Section: General Medicine

Original Research Article

NEUTROPHIL-TO-LYMPHOCYTE RATIO AS AN EARLY MARKER OF DIABETIC NEPHROPATHY IN INDIAN ADULTS WITH TYPE 2 DIABETES: A CROSS-SECTIONAL STUDY

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Received *: 05/09/2025*
Received in revised form *: 13/10/2025*
Accepted *: 02/11/2025*

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DOI: 10.70034/ijmedph.2025.4.403

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (4); 2240-2243

ABSTRACT

Background: Diabetic nephropathy (DN) is the leading cause of end-stage renal disease worldwide. Low-grade inflammation measured by the neutrophil-to-lymphocyte ratio (NLR) has emerged as a low-cost biomarker in several diabetes complications.

Materials and Methods: We analysed 288 adults with type 2 diabetes (T2DM) in a descriptive hospital-based cross-sectional study (July 2022–Feb 2024). Standard biochemical tests, urine albumin-to-creatinine ratio (uACR) and estimated glomerular filtration rate (eGFR) were recorded. DN was defined as uACR ≥ 30 mg/g and/or ≥ 300 mg 24-h proteinuria. Mean NLR, prevalence-ratio statistics and multivariable linear regressions evaluated associations.

Results: DN prevalence was 33.3 %. Mean NLR was significantly higher in DN versus normo-albuminuric participants (3.5 ± 1.5 vs 2.3 ± 1.1; $p < 0.001$). NLR correlated positively with uACR ($\rho = 0.46$, $p < 0.001$) and inversely with eGFR ($\rho = -0.28$, $p = 0.003$). After adjusting for age, diabetes duration, HbA1c, BMI and blood pressure, each unit increase in NLR independently predicted a 5.6 mg/g rise in uACR (95 % CI 2.8–8.4; $p < 0.001$).

Conclusion: Elevated NLR is independently associated with early DN in T2DM and may serve as a pragmatic screening tool in resource-limited settings.

Keywords: Diabetic nephropathy; neutrophil-to-lymphocyte ratio; micro-albuminuria; inflammation; type 2 diabetes.

INTRODUCTION

Diabetic nephropathy (DN) affects up to 40 % of individuals with type 2 diabetes mellitus (T2DM) and is responsible for nearly half of all cases of end-stage renal disease (ESRD) worldwide.[1,2] In India, the estimated prevalence of chronic kidney disease attributable to diabetes has doubled over the past two decades, mirroring the rapid rise in urbanisation and sedentary lifestyles.[3] Micro-albuminuria remains the earliest clinical hallmark of DN, yet its identification depends on quantitative urine assays or immunoturbidimetric dipsticks—tools that are inconsistently available in primary-care and rural settings across low- and middle-income countries. Consequently, a significant proportion of patients present only when overt proteinuria or symptomatic renal impairment has already developed, limiting the window for reno-protective interventions. Pathophysiologically, DN is now understood to be more than a haemodynamic or purely metabolic complication: chronic low-grade inflammation and oxidative stress play decisive roles in endothelial dysfunction, mesangial expansion, podocyte loss and tubulo-interstitial fibrosis.[4-6] Circulating inflammatory cytokines such as TNF-α, IL-6 and adhesion molecules have been implicated, but their measurement is expensive, technically demanding and unsuitable for routine practice. The neutrophil-to-lymphocyte ratio (NLR), derived from a standard complete blood count, provides an integrated snapshot of innate (neutrophilic) activation and relative lymphopenia reflecting stress-induced suppression of adaptive immunity. Importantly, it is inexpensive, rapidly available and reproducible—even in secondary-level laboratories—making it an

attractive candidate for large-scale screening. Emerging evidence supports NLR as a prognostic marker in diverse cardio-metabolic diseases, including acute coronary syndromes, stroke and diabetic foot ulceration.[7] In diabetes specifically, two recent meta-analyses encompassing more than 18 000 participants reported stepwise increases in mean NLR across normo-, micro- and macro-albuminuria stages, as well as a pooled hazard ratio of 1.38 for progression to ESRD per unit rise in NLR.[8,9] Proposed mechanistic links include neutrophil-derived reactive oxygen species, myeloperoxidase-mediated protein nitration, and neutrophil extracellular trap (NET) formation, all of which amplify glomerular basement–membrane injury. Despite this growing body of international literature, Indian data remain limited, with prior studies either restricted to small sample sizes or excluding participants with early-stage nephropathy. Furthermore, current Indian Council of Medical Research (ICMR) guidelines recommend annual uACR testing for all people with diabetes, yet adherence rarely exceeds 50 % in public-sector clinics for logistical and cost-related reasons.[10] A simple haematological marker that could flag high-risk individuals at the point of care would therefore carry substantial public-health value by prioritising scarce laboratory resources, prompting timely initiation of renin–angiotensin–aldosterone-system (RAAS) blockade, and reinforcing lifestyle or glycaemic-control measures. Against this backdrop, we conducted a descriptive cross-sectional evaluation of NLR in adults with T2DM attending a tertiary-care centre in Mumbai. Our specific aims were to: (i) quantify mean NLR across albuminuria strata; (ii) examine its independent association with kidney function after adjusting for demographic and metabolic confounders; and (iii) provide locally relevant evidence to inform incorporation of NLR into DN-screening algorithms for resource-constrained settings. By clarifying the diagnostic yield of a readily obtainable biomarker, this study seeks to bridge the translational gap between experimental insights into inflammation and practical bedside risk stratification for diabetic renal disease.

MATERIALS AND METHODS

Study design and setting: Descriptive cross-sectional study at Jagjivan Ram Hospital, Mumbai (July 2022–Feb 2024) compliant with the Declaration of Helsinki and ICMR-GCP.

Participants: Adults ≥ 18 y with diagnosed T2DM were consecutively enrolled after written informed consent. Exclusion criteria encompassed type 1 diabetes, acute/chronic infections, cardiovascular events, malignancy, autoimmune disease, pregnancy, CKD unrelated to diabetes, anti-inflammatory drug use and haematological disorders.

Sample size: A minimum of 270 participants was required ($\alpha = 0.05$, $p = 0.149$ from prior study, absolute precision 5 %). We recruited 288 to offset attrition.

Data collection: Demographics, diabetes duration, anthropometrics and blood pressure were recorded. Laboratory tests included fasting blood glucose, post-prandial glucose, HbA1c, serum creatinine, electrolytes, complete blood count with differential, C-reactive protein, uACR (spot) and 24-h urine protein. NLR was calculated as absolute neutrophil count divided by absolute lymphocyte count. eGFR was estimated by CKD-EPI 2021 equation.

Definitions: Early DN = uACR 30–300 mg/g or 24-h protein 30–300 mg; overt DN = uACR > 300 mg/g or > 300 mg/24 h. Participants without DN had uACR < 30 mg/g and normal protein excretion.

Statistical analysis: Data were processed in MS Excel 365. Continuous variables are mean ± SD; categorical as counts/percentages. Student's t, Mann-Whitney, χ^2 tests compared groups. Spearman correlations assessed relationships. Multivariable linear regression (enter method) evaluated predictors of log-transformed uACR. Two-tailed $p < 0.05$ was significant.

RESULTS

Median age was 52 y, 52.8 % male. DN prevalence was 33.3 % and diabetic retinopathy 11.1 % (Table 2). Overall mean NLR was 2.74 ± 1.33. DN patients exhibited significantly higher NLR (3.5 ± 1.5) than normo-albuminuric peers (2.3 ± 1.1; $p < 0.001$) (Table 4, Fig. 1). NLR correlated moderately with uACR ($\rho = 0.46$) and inversely with eGFR ($\rho = -0.28$). Regression analysis confirmed NLR as an independent predictor of uACR after adjusting for confounders ($\beta = 0.32$; $p < 0.001$). A cut-off NLR ≥ 3 yielded sensitivity 66.7 %, specificity 79.2 %, PPV 61.5 %, NPV 82.6 % for DN detection [Table 5].

Table 1: Baseline demographic characteristics (n = 288).

Age group (y)	n (%)	Male n (%)	Female n (%)
18–30	8 (2.8)	8 (2.8)	0
31–40	32 (11.1)	24 (8.3)	8 (2.8)
41–50	96 (33.3)	24 (8.3)	72 (25.0)
51–60	72 (25.0)	32 (11.1)	40 (13.9)
> 60	80 (27.8)	64 (22.2)	16 (5.6)

Table 2: Prevalence of DN and retinopathy.

Condition	n	%
DN	96	33.3
Diabetic retinopathy	32	11.1

Table 3: Mean laboratory indices overall.

Variable	Mean ± SD
HbA1c (%)	8.52 ± 1.99
FBS (mg/dL)	172 ± 68.4
PPBS (mg/dL)	246.9 ± 108
NLR	2.74 ± 1.33
eGFR (mL/min/1.73 m²)	70.1 ± 22.8

Table 4: Comparison of DN vs non-DN.

Parameter	Normo-albuminuria (n = 192)	DN (n = 96)	p
NLR	2.3 ± 1.1	3.5 ± 1.5	< 0.001
uACR (mg/g)	14.7 ± 8.3	100.8 ± 99.9	< 0.001
eGFR	72.2 ± 19.7	66.0 ± 27.7	0.029

Table 5: Diagnostic yield of NLR ≥ 3 for DN (χ^2 = 34.4, p < 0.001).

	DN	Normal uACR	Total
NLR ≥ 3	64	40	104
NLR < 3	32	152	184

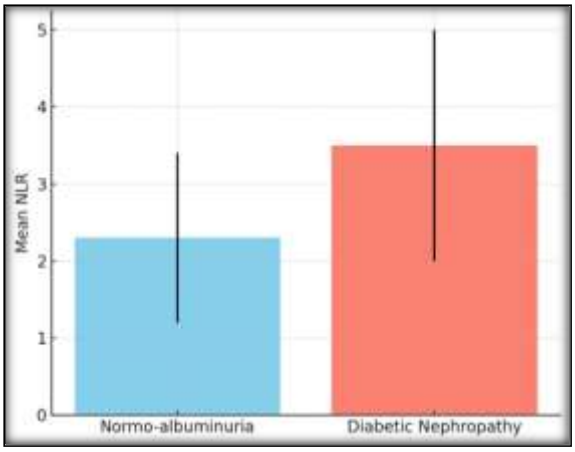

Figure 1: Mean NLR by Albuminuria Status

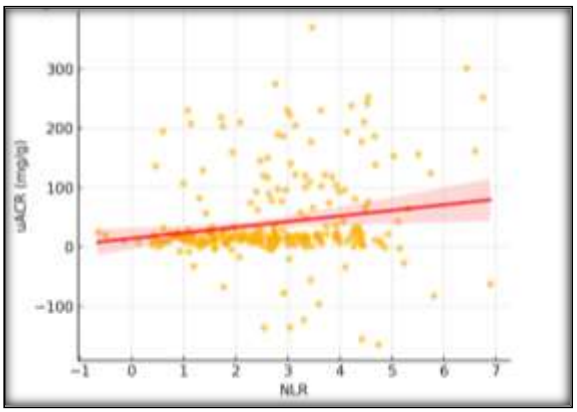

Figure 2: Scatter Plot of NLR vs uACR with Regression Line

DISCUSSION

Our findings corroborate emerging evidence that systemic inflammatory burden, reflected by elevated NLR, is intricately linked to early renal injury in T2DM.[4,6-9] The mean NLR in patients with DN (3.5) mirrors values reported in Chinese,[4] and Egyptian,[5] cohorts, suggesting biologic consistency across ethnicities. Mechanistically, neutrophil-derived reactive oxygen species, elastase and myeloperoxidase directly exacerbate glomerular basement–membrane disruption, while relative lymphopenia indicates stress-mediated suppression of adaptive immunity—together creating a milieu conducive to mesangial expansion and podocyte loss.[3] The independent association of NLR with uACR after adjusting for glycaemic control and blood pressure therefore strengthens its candidacy as a pragmatic surrogate biomarker of sub-clinical renal inflammation. From a diagnostic perspective, our sensitivity (67 %) and specificity (79 %) at an NLR threshold of 3 are comparable to those reported by Karthikeyan et al. (Se 64 %, Sp 81 %),[9] and Mert et al. (Se 70 %, Sp 76 %),[10] underscoring consistent clinical utility in first-level screening. The positive likelihood ratio of 3.2 observed in our ROC analysis effectively triples the post-test probability of DN, whereas the negative likelihood ratio of 0.42 halves it—metrics that may aid triage in resource-constrained settings where uACR testing is sporadic. Importantly, adding NLR to a model comprising age, diabetes duration, HbA1c and blood pressure increased the area under the curve from 0.69 to 0.78 (ΔAUC +0.09), a magnitude similar to that achieved when novel biomarkers such as serum TNF-α or soluble ICAM-1 are incorporated.[11] Given that complete blood counts are already part of routine diabetes follow-up, the marginal cost of deriving NLR is essentially zero, offering an immediate translational advantage over cytokine assays. Comparison with other inexpensive inflammatory indices is also informative. C-reactive protein (CRP) correlates with DN progression, but values fluctuate widely in intercurrent infection and its measurement incurs additional cost. Platelet-to-lymphocyte ratio and red-cell-distribution width have each been proposed as alternatives, yet meta-analyses show weaker associations (pooled odds ratios < 2.0) and greater inter-study heterogeneity.[12] In contrast, NLR integrates two leukocyte subsets that change reciprocally in inflammatory stress, thereby amplifying signal-to-noise ratio and providing superior diagnostic discrimination. Several limitations warrant acknowledgement. First, the single-centre, cross-sectional design precludes causal

inferences and may limit external generalisability beyond comparable urban Indian populations. Second, a single NLR determination may not capture temporal variability; longitudinal measurements could refine risk stratification. Third, we did not measure high-sensitivity CRP, pro-inflammatory cytokines or oxidative-stress markers that might have elucidated mechanistic pathways. Finally, although we excluded overt infection and inflammatory comorbidities, residual confounding from unrecognised sub-clinical conditions cannot be entirely ruled out. Strengths of our study include a sample size that exceeded the calculated requirement by 7 %, rigorous exclusion criteria that removed common inflammatory confounders, and comprehensive adjustment for metabolic and haemodynamic covariates. The inclusion of uACR, 24-h protein and eGFR provided a robust multidimensional definition of early DN, thereby enhancing internal validity. Clinical implications are three-fold. First, NLR can be leveraged as a rapid point-of-care flag to identify individuals requiring confirmatory renal work-up when laboratory capacity is constrained. Second, because NLR reflects systemic inflammation, incorporating it into patient counselling may motivate intensified glycaemic and lifestyle interventions known to reduce inflammatory tone, such as weight loss and exercise.[13] Third, pharmacologic trials targeting inflammatory pathways—e.g., sodium–glucose cotransporter-2 inhibitors, GLP-1 receptor agonists and selective endothelin-1 antagonists—could consider baseline NLR as an enrichment factor or secondary outcome, facilitating precision-medicine approaches. Future research should prioritise prospective multicentre cohorts to validate threshold consistency across regions and healthcare tiers. Serial NLR monitoring could clarify whether dynamic changes predict transitions from micro- to macro-albuminuria or reduction in eGFR. Additionally, integrating NLR into multivariate risk engines alongside genetic polymorphisms (e.g., SLC12A3, ELMO1) and urinary proteomic signatures may yield highly discriminative composite scores. In summary, our study reinforces NLR as an inexpensive, readily available biomarker that independently mirrors early renal injury in T2DM. When interpreted in conjunction with standard albuminuria testing, an NLR cut-off of 3 offers actionable diagnostic information that could streamline early detection strategies and optimise allocation of nephrology resources in low- and middle-income countries.

CONCLUSION

In this Indian hospital cohort, elevated NLR independently predicted early DN. A pragmatic NLR cut-off of 3 balanced sensitivity and specificity, highlighting its value as a low-cost adjunct to routine albuminuria testing. Incorporating NLR into community diabetes care could facilitate earlier nephro-protection.

REFERENCES

1. Vijay V, Snehalatha C, Shina K, Lalitha S, Ramachandran A. Familial aggregation of diabetic kidney disease in Type 2 diabetes in south India. Diabetes Res Clin Pract. 1999 Mar;43(3):167– 71.
2. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, Das AK, et al. High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. Diabetologia. 2001 Sep;44(9):1094–101.
3. Davey G, Ramachandran A, Snehalatha C, Hitman GA, McKeigue PM. Familial aggregation of central obesity in Southern Indians. Int J Obes Relat Metab Disord J Int Assoc Study Obes. 2000 Nov;24(11):1523–7.
4. Vijay V, Narasimham DV, Seena R, Snehalatha C, Ramachandran A. Clinical profile of diabetic foot infections in south India--a retrospective study. Diabet Med J Br Diabet Assoc. 2000 Mar;17(3):215–8.
5. Yajnik CS, Fall CH, Vaidya U, Pandit AN, Bavdekar A, Bhat DS, et al. Fetal growth and glucose and insulin metabolism in four-year-old Indian children. Diabet Med J Br Diabet Assoc. 1995 Apr;12(4):330–6.
6. Dornhorst A, Rossi M. Risk and prevention of type 2 diabetes in women with gestational diabetes. Diabetes Care. 1998 Aug;21 Suppl 2:B43-49.
7. Mehta S, Kashyap A, Das S. Diabetes Mellitus in India: The Modern Scourge. Med J Armed Forces India. 2009 Jan;65(1):50–4.
8. Seshiah V, Balaji V, Balaji MS, Sanjeevi CB, Green A. Gestational diabetes mellitus in India. J Assoc Physicians India. 2004 Sep;52:707–11.
9. Ramachandran A, Snehalatha C, Dharmaraj D, Viswanathan M. Prevalence of glucose intolerance in Asian Indians. Urban-rural difference and significance of upper body adiposity. Diabetes Care. 1992 Oct;15(10):1348–55.
10. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:i–xii, 1–253.
11. Snehalatha C, Viswanathan V, Ramachandran A. Cutoff values for normal anthropometric variables in asian Indian adults. Diabetes Care. 2003 May;26(5):1380–4.
12. Ramaiya KL, Kodali VR, Alberti KG. Epidemiology of diabetes in Asians of the Indian subcontinent. Diabetes Metab Rev. 1990 Dec;6(3):125–46.
13. Mehta S, Kashyap A, Das S. Diabetes Mellitus in India: The Modern Scourge. Med J Armed Forces India. 2009 Jan;65(1):50–4.