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Correlation of High Glycemic Index with Platelet Indices

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Abstract

Background: *The increased platelet count has its association with increased prothrombotic activity in diabetics population and play a role in microvascular complications. Various platelet indices play a role in measurement of platelet activity, prothrombotic activity and atherogenic mechanisms. We aim to evaluate role of various platelet indices in a diabetic group, the relationship between increase in platelet parameters with increasing HBA1C value and also comparison of various platelet indices in diabetics from its healthy controls.* ***Material and methods:*** *This isa retrospective cross-sectional observational study carried out at Department of Pathology, Jag Parvesh Chand Hospital, Shastri Park, Delhi, India, on 108 patients who were advised for HbA1C, blood sugar levels and CBC. The CBC was run in 6-part hematology analyzer Mindray BC 6200 whereas all the biochemistry tests were run on Randox RX Monaco series analyzer. Data for various values were then tabulated and analyzed for p value by using Microsoft excel 2008.****Results and Conclusion:*** *The platelet parameters and Hba1c are correlating with each other. Mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR) was significantly higher in the diabetic group with increasing HBA1C levels. Also, largely underestimated parameters like Plateletcrit and PLCC were increased in diabetic group in comparison to non-diabetics. Studying platelet parameters in patients with higher Hba1c values/ diabetics can be of utility in knowing platelet related coagulation activity which are easily determined by routine automated analyzers and are available at low costs*

Key words*: Platelet Indices, HbA1c and platelet parameters, High glycemic index.*

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I. Introduction

Diabetes and other non-communicable diseases in the present world have shown an increasing trend and, along with the adverse associated complications are important cause of morbidity and mortality. Diabetes is now commonly recognized as a coronary heart disease risk equivalent. This is mainly attributed to the high rates of dyslipidemia among diabetic patients which is believed to be one of the major factors accounting for the high percentage of deaths among diabetics due to cardiovascular disease (CVD).[1,2,3]The prothrombotic tendency and increased platelet reactivity in diabetics play a role in microvascular complications. Various platelet indices that have been included in the present study are platelet count, MPV (mean platelet volume), PDW (platelet distribution width), PCT (Plateletcrit), PLCC (Platelet large cell count), & PLCR (Platelet large cell ratio) and are corelated with the HbA1c values in diabetics as well as non-diabetics.

The increased platelet count has its association with increased prothrombotic activity in diabetics compared to non-diabetics.[9]MPV reflects changes in either platelet stimulation or the rate of platelet production.[10]Mean platelet volume is strongly and independently associated with the presence and severity of diabetes.[11]Higher MPV values has shown to be associated with diabetic retinopathy in some studies.[12]Also, the association of increased MPV has been seen in diabetes, stroke and metabolic syndrome.[13]The heterogenicity/ variability in the platelet size is measured by platelet distribution width (PDW), which may be due to aging of platelets or heterogenous demarcation of megakaryocytes. Plateletcrit (PCT) is the volume occupied by platelets in the blood as a percentage and calculated according to the formula PCT= platelet count × MPV/10,000 (Range = 25-27). P-LCR is calculated in automated hematology analyzers using the formula: PLCR = PLCC/PLT.

In our study we aim to evaluate role of various platelet indices in a diabetic group, the relationship between increase in platelet parameters with increasing HBA1C value and also comparison of various platelet indices in diabetics from its healthy controls.

II. Material And Methods

This is a retrospective study carried out on 108 patients at Department of Pathology, Jag Pravesh Chand Hospital, Shastri Park, Delhi, India. **Study Design:** Retrospective, cross-sectional, observational study. **Study Location**: This was a tertiary care hospital-based study done in Department of Pathology, Jag Pravesh Chand Hospital, Shastri Park, Delhi, India – 110053. **Study Duration:** September 2022 to December 2022.**Sample size:** 108 patients. **Subject & selection method**: The study population was drawn from the patients who were prescribed for HBA1c, CBC and blood sugar from September 2022 to December 2022. According level of HbA1c, patients were divided into two groups (Diabetics, HbA1c ≥7 and Non-Diabetics, HbA1c≤ 7). Criteria for diagnosis of diabetes was taken from WHO guidelines 2020.[4]

Inclusion criteria:

1. Diabetic patients (fasting blood glucose ≥ 110 mg/dL [HbA1c ≥ 7.0mmol/L])
2. Control group (HbA1c ≤ 7.0mmol/L)
3. Either sex
4. Aged ≥ 18 years

Exclusion criteria:

1. Pregnant women;
2. Young patient.
3. Patients with genetic disorders
4. Patients taking concurrent corticosteroids.
5. Anemic patients, Hb < 13 gm% in males and < 12 gm% in females.
6. Any known platelets disorder.
7. Patients on antiplatelet drug.
8. Pre analytical errors such as clotted sample, inadequate sample, hemolyzed sample.

Procedure methodology: Blood samples for routine hematology and biochemistry tests were collected in patients who presented to our hospital after eight hours of overnight fasting. Under all aseptic precautions, a fasting venous sample was collected in EDTA vacutainers for glycated hemoglobin (HbA1C), complete blood count (CBC)with detailed platelet analysis were tabulated. For blood glucose level (BGL) estimation, fasting (FBGL), post prandial (PPBGL) and random (RBGL) blood samples were collected in fluoride vacutainers (grey top). FBGL was collected in patients with eight hours of fasting, post prandial blood after two hours post meal. All the tests were conducted within 1 hour of sample collection and was carried out by the same team of laboratory technicians using the same method, throughout the study period. The CBC was run in 6-part hematology analyzer Mindray BC 6200 which is based on SF Cube technology and for biochemistry samples were on Randox RX Monaco series which is a fully automated clinical chemistry analyzer relies on biochip array technology which in turn relies on the basic principle of immunology using competitive and sandwich immunoassay. Horseradish peroxidase labelled detection creates chemiluminescence signals at each discrete test region, all of which are simultaneously measured by CCD camera and interpretated by analyzer software. Generation of Levey-Jennings charts, calibration curves and QC statistics done for reliable results.

Statistical analysis: Data was analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Student's *t*-test was used to ascertain the significance of differences between mean values of two continuous variables. In addition, paired *t*-test was used to determine the difference between baseline wherever necessary. The level $P < 0.05$ was considered as the cutoff value or significance.

III. Results

All the cases studied, are divided into two major group on the basis of cut off value of Hba1c which is 7. In our study we have found that 41 (37.96 %) cases were having HbA1c ≥ 7%, whereas 67 cases (62.04 %) were having Hba1c< 7%. Platelet indices includes platelet count, MPV (mean platelet volume), PDW (platelet distribution width), PCT (Plateletcrit), PLCC (Platelet large cell count), & PLCR (Platelet large cell ratio). The indices were further subdivided into subgroups on the basis of their cutoff values.

In group A (Table 1; HBA1C ≥ 7%, Diabetics), 87.8% (36) cases have value more than 1.5 lakhs/mm^3 and 12.1% (05) cases have value less than 1.5 lakhs/mm^3. MPV is higher (≥12 f) in 70.7% (29) cases whereas normal (< 12 fL) in 29.2% (12) cases. PDW is higher (>17) in 19.5% (08) cases whereas it is normal in 80.5%

(33) cases. PCT is higher in 95.1% (39) cases whereas it is normal in 4.8% (02) case. PLCC is higher in 78% (32) cases and is normal in 21.9% (09) cases. PLCR is higher than normal in 58.5% (24) cases and normal in 41.4% (17) cases.

Table 1: DISTRIBUTION OF CASES OF DIFFERENT PARAMETERS IN DIABETICS WITH HBA1C ≥ 7 % (GROUP A)

S.No	PARAMETERS	CUT OFF VALUES	TOTAL CASES	% CASES	CUT OFF VALUES	TOTAL CASES	% CASES
1	PLATELET (lacs/mm³)	≥ 1.5	36	87.8%	< 1.5	5	12.1%
2	MPV (fL)	≥ 12 fL	29	70.7%	< 12	12	29.2%
3	PDW	≥ 17	8	19.5%	< 17	33	80.5%
4	PCT (%)	≥ 0.28	39	95.1%	< 0.28	2	4.8%
5	PLCC (10^9/L)	≥90	32	78.0%	< 90	9	21.9%
6	PLCR (%)	≥45	24	58.5%	< 45	17	41.4%

TOTAL CASES 109; HBA1C ≥ 7.0, Total cases = 41; HBA1C < 7.0, Total cases = 67

Table 2: DISTRIBUTION OF CASES OF DIFFERENT PARAMETERS IN NON-DIABETICS WITH HBA1C < 7 % (GROUP B)

S.No	PARAMETERS	CUT OFF VALUES	TOTAL CASES	% CASES	CUT OFF VALUES	TOTAL CASES	% CASES
1	PLATELET (lacs/mm³)	≥ 1.5	58	86.6	< 1.5	9	13.4
2	MPV (fL)	≥ 12 fL	44	65.7	< 12	22	32.8
3	PDW	≥ 17	3	4.4	< 17	64	95.5
4	PCT (%)	≥ 0.28	65	97	< 0.28	2	2.9
5	PLCC (10^9/L)	≥90	46	68.6	< 90	21	31.3
6	PLCR (%)	≥45	35	52.2	< 45	32	47.7

TOTAL CASES 109; HBA1C ≥ 7.0, Total cases = 41; HBA1C < 7.0, Total cases = 67

In group B (Table 2; HBA1C < 7%/ non-Diabetics), 86.6% (58) cases have value more than 1.5 lakhs/mm^3 and 13.4% (09) cases have value less than 1.5 lakhs/mm^3. MPV is higher (≥12 fL) in 65.7% (44) cases whereas normal (< 12fL) in 32.8% (22) cases. PDW is higher (>17) in 4.4% (03) cases whereas it is normal in 95.5% (64) cases. PCT is higher in 97.0% (65) cases whereas it is normal in 2.9% (02) case. PLCC is higher in 68.6% (46) cases and is normal in 31.3% (21) cases. PLCR is higher than normal in 52.2% (35) cases and normal in 47.7% (32) cases.

Table 3: COMPARISON OF VARIOUS PARAMETERS OF PLATELET INDICES TO RAISED HBA1C/ DIABETIES

S.No		PARAMETERS	P value	SIGNIFICANCE
1	HBA1C >7	PLATELET COUNT (PC)	0.075198	NS
2	HBA1C >7	MPV (fL)	<0.0001	SIGNIFICANT
3	HBA1C >7	PDW	<0.0001	SIGNIFICANT
4	HBA1C >7	PCT (%)	0.127703	NS
5	HBA1C >7	PLCC (10^9/L)	<0.0001	NS
6	HBA1C >7	PLCR (%)	<0.0001	SIGNIFICANT
7	HBA1C >7	F BGL	<0.0001	SIGNIFICANT
8	HBA1C >7	PP BGL	<0.0001	SIGNIFICANT

NS (Non-Significant), TOTAL CASES 109; HBA1C ≥ 7.0, Total cases = 41; HBA1C < 7.0, Total cases = 67

Comparison of various platelet indices is done (Table 3) in diabetics (group A) and it is found that with increasing blood sugar levels, there is an increase in MPV, PDW and PLCR and is statistically significant (P value> 0.05). Also, it is noticed that with increasing HBA1C levels, there is an increase in the value of fasting and post prandial blood glucose level. Maximum and minimum values observed were also recorded in the present study.

Table 4: MAXIMUM AND MINIMUM VALUES OBSERVED AMONG DIFFERENT PARAMETERS IN PRESENT STUDY

S.No	PARAMETERS	MINIMUM VALUE	MAXIMUM VAUE
1	**HBA1C (%)**	3.7	15.8
2	**PC* (lacs/mm³)**	1.05	6.38
3	**MPV (fL)**	9	16
4	**PDW**	15	19
5	**PCT (%)**	0.1	0.9
6	**PLCC (10^9/L)**	57	241
7	**PLCR (%)**	19	90
8	**F BGL**	60	381
9	**PP BGL**	84	520

*PLATELET COUNT (PC)

Table 5: TABLE OF COMPARISION OF PARAMETERS IN DIABETICS (HBA1C ≥ 7) WITH OTHER STUDIES

AUTHORS	PRESENT STUDY	DUBEY et. al[5]	APOORVA et. al[6]	BHATTACHARYA et. al[7]	VARSHINI et. al[8]
MEAN VALUES	MEAN HBA1C ≥7 (%)	MEAN HBA1C ≥7 (%)	MEAN HBA1C ≥7 (%)	MEAN HBA1C ≥7 (%)	MEAN HBA1C ≥7 (%)
F BGL	207.4 ± 80.6 (S)	177.1 ± 22.27 (S)	175 ± 15(S)	*	*
PP BGL	299.8 ± 110.1 (S)	*	252.9 ± 94	*	*
PC (lacs/mm³)	278.4 ± 137	270 ± 79	270 ± 79	*	227.4 ± 77.6
MPV (fL)	12.8 ± 1.79 (S)	9.06 ± 1.72 (S)	11.8 ± 1.0(S)	12.98 ± 0.95(S)	10.50 ± 0.86
PDW	16.1 ± 0.82 (S)	18.6 ± 10.35	18.6 ± 10.35	21.6 ± 2.4(S)	14.16 ± 3.35
PCT (%)	0.34 ± 0.17	*	*	*	*
PLCC (10^9/L)	122 ± 51.8	*	*	*	*
PLCR (%)	48.8 ± 12.8 (S)	*	*	52.36 ± 6.49(S)	*

Table 6: PLATELET INDICES WERE COMPARED AMONG THE DIABETICS (HBA1C≥ 7) AND NON-DIABETIC (HBA1C <7) CASES

	DIABETICS	NONDIABETICS		
PLATELET INDICES	HBA1C ≥ 7.0	HBA1C < 7.0	p VALUE	STATASTICAL SIGNIFICANCE
	Total cases = 41	Total cases = 67		
MEAN PLATELET COUNT	278.4 ± 137	249.14 ± 87.69	P = 0.1785	NS
MEAN MPV	12.8 ± 1.79	12.6 ± 2.05	P = 0.6071	NS
MEAN PDW	16.1 ± 0.82	15.9 ± 0.47	P = 0.1098	NS
MEAN PCT	0.34 ± 0.17	0.28 ± 0.08	P = 0.0147	SIGNIFICANT
MEAN PLCC	122 ± 51.8	104.1 ± 27.78	P = 0.0214	SIGNIFICANT
MEAN PLCR	48.8 ± 12.8	46.1 ± 14.42	P = 0.3271	NS
F BGL	207.4 ± 80.6	87 ± 27.98	P < 0.0001	SIGNIFICANT
PP BGL	299.8 ± 110.1	119 ± 36.44	P < 0.0001	SIGNIFICANT

IV. DISCUSSION

In our study, patients with value of HbA1c ≥7(Diabetics) are compared and it is observed mean fasting blood glucose is 206.4±80.6which is comparable with the study of Dubey et.al.[5] and Apoorva et.al.[6]where mean fasting blood glucose level is 177±15 and 175±15 respectively. In all three studies value of mean HbA1C in relation to mean fasting blood glucose found to be statistically significant (p value ≤ 0.05).

Mean Value of post prandial blood glucose level in present study is 299.8±110, which is comparable with the study of Apoorva et.al.[6]whereit is 252.9±94. In both the studies value of mean post prandial blood glucose is found to be statistically significant (p value ≤ 0.05).

In present study value of mean platelet count is 278±137 whereas in Dubey et.al.[5]and Apoorva et.al.[6], the value of mean platelet count is 270±79 and 270±79 respectively. In study of Varshini et.al.[8] the value of mean platelet count is 227±77.6. Platelet count is comparable among these studies but none of them (including our study) found it to be statistically significant in relation to mean HbA1c and mean fasting blood glucose.

In our study mean of mean platelet volume is 12.8 ± 1.79 whereas in that of Dubey et.al.[5] and Apoorva et.al[6], it was 9.06 ± 1.72 and 11.8 ±1.0 respectively, and in study byBhattacharyya[7] et.al. and Varshini et.al.[8]values of mean MPV is 12.98± 0.95 and 10.50 ±0.86 respectively, which is comparable to present study.

Value of mean PDW in our study is 16.1 ±0.82 which is statistically significant (p value ≤ 0.05) in relation to mean HbA1c, where as in study of both Dubey et.al.[5] and Apoorva et.al.[6] it is 18.6 ± 10.35 each. In study of Bhattacharya et.al.[7] it was 21.6 ±13.4, whereas in Varshini et.al.[8] it is 14.16 ± 3.25. PDW is statistically significant in study of Bhattacharya et.al.[7] which is comparable with our study.

Value of mean PCT AND P-LCC in our study is 0.34 ± 01 and 122±51.8 respectively but it is not statistically significant in relation to HBA1c, study of PCT and P-LCC in relation to HbA1c are rarely done by any other author to compare with.

Mean value of P-LCR is 48.8 ±12.8, which is comparable to study of Bhattacharya et.al.[7] where their value is 52.36± 6.49. Mean value P-LCR in relation to mean HbA1c is found to be statistically significant in both the studies.

Platelet indices among the diabetics were compared with those of the healthy controls and we find that the Platelet count (PC), Plateletcrit and PLCC was significantly higher in the diabetic group (Table 6). Also, when the two groups were compared, the mean Plateletcrit and PLCC are found to statistically significant (p value ≤ 0.05) in patients with diabetes (HBA1C≥ 7). There is also increased fasting blood sugar and post prandial blood sugar levels in diabetic population compared to non-diabetics, which is statistically significant. (p value ≤ 0.05)

V. Conclusion

In current study, we find that mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (PLCR) was significantly higher in the diabetic group with increasing HBA1C level. Also, largely underestimated parameters like Plateletcrit and PLCC are increased in with diabetic group or increased HBA1C≥ 7 levels in comparison to non-diabetics. The value of increased HbA1C in relation to increased mean fasting and post prandial blood glucose found to be statistically significant.

MPV, is significantly higher in the diabetic population compared to healthy subjects, which may be attributed to the osmotic swelling of platelets as a result of hyperglycemia.[15]

Platelet activity and its contribution to atherosclerosis, micro and macrovascular complications in diabetes can be measured by various complicated methods which can be time consuming, tedious and expensive. Apart from this, it requires skilled manpower and a dedicated person to do the task with a specialty training. A simple alternative to all these hurdles can be simply measuring and monitoring of platelet indices in diabetics during routine screening. Mean platelet volume, Plateletcrit, PLCC, PLCR, PDW, and platelet counts are easily determined by routine automated analyzers and are available at low costs.[16-22] The current study analysis do support the link between an underlying abnormal glucometabolic state, poor glycemic control, and platelet activity as measured by MPV, PLCC, PLCR, PDW, PCT but has the limitation of small sample size and an observation study. Large prospective studies correlating vascular complications of diabetes with platelet indices should be considered which also support the role of monitoring platelet indices in the diabetic population.

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