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Evaluation of Platelet Indices in Diabetes Mellitus in Relation to Glycemic Control (HbA1c) and Diabetic Complications

Dr Pradip B. Rathod[1], Dr Shambhro Nath Bhoi[2], Dr. Rupendra Kumar Sao[3]

1. Dr Pradip B. Rathod, Associate Professor, Department of Radio-Diagnosis, Chandulal Chandraker Memonal Medical College, Durg (CG)
2. Dr Shambhro Nath Bhoi, Assistant Professor, Department of Pathology, Chandulal Chandraker Memonal Medical College, Durg (CG)
3. Dr. Rupendra Kumar Sao, Assistant Professor, Department of Biochemistry, SSIMS, Junwani, Bhilai, CG

Corresponding author:

Dr Shambhro Nath Bhoi, Assistant Professor Department of Pathology, Chandulal Chandraker Memonal Medical College, Durg (CG)

Abstract

Introduction: Diabetes mellitus (DM) is a global pandemic and is recognized as a prothrombotic state characterized by enhanced platelet activity. Increased platelet activation is believed to play a significant role in the development of vascular complications associated with diabetes. Mean platelet volume (MPV) reflects platelet size and activity and may serve as a marker of thrombotic risk. This study aimed to evaluate the correlation between platelet indices and glycemic control (HbA1c) in patients with diabetes mellitus, with and without vascular complications. **Materials and Methods:** A total of 90 patients with type 2 diabetes mellitus attending the Outpatient Department of Pathology, Chandulal Chandraker Memonal Medical College, Durg (CG), were included in the study conducted from February 2019 to January 2020.. Platelet indices were measured using an automated hematology analyzer. Statistical analysis was performed using SPSS version 22. Analysis of variance (ANOVA) was used to compare platelet indices between patients with HbA1c <7 and ≥7, and between diabetic patients with and without vascular complications. **Results:** Mean platelet volume was significantly higher in patients with poor glycemic control (HbA1c ≥7) compared to those with HbA1c <7. MPV was also elevated in patients with vascular complications compared to those without complications. **Conclusion:** Elevated platelet indices, particularly MPV, are associated with poor glycemic control and the presence of vascular complications in patients with diabetes mellitus. Platelet indices may serve as simple, cost-effective markers for early identification of patients at increased risk of vascular complications.

Keywords: diabetes mellitus, mean platelet volume, platelet indices, vascular complications

INTRODUCTION

Diabetes mellitus (DM) is a global pandemic and a chronic metabolic disorder principally characterized by persistent hyperglycemia.[1] Impaired fasting glucose is a common glycemic abnormality in the general population and is considered a pre-diabetic state.[2] According to estimates from 2014, approximately 387 million people

worldwide were living with diabetes.[3] In the same year, diabetes accounted for nearly 4.9 million deaths, with one death occurring every seven seconds. Type 2 diabetes mellitus (T2DM) constitutes approximately 90% of all diabetes cases.[3] The prevalence of diabetes is steadily increasing and is expected to more than double within the next 15 years, largely due to adverse lifestyle changes, including excessive caloric intake and reduced physical activity.[4] Currently, diabetes affects about 8.3% of the adult population, with a similar prevalence among men and women.

Diabetes predominantly affects individuals between 40 and 59 years of age and is associated with at least a two-fold increase in mortality.[5] India bears one of the highest burdens of diabetes globally. A majority of patients with T2DM, as well as individuals with impaired glucose tolerance (IGT), exhibit features of metabolic syndrome (also known as dysmetabolic syndrome, insulin resistance syndrome, or syndrome X). This syndrome is characterized by a cluster of metabolic abnormalities, including central obesity, hypertension, dyslipidemia (low high-density lipoprotein cholesterol, elevated triglycerides, and small dense oxidized low-density lipoprotein particles), and endothelial dysfunction manifested as microalbuminuria.[6] Insulin resistance plays a central role in the pathogenesis of metabolic syndrome and substantially increases the risk of cardiovascular disease (CVD).

Diabetes mellitus is associated with worse early and late outcomes in acute coronary syndromes and following coronary interventions. Current consensus recommends that patients with diabetes without a prior myocardial infarction should receive aggressive multifactorial management of modifiable cardiovascular risk factors, similar to non-diabetic individuals with a history of myocardial infarction.[7] Although T2DM is strongly associated with traditional cardiovascular risk factors, the precise mechanisms underlying the markedly increased risk of CVD are not fully understood. Accelerated and premature macrovascular disease occurs in both type 1 and type 2 diabetes mellitus. Epidemiological studies suggest that type 1 DM confers a cardiovascular mortality and stroke risk comparable to that of type 2 DM, and these complications may occur at a younger age.[8]

The majority of diabetic patients develop complications primarily due to chronic hyperglycemia resulting from poor glycemic control, along with altered platelet morphology and function. Larger platelets are metabolically and enzymatically more active and exhibit increased prothrombotic potential, contributing to both microvascular and macrovascular complications.[9,10] Glycemic control can be assessed using fasting blood glucose (FBG) and glycated hemoglobin (HbA1c). Platelet function can be indirectly evaluated through platelet indices, which are routinely measured by automated hematology analyzers.[11] Increased platelet indices may reflect enhanced thrombogenic potential. Mean platelet volume (MPV) indicates the average size and activity of platelets, while platelet distribution width (PDW) reflects variability in platelet size. PDW is often elevated earlier than other platelet parameters in disorders affecting platelets.

The present study was undertaken to evaluate variations in platelet indices among patients with diabetes mellitus, to assess their association with diabetic complications, and to determine the correlation between platelet indices and glycemic control (HbA1c). This may help establish platelet indices as potential early markers for thromboembolic events in patients with diabetes mellitus.

MATERIALS AND METHODS

The present study was a prospective, cross-sectional study carried out in the Department of Pathology, Chandulal Chandrakar Memorial Government Medical College, Durg, Chhattisgarh. A total of 90 patients with type 2 diabetes mellitus attending the Outpatient Department (OPD) were included in the study. The study was conducted over a period from February 2019 to January 2020.

Inclusion Criteria

- OPD-based patients diagnosed with type 2 diabetes mellitus.

Exclusion Criteria

- Patients with anemia (hemoglobin <12 g/dL in males and <11 g/dL in females)
- Patients with diagnosed malignancy
- Patients receiving antiplatelet therapy
- Known cases of quantitative or qualitative platelet disorders

All diabetic patients underwent a detailed clinical evaluation with special emphasis on the presence of diabetic complications and current drug therapy. After obtaining informed consent, a detailed history and clinical examination were performed. Venous blood samples were collected under aseptic conditions.

Blood samples for platelet indices were collected in ethylenediaminetetraacetic acid (EDTA) tubes and analyzed within two hours of collection using an automated hematology analyzer (HORIBA XLR) to minimize variations due to sample aging. Samples for fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) estimation were collected in sodium fluoride and EDTA vacutainers, respectively. All samples were maintained at room temperature until analysis. FBS was measured using a Lablife chemistry analyzer, and HbA1c was estimated using a Proviso Merilyzer by the nephelometric method.

Based on the presence of diabetic complications, all 90 patients were divided into two groups:

Group A: Patients without diabetic complications (n = 30; 33.3%)

Group B: Patients with diabetic complications (n = 60; 66.7%)

Patients were further classified according to glycemic control based on HbA1c levels:

Group I: HbA1c <7%

Group II: HbA1c ≥7%

Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 16. Data were expressed as mean ± standard deviation (SD). Analysis

of variance (ANOVA) was used to compare variables among groups. Student's *t*-test was applied to compare two groups, namely patients with HbA1c <7% versus ≥7%, and diabetic patients with vascular complications versus those without complications. A *p*-value <0.05 was considered statistically significant.

RESULTS

The diabetic patients were divided into two groups based on HbA1c levels. Group I comprised patients with HbA1c ≤7%, while Group II included patients with HbA1c >7%. Out of the total 90 patients, 20 patients (22.2%) had HbA1c levels ≤7%, whereas 70 patients (77.8%) had HbA1c levels >7%.

Fasting plasma glucose levels were significantly higher in Group II patients with HbA1c >7% compared to those with HbA1c ≤7%. The majority of patients belonged to the age group of 40–59 years. Male patients constituted 55.6% of the study population, showing a slight male predominance.

Table 1: Age distribution of cases and controls

Age Group	No. of Patients/Controls	Percentage (%)
20-40	9	10
41-60	41	45.6
61-80	30	33.3
>81	10	11.1

Table 2: Comparison of various parameters in two groups of diabetic patients with reference to HbA1c level.

Parameters	HbA1c ≤7%	HbA1C >7%	p-value
Mean fasting plasma glucose(mg/dl)	135.6±20.4	177.7±32.5	0.0001
Mean platelet count(lacs/cmm)	2.68±1.01	2.85±1.07	0.528
Mean platelet volume (fl)	7.81±2.16	9.8±2.25	0.001
Platelet Distribution Width (PDW)	16.7±2.6	18.2±3.2	0.058

All platelet indices, including platelet count, mean platelet volume (MPV), and platelet distribution width (PDW), were found to be higher in Group II patients with HbA1c >7% compared to Group I patients with HbA1c ≤7%. However, among these parameters, only MPV showed a statistically significant difference between the two groups ($p < 0.05$).

Out of the 90 patients included in the study, 70 patients (77.8%) presented with one or more diabetic complications, while 20 patients (22.2%) had no documented complications. The observed complications included diabetic foot, hypertension, coronary artery disease, diabetic retinopathy, diabetic nephropathy, autonomic neuropathy, peripheral neuropathy, peripheral vascular disease, hypercholesterolemia, and hypertriglyceridemia.

Cardiovascular complications were the most prevalent and represent a major cause of morbidity and mortality among patients with diabetes mellitus. In the present study, cardiovascular disease was observed in 35.5% of diabetic patients, making it the most common complication identified.

Table 3: Various complications developed in patents of DM

Complications	No. of Patients/Controls	Percentage
Cardiovascular	22	35.5
Diabetic retinopathy	3	4.8
Diabetic nephropathy	2	3.2
Cerebrovascular	1	1.6
Diabetic foot	18	29.03
Others	5	8.06
Multiple	11	17.7
Total	62	100

Table 4: Comparisons of glycemic characteristics of diabetic patients without diabetic complications (Group A) and with diabetic complications (Group B)

Parameters	Group A	Group B	P-value
FPG (mg/dl)	144.65±12.9	187.7±48.8	0.0001
HbA1C (%)	8.6±2.4	11.1±3.5	0.004

Both FBS and HbA1c were higher in patients with complications due to DM than patients without complications and statistically significant.

Table 5: Comparison of platelet indices in diabetic patient without diabetic complications (Group A) and with (Group B) diabetic complications

Platelet Indices	Group A (mean+SD)	Group B (mean+SD)	P -Value
Mean platelet count(lacs/cumm)	2.6±1.04	2.7±1.1	0.718
Mean Platelet Volume (MPV) (fl)	8.3±2.3	10.7±3.4	0.004

From the tabulated data, it was observed that platelet indices increased in patients with poor glycemic control. Mean platelet volume (MPV) was significantly higher in diabetic patients with vascular complications compared to those without complications ($p < 0.05$). Both HbA1c and MPV were elevated in diabetic patients with vascular complications, suggesting a strong association between poor glycemic control, platelet activation, and the development of vascular complications.

DISCUSSION

Diabetes mellitus is the most common endocrine disorder worldwide and has a multifactorial etiology. Platelet dysfunction plays a crucial role in the development of diabetic vascular complications. Larger and more reactive platelets are frequently observed in diabetes mellitus and are considered key contributors to the prothrombotic state associated with the disease.

Abnormal platelet function in diabetes is attributed to the presence of immature, larger platelets and increased platelet activation. Vascular endothelial damage leads to enhanced platelet hyperaggregability and activation, resulting in increased release of platelet granules. This process reduces platelet survival and stimulates the bone marrow to release larger platelets due to increased megakaryocyte ploidy and activation.

In the present study, diabetic patients were classified based on glycemic control (HbA1c ≤7% and >7%) and the presence or absence of diabetic complications. Patients with poor glycemic control (HbA1c >7%) demonstrated higher platelet indices compared to those with good glycemic control. However, statistically significant differences were observed only for fasting plasma glucose (FPG) and MPV.

The mean fasting plasma glucose level was significantly higher in diabetic patients with vascular complications (177.7 ± 32.5 mg/dL) compared to those without complications (135.6 ± 20.4 mg/dL), with a p value <0.0001. Similarly, MPV was significantly elevated in patients with vascular complications (9.8 ± 2.25 fL). HbA1c levels were also higher in patients with vascular complications (11.1 ± 3.5%) compared to those without complications (8.6 ± 2.4%), and this difference was statistically significant (p <0.0001).

These findings are consistent with previous studies. Li et al. reported significantly higher MPV values in patients with type 2 diabetes, particularly in those with HbA1c ≥7%, and identified MPV as an important risk factor for peripheral arterial disease.[10] Demirtune et al. also observed significantly higher MPV in diabetic patients compared to controls and found a positive correlation between MPV and HbA1c in patients with vascular complications.[2]

If vascular damage were solely due to an increased number of large, reactive platelets, vascular injury would be constant and independent of glycemic control. However, the observed association between MPV and HbA1c suggests that platelet reactivity alone does not fully explain the progression of vascular complications. Other factors influenced by glycemic control likely contribute to vascular injury. This is further supported by the lack of significant correlation between MPV and duration of diabetes in the present study.

Microvascular complications such as diabetic retinopathy, nephropathy, and neuropathy significantly contribute to morbidity in diabetes mellitus, being major causes of blindness and end-stage renal disease. However, macrovascular complications remain the leading cause of mortality among diabetic patients. A substantial proportion of diabetic patients die due to cardiovascular disease. Insulin resistance, impaired glucose tolerance, and overt type 2 diabetes are strongly associated with increased cardiovascular risk, including coronary artery disease, peripheral arterial disease, and stroke.[6,12]

Platelets in diabetes mellitus exhibit dysregulated signaling pathways that result in enhanced activation and aggregation. This promotes thrombus formation, microvascular embolization, and release of vasoactive and mitogenic substances such as platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF), accelerating vascular lesion progression, particularly in diabetic retinopathy.[13]

In the present study, MPV was significantly higher in patients with HbA1c >7% compared to those with HbA1c ≤7% (p <0.0001), whereas platelet count and PDW did not show significant differences. Similar findings were reported by Ozder et al., who observed no significant difference in platelet count between diabetic groups.[14] Multiple studies have emphasized HbA1c as a sensitive and specific marker of long-term glycemic control and have demonstrated its positive correlation with MPV.[1,2,15–17]

Overall, the present study supports the association between poor glycemic control, increased MPV, and diabetic vascular complications, highlighting MPV as a potential prognostic marker for cardiovascular risk in patients with diabetes mellitus.

CONCLUSION

The present study demonstrates that platelet indices, particularly mean platelet volume, are significantly increased in diabetic patients with poor glycemic control (HbA1c >7%). Larger platelets are hemostatically more active and contribute to the prothrombotic state observed in diabetes mellitus, thereby increasing the risk of both microvascular and macrovascular complications.

MPV showed a strong association with HbA1c and the presence of vascular complications, suggesting its utility as a simple, cost-effective laboratory marker for monitoring platelet activity and predicting thrombotic risk in diabetic patients. Early identification of increased platelet activation may aid in timely intervention and prevention of diabetic vascular complications.

The main limitations of this study include a relatively small sample size and the lack of assessment of confounding factors such as hypertension, obesity, and dyslipidemia, which may also influence platelet indices. Further studies with larger sample sizes and comprehensive risk factor analysis are recommended to better elucidate the role of platelet indices in diabetes mellitus and its complications.

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