficient amount of glucose reached to the cells[2].

Diabetes mellitus (DM) is rapidly increasing across the Indian subcontinent and worldwide, posing a significant public health challenge[3]. According to the World Health Organization (WHO), the prevalence of diabetes in India is estimated to be around 9%, and this figure is expected to rise due to various factors such as urbanization, sedentary lifestyles, and changing dietary habits[4]. Among the complications associated with diabetes, diabetic nephropathy stands out as a critical microvascular complication. Diabetic nephropathy is not only a leading cause of chronic kidney disease (CKD) but also contributes significantly to cardiovascular morbidity and mortality. The pathogenesis of diabetic nephropathy is primarily driven by subendothelial inflammation and vasculopathy, which are hallmarks of the disease process[5].

The Neutrophil Lymphocyte Ratio (NLR) and Platelet Lymphocyte Ratio (PLR) are emerging as inexpensive and accessible markers of inflammation that could have significant clinical utility in monitoring diabetic complications[6]. In diabetic patients, albuminuria serves as a key indicator of endothelial inflammation, reflecting the damage to the microvasculature caused by persistent hyperglycemia. The Urine Albumin Creatinine Ratio (UACR) is a widely used marker that helps detect early kidney disease in diabetic individuals by measuring urine microalbumin levels. Normally, the amount of albumin in the urine is  $\leq 30$  mg/gm, and any value above this threshold is indicative of kidney disease, even if the estimated glomerular filtration rate (eGFR) remains within the normal range. A raised UACR is considered an early sign of kidney disease, and its progression is closely monitored in patients with diabetes to prevent further renal damage and associated complications[7].

Given the critical importance of early detection and monitoring of diabetic nephropathy, we undertook this study to investigate the potential correlation between NLR and PLR with different grades of UACR in patients with diabetic nephropathy. The goal was to explore the utility of NLR and PLR as surrogate markers for assessing the severity of diabetic nephropathy, especially in resource-limited settings where facilities for UACR estimation may not be readily available[8].

Several studies have explored the relationship between NLR,

PLR, and diabetic nephropathy, highlighting the potential of these markers in clinical practice. For instance, a study conducted by Kamrul-Hasan AB et al. on patients with Type 2 Diabetes Mellitus in Bangladesh found significantly higher NLR and PLR values in subjects with diabetic nephropathy compared to those without the condition. The study reported NLR values of  $2.16 \pm 1.1$  in patients with diabetic nephropathy versus  $1.92 \pm 0.96$  in those without ( $P=0.04$ ), and PLR values of  $115.45 \pm 57.07$  versus  $101.02 \pm 40.06$ , respectively ( $P = 0.010$ ). These findings suggest that elevated NLR and PLR could be indicative of the presence of diabetic nephropathy, potentially serving as predictive markers for this condition[9].

Another study corroborated these findings by demonstrating a significant correlation between increased NLR and PLR with diabetic nephropathy. The researchers concluded that these inflammatory markers could be effectively used as predictors and prognostic risk markers for diabetic nephropathy. This has important implications for clinical practice, particularly in settings where advanced diagnostic tools are not available, and there is a need for cost-effective, reliable markers to assess disease progression and manage patient care effectively[8].

Further supporting evidence comes from a study conducted in 2020 by Indian researchers, who evaluated the Neutrophil Lymphocyte Ratio as a marker of Diabetic Nephropathy in a cohort of 127 diabetic patients from the Indian population. This study found a significant correlation between the urinary Protein Creatinine Ratio and NLR, with a correlation coefficient ( $r$ ) of 0.813 and a  $p$ -value of 0.0001. Using a cutoff value of 7 for NLR, the researchers reported a sensitivity of 88.89% and a specificity of 94.9%, suggesting that NLR is a highly sensitive and specific marker for detecting diabetic nephropathy. These findings underscore the potential of NLR as a valuable tool in the early detection and management of diabetic nephropathy[10].

Our study aimed to investigate the correlation between NLR and PLR with different grades of UACR specifically in the Indian population. We sought to determine whether NLR and PLR could serve as effective surrogate markers for diabetic nephropathy, particularly in settings where UACR estimation is not feasible. By establishing a strong correlation between these markers and UACR grades, we hope to provide clinicians with additional tools to identify and manage diabetic nephropathy more effectively, ultimately improving patient outcomes and reducing the burden of this complication in diabetic patients.

## MATERIAL AND METHODS

This is a cross-sectional study was conducted at HIMS, Barabanki, in a tertiary care hospital in the northeastern part of UP, India. A total of 200 patients were included in the study with their prior consent and ethical clearance from the Institutional ethical committee.

## STUDY POPULATION

The study included patients with type 2 diabetes mellitus, male and female, over 25 years old, with HbA1C levels of 6.5% or higher, attending the outpatient department. Both newly diagno-

- sed patients and those already receiving treatment (oral antidiabetic drugs or insulin) were considered. Excluded were patients with Type 1 or secondary diabetes, uncontrolled hypertension (>140/90 mmHg), heart failure, urinary tract infections, conditions affecting albumin status (such as HIV, chronic liver diseases, or malignancies), diseases affecting neutrophil or lymphocyte counts (such as blood disorders, autoimmune disorders, or active infections), and pregnant or lactating women. Patients were grouped according to their UACR values into three categories: A1 (0-30 mg/g), A2 (30-300 mg/g), and A3 (≥300 mg/g), and their data were subsequently compared and analyzed.

**DATA ANALYSIS**

Patient data for the study were collected in Excel and analyzed

using the Statistical Package for Social Sciences (SPSS 28, Inc., Chicago, USA). Categorical variables were reported as numbers and percentages (%), while continuous variables were presented as mean ± standard deviation (SD) and median. For comparing quantitative variables, a Student's t-test or unpaired t-test was used for two groups, and ANOVA was applied for comparisons among three groups.

**RESULTS**

The study included 105 males and 95 females. Among males, the largest age group was 41-50 (31.5%), followed by ≤40 (30.5%), 51-60 (19.0%), and >60 (19.0%). In females, the 41-50 age group also had the most patients (31.6%), followed by ≤40 (25.3%), 51-60 (25.3%), and >60 (17.8%). The distribution of age groups between genders was not statistically significant (p>0.05).

**Table 1: NLR and PLR Among The Patients.**

	Mean±SD	Minimum	Maximum
<b>NLR</b>	4.18±3.71	0.65	32.00
<b>PLR</b>	132.03±110.03	36.86	873.02

	Age Group (Years)				P Value
	≤40 (N=44)	41-50 (N=63)	51-60 (N=56)	>60 (N=37)	
<b>NLR</b>	4.84±4.27	4.27±2.85	5.01±4.73	6.09±3.25	0.157
<b>PLR</b>	150.41±137.34	113.85±66.89	124.38±87.25	146.45±71.43	0.150

The table presents data on the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) across different age groups of patients. The overall mean NLR is 4.18±3.71, with values ranging from 0.65 to 32.00, while the mean PLR is 132.03±110.03, ranging from 36.86 to 873.02. When broken down by age groups (<40, 41-50, 51-60, and >60 years), the NLR increases with age, peaking in the >60 group

(6.09±3.25), and the PLR also shows variability, with the highest mean in the <40 group (150.41±137.34). However, the p-values (0.157 for NLR and 0.150 for PLR) indicate that these differences across age groups are not statistically significant, suggesting that there is no strong association between age and these ratios in the study population.

**Table 2: Correlations of Parameters with Type of Albuminuria Among the Patients**

Parameter	Albuminuria A1	Albuminuria A2	Albuminuria A3	P- Value
Number	19	52	19	NS
Percentage	9.5	26	64.5	NS
FBS	148.64±62.82	153.08±47.76	173.20±67.56	0.070
PPBS	212.26±75.08	241.67±82.31	273.52±99.03	0.009
RBS	204.84±55.77	217.13±66.59	229.10±76.52	0.298
HbA1c	8.53±2.59	9.03±2.18	10.35±9.11	0.406
Neutrophil Lymphocyte Ratio (NLR) Mean±SD	2.44±1.42	3.82±4.43	5.76±3.61	<0.001
Platelet Lymphocyte Ratio (PLR) Mean±SD	86.61±34.46	96.08±44.82	151.42±106.76	<0.001

The table compares various clinical parameters among patients with different levels of albuminuria (A1, A2, A3). As albuminuria severity increases from A1 to A3, both the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) also increase significantly (NLR: p <

0.001; PLR: p < 0.001), indicating a potential association between higher albuminuria levels and inflammatory markers. Fasting Blood Sugar (FBS) and Postprandial Blood Sugar (PPBS) levels are also higher in the A3 group, but only PPBS shows a statistically significant difference (p = 0.009). Other par-

ameters, like Random Blood Sugar (RBS) and HbA1c, do not show significant differences across the groups, suggesting that

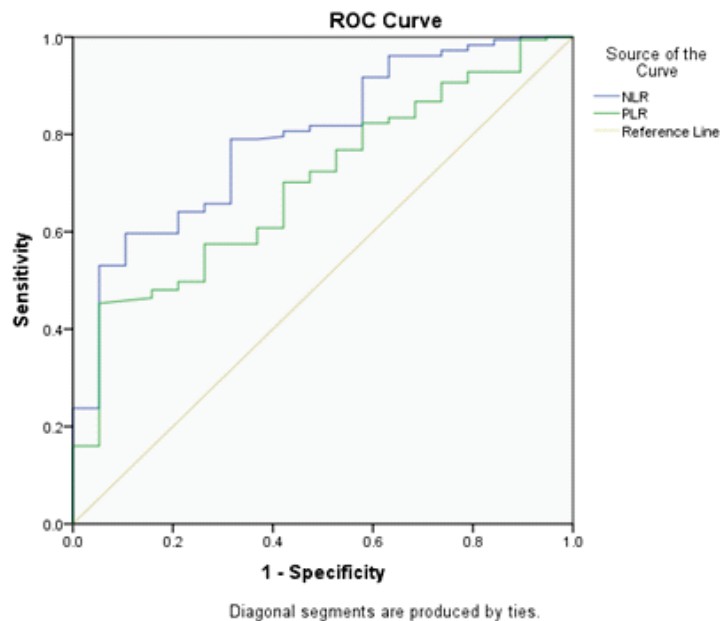
NLR and PLR are more sensitive indicators of increasing albuminuria in this cohort.

**Table 4: NLR and PLR Mean Distribution According Albumin Creatinine Ratio Grade**

		Neutrophil Lymphocyte Ratio (NLR) Mean $\pm$ SD	Platelet Lymphocyte Ratio (PLR) Mean $\pm$ SD
UACR Grade	A1	2.44 $\pm$ 1.42	86.61 $\pm$ 34.46
	A2	3.82 $\pm$ 4.43	96.08 $\pm$ 44.82
	A3	5.76 $\pm$ 3.61	151.42 $\pm$ 106.76
F Value		9.853	9.624
P Value		<0.001	<0.001

The table shows the mean distribution of the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) across different UACR (Urinary Albumin-Creatinine Ratio) grades (A1, A2, A3). As the UACR grade increases from A1 to A3, both NLR and PLR values significantly rise, indicating a trend of higher inflammatory markers with worsen-

-ing albuminuria. The F-values for both NLR (9.853) and PLR (9.624) are substantial, and the p-values are less than 0.001, confirming that the differences across the UACR grades are statistically significant. This suggests a strong association between increased albuminuria and elevated NLR and PLR levels in the study population.



**Figure 1**

The ROC curve analysis shows that the NLR has an Area Under the Curve (AUC) of 0.793, indicating good diagnostic accuracy. A low standard error of 0.049 suggests precision in the AUC estimate. The asymptotic significance of 0.000 indicates that the AUC is significantly different from 0.5, confirming strong diagnostic potential. The 95% confidence interval for the AUC ranges from 0.696 to 0.890.

## DISCUSSION

This study aimed to examine the correlation between the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) with various grades of Urinary Albumin-to-Creatinine Ratio (UACR) in the Indian population of our region. In our study, we included 105 males and 95 females, with the majority of male patients (31.5%) and female patients (31.6%) falling within the 41-50 age group. This was

followed by the  $\leq 40$  age group (30.5% in males and 25.3% in females), the 51-60 age group (19.0% in males and 25.3% in females), and the  $>60$  age group (19.0% in males and 17.8% in females). The age distribution between genders was found to be statistically non-significant ( $p > 0.05$ ), indicating no significant difference in age distribution between males and females in our cohort. This age distribution pattern is consistent with findings from previous studies by **Kahraman C et al. (2016)** and **Afsar B et al. (2014)**, which also reported that most patients were within the 40-60 age range, with the highest concentration of patients between 40-50 years, regardless of gender [11-12].

In our study, we observed the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) across different age groups of patients. The overall mean NLR was  $4.18 \pm 3.71$ , ranging from 0.65 to 32.00, while the mean PLR was  $132.03 \pm 11$



0.03, with a range from 36.86 to 873.02. When analyzed by age groups (<40, 41-50, 51-60, and >60 years), the NLR showed an increasing trend with age, reaching its highest mean in the >60 age group (6.09±3.25). In contrast, the PLR demonstrated variability across age groups, with the highest mean observed in the <40 group (150.41±137.34). Despite these trends, the p-values for NLR (0.157) and PLR (0.150) suggest that these differences are not statistically significant, indicating no strong association between age and these ratios in our study population. These findings align with those reported by **Wu Y et al. (2016)** and **Seyit M et al. (2021)** who found a similar mean NLR of approximately 5.0 and PLR around 130. Additionally, both studies noted that NLR tends to peak in patients over 60 years, and PLR shows variability, with the highest means typically found in the younger (<40 years) age group, consistent with our observations[13-14].

In our study, we compared various clinical parameters among patients with different levels of albuminuria (A1, A2, A3). We observed that as the severity of albuminuria increased from A1 to A3, both the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) also showed a significant increase (NLR:  $p < 0.001$ ; PLR:  $p < 0.001$ ). This suggests a potential link between higher albuminuria levels and elevated inflammatory markers, indicating that these ratios could be useful indicators of inflammation associated with worsening renal function. Additionally, Fasting Blood Sugar (FBS) and Postprandial Blood Sugar (PPBS) levels were higher in the A3 group, although only the PPBS differences were statistically significant ( $p = 0.009$ ). In contrast, other parameters like Random Blood Sugar (RBS) and HbA1c did not show significant differences across the albuminuria levels, highlighting NLR and PLR as more sensitive markers in this context. These findings are consistent with previous studies by **Viswanathan V et al. (2004)** and **Sun K et al. (2015)** which also reported a progressive increase in albuminuria severity from A1 to A3 and an associated rise in inflammatory markers. Both studies reinforce the idea that there is a significant association between increased albuminuria levels and inflammatory responses in patients, similar to what we observed in our cohort[15-16].

In our study, we examined the mean distribution of the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) across different Urinary Albumin-Creatinine Ratio (UACR) grades (A1, A2, A3). We found that as the UACR grade increased from A1 to A3, there was a significant rise in both NLR and PLR values. This trend suggests that higher levels of albuminuria are associated with increased inflammatory markers, reflecting a potential link between worsening renal function and systemic inflammation. The F-values for NLR (9.853) and PLR (9.624) were high, and the p-values were less than 0.001, indicating that the observed differences across UACR grades are statistically significant. This confirms a strong association between increased albuminuria and elevated levels of NLR and PLR within our study population. Our findings align with those reported by **Qin**

**B et al. (2016)** and **Sun K et al. (2015)**, which also demonstrated that as UACR grades increase, both NLR and PLR values rise significantly. These studies similarly indicated a trend of higher inflammatory markers with worsening albuminuria, supporting the idea that these ratios can serve as effective indicators of inflammation and potential renal damage progression in diabetic patients[16-17].

In our study, the ROC curve analysis revealed that the Neutrophil-to-Lymphocyte Ratio (NLR) had an Area Under the Curve (AUC) of 0.793, indicating a high level of diagnostic accuracy for detecting certain clinical conditions. The low standard error of 0.049 reflects the precision of this AUC estimate, while the asymptotic significance value of 0.000 suggests that the AUC is significantly greater than 0.5, further validating the strong diagnostic potential of NLR. Additionally, the 95% confidence interval for the AUC, ranging from 0.696 to 0.890, suggests that the observed diagnostic performance is reliable and likely to be reproducible. Our findings are consistent with those reported by **Jaaban M et al. (2021)** and **Qiao S et al. (2020)** who also found that the asymptotic significance of 0.000 indicated an AUC significantly different from 0.5, underscoring the robust diagnostic capabilities of NLR. These studies, like ours, demonstrate the potential utility of NLR as a valuable marker in clinical diagnostics, particularly for conditions where inflammation plays a critical role[18-19]. Our findings contribute to the growing body of evidence supporting the clinical utility of these ratios in predicting and monitoring renal complications in patients with type-2 diabetes mellitus.

## CONCLUSION

This study concludes that both Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) are valuable biomarkers for assessing the severity of diabetic nephropathy in patients with Type-2 Diabetes Mellitus. The significant correlation between elevated NLR and PLR values and higher Urine Albumin-Creatinine Ratio (UACR) grades suggests that these ratios effectively reflect the progression of albuminuria, a key indicator of kidney damage in diabetic patients. With good diagnostic accuracy demonstrated by the Receiver Operating Characteristic (ROC) curve analysis, particularly for NLR with an Area Under the Curve (AUC) of 0.793, these biomarkers offer practical and cost-effective tools for clinical use, especially in settings with limited access to advanced diagnostic technologies. The findings reinforce the potential of NLR and PLR to serve as reliable, accessible indicators for monitoring diabetic nephropathy, enabling earlier intervention and better management of the disease.

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