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White Blood Cell Ratios are an Indicators for Diabetic Nephropathy among Sudanese with Type 2 Diabetes

Samia Saeed Ahmed[1], M. A. Adris[2]

[1]Basic Medical Sciences Department, Al-Rayan National College of Health Sciences, Al-Rayan National Colleges, Al-Madinah Al-Munawwarah, Saudi Arabia
Email: *ss.ahmed[at]amc.edu.sa.*

[2]Department of Biochemistry, Faculty of Medicine, University of Al-butana, Rifaa, East Gezira State, Sudan
Email: *maidris71[at]gmail.com*

Abstract: ***Background: Diabetic nephropathy is one of the most serious microvascular complications of diabetes mellitus, and a major cause of chronic kidney disease (CKD) globally. Inflammation is implicated in its pathogenesis. More recently, easy inflammatory indices from CBC such as PLR (platelet-to-lymphocytes ratio), NLR (neutrophil-to-lymphocyte ratio) and MLR (monocyte-to- lymphocyte ratio) have been proposed as potential biomarkers. Aim: To analyze the correlation of PLR, NLR and MLR with diabetic nephropathy and estimate their diagnostic values in diabetes mellitus (DM) patients. Methods: In this cross-sectional study, a total of 150 subjects were recruited and divided into three groups: healthy control (Group A), diabetic patients without nephropathy (Group B) and diabetic nephropathy group (Group C) containing 50 subjects each. Clinical information and laboratory analyses such as urine albumin/creatinine ratio and indicators of inflammation (PLR, NLR, MLR) were recorded. Spearman's rank correlation test was performed to analyze correlations. Receiver operating characteristic (ROC) curve analysis was used to determine the diagnostic efficacy of markers under study. Results: Inflammatory markers were significantly higher in patients with diabetic nephropathy versus diabetics without nephropathy and controls ($p < 0.001$). The UACR had a significant positive association with PLR, NLR and MLR, especially in DN group. Among the measured parameters, MLR had the closest relationship with UACR. ROC curve analysis revealed that MLR had the most accurate diagnostic performance for diabetic nephropathy (AUC = 0.83) (76% sensitivity and 74% specificity), which differed significantly compared with PLR and NLR ($p < 0.001$).***

Keywords: Diabetes, Nephropathy, PLR, NLR, MLR. Type 2 DM

1. Introduction

Diabetes mellitus represents one of the most significant global public health challenges, with a continuously rising prevalence. According to the International Diabetes Federation, approximately 10.5% of the adult population worldwide was affected by diabetes in 2024, and this proportion is projected to increase to 12.2% by 2045 (1). The growing burden of diabetes has been accompanied by an increase in chronic complications, particularly diabetic kidney disease (DKD), which substantially contributes to morbidity, mortality, and healthcare costs (2).

Diabetic kidney disease is a common microvascular complication affecting nearly 40% of individuals with diabetes and remains the leading cause of end-stage kidney disease globally, accounting for approximately 30–50% of cases. DKD is clinically defined by persistent albuminuria (urine albumin-to-creatinine ratio ≥30 mg/g) and/or a reduction in estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m²) for more than three months, in the absence of other causes of kidney damage in patients with diabetes (3,4). Early identification of renal dysfunction is critical for delaying disease progression; however, conventional biomarkers such as serum creatinine are limited by their dependence on muscle mass, age, and sex, and often fail to detect early declines in renal function.(3).(4).

2. Methods

Study design
This is a cross-sectional study was conducted between 2023-2025 in Gazira hospital for renal diseases. Wad-Madani, Sudan, the study aimed to evaluate WBCs ratios as an early diagnostic biomarker of diabetic kidney disease (DKD) in patients with type 2 diabetes mellitus (T2DM).

Inclusion and exclusion criteria

Inclusion criteria were adults aged 40-60 years, confirmed diagnosis of type 2 diabetes mellitus based on the American Diabetes Association criteria, and willingness to participate with written informed consent.

- Sudanese patients' age range (40-60 years old), who agreed to participate in the study.
- T2DM without chronic kidney disease.
- T2DM with chronic kidney disease.

Exclusion criteria i

- Known non-diabetic kidney disease
- Acute kidney injury
- Patients suffer from acute or chronic inflammatory or autoimmune diseases, endocrine disorders and hepatic disease.
- Active infection or malignancy
- Pregnancy
- Use of nephrotoxic medications

Data Collection

Demographic and clinical data were collected through face-to-face structured interviews using a standardized questionnaire. Collected variables included age, sex, occupation, marital status, smoking status, physical activity, duration of diabetes, and medical history (hypertension, cardiovascular disease, and medication use).

Blood pressure was measured using a calibrated sphygmomanometer after at least 5 minutes of rest, and body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

Blood sample collection and laboratory analysis
Venous blood samples were collected in the early morning after an overnight fast of 8–10 hours. Samples were processed according to standard laboratory procedures.

The following biochemical parameters were measured:
Fasting blood glucose (FBG), Glycated hemoglobin (HbA1c), Serum creatinine, Complete blood count (CBC), urine albumin and urine creatinine

3. Results

Baseline characteristics of the studied groups:
One hundred and fifty subjects were included in the study, and they were equally divided into three groups of 50 patients each; (A) a normal control group, (B) a diabetes mellitus without nephropathy and (C) diabetic nephropathy group.

There was no significant difference between the groups in terms of age and sex distribution ($p > 0.05$). But there were extremely significant differences in the course of DM, systolic pressure, Cr, eGFR, UA level, UACR, HbA1c level and fasting glucose as well as PLR, NLR and MLR ($p < 0.001$ for all), which were demonstrated in Table 1.

Diabetic nephropathy patients (Group C) presented with office serum creatinine, urine albumin/creatinine ratio, HbA1c, fasting blood sugar and inflammatory markers that were significantly higher than those without nephropathy (Group B) and normal controls and eGFR was found to be significantly reduced as shown in table (1) below.

Table 1: Characteristics of the three groups

Characteristics	Normal group(A) N=50		Diabetic group(B) N=50		Diabetic nephropathy group (C) N=50		p- value
	Mean	SD	Mean	SD	Mean	SD	
Age	51.76	7.13	53.64	6.70	53.86	6.71	NS
Gender	F (48%), M (52%)		F (52%), M (48%)		F (54%), M (46%)		NS
Duration of DM	0.00	0.00	6.68	2.63	6.90	2.55	0.000*
SBP	120.86	7.82	127.60	10.65	127.80	10.97	.001*
DBP	81.70	5.35	83.80	14.02	83.60	13.85	.619
serum creatinine	0.68	0.13	1.94	0.75	2.36	0.89	.000*
cr eGFR	135.02	23.90	101.58	11.88	47.96	14.33	.000*
serum uric acid	3.16	0.70	6.36	1.37	3.83	1.29	.000*
Urine/albumin/creatinine ratio	10.54	5.48	39.96	26.42	265.86	157.22	.000*
HbA1c%	3.89	0.95	8.29	2.42	8.82	1.82	.000*
fasting blood sugar	84.74	10.89	156.42	61.19	139.10	48.85	.000*
PLR	88.84	55.50	82.33	31.72	108.10	56.78	.027*
NLR	1.30	1.07	1.52	1.08	1.93	1.56	.042*
MLR	0.13	0.06	0.34	0.50	1.27	0.79	.000*

Table 1 shows that there is no significant difference between the three groups regarding initial characteristics which are age and gender while there is a significant difference regarding all measurements and clinical blood tests(pvalue<0.001).

Comparison of inflammatory markers among groups
Urinary albumin/creatinine ratio increased significantly in a progressive and striking manner from Group A [9.7 (IQR: 6.9–14.6)] to B [29 (IQR: 20.7–60)], with the highest median value being recorded in the group C [240 (IQR: 150–320)].

For the PLR, it was observed that group C showed the highest median [91.4 (63–161)], while group B demonstrated the lowest one [77.7 (62–99)] and group A presented intermediate values [88.2 (41–126)].NLR was rather high in Group C [1.2 (IQR: 0.81–2.9)], compared with Groups A and B, both documenting similar median value at 1.1.

In addition, group C showed a significant increase in MLR [1.1 (IQR: 0.78–1.5)] when compared with that of group B [0.12 (IQR: 0.09–0.19)] and A [0.1 (IQR: 0.09–13)], suggesting an inverse relationship with the stage of diabetic nephropathy severity as shown in (Table 2) below.

Table 2: Comparison of clinical blood tests data between Groups

Variables		Normal group (A) (n=50)	Diabetic group (B) (n=50)	Diabetic nephropathy group (C) (n=50)
Urine/albumin/ creatinine ratio	Median (IQR)	9.7(6.9-14.6)	29(20.7-60)	240(150-320)
	Min- Max	2.1-22	10-100	50-700
PLR	Median (IQR)	88.2(41-126)	77.7(62-99)	91.4(63-161)
	Min- Max	0.9-241	26-170	26-226
NLR	Median (IQR)	1.1(0.69-1.5)	1.1(0.76-2.1)	1.2(0.81-2.9)
	Min- Max	0.26-5.5	0.03-4.9	0.12-5.9
MLR	Median (IQR)	0.1(0.09-0.13)	0.12(0.09-0.19)	1.1(0.78-1.5)
	Min- Max	0.05-0.36	0.0-2.1	0.03-3.8

Diagnostic performance of inflammatory markers

The ROC curve analysis demonstrated that the MLR had the best diagnostic accuracy to identify diabetic nephropathy patients (AUC: 0.83; sensitivity: 76%; specificity: 74%) at a cutoff value of 0.13.

PLR and NLR, however, had relatively lower diagnostic performance with AUCs of 0.55 and 0.57, respectively. DeLong's test revealed that the AUC of MLR was significantly higher than PLR and NLR ($p < 0.001$), suggesting its excellent diagnostic performance as shown in (Table 4, Figure 1) below

Table 4: Diagnostic values of PLR, NLR and MLR

	AUC	Threshold	Sensitivity	Specificity	Delong's test p- value
PLR	0.55	126	44%	53%	<0.001***
NLR	0.57	1.5	49%	55%	
MLR	0.83	0.13	76%	74%	

*** *p < .001: High significant* AUC: Area Under the Curve.*

In this table it is more sensitive (76%) than NLR (49%) and PLR (44%) as biomarker of chronic kidney disease diabetic patients. MLR showed higher significant AUC than PLR and NLR in diagnosing chronic kidney disease diabetic patients (p- value < 0.001).

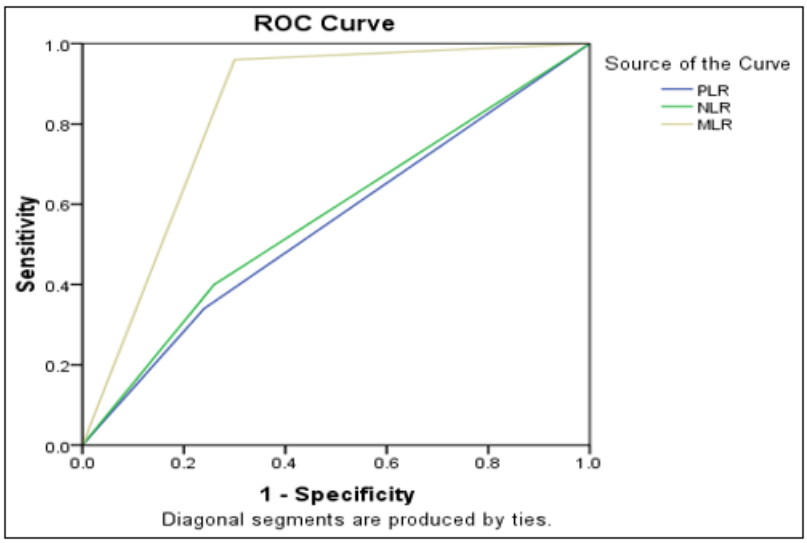

Figure 1: ROC curve of PLR, NLR and MLR as biomarkers of chronic kidney disease diabetic Patients

4. Discussion

Recently, inflammatory indices calculated using complete blood count (CBC), such as platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and monocyte-to-lymphocyte ratio (MLR) have been proposed as surrogate markers of systemic inflammation. These indices have been studied in various cardiovascular, metabolic and renal diseases and have been found to correlate with disease severity and outcome. These ratios might better reflect the balance between pro-inflammatory and regulatory immunity than absolute numbers of individual leukocyte populations (5).

The current study aimed at analyzing the significance of the inflammatory hematological markers, namely platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and monocyte-tolymphopcyte ratio (MLR) in diabetic patients with or without nephropathy and their relationships to urine albumin/creatinine as a renal damage marker.(6). Results of us showed that inflammatory markers were significantly higher in patients with diabetic nephropathy as compared to those diabetics without nephropathy and healthy controls, suggesting the close association between systemic inflammation and development of DKD (7). Although PLR and NLR increased slightly, MLR demonstrated a significant and stable extremity compared with healthy controls group, implying that monocyte-driven inflammation might be crucial in the course of renal injury to diabetic nephropathy(8).

The gradual increase in urine albumin/creatinine ratio with increasing severity of diabetic nephropathy is indicative of the progressive degree of renal involvement, which corresponds closely with the rise in inflammatory markers especially in Group C. The significant positive correlation found between

urine albumin/creatinine ratio and both PLR, NLR and MLR for patients with diabetic nephropathy also supports the idea that inflammation significantly contributes to glomerular damage and subsequent increased permeability to albumin (9).

Correlation analysis indicated that MLR was most robust and consistently associated with urine albumin/creatinine ratio in diabetic and DN populations. This observation implicates monocytes potentially in mediating chronic inflammation, endothelial dysfunction and renal fibrosis, all pivotal pathological pathways of DN (10), (11).The high association between NLR and MLR also implies the complementary activation of innate pathways in late stages of disease.Notably, MLR was indicated as a better diagnostic biomarker for DN than PLR and NLR by ROC curve analysis (12),(11).MLR had significant larger area under the curve, sensitivity and specificity, which suggested that MLR was more accurate to detect patients with diabetic kidney disease. PLR and NLR were not as useful, perhaps reflecting their susceptibility to short-term physiological fluctuations or more indirect involvement in chronic renal inflammation.(11).

As the MLR exhibits a higher AUC, it may be utilized as an inexpensive, convent and easily measured indicator to discriminate against the early stage and stratify the risk of diabetic kidney. Since CBC parameters are received readily in clinical practice, MLR can be added to standard evaluation protocols at little extra financial cost (13),(14).

Notwithstanding the magnitude of these inferences, there are some limitations which must be considered. The cross-sectional nature hinders the causal relationship, and longitudinal research is called for to explore whether elevated MLR allows prediction of disease progression or therapy response. Also, the research examined only the other inflammatory cytokines or markers that might enrich our understanding of mechanisms lying beneath inflammation in DN (15),(16),(17).

In conclusion, the present study emphasizes the close relationship between inflammatory hematological indices and diabetic nephropathy with MLR being the most predictive one of all markers we studied. These findings underscore the role of inflammation in DKD and provide support for the potential clinical application of MLR as a noninvasive marker for diagnosis and monitoring of disease (18),(19).

5. Conclusion

MLR is a better and more stable inflammatory marker for the identification of diabetic nephropathy than PLR and NLR. Its significant correlation with renal damage, however, emphasizes the inflammatory response in diabetic nephropathy and may provide a possible practical application of MLR as an inexpensive cost-effective diagnostic biomarker.

Declarations

Ethics approval and consent to participate.
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. Written informed consent was obtained from all the participants. The study was approved by the Institutional Ethical Committee of the Faculty of Medicine, Albutana University, Sudan.

Consent to publication
Not applicable.

Availability of data and materials
The data generated in this study are available from the corresponding author upon reasonable request with a completed Materials Transfer Agreement, excluding the materials, which included personally identifiable information.

Competing interests
The authors declare that they have no competing interests.

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Author contributions:
M.A. Adris was involved in writing and revising the manuscript critically for important intellectual content, generated the Idea and participated in drafting and revising the manuscript. SSA enrolled and randomly allocated participants, acquired measurements and data, followed the study, statistically analysed the data, and wrote and drafted the manuscript.

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References

[1] Liu J, Liu X, Li Y, Quan J, Wei S, An S, et al. The association of neutrophil to lymphocyte ratio , mean platelet volume, and platelet distribution width with diabetic retinopathy and nephropathy : a meta-analysis. 2018;0:1–18.
[2] Li L. Association of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio with diabetic kidney disease in patients with type 2 diabetes. 2022;1–15.
[3] Houeiss P, Njeim R, Tamim H, Hamdy AF, Azar TS, Azar WS, et al. Urinary 20-HETE : A prospective Non-Invasive prognostic and diagnostic marker for diabetic kidney disease. J Adv Res [Internet]. 2023;44:109–17. Available from: https://doi.org/10.1016/j.jare.2022.04.013
[4] Yu MG, Gordin D, Fu J, Park K, Li Q, King GL. Protective Factors and the Pathogenesis of Complications in Diabetes. Vol. 45, Endocrine Reviews. 2024.
[5] Li L. Association of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio with Diabetic Kidney Disease in Chinese Patients with Type 2 Diabetes : A Cross-Sectional Study. 2022;(December):1157–66.
[6] Syndr M, Wang JR, Chen Z, Yang K, Yang HJ, Tao WY, et al. Association between neutrophil - to - lymphocyte ratio, platelet - to - lymphocyte ratio , and

diabetic retinopathy among diabetic patients without a related family history. Diabetol Metab Syndr [Internet]. 2020;1–10. Available from: https://doi.org/10.1186/s13098-020-00562-y

[7] Stringhini S, Batty GD, Bovet P, Shipley MJ, Marmot MG. Association of Lifecourse Socioeconomic Status with Chronic Inflammation and Type 2 Diabetes Risk : The Whitehall II Prospective Cohort Study. 2013;10(7):1–15.

[8] Manuscript A. NIH Public Access. 2012;30(5):343–58.

[9] Almalki AH, Khobrani FM, Mohammed S. Neutrophil to Lymphocyte Ratio in Early Diabetic Kidney Disease among Patients with Type 2 Diabetes Mellitus. 2020;4(5):453–64.

[10] Azab B, Daoud J, Naeem F Ben, Nasr R, Ghimire P, Siddiqui A, et al. Neutrophil-to-Lymphocyte Ratio as a Predictor of Worsening Renal Function in Diabetic Patients (3- Year Follow-Up Study) Neutrophil-to-Lymphocyte Ratio as a Predictor of Worsening Renal Function in Diabetic Patients (3-Year Follow-Up Study). 2012;6049.

[11] Li X, Wang L, Liu M, Zhou H. Association between ratio and diabetic kidney disease in type 2 diabetes mellitus patients : a cross- sectional study. 2024;(January):1–17.

[12] Yu Y, Lin Q, Ye D, Wang Y, He B, Li Y, et al. Neutrophil count as a reliable marker for diabetic kidney disease in autoimmune diabetes. 2020;1–12.

[13] Wheelock KM, Saulnier P jean, Tanamas SK, Vijayakumar P, Weil EJ, Looker HC, et al. White blood cell fractions correlate with lesions of diabetic kidney disease and predict loss of kidney function in Type 2 diabetes. 2018;1001–9.

[14] Lin J, Cheng A, Cheng K, Deng Q, Zhang S, Lan Z, et al. New Insights into the Mechanisms of Pyroptosis and Implications for Diabetic Kidney Disease.

[15] 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. 2020;2020.

[16] Provenzano M, Maritati F, Abenavoli C, Bini C, Corradetti V. Precision Nephrology in Patients with Diabetes and Chronic Kidney Disease. 2022;

[17] Zhang H, Cui Y, Dong R, Zhang H, Cui Y, Dong R, et al. Vitamin D is associated with blood lead exposure through bone turnover in type 2 diabetes patients. 2021;378–86.

[18] Bai Y, Huang L, Li Y, Zhou S, Li L, Jiang H, et al. Neutrophil / Lymphocyte Ratio and All-Cause Mortality in Diabetic Kidney Disease : A Retrospective Cohort Study. 2024;(November):10739–53.

[19] Zwolak R, Piotrowski M, Grzechnik K, Majdan M. The Relationship between Hematological Markers of Systemic Inflammation (Neutrophil-To-Lymphocyte , Ratios) and Ultrasound Disease Activity Parameters in Patients with Rheumatoid Arthritis. :1–11.

Author Profile

Samia Saeed Ahmed [(1)], Basic Medical Sciences Department, Al-Rayan National College of Health Sciences and Nursing, Al-Madinah, Saudi Arabia**.** Email: *ss.ahmed[at]amc.edu.sa.*

M. A. Adris [(2)], Department of biochemistry, faculty of medicine, University of Al-butana. Sudan. *maidris71[at]gmail.com.*