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Evaluating platelet indices as predictive marker for microvascular complications in type 2 diabetes mellitus

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder marked by insulin resistance and impaired insulin secretion. It is associated with long-term complications, particularly microvascular complications such as retinopathy, nephropathy, neuropathy and diabetic foot. These complications are major contributors to morbidity and mortality. Early detection and intervention are crucial, but screening is often resource-intensive. Platelet indices—Mean Platelet Volume (MPV), Platelet Distribution Width (PDW), and Platelet Large Cell Ratio (P-LCR)—reflect platelet activation and may serve as cost-effective biomarkers to predict diabetic complications.

Aims and Objectives: This study aims to assess platelet indices in patients with T2DM and to determine their association with microvascular complications.

Materials and Methods: A cross-sectional study was conducted at Navodaya Medical College Hospital & Research Centre, Raichur, including 60 participants—30 T2DM patients (disease duration >5 years) and 30 healthy controls. Platelet indices were measured using an automated analyser, and HbA1C was estimated using HPLC. Diabetic patients were further categorized based on the presence or absence of microvascular complications.

Results: MPV, PDW, and P-LCR were significantly elevated in diabetics compared to non-diabetics ($p < 0.05$). Diabetic patients with complications exhibited higher MPV, PDW, and P-LCR compared to those without complications, although these differences did not reach statistical significance. HbA1C levels were significantly higher in diabetics with complications ($p = 0.003$), while platelet count was significantly lower ($p = 0.045$).

Conclusion: This study demonstrates a significant alteration in platelet indices among T2DM patients. While MPV, PDW, and P-LCR levels were higher in patients with complications, further research with larger sample sizes and longitudinal follow-up is needed. Platelet indices may serve as valuable, cost-effective indicators for identifying diabetic patients at risk of microvascular complications, enabling earlier diagnosis and intervention.

Keywords: Diabetes mellitus, Microvascular complications, Platelet indices.

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1. Introduction

Diabetes mellitus (DM) refers to a group of metabolic conditions characterized by chronic hyperglycaemia. These conditions arise from disrupted insulin production, reduced insulin sensitivity or a combination. The classic symptoms—polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (heightened appetite)—are common.[1]

1.1. DM can be broadly classified into 2 classes

Type 1 Diabetes (T1D) is an autoimmune disease leading to destruction of pancreatic β-cells, resulting in a complete lack of insulin. This type is most frequently diagnosed in people under 20 years of age and accounts for 5-10% among all the diabetic cases.[2]

Type 2 Diabetes (T2D) is a Complex metabolic syndrome which involves a combination of reduced insulin secretion by pancreatic β-cells and impaired insulin sensitivity in peripheral tissues. This results in a relative insulin deficiency, rendering the body unable to effectively regulate blood glucose levels. T2D accounts for 90-95% of all diabetes cases.[2]

According to the International Diabetes Federation (IDF), approximately 537 million adults aged between 20-79 years worldwide had diabetes mellitus in 2021. DM is

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proving to be a global public health burden as the number is likely to go higher by another 200 million by 2045.[3]

In the year 2010 the American Diabetes Association adopted glycated haemoglobin (HbA1C) testing (with a diagnostic threshold of ≥6.5%) as an accepted method for diagnosing diabetes. HbA1C provides a retrospective assessment of blood glucose control over 6-8 weeks, offering advantages in convenience, stability and less susceptibility to day-to-day variations. Patients having HbA1C levels greater than 6.5% are diagnosed as having DM.[4]

Persistent raised blood glucose levels, combined with other metabolic derangements in patients of diabetes mellitus can damage various organ systems, predisposing them to severe complications. Most prominent are microvascular (retinopathy, nephropathy and neuropathy) and macro vascular complications with significant increase in the risk of cardiovascular disease.[1] Diabetic patients exhibit modified platelet behaviour and increased platelet responsiveness, inducing a prothrombotic state that contributes to risk of vascular disease.[5]

Screening diabetic patients for microvascular complications is economically challenging due to the need for lifelong follow-up and multispecialty involvement. A parameter to predict high-risk patients would be valuable. Diabetic patient's exhibit altered platelet function, characterized by increased size, activity and granule release, which contributes to thrombotic events and complications. Routine haematological analysis can provide platelet indices, which may aid in early detection and diagnosis of diabetes-related complications, allowing timely interventions. Estimation of Platelet indices can easily be performed from simple Complete Blood Count (CBC) test making it an inexpensive and easily available investigation.[6]

Platelet indices measure the platelet function and activity. The mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (P-LCR) show crucial role of platelets in maintaining the normal homeostasis.[7] Larger platelets have increased number of dense granules, making them more potent and thrombogenic. Therefore, higher platelet indices signal an increased tendency toward thrombosis. In diabetic patients, Microvascular damage is linked to an increased risk of cardio and cerebrovascular events, leading to higher rates of morbidity and death.[8]

Our study population included patients of type 2 diabetes mellitus, were subjected to discriminant analysis to evaluate the utility of platelet indices as indicators and predictive biomarker for microvascular complication.

2. Aims and Objective

1. To determine and compare platelet indices in type 2 Diabetes Mellitus patients and healthy controls.
2. To assess whether platelet indices correlate with the presence of microvascular complications in type 2 diabetic patients.

3. Materials and Methods

The present cross-sectional analysis was undertaken from April 2024 to September 2024, on 60 patients, aged 18 years and above, at Navodaya Medical College Hospital & Research Center, Raichur. The sample size was calculated based on the study done by Khanna P.et al.[8] They were further categorized into 2 groups of 30 subjects each.

Group 1: Patients of Diabetes diagnosed based on American Diabetes Association criteria, with more than 5 years disease duration.

Group 2: Healthy non-diabetic controls.

3.1. Inclusion criteria

Patients, both male and female aged above 18 years, suffering from type 2 Attending OPD.

3.2. Exclusion criteria

1. Patients aged <18 years, patients with anaemia or haematological disorders or active infection or malignancies, patients already on antiplatelet drugs or anticoagulants, immunosuppressants, steroids and pregnant females.
2. Patients who received blood transfusion in past 2 weeks, patients with renal, cardiac and hepatic failure.
3. Patients not willing to participate in the present study.

3.3. Methods

After taking the detailed history and clinical examination of patients, 2ml of EDTA blood sample was collected from the antecubital vein. The samples were then labelled with the identification numbers along with patients' age and sex. HbA1C was estimated by AFINION-2 (ABBOT) high-performance liquid chromatography (HPLC) method. Within 4 hours of blood collection, CBC was performed by an automated cell counter, BC-720, which provided the platelet count and platelet indices (MPV, P-LCR, and PDW).

3.4. Statistical analysis

The following statistical formula was used to calculate the sample size of 60:

$$n = 2\frac{S^2(Z1+Z2)^2}{(M1-M2)^2}$$

M1=12.59*
M2= 11.58*
S1 = 0.956*
S2 = 1.67*
S=1.36
AH=2

1-α= 0.95
1-β= 0.80
Z1= 1.96
Z2= 0.84
n = 30
Substituting the values in the above formula, sample size obtained is 30.
Since there are 2 groups, total sample size is 30*2= 60.

4. Results

Table 1 shows the comparison of mean age between diabetic and non-diabetic groups. The mean age among diabetic group (n = 30) was 51.37 years (SD = 13.02), while the non-diabetic group (n = 30) had a mean age of 51.23 years (SD = 13.90). The difference in mean age was 0.133 years, which showed no statistical significance (p = 0.97).

Table 2 shows the age distribution of diabetic and non-diabetic participants. Although we observed percentage variation across different age groups, the overall age distribution was similar in the two groups (p=0.726).

The distribution of gender was identical between the diabetic and non-diabetic groups. Both groups comprised 50.0% females (n = 15) and 50.0% males (n = 15). Overall, the total sample of 60 participants was evenly distributed by gender, with no differences observed between the groups.(**Table 3**)

Among the DM patients, 43.3% (n = 13) had illness for less than 10 years, while 56.6% (n = 17) had DM for more than 10 years.(**Table 4**)

Table 1: Comparison of the mean age between the groups using independent sample t test

Groups	N	Minimum	Maximum	Mean	S.D	Mean diff	p value
Diabetic	30	32	75	51.37	13.02	0.133	0.97
Non-Diabetic	30	32	78	51.23	13.90		

Table 2: Distribution of the subjects based on age groups

Age Groups		Groups		Total
		Diabetic	Non-Diabetic	
30 to 45 yrs	Count	10	12	22
	%	33.3%	40.0%	36.7%
46 to 60 yrs	Count	13	10	23
	%	43.3%	33.3%	38.3%
> 60 yrs	Count	7	8	15
	%	23.3%	26.7%	25.0%
Total	Count	30	30	60
	%	100.0%	100.0%	100.0%
Chi-square value-0.64				
p value-0.726				

Table 3: Distribution of the subjects based on gender

Gender		Groups		Total
		Diabetic	Non-Diabetic	
Females	Count	15	15	30
	%	50.0%	50.0%	50.0%
Males	Count	15	15	30
	%	50.0%	50.0%	50.0%
Total	Count	30	30	60
	%	100.0%	100.0%	100.0%

Table 4: Distribution of the subjects based on duration of DM

Duration of DM	Frequency	Percent
<10 yrs	13	43.3
>10 yrs	17	56.6
Total	30	100.0

Table 5: Comparison of the mean indices between the groups using independent sample t test

	Groups	N	Minimum	Maximum	Mean	S.D	Mean diff	p value
HbA1C	Diabetic	30	6.5	14.9	9.5	2.4	4.43	0.001*
	Non-Diabetic	30	4.3	5.6	5.090	.2683		
Platelet count	Diabetic	30	77000	440000	259700.0	84706.9	-13233.3	0.467
	Non-Diabetic	30	189000	385000	272933.3	51136.7		
MPV	Diabetic	30	8.5	18.3	10.70	1.82	0.91	0.012*
	Non-Diabetic	30	8.8	11.0	9.79	0.58		
PDW	Diabetic	30	11.4	46.9	16.34	6.09	2.99	0.012*
	Non-Diabetic	30	10.3	17.8	13.34	1.76		
P-LCR	Diabetic	30	17.6	64.5	30.09	10.07	6.75	0.001*
	Non-Diabetic	30	15.0	32.0	23.34	4.35		

*Significant P-value - ≤ 0.05
Non-significant P-value- > 0.05

Table 6: Distribution of the subjects based on diabetic complications

Diabetic Complications	Frequency	Percent
Absent	19	63.3
Present	11	36.6
Total	30	100.0

Table 7: Distribution of the subjects based on type of diabetic complications

Diabetic Complications	Frequency	Percent
Diabetic Foot	2	6.7
Retinopathy	3	10.0
Nephropathy	4	13.3
Neuropathy	7	23.3

Table 8: Comparison of the mean indices between the groups based on complications using independent sample t test

	Diabetic	N	Minimum	Maximum	Mean	S.D	Mean diff	p value
HbA1C	Without Complications	19	6.5	13.6	8.60	1.92	-2.52	0.003*
	With Complications	11	8.6	14.9	11.13	2.36		
Platelet count	Without Complications	19	151000	440000	283105.26	71614.63	63832.5	0.045*
	With Complications	11	77000	399000	219272.73	93477.37		
MPV	Without Complications	19	8.5	12.5	10.24	1.08	-1.27	0.064
	With Complications	11	9.4	18.3	11.51	2.53		
PDW	Without Complications	19	12.7	16.9	15.19	1.51	-3.12	0.18
	With Complications	11	11.4	46.9	18.32	9.84		
P-LCR	Without Complications	19	17.6	43.2	27.85	7.33	-6.1	0.11
	With Complications	11	18.7	64.5	33.95	13.09		

*Significant P-value - ≤ 0.05
Non-significant P-value- > 0.05

The comparison of various haematological parameters between diabetic and non-diabetic groups revealed significant differences.(**Table 5**)

The mean value For HbA1C, was significantly greater in the diabetic group (9.5 ± 2.4) as compared to the non-diabetic group (5.09 ± 0.27), having a mean difference of 4.43 (p = 0.001). There was no notable difference in Platelet count among diabetic (259,700 ± 84,706.9) and non-diabetic (272,933.3 ± 51,136.7) subjects, with a mean difference of -13,233.3 (p = 0.467).

However, diabetic patients had considerably greater Mean platelet volume (MPV) (10.7 ± 1.82) than controls (9.79 ± 0.58), with a mean difference of 0.91 (p = 0.012).

Platelet distribution width (PDW) was also raised in diabetics (16.34 ± 6.09) as compared to non-diabetics (13.34 ± 1.76), by a mean difference of 2.99 (p = 0.012).

Similarly, the platelet large cell ratio (P-LCR) was higher in diabetics (30.09 ± 10.07) than in controls (23.34 ± 4.35), having a mean difference of 6.75 (p = 0.001).

These findings highlight substantial alterations in platelet indices among diabetics.

The distribution of subjects based on diabetic complications indicates that 63.3% (n = 19) of the diabetic participants had no complications, while 36.6% (n = 11) presented with diabetic complications.(**Table 6**)

Among the diabetic complications observed, neuropathy was the most common (n=7; 23.3%), followed by nephropathy (n=4; 13.3%), retinopathy (n = 3; 10.0%), and the least common was diabetic foot (n = 2; 6.7%).(**Table 7**)

A comparison of haematological values in diabetics—those with complications versus those without—showed notable variations in several indices. Significantly higher values of HbA1C were observed in participants with complications (11.13 ± 2.36) in contrast to individuals without complications (8.60 ± 1.92), with a mean difference of -2.52 (p = 0.003). Platelet count was significantly reduced in patients having complications (219,272.73 ± 93,477.37) compared to those with no complications (283,105.26 ± 71,614.63), showing a mean difference of 63,832.5 (p = 0.045). Although Mean Platelet Volume (MPV) was higher in those with complications (11.51 ± 2.53) compared to those without (10.24 ± 1.08), this difference did not attain statistical significance (p = 0.064).(**Table 8**)

Similarly, platelet distribution width (PDW) and platelet large cell ratio (P-LCR) were greater in participants having complications (PDW: 18.32 ± 9.84, P-LCR: 33.95 ± 13.09) as against to those who do not have complications (PDW: 15.19 ± 1.51, P-LCR: 27.85 ± 7.33), but these variations were not statistically significant (PDW: p = 0.18; P-LCR: p = 0.11).

These results suggest that HbA1C and platelet count are significantly associated with the presence of complications in diabetic individuals.

5. Discussion

Diabetes Mellitus (DM) is a long-term metabolic disorder characterized by elevated blood glucose levels due to impaired insulin production or function.[9] Type 2 DM, which represents the majority of cases (90-95%), is linked to lifestyle and dietary factors. As a complex disorder influenced by genetic and environmental factors, diabetes can lead to major complications. Regular assessment of blood glucose and glycated haemoglobin (HbA1C) levels is essential for effective disease control.[5,10] Diabetes Mellitus (DM) produces a prothrombotic state characterized by increased platelet reactivity. This increased reactivity is thought to play a key role in the development of microvascular complications, affecting multiple organs including the ocular, cardiovascular, neurological, renal and gastrointestinal system, leading to severe long-term complications, resulting in increased morbidity and mortality.[5,11]

Platelets are essential for maintaining normal haemostasis. When activated, platelets undergo morphological changes, including swelling and degranulation, which are reflected in platelet indices (PI).[12]

The present study aimed to evaluate total platelet count and platelet indices like mean platelet volume (MPV), platelet large cell ratio (P-LCR) and platelet distribution width (PDW) in individuals with diabetes and to analyse their association with microvascular complications.

In this study, the age of diabetic patients ranged from 32-75 years, with mean age of 51.37 years and non-diabetic control subjects had a mean age of 51.23 years, which do not show any statistical disparity between the patients and control groups. Additionally, no significant sex-related differences were observed between diabetic and non-diabetic subjects.

HbA1C levels were significantly higher in diabetic patients (9.5±2.4) compared to the non-diabetic subjects (5.09±0.27) with a significant p-value of 0.001. Similarly, HbA1C levels in diabetic patients with complications (11.13±2.36) was higher than diabetic patients without complications (8.60 ±1.92), and is statistically significant with a p value of 0.003.

There was no significant difference in platelet count between diabetic and control groups. However, among diabetic patients, those with microvascular complications had significantly lower platelet counts. This finding aligns with the results reported by Dwivedi T. et al.[5] Nevertheless, the absence of a correlation between total platelet counts and microvascular complications in diabetic patients may be attributed to factors such as decreased platelet lifespan and increased platelet turnover.[5]

Mean Platelet Volume (MPV) reflects the average platelet size in blood, providing insight into platelet size distribution, function, and activation. Elevated MPV is linked to increased platelet aggregation, greater release of adhesion molecules and a higher risk of cardiovascular and peripheral arterial diseases.[12] In this study the MPV was significantly elevated in diabetic patients (10.7±1.82) compared to the control group (9.79±0.58) with a p value 0.01, which was also seen in the study done by K.Uma Maheshwari.et al. [12]

MPV was also higher among diabetic patients with complications (11.5±2.53) as compared to those without any complications (10.24±1.08), however this difference with a p value of 0.06 did not reach the statistical significance, consistent with findings by Taderegew et al.[6]

Platelet distribution width (PDW) depicts the variation in platelet size, with increased values suggesting platelet anisocytosis. Furthermore, PDW is a sensitive marker to

inflammatory responses and thrombotic activity. While its role in diabetes is still unclear, research suggests that PDW differs significantly between diabetic and non-diabetic individuals, especially in those with microvascular complications. A positive association has been observed between PDW and the severity of diabetic microvascular complications, like nephropathy and retinopathy, as well as disease duration and HbA1C levels.[13]

The Platelet Large Cell Ratio (PLCR) indicates the fraction of large platelets or macro platelets, among the total platelet count. It serves as a diagnostic indicator of platelet function and production, with higher levels suggesting increased platelet production and activation.[14]

In this study, both PDW and PLCR among the diabetics was elevated when compared to non-diabetic subjects with a significant p value of 0.01 and 0.001 respectively, these findings were consistent with those reported by walinjkar et al.[15] Studies conducted by Taderegew et al.[16] and Pradeep Nigam et al.[16] also demonstrated higher PDW and PLCR values in diabetic patients with complications. This similar trend was also observed in our study although the differences did not reach statistical significance (PDW, p=0.18; PLCR, p=0.11).

6. Conclusion

This study revealed significantly elevated MPV, PDW, PLCR values in patients with poor glycaemic control and microvascular complications. While the causal relationship between these increased platelet indices and vascular complications remains unclear, findings of present study suggest that platelet indices can serve as easy and affordable indicator for glycaemic control and predicting microvascular complications in patients with Type 2 Diabetes Mellitus.

7. Limitations

A key limitation of present study is the limited sample size, which cannot represent the broader population. Additionally, the lack of follow-up data prevented us from assessing the prognostic value of our findings and exploring their relationship with the progression of microvascular complications. Long-term monitoring would facilitate us to investigate the reversibility of platelet dysfunction, in response to glycaemic control.

8. Scope of the Study

This study evaluates platelet indices—MPV, PDW, and P-LCR—as predictive markers of microvascular complications in Type 2 Diabetes Mellitus (T2DM), owing to their association with platelet activation and thrombogenicity. It compares T2DM patients with disease duration >5 years to age-matched healthy controls, assessing key microvascular outcomes such as neuropathy, nephropathy, retinopathy, and diabetic foot. Given that platelet indices are inexpensive and routinely obtainable from CBC, they may aid early detection of high-risk patients and enable timely intervention. The study is restricted to a single-centre, cross-sectional design and excludes confounding conditions affecting platelets.

9. Source of Funding

None.

10. Conflict of Interest

None.

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