



## UTILIZE MPV, PDW, AND P-LCR AS PREDICTIVE MARKERS FOR THE EARLY DETECTION OF DIABETES MELLITUS COMPLICATIONS.

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### Abstract

Diabetes Mellitus, one of the oldest and most widespread diseases globally, poses a significant risk due to its association with an unstable thrombogenic state resulting from impaired platelet and endothelial function, coagulation, and fibrinolysis. This cross-sectional, observational study conducted over one year (January to December 2024) at the Pathology Department of Santosh Medical College involved 152 Type 2 Diabetes Mellitus patients, with a male-to-female ratio of 1.5:1 and a majority aged between 41–50 years. The study aimed to evaluate mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR) as predictive markers for early detection of diabetic complications. Results demonstrated a significant association between these platelet indices and diabetic complications ( $p < 0.001$ ), and a strong correlation with HbA1c levels through Pearson correlation analysis. These findings suggest that regular monitoring of MPV, PDW, and P-LCR may aid in the early detection and prevention of microvascular complications in diabetic patients, potentially averting severe outcomes.

**Keywords-** Glycosylated hemoglobin, Mean Platelet Volume, Platelet Distribution Width, Platelet Large Cell Ratio

### Introduction

The World Health Organization (WHO) defines diabetes mellitus (DM) as a multifaceted metabolic disorder characterized by persistent hyperglycemia that disrupts the metabolism of carbohydrates, fats, and proteins, resulting from issues with insulin secretion, insulin action, or both <sup>1</sup>. Diabetes mellitus (DM) stands as a global pandemic, posing significant challenges to healthcare systems worldwide. This condition represents the most prevalent group of metabolic disorders, characterized by persistent hyperglycemia. The ramifications extend far beyond mere elevated blood sugar levels, manifesting in secondary damage to multiple organ systems, notably the kidneys, eyes, peripheral nerves, and blood vessels. Within this complex web of pathophysiology, platelet activation emerges as a pivotal player implicated in the development of vascular complications. Moreover, hyperglycemia drives the up-regulation of glycoproteins (Ib and IIb/IIIa) and P2Y<sub>12</sub> signaling, both critical processes that increase atherothrombotic risk in T1DM and T2DM. Elevated glucose can lead to vascular

abnormalities through several mechanisms, including disturbances in polyol pathways, the activation of protein kinase C, and the formation of advanced glycation end products. Additionally, an increase in thromboxane A<sub>2</sub>, serotonin, and thromboglobulin, along with a decrease in prostacyclin synthesis, is linked to heightened platelet activity. One possible reason for the increased mean platelet volume (MPV) in diabetes mellitus (DM) may be osmotic edema caused by high blood sugar, potentially combined with a reduced platelet lifespan in diabetic patients <sup>2,3,4</sup>. Platelet parameters encompass mean platelet volume (MPV), platelet distribution width (PDW), and platelet large cell ratio (P-LCR). MPV indicates the size or volume of platelets, PDW assesses platelet heterogeneity, and P-LCR gauges the proportion of larger platelets <sup>3</sup>. Consequently, variations in MPV, PDW, and P-LCR signify changes in thrombogenesis, making them valuable predictive markers for the vascular complications associated with diabetes mellitus (DM) <sup>5,6,7</sup>. These platelet parameters are cost-effective and practical tests that can signal the diagnosis and progression of DM complications. Therefore, we will examine the platelet parameters in diabetic patients.

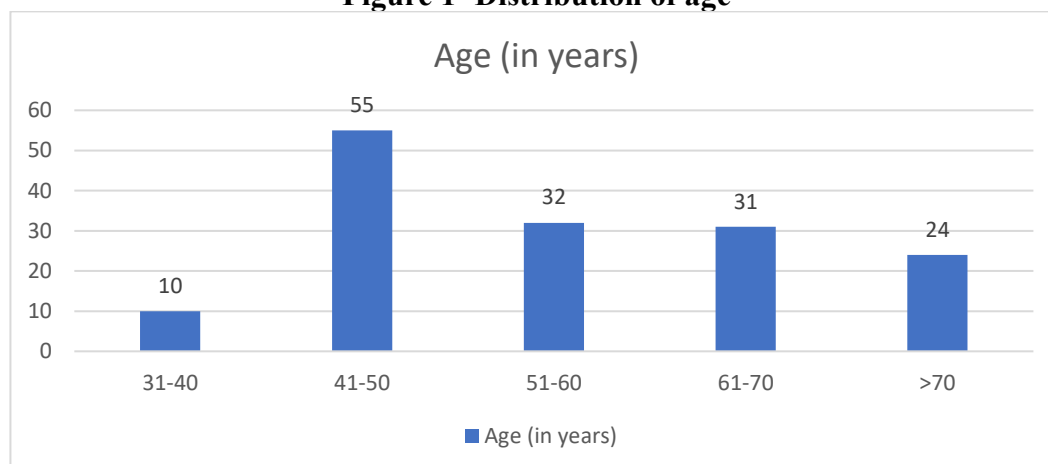
## Materials and Methods

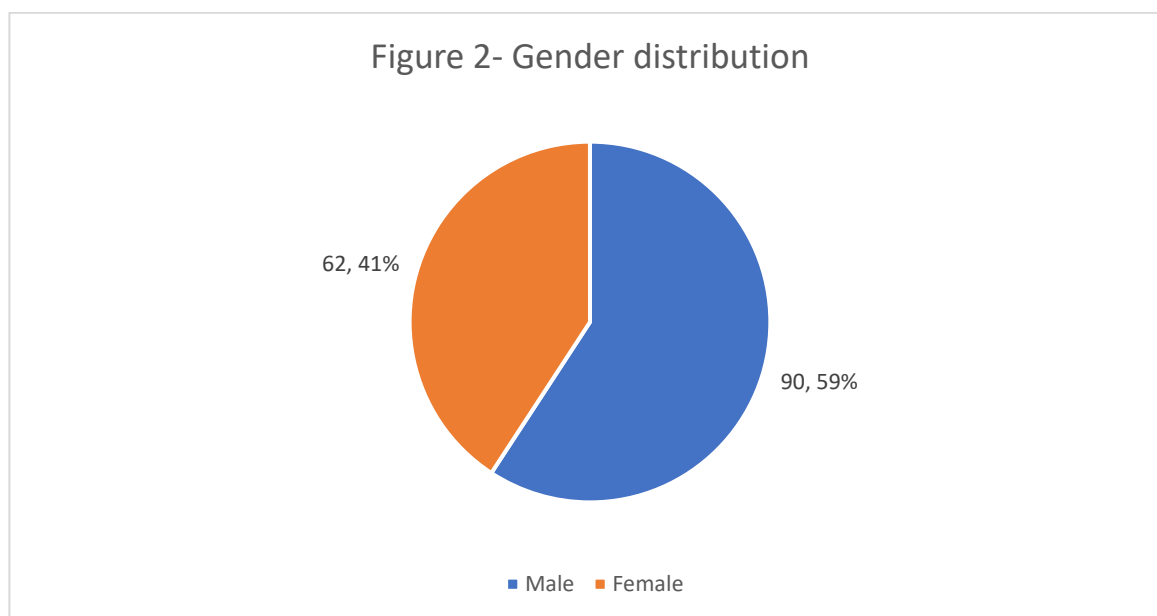
A cross-sectional observational study was conducted in the Clinical Laboratory, Pathology Department, Santosh Medical College, Ghaziabad, over a period of 1 year (January 2024- December 2024). The sample size determined was 152 cases. All the patients between the ages of 31-70 years who gave consent were included in this study. All anemic patients (male <12gm/dl, and female <10gm/dl), pregnant females, patients with acute febrile illness, thrombocytopenia, or thrombotic disorder, malignancy, or patients with a history of anti-platelet drug intake were excluded from the study. A complete clinical history and investigations were taken when the patient visited the Laboratory for sample collection. A preformed questionnaire was filled out by the patient, including his/her name, gender, and symptoms. The prior history of ischemic heart disease, stroke, retinopathy, and deranged KFT was noted. Physical examination was done at the same time. Following standard protocol of sample collection, 5 mL of venous blood was collected in a lavender vial and sent for CBC and HbA1c. Complete blood count (CBC) was carried out in Erba 360- Five-part auto analyzer, and HbA1c was carried out in COBAS-c 311, and their printed reports were taken into consideration. SPSS Statistics version 29 trial was used for statistical analyses.

## Results

During 1 year of study, a total of 152 cases were studied. All the cases were segregated according to a range variance of 10 years, from 31 to 70 years. The maximum cases were observed in 41-50 years (36.2%), followed by 51-60 years (21%). 20.4% of cases were seen in 61-70 years of age. Less case was seen in patients less than 36 years, i.e., only 2 cases. This is shown in Figure 1. Among 152 cases, more males were represented than females, i.e., 90 and 62, respectively. The Male: Female ratio is 1.5:1, which shows that more males are affected than females. This distribution is shown in Figure 2.

**Figure 1- Distribution of age**





**Table 1: Presents the distribution of common symptoms among diabetes patients.**

Symptoms	Cases	Percentage
No	84	55.3
Malaise, Polyuria	11	7.2
Polyuria, Blurry vision	13	8.5
Polyphagia, Polydipsia	17	11.2
Weight loss, Weakness	12	7.9
Difficulty in breathing, Polyphagia	15	9.9
Total	152	100

Table 1 presents the distribution of common symptoms among the cases. While 84 participants reported no symptoms, various symptom combinations were exclusively present in the case group. These included malaise and polyuria (11 cases), polyuria with blurry vision (13 cases), weight loss with weakness (12 cases), polyphagia with polydipsia (17 cases), and difficulty breathing with polyphagia (15 cases). Cases with no symptoms include patients with good glycemic control. Among 84 patients, 8 were present with poor glycemic control, while the rest, 76, presented with good glycemic control. The chi-square test result is 123, with a p-value of  $<0.001$ , indicating a statistically significant difference in symptom distribution between the groups. This highlights the symptomatic burden experienced by diabetic patients with poor glycemic control compared to diabetic patients with good glycemic control.

**Table 2: Presentation of diabetic complications among cases**

Diabetic complications	Cases	Percentage
Absent	20	13.2
Diabetic foot	28	18.4
Retinopathy	13	8.5
Nephropathy	26	17.1
Cardiovascular	16	10.5
Cerebrovascular	13	8.5
Multiple complications	36	23.8
Total	152	100

Table 2 presents the different diabetic complications of patients at the time of study data collection. In this, we observed that out of 152 cases, only 20 cases (13.2%) present with no complications, while

36 cases (23.8%) present with multiple complications. Our study population presents with diabetic foot and nephropathy as common presentations, i.e., 18.4% and 17.1%, respectively. Cardiovascular complications were presented in 16 cases (10.5%), while retinopathies and cerebrovascular complications were presented in 13 cases each (8.5%). This table highlights the implications of diabetic complications and gist for the need of rational treatment strategies to control the microvascular complications among diabetics.

**Table 3: Comparison of mean MPV between Age groups.**

Age Range	MPV (fL) (Mean $\pm$ SD)
31–40	4.64 $\pm$ 1.67
41–50	4.51 $\pm$ 1.90
51–60	5.68 $\pm$ 2.14
61–70	5.40 $\pm$ 2.20
>70	5.16 $\pm$ 1.93

Table 3 presents the comparison of mean MPV (Mean Platelet Volume) across different age groups. The mean MPV varies slightly across the age ranges, with the lowest value observed in the 41–50 age group (4.51  $\pm$  1.90 fL) and the highest in the 51–60 age group (5.68  $\pm$  2.14 fL). Participants in the 31–40, 61–70, and >70 age groups show mean MPV values of 4.64  $\pm$  1.67 fL, 5.40  $\pm$  2.20 fL, and 5.16  $\pm$  1.93 fL, respectively. The data indicate a modest variation in MPV across age groups, suggesting age-related changes in platelet size. However, further statistical analysis is required to determine if these differences are significant.

**Table 4: Comparison of mean MPV among genders**

Gender	Male	Female	P value
MPV (fL)	5.16 $\pm$ 2.07	4.95 $\pm$ 1.85	0.520

Table 4 presents the comparison of mean MPV (Mean Platelet Volume) between male and female participants. The mean MPV for males is 5.16  $\pm$  2.07 fL, while for females, it is 4.95  $\pm$  1.85 fL. The p-value for the comparison is 0.520, indicating no statistically significant difference in MPV between genders. This suggests that platelet size, as measured by MPV, is comparable between male and female participants, and gender does not appear to influence MPV significantly in this study population.

**Table 5: Comparison of MPV, PDW, and P-LCR levels among diabetics with good control (HbA1c <7) and poor control (HbA1c > 7)**

Parameters	Good glycemic control	Poor glycemic control	P -value
MPV	5.16 $\pm$ 1.86	6.98 $\pm$ 1.50	<0.001
PDW	6.53 $\pm$ 1.40	11.5 $\pm$ 2.01	<0.001
P-LCR	12.3 $\pm$ 4.17	22.4 $\pm$ 3.43	<0.001

Table 5 illustrates the comparison of platelet parameters with glycated hemoglobin levels (HbA1c). Good glycemic control is defined as patients' HbA1c levels < 7, and poor glycemic control is labelled to patients with HbA1c levels >7 (According to ADA guidelines). The MPV is 5.16 $\pm$ 1.86 in good glycemic control patients and slightly higher in poor glycemic control patients. A similar pattern is shown by PDW. It is 6.53 $\pm$ 1.40 in patients with good control and 11.5 $\pm$ 2.01 in patients with poor control. P-LCR also showed an increase in value in poor control of glycemic levels. These findings suggest that an increase in HbA1c levels or patients with poor glycemic control compared to good glycemic control shows statistically significant change and emphasize that an increase in glucose levels in blood can lead to an increase in platelet activation, which in the end results in vascular complications.

**Table 6: Correlation matrix**

		HbA1c levels	MPV (fL)	PDW (fL)	P-LCR (%)
HbA1c levels	Pearson's r	—	0.967	0.982	0.978
	p-value	—	< .001	< .001	< .001
MPV (fL)	Pearson's r		—		
	p-value		—		
PDW (fL)	Pearson's r		0.954	—	
	p-value		< .001	—	
P-LCR (%)	Pearson's r		0.951	0.962	—
	p-value		< .001	< .001	—

Table 6 presents the Pearson correlation analysis between HbA1c levels, MPV, PDW, and P-LCR in Type 2 Diabetes Mellitus patients. A positive and highly significant correlation is observed between HbA1c levels and MPV ( $r = 0.967$ ,  $p < 0.001$ ), HbA1c and PDW ( $r = 0.982$ ,  $p < 0.001$ ), and HbA1c with P-LCR ( $r = 0.978$ ,  $p < 0.001$ ), suggesting that as glycemic levels increase, platelet activation parameters also increase. Similarly, MPV shows a significant association with PDW ( $r = 0.954$ ,  $p < 0.001$ ) and P-LCR ( $r = 0.951$ ,  $p < 0.001$ ), indicating a strong interrelationship among these platelet indices. Additionally, PDW is positively correlated with P-LCR ( $r = 0.962$ ,  $p < 0.001$ ). These findings underscore the potential of platelet indices as markers of glycemic status and platelet function in diabetic individuals, emphasizing their role in the early detection of complications in Type 2 Diabetes Mellitus.

## Discussion

Type II Diabetes Mellitus is a chronic metabolic disorder marked by hyperglycemia and metabolic dysregulation. Various mechanisms have been proposed to illustrate the crucial role of metabolic abnormalities in developing diabetic vascular complications. These include: (i) diminished nitric oxide production from damaged endothelial cells and elevated endothelin-1 levels, leading to vasoconstriction; (ii) activation of genes that increase the production of mediators associated with atherogenesis; (iii) reduced collagen production, resulting in unstable plaque formation; and (iv) changed platelet function, which encourages thrombus formation<sup>8</sup>. Typically, insulin inhibits thrombus formation by blocking platelet-collagen interactions. Consequently, insulin resistance in type 2 diabetes patients heightens thromboembolic activity, which contributes to vascular complications<sup>9</sup>. Additionally, the average platelet size, determined by the mean platelet volume, facilitates the identification of large, aggregable platelets involved in thrombus formation<sup>10</sup>.

This one-year, cross-sectional, observational study was conducted in Santosh Medical College. A total of 152 patients were included of 31-70 years and above. The maximum cases were reported in the 41-50 age group, followed by the 51-60 age group. This was in concordance with Jatin A et al.<sup>11</sup>, whose mean age was  $42.26 \pm 6.42$  years. A similar higher incidence is found in a study done by Yadav G et al.<sup>9</sup> in the age group 46-50 years. All other related studies show their peak incidence in 51-60 years of age<sup>2,12,13,14</sup>.

In our study, we found male predominance with 59 % of the total population, while only 41% of the female population were recorded. These were similar to many studies conducted across the globe,<sup>9,13-16</sup>. The study conducted by Khanna et al.<sup>2</sup> found that females were more affected than males, with 57 % and 43 %, respectively. This variation can be due to demographic differences. Also, a study done by Samaddar et al.<sup>17</sup> reported different gender distribution. They found 51.19% of females and 48.8% of males in the uncontrolled group.

A study on the differences in type 2 diabetes mellitus risk, pathogenesis, and consequences by sex and gender was conducted by Kautzky-Willer et al.<sup>19</sup>. Men are more likely to develop diabetes mellitus, while women are more likely to experience its consequences, according to this study. Although the most significant risk factor, obesity, is more common in women, type 2 diabetes is more commonly diagnosed in men at younger ages and with lower body mass indices. There are typically

significant variations in sex ratios between nations. Differences in propensity, development, and clinical presentation between males and females are influenced by biological, cultural, lifestyle, environmental, and socioeconomic factors. Risk and complications are impacted differentially in men and women by sedentary lifestyle, nutritional variables, and genetic and epigenetic pathways<sup>19,21</sup>.

Sex hormones also significantly affect vascular function, body composition, inflammation, and energy metabolism<sup>20</sup>. Men with hypogonadism or women with excess androgen exhibit negative cardiometabolic characteristics, which are linked to endocrine abnormalities. Sex and gender disparities in diabetes risk and outcome are caused by both biological and psychological variables. Overall, it seems that women are more affected by psycho-social stress than males are. Furthermore, as compared to patients without diabetes, women experience higher increases in cardiovascular risk, myocardial infarction, and stroke mortality than males.

On tabulating the clinical symptoms of the patients, we found that more patients were asymptomatic (55.3%). Patients with good glycemic control showed no symptoms, while 8 cases of poor glycemic control were asymptomatic. Many patients came with the characteristic feature of a symptomatic triad, i.e., polyphagia, polydipsia, and polyuria. Complications of diabetes lead to organ-targeted symptoms like blurring of vision, difficulty in breathing, weakness, malaise, weight loss, or weight gain. Diabetes Mellitus type 2 often progresses to one or more complications.

In this study, we also examined patients for any diabetic complications at the time of examination and sample collection. We observed that maximum cases were presented with multiple complications, i.e., 36/152 (23.8%). On accounting for individual complications, diabetic foot was the most common presentation, with a prevalence of 18.4%, followed by nephropathy, 17.1%, and 10.5% cases had a history of cardiovascular complications. Diabetic foot was the common presentation found in other studies, also. A study conducted by Yadav et al.<sup>9</sup> and Dwivedi and Davangeri<sup>18</sup> reported patients affected with 21.05% and 44.76% diabetic foot, respectively. A study conducted by Thakur et al.<sup>14</sup> shows that more patients are affected by diabetic nephropathy (N-28), followed by cardiovascular (N-22) and retinopathy (N-20). Diabetic foot was the least common presentation in his study (N-2).

On assessing various platelet parameters, MPV, PDW, and P-LCR show significant variation. On comparing mean MPV across the different age groups, it shows an increase in mean MPV values is observed, suggesting an age-related change in platelet size. Also, on comparing mean MPV between genders, the mean MPV was higher among males ( $5.16 \pm 2.07$ ) than females ( $4.95 \pm 1.85$ ). This shows a statistically significant difference between genders. A similar finding of men having higher MPV than females was reported in research done by Christabel Anyika et al.<sup>13</sup> They found men have higher MPV (9.2fL) as compared to women (8.4fL), indicating differences in platelet characteristics based on gender in a diabetic population.

When comparing MPV, PDW, and P-LCR with HbA1c levels, there was a significant change seen between the good glycemic control group and the poor glycemic control group. This suggests that an increase in blood glucose levels can cause activation of platelets, which can result in vascular complications. Similar findings were observed in different studies<sup>2,5,9,11,12,14,16</sup>. Khanna et al.<sup>2</sup> showed mean MPV in HbA1c <7.5 was  $1.094 \pm 1.88$  fL and mean MPV in HbA1c > 10 was  $12.37 \pm 1.03$  fL. A study done by Yadav et al.<sup>9</sup> shows significantly higher platelet indices among good glycemic controls as compared to poor glycemic control cases.

The Pearson correlation analysis between HbA1c levels, MPV, PDW, and P-LCR in type 2 DM patients. There was a positive and highly significant correlation ( $p < 0.001$ ) between HbA1c with MPV ( $r = 0.967$ ), with PDW ( $r = 0.982$ ), and with P-LCR ( $r = 0.978$ ). Interestingly, MPV shows a significant association with PDW ( $r = 0.954$ ) and P-LCR ( $r = 0.951$ ). A study by Jatin et al.<sup>11</sup> showed a statistically significant difference in comparison of the HbA1c and MPV in T1DM and T2DM with  $p = 0.006$ ,  $r = 0.4968$  and  $p = 0.013$ ,  $r = 0.316$ , respectively. Another study, Binish et al.<sup>16</sup>, reported a statistically significant correlation between MPV and HbA1c as  $p < 0.001$  and  $r = 0.62$ . Thakur et al.<sup>14</sup> also observed a similar correlation between MPV and HbA1c. They reported  $p < 0.001$  and  $r = 0.578$ . The results indicate that platelet indices can serve as valuable indicators of glycemic control and platelet function in diabetic patients, highlighting their potential for early complication detection in type 2 diabetes mellitus.

**Conclusion**

The study found that MPV, PDW, and P-LCR were significantly higher in diabetics, suggesting a prothrombotic state. Diabetics with poor glycemic control exhibited even higher platelet indices, highlighting the potential for increased vascular complications with poorer glucose management. The findings also illustrated that platelet indices showed a notable variation in indices with glycemic control. Overall, the study reinforced the importance of monitoring platelet indices as part of the clinical management of Type 2 Diabetes Mellitus to predict and prevent associated vascular complications, especially in patients with poor glycemic control.

**Limitations of the study**

The limited sample size of 152 diabetic patients in this cross-sectional study may restrict future research, highlighting the need for a larger study sample, prospective studies with additional parameters.

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