Original Article

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Pathology Section

Association of Platelet Volume Indices with HbA1c Levels in Type 2 Diabetes Mellitus and Non-diabetic Individuals: A Cross-sectional Analytical Study

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ABSTRACT

Introduction: Platelets play a significant role in the pathophysiology of diabetes-related vascular complications. Chronic hyperglycaemia contributes to endothelial dysfunction, oxidative stress and increased platelet activation, which all together promote a prothrombotic state. Platelet Volume Indices (PVI), including Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW), are considered markers of platelet activation and reactivity, early estimation of which can help in early detection of diabetes related complications.

Aim: To study association of PVI (MPV and PDW) with HbA1c in diabetes mellitus type 2 patients and non diabetics.

Materials and Methods: This cross-sectional comparative study was conducted in the Department of Pathology and the Department of Immunohaematology and blood transfusion in a tertiary care hospital of Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India on 300 subjects: 200 Type 2 Diabetes Mellitus (T2DM) patients and 100 healthy controls (blood donors) from 1st November 2018 to 31st January 2020. Diabetics were sub-divided based on HbA1c: Group A (HbA1c ≥7.5%), Group B (HbA1c 6.5-7.4%) and Group C was of controls (HbA1c ≤6.4%). Platelet indices (MPV and PDW) and HbA1c were measured and statistically analysed using Statistical Packages of Social Sciences (SPSS) version 26.0 Quantitative variables were expressed as mean±standard deviation. Chi-square test, Mann-Whitney U/Z-score test and Pearson's/Spearman correlation were applied considering p-value <0.05 statistically significant.

Results: Mean MPV of Group A was 10.83±1.69 fL, Group B was 10.53±1.51 fl and Group C was 10.00±1.36 fL. Mean PDW of Group A was 16.43±0.68 fL, Group B was 16.38±0.50 fL and Group C was 16.17±0.37 fL. MPV and PDW were significantly higher in both diabetic sub groups compared to controls (p <0.001). Group A showed the highest values, suggesting greater platelet activation. However, correlation between HbA1c and platelet indices was not statistically significant within two diabetic sub-groups (Group A and B).

Conclusion: Elevated MPV and PDW in T2DM patients suggest their potential as markers for vascular risk may serve as a practical tool for early identification of complications in T2DM. MPV may be considered a simple supportive marker for glycaemic control in T2DM patients, though validated clinical cut-off values require further studies.

Keywords: Glycated haemoglobin, Mean platelet volume, Platelet activation, Platelet distribution width, Poor glycaemic control

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder marked by insulin resistance and persistently elevated blood glucose levels. With India facing an ever-growing diabetic population, there is mounting concern over the long-term complications associated with this condition, particularly vascular risks. Chronic hyperglycaemia contributes to endothelial dysfunction, oxidative stress and increased platelet activation, which all together promote a prothrombotic state. In this context, platelet indices such as MPV and PDW have emerged as potential markers reflecting increased platelet reactivity and size factors closely linked to thrombotic events [1,2].

Glycated Haemoglobin (HbA1c) remains the standard marker for long-term glycaemic control. However, it offers limited insight into the actual thrombotic or vascular complications in diabetic patients [3]. Several regional studies have reported that T2DM patients exhibit significantly elevated MPV and PDW levels, which appear to correlate positively with higher HbA1c values, indicating that poor glycaemic control may be linked to enhanced platelet activity and potential vascular risk [4-6].

Despite these insights, critical knowledge gaps remain. Most of the current data originates from small-scale or single-center studies with limited geographic scope. There is no established national reference for platelet indices in diabetic versus non diabetic populations and studies rarely account for confounding factors such as medications, comorbidities, or lifestyle variables [7]. Moreover, the utility of combining multiple platelet indices (rather than just MPV alone) as a comprehensive predictive tool remains underexplored [8].

Furthermore, few studies have directly compared diabetic individuals with healthy blood donors under standardised lab conditions, a necessary step for establishing diagnostic relevance [9,10]. The present study, therefore, aimed to bridge these gaps by evaluating PVI in T2DM patients alongside healthy controls, to better understand their potential role as accessible, cost-effective markers of vascular risk in diabetes care. The aims and objectives of the study were to study the association of PVI with HbA1c in Diabetes mellitus type 2 patients and non diabetic healthy controls and to determine the effect of glycaemic control on platelet indices.

MATERIALS AND METHODS

The present cross-sectional comparative study was conducted in the Department of Pathology and the Department of immunohaematology and blood transfusion at Adesh Institute of Medical Sciences and Research, Bathinda, Punjab, India from 1st November 2018 to 31st January 2020. Ethical approval for the study was obtained from the

Institutional Ethics Committee before commencement vide ref no: AU/EC/FM/138/2018 dated 31st October 2018.

Sample size calculation: Minimum sample size calculated was 91 for each group as per the values of MPV observed in a pilot study run on 30 subjects (15 T2DM patients and 15 non diabetic healthy controls).

The following formula has been used to calculate the sample size:

$(Z\alpha+Z\beta)^2 (SD_1^2+SD_2^2)/(X_1-X_2)^2$

$= (1.96+2.326)^2 (0.942+1.012)/(10.66-10.04)^2$

(Where Zβ=2.326 at power of 99%, Zα=1.96 at significance level 5%)

X1= 10.66 (mean MPV of T2DM patients)

X2= 10.04 (mean MPV of non diabetic healthy controls)

Minimum sample size calculated was 91 for each group, but for the convenience of present study, sample size was taken as 200 in diabetic group and 100 in non diabetic control group.

The study included 200 diagnosed T2DM patients (cases) and 100 healthy non diabetic individuals (controls), all aged between 18 and 70 years and diabetics were further categorised into two groups for comparative analysis [11].

- **Group A (n=100):** T2DM with poor glycaemic control (HbA1c ≥7.5%)
- **Group B (n=100):** T2DM with good glycaemic control (HbA1c 6.5-7.4%)

  Group C (n=100): Non diabetic healthy controls who were taken from blood donors after taking a proper history of no co-morbidities. (HbA1c ≤6.4%)

Inclusion criteria:

Cases (Group A and B): All the confirmed T2DM patients, aged between 18 and 70 years, irrespective of duration of disease, with no history of known thromboembolic events.

Controls (Group C): Healthy individuals of either gender with no history of coronary artery disease, cerebrovascular disease, or peripheral vascular disease were included. These were taken from blood donors after taking a proper history of no above-mentioned co-morbidities.

Exclusion criteria: Subjects with anemia (Hb <13 g/dL in males, <12 g/dL in females), known malignancy, recent surgery, pregnancy, substance abuse, or those on antiplatelet/anticoagulant therapy were excluded.

Study Procedure

Sample collection and processing procedure: Written informed consent was obtained from each participant prior to inclusion in the study and venous blood was collected under standard aseptic precautions. A 3 mL of blood was drawn into Ethylenediaminetetraacetic acid (EDTA) vacutainers. Complete Blood Count (CBC) was done including PVI (MPV and PDW) by Mindray BC-6800 fully automated haematologyanalyser (6-part differential) for platelet indices. Glycated haemoglobin (HbA1c) estimation was also performed using Biorad D-10 haemoglobin testing system. Normal reference ranges of MPV and PDW as per analysers used were:

Mean Platelet Volume (MPV): 6.8-10.9 fL

Platelet Distribution Width (PDW): 11.1-19.7 fL

According to American Diabetes Association (ADA) guidelines [12], normal reference ranges of HbA1c and Random Blood Sugar (RBS) considered were:

Glycated Haemoglobin (HbA1c): Non diabetic <5.7%,

Prediabetic- 5.7 to 6.4%,

Diabetic >=6.5%

Random Blood Sugar (RBS): Non diabetic <140mg/dL

Prediabetic-140- 199 mg/dL

Diabetic >= 200mg/dL

All samples were part of routine hospital investigations and no additional cost was charged to the participants.

STATISTICAL ANALYSIS

Data were analysed using SPSS version 26.0. Quantitative variables were expressed as mean±standard deviation. Chi-square test, Mann-Whitney U/Z-score test and Pearson's/Spearman correlation were applied. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 300 participants were included in the study, with 100 subjects in each of the three groups: Group A, Group B and Group C. The mean age was highest in Group B (57.39±10.05 years), followed by Group A (54.34±9.25 years) and Group C (50.79±14.90 years). A male predominance was observed across all groups, with 58% males in Group A, 59% in Group B and 60% in Group C [Table/Fig-1].

Glycaemic and haematologic profile

Group A demonstrated markedly higher glycaemic parameters, with mean HbA1c of 11.05±2.51% and RBS of 257.58±108.05 mg/dL. Group B showed moderately elevated values (HbA1c: 6.93±0.30%, RBS: 154.14±52.04 mg/dL), whereas Group C exhibited values within the normal range (HbA1c: 5.83±0.51%, RBS: 114.51±30.68 mg/dL) [Table/Fig-1].

Platelet Volume Indices (PVI)

The MPV and PDW were higher in diabetic groups compared to the non diabetic group. The mean MPV was 10.83±1.69 fL in Group A, 10.53±1.51 fL in Group B and 10.00±1.36 fL in Group C. Similarly, the mean PDW was 16.43±0.68 fL in Group A, 16.38±0.50 fL in Group B and 16.17±0.37 fL in Group C [Table/Fig-1].

The differences in MPV and PDW between diabetic groups and the control group were statistically significant (p<0.05). However, no statistically significant difference was observed between Group A and Group B (MPV: p=0.342; PDW: p=0.770) [Table/Fig-2].

Groups	Mean age (years)	Male n (%)	Female n (%)	HbA1c (%)	RBS (mg/dL)	MPV (fL)	PDW (fL)
A	54.34 ±9.25	58 (58%)	42 (42%)	11.05 ±2.51	257.58±108.05	10.83±1.69	16.43±0.68
B	57.39±10.05	59 (59%)	41 (41%)	6.93±0.30	154.14±52.04	10.53±1.51	16.38±0.50
C	50.79±14.90	60 (60%)	40 (40%)	5.83±0.51	114.51±30.68	10.00±1.36	16.17±0.37

[Table/Fig-1]: Demographic and laboratory parameters by study group.
HbA1c: Glycated haemoglobin; RBS: Random blood sugar; MPV: Mean platelet volume; PDW: Platelet distribution width

Group Comparisons

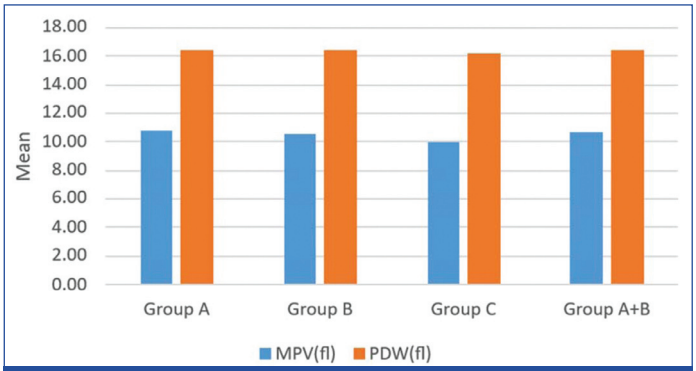
The PVI were compared between:

- Diabetic group (Group A + Group B) and non diabetic group (Group C)
- Poor glycaemic control (Group A) and good glycaemic control (Group B)
- Poor glycaemic control (Group A) and non diabetic group (Group C)
- Good glycaemic control (Group B) and non diabetic group (Group C)

When diabetic groups (Group A + Group B) were combined and compared with the non diabetic group (Group C), both MPV and PDW were significantly higher in the diabetic group. The mean MPV was 10.68±1.61 fL in Group A+B compared to 10.00±1.36 fL in Group C (Z=–3.386, p=0.001). The mean PDW was 16.40±0.60 fL in Group A+B versus 16.17±0.37 fL in Group C (Z=–3.482, p=0.001) [Table/Fig-2,3].

	Group A+B	Group C		
	Mean±SD	Mean±SD	Z	p-value
MPV (fl)	10.68±1.61	10.00±1.36	-3.386	0.001
PDW (fl)	16.40±0.60	16.17±0.37	-3.482	0.001
	Group A versus B	Group A versus C	Group B Versus C	
	p-value	p-value	p-value	
MPV (fl)	0.342	0.001	0.042	
PDW (fl)	0.770	0.002	0.016	

[Table/Fig-2]: Comparison of platelet volume indices across three study groups.
MPV: Mean platelet volume, PDW: Platelet distribution width



[Table/Fig-3]: Comparison of MPV and PDW across the study groups.
MPV: Mean platelet volume, PDW: Platelet distribution width

Pair-wise comparisons revealed no significant difference between Group A and Group B for both MPV and PDW. However, statistically significant differences were observed between Group A and Group C (MPV: p=0.001; PDW: p=0.002) and between Group B and Group C (MPV: p=0.042; PDW: p=0.016) [Table/Fig-2,3].

Correlation Analysis

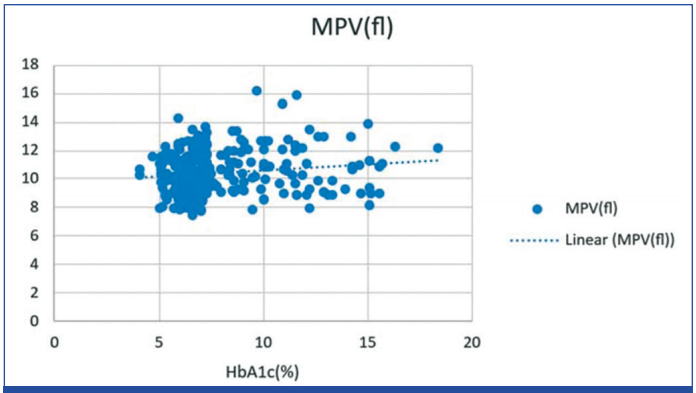
Correlation analysis for the overall study population demonstrated a weak but statistically significant positive correlation between HbA1c and MPV (Spearman's rho=0.175, p=0.002). However, within the diabetic subgroups (Group A and Group B), the correlations between HbA1c and platelet indices were not statistically significant.In contrast, in the control group (Group C), MPV showed a weak but statistically significant negative correlation with HbA1c (Spearman's rho=-0.205, p=0.040) [Table/Fig-4-6].

DISCUSSION

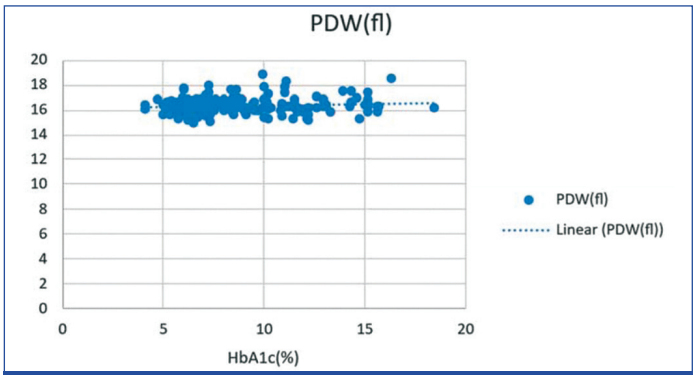
The majority of subjects were males over 50 years as consistent with earlier studies as done in Guntur, India where majority of subjects were males (male: female= 2.01:1) with mean age of diabetics being 54.44±12.16 years [13] and Lucknow, India where mean age of diabetics was 47.24±11.02 years [14], thus signifying that older age and male sex are significant risk factors for T2DM. Another study from Bengaluru, India also reported similar demographic trends, emphasising the hormonal and lifestyle-related predisposition in elderly males [15]. The pathophysiological underpinning might involve testosterone deficiency in aging males, contributing to visceral adiposity and increased T2DM risk [16].

Glycaemic and Haematological Parameters

HbA1c and RBS levels were significantly elevated in Group A (mean HbA1c: 11.05%) compared to Group B (6.93%) and Group C



[Table/Fig-4]: Scattered diagram showing correlation of HbA1c with MPV overall (Group A + Group B + Group C).
MPV: Mean platelet volume; HbA1c: Glycated haemoglobin



[Table/Fig-5]: Scattered diagram showing correlation of HbA1c with PDW overall (Group A + Group B + Group C).
PDW: Platelet distribution width; HbA1c: Glycated haemoglobin

(5.83%). These findings mirror some previous studies, reinforcing the direct link between poor glycaemic control and systemic metabolic imbalance i.e., higher HbA1c levels and increased MPV values in patients with T2DM [15,17].

Platelet Volume Indices (PVI) and Glycaemic Status

A clear gradation in MPV and PDW was observed across groups. MPV was highest in Group A (10.83 fL), followed by Group B (10.53 fL) and Group C (10.00 fL). Similarly, PDW followed the same pattern: Group A (16.43 fL), Group B (16.38 fL) and Group C (16.17 fL). These results align with the observations of other studies where MPV was significantly higher in diabetics as compared to healthy controls with MPV in diabetics being 7.91±0.87 fL, 9.48±0.8 fL and 9.21±0.76 fL, versus MPV in non- diabetics (healthy controls) being 6.91±0.71 fL, 9.34±0.8 fL and 8.29±0.46 fL, respectively [13,15,18] all of whom emphasised the impact of hyperglycaemia on platelet morphology and function. Although the absolute MPV values differed from those reported in some earlier studies, such variation can be attributed to differences in haematology analysers pre-analytical conditions and population characteristics.

Elevated MPV reflects increased platelet size and reactivity, which are central to thrombotic risk in diabetes, as emphasised in various studies and literature [19-21]. When comparing diabetic (Group A + B) versus non diabetic (Group C) Groups, MPV and PDW were significantly higher in diabetics. It was also observed in various studies that platelet indices like MPV and PDW are significantly higher in type 2 DM with microvascular and macrovascular complications such as thrombosis, thromboembolism, stroke, myocardial infarction and chronic complications like diabetic nephropathy, retinopathy etc., suggesting that these indices can be used as early marker for risk prediction of these complications in diabetics and as markers of vascular pathology [8,22].

Correlation Analysis

While MPV and PDW showed rising trends with increasing HbA1c, no significant correlation was found between glycaemic control and

Correlations		Overall	Group A	Group B	Group C	Group A+B
Spearman's rho		HbA1c (%)	HbA1c (%)	HbA1c (%)	HbA1c (%)	HbA1c(%)
MPV(fl)	Correlation coefficient	0.175	-0.051	0.151	-0.205	0.085
	p-value	0.002	0.612	0.133	0.040	0.231
PDW(fl)	Correlation coefficient	0.126	-0.028	0.021	-0.189	-0.010
	p-value	0.030	0.779	0.837	0.060	0.891

[Table/Fig-6]: Correlation of HbA1c with platelet volume indices across study groups (Spearman's rho correlation).
HbA1c: Glycated haemoglobin; MPV: Mean platelet volume; PDW: Platelet distribution width

platelet indices within diabetic sub-groups (Groups A and B). This was in line with findings from some studies which also suggested no significant correlation between poor glycaemic control and MPV [8,23,24]. However, when the entire diabetic group was analysed collectively, a weak positive correlation was observed between HbA1c and MPV.

One of the studies demonstrated a correlation coefficient of r=0.5 between HbA1c and MPV, reinforcing the hypothesis that hyperglycaemia contributes to platelet activation [13].

Clinical implications and prognostic value of MPV: Chronic hyperglycaemia promotes endothelial dysfunction and platelet hyperactivity, contributing to micro and macrovascular complications. Elevated MPV has been linked to ischaemic heart disease, retinopathy and stroke risk in diabetics [9,25]. Given the simplicity and cost-effectiveness of measuring MPV, it can serve as a practical adjunct marker to gauge vascular risk in routine diabetic monitoring.

Limitation(s)

Being a single-centre, cross-sectional study, the findings may not be generalisable to the wider population and cannot establish causality. Moreover, the sub- grouping of diabetic patients into good control and poor control was based on the single study reference [11]. Potential confounders like smoking, infections, or medications affecting platelet function were not accounted for. Inclusion of individuals with HbA1c in the prediabetic range (5.7-6.4%) in the control group may have influenced the results and represents a potential limitation of the study. The absence of follow-up limits the assessment of long-term diabetic complications. Additionally, reliance on basic platelet indices without advanced platelet function tests restricts mechanistic insight. Minor pre-analytical variability may also have influenced results.

CONCLUSION(S)

The study reaffirms that PVI MPV and PDW are significantly elevated in individuals with T2DM compared to healthy controls appears to be a practical threshold indicating heightened thrombotic risk, especially in patients with poor glycaemic control. MPV may be considered a simple supportive marker for glycaemic control in T2DM patients, though validated clinical cut-off values require further studies. While intragroup correlations with HbA1c were not statistically significant, the overall trend supports the role of MPV as a supplementary biomarker in diabetic vasculopathy. Multi-centric studies with larger sample sizes are recommended to validate these findings and further explore the predictive role of PVI in diabetes-related complications.

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