Panacea Journal of Medical Sciences 2023;13(3):747–750

Content available at: https://www.ipinnovative.com/open-access-journals

Panacea Journal of Medical Sciences

Journal homepage: http://www.pjms.in/

Original Research Article

Evaluation of neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) as inflammatory markers in patients with type 2 diabetes mellitus

Dharmveer Sharma[1], Vivek Kumar Jain[1], Vidyanand Pandit[2]*, Shashsank Tyagi[1]

[1]*Dept. of Biochemistry, SRVS Government Medical College, Shivpuri, Madhya Pradesh, India*
[2]*Dept. of Pathology, SRVS Government Medical College, Shivpuri, Madhya Pradesh, India*

ARTICLE INFO

Article history:
Received 29-03-2022
Accepted 11-05-2022
Available online 07-12-2023

Keywords:
Inflammation Neutrophil-lymphocyte Ratio
Platelet-lymphocyte Ratio
Type 2 diabetes mellitus

ABSTRACT

Background: Diabetes Mellitus (DM), chronic metabolic disease and its complications are diabetic nephropathy, retinopathy, and neuropathy. Systemic inflammation play a significant role and could lead to insulin resistance. This study aimed to investigate NLR and PLR in T2DM patients in comparison with healthy controls.

Materials and Methods : This prospective study, conducted in SRVS Government Medical College, Shivpuri, Madhya Pradesh, India. In this study, a total of 220 subjects were involved, among them 110 were T2DM patients were cases and 110 healthy subjects were controls. Demographic details, physical and clinical examination were done for all the study subjects. Under aseptic conditions, five ml of fasting venous blood sample was collected and aliquoted into plain (3ml) and EDTA (2 ml) tubes and allowed to clot and centrifuged at 3000 rpm for 10 minutes. The obtained serum sample was used for the estimation of fasting and post-prandial glucose, renal profile, lipid profile using commercially available autoanalyzer kits. Whole blood sample was used for the Complete Blood Count (CBC) in EDTA vials. Neutrophil to Lymphocyte Ratio (NLR) and Platelet to Lymphocyte (PLR) were calculated. Whole blood sample was used for the estimation of HbA1c and BMI was calculated.

Statistical analysis: The variables were represented in Mean±SD. Categorical variables were represented in percentage. Spearman's correlation was applied. The p value <0.05 considered as significant.

Results: In the current study, mean age 60.2±4.2 yrs, BMI 27.1±2.4 (kg/m^2), Systolic blood pressure 132.1±12.3 mmHg, Diastolic blood pressure 90.2±10.5 mmHg, fasting blood sugar (FBS) 169.7±19.3 mg/dl, Post-Prandial blood sugar 238.1±39.5 mg/dl, HbA1c 7.9±0.8 %, Serum Urea 36.1±7.1 mg/dl, Creatinine 1.0±0.3 mg/dl, UA 6.5±2.3 mg/dl, Serum Total Cholesterol 241.1±30.5 mg/dl, Serum Triglycerides 170.0±16.2 mg/dl, Serum low density lipoprotein cholesterol (LDLC) 176.4±35.2 mg/dl, Serum very low density lipoprotein cholesterol (VLDL) 34.1±3.2 mg/dl, Lymphocytes 17.2±4.1 %, NLR 6.7±2.3 and PLR 19.1±6.9 were significantly increased in Type 2 Diabetes Mellitus (T2DM) cases whereas high low density lipoprotein cholesterol (HDLC) 30.7±3.9 mg/dl was significantly decreased in T2DM cases.

Conclusion: The present study results may conclude that increased NLR and PLR may be used as a markers for inflammation in T2DM. These may serve as an alternative to the other costly inflammatory markers.

1. Introduction

Diabetes Mellitus (DM), chronic metabolic disease with increasing prevalence. In 2019, 463 million were affected

* *Corresponding author*.
E-mail address: panditvidya@gmail.com (V. Pandit).

https://doi.org/10.18231/j.pjms.2023.137

with diabetes and this may be projected to increase 700 million by 2045 according to International Diabetes Federation (IDF).[1,2] The micro-vascular complications of diabetes mellitus such as diabetic nephropathy, retinopathy, and neuropathy and macro-vascular diseases such as peripheral vascular diseases, stroke and cardiovascular diseases.[3]

The inflammatory mediators play a significant role in diabetes pathophysiology. These inflammatory mediators may inhibit β-cell function, promote apoptosis, and finally leads to insulin resistance.[4] The inflammatory markers released from blood was found to be associated with diabetes mellitus.

Mean platelet volume (MPV), may indicate the prognosis of many inflammatory diseases.[5] Red blood cell distribution width (RDW) is associated with CVDs, tumors and sepsis. Recently, a few studies documented that NLR and RLR may serve as a systemic marker in inflammatory conditions like cardiovascular disease, metabolic syndrome and malignancies.[6,7] These are novel, available, and less expensive markers of Inflammation. White blood cell (WBC) count (Total and differential) is an indicator of inflammation and it is a cost-effective and routine investigation. NLR, emerged as a novel alternative marker for inflammation.[8] A study by Turkmen et al. reported that platelets may be involved in atherosclerosis by secreting proinflammatory cytokines and their bounding to endothelial cells.[9] Platelets secretes thromboxanes, which may accelerate the inflammatory response in patients with increased platelets.[10,11]

The promising ratios NLR and PLR conveyed a systematic inflammatory response and has been evidenced as predictive and prognostic factors for DM and the related complications.[12,13] In this study, we evaluated NLR and PLR in T2DM patients.

2. Materials and Methods

This prospective case-control study was conducted in SRVS Government Medical College, Shivpuri, Madhya Pradesh, India. In this study, a total of 220 subjects were involved, among them 110 were T2DM patients were cases and 110 healthy subjects were controls. Among the 110 cases, 65 were males 45 were females. In controls, 70 were males and 40 were females. Institutional ethics committee approval is obtained for this study. Demographic details, physical and clinical examination were done for all the study subjects. Patients with cardiovascular diseases, thyroid diseases, liver disease, pregnant women were excluded from the study.

Under aseptic conditions, five ml of fasting venous blood samples were collected from each study participant and aliquoted into plain (3ml) and EDTA (2 ml) tubes and allowed to clot and centrifuged at 3000 rpm for 10 minutes. The obtained serum sample was used for the estimation of fasting and post-prandial glucose, renal profile [serum urea, creatinine and uric acid], lipid profile [serum total cholesterol, triglycerides, HDLC, LDLC (calculated) and VLDL (calculated)] using commercially available autoanalyzer kits. Whole blood sample was used for the Complete Blood Count (CBC) in EDTA vials. NLR and PLR were calculated. Whole blood sample was used for the estimation of HbA1c (Immunoturbidimetry). BMI was calculated.

2.1. Statistical analysis

The variables were represented in Mean±SD. Categorical variables were represented in percentage. Spearman's correlation was applied as the data was non-normally distributed. The p value <0.05 considered significant.

3. Results

In this study, mean age 60.2±4.2 yrs, BMI 27.1±2.4 (kg/m^2), Systolic blood pressure (SBP) 132.1±12.3 mmHg, Diastolic blood pressure (DBP) 90.2±10.5 mmHg, fasting blood sugar (FBS) 169.7±19.3 mg/dl, Post-Prandial blood sugar 238.1±39.5 mg/dl, HbA1c 7.9±0.8 %, Serum Urea 36.1±7.1 mg/dl, Creatinine 1.0±0.3 mg/dl, Serum uric acid (UA) 6.5±2.3 mg/dl, Serum Total Cholesterol 241.1±30.5 mg/dl, Serum Triglycerides 170.0±16.2 mg/dl, Serum LDLC 176.4±35.2 mg/dl, VLDL 34.1±3.2 mg/dl, Lymphocytes 17.2±4.1 %, NLR 6.7±2.3 and PLR 19.1±6.9 were significantly increased in T2DM cases whereas HDLC 30.7±3.9 mg/dl was significantly decreased in T2DM cases as indicated in Table 1.

4. Discussion

In this study, NLR and PLR were increased in patients of T2DM than the healthy controls. WBC count and its subtypes serves as inflammatory markers. NLR, a marker of inflammation that reflects a counterbalance between two complementary components of the immune system; Neutrophils, being the active, non-specific mediator of inflammation, forming the 1^{st} line of defense, whereas lymphocytes acting as the protective or regulatory component of inflammation.[12] Platelets can interact with various cell types, including endothelial cells, T-lymphocytes, neutrophils, and mononuclear phagocytes. It has been reported that chronic inflammation may contribute to the development of atherosclerosis. Besides, PLR was found to be higher in some inflammatory conditions.[14]

Studies have indicated that inflammatory markers, such as neutrophilia and lymphocytopenia, serves as independent markers of many diseases, especially complications of DM.[15,16] Study by Rahar S et al. reported, NLR is a novel, inexpensive marker and may be used to measure inflammation in diabetes.[17] Study by Duman TT et al, reported that elevated NLR may be used as a marker of diabetic control in addition to HbA1c in T2DM

Table 1: Comparison of Baseline, Biochemical and Haematological Parameters between T2DM cases and Healthy controls

Parameters	T2DM Cases (n=110)	Healthy Controls (n=110)	P Value
Baseline characteristics			
Age (years)	60.2±4.2	50.0±4.5	<0.001
Male	65 (59.1%)	70 (63.6%)	-
Female	45 (40.9%)	40 (36.4%)	-
BMI (kg/m^2)	27.1±2.4	23.0±2.1	<0.001
SBP (mmHg)	132.1±12.3	110.1±6.0	<0.001
DBP (mmHg)	90.2±10.5	78.0±4.0	<0.001
Biochemical parameters			
Fasting blood sugar (mg/dl)	169.7±19.3	90.5±10.1	<0.001
Post-Prandial blood sugar (mg/dl)	238.1±39.5	129.1±5.2	<0.001
HbA1c (%)	7.9±0.8	5.2±0.6	<0.001
Serum Urea (mg/dl)	36.1±7.1	26.1±5.2	<0.001
Serum Creatinine (mg/dl)	1.0±0.3	0.5±0.2	<0.001
Serum Uric Acid (mg/dl)	6.5±2.3	4.2±0.8	<0.001
Serum Total Cholesterol (mg/dl)	241.1±30.5	165.9±6.2	<0.001
Serum Triglycerides (mg/dl)	170.0±16.2	140.2±3.9	<0.001
Serum HDLC (mg/dl)	30.7±3.9	41.9±5.6	<0.001
Serum LDLC (mg/dl)	176.4±35.2	96.2±8.2	<0.001
Serum VLDL (mg/dl)	34.1±3.2	28.0±0.8	<0.001
Haematological parameters			
Haemoglobin (%)	11.4±1.9	11.35±1.77	0.429
WBC ($10^3/\mu L$)	12.4±3.8	13.9±3.99	0.050
Neutrophils (%)	76.5±5.9	75.4±6.9	0.545
Lymphocytes (%)	17.2±4.1	15.2±4.7	0.008
Platelets, x (10^9/L)	242.5±84.6	245.1±61.9	0.624
NLR	6.7±2.3	5.2±1.4	0.008
PLR	19.1±6.9	16.1±5.9	0.007

subjects.[18] Yet, another study by Walaa H. Mohammad et al. reported that, NLR may serve an independent predictor of carotid artery intima media thickness (cIMT) and albuminuria in diabetic patients with micro and macrovascular complications. Therefore, NLR may serve as readily accessible marker of vascular complications of diabetes.[19]

Similarly, Fawwad et al. also found NLR to be an important predictor of microvascular complications in subjects with T2DM.[20] Study by A. Velayutharaj et al. reported WBC count is one of the markers of subclinical inflammation. In diabetes, due to the presence of low-grade inflammation, the white cell count, NLR and hsCRP were increased. Therefore, by assessing NLR will be useful in T2DM patients to control future vascular risk events.[21]

PLR is also a novel inflammatory biomarker used as prognostic factor in various diseases. Abdelaziz et al. observed a higher PLR in subjects with T2DM with macroalbuminuria in comparison to those with microalbuminuria and normoalbuminuria.[22] Akbas et al. and Alsayyad et al. also had similar observations.[23,24]

5. Conclusion

The present study results may conclude that increased NLR and PLR may be useful as a marker of inflammation in T2DM. These are easy to calculate from CBC, which is almost a routine investigation. These may serve as an alternative choice to other costly inflammatory markers. Further, studies are recommended with large sample size.

6. Source of Funding

No financial support was received for this study.

7. Conflict of Interest

The authors declare they have no conflict of interest.

8. Acknowledgement

None.

References

1. Jaaban M, Zetoune AB, Hesenow S, Hessenow R. Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio as novel risk markers for diabetic nephropathy in patients with type 2 diabetes. *Heliyon*. 2021;7(7):e07564. doi:10.1016/j.heliyon.2021.e07564.
2. Williams R. IDF Diabetes Atlas Ninth Edition 2019, in: IDF Diabetes Atlas, 9th, International Diabetes Federation; 2019. Available from: IDFDiabetesAtlasNinthEdition2019,in:IDFDiabetesAtlas,9th, InternationalDiabetesFederation.
3. Okur ME, Karantas ID, Siafaka P. Diabetes Mellitus: a review on pathophysiology, current status of oral pathophysiology, current

status of oral medications and future perspectives. *ACTA Pharm Sci*. 2017;55(1):61–82.
4. Chen M, Zhu Y, Wang J, Wang G, Wu Y. The Predictive Value of Neutrophil-toLymphocyte Ratio and Platelet-to-Lymphocyte Ratio Levels of Diabetic Peripheral Neuropathy. *J Pain Res*. 2021;(14):2049–58.
5. Korniluk A, Koper-Lenkiewicz OM, Kamińska J, Kemona H, Dymicka-Piekarska V. Mean Platelet Volume (MPV): New Perspectives for an Old Marker in the Course and Prognosis of Inflammatory Conditions. *Mediators Inflamm*. 2019;p. 9213074. doi:10.1155/2019/9213074.
6. Afari ME, Bhat T. Neutrophil to lymphocyte ratio (NLR) and cardiovascular diseases: an update. *Expert Rev Cardiovasc Ther*. 2016;14(5):573–7.
7. Diem S, Schmid S, Krapf M, Flatz L, Born D, Jochum W, et al. Neutrophil-to-Lymphocyte ratio (NLR) and Platelet-to-Lymphocyte ratio (PLR) as prognostic markers in patients with non-small cell lung cancer (NSCLC) treated with nivolumab. *Lung Cancer*. 2017;111:176–81. doi:10.1016/j.lungcan.2017.07.024.
8. 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 (Lausanne)*. 2018;9:225. doi:10.3389/fendo.2018.00225.
9. 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.
10. 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.
11. 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:BSR20180172. doi:10.1042/BSR20180172.
12. Turkmen K, Tonbul HZ, Toker A, Gaipov A, Erdur FM, Cicekler H, et al. The relationship between oxidative stress, inflammation, and atherosclerosis in renal transplant and end-stage renal disease patients. *Ren Fail*. 2012;34(10):1229–37.
13. Liu N, Sheng J, Pan T, Wang Y. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio are associated with lower extremity vascular lesions in Chinese patients with type 2 diabetes. *Clin Lab*. 2019;65(3):1–8.
14. 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.
15. 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 Metab*. 2017;21(3):387–92.
16. Lim AK, Tesch GH. Inflammation in diabetic nephropathy. *Mediators Inflamm*. 2012;p. 146154. doi:10.1155/2012/146154.
17. Rahar S, Marwah S, Kulshreshtha B. Neutrophil lymphocyte ratio (NLR) in type 2 diabetes mellitus and its correlation with renal function: An institutional experience. *J NTR Univ Health Sci*. 2021;10(2):82–7.
18. Duman TT, Aktas G, Atak BM, Kocak MZ, Erkus E, Savli H, et al. Neutrophil to lymphocyte ratio as an indicative of diabetic control level in type 2 diabetes mellitus. *Afri Health Sci*. 2019;19(1):1602–6.
19. Mohammad W, Ahmad A, Al-Maghraby M, et al. Is neutrophil-lymphocyte ratio a novel biomarker for macrovascular and microvascular complications of type 2 diabetes. *Egypt J Intern Med*. 2019;31(1):1–7. doi:10.4103/ejim.ejim_54_18.
20. Fawwad A, Butt AM, Siddiqui IA, Khalid M, Sabir R, Basit A, et al. Neutrophil-to-lymphocyte ratio and microvascular complications in subjects with type 2 diabetes: Pakistan's perspective. *Turk J Med Sci*. 2018;48(1):157–61.
21. Velayutharaj A, Saraswathi R, Muthumani L, Shivakumar R, Sivakumar M. Significance of Neutrophil Lymphocyte Ratio and High Sensitivity C-Reactive Protein in Type 2 Diabetic Patients. *Int J Cur Res Rev*. 2020;12(22):66–9.
22. Abdelaziz AA, El-Sayed EE, Emran TM, Abdallah AI. Study of neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) as a predictor inflammatory marker for diabetic nephropathy in type 2 diabetic patients. *Egypt J Hospital Med*. 2018;72(7):4800–7.
23. Akbas EM, Demirtas L, Ozcicek A, Timuroglu A, Bakirci EM, Hamur H, et al. Association of epicardial adipose tissue, neutrophilto-lymphocyte ratio and platelet-to-lymphocyte ratio with diabetic nephropathy. *Int J Clin Exp Med*. 2014;7(7):1794–801.
24. Alsayyad M, Alsamie HA. The prognostic value of lymphocyte-to-monocyte ratio in nephropathy of type 2 diabetes mellitus. *Sci J Al-Azhar Med Fac Girls*. 2019;3:181–8.

Author biography

Dharmveer Sharma, Associate Professor

Vivek Kumar Jain, Assistant Jain

Vidyanand Pandit, Assistant Professor

Shashsank Tyagi, Professor & HOD

Cite this article: Sharma D, Jain VK, Pandit V, Tyagi S. Evaluation of neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) as inflammatory markers in patients with type 2 diabetes mellitus. *Panacea J Med Sci* 2023;13(3):747-750.