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Metabolic consequences on platelet parameters: Mean platelet volume and platelet distribution width in type 2 diabetes mellitus

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ABSTRACT

Background: Diabetes mellitus encompasses metabolic disorders marked by chronic hyperglycemia, leading to various complications. It is considered a prothrombotic state associated with increased platelet reactivity. Parameters such as mean platelet volume (MPV) and platelet distribution width (PDW), which are indicative of platelet size, enzymatic activity, and prothrombotic risk, can be readily assessed during routine hematological analysis, facilitating early detection of this prothrombotic state. **Aims and Objectives:** The study aimed to investigate the varied alterations in platelet parameters in type 2 diabetes mellitus (T2DM) patients and tried to elucidate these parameters' predictive role in diabetes complications. **Materials and Methods:** This prospective cross-sectional study was conducted between February 2022 and February 2024, involving 100 patients with T2DM and 100 healthy non-diabetic individuals. MPV, PDW, fasting blood glucose (FBS), and glycated hemoglobin (HbA1c) levels were measured and analyzed. Statistical analysis was carried out using the Student's t-test, Mann–Whitney U-test, Chi-square test, and Spearman's correlation tests in the Statistical Package for the Social Sciences software (version 21.0). **Results:** Most of the patients were in the age group of 40–70 years with male predominance. In comparing the 100 diabetics and 100 non-diabetics groups, MPV and PDW levels were notably higher in diabetics (11.46 ± 1.75 vs. 9.40 ± 1.02 fl, 21 ± 2.57 vs. 16.72 ± 1.48%) with statistical significance ($P < 0.01$). Similarly, FBS and HbA1C levels were elevated among diabetics (179.38 ± 70.25 vs. 90.64 ± 5.93, 7.83 ± 2.24 vs. 5.02 ± 0.64) along with a positive correlation between platelet indices (MPV and PDW) and FBS, HbA1c levels in patients with T2DM. In addition, diabetic patients with complications exhibit significantly higher MPV, PDW, FBS, and HbA1c levels compared to those without complications. **Conclusion:** MPV and PDW levels show significant alterations in T2DM patients, with consistently elevated values, especially in those with complications. This underscores their potential importance as key indicators alongside glycemic indices such as FBS and HbA1c, in monitoring diabetes progression and anticipating associated complications.

Key words: Diabetes mellitus; Platelet indices; Diabetes complications

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INTRODUCTION

Diabetes mellitus (DM) comprises a spectrum of metabolic dysfunctions characterized by hyperglycemia resulting from inadequate insulin secretion, insulin insensitivity, or a combination of both. Hyperglycemia, which constitutes the foremost clinical sign of diabetes, is strongly associated with the onset of diabetic complications, such as neuropathy, nephropathy, retinopathy, and cardiovascular diseases.[1] Diabetes has become a global pandemic disease.

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The global diabetes prevalence in 2019 was estimated at 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045.[2] According to the international diabetes federation, the prevalence of diabetes in the Indian population is as high as 8.9%, with one out of every six adults with diabetes.[3] For this magnitude of the diabetes burden in India, it has earned the title "Diabetes Capital of the World."

DM is considered to be a thrombotic state. The prothrombotic condition is contributed by prolonged hyperglycemia, dyslipidemia, and insulin resistance resulting in endothelial injury and changes in platelet structure, functions, and activity.[4] Mean platelet volume (MPV) indicates alterations in platelet activation or the rate of platelet production. On the other hand, platelet distribution width (PDW) measures the heterogeneity of platelets, which is influenced by aging or heterogeneous megakaryocyte demarcation. These platelet alterations affect MPV and PDW thereby contributing to the progression of vascular complications in diabetes.[5-7] MPV and PDW can be easily determined on routine automated hematological analyzers at a relatively low cost. Evaluating the platelet parameters can serve as an early warning in identifying the disease and monitoring the progression of complications associated with DM.

Aims and objectives

The present study aimed to compare the platelet parameters (specifically MPV and PDW) in individuals with type 2 diabetes mellitus (T2DM) and healthy control subjects. In addition, we sought to establish any correlations between these parameters and glycemic control, as measured by fasting blood sugar levels (FBS) and glycated hemoglobin (HbA1c) levels in individuals with T2DM.

MATERIALS AND METHODS

Study design and participants

A cross-sectional study was conducted over 24 months, from February 2022 to February 2024. The study included 100 T2DM patients who met the inclusion and exclusion criteria, as well as 100 non-diabetic healthy controls.

Inclusion and exclusion criteria

All patients diagnosed with T2DM, as per the criteria by the American Diabetes Association, were included in the study.[8] Patients with thrombocytopenia, or those on antiplatelet and anticoagulant medications, pregnant women, females with hemoglobin <11 g/dL, males with hemoglobin <12 g/dL and patients with inflammatory conditions or diagnosed malignancy were excluded from the study.

Sample size calculation

At a 95% confidence interval and ±5% margin of error, the required sample size was calculated using the statistical formula:

$$N = 2 \times \left\{ \frac{\sigma(Z\alpha / 2 + Z (1-\beta)}{(\mu A - \mu B)} \right\}^2$$ where,

N = sample size, σ = standard deviation, α = 0.05 (95% confidence interval), and β = 0.80 (power of study),
Zα =1.96 (constant set by convention according to accepted α error),
Zβ = 0.84 (constant set by convention according to the power of the study),
μA = mean value of MPV, μB = mean value of PDW.

The sample size was determined to be 100 cases and 100 controls.

Data collection

All the study participants underwent detailed clinical evaluation for both macrovascular and microvascular complications. Further, from all the subjects, 2 mL of blood was drawn with minimal stasis from the antecubital vein using a dry sterile disposable syringe and needle. The fluoride samples (for FBS estimation) and EDTA samples (for complete blood count and HbA1c level) were kept at room temperature until processed within 4 h of collection. Complete blood count was analyzed using the five-part differential automated Hematology Analyzer Coulter LH 750 (Beckman Coulter, Inc. CA, USA). FBS or glucose estimation was carried out by AU680 Clinical Chemistry Analyzer Beckmann Coulter (Beckman Coulter, Inc. CA, USA). HbA1c estimation was carried out by HEMO ONE autoanalyzer (I.S.E. Srl Company).

Statistical analysis

Data were assessed using the Statistical Package for the Social Sciences version 21.0. Results were expressed as mean±SD (Min-Max). Student's t-test and Mann–Whitney U-test were used for comparative analysis whereas the Chi-square test was used for an association between two variables. For correlation, the Spearman rho correlation coefficient was used. A $P<0.01$ was considered statistically significant.

Ethical considerations

This study was conducted following the Declaration of Helsinki after obtaining approval from the Institutional Ethics Committee under reference no. IEC/VMMC/SJH/Thesis/06/2022/CC-231. All the subjects provided their informed written consent for participation in the present study.

RESULTS

The study was a cross-sectional study conducted on 100 T2DM patients (35 females and 65 males) and 100 non-diabetic controls (13 females and 87 males). The mean age was 56.85±8.95 and 34.65±7.02 in both groups, respectively. Platelet indices, namely MPV and PDW, were compared in patients with T2DM and healthy non-diabetic controls, and correlation with HbA1c levels and FBS was done in patients with T2DM. The following observations were made after data compilation and statistical analysis.

The mean HbA1c in diabetics was 7.83±2.24 whereas the non-diabetics had a mean HbA1c of 5.02±0.64 with P<0.001. Similarly, the mean FBS was 179.38±70.25 and 90.64±5.93 in diabetics and non-diabetics, respectively, with significant P<0.001. The platelet count was 218530.00±58892.55 in diabetics and 225320.00±59687.5 in non-diabetics which was statistically non-significant (P=0.33).

The MPV of diabetics was 11.46±1.75fl compared to 9.40±1.02fl in non-diabetics. The PDW of diabetics was calculated to be 21.97±2.57% compared to 16.72±1.48% in non-diabetics. Our study observed a statistically significant P-value (<0.001) in mean HbA1C, MPV, and PDW when diabetics and non-diabetics were compared (using the Mann–Whitney U-test). A comparison of platelet indices and blood sugar levels between type 2 diabetics (cases) and non-diabetics (controls) can be seen in Table 1.

Platelet indices were also compared between diabetic patients with and without complications. Out of 100 diabetic patients, 32 had diabetes with complications whereas 68 of them had diabetes without complications. It was observed that all the platelet indices (MPV and PDW) and blood sugar levels (FBS and HbA1c) were higher in diabetics with complications as compared to diabetics without complications and these differences were statistically significant as shown in Table 2.

A positive correlation between platelet indices with HbA1c and FBS was seen in diabetics using Spearman's rho correlation, which was also statistically significant (Table 3).

Table 1: Sample distribution based on blood sugar levels (HbA1c and FBS) and platelet indices (MPV, PDW, and platelet count)

Parameters	Cases			Controls			P-value
	Mean±SD	Min-Max	Median (IQR)	Mean±SD	Min-Max	Median (IQR)	
HbA1c	7.83±2.24	4.10–13.60	7.50 (6.13–9.37)	5.02±0.64	4.00–6.40	4.95 (4.50–5.50)	<0.001*
FBS	179.38±70.25	85–326	162.50 (119–249.50)	90.64±5.93	80–107	91 (86–95)	<0.001*
Platelet count	218530.00±58892.55	127000–400000	210000 (168250–247000)	225320.00±59687.55	103000–402000	218500 (182250–261750)	0.333
MPV	11.46±1.75	8.2–15.3	11.90 (9.75–12.60)	9.40±1.02	6.5–11.0	9.50 (8.63–10.20)	<0.001*
PDW	21.97±2.57	15.3–26.8	22.30 (20.08–23.95)	16.72±1.48	12.0–19.3	17 (16–17.80)	<0.001*

HbA1c: Glycated hemoglobin, FBS: Fasting blood glucose, MPV: Mean platelet volume, PDW: Platelet distribution width, SD: Standard deviation, IQR: Interquartile range. *Correlation is significant at P<0.001 level.

DISCUSSION

Diabetes is a common metabolic disorder that accounts for a major amount of morbidity and mortality mainly due to its microvascular and macrovascular complications. While the etiology of DM is multifactorial, platelets, especially large platelets play a significant role in both the pathogenesis of diabetes and the development of its

associated complications.[5] Patients with larger platelets as seen in T2DM can easily be identified during routine hematological analysis which helps in the easy detection of the prothrombotic state of the patient.

MPV is a parameter used to assess platelet size, as it reflects either changes in platelet stimulation or the rate of platelet production. It has been shown that large platelets are more reactive than smaller ones.[5] PDW is a measure of platelet heterogeneity, which in turn may be due to platelet aging or heterogeneous demarcation of megakaryocytes. PDW can directly measure the variability in platelet size, and its high value suggests increased production of larger platelets.[9]

Our study revealed a significant elevation in MPV with a mean of 11.46±1.75 among patients diagnosed with T2DM compared to non-diabetic controls which has a mean of 9.40±1.02, which was statistically significant (P<0.001). This corroborates findings from previous studies conducted by Papanas et al.,[9] Jindal et al.,[7] Zuberi et al.,[6] Ateş et al.,[10] Hekimsoy et al.,[11] Bhattacharjee et al.,[12] highlighting a consistent association between diabetes and increased MPV. A study conducted by Akinsegun et al. demonstrated that there was no significant difference in the MPV between the diabetics and the non-diabetic group.[13]

Table 2: Comparison of selected parameters (HbA1c, FBS, MPV, and PDW) among diabetics with complications and diabetics without complications

Parameters	Complications present (n=32) Mean±SD	Complications absent (n=68) Mean±SD	P-value
HbA1c	10.32±1.26	6.45±1.39	<0.001*
FBS	260.15±30.2	134±45.19	<0.001*
MPV	12.67±1.19	10.73±1.63	<0.001*
PDW	22.35±2.20	21.55±2.67	0.22

HbA1c: Glycated hemoglobin, FBS: Fasting blood glucose, MPV: Mean platelet volume, PDW: Platelet distribution width, SD: Standard deviation. *Correlation is significant at P<0.001 level.

Similarly, the mean PDW levels were elevated among the diabetic population (mean of 21±2.57) compared to the non-diabetic controls (mean of 16.72±1.48). It was further noted that there was a statistically significant difference in PDW, that is, P<0.001 between the diabetic population and non-diabetic controls. Observations in our study correlated with studies conducted by Alhadas et al.,[14] Jabeen et al.,[15] and Buch et al.[4]

This increase in PDW was attributed to aberrant platelet activation, culminating in the formation of pseudophilias, a characteristic feature often encountered in people with long-standing uncontrolled diabetes. This assertion was supported by Vagdatli et al.,[16] suggesting that such alterations represent a significant aspect of the pathogenic cascade in diabetic microvascular complications. This observation underscores the interplay between platelet physiology and the progression of diabetic vascular pathology. Conversely, the studies done by Citirik et al.,[17] and Gupta et al.,[18] yielded inconsistent results.

Our study analysis unveiled a significant elevation in MPV among the diabetic subjects exhibiting HbA1c levels exceeding 6.5% (HbA1c >6.5%) in contrast to non-diabetic controls with HbA1c below this threshold (HbA1c <6.5%). This finding emphasizes the potential utility of MPV as a sensitive indicator for glycemic dysregulation and underscores its intricate interplay with the pathophysiological milieu of DM. Our findings align

Table 3: Correlation of HbA1c, FBS with MPV, PDW, and platelet count in diabetic patients

	Correlations			
Spearman's rho	**HbA1c**	**Platelet count**	**MPV**	**PDW**
HbA1c				
Correlation Coefficient	1	−0.108	0.688	0.177
P-value		0.286	<0.001*	0.078
n	100	100	100	100
FBS				
Correlation Coefficient		−0.106	0.668	0.206
P-value		0.294	<0.001*	0.040**
n		100	100	100
Platelet count				
Correlation Coefficient		1	−0.047	−0.514
P-value			0.641	<0.001*
n		100	100	100
MPV				
Correlation Coefficient			1	0.285
P-value				0.004**
n			100	100

n=Total number of samples, HbA1c: Glycated hemoglobin, FBS: Fasting blood glucose, MPV: Mean platelet volume, PDW: Platelet distribution width. *Correlation is significant at P<0.001 level, **Correlation is significant at P<0.05 level.

with studies reported by Bhattacharjee et al.,[12] Demirtas et al.,[19] and Kodiatte et al.[5]

Furthermore, our study revealed that MPV levels exhibited a notable increase in diabetic patients with complications compared to those without complications, demonstrating a statistical significance (P<0.001). Conversely, although PDW levels appeared to be elevated in diabetics with complications, the statistical analysis was non-significant. Few studies conducted arrived at similar conclusions.[4,9,10] However, studies by Hekimsoy et al.,[11] and Demirtunc et al.,[20] indicated that there was no significant difference in MPV and PDW among subjects with diabetic complications.

We also observed in our study that, in T2DM patients, there was a significant positive correlation of FBS and HbA1c levels with the indices of platelet function, namely MPV and PDW. This observation resonates with studies conducted by Demirtunc et al.,[20] and Bhattacharjee et al.,[12] which also reported a similar positive correlation between FBS, HbA1c, and platelet indices. However, studies conducted by Ünübol et al.,[21] and Bavbek et al.[22] present contrasting results.

Limitations of the study

The limitation of our study is that it involved mainly male subjects in comparison to females, therefore, the data obtained in the present study may not be representative of diabetic and non-diabetic females. Hence, a larger and multi-institutional study can provide a wider perspective and deeper insight into the role of platelet parameters in the diabetic population in the near future.

CONCLUSION

The present study highlights that the alterations in MPV and PDW in T2DM can be easily identified through routine hematological analysis. Consistently elevated MPV and PDW values were observed in T2DM patients compared to non-diabetic controls, along with higher values noted in diabetics with complications than those without complications. These indices in conjunction with glycemic indices such as HbA1c and FBS serve as valuable indicators for tracking the progression of DM and anticipating associated complications such as cardiovascular disease, nephropathy, neuropathy, and others. Regular monitoring of MPV and PDW could enable clinicians to actively intervene and implement timely measures for managing the disease, potentially mitigating its progression, and reducing the risk of complications.

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Authors' Contribution:
NN- Implementation of the study protocol, literature survey, data collection, data analysis, and manuscript preparation; **PK-** Concept, design, and manuscript preparation; **SS-** Design, manuscript preparation, editing, and manuscript revision; **TBS-** Literature survey and data collection.

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