JPSIM Journal of Pakistan Society of Internal Medicine

Original Article

Study of Platelet to Lymphocyte Ratio as a Predictor Inflammatory Marker for Diabetic Nephropathy in Patients with Type 2 Diabetes Mellitus

Heba Tul Noor, Nasir Farooq Butt, Hina Latif, Rabia Rathore, Anam Fatima Bangash, Adil Iqbal

King Edward Medical University/Mayo Hospital Lahore

Abstract

Objective: To compare ratio of platelet to lymphocyte (PLR) in diabetic patients with nephropathy to those diabetics without nephropathy.

Methods: It was an observational study carried out in the medical department from June 2022 to May 2023. A total of 246 patients of type 2 diabetes mellitus hospitalized in all medical wards were included. Based on urinary albumin excretion, two groups of patients were formed: diabetics without nephropathy (Group A) and diabetics with nephropathy (Group B). Ratio of Platelet to lymphocyte was calculated by dividing platelet count with lymphocyte count and ratio of neutrophil to lymphocyte (NLR) was calculated by dividing neutrophil to lymphocyte count. PLR and NLR were compared amongst both groups.

Results: There were 246 subjects (111 females, 134 males). 131 subjects did not have nephropathy, 115 patients had nephropathy. Comparison of hematological parameters showed that NLR of patients with type 2 DM with nephropathy was 2.59 ± 0.51 and without nephropathy group was 1.70 ± 0.44. The PLR of diabetic nephropathy group was 251 ± 62.4 and that without nephropathy was 213 ± 59.6. Statistical significance ($p < 0.05$) was seen in the NLR and PLR values of the two groups when compared using the student t-test.

Conclusion: Increased ratio of platelet-to-lymphocyte significantly correlates with diabetic nephropathy, and may serve as a predictor inflammatory marker for diabetic nephropathy.

Keywords: Diabetic Nephropathy, platelet-to-lymphocyte ratio, type 2 Diabetes mellitus

How to cite this:

Noor HT, Butt NF, Latif H, Rathore R, Bangash AF, Iqbal A. Study of Platelet to Lymphocyte Ratio as a Predictor Inflammatory Marker for Diabetic Nephropathy in Patients with Type 2 Diabetes Mellitus. J Pak Soc Intern Med. 2025;6(1): 16-21

Corresponding Author: Dr. Heba Tul Noor **Email:** hebatulnoor@gmail.com

Received: 17-09-2024 **Revised:** 23-01-2025 **Accepted:** 24-02-2025

DOI: https://doi.org/10.70302/jpsim.v6i1.2504

Introduction

Diabetes Mellitus, whose incidence rates are rising, poses a severe danger to global health.[1] Elevated blood sugar levels are the hallmark of this chronic metabolic disorder, caused by either increased cellular resistance to insulin or decreased insulin secretion, or both.[2] Because diabetes raises blood glucose levels over time, it can cause a variety of problems that fall under the categories of microvascular and macrovascular illnesses. Neuropathy, nephropathy, and retinopathy are examples of microvascular consequences.[3] Accelerated cardiovascular diseases, myocardial infarction and cerebrovascular disease resulting in strokes are the main macrovascular consequences.

A steady decrease in renal function and chronic albuminuria are the hallmarks of diabetic nephropathy (DN).[4] DN is estimated to affect 20% to 50% of diabetics, and in many populations, it becomes a leading cause of end stage kidney disease. While renal involvement can be caused by both type of diabetes, type 2 diabetes is far more common in ESRD patients than type 1 diabetes. The clinical symptom of DN is an increase in urine albumin excretion, which progresses from micro albuminuria to macro albuminuria and ultimately ESRD.[5]

Due to a number of its inherent shortcomings, albuminuria, the biomarker used for the current diagnosis of DN, is not a very reliable indicator of the disease.[6] One possible pathophysiology thought to be in charge of the emergence of diabetic complications is chronic inflamma-

tion.[7,8] According to research by Rudiger et al., there is a connection between systemic inflammation and vascular disease, and patients with diabetes who have chronic inflammation are more likely to experience micro and macroangiopathic problems.[9] Numerous inflammatory cytokines, like tumor necrosis factor α, interleukin-1, 6 and 8 participate in the pathophysiology of diabetic nephropathy.[10] The expense and measurement challenges of these inflammatory indicators limit their application in routine clinical practice. So there remains a need for early predictors of diabetic nephropathy which is readily available, cost effective and reliable. [11]

The ratios of neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte (PLR) have been proposed as possible biomarkers of systemic inflammation that can be easily incorporated into clinical practice and can be obtained from regular blood exams. It has been shown that in populations with cancer and cardiovascular disease, the PLR and NLR ratios can predict mortality. Although the precise process by which elevated PLR and NLR leads to increased mortality is yet unknown, inflammation most certainly plays a significant part. It has also recently been shown that PLR and NLR have predictive potential for issues related to diabetes.[6,7] Notably, standard blood counts can be used to compute the neutrophil-to-lymphocyte ratio (NLR), a cheap and easily detectable laboratory measure.

It has been suggested that the platelet-to-lymphocyte ratio (PLR) is a measure of inflammation and endothelial dysfunction.[12,13] In order to ascertain whether PLR may be utilized as a prognostic marker and predictor for DN, as well as to assess its connection with DN, this study was conducted. This will further aid in reducing the emergence of problems in patients with uncontrolled diabetes, perhaps leading to improved patient management and a better understanding of the function of inflammation in diabetic nephropathy. Our research was conducted to determine and compare ratio of platelet to lymphocyte in diabetic patients with nephropathy to those diabetics without nephropathy.

Methods

It was an observational study conducted in the department of medicine from June 2022 to May 2023. Type 2 diabetics who were hospitalized in the medical wards were included. A total of 246 patients were taken by using non probability convenient sampling technique. Ethical approval was granted by King Edward Medical University's Institutional Review Board (IRB).

Patients aged between 18 to 75 years, of either gender, who had type 2 diabetes mellitus were included. Patients with other chronic ailments like severe liver disease and cancers were excluded. Similarly patients suffering from hematological disorders like immune thrombocytopenic purpura, leukemia, lymphoma leading to abnormalities in leukocyte and platelet production were also not included. Patients on drugs causing thrombocytopenia like NSAIDS, furosemide, penicillin, sulfonamide, linezolid were also not taken.

According to clinical definitions, individuals with type 2 Diabetes mellitus are those who are previously diagnosed based on history or previous records showing more than 126 mg/dl fasting blood sugar or more than 200 mg/dl for random blood sugar or HbA1c more than 6.4%. Normal platelet count is taken as a count between 150,000-450,000 per microliter, normal lymphocyte count 800-5000 per microliter, and normal range for platelets to lymphocyte ratio is 30-562.5. The urine albumin-to-creatinine ratio exceeding 30 mg/g is considered indicative of diabetic nephropathy.

Based on the urinary albumin-to-creatinine ratio, two groups were made; diabetes without nephropathy (Group A) and with nephropathy (Group B). Ratio of platelet to lymphocyte was computed by dividing platelet count with lymphocyte count and ratio of neutrophil tolymphocyte was calculated by diving neutrophil to lymphocyte count. PLR and NLR were compared amongst both groups. Record of all patients with diabetic nephropathy were entered from hospital records according to operational definition. Patients identity was kept confidential. All patients demographic information such as name, age and gender were noted from hospital records. Ratios of urinary albumin to creatinine(UACR), neutrophil to lymphocyte, platelet to lymphocyte ratio, serum creatinine and eGFR were recorded for all patients. Patients were categorized into two groups depending on UACR; Group A termed as diabetics without nephropathy were those with UACR<30 mg/g while Group B was designated as diabetics with nephropathy with a UACR>30 mg/g. PLR, NLR, serum creatinine, eGFR was compared amongst the groups. A pre-designed proforma was used to collect all information.

SPSS version 26 was used for data entry and analysis. Quantitative variables like age, PLR, NLR, serum creatinine and eGFR ratio was presented as mean and standard deviation. Frequencies and percentages were used to represent the qualitative factors, such as gender and the presence or absence of disease. To compare the two groups, student t-test was employed. Pearson's test was used to assess correlations. A receiver operating characteristic (ROC) curve was employed to forecast diabetic patients' nephropathy. Statistical significance was defined as a p-value of less than 0.05.

Results

In this study, 246 patients with type 2 diabetes were enrolled. These patients were classified into two groups, whether they did not have diabetic nephropathy (n=131)

or if they had diabetic nephropathy (n=115). Presence and absence of nephropathy was designated by presence or absence of albuminuria.

Mean age of patients was 52.23±8.42 years for group A and 59.63±11.54 years for group B. 134 were male and 111 females (Table 1).

Table 2 shows comparison of hematological parameters

Table 1: *Study groups characteristics*

	Group A DM without nephron-pathy	Group B DM with nephro-pathy	Total No. of cases	P value
Age (mean±SD)	52.23±8.42	59.63± 11.54		0.002
Male	72	63	134 (64.4%)	0.08
Female	59	52	111 (45.1%)	0.06

Table 2: *Hematological Parameters in DM without Nephropathy and DM with Nephropathy*

Parameters	Group A (DM without nephropathy) Mean and std. dev.	Group B (DM with nephropathy) Mean and std. dev.	P value
WBC	7.48 ± 1.71	8.3 ± 1.52	0.003
Absolute Neutrophil count	4328 ± 1221	5241 ± 1385	0.001
Absolute lymphocyte count	2543 ± 654	2016 ± 438	0.002
NLR	1.70 ± 0.44	2.59 ± 0.51	0.013
Platelet	213 ± 59.6	251 ± 62.4	0.001
PLR	91.6 ± 21.5	129.5 ± 37.8	0.001
Creatinine	0.88 ± 0.52	2.43 ± 0.76	0.001
e GFR	107.3 ± 8.3	63.2 ± 11.7	0.012

WBC, white blood count; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; eGFR, estimated glomerular filtration rate

in Group A and Group B. It is observed that NLR of patients with type 2 DM with nephropathy was 2.59 ± 0.51 and that of the patients without nephropathy was 1.70 ± 0.44. The PLR of patients with nephropathy was 251 ± 62.4 and those without nephropathy was 213 ± 59.6. When the t-test was used to compare the NLR and PLR values of the two groups, statistical significance was revealed in the results. ($p < 0.05$) (Table 2).

Pearson test was applied and it found significant correlation between NLR, PLR, creatinine and eGFR. It is evident that NLR and serum creatinine have a positive correlation, while NLR and eGFR have a negative correlation. Likewise, a negative association was discovered between PLR and eGFR and a positive link between PLR and serum creatinine. (Table 3)

Prediction of diabetic kidney disease by using receiver operating characteristic had an area under curve of 0.804. Value of 116.6 for PLR had 77.8 % sensitivity and 87.4% specificity for prediction of diabetic kidney disease, which is sufficiently accurate. (Figure 1)

Table 3: *Pearson's correlation analysis of NLR and PLR in diabetic nephropathy*

Variable	NLR	PLR
NLR	-	0.53
PLR	0.53	-
Creatinine	0.45	0.58
eGFR	-0.65	-0.43

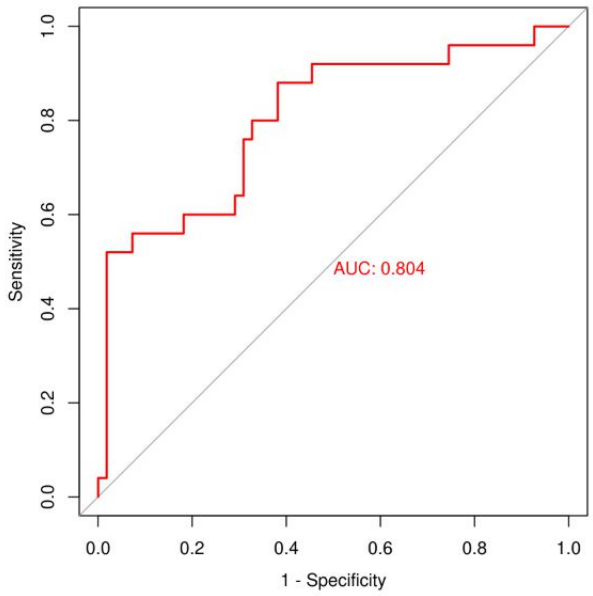

Figure1: *ROC curve analysis of PLR for prediction of diabetic kidney disease.*

Discussion

Diabetic nephropathy is a common microvascular complication of diabetes. Our present study demonstrated that PLR was significantly higher in patients having type 2 diabetes who suffered from nephropathy as compared to subjects without evidence of diabetic kidney disease. Over the past few decades, studies on

the ratios of neutrophils to lymphocytes and platelets to lymphocytes have drawn more attention.

Diabetic complications may occur as a result of chronic inflammation, which has been proposed as a possible etiology.[14] Numerous inflammatory cytokines, including NLRP, tumor necrosis factor, and interleukins cause pathological alterations in kidney structure through a variety of inflammatory pathways. They worsen glomerular sclerosis and renal fibrosis leading to increase in urinary albumin excretion[15].

The clinical symptom of diabetic kidney disease (DN) is an increase in urine albumin excretion, which progresses from microalbuminuria to macroalbuminuria and ultimately ESRD. Diagnosis of DN depends on albuminuria as a biomarker but because of some of its own limitations, it is not a predictor of DN that is accu-rate enough. Novel inflammatory markers have been found as an independent risk factors for the progression of renal disease in diabetes.[16] The ratios of fibrinogen to albumin, CRP to serum albumin, NLR, and PLR are a few examples. White blood cells lymphocytes and neutrophils are known markers of inflammation but the combination of two components is represented by the NLR and PLR indices, which have emerged as novel indicators of the systemic inflammatory response. Research has validated their correlation with type 2 diabetes and its associated consequences. High NLR indicates an increased quantity of neutrophils adhering to endothelial cells, resulting in endothelial damage. Lymphocytes play an important role in the immunological response of the body regulating inflammatory responses.[17] Continuous inflammation causes a number of megakaryocytes to proliferate more rapidly. This raises the platelet count as a result. In response to prolonged stress, the bone marrow produces more neutrophils and fewer lymphocytes leading to a rise in neutrophils and a fall in lymphocytes in instances of persistent inflammation.

This study set out to determine PLR's predictive significance for diabetic nephropathy in people with type 2 diabetes. Depending on whether they had proteinuria or not, the patients were split into two groups. The comparision to various parameters including inflammatory markers (PLR, NLR) was made in the groups. The findings showed that patients with DN had considerably higher PLR, their levels also correlates with renal function indices. Moreover, ROC curve showed PLR had diagnostic value for DN.

Multiple studies done in recent few years also reveal similar results. Huang et al.'s[18] studied 253 patients including 115 early diabetic nephropathy patients. They revealed that high NLR was predictive of early diabetic kidney impairment and linked with DN. Li L investigated the potential utility of these two indicators as DN predictors by examining their association with renal function in individuals with DM Type 2. In retrospect, 655 people with DM type 2 were selected. The urine albumin-to-creatinine ratio was used to divide the individuals into three groups. The NLR and PLR varied considerably between the three groups and increased with increasing albuminuria levels.[19] Onalan E et al. found that PLR was a predictor of microvascular compication in diabetes.[20] Moreover, Sagar and colleagues[21] discovered a noteworthy association between NLR and DN, indicating that endothelial dysfunction brought on by inflammation may be a major factor in DN. Turkmen et al. examined how NLR and PLR related to IL-6 and TNF-α. In terms of inflammation, PLR was found to be better in ESRD patients than NLR. PLR may be calculated simply and is more accurate in predicting inflammation in ESRD patients than NLR. Furthermore, they mentioned that platelets may bind to endothelial cells and release pro-inflammatory cytokines, which could lead to atherosclerosis.[22] Patients with greater platelet counts may have increased inflammation as a result of the production of thromboxanes and other mediators by platelets.[23]

A study done by Duan S, et al. studied the association of PLR with proteinuria and they found that PLR had a positive correlation with urinary protein excretion and prognosis in DN patients. Additionally, he discovered that in DN with biopsy-proven renal advancement, it is an independent risk factor.[24]

PLR is emerging as a new prognostic marker, providing the concept of platelet aggregation and inflammatory pathways. Elevated PLR has been linked to unfavorable results in clinical practice, demonstrating a predictive value in numerous diseases like cardiovascular diseases, cancer patients, survival rates after MI, critical limb ischemia in peripheral arterial disease and diabetic microvacular complications.[25]

Conclusion

Platelet to lymphocyte is an inexpensive, readily quantifiable inflammatory marker that highly correlates with renal function in patients of type 2 diabetes mellitus. It can also be utilized as a prognostic risk marker and predictor for diabetic nephropathy. It is still necessary to validate the conclusion of this study in further large scale studies and also to determine its effectiveness as a probable risk factor for diabetic nephropathy.

Ethical Approval: The IRB/EC approved this study via letter no.343/RC/KEMU dated 22-02-2022.

Conflict of Interest: None

Funding Source: None

Authors' Contribution:

HTN: Conception

NFB, HL: Design of the work

RR, AFB, AI: Data acquisition, analysis, or interpretation
HTN, HL: Draft the work
NFB, RR, AFB, AI: Review critically for important intellectual content
HTN, NFB, HL, RR, AFB, AI: Approve the version to be published
HTN, NFB, HL, RR, AFB, AI: Agree to be accountable for all aspects of the work

References

1. Williams R. IDF Diabetes Atlas Ninth Edition 2019 IDF Diabetes Atlas, 9th, International Diabetes Federation. 2019.
2. Punthakee Z, Goldenberg R, Katz P. Definition, classification and diagnosis of diabetes, prediabetes and metabolic syndrome. Can J Diabetes. 2018; 42(S): S10-15.
3. American Diabetes Association. 10. Microvascular complications and foot care: standards of medical care in diabetes 2018. Diabetes Care. 2018;41(Supp 1):S105-18.
4. Warren AM, Knudsen ST, Cooper ME. Diabetic nephropathy: an insight into molecular mechanisms and emerging therapies. Expert Opin Ther Targets England. 2019;23(4):579–91.
5. Ninomiya T, Perkovic V, de Galan BE. Albuminuria and kidney function independently predict cardiovascular and renal outcomes in diabetes. JASN. 2009; doi: 10.1681/ASN.2008121270
6. Winter L, Wong LA, Jerums G, Seah JM, Clarke M, Tan SM, et al. Use of readily accessible inflammatory markers to predict diabetic kidney disease. Front Endocrinol. 2018;9(2):225.
7. Fiseha T. Urinary biomarkers for early diabetic nephropathy in type 2 diabetic patients. Biomarker research. 2015;3(4):1-7.
8. 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. Biosci Rep. 2018;38(3):BSR20180172.
9. Rudiger A, Burckhardt OA, Harpes P, Müller SA, Follath F. The relative lymphocyte count on hospital admission is a risk factor for long term mortality in patients with acute heart failure. Am J Emerg Med. 2006; 24(4): 451-4.
10. Winter L, Wong LA, Jerums G, Seah JM, Clarke M, Tan SM, et al. Use of readily accessible inflammatory markers to predict diabetic kidney disease. Front Endocrinol. 2018;9(3):225.
11. Uwaezuoke SN. The role of novel biomarkers in predicting diabetic nephropathy: a review. Int J Nephrol Renovasc Dis. 2017: https://doi.org/10.2147/IJNRD.S143186.
12. Balta S, Demırkol S, Kucuk U. The platelet lymphocyte ratio may be useful inflammatory indicator in clinical practice. Hemodial Int.2013;4(17): 668-9
13. 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. Biosc. Rep. 2018;38(3):BSR20180172.
14. Jeong Y, Jeon SR, Kim HG, et al. The role of platelet to lymphocyte ratio and neutrophil to lymphocyte ratio in ulcerative colitis. Intest Res. 2021;19(1):62–70. doi:10.5217/ir.2019.09156
15. Lin J, Cheng A, Cheng K, Deng Q, Zhang S, Lan Z, et al. New Insights into the Mechanisms of Proptosis and Implications for Diabetic Kidney Disease. Int J Mol Sci. 2020; 21(19):doi: 10.3390/ijms21197057
16. Fujita T, Hemmi S, Kajiwara M, Yabuki M, Fuke Y, Satomura A, et al. Complement-mediated chronic inflammation is associated with diabetic microvascular complication. Diabetes Metab Res Rev. 2013;29(2): 220 – 6.
17. Moursy EY, Megallaa MH, Mouftah RF. Relationship between neutrophil lymphocyte ratio and microvascular complications in Egyptian patients with type 2 diabetes. Am J Intern Med. 2015;3(2):250-5.
18. Huang W, Huang J, Liu Q, Lin F, He Z, Zeng Z, et al. Neutrophil-lymphocyte ratio is a reliable predictive marker for early-stage diabetic nephropathy. Clin Endocrinol (Oxf). 2015;82(2):229-33.
19. Li L, Shen Q, Rao S. 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. Therapeut Clin Risk Manage. 2022:8(12):1157-66.
20. Onalan E, Gozel N, Donder E. Can hematological parameters in type 2 diabetes predict microvascular complication development? Pak J Med Sci. 2019;35(6): 1511 -5.
21. Khandare SA, Chittawar S, Nahar N, Dubey TN, Qureshi Z. Study of Neutrophil-lymphocyte Ratio as Novel Marker for Diabetic Nephropathy in Type 2 Diabetes. Indian J Endocrinol Metabol. 2017 May 1;21(3):387-92.
22. Turkmen K, Erdur FM, Ozcicek F, Ozcicek A, Akbas EM, Ozbicer A, et al. Platelet-to-lymphocyte ratio better predicts inflammation than neutrophil-to-lymphocyte ratio in end-stage renal disease patients. Hemodial Int. 2013;17(3):391-6

23. 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 Diabet Res. 2020; https://doi.org/10.1155/2020/6219545.

24. Duan S, Sun L, Zhang C, Wu L, Nie G, Huang Z, et al. Association of platelet-to-lymphocyte ratio with kidney clinicopathologic features and renal outcomes in patients with diabetic kidney disease. Int Immunopharmacol. 2021; doi:10.1016/j.intimp.2021.107413.

25. Temiz A, Gazi E, Güngör Ö, Barutçu A, Altun B, Bekler A, et al. Platelet/lymphocyte ratio and risk of in-hospital mortality in patients with ST-elevated myocardial infarction. Med Sci Monit. 2014;22(20):660–5.