

Role of platelet indices and vitamin D in forecasting deterioration of glycemic control and vascular complications in type 2 diabetes

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ABSTRACT

Type 2 diabetes mellitus (T2DM) is a prevalent chronic condition associated with various complications, including vascular ones. Platelet indices and vitamin D have been proposed as potential predictors of glycemic control deterioration and vascular complications in T2DM patients. This study aimed to investigate the predictive role of platelet indices and vitamin D in the development of vascular complications and deterioration of glycemic control in type 2 diabetic patients attending Thumbay Hospital, Ajman. In this cross-sectional study, data were collected from individuals divided into two groups: a controlled group and a patient group with T2DM from the Thumbay University Hospital and Thumbay Laboratory. A total of 100 individuals aged between 20 and 75 years was included. Demographic information, vitamin D levels, and platelet indices were collected and analyzed using appropriate statistical tests. The demographic distribution of T2DM patients revealed that males accounted for 56.76% of the sample, while females represented 43.22%. The analysis of vitamin D levels showed that 58% had a deficiency, 23% had an insufficiency, and 19% fell within the optimal range. Platelet indices were evaluated in relation to glycemic control, and significant associations were found between vitamin D levels and mean platelet volume (MPV) as well as platelet distribution width (PDW). Post-hoc tests indicated significant differences in plateletcrit values among specific glycemic control groups. Furthermore, diabetic patients had significantly higher levels of fasting blood glucose and hemoglobin A1C compared to the control group, along with higher MPV and slightly lower PDW. The findings suggest a potential predictive role of platelet indices and vitamin D in the deterioration of glycemic control and the development of vascular complications in T2DM patients attending Thumbay Hospital, Ajman.

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Introduction

Type 2 diabetes mellitus (T2DM) is a multifactorial chronic disease and constitutes one of the 21st century's major health challenges that demand urgent attention from shareholders in healthcare globally. The rise in the incidence of diabetes is due to various factors, such as a sedentary lifestyle, obesity, and an aging population. Diabetes is a group of metabolic diseases characterized by hyperglycemia caused by defects in insulin secretion, insulin action, or both,^{1,2} which causes the body to gradually lose the capacity to produce enough insulin in the pancreas.³

Platelet indices [platelet count (PLT), plateletcrit (PCT), mean platelet volume (MPV), platelet distribution width (PDW)] are determinants of platelet functionality, among which increased MPV and PDW were found to be important

contributory factors causing thromboembolic complications like thrombosis and recurrent pregnancy loss.⁴ MPV is a determinant of platelet functionality, and increased MPV is related to a high risk of cardiovascular disease like myocardial infarction, stroke, and transient ischemic attacks.⁵ Altered platelets have been reported in patients with diabetes mellitus (DM) and have been considered as a prothrombotic state with enhanced platelet reactivity, and they have been associated with an increased risk of vascular complications in these patients. Platelet indices correlate with the functional status of platelets and are an emerging risk factor for vascular complications in diabetes.⁶ People with T2DM secretly enhance platelet reactivity. In this case, hyperglycemia leads to higher platelet reactivity by directly affecting as well as stimulating the platelet protein glycation.⁷

In previous studies, it has been demonstrated that MPV is an indicator of the activity and average size of the platelets and is reported to be higher in diabetic patients, a risk factor for various cardiovascular diseases.^{1,8} Vitamin D deficiency, increased platelet indices, and abnormal lipid profile are closely associated with increased vascular complications in T2DM patients. Accumulating evidence has shown a close association between poor glycemic control and the development and progression of diabetes-related complications such as cardiovascular disease, nephropathy, and retinopathy.⁹

Alterations in platelet morphology, number, and functions are associated with pathological processes and increased risk of vascular complications in patients with diabetes. The purpose of the study was to find the role of platelet indices and vitamin D in predicting deterioration of glycemic control and causing vascular complications in T2DM patients attending Thumbay Hospital (Ajman, United Arab Emirates).

Materials and Methods

This cross-sectional study took place at Thumbay Hospital and Laboratory, located in Ajman, United Arab Emirates. The samples collected for the study were processed and analyzed within the facilities of Thumbay Laboratory. Data was collected at a single point in time, allowing for an examination of correlations and associations. The study population consisted of individuals diagnosed with T2DM, aged between 20 and 75 years, who were patients of Thumbay Hospital and Thumbay Laboratory. This specific group was selected to ensure relevance and accessibility for data collection and analysis. All T2DM patients who attended Thumbay Hospital and Thumbay Laboratory during the most specified period were included in the study. Exclusion criteria included patients who were taking antiplatelet medications like aspirin and clopidogrel, individuals who declined to provide consent for participation, and pregnant women. These exclusions aimed to minimize confounding factors and ensure the safety and ethical considerations of the study.

Samples for complete blood count (CBC) and hemoglobin A1C (HbA1c) were collected in an ethylene diamine tetra acetic acid (EDTA) tube. For platelet indices, venous blood samples were collected *via* a 21-gauge needle into polypropylene tubes, including 7.5% Tri potassium EDTA, and we added sodium citrate (0.5 mL 3.8% citrate/2 mL blood) to avoid the platelet swelling induced by EDTA. MPV and PLT were measured by an automated cell counter (Abbot Cell-Dy 3500). Platelet mass was calculated as MPV

and PLT. For measuring 25-hydroxyvitamin D levels, 2 mL of blood in a lithium heparin tube was collected. The CBC test was carried out using UniCel DxH- 800/900 (Beckman Coulter) automated hematology analyzer that has a 5-part autoanalyzer able to test 23 parameters per sample. While HbA1c and 25-hydroxyvitamin D tests were performed using a DxC 800 analyzer by a competitive immunoenzymatically chemiluminescence method and cobas 6000e/601 by electrochemiluminescence immunoassay analyzer.¹⁰ All patients consulting Thumbay Hospital during the 4 months of the study period were considered as the subjects for the research. Demographic information of the participants was captured from the laboratory data manager system.

Version 29 of the Statistical Package for Social Science (IBM, Armonk, NY, USA) was used to analyze the data. The study uses both quantitative and qualitative factors, among other sorts. To determine the difference in the mean vitamin D level and other clinical parameters between the groups of diabetic duration (5 years, ≥ 5 years), parametric statistical tests such as two-sample Z or *t*-tests were used. Analysis of variance is used if the duration of diabetes is divided into more than two groups. Alternative non-parametric tests, like the median test or the Wilcoxon rank sum test/Kruskal Wallis test, were selected properly if the variables were non-normal. Spearman's rank correlation or Pearson's correlation method were used. A p-value of 0.05 or lower was regarded as statistically significant.

Results

The demographic characteristics of the study participants, totaling 100 individuals, reveal several important findings. In terms of age distribution, most participants were over 50 years old, comprising 57% of the sample, while those aged 31 to 40 years and 41 to 50 years accounted for 21% and 19%, respectively. Only 3% of participants were under 30 years of age. Regarding gender, a larger proportion of the participants were male (59%) compared to female participants (41%). Examining DM status, 67% of the participants had non-controlled DM, whereas 33% had controlled DM. When assessing the presence of complications, 33% of participants reported having complications, while 67% did not. In terms of the duration of diabetes, 28% of participants had DM for less than 5 years, while a significant 72% had lived with DM for more than 5 years. Additionally, the vitamin D status of the participants indicated a concerning trend, with 58% classified as having vitamin D deficiency, 23% categorized as vitamin D insufficiency, and only 19% achieving optimal vitamin D levels. These findings underscore the noteworthy demographic profile and health concerns of the study participants (Table 1). The PLT results demonstrate that a substantial majority, 84% of participants, fell within the normal range, while 9% exhibited high PLT, and 7% were classified as having low counts. Similarly, for MPV, 87% of individuals had normal values, with 10% showing elevated levels and 3% indicating low levels. In terms of PCT, once again, the majority (82%) of participants maintained normal PCT levels; however, high PCT was observed in 7% of cases, and 11% of participants exhibited low levels. The distribution of PDW presented a noteworthy finding, as a high PDW was noted in 67% of participants, with only 23% classified as having low PDW values and 10% within the normal range (Table 2).

The tabulation of PLT with DM status, DM complications, and vitamin D status indicates no significant associations, as reflected in the p-values of 0.543, 0.220, and 0.537, respectively. Among participants with controlled DM, 4 were classified as thrombocytosis, 29 as normal, and none as thrombocytopenia. In contrast, those with non-controlled DM showed 5 cases of thrombocytosis, 55 normal counts, and 7 thrombocytopenic cases. Similarly, for those with complications, 5 had thrombocytosis, 58 were normal, and 4 were thrombocytopenic, while participants without complications recorded 4 thrombocytosis, 26 normal, and 3 thrombocytopenia.

Table 1. Demographic characteristics of study participants.

Factors	Cases (n=100)
Age group, n (%)	
Less than 30 years old	3 (3)
31-40 years old	21 (21)
41-50 years old	19 (19)
More than 50 years old	57 (57)
Gender, n (%)	
Male	59 (59)
Female	41 (41)
Diabetes mellitus status, n (%)	
Controlled	33 (33)
Non-controlled	67 (67)
Complications, n (%)	
Yes	33 (33)
No	67 (67)
Diabetes mellitus duration, n (%)	
Less than 5 years	
More than 5 years	28 (28) 72 (72)
Vitamin D status, %	
Deficiency	58
Insufficiency	23
Optimal	19

Regarding vitamin D status, 7 individuals with deficiency had thrombocytosis, 49 were normal, and 2 were thrombocytopenic, while those with insufficient vitamin D had no thrombocytosis, 20 were normal, and 3 were thrombocytopenic. Overall, the results suggest that PLT is not significantly influenced by DM status, complications, or vitamin D status in this study population (Table 3). The cross-tabulation analysis of MPV, PCT, and PDW in relation to DM status, complications, and vitamin D status yielded several noteworthy findings. A significant association was observed between MPV and DM status ($p=0.003$), with participants who had controlled DM showing predominantly normal MPV levels (33 cases), while those with non-controlled DM had a higher incidence of high MPV (10 cases). The associations with DM complications ($p=0.373$) and vitamin D status ($p=0.397$) were not significant. For PCT, no significant differences were found across DM status ($p=0.159$), complications ($p=0.200$), or vitamin D status ($p=0.444$). In contrast, PDW showed no significant relation to DM status ($p=0.545$) but indicated a significant association with vitamin D status ($p=0.041$), where 37 individuals with insufficient vitamin D levels exhibited high PDW. These findings suggest that while MPV is influenced by DM status, PCT and PDW levels are affected by vitamin D status, highlighting the need for further exploration of these relationships in the context of hematological health (Table 4).

The cross-tabulation analysis of vitamin D status in relation to DM status and complications indicates notable findings. The association between vitamin D status and DM status was not statistically significant ($p=0.273$). Among participants with controlled DM, 5 were classified as sufficient, 7 as insufficient, and 21 as deficient in vitamin D. In contrast, non-controlled diabetics had 14 sufficient, 16 insufficient, and 37 deficient cases, highlighting a higher prevalence of deficiency in non-controlled DM. Conversely, a significant association was observed between vitamin D status and DM complications ($p=0.027$). Among those with complications, 8 participants had sufficient vitamin D, 17 were insufficient, and 42 were deficient, suggesting that vi-

Table 2. Frequency of platelet parameters among cases.

Parameters	Normal, n (%)	Low, n (%)	High, n (%)
Platelet count	84 (84)	7 (7)	9 (9)
Mean platelet volume	87 (87)	3 (3)	7 (7)
Plateletcrit	82 (82)	11 (11)	7 (7)
Platelet distribution width	10 (10)	23 (23)	67 (67)

Table 3. Cross-tabulation between platelet count and diabetes mellitus (DM) status, DM complications and vitamin D status.

Parameters		Platelet count			p
		Thrombocytopenia	Normal	Thrombocytosis	
Diabetes mellitus status	Controlled	-	29	4	0.543
	Non-controlled	7	55	5	
Complications	Complicated	4	58	5	0.220
	Non-complicated	3	26	4	
Vitamin D status	Deficient	2	49	7	0.537
	Insufficient	3	20	-	
	Sufficient	2	15	2	

tamin D deficiency is more common in individuals experiencing DM complications (Table 5).

Discussion

Both diabetes and cancer are associated with chronic inflammation, which often complicates vascular health. The role of platelet indices in predicting complications implies a pro-inflammatory state, which may be similar in cancer patients with elevated angiogenesis.^{11,12} Also, in the context of thrombophilia during pregnancy, it is crucial to consider the role of platelets, as they play a significant part in hemostasis and vascular health.^{13,14}

The study found substantial variations in the prevalence of both microvascular and macrovascular complications among cases. Factors associated with higher complication prevalence included older age, male sex, low level of education, longer diabetes duration, and history of hypo-

glycemia. Additionally, higher HbA1c levels were correlated with microvascular complications, consistent with previous studies on the impact of glycemic control on microvascular outcomes.^{1,15}

Another article studied the importance of predicting deterioration of glycemic control found in their analysis. The researchers identified predictors of loss of glycemic control in youth-onset T2DM over a 5-9-year follow-up period. They confirmed that the population of youth with T2DM is heterogeneous, consisting of subsets at risk of rapid glycemic control loss and those maintaining control for a longer period.^{16,17}

Previous findings demonstrated that baseline HbA1c levels after a few months of metformin monotherapy were predictive of glycemic control loss within 48 months.¹⁸ The study demonstrated that an increase in HbA1c of more than 0.5% over any interval was predictive of future loss of glycemic control. Importantly, this prediction held true regardless of the starting HbA1c level, indicating that even a

Table 4. Cross-tabulation between mean platelet volume, plateletcrit, platelet distribution width, diabetes mellitus (DM) status, DM complications and vitamin D status.

Parameters		Low	Normal	High	p
Mean platelet volume					
DM status	Controlled	-	33	-	0.003
	Non-controlled	3	54	10	
Complications	Complicated	2	59	6	0.373
	Non-complicated	1	28	4	
Vitamin D status	Deficient	2	49	7	0.397
	Insufficient	-	22	1	
	Sufficient	1	16	2	
Plateletcrit					
DM status	Controlled	3	29	1	0.159
	Non-controlled	3	29	1	
Complications	Complicated	8	53	6	0.200
	Non-complicated	6	57	4	
Vitamin D status	Deficient	5	25	3	0.444
	Insufficient	8	45	5	
	Sufficient	-	23	-	
Platelet distribution width					
DM status	Controlled	8	3	22	0.545
	Non-controlled	8	3	22	
Complications	Complicated	15	7	45	0.064
	Non-complicated	18	8	41	
Vitamin D status	Deficient	5	2	26	0.041
	Insufficient	17	4	37	
	Sufficient	1	5	17	
DM status	Controlled	5	1	14	

DM, diabetes mellitus.

Table 5. Cross-tabulation between vitamin D status, diabetes mellitus (DM) status and DM complications.

Parameters		Vitamin D status			p
		Deficient	Insufficient	Sufficient	
Diabetes mellitus status	Controlled	21	7	5	0.273
	Non-controlled	37	16	14	
Complications	Complicated	42	17	8	0.027
	Non-complicated	16	6	11	

rise in HbA1c within the non-diabetes range (within current treatment targets) should raise concern. In other words, an HbA1c increase exceeding 0.5% did not merely indicate a gradual, continuous rise in HbA1c over time but predicted rapid deterioration in glycemic control, even if overall control appeared initially acceptable.

Other factors demonstrated to be examined within the T2DM complication was the platelet indices, including MPV, PDW, and PLT, which play a crucial role in understanding platelet function and activation in individuals with T2DM. In a similar study conducted by Kodiatte *et al.*, platelet activation was found to contribute to the development of vascular complications by triggering thrombus formation and releasing substances like platelet-derived growth factor and vascular endothelial growth factor, which accelerate the progression of vascular lesions.⁸

MPV can also be elevated because of atherosclerotic events such as myocardial infarction, which leads to the consumption of smaller platelets and compensatory production of reticulated platelets.^{8,19}

Glycemic control, as indicated by HbA1c levels, was associated with lower MPV values, suggesting that better glycemic control may reduce platelet hyperactivity and prevent or delay diabetic vascular complications. Higher MPV in diabetic patients with higher HbA1C indicates poor glycemic control. This means that elevated MPV could be the cause of vascular complications.²⁰

Also, other studies reported MPV, PDW, and platelet-large cell ratio (P-LCR) were significantly higher among T2DM patients with microvascular complications, and this indicates that platelet indices can be used as prognostic markers of vascular complications.²¹

The correlation between HbA1c and PDW was found to be significant in current study, suggesting that PDW may reflect changes in diabetic regulation over shorter periods compared to HbA1c. The elevated PDW in T2DM patients with neuropathy and nephropathy is noteworthy, as higher PDW values have been associated with increased mortality in patients with acute myocardial infarction and poor glycemic control in diabetic populations.^{22,23}

It has also been observed that these three factors (P-LCR, PDW and MPV) have been deranged among diabetic patients with complexities in comparison to those without complications. However, PCT has not shown any significant interlink in certain studies.

On the other hand, vitamin D deficiency has also been associated with an increased risk of vascular complications. Vitamin D plays a crucial role in regulating blood pressure, reducing inflammation, and improving endothelial function. Its deficiency has been linked to hypertension, chronic low-grade inflammation, and insulin resistance, all of which contribute to vascular damage and atherosclerosis.^{24,25}

Although many studies have sought to establish an association between vitamin D levels and DM, only a few studies have included Korean patients with DM.^{26,27} Furthermore, the mechanism by which vitamin D affects glucose control in DM patients is unclear. Therefore, in this study, we examined differences in the associations between vitamin D levels and glucose in individuals with and without DM.

In the current study, we investigate the predictive role of platelet indices and vitamin D in the deterioration of glycemic control and the development of vascular compli-

cations in T2DM patients. The demographic distribution of the T2DM patients was analyzed, revealing that males accounted for 56.76% of the sample, while females represented 43.22%. Secondly, an examination of the patients' vitamin D levels showed that 58% had a deficiency, 23% had an insufficiency, and 19% fell within the optimal range. This finding is in line with that of several studies that concluded that early screening for vitamin D serum level is recommended for T2DM patients.^{1,28,29}

Regarding the relationship between vitamin D and platelet indices, several cross-tabulation tables were utilized. The analysis revealed a significant association between vitamin D levels and MPV, suggesting that vitamin D may impact MPV. However, no significant associations were found between vitamin D levels and PLT or PCT. This finding, supported by several previous studies, concludes that there was a strong association between a low vitamin D level and a high MPV; therefore, vitamin D deficiency may be associated with increased MPV.^{1,8} Additionally, the relationship between vitamin D and PDW was explored, and a significant association between these variables was identified through the Chi-Square test. This suggests that vitamin D might have an influence on PDW.

Finally, a comparison between the controlled group and the diabetic patients was made in terms of fasting blood glucose (FBG), HbA1c, and platelet indices. It was found that diabetic patients had significantly higher levels of FBG and HbA1c compared to the controlled group. Moreover, diabetic patients exhibited significantly higher MPV and slightly lower PDW. However, there were no statistically significant differences in PLT and PCT between the two groups.

The research has several limitations that should be considered when interpreting the findings. Firstly, the sample size is limited and may not be representative of the entire population of T2DM patients. A larger and more diverse sample is needed to ensure more generalizable results. Additionally, the study focuses on a specific demographic distribution of gender, which may not apply to other demographic groups or regions.

Another limitation is the cross-sectional design of the study that limits the ability to establish causal relationships between variables. Longitudinal studies would be more suitable for exploring temporal associations.

Conclusions

The findings suggest a potential predictive role of platelet indices and vitamin D in the deterioration of glycemic control and the development of vascular complications in T2DM patients attending Thumbay Hospital, Ajman. Overall, the results of the analysis provide valuable insights into the relationships between platelet indices, glycemic control, and vitamin D levels in T2DM patients. While some associations were observed, such as the significant association between vitamin D levels and MPV, further research is needed to fully understand these relationships and their clinical significance. The findings emphasize the complexity of T2DM and the need for a comprehensive approach to its management, considering various factors that may contribute to the disease's progression and complications.

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