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Assessment of neutrophil and platelet-to-lymphocyte ratio as inflammatory markers in type 2 diabetes mellitus patients

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ABSTRACT

Background: Diabetes mellitus (DM), metabolic disease, and its prevalence are increasing in India. DM causes micro- and macrovascular complications. Inflammation is one of the contributing factor in the pathophysiology of DM. **Aims and Objectives:** This study aimed to evaluate neutrophil and platelet-to-lymphocyte ratio (PLR) in T2DM patients. **Materials and Methods:** This study was carried out in Biochemistry Department, Lt. B.R.K.M Government Medical College, Chhattisgarh, India. In this study, 150 type 2 DM patients were considered as cases and 150 normal subjects were considered as controls. Baseline data was collected from subjects. All subjects underwent physical and clinical examination. Fasting and post prandial venous blood samples were collected. FBS, PPBS, renal profile (urea, creatinine and uric acid) were estimated in serum sample. EDTA samples were used for complete blood count (CBC). Neutrophil-to-lymphocyte ratio (NLR) and PLR ratio were calculated from CBC values. HbA1c was estimated using whole blood sample. Blood pressure and BMI were recorded. **Results:** In this study, mean age of 61.2 ± 4.0 years, systolic blood pressure 136.2 ± 14.4 mmHg, diastolic blood pressure 100.1 ± 12.5 mmHg, BMI 28.1 ± 2.6 (kg/m^2), FBS 180.7 ± 22.3 mg/dL, PPBS 289.3 ± 33.2 mg/dL, HbA1c 8.1 ± 0.7%, serum urea 39.1 ± 8.3 mg/dL, creatinine 1.1 ± 0.2 mg/dL, uric acid 7.1 ± 2.0 mg/dL, lymphocytes 18.3 ± 3.0%, NLR 8.1 ± 3.1, and PLR 20.3 ± 7.1 were significantly increased in cases than controls. **Conclusion:** Elevated ratios of NLR and PLR may serve as markers of inflammation in T2DM. These are inexpensive and helpful to assess the inflammatory status in T2DM.

Key words: Neutrophil–lymphocyte ratio; Platelet–lymphocyte Ratio; Inflammation

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease with increasing prevalence in India.[1] According to International Diabetes Federation, the prevalence of diabetes in adults was approximately 9.3% in 2019 and may increase 10.9% by 2045.[2] DM is associated with micro- and macrovascular complications. Inflammation is one of the contributing factor in the pathophysiology of DM. The inflammatory markers may cause insulin resistance by inhibiting β-cell function and by accelerating apoptosis.[3,4]

Recently, neutrophil–lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are proposed as biomarkers of inflammation.[5-7] Rudiger et al., reported the correlation between systemic inflammation and vascular disease, suggested that underlying chronic inflammation promotes the development of micro- and macroangiopathic complications in diabetic patients. White blood cell (WBC) count is also a sensitive indicator of inflammation.[8]

Studies have reported many inflammatory markers found to be related with T2DM, include interleukin-1 (IL1), IL-6, IL-8, TGF-β1, and TNF-α. However, measurement of

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these markers is not done routinely and is costly. Therefore, NLR and PLR have emerged as a novel surrogate markers.[3,4]

Turkmen et al., reported the platelet involvement in atherosclerosis by secreting proinflammatory cytokines.[9] However, platelets releases thromboxanes, which may exacerbate inflammation in patients with elevated platelet count.[10,11] It has been reported in few studies that NLR and PLR are potential inflammatory markers for diabetes.[12-14]

Aims and objectives

The study aimed to evaluate neutrophil and PLR in T2DM patients.

MATERIALS AND METHODS

This prospective study was conducted in Biochemistry Department, Lt. B.R.K.M Government Medical College, Chhattisgarh, India. In this, 150 type 2 DM patients were considered as cases and 150 normal subjects were considered as controls. Baseline data were collected from subjects. All subjects underwent physical and clinical examination. Approval from the Institutional Ethical Committee and informed consent was obtained from study participants. Patients with cardiovascular diseases, thyroid diseases, liver diseases, renal diseases, and pregnant women were excluded from the study.

After 12 h fasting, 5 mL of fasting and 2 mL post-prandial blood samples were collected. FBS, PPBS, and renal profile (urea, creatinine, and uric acid) were estimated in serum using commercially available autoanalyzer kits. EDTA samples were used for complete blood count (CBC). Neutrophil-to-lymphocyte and PLR were calculated from CBC values. HbA1c was estimated using whole blood sample. Blood pressure and BMI were recorded.

Statistical analysis

Data were expressed in Mean±SD. Categorical variables were expressed in percentage. $P<0.05$ considered significant. Data analysis was done by SPSS version 18.0.

RESULTS

In this study, mean age of 61.2±4.0 years, systolic blood pressure 136.2±14.4 mmHg, diastolic blood pressure 100.1±12.5 mmHg, BMI 28.1±2.6 (kg/m^2), FBS 180.7±22.3 mg/dL, PPBS 289.3±33.2 mg/dL, HbA1c 8.1±0.7%, urea 39.1±8.3 mg/dL, creatinine 1.1±0.2 mg/dL, uric acid 7.1±2.0 mg/dL, lymphocytes 18.3±3.0%, NLR 8.1±3.1, and PLR 20.3±7.1 were significantly increased in T2DM cases compared to controls (Table 1).

DISCUSSION

In this study, significantly elevated NLR and PLR were observed in cases. Neutrophils mainly associated with inflammation, whereas lymphocytes indicate immunoregulation.[15,16] These can indicate the systemic

Table 1: Demographic details, biochemical, hematological, and inflammatory markers between two groups

Parameters	Cases (T2DM) (n=150)	Controls (n=150)	P-value
Demographic details			
Age (years)	61.2±4.0	51.0±4.4	<0.001*
Male	90 (60%)	85 (56.6%)	-
Female	60 (40%)	65 (43.4%)	-
SBP (mmHg)	136.2±14.4	112.1±8.0	<0.001*
DBP (mmHg)	100.1±12.5	76.0±6.0	<0.001*
BMI (kg/m^2)	28.1±2.6	22.0±3.2	<0.001*
Biochemical parameters			
FBS (mg/dL)	180.7±22.3	89.2±11.2	<0.001*
Post-Prandial blood sugar (mg/dL)	289.3±33.2	120.0±7.4	<0.001*
HbA1c (%)	8.1±0.7	5.1±0.8	<0.001*
Urea (mg/dL)	39.1±8.3	25.2±6.4	<0.001*
Creatinine (mg/dL)	1.1±0.2	0.6±0.1	<0.001*
Uric acid (mg/dL)	7.1±2.0	5.1±0.9	<0.001*
Hematological parameters			
Hb (%)	11.2±1.5	11.5±1.4	0.419
White blood cells (10^3/µL)	13.0±3.2	13.2±3.7	0.050
Neutrophils (%)	77.5±4.8	74.4±5.8	0.544
Lymphocytes (%)	18.3±3.0	14.2±3.6	0.007*
Platelets, × (10^9/L)	241.5±83.4	244.1±60.2	0.523
Inflammatory markers			
NLR	8.1±3.1	4.2±1.9	<0.001*
PLR	20.3±7.1	14.1±6.2	<0.001*

*Significant, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, NLR: Neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio

inflammation and also innate and adaptive immune responses.[17,18] Inflammation caused by hyperglycemia may cause alterations in peripheral blood cell levels.[19]

Duman et al., study reported strong correlation of NLR with age, plasma glucose, and HbA1c.[20] Study by Kawamoto et al., demonstrated that NLR may be potential marker for evaluating higher degree of albuminuria in diabetics.[21] Fawwad et al., suggested that NLR may be helpful to predict microvascular complications in diabetes.[22] Rahar et al., indicated that NLR is less expensive marker to assess inflammation in diabetes.[23] Yet, another study by Liu et al., indicated that T2DM patients with elevated NLR might be more likely to develop peripheral neuropathy.[24]

Moursy et al., reported elevated NLR in diabetic patients with microvascular complications than diabetics without complications.[25] Mohammad et al., conducted a study in diabetic subjects reported that NLR is useful to assess albuminuria and carotid artery intima media thickness.[26]

Abnormal insulin action in DM may lead to increased adhesion of platelets. In addition, hyperglycemia may lead to increased platelet metabolism, imbalance in coagulation, and anticoagulation, which may be involved in atherogenesis, thrombosis, and microcirculation disturbance.[27]

It had been documented that PLR is a prognostic marker of inflammation for many conditions including peripheral arterial disease and hypertension.[5,28] Recently, PLR is shown to be useful to predict complications of diabetes. Mineoka et al., reported that PLR may be a marker for diabetic foot.[29] Duan et al., showed that PLR was correlated with proteinuria and prognosis in diabetic kidney disease.[30] Another study by Abdelaziz et al., reported elevated PLR in T2DM cases with macroalbuminuria.[3] Similarly, Akbas et al., also showed increased PLR in patients T2DM and its correlation with HbA1c.[31]

Limitations of the study

The present study has some limitations. The sample size was small. Established inflammatory markers such as CRP and IL-6 were not assessed.

CONCLUSION

The study concludes that elevated NLR and PLR in type 2 DM may serve as markers of inflammation. NLR and PLR are easy to calculate from CBC parameters. These are alternative markers for other costlier inflammatory markers such as ILs, TNF, and cytokines. These simple and inexpensive laboratory parameters are helpful to assess the impact of systemic inflammatory response in T2DM. Further, studies are recommended.

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