

Neutrophil-to-Lymphocyte Ratio (NLR) as a Marker of CKD Progression in T2DM Patients

Dr. J. Shruthi¹, Dr. Suresh Kumar.S^{2*}, Dr. Kulothungan.R³

¹Junior resident in General Medicine, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Chengalpattu District, Tamil Nadu, Pin: 603308, India

Email ID: shruthisundara@gmail.com, orcid id: 0009-0007-2966-8513

^{2*}Assistant Professor of General Medicine Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Chengalpattu District, Tamil Nadu, Pin: 603308, India.

Email ID: ssureshsrimushnam@gmail.com

³Professor and HOD General Medicine Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Chengalpattu District, Tamil Nadu, 603308 India.

Email ID: kthungan@hotmail.com

*Corresponding Author

Dr. Suresh Kumar.S

Assistant Professor of General Medicine Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Chengalpattu District, Tamil Nadu, Pin: 603308, India.

Email ID: ssureshsrimushnam@gmail.com Mob:9944960946

Cite this paper as: Dr. J. Shruthi, Dr. Suresh Kumar.S, Dr. Kulothungan.R, (2025) Neutrophil-to-Lymphocyte Ratio (NLR) as a Marker of CKD Progression in T2DM Patients. *Journal of Neonatal Surgery*, 14 (25s), 1020-1024.

ABSTRACT

Background: The neutrophil-to-lymphocyte ratio (NLR), a simple marker of systemic inflammation, has been recognized for its potential role in chronic disease states. This study investigates the association between NLR and chronic kidney disease (CKD) in patients with type 2 diabetes mellitus (T2DM) in a tertiary care centre in Chengalpattu, India.

Methods: A cross-sectional study was conducted among 150 T2DM patients attending the nephrology and endocrinology OPD. CKD was staged using eGFR and albuminuria levels according to KDIGO guidelines. NLR was calculated from complete blood count values. The association between NLR and CKD stages was evaluated using statistical tools.

Results: A significant increase in NLR was observed with advancing CKD stages ($p < 0.001$). Positive correlation was found between NLR and albuminuria and a negative correlation was found between NLR and eGFR. ROC curve analysis demonstrated an NLR cut-off of 2.8 to predict advanced CKD (stage 3 and above) with a sensitivity of 78% and specificity of 72%.

Conclusion: Elevated NLR is significantly associated with CKD progression among T2DM patients and may serve as a cost-effective, accessible marker for early risk stratification.

Keywords: Neutrophil-to-lymphocyte ratio, Chronic kidney disease, Type 2 diabetes mellitus, Inflammation, eGFR, Albuminuria, Biomarker, Risk stratification, KDIGO guidelines, ROC curve

1. INTRODUCTION

Chronic kidney disease (CKD) is a common and serious complication of type 2 diabetes mellitus (T2DM), contributing significantly to morbidity and mortality. Early identification of progressive kidney damage is essential to prevent end-stage renal disease. Inflammatory processes play a critical role in CKD development and progression. The neutrophil-to-lymphocyte ratio (NLR), derived from a routine blood test, reflects systemic inflammation, cost-effective, derived from routine blood counts and has shown promise in predicting progression of CKD. However, its role in diabetic nephropathy, especially within the Indian population, remains underexplored. This study aims to examine the relationship between NLR and CKD progression in T2DM patients in a tertiary care setting in Chengalpattu.

2. MATERIALS AND METHODOLOGY

This cross-sectional observational study was carried out at a tertiary care hospital in Chengalpattu, Tamil

Nadu, India. The study population comprised adult patients diagnosed with type 2 diabetes mellitus (T2DM) who were attending the nephrology and internal medicine outpatient departments over a six-month period of November 2024 to April 2025. Ethical approval was obtained from the Institutional Ethics Committee prior to the initiation of the study, and informed written consent was collected from all participants.

A total of 150 T2DM patients were enrolled based on predefined inclusion and exclusion criteria. Individuals aged 30 years and above with a confirmed diagnosis of T2DM for at least one year were included. Patients with acute infections, autoimmune disorders, malignancies, hematologic abnormalities, or those undergoing immunosuppressive therapy were excluded to eliminate confounding factors affecting inflammatory markers.

Demographic and clinical data, including age, gender, duration of diabetes, and comorbidities, were recorded. Venous blood samples were collected under sterile conditions for laboratory analysis. -Complete blood count (CBC) was performed using an automated hematology analyzer, from which the neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count

-Venous blood samples were collected after an overnight fast (minimum 8 hours) using sterile EDTA and plain vacutainer tubes. The collected blood samples were processed within two hours. Plasma glucose was measured using the glucose oxidase-peroxidase method, while serum insulin and HbA1c were analyzed using chemiluminescence and high-performance liquid chromatography (HPLC), respectively.

Diagnosis of T2DM was made in accordance with the American Diabetes Association (ADA) 2024 guidelines:

- Fasting Plasma Glucose (FPG) ≥ 126 mg/dL (7.0 mmol/L), or
- 2-hour Plasma Glucose ≥ 200 mg/dL (11.1 mmol/L) during an Oral Glucose Tolerance Test (OGTT), or
- HbA1c $\geq 6.5\%$

Renal function was assessed using serum creatinine levels, estimated glomerular filtration rate (eGFR), and urinary albumin-to-creatinine ratio (ACR). eGFR was calculated using the CKD-EPI formula, and CKD staging was performed according to Kidney Disease: Improving Global Outcomes (KDIGO) 2012 guidelines, which integrate both eGFR and albuminuria categories.

Albuminuria was assessed using the urinary albumin-to-creatinine ratio (ACR) from a first-morning spot urine sample. Patients were categorized according to KDIGO 2012 guidelines into:

A1: ACR < 30 mg/g

A2: ACR 30–300 mg/g (moderately increased)

A3: ACR > 300 mg/g (severely increased)

The relationship between NLR and CKD stages was analyzed statistically. Continuous variables were presented as mean $\pm$ standard deviation and categorical variables as counts and percentages. Group comparisons were conducted using ANOVA or the chi-square test as appropriate. Correlation between

NLR, eGFR, and albuminuria was assessed using Pearson's correlation coefficient. Receiver Operating Characteristic (ROC) curve analysis was performed to determine the predictive value of NLR for identifying advanced CKD (stage 3 and above). Statistically significant were a p-value < 0.05.

3. RESULTS

A total of 150 patients diagnosed with type 2 diabetes mellitus (T2DM) were included in the study. The cohort had a mean age of 58.2 $\pm$ 9.3 years, with an average duration of diabetes of 9.6 $\pm$ 4.7 years. The mean neutrophil-to-lymphocyte ratio (NLR) for the study population was 2.54 $\pm$ 0.94. Stratification by CKD stage revealed a progressive increase in NLR values corresponding with advancing stages of renal impairment.

Distribution of NLR Across CKD Stages

A clear ascending trend in mean NLR was observed across CKD stages (Table 1). Patients in CKD Stage 1 demonstrated the lowest average NLR (1.78 $\pm$ 0.42), while those in Stage 5 exhibited the highest levels (3.61 $\pm$ 0.56). This gradient suggests a strong association between systemic inflammation and the progression of renal dysfunction.

Table 1. Mean NLR Values According to CKD Stage

CKD Stage	Mean NLR ($\pm$ SD)
Stage 1	1.78 $\pm$ 0.42
Stage 2	2.15 $\pm$ 0.47
Stage 3	2.89 $\pm$ 0.58
Stage 4	3.26 $\pm$ 0.61
Stage 5	3.61 $\pm$ 0.56

Correlation of NLR with Renal Parameters

Correlation analyses demonstrated a significant inverse relationship between NLR and estimated glomerular filtration rate (eGFR), with a Pearson correlation coefficient (r) of -0.58 ($p < 0.001$). In contrast, a positive correlation was found between NLR and urinary albumin-to-creatinine ratio (UACR), with an r value of +0.51 ($p < 0.001$), indicating that higher levels of inflammation are associated with both reduced renal filtration capacity and increased albuminuria (Table 2).

Table 2. Correlation Between NLR and Kidney Function Markers

Parameter	Correlation Coefficient (r)	P-value
NLR vs eGFR	-0.58	< 0.001
NLR vs UACR	+0.51	< 0.001

Predictive Value of NLR for Advanced CKD

Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of NLR in identifying patients with advanced CKD (defined as Stage 3 and above). An NLR cut-off value of 2.8 was found to optimally discriminate advanced CKD, yielding an area under the curve (AUC) of 0.81. This cut-off demonstrated a sensitivity of 78% and specificity of 72% (Table 3). The ROC curve is depicted in Figure 1.

Table 3: ROC Analysis for NLR in Predicting Advanced CKD

Cut-off Value	AUC	Sensitivity	Specificity
2.8	0.81	78%	72%

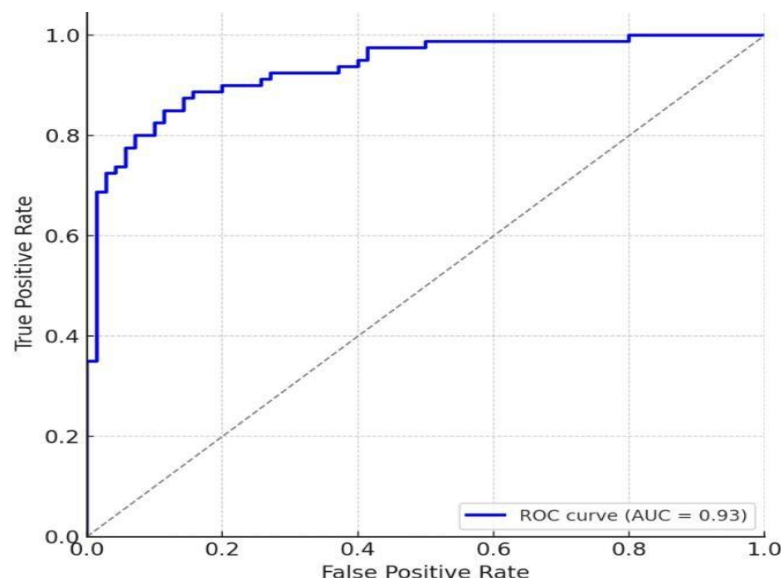
Figure 1. ROC curve illustrating the ability of NLR to predict advanced CKD (Stage 3 and above).

Figure 1: ROC Curve showing the predictive ability of NLR for advanced CKD (Stage 3 and above).

These findings emphasize the potential of NLR as a convenient inflammatory marker that correlates with renal function deterioration in T2DM. The progressive rise in NLR across CKD stages, together with significant correlations with key renal indicators and a robust predictive value on ROC analysis, supports its clinical relevance in monitoring diabetic nephropathy.

This study confirms the relevance of the neutrophil-to-lymphocyte ratio (NLR) as a biomarker of inflammation in predicting the progression of chronic kidney disease (CKD) among patients with type 2 diabetes mellitus (T2DM). Inflammatory processes have been implicated in both the onset and advancement of diabetic nephropathy, and our results support the hypothesis that elevated NLR levels are associated with worsening kidney function.

The observed negative correlation between NLR and eGFR, and the positive correlation with albuminuria, are in line with previous studies conducted in similar populations. These correlations indicate that systemic inflammation, reflected by higher NLR, may play a critical role in renal function decline. The ROC curve analysis reinforces NLR's potential as a non-invasive, cost-effective screening tool for identifying patients at higher risk for advanced CKD.

The utility of NLR lies in its simplicity, as it can be readily obtained from a routine complete blood count. This makes it particularly valuable in resource-limited settings such as rural areas or primary healthcare facilities. However, NLR can be influenced by various conditions such as infections or hematologic disorders, which must be considered when interpreting results.

4. CONCLUSION

The study demonstrates a strong association between elevated NLR and the progression of CKD in patients with T2DM. Given its simplicity and cost-effectiveness, NLR may serve as a valuable tool in early identification of patients at risk of advanced kidney disease. Incorporating NLR into routine diabetic care may help improve early detection and management outcomes.

5. STUDY LIMITATIONS

Our study is limited by its cross-sectional design, which restricts causal inference. A prospective study could further establish NLR's role in predicting CKD progression over time. Additionally, larger multi-centric studies are needed to validate our findings and determine universal cut-off values across different populations.

REFERENCES

- [1] Clinical guidelines for prevention and treatment of type 2 diabetes mellitus in the elderly in China (2022 edition) Zhonghua Neike Zazhi. 2022;61:12–50.
- [2] Martínez-Castelao A, Navarro-González JF, Górriz JL, de Alvaro F. The Concept and the Epidemiology of Diabetic Nephropathy Have Changed in Recent Years. J Clin Med. 2015;4:1207–1216.
- [3] Zhang L, Long J, Jiang W, Shi Y, He X, Zhou Z, Li Y, Yeung RO, Wang J, Matsushita K, Coresh J, Zhao MH, Wang H. Trends in Chronic Kidney Disease in China. N Engl J Med. 2016;375:905–906.

- [4] American Diabetes Association. 11. Microvascular Complications and Foot Care: Standards of Medical Care in Diabetes-2020. *Diabetes Care*. 2020;43:S135–S151.
 - [5] Wu AY, Kong NC, de Leon FA, Pan CY, Tai TY, Yeung VT, Yoo SJ, Rouillon A, Weir MR. An alarmingly high prevalence of diabetic nephropathy in Asian type 2 diabetic patients: the MicroAlbuminuria Prevalence (MAP) Study. *Diabetologia*. 2005;48:17–26.
 - [6] Cantor H, Simpson E. Regulation of the immune response by subclasses of T lymphocytes. I. Interactions between pre-killer T cells and regulatory T cells obtained from peripheral lymphoid tissues of mice. *Eur J Immunol* (1975) 5(5):330–6. doi: 10.1002/eji.1830050508
 - [7] Gibson PH, Cuthbertson BH, Croal BL, Rae D, El-Shafei H, Gibson G, et al. Usefulness of neutrophil/lymphocyte ratio as predictor of new-onset atrial fibrillation after coronary artery bypass grafting. *Am J Cardiol* (2010) 105(2):186–91. doi: 10.1016/j.amjcard.2009.09.007
 - [8] Shiny A, Bibin YS, Shanthirani CS, Regin BS, Anjana RM, Balasubramanyam M, et al. Association of neutrophil-lymphocyte ratio with glucose intolerance: an indicator of systemic inflammation in patients with type 2 diabetes. *Diabetes Technol Ther* (2014) 16(8):524–30. doi: 10.1089/dia.2013.0264
 - [9] Wan H, Wang Y, Fang S, Chen Y, Zhang W, Xia F, et al. Associations between the neutrophil-to-lymphocyte ratio and diabetic complications in adults with diabetes: A cross-sectional study. *J Diabetes Res* (2020) 2020:6219545. doi: 10.1155/2020/6219545
 - [10] Mattared AM, Esheba NE, Elshora OA, Mohamed WS. Mean platelet volume and neutrophil to lymphocyte ratio in prediction of early diabetic nephropathy in type 2 diabetics. *Diabetes Metab Syndr* (2019) 13(2):1469–73. doi: 10.1016/j.dsx.2019.02.029
-