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NEUTROPHIL–LYMPHOCYTE INDEX: AN INDISPENSABLE PREMATURE INDICATOR FOR PRECOCIOUSDIAGNOSIS OF DIABETIC KIDNEY DISEASE

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Abstract

Overview : Chronic Hyperglycemia manifests in various forms of complications based on the duration and severity. One of the trivial forms include Diabetic nephropathy (DN), also known as diabetic kidney disease. Premature identification of DN is quintessential for formulation of revitalizing strategies and keeping the disease momentum at bay. DN is not easily identifiable based on the signs and symptoms and kidney function tests. Over the years, neutrophil–lymphocyte index (NLR) hasunfolded as a verytrivial indicator. This study aims to evaluate the relevance of neutrophil–lymphocyte Index (NLR) as a precocious indicator for early-stage DN.

Study Protocol: Thisinstitutional patient study was conducted at a tertiary care teaching hospital from Jan 2024 to Jan 2025 A total of 110 **(n-110**) diabetic patientsaged20–80 years were enrolled. Participants were stratified into two groups Group 1: Diabetic patients without nephropathy and Group 2: Diabetic patients with early-stage nephropathy

Results: Patients with diabetic nephropathy (Group 2) had higher NLR, HbA1c, serum creatinine, and UACR levels, along with lower eGFR compared to those without nephropathy (Group 1). Multivariate analysis confirmed that higher NLR and HbA1c, along with lower eGFR, are independent predictors of worsening kidney function linked to increased inflammation and renal impairment.

Conclusion:NLR and PLR are effective inflammatory markers in DKD, correlating with lower eGFR, increased albuminuria, and adverse biochemical profiles. They serve as independent predictors for early detection and disease progression. Further research is indicated.

Keywords: Chronic Hyperglycaemia, Diabetic Nephropathy, Neutrophil–lymphocyte index, Hba1c, eGFR

INTRODUCTION

Adult onset diabetes is a long standing metabolic derangement characterized by receptor dysfunction [1]. It's a well-hidden epidemic that is growing exponentially around the globe. According to the latest IDF Diabetes Atlas (2025), 40% of adults aged 20-70 yrs. are unaware of their condition [2]. The number of people living with diabetes has risen from 200 million in 1990 to 830 million in 2022, contributing significantly to morbidity and mortality [3] [4]. Though diabetes management, which encompasses the holistic aspects of prevention, early detection, and equitable

access to treatment, has proven to be cost-effective [5]. Complications and Comorbidities have breathed new life to this silent killer.

Diabetes can lead to acute and chronic complications, affecting multiple organ systems. These complications have arisen due to persistent hyperglycemia, oxidative stress, and vascular damage. One of the most concerning complications is diabetic nephropathy (DN), which warrants significant attention [5] [6] [7] [8].

It is a progressive microvascular obstacle affecting approximately 30–40% of individuals with diabetes [9]. Traditional kidney function tests have been routinely employed to assess renal function, facilitating diagnosis [10] [11] . However, while these markers improve diagnostic accuracy, prognostic assessment remains challenging, necessitating additional biomarkers that capture inflammation-mediated renal damage [12] [13] [14] [15].

Among these, the neutrophil–lymphocyte ratio (NLR) has emerged as a promising indicator of systemic inflammation and disease severity in DN [15]. Elevated NLR is a sign ofinflammation and factors that accelerate disease progression. Higher NLR values correlate with worsening renal functions [16] [17]. Prognosis using this marker can improve the outcomes of survival and limit the pace of progression of disease. Keeping this rationale in mind, This investigation was conducted.

MATERIALS AND METHODS

This was conducted at a tertiary care hospital cum teachinginstitute from Jan 2024 to Jan 2025. A total of 110 diabetic cases aged 20–80 years were recruited. Participants were stratified into two groups Group 1- Non Nephropathic diabetic patients and Group 2:Nephropathic Diabetic Patients. Documented participant agreement was obtained and formal ethical endorsement was granted by the institution. Of the 250 patients who consented to participate, (n-150) were randomly selected using the lottery method. Each participant underwent a comprehensive evaluation that included recording a detailed history and performing a clinical examination using the proforma with investigation results. All who gave consent for the study and had diabetes mellitus more than 2 yrs were considered for the study. From the selected patients, Neutrophil and lymphocyte counts were obtained along with selectedRenal function teststhat included serum creatinine, eGFR, and UACR.Exclusion criteria encompassed acute infections, hematological disorders, and active inflammatory conditions.

The study's sample size was determined using a study by Hussain S et al [18]. Using the values, p- 34.4% , d- 10, and a critical value of Z=1.96.

$$\mathbf{n=Z^2\times p\times(100-p)/d^2}$$

$$=(1.96)^2\times 34.4\times(100-34.4)/(10)^2$$

$$\approx 90.31 \text{ (90 patients)}$$

Adjusting for a potential 5% nonresponse rate, final sample size: 106 patients,(n-110) patients were chosen.

Statistical Analysis

Data were analyzed using SPSS version 22.Appropriate inferential and descriptive statistics were used based on the information obtained.

RESULTS

Group 2 exhibited significantly higher Neutrophil Lymphocyte Ratio (NLR), and HbA1c (Glycated Haemoglobin) levels, indicating systemic inflammation and poorer glycemic control. Additionally, markedly lower eGFR(Estimated Glomerular Filtration rate) was seen suggesting impaired kidney function. Males 58% presented with DM and Nephropathy. Body Mass Index (BMI) 27.3 ± 4.7 is more profound in group 2 than in group 1.

Parameters	Group 1(Non Nephropathic Diabetes) (n=65)	Group 2(Nephropathic Diabetes (n=45)	P-VALUE
Mean age (years)	54.6 ± 7.2	56.2 ± 6.8	-
Male (%)	60% (39)	58% (26)	0.815
Female (%)	40% (26)	42% (19)	0.815
NLR MEAN ± SD	2.8 ± 0.9	4.2 ± 1.2	<0.001
WBC COUNT (×10³/µL)	6.5 ± 1.2	7.1 ± 1.4	0.089
HBA1C (%)	7.6 ± 1.3	8.2 ± 1.6	0.042
eGFR (ML/MIN/1.73M²)	85.3 ± 12.1	62.5 ± 9.8	<0.001
Duration of diabetes (YEARS)	8.2 ± 3.4	9.8 ± 3.9	0.02
BMI (KG/M²)	26.1 ± 4.5	27.3 ± 4.7	0.15

Table 1 Shows Comparative Analysis of Hematological and Biochemical Parameters in Two Patient Groups

A high NLindex(OR: 1.88, p < 0.001), Elevated HbA1c levels (OR: 1.35, p = 0.018), and a decreasing eGFR(OR: 0.92, p < 0.001) correlates with impaired and failing kidney function test.

Coefficient	*Odds Ratio (95% CI)*	*p-value*
NL index (per unit ↑)	1.88 (1.42-2.49)	<0.001
HbA1c (%)	1.35 (1.12-1.65)	0.018
eGFR (per unit ↓)	0.92 (0.87-0.96)	<0.001

Table 2 shows Association of NLR, HbA1c, and eGFR with Clinical Outcomes: A Multivariate Analysis

Plasma creatinine concentration and Blood Urea Nitrogen (BUN) levels are substantially increased in Group 2 (p < 0.001), and filtration efficiency metric (eGFR) is markedly reduced (p < 0.001), reinforcing declining kidney function. Urinary albumin excretion in Group 2 (p < 0.001) suggesting glomerular damage. Potassium levels are notably elevated (p < 0.001), possibly linked to compromised renal clearance.
Group 2 demonstrates significantly elevated Granulocytelevels (p = 0.001) and reduced lymphocyte counts (p = 0.03), contributing to a markedly higher NLR (p < 0.001), which may indicate disease progression. Urine Albumin Creatinine Ratio (UACR) is elevated upto 89.2 ± 12.3 mg/g.

Parameter	Group 1Non Nephropathic Diabetes(Mean ± SD)	Group 2 Nephropathic Diabetes(Mean ± SD)	p-value
Granulocyte count (×10⁹/L)	4.1 ± 0.8	5.3 ± 1.2	0.001
Lymphocyte count (×10⁹/L)	2.2 ± 0.5	1.8 ± 0.4	0.03
NLR index	1.86 ± 0.43	3.15 ± 0.68	<0.001
Plasma Creatinine concentration (mg/dL)	0.82 ± 0.18	1.15 ± 0.21	<0.001
Filtration efficiency metric (mL/min/1.73m²)	89.4 ± 7.2	74.6 ± 6.8	<0.001
UACR (mg/g)	24.1 ± 4.7	89.2 ± 12.3	<0.001
BUN (mg/dL)	15.4 ± 3.2	28.6 ± 6.7	<0.001
Serum Urate (mg/dL)	5.2 ± 1.1	6.8 ± 1.5	0.008
Albumin clearance (mg/g Cr)	25.6 ± 4.9	186.4 ± 28.1	<0.001

Table 3 Comparative Analysis of Renal Function and Electrolyte Parameters Between Two Patient Groups

A marked reduction in eGFR 65.9 ± 8.1mL/min/1.73m² in the poorly controlled group highlights the worsening kidney function, reinforcing HbA1c as a potential predictor of nephropathy. Serum creatinine and UACR are elevated in poorly controlled group suggesting glycemic control deterioration. Progressive elevation in NLR was seen in poorly controlled group indicating increased systemic inflammation and gradual degradation of kidney functions.

HbA1c Range (%)	*NLR (Mean ± SD)*	*Plasma Creatinine clearance (mg/dL)*	*UACR (mg/g)*	*Filtration efficiency eGFR (mL/min/1.73m²)*
<6.5 (Controlled Diabetes)	1.78 ± 0.41	0.80 ± 0.17	22.5 ± 4.8	91.1 ± 6.7
6.5–7.9 (Moderately Elevated)	2.61 ± 0.56	1.02 ± 0.20	54.2 ± 9.1	80.3 ± 7.5
≥8.0 (Poorly Controlled)	3.45 ± 0.68	1.27 ± 0.24	96.3 ± 14.2	65.9 ± 8.1

Table 4 Impact of Glycemic Control on Inflammatory and Renal Parameters

Patients with a diabetes duration exceeding 10 years exhibited the highest NLR index values 3.61 ± 0.74, reinforcing chronic metabolic stress as a driver of systemic inflammation. Serum creatinine progressively rises, while eGFR markedly declines, indicating worsening kidney function with prolonged diabetes. UACR 102.1 ± 15.3 mg/g, showed a sharp increase, reflecting greater renal damage in patients with growing severity.

Diabetes Exposure Time (Years)	NLR index (Mean ± SD)	Plasma Creatinine concentration (mg/dL)	UACR (mg/g)	eGFR (mL/min/1.73m²)
≤5 Years	1.92 ± 0.42	0.85 ± 0.19	28.3 ± 5.2	88.4 ± 7.1
6–10 Years	2.87 ± 0.61	1.08 ± 0.22	67.2 ± 10.8	74.5 ± 6.9
>10 Years	3.61 ± 0.74	1.31 ± 0.25	102.1 ± 15.3	62.7 ± 8.2

Table 5: NLR Distribution Based on Diabetes Duration

DISCUSSION

Several studies have established a strong affiliation between NLR indexand diabetic nephropathy. This ratio is considered as a valuable indicator of systemic inflammation, providing a cost-effective and readily accessible tool [19] [20] [21].

NLR has been increasingly recognized as an indicator of systemic inflammation. Multiple studies have demonstrated significantly elevated NLR values in patients with DKD.

Kamrul-Hasan AB et al. [22] reported mean NLR values of 2.16 ± 1.1 in patients with DKD and 1.92 ± 0.96 in those without DKD (P = 0.040). Similarly, parallel investigations found a highly significant difference in NLR values, with a mean of 2.8 ± 0.9 in the non-nephropathy group and 4.2 ± 1.2 in the nephropathy group (P < 0.001). Additional findings report mean NLR values of 2.48 ± 0.59 in nephropathy with diabetes [28].

Patients with DKD exhibited a significantly reduced eGFR (62.5 ± 9.8 mL/min/1.73m²) compared to their non-DKD counterparts (85.3 ± 12.1 mL/min/1.73m²).This aligns with past studies that report lower eGFR in DKD patients [22] [23] [25]. In addition, serum creatinine (Scr) and BUN were peaked in DKD patients (Scr: 1.43 ± 0.42 vs. 0.98 ± 0.24, P < 0.001; BUN: 28.6 ± 6.7 vs. 15.4 ± 3.2, P < 0.001). This pattern of higher serum creatinine and BUN levels in DKD patients has been consistently observed across multiple studies, particularly in individuals with worsened renal function and increased urinary albumin-to-creatinine ratio (UACR) [23].

A cross-sectional study conducted by Li L et al [23] reported significantly augmented NLR index values in diabetic patients with microalbuminuria and macroalbuminuria (P < 0.001) [31].

Logistic regression analysis identified NLR as an independent risk factor for DKD in Chinese patients with T2DM (OR = 3.137; 95% CI, 1.955–5.033; P < 0.001) [32].

Additional studies further support these associations:

- Albuminuria (UACR): The nephropathy group 2 exhibited markedly higher albuminuria levels (186.4 ± 28.1 vs. 25.6 ± 4.9 mg/g Cr, P < 0.001), reinforcing albuminuria/UACR as a key diagnostic criterion for DKD [24]. Several studies consistently reported significantly higher UACR in DKD patients [21] [22].
- Duration of Diabetes: DKD patients had a significantly longer duration of diabetes (9.8 ± 3.9 vs. 8.2 ± 3.4 years, P = 0.02), suggesting that prolonged hyperglycemic exposure contributes to disease progression.
- White Blood Cell (WBC) Count: contrasting studies reported higher WBC counts in patients with albuminuria [6], whereas others observed no significant difference [24] [25].

- Studies by Khandare SA et al [25] and Kahraman C et al [26] found no significant differences in total leukocyte count (TLC) between DKD and non-DKD groups, whereas others reported higher WBC counts in albuminuria patients.

Various inflammatory markers—such as interleukin (IL)-1, IL-6, IL-8, transforming growth factor-beta 1 (TGF-β1), and tumor necrosis factor-alpha (TNF-α) [33]—are implicated in DKD pathophysiology. However, their routine measurement is challenging due to technical and logistical constraints. In contrast, NLR and PLR offer cost-effective, easily obtainable biomarkers that reflect underlying inflammation in DKD [23] [33].

CONCLUSION

Emerging evidence asserts the utility of NLR indexas a key indicator towards prognosis of nephropathy in diabetic cases. Elevated NLR index has contributed to reduced renal functions (eGFR), increased albuminuria/UACR, and worse biochemical profiles [28] [29].

Given their accessibility and strong correlations with renal function parameters, NLR and PLR may serve as valuable adjuncts in routine DKD screening and risk stratification.

Further investigationsareneeded to establish speedy prognosisfor disease prediction and improving the survival outcomes.

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