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ORIGINAL ARTICLE

Correlation of Glycosylated Hemoglobin (HbA1c) and Mean Platelet Volume (MPV) in Type II Diabetes Mellitus patients and Non Diabetic subjects

Mukund W.Pujari[1], Padmaja R.Desai[2]

[1]PG Resident, [2] Professor and Head of Department, Department of Physiology, D.Y.Patil Medical College, Kolhapur, Maharashtra, India

ABSTRACT:
Background: Type II Diabetes Mellitus (T2DM) is one of the pandemics in the modern era. It is a metabolic disease which leads to macrovascular complications like Coronary Artery Disease (CAD). HbA1c laboratory test is used to diagnose DM and to assess control in diabetes mellitus. Large platelets are more thrombogenic and put the patient at higher risk. Mean Platelet Volume (MPV) is the determinant of platelet functionality and increased MPV is associated with increased risk of macrovascular complications like myocardial infarction, stroke and Transient Ischaemic Attacks (TIA). **Aims and Objectives**: To study the HbA1c levels and mean platelet volume in Type II Diabetes Mellitus patients and nondiabetic subjects. To correlate HbA1c levels and MPV in T2DM patients and nondiabetic subjects. **Materials and metod:** This study was undertaken at D.Y. Patil Medical College, Hospital and Research Institute, Kolhapur. The duration of study was from May 2015 to April 2017. Total sample size was 110 out of which 56 were patients with T2DM and 54 were non-diabetic control subjects. Type II DM patients attending the outdoor and indoor patient department of D.Y.Patil Hospital, Kolhapur were taken as sample (cases).This is a cross sectional study. Only known cases of Type II Diabetes Mellitus without any cardiovascular manifestation were included in the study. Non-diabetic asymptomatic cases as sample control. A detailed history with thorough clinical examination was carried out. HbA1c and MPV investigations were carried out in all subjects (both groups). **Results**: MPV in T2DM patient group was 9±0.9 fl.; MPV in the non-diabetic group was 8.08±0.45 fl. Comparison of MPV values in two groups show statistically significant difference and p values < 0.0001. **Conclusion**: MPV was found to be higher in T2DM patients. Increased MPV was associated with higher HbA1c values. MPV can be used as a prognostic marker of vascular complications in patients with T2DM.
Keywords: Type II Diabetes Mellitus (T2DM), HbA1c, Mean Platelet Volume (MPV).

Correspondence Info: Dr.Mukund Pujari, PG student, Dept. of Physiology, D.Y Patil Medical College, Kolhapur, 416006 (M.S.), India.

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INTRODUCTION:

Diabetes Mellitus (DM) is a major global health problem.[1] T2Dm has reached an epidemic level in both developed and developing countries.[2] It is projected that by the year 2025, 80.9 millions will have diabetes in India. India has become the capital of diabetes. Prevalence of myocardial infarction is three times higher in diabetic subjects. India is predicted to bear the greatest Coronary Artery Disease (CAD) burden, according to the estimates from the Global Burden of Disease study.[3]

T2DM characterized by persistent hyperglycemia, is a consequence of a progressive defect of insulin secretion on the background of insulin resistance and represent about 90 to 95% of those with diabetes. Consequential hyperglycemia causes accelerated atherosclerosis and long term vascular complications.[4]

HbA1c is the glycated form of hemoglobin (Hb) formed by the non-enzymatic glycation pathway by hemoglobin exposure to plasma glucose. Normal levels of glucose produce normal amount of glycated Hb. As the average amount of plasma glucose increases the fraction of glycated Hb increases in a predictable way. This serves as a marker of average blood glucose level over last three months prior to the measurement, as this is the half life of RBCs. In DM higher amounts of glycated Hb indicates

poorer control of blood glucose levels and it is associated with cardiovascular diseases, nephropathy and retinopathy.

Functional and morphological abnormalities of platelets in diabetes mellitus are reported.[5] Platelets are tiny, disc shaped, non-nucleated, flattened structures 1-4µm in diameter. They are derived from cytoplasm of megakaryocytes. Mean platelet volume varies between 7.5 and 10.5fl.The size of platelets depends on the density of granules present in them. MPV has become an important marker/determinant of platelet function.[6] Platelet activity and aggregation potential which are essential in atherogenesis and thrombogenesis, can be easily estimated by measuring Mean Platelet Volume (MPV) as a part of complete blood count (CBC).[7] Large platelets contain more dense granules, metabolically and enzymatically more active than small platelets and show more dense granules producing more procoagulant factors like serotonin β thromboglobulin and thromboxane A2, thus playing an important role in thromboembotic diseases. Several studies have shown that patients with diabetes have an altered population of circulating platelets compared with non-diabetics.[5]

In our study, we correlated glycosylated hemoglobin levels and mean platelet volume in type II diabetes mellitus patients and compare them with non-diabetic subjects.

Materials and Method:

The present study was non-interventional, cross sectional study comprising 56 diabetic patients (study group) and 54 non-diabetic subjects (control group). Approval for this work was obtained from the Institutional Ethical Committee of D.Y.Patil Medical College, Hospital and Research Center, Kolhapur. This study was carried out at Department of Physiology, D.Y. Patil Medical College, Hospital and Research Center, Kolhapur. Informed written consent was taken from each patient and subject included in the study and control group. The duration of study was from May 2016 to April 2017 (one year). Patients attending the outdoor and indoor patient department of D.Y. Patil Hospital, Kolhapur were taken as sample (cases). This is a cross sectional study.

Known cases of Type II Diabetes Mellitus without any cardiovascular manifestations were included in the study. Near relatives and other persons attending along with their patients were encouraged for blood glucose testing and those with fasting blood glucose values less than 126 mg% were taken as non-diabetic subjects (control group). Type II diabetes mellitus patients with cardiovascular disease, patients with renal failure and peripheral vascular disease and those with anaemia (Hb<10gms %) and blood dyscrasias were excluded from study.

All the subjects were studied between 10 am to 12 noon. A detailed history with thorough clinical examination, height, weight and blood pressure was recorded. Body mass index was calculated as weight in kg divided by height in meter squared. Blood pressure was a cuff type Sphygmomanometer device.

In diabetic subjects the duration of diabetes was recorded. Venous blood samples were collected from all subjects in both groups with proper aseptic precaution for complete blood count (MPV is a part of complete blood count), blood glucose levels and HbA1c assays. 3ml blood was collected in vials containing EDTA for complete blood counts (MPV) and HbA1c. 2ml blood was collected in Fluoride vial for blood glucose estimation. All samples were maintained at room temperature and tested within one hour of collection to minimize variation due to sample aging. MPV was analyzed by auto hematology analyzer (BC-1800 Mindray).

Blood glucose was done by GOD-POD method on Biochemistry Analyzer (BS 3000P Sinnowa). HbA1c estimation was done by direct enzymatic HbA1c assay (Diazyme) on Selectra Auto analyser. It is IFCC certified method of HbA1c estimation.

All the data was recorded, documented and subjected for statistical analysis. Blood glucose levels, HbA1c and MPV were studied for possible correlation.

Statistical Analysis:

Statistical data analysis for all quantitative variables is performed using Z-test for means and proportion is compared by Z-test or Chi-square test. Data analysis is performed by MS Excel 2007 and Graph Pad Instand Software. P< 0.0001 shows statistical significance.

Results:

In this study, blood samples from 56 diabetic individuals and 54 healthy controls were analyzed for blood sugar, HbA1c and MPV .The mean age of diabetic patients was 52.37± 10.42 years whereas the mean age of non diabetic subjects was 49.07± 11.77 years. There was no significant difference with reference to age. The BMI of diabetic group is 27.37 ± 3.12 kg/m^2 and that of non diabetic group was 23.74 ± 2.65 kg/m^2. There is a significant difference between these two groups (p< .0001). The mean HbA1c in diabetic subjects is 9.15 ±1.87 mmol/mol and that in control group is 5.58 ±0.46 mmol/mol. This is significant difference between two groups (p< .0001). Mean MPV in diabetic subjects is 9 ±0.9 fl and that in control group is 8.08 ±0.45 fl again this is significant difference among two groups. Average blood sugar in diabetic group was 233.94 ± 58.57 mg/dl and average blood sugar in non diabetic group was 102.8 ±15.69 mg/dl **[Table 1]**.

	Diabetic mean	Sd	Non Diabetic mean	Sd	P-Value	
AGE	52.37	10.42	49.07	11.77	0.12	NS
HEIGHT	159.04	8.27	159.64	15.53	0.79	NS
WEIGHT	68.74	9.2	59.25	8.73	P<.0001***	
BMI	27.37	3.12	23.74	2.65	P< .0001***	
BSL	233.94	58.57	102.8	15.69	P<.0001***	
HbA1c	9.15	1.87	5.58	0.46	P<.0001***	
MPV	9	0.9	8.08	0.45	P<.0001***	

Table 1: Comparison of various parameters between diabetic and non diabetic subjects

Discussion:

From our study it is clearly seen that the MPV was significantly elevated in T2DM (Study group, 9± 0.9fl) as compared to MPV in non-diabetic group (Control group, 8.08±0.45fl). Previous studies have shown that MPV increased in diabetic populations.[12] The Mean Platelet Volume is increased in T2DM.This increase can be due to increased number of younger platelets in circulation in diabetics. Younger platelets have increased platelet volume. Increased endothelial damage is seen in diabetes mellitus, which reduces survival of platelets and increases turnover of younger platelets in diabetes mellitus. Larger platelets are younger, more reactive and aggregable as they contain denser granules ,secrete more serotonin and β-thromboglobulin and produce more thromboxaneA2 than smaller platelets. All these can produce a procoagulant effect and cause thrombotic vascular complications.[8]

Demirtunc R et al investigated the relationship among MPV, glycemic control, and micro- and macrovascular complications in type 2 DM. Seventy patients with type 2 DM and 40 age- and sex-matched healthy individuals were enrolled. Diabetic patients were grouped into those with glycated hemoglobin (HbA1c) levels <or=7% (Group A, n=35 patients) and those with HbA1c >7% (Group B, n=35 patients). Initially, both groups were compared with regard to MPV, HbA1c, serum lipid levels, coronary artery disease, retinopathy, neuropathy, and nephropathy. Thereafter, Group B was called to monthly visits to obtain improved control glycemic control, which was defined as achievement of HbA1c <or=7%. At the end of 3 months of follow-up, Group B was reevaluated. MPV was significantly higher in patients with DM than in controls (8.7+/-0.8 fl vs. 8.2+/-0.7 fl, P=.002). In diabetic patients, there was a significant positive correlation between MPV and HbA1c levels (r=.39, P=.001) but not diabetic vascular complications. When we compared the two diabetic groups, Group B patients had significantly higher MPV than Group A (9.0+/-0.7 fl vs. 8.4+/-0.8 fl, P=.01). Thirty patients (86%) of Group B achieved improved glycemic control at the end of the 3 months. MPV of the patients with improved glycemic control were significantly decreased compared to baseline MPV (8.4+/-0.8 fl vs. 9.0+/-0.7 fl, P=.003). Their results suggested a close relationship between poor glycemic control and increased platelet activity in patients with type 2 DM. Furthermore, platelet activity recovered through improved glycemic control, which may prevent the possible role of platelets in cardiovascular events in these patients.[7]

Olaleye D et al conducted a study with the aim of evaluating predictive power, investigated three simple screening tests as alternates to nerve conduction tests for diagnosing diabetic peripheral neuropathy (DPN). Results of the screening tests, along with the subjects' demographic and clinical characteristics, were planned as the variables for the development of a risk assessment tool for predicting DPN. Data come from 478 subjects consisting of non-diabetic reference subjects, and patients with type 1 and type 2 diabetes mellitus. The three screening tests are significantly and positively correlated with NCS. An increase in the number of insensate responses in the screening test is associated with an increase in the abnormal NCS score. The strength of the association between NCS and each sensory test was greater when the neuropathy severity stage of the subject was added to the model. Both the SWME and vibration by the on-off method tests demonstrated sufficient statistical power to differentiate non-diabetic control subjects from subjects with diabetes, as well as to differentiate subjects with diabetes with and without neuropathy. These two tests, when compared with NCS, also demonstrated acceptable diagnostic performance characteristics in terms of high sensitivity and specificity, total number of correctly predicted cases, and receiver-operating characteristic curves.[13]

One more mechanism of increase in MPV in T2DM could be osmotic swelling of platelets due to raised levels of some glucose metabolites.[6] Hyperglycemia induce non-enzymatic glycation of proteins on the surface of platelets, which

decreases membrane fluidity and increases its reactivity. Thrombi contents is increased in diabetes causing phosphorylation of light myosin chain leading to change in MPV.[8]

Our study shows positive correlation between MPV and markers of short and long term glycemic control such as regular blood glucose levels and HbA1c in T2DM. Thus it can be seen that diabetic patients have significantly larger platelets with increased MPV than non-diabetic controls. Studies show increased platelet aggregation in DM which have a role in its vascular complications.[10]

Limitations:

Small sample size.

Study single centered and restricted to a small geographical area.

As it is a cross sectional study no follow-up was done.

Despite these limitations, the study suggests that MPV could be used as a cost effective tool to monitor Type II DM patients, although large prospective trials are needed.

Conclusion:

Within the limitations of the study, we conclude from the results of present study that MPV has positive correlation with the long term (HbA1c) and short term (Blood glucose levels) markers of glycemic control. As the diabetic subjects have higher baseline platelet reactivity, assessment of MPV, a simple and cost effective laboratory test would be a useful prognostic marker of cardiovascular complications in diabetes and thereby help reduce the morbidity and mortality.

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