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Platelet-to-lymphocyte ratio: A useful predictor of glycemic control in patients with diabetes mellitus

Mohammed Fabin [1], Jayakrishnan Jayakumar [2], Swathy Shanker [3*]

1. Department of Emergency Medicine, KMCT Medical College, Mukkam, Kerala, India
2. Department of Radiology, KMCT Medical College, Mukkam, Kerala, India
3. Department of Pathology, KMCT Medical College, Mukkam, Kerala, India
* Correspondence: Swathy Shanker. Department of Pathology, KMCT Medical College, Mukkam, Kerala, India. Tel: +918593886723;
Email: swathyshanker.ss@gmail.com

Abstract

Background: Diabetes Mellitus (DM) is a metabolic disorder whose pathophysiology has been linked to various genetic and environmental factors. The main mechanism of the development of complications has been implicated as inflammation-mediated. Various blood cell parameters are being used as early indicators of inflammation-mediated endothelial dysfunction; thereby predicting the severity or prognosis of DM. In this study, we aimed to evaluate the role of platelet-to-lymphocyte ratio (PLR) in predicting glycemic control in patients with DM.

Methods: This is a retrospective, hospital-based study conducted from August 2023 to December 2023. A total of 134 patients were included in the study. The hematological and biochemical reports of the study population were retrieved, and the data obtained was analyzed using SPSS software version 16.0.

Results: In this study, it has been found that PLR is significantly increased in patients suffering from DM with poor glycemic control compared to those patients with good glycemic control (P<0.001). In concordance with other studies, a positive association was observed between PLR and disease severity.

Conclusion: Based on the findings of the study, PLR may be used as a predictive marker in assessing the severity and prognosis of DM; however, the exact cut-off value is yet to be determined.

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Introduction

Diabetes Mellitus (DM) is a chronic metabolic disorder that has been increasing in incidence globally, especially in developing countries like India. According to a study published by the Indian Council of Medical Research - India Diabetes (ICMR INDIAB) in 2023, the prevalence of DM is 10.1 crores (1). This increase in number can be attributed to an unhealthy lifestyle, as evidenced by the increase in weight- and obesity-related issues. Early intervention and lifestyle modifications can effectively improve the standard of living and prevent the onset of adverse complications like end-organ damage.

Diabetes mellitus is a complex disorder with multiple factors playing complex functions (2). The pathogenesis of Type 2 DM (T2DM) has been found to be connected to various genetic and environmental factors. An individual with a family history of DM has been reported to have a 2-4 times increased risk of developing DM compared to an individual without a family history (3). Diabetes mellitus comes into play when the pancreatic beta cells are unable to synthesize insulin or if the insulin-sensitive tissues are unable to respond to the insulin released. Progression of the disease leads to defective glucose homeostasis, causing hyperglycemia (4). Elevated blood sugar levels for a long period of time lead to various complications involving organs like the kidney, heart, eyes, etc. Glycosylated hemoglobin (HbA1c) is routinely monitored along with blood glucose levels in diabetic individuals to ensure good glycemic control (5). A diabetic patient with HbA1c less than 7% is said to have good glycemic control. HbA1c values greater than 7% indicate poor glycemic control (6).

Numerous blood cell parameters have been implicated as important in indicating endothelial dysfunction. These parameters include Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), White Blood Cell (WBC) count, and platelet count (7). Recently, ratios like neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio have been widely used. Platelet-to-lymphocyte ratio (PLR) is a hematological parameter that has been utilized as an indicator of systemic inflammation. PLR is a cheap, easily available, and simple parameter for evaluating systemic inflammation (8). Over the last 10 years, PLR has been increasingly used as a biomarker for predicting inflammation and mortality. As routine blood test is the primary investigation requested by clinicians, the importance of blood cell ratios has been emphasized in previous studies. In this study, we aimed to evaluate the role of PLR and assess the cut-off value in predicting glycemic control of patients with DM based on HbA1c values.

Methods

This was a single-center, retrospective study conducted in a tertiary hospital in Kerala, India. A total of 134 patients were included in the study. All patients with DM referred to the Emergency Medicine/Medicine Department for minor ailments were included in the study. Patients with coexisting terminal illnesses or infections/sepsis were excluded from the study. The study was conducted by including case records of patients with DM who attended the hospital from August 2023 to December 2023. Blood samples were processed by Auriba ABX Penta XLR hematology analyzer for CBC and by Tosoh GX HPLC analyzer for HbA1c reports.

HbA1c values and CBC reports were obtained from the records and tabulated in Microsoft Excel. Total White Blood Cell (WBC) counts, differential counts, and platelet counts were recorded. Absolute lymphocyte counts were calculated using multiplying the total WBC count with the percentage of lymphocytes recorded in the differential counts. The PLR was calculated by dividing platelet count with absolute lymphocyte count. The PLR = Platelet count/absolute lymphocyte counts. HbA1c values less than or equal to 7% were reported as good glycemic control, whereas HbA1c values higher than 7% were reported as having poor glycemic control (6). The data were analyzed using SPSS software version 16.0. Descriptive statistics were recorded for the continuous and categorical variables. P-value was calculated using T-test. If the parameter had a p-value of less than 0.001, it was considered to be statistically significant.

Results

A total of 134 patients with DM were included in the study, including 70 females and 64 males. The sex distribution of the study population is illustrated in (Figure 1a). The majority of patients were in the age group of 50-70 years. A total of 79 patients were in this age group. Moreover, 29 patients were in the age group of 71-90 years and 25 patients were in the age group of less than 50 years. One subject in the study population was over 90 years old (Figure 1b). The platelet counts in the study population ranged from 79,000/mm^3 to 6.9 lakh/mm^3 with a mean value of 2.84 lakh/mm^3. The majority of patients (69.4%) had platelet counts in the range of 1.5-4 lakh/mm^3. Only eight patients had platelet counts less than 1.00 lakh/mm^3 (Table 1, Figure 3).

Total WBC counts of the patients ranged from 4 300 cells/mm3 to 31 800 cells/mm3, with a mean value of 11 120 cells/mm3. The absolute lymphocyte count ranged from 472 cells/mm3 to 5 980 cells/mm3. The majority of patients (81.4%) had an absolute lymphocyte count in the range 1 000-4 800 cells/mm3 (Table 2, Figure 3). HbA1c of the patients was classified as those with good glycemic control and patients with poor glycemic control. Out of 134 cases, 79 cases had good glycemic control with HbA1c ⩽7%, and 55 cases had poor glycemic control with HbA1c >7% (Figure 4). The PLR was calculated and the following trends were observed: Patients with HbA1c less than 7% had a PLR ranging from 46.8 to 357.1 with a mean value of 132.5. Whereas in patients with HbA1c, more than 7% had PLR ranging from 58.4 to 673.1 with a mean value of 260.5. This parameter had a p-value less than 0.001 and it was statistically significant. Among 79 cases with good glycemic control, 62 patients had a PLR ⩽150, while 17 had PLR in the range of 151-500. Among 55 cases with poor glycemic control, 45 patients had a PLR in the range 151-500, while five patients

had PLR >500 and five patients had PLR ⩽150 (Figure 5). The above data shows that the majority of patients with a PLR value higher than 150 were related to poor glycemic control, whereas the majority of patients with a PLR value less than or equal to 150 showed good glycemic control.

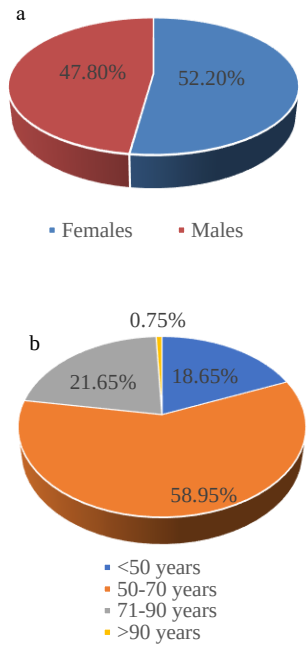

Figure 1. a. Sex distribution and **b.** Age distribution of the study population

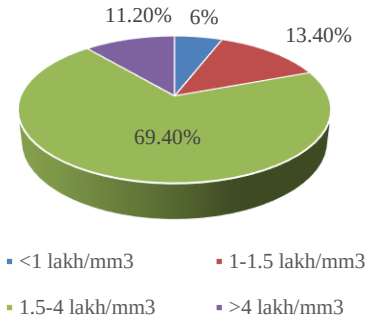

Figure 2. Platelet count in the study population and the percentage of patients

Table 1. Platelet counts in the study population

Platelet counts	Number of patients
< 1 lakh/mm^3	8
1-1.5 lakh/mm^3	18
1.5-4 lakh/mm^3	93
> 4lakh/mm^3	15

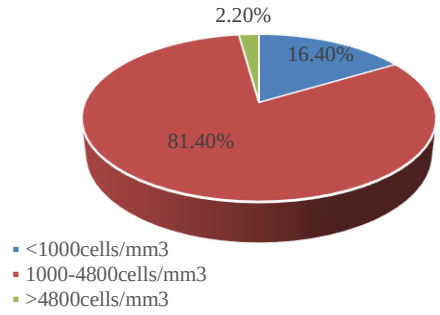

Figure 3. Absolute Lymphocyte count with percentage distribution in the study population

Table 2. Absolute lymphocyte counts in the study population

Absolute lymphocyte counts	Number of patients
< 1000 cells/mm^3	22
1000-4800 cells/mm^3	109
> 4800 cells/mm^3	3

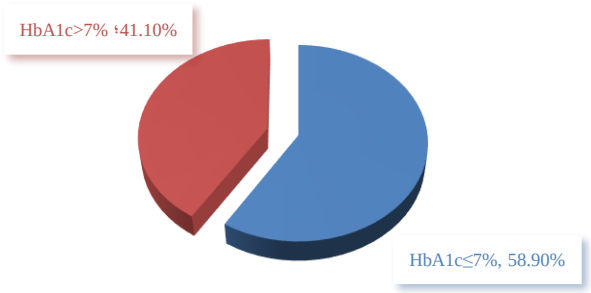

Figure 4. Glycemic control in the study population
HbA1c: Glycosylated hemoglobin

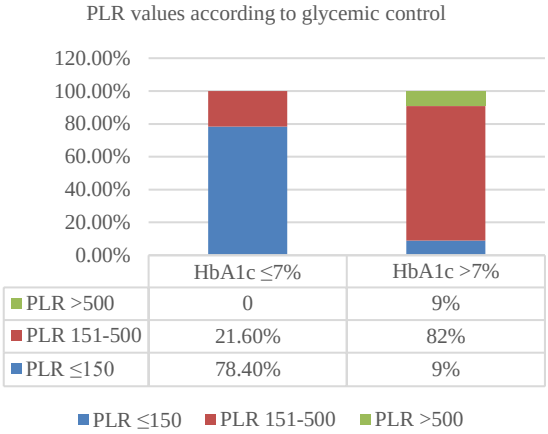

Figure 5. PLR values according to glycemic control
*PLR:Platelet-to-Lymphocyte Ratio; HbA1c:Glycosylated hemoglobin

Discussion

Diabetes mellitus can result in numerous microvascular and macrovascular complications, including retinopathy, stroke, and cardiovascular disease. Chronic inflammation plays an important role in the progression of T2DM (7). This facilitates the deterioration of micro- and macro-vascular diseases in patients with DM (8). Previous studies have shown a decrease in lymphocyte counts in patients with complications related to T2DM, such as peripheral neuropathy (9). This may be due to the fact that DM causes an increase in reactive oxygen species, which in turn leads to increased DNA damage and apoptosis of the lymphocytes (10).

The increased release of inflammatory mediators causes a decrease in absolute lymphocyte count (11). Numerous inflammatory cytokines, like interleukin-6 (IL-6), IL-8, tumor necrosis factor-α (TNF-α), and interferon-γ (IFN-γ) have been reported to be elevated in patients with DM. The decrease in lymphocyte counts reflects ineffective immune regulation (12). An increase in platelet counts shows that patients with DM have a higher inflammatory state and an increased risk of thrombosis. Thereby, PLR, as a combination of these two parameters, has a better correlation with diabetic complications (13). However, the mechanism is yet to be elucidated.

A study conducted by Liu N. et al. has shown that PLR is associated with vascular disease of the lower extremities in patients with DM (14). A study conducted by Kuanxin Zhang et al. showed that increased PLR was significantly related to the development of diabetic foot ulcers (15). A study conducted by Atak et al. also found that PLR of patients with DM was higher than that of healthy subjects. This suggests that the PLR may be a useful predictor of glycemic control. The study has shown that PLR can be used to assess the progress and severity of DM (16). Moursy et al. showed that PLR values were significantly higher in patients suffering from DM with microvascular complications compared to PLR values of patients with uncomplicated diabetes (17).

A study conducted by Mertoglu et al. showed that increased PLR was associated with high insulin resistance. Moreover, PLR was found to be higher in the diabetic group when compared to the control group (18). A study conducted

by Yue et al. showed that PLR was significantly higher in patients suffering from DM with diabetic retinopathy compared to patients without diabetic retinopathy. This study shows that increased PLR values are linked with microvascular complications in patients with DM (19). Wang JR et al. reported that PLR values were significantly higher in patients with diabetic retinopathy and PLR remained an independent risk factor for diabetic retinopathy (20).

A study conducted by Li L et al. showed that PLR values increased in patients with DM, which is associated with increased levels of albuminuria (21). According to a study conducted by Duan S et al., PLR was significantly associated with proteinuria in patients suffering from DM with diabetic kidney disease. It was reported as an independent prognostic indicator in patients with renal involvement (22). A study conducted by Kamrul Hasan et al. reported higher PLR values in patients with diabetic kidney disease compared to patients without diabetic kidney disease (23). A study conducted by Du L et al. showed that a higher PLR was associated with cognitive decline in diabetic patients (24).

This study is in concordance with the previous studies and shows that increased PLR is a good indicator of poor glycemic control in patients with DM. PLR values are an indicator of the inflammatory state of the patient, and a higher value shows that the patient is more likely to develop complications related to the condition. In our study, the increase in PLR values may be attributed to the increase in platelet counts rather than the decrease in lymphocyte counts. The majority of patients showed an absolute lymphocyte count within the normal range. The increase in platelet counts is an indicator that the patient is at increased risk of thrombosis and micro- and macro-vascular complications. The exact mechanism causing the rise in platelet counts in patients with DM remains unknown.

The major limitation of this study is that the anti-inflammatory effects of certain diabetic medications could not be taken into account and the patients on such medications could not be evaluated separately.

Conclusion

The present study is in concordance with previous studies and shows that increased PLR values are directly linked to poor glycemic control in patients with DM. The underlying mechanism of DM-induced complications has been reported to be linked to the inflammatory state of the patient. Although previous studies have shown that PLR is an excellent marker of inflammation (25), the exact cut-off values to assess disease severity are yet to be understood. A larger, population-based analysis is warranted to suggest a universal cut-off value of PLR that is accurate in prediction of glycemic control in patients with DM.

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Ethical statement

There were no ethical considerations to be considered in this research. This protocol was approved by the Institution and was performed in accordance with the principles of the Declaration of Helsinki. Retrospective nature of the study obviated the need for informed consent.

Conflicts of interest

The authors declare that there is no conflict of interest.

Author contributions

The authors equally contributed to preparation of this article. All authors read and approved the final draft of the manuscript.

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