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"CORRELATION BETWEEN PLATELET INDICES AND HBA1C IN TYPE 2 DIABETIC PATIENTS"

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Abstract

Diabetes is a major health pandemic with increased risk of micro- and macrovascular disease and platelets may be involved as a causative agent with respect to altered platelet morphology and function. Hyperglycemia contributes to greater platelet reactivity through direct effects and by promoting glycation of platelet proteins. Platelet indices are markers of platelet activation and are parameters obtained daily as a part of an automated blood count. This study is done to find out any correlation of platelet indices like MPV and PDW with Hba1c and comparisons of platelet indices in good (HbA1c<7) and poor (HbA1c≥7) glycemic control in type 2 diabetic patients which could be helpful in predicting an impending thrombotic state and complications of diabetes.

A Prospective study was undertaken at the central laboratory of Sir T Hospital, Bhavnagar, on selected diabetic patients according to inclusion and exclusion criteria. From the EDTA vacuette, samples were aspirated for various parameters like platelet count, MPV, PDW and HbA1c. Reports were collected, data were entered into a Master chart and Statistical analysis was done.

The poor glycemic control group (HbA1c≥7) has increased mean Hba1c, mean MPV and mean PDW compared to good glycemic control (HbA1c<7) which are statistically significant ($p<0.05$). Positive correlation were found between HbA1c and MPV and HbA1c and PDW.

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Platelet indices like MPV and PDW along with HbA1c could be used as a cost-effective tool to monitor diabetes mellitus patients and could be helpful in predicting an impending thrombotic state and complications of diabetes.

Key Words: Diabetes, Good glycemic control, Hba1c, Platelet indices, Poor glycemic control.

Main Text

Introduction: Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation. The number of people with diabetes has increased from 108 million in 1980 to 422 million in 2014. Prevalence has been rising more rapidly in low- and middle-income countries than in high-income countries. In 2019, diabetes and kidney disease due to diabetes caused an estimated 2 million deaths, as per WHO. In India, there are estimated 77 million people above the age of 18 years are suffering from diabetes (type 2) and nearly 25 million are pre-diabetics. More than 50% of people are unaware of their diabetic status which leads to health complications if not detected and treated early. Adults with diabetes have a two- to three-fold increased risk of heart attacks and strokes, as per WHO-India.

Patients with diabetes are at increased risk of developing micro- and macrovascular disease and platelets may be involved as a causative agent with respect to altered platelet morphology and function. [1]

Hyperglycemia can increase platelet reactivity by inducing non-enzymatic glycation of proteins on the surface of the platelet. Such glycation decreases membrane fluidity and increases the propensity of platelets to activate. The osmotic effect of glucose and activation of protein kinase C may increase platelet reactivity. People with diabetes have increased expression of the surface glycoproteins Ib and IIb/IIIa, these glycoproteins mediate platelet adhesion and adherence. People with diabetes typically manifest hypertriglyceridemia,

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VLDL which is rich in triglycerides increases platelet reactivity.

Insulin antagonizes the effect of platelet agonists such as collagen, ADP, epinephrine and platelet-activating factor. Thus, resistance to the effects of insulin (relative insulin deficiency) or absolute deficiency of insulin reduces insulin-mediated antagonism of platelet activation and increases platelet reactivity.

Oxidative stress that may contribute to increased platelet reactivity. Superoxide has been shown to increase platelet reactivity by enhancing release of intraplatelet calcium after activation. In addition, superoxide inhibit the biological activity of NO and impairs endothelial function. Thus, the inflammation increased platelet reactivity.

Platelets from diabetic patients have increased sensitivity to secondary aggregation in response to agonists including ADP, collagen, arachidonic acid, PAF and thrombin. The platelet-specific proteins, platelet factor 4 and β thromboglobulin, contained in platelet alpha-granules occur in greater concentrations in the plasma of diabetic subjects, suggesting increased release of these proteins in vivo. [2]

Platelet indices are markers of platelet activation that are obtained daily as a part of an automated blood counts. The most commonly assessed Platelet indices include the mean platelet volume (MPV), platelet distribution width (PDW), platelet-large cell ratio (P-LCR), and plateletcrit (PCT). [3]

HbA1c (glycated hemoglobin) reflects the amounts of glucose bound to hemoglobin over the life span of the red blood cells (120 days) which correlated with exposure to blood glucose. This means that clinically meaningful changes in HbA1c can be used as an index of long-term blood glucose level and as a measure of the risk for the developing macrovascular and microvascular complications in patients with diabetes mellitus.

This study was done to find out any correlation of platelet indices such as MPV and PDW with HbA1c and to comparisons of platelet indices in good (HbA1c<7) and poor

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(HbA1c≥7) glycemic control in type 2 diabetic patients which could be helpful in predicting an impending thrombotic state and complications of diabetes.

Materials and Methods: After obtaining permission from the Scientific Review Committee and Ethical Committee, study was conducted at central pathology laboratory, Sir T Hospital, Government Medical College, Bhavnagar. This study was conducted with the aim to find a correlation between HbA1c and platelet indices among type 2 diabetic patients. Study design was cross-sectional, duration was 12 months and sample size were 175.

Inclusion Criteria:

Patients with type 2 diabetes mellitus age > 30 years.

Exclusion Criteria:

Severe anemic patients (Hb<8gm/dl).

Drugs affecting platelet count.

Gestational diabetes mellitus patients.

Patients diagnosed with malignancy.

Patients diagnosed with chronic kidney disease.

Patients diagnosed with heart disease.

Sample taken from the EDTA vacuette, every sample was aspirated on 5-part differential automated hematology analyzer namely (Horiba Pentra ES 60) for various parameters like platelet count, MPV and PDW. HbA1c measured by the (BIO-RAD D10 Hemoglobin testing system) based on the principle of High-Performance Liquid Chromatography (HPLC) method and reports were collected.

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Data were entered into a Master chart and statistical analysis was done using Jamovi Version 2.3 software.

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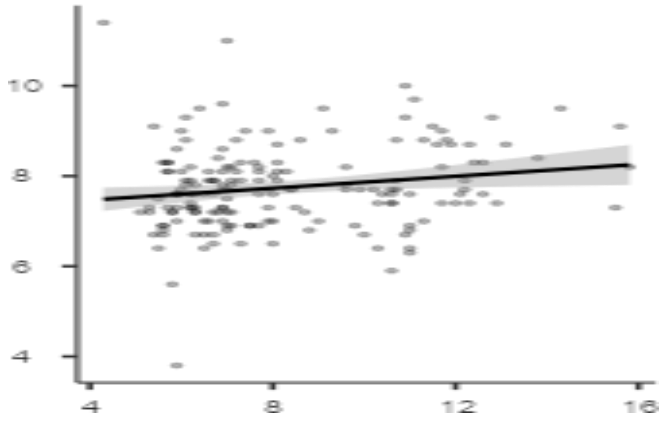
Results: Out of 175 cases; (53.71%) were females and (46.29%) were males. According to Age group wise cases were 30-50 years (38.29%), 51-70 years (56%), >70 years (5.71%). According to duration of diabetes, cases with 0-5 years (50.29%), 6-10 years (36.57%) and >10 years were (13.14%). Glycemic control wise (45.14%) were in good glycemic control (HbA1c<7) and (54.86%) were in poor glycemic control group (HbA1c≥7).

Comparison of Mean of HbA1c, Mean Platelet, Mean MPV, Mean PDW, among the good and poor glycemic control shows increased Mean HbA1c (9.90±2.18), Mean MPV(7.88±0.903) and Mean PDW(13.6±2.75) in poor glycemic control group compared to good glycemic control group which show Mean HbA1c(6.19±0.548), Mean MPV(7.58±0.949) and Mean PDW(12.7±2.78) which is statistically significant($p<0.05$). Mean Platelet in poor glycemic control group were (3.37±0.977) and in good glycemic control group (3.29±0.985). No statistical significance is found in platelets between good and poor glycemic control ($p>0.05$).

Correlation statistics between HbA1c vs MPV show Positive Pearson's R-value (0.176) and p value (0.020) suggesting a positive correlation between HbA1c and MPV ($p<0.05$-Stastically significant). (Graph 1).

Graph 1: Correlation Statistics – Hba1c vs. MPV



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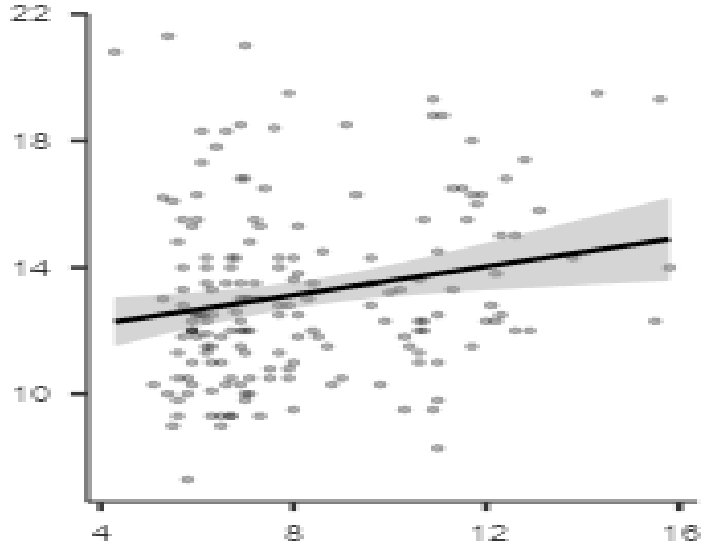
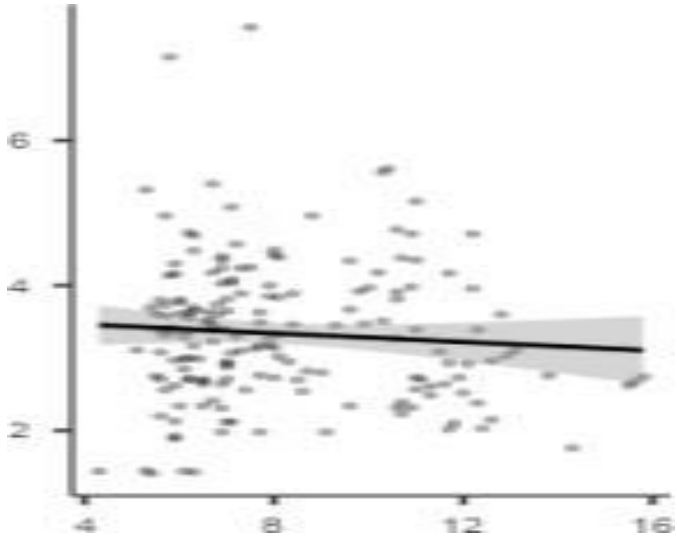
Correlation statistics between HbA1c vs PDW show Positive Pearson's R-value (0.202) and p value (0.007) suggesting a positive correlation between HbA1c and PDW (p<0.05-Stastically significant). (Graph 2).

Graph 2: Correlation statistics-Hba1c vs. PDW



Correlation statistics between HbA1c vs. Platelet count show a Negative Pearson's R-value (-0.076) and p value (0.315) suggesting a negative correlation between HbA1c and platelet count. (p>0.05-Stastically insignificant). (Graph 3).

Graph 3: Correlation Statistics – Hba1c vs. Platelet



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Discussion: In the present study, we observed that the majority of cases of female gender (53.71%). Similar results were also found in the study conducted by Kadić et al(65.1%)[4] while the study conducted by following authors shows a majority of cases of the male gender; Dr Aparajita Sharma et al(54.63%)[5], Kodiatte et al(65%)[6] and Bhattcharji P et al(51%).[7] Variation of results in different studies was due to factors like lifestyle, culture, and attitudes and behaviors related to diabetes care.

In the present study, we observed the majority of cases in the 51-70-year-old age group(56%). Similar results were also found in a study conducted by Aparajita et al(45.38%)[5] and Bhattacharjee P et al(48%).[7]

In the present study, we observed the majority of cases with 0-5 years of duration of diabetes (50.29%). Similar result was also found in a study conducted by Tanima et al.[8]

In the present study, we observed the majority of cases with poor glycemic control (54.86%). Similar results were also found in a study conducted by kadic et al[4] (58.5%), Apupoora at al[9](73.6%), A gohil et al[10](77.3%) and Sangapur SM et al[11] (71%). While a study conducted by Anandhalakshmi et al[12](56%) shows the majority of cases with good glycemic control. Variation in result was due to factors such as age, gender, duration of disease, type of treatment, medical adherence, presence of comorbidities, occupation and level of education.

In the present study, MPV values were higher in diabetic patients with poor control as compared to the diabetic population with good control and there was a statistically significant difference between both the groups (p 0.031). The results were similar to those obtained in a study done by Sangapur SM et al[11] ($p< 0.001$), Bhattacharjee P et al[7](p 0.02) and Anandhalakshmi et al[12] (p 0.008). (Table 1).

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Table 1: Comparison of MPV in good and poor glycemic control group.

Studies	Parameter	Mean ±SD	p VALUE
Present study	Good glycemic control	7.58±0.94	0.031
	Poor glycemic control	7.88±0.90	
Sangapur SM et al[11]	Good glycemic control	7.89±0.63	<0.001
	Poor glycemic control	12.32±1.94	
Bhattacharjee P et al[7]	Good glycemic control	11.97 ± 1.15	0.02
	Poor glycemic control	12.98 ± 0.95	
Anandhalakshmi et al[12]	Good glycemic control	10.01±0.70	0.008
	Poor glycemic control	10.54±0.85	

In the present study, the PDW values were higher in diabetic patients with poor control as compared to the diabetic patients with good control and there was a statistically significant difference between both the groups (p 0.026). The results were similar to those obtained in a study done by Sangapur SM et al[11] (0.008), Bhattacharjee et al[7](0.01) and Anandhalakshmi et al[12] (0.01).

In the present study, no statistically significant differences were found in platelet value between good and poor glycemic control group (p 0.565) which is >0.05. The results were similar to those obtained in a study done by Apuroopa et al[9] (p 0.31), A Gohil et al[10] (p>0.05), and Anandhalakshmi et al[12] (p 0.41).

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In the present study, we observed a Positive Pearson's R-value and p value (≤0.05) suggesting positive correlation between HbA1c and MPV. Similar results were also found in a study conducted by Kodiatte et al[6], Tanima et al[8], Mitakshara et al[13], Lavanya et al[14], S. Nirangjhana et al[15], Demirtunc et al[16]. While a study conducted by Hekimsoy et al[17] shows a Negative correlation between HbA1c and MPV. (Table 2).

Table 2: Comparison of correlation statistics of HbA1c vs. MPV

Study	Pearson's R	P value
Present	0.176	0.020
Kodiatte, et al[6]	0.29	<0.0001
Tanima et al[8]	0.297	<0.0001
Mitakshara et al[13]	0.875	0.000
Lavanya et a[14]	0.703	0.0001
S. Nirangjhana et al[15]	0.382	0.004
Demirtunc et al[16]	0.39	0.001
Hekimsoy et al[17]	-0.33	0.79

Platelet hyper-reactivity and increased baseline activation in patients with diabetes are multifactorial. It is associated with biochemical factors such as hyperglycemia, hyperlipidemia, insulin resistance, an inflammatory and oxidant state and also with increased expression of glycoprotein receptors and growth factors. [2,6,18,19,20,21] Hyperglycemia can Increase mean platelet volume (MPV) by inducing nonenzymatic glycation of proteins on the surface of the platelet, by the osmotic effect of glucose and activation of protein kinase C.

In the present study, we observed Positive Pearson's R-value and p value (≤0.05) suggesting a positive correlation between HbA1c and PDW, Similar results were also found

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in a study conducted by Tanima et al[8], Mitakshara et al[13], Lavanya et al[14], S. Nirangjhana et al[15]. (Table 3).

Table 3: Comparison of correlation statistics of HbA1c vs. PDW

Study	Pearson's R	P value
Present	0.202	0.007
Tanima et al[8]	0.204	0.001
Mitakshara et al[13]	0.951	0.000
Lavanya et al[14]	0.663	0.0001
S. Nirangjhana et al[15]	0.164	0.387

For their activation, platelets change their shape from discoid to spherical forms along with the formation of pseudopodia that differ in size possibly affecting PDW.[15]

In the present study, we observed negative Pearson's R-value (-0.076) and p value (>0.05) suggesting a negative correlation between HbA1c and platelet. A similar result was found in a study conducted by Mitakshara et al[13] show negative Pearson's R-value(-0.164) While a study conducted by Lavanya et al[14] with positive Pearson's R-value(0.108) and S. Nirangjhana et al[15] with positive Pearson's R-value(0.513) shows a positive correlation between HbA1c and platelet.

Platelet count could be dependent on several variables, that is, mean platelet survival, platelet production rate and turnover rate in Diabetes mellitus.[5]

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Conclusion: In our study of 175 type 2 diabetes mellitus cases, poor glycemic control cases (HbA1c≥7) have increased mean MPV (p=0.031) and Mean PDW (p=0.026) compared to good glycemic control (Hba1c<7) which are statistically significant (p<0.05).There is also positive correlation between HbA1c and MPV (r=0.176, p=0.020) and HbA1c and PDW (r=0.202, p=0.007).Platelet indices like MPV and PDW along with HbA1c could be used as a cost-effective tool to monitor diabetes mellitus patients which could be helpful in predicting an impending thrombotic state and complications of diabetes.

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