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Study of relationship between Mean platelet volume and prediabetes and to evaluate the relationship between MPV, HbA1c and Fasting plasma glucose levels (FPG)

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Abstract

Background: Prediabetes is a preclinical stage in the hyperglycemia continuum where subjects are at increased risk of developing diabetes in the near future. The purpose of the present study was to compare MPV in prediabetic and normoglycemic subjects, and to evaluate the relationship between MPV,HbA1c and fasting plasma glucose (FPG) levels in these two groups. **Material and Methods:** Present study was single-center, case-control study, conducted in 100 individuals, 50 prediabetics and 50 normoglycemics, of age > 18 years, either gender, willing to participate in present study. **Results:** The mean BMI in controls was 22.6 ± 1.972 and 25.3 ± 3.825 in cases, difference was highly significant ($p<0.001$). The mean FBS, PPBS and HbA1c in controls were 90.08±10.089, 113.68 ± 9.696, 5.25 ± 0.308 and 111.36 ± 15.398, 156.68 ± 12.099, 6.02 ± 0.222 in cases respectively, difference was highly significant ($p<0.001$). We observed that MPV in prediabetic subjects was higher than that in normoglycemic subjects. The mean MPV in normoglycemics and prediabetics was 9.24 ± 0.950 and11.62 ± 0.442 respectively, difference was highly significant ($p<0.001$). We observed a positive correlation between MPV and FPG, PPG, HbA1c levels, not only in the prediabetic but also in the normoglycemic subjects [FPG (r=0.540), PPG (r=0.748), HbA1c (r=0.815) for prediabetics and FPG (r=0.585), PPG (r=0.809), HbA1c (r=0.817)]. We studied correlation of MPV with HbA1C values of prediabetic patients (in 2 groups as 5,7-6 % & 6.1-6.4 %), a positive correlation was noted between MPV with HbA1C values of prediabetic patients. **Conclusion:** Mean platelet volume was found to be increased in prediabetics compared to normoglycemics. In prediabetic and normoglycemic subjects, MPV showed positive correlation with FPG, PPG and HbA1c levels.

Keywords: mean platelet volume, prediabetics, normoglycemics, HbA1c

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Introduction

Diabetes Mellitus is a common and a serious disease with chronic complications and constitutes a substantial burden for both patient and health care system. The leading risk factor for type 2 diabetes is a condition called *pre-diabetes.* The criteria for determining prediabetes are generally defined as impaired fasting glucose (IFG) levels, impaired glucose tolerance (IGT), or both.[1]

Prediabetes is a preclinical stage in the hyperglycemia continuum where subjects are at increased risk of developing diabetes in the near future.[2] Individuals with prediabetes are at a high risk of not only developing diabetes but also of adverse cardiovascular events (myocardial infarction, stroke, or cardiovascular death) in the later life.[3,4]

Mean platelet volume (MPV) is a new and independent risk factor for atherothrombosis. Altered platelet morphology and function have been reported in patients with Diabetes Mellitus (DM) and MPV was found to be significantly higher in diabetic patients,[5] thereby playing role in the micro and macro-vascular complications of diabetic patients.[6] However, the relationship between MPV and prediabetes is poorly understood. The purpose of the present study was to compare MPV in prediabetic and normoglycemic subjects, and to evaluate the relationship between MPV,HbA1c and fasting plasma glucose (FPG) levels in these two groups.

Material and Methods

Present study was single-center, case-control study, conducted in Department of General Medicine, ESIC MEDICAL COLLEGE , PGIMSR & HOSPITAL, KALABURAGI, India. Study duration was of 18 months (November 2021-April 2023). Prior approval for the study protocol was obtained from institutional ethical committee.

Inclusion criteria

- Patients of age > 18 years, either gender, willing to participate in present study.
- Cases – 50 prediabetic (according to ADA criteria)
- Controls – 50 normal euglycemic subjects

Exclusion criteria

- Hb <13gm% in males, Hb <12gm% in females
- Diabetic subjects with the history of antidiabetic therapy.
- Individuals on antiplatelet therapy.
- Subjects with any diagnosed hematological malignancy.

Study was explained to patients in local language & written consent was taken for participation & study. Data was collected from patients fulfilling the inclusion and exclusion criteria attending either outpatient department or inpatient. Baseline data including age and sex, detailed medical history including conventional risk factors, clinical examinations and relevant investigations were done.

Investigations done were Complete hemogram- (including Hb, Mean Platelet Volume, total count, platelets), ESR, Peripheral smear, Urine examination for sugar and albumin, fasting blood sugar, Post prandial blood sugar & glycosylated hemoglobin Venous blood samples were collected in sodium citrate and tested within 1 hour of collection to minimize variations due to sample aging. Samples were be maintained at room temperature.

The diagnosis of prediabetis was made by FBS, PPBS and HbA1c levels. Blood for FBS & PPBS was collected in fluoride tubes and was done by HEXOKINASE method. Fasting is defined as no caloric intake for at least 8 h. Post prandial blood was collected after 2 hours. Samples for HbA1c were collected in di-potassium EDTA. HbA1c was calculated by COBAS b 101 instrument from Roche Diagnostics International Ltd by Immuno-assay

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method. MPV was done as a part of complete blood count using an automatic blood counter, Coulter 800 series, Miami , FL.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. The student 't' test was used to determine whether there was a statistical difference between the groups in the parameters measured. To assess independent relationships between MPV and the clinical variables, a multiple linear regression analysis was performed. P value less than 0.05 was considered as statistically significant.

Results

The present study included 100 individuals, 50 prediabetics and 50 normoglycemics. A detailed history, examination and investigations were done for each patient. Patients in the study were aged from 22-76 yrs and the mean age of the patients in control group and case group was 43.4 ± 10.50 and 54.4 ± 9.40 respectively, difference was statistically significant ($p < 0.001$). Among controls 58 % were male and 42 % were female and in cases group 68 % were male and 32 % were female, difference was not significant statistically. Family history of diabetes, smoking habit & alcoholic habits were comparable among both groups & difference was not significant statistically.

Table 1: General characteristics

Characteristics	Control	Case	P value
Mean age (in years)	43.4 ± 10.50	54.4 ± 9.40	*<0.001*
Gender			0.3
Male	29 (58 %)	34 (68 %)	
Female	21 (42 %)	16 (32 %)	
Other			
Family History Of Diabetes	18(36.0%)	26 (52.0%)	0.107
Smoker	13(26.0%)	15(30.0%)	0.656
Alcoholic	5 (10.0%)	9 (18.0%)	0.249

The mean BMI in controls was 22.6 ± 1.972 and 25.3 ± 3.825 in cases, difference was highly significant ($p<0.001$). The mean FBS, PPBS and HbA1c in controls were 90.08±10.089, 113.68 ± 9.696, 5.25 ± 0.308 and 111.36 ± 15.398, 156.68 ± 12.099, 6.02 ± 0.222 in cases respectively, difference was highly significant ($p<0.001$). We observed that MPV in prediabetic subjects was higher than that in normoglycemic subjects. The mean MPV in normoglycemics and prediabetics was 9.24 ± 0.950 and11.62 ± 0.442 respectively, difference was highly significant ($p<0.001$).

Table 2: Clinical and metabolic characteristics of study participants

	Normoglycemics (n=50)	Prediabetics (n=50)	P value
BMI (kg/M^2)	22.6±1.972	25.3±3.825	*<0.001*
SBP (mm Hg)	125.88±12.198	119.00±8.144	*0.001*
DBP (mm Hg)	85.32±9.711	83.20±9.134	0.264
Hypertension (%)	0 (0.0%)	0 (0.0%)	-
FPG (mg/dl)	90.08 ±10.089	111.36±15.398	*<0.001*
PPG (mg/dl)	113.68±9.696	156.68±12.099	*<0.001*
HBA1C (%)	5.25± 0.308	6.02±0.222	*<0.001*

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MPV (fl)	9.24±0.950	11.62±0.442	*<0.001*
Platelet (lakhs/mm^3)	2.647±0.7348	2.454±0.600	0.154

We observed a positive correlation between MPV and FPG, PPG, HbA1c levels, not only in the prediabetic but also in the normoglycemic subjects [FPG (r=0.540), PPG (r=0.748), HbA1c (r=0.815) for prediabetics and FPG (r=0.585), PPG (r=0.809), HbA1c (r=0.817)].

Table 3: Correlations between mean platelet volumes and various parameters

	MPV					
	in total subjects (n=100)		**In Normoglycemics (n=50)**		**In prediabetics (n=50)**	
	R	**p value**	**r**	**p value**	**r**	**p value**
AGE (yrs)	0.443	*<0.001*	0.134	0.355	-0.108	0.456
Gender	-0.079	0.434	0.099	0.493	-0.165	0.253
BMI (kg/M^2)	0.499	*<0.001*	0.269	0.059	0.530	*<0.001*
SBP (mmhg)	-0.192	0.056	0.183	0.203	0.086	0.552
DBP (mmhg)	-0.182	0.071	-0.202	0.159	-0.105	0.467
Family History Of Diabetes	-0.121	0.229	0.141	0.328	-0.190	0.187
FPG (mg/dl)	0.585	*<0.001*	-0.039	0.789	0.540	<0.001
PPG (mg/dl)	0.809	*<0.001*	-0.068	0.639	0.748	*<0.001*
HBA1C (%)	0.817	*<0.001*	0.249	0.081	0.815	*<0.001*
PLATELET(lakhs/cumm)	-0.125	0.217	-0.133	0.356	0.335	*0.017*

We studied correlation of MPV with HbA1C values of prediabetic patients (in 2 groups as 5,7-6 % & 6.1-6.4 %), a positive correlation was noted between MPV with HbA1C values of prediabetic patients.

Table 4: Correlation of MPV with HbA1C values of prediabetic patients

Hba1c (%)	**N**	**Mean**	**SD**	**Min.**	**Max.**	**T value**	**P value**
5.7-6.0	28 (56 %)	11.37	0.418	10.1	12.1	37.002	*<0.001*
6.1-6.4	22 (44 %)	11.95	0.182	11.6	12.2		

Discussion

Prediabetes is a preclinical stage in the hyperglycemia continuum where subjects are at increased risk of developing diabetes in the near future. Pre diabetes generally is defined by either an elevation of fasting or post-prandial plasma glucose levels.[1] Elevated hemoglobin A1c, or glycosylated hemoglobin (HbA1c), which integrates plasma glucose over time, is promoted by some as another indicator of pre-diabetes.[2]

In the present study, 18(36%) of normoglycemics and 26(52%) of prediabetics had a family history of diabetes. Though family history of diabetes is a risk factor for diabetes and prediabetes, it did not make much impact in our study(p=0.107). Similar observation was seen in a study done by Shimodaira et al.,[7] 26% of normoglycemics, 30% of prediabetics were smokers and 10% of normoglycemics and 18% of prediabetics were alcoholics in our study. Smoking and consumption of alcohol did not affect MPV (p=0.590) & (p=0.342) respectively, which was also seen in the study done by Shimodaira et al.,[7] BMI was also significantly high in prediabetics(25.3kg/M^2) compared to normoglycemics (22.6kg/M^2)

The mean FBS,PPBS and HbA1c in controls were 90.08±10.089, 113.68±9.696, 5.25± 0.308 and 111.36± 15.398, 156.68±12.099, 6.02±0.222 in cases respectively. We observed that

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MPV in prediabetic subjects was higher than that in normoglycemic subjects. The mean MPV in normoglycemics and prediabetics was 9.24±0.950 and 11.62±0.442 respectively. Moreover, we observed a positive correlation between MPV and FPG,PPG, HbA1c levels, not only in the prediabetic but also in the normoglycemic subjects [FPG (r=0.540), PPG (r=0.748), HbA1c (r=0.815) for prediabetics and FPG (r=0.585), PPG (r=0.809), HbA1c (r=0.817)]. Our study correlated with the study done by Shimodaira et al.,[7,8] Similar observations were seen in other studies, A study was done in turkey by Aclan Ozder[9], In the patients with diabetes and subjects with IFG, MPV was significantly higher (10.66 ± 0.94 fL and 10.49 ± 0.96 fL, respectively) as compared to the non-diabetic group (10.04 ± 1.01 fL) (p = 0.000).

In one study done by Kapoor et al.,[10] where subjects were analyzed retrospectively and categorized into three groups based on the fasting blood glucose levels as Group I - normoglycemics (FBG ≤ 109 mg/dl), Group II- impaired fasting blood glucose (FBG ≤ 126 mg/dl) and Group III – Diabetics (FBG ≥ 127 mg/dl) and they found progressive increase in value of MPV with the increasing FBG levels, in the following order: G1 (8.44 ± 0.842 fl), G2 (8.98 ± 0.898 fl), G3 (9.31 ± 0.967 fl). Unlike our results, Kim et al.,[11] reported a negative correlation between MPV and FPG in Korean subjects with normal glucose tolerance and intermittent hyperglycemia.

In Study done by Shimodaira et al.,[7] subjects were divided into 4 groups based on FPG levels but In our study individuals were divided into 3 groups based on HbA1c levels, group 1 with HbA1c <5.7, group 2 with HbA1c between 5.7-6% and group 3 with HbA1c between 6.1-6.4% to check the raise in MPV with HbA1c values. There were 50 individuals in group 1, 28 in group 2 and 22 in group 3. It was found that there was a significant increase in MPV with increasing HbA1c levels (p=<0.001). The MPV in group 1 was 9.24fl,group 2 was 11.37fl and in group 3 was 11.95fl.

Larger platelets are younger, more reactive and aggregable. Hence, they contain denser granules, secrete more serotonin and β-thromboglobulin, and produce more thromboxane A2 than smaller platelets. All these can produce a pro-coagulant effect and cause thrombotic vascular complications. There might be small bleeds due to the rupture of atherothrombotic plaques leading to increased platelet recruitment, hyper reactivity, and bone marrow stimulation. High MPV is emerging as a new risk factor for the vascular complications of DM of which atherothrombosis plays a major role.

Conclusion

The present study demonstrated that mean platelet volume was found to be increased in prediabetics compared to normoglycemics. In prediabetic and normoglycemic subjects, MPV showed positive correlation with FPG, PPG and HbA1c levels. Hence we conclude that MPV is an useful tool which should be looed in the individuals with prediabetes as increased MPV is related to cardiovascular risk.

Conflict of Interest: None to declare
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