ORIGINAL RESEARCH

Comparison Of Mean Platelet Volume In Type 2 Diabetics On Insulin Therapy And Oral Hypoglycaemic Agents

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ABSTRACT

Introduction: Diabetes mellitus (DM) is a global pandemic1. It is the most common group of metabolic disorder characterized by chronic hyperglycemia associated with secondary damage in multiple organ systems especially kidneys, eyes, peripheral nerves and blood vessels.

Aims And Objectives: To determine the association between Mean platelet volume and type 2 diabetes mellitus. To determine the association of microvascular complications with Mean platelet volume.

Materials And Methods: This study was performed at Mahatma Gandhi Memorial Hospital, Warangal from November 2018 to May 2020**.**

Observation And Results: The study population of 100 analysed 40 subjects were above 55 yrs of age and had a mean MPV of 10.770 fl. 56 of them were in the age group of 41- 55 years and the mean MPV of this age group was 10.886 fl and standard deviation of ± 0.5038.

Discussion: DM is a complex metabolic syndrome characterized by chronic hyperglycemia resulting in complications affecting the peripheral nerves, kidneys, eyes, and micro- and macrovascular structures**.**

Key Words: Diabetes mellitus; Insulin therapy; Vascular.

INTRODUCTION

Diabetes mellitus (DM) is a global pandemic1. It is the most common group of metabolic disorder characterized by chronic hyperglycemia associated with secondary damage in multiple organ systems especially kidneys, eyes, peripheral nerves and blood vessels. Increased platelet activation has been suggested to be involved in the pathogenesis of vascular complications22. It is being found that Mean platelet volume (MPV) values are high in patients with diabetes mellitus, more so in uncontrolled diabetes. Platelet volume, a marker of the platelet function and activation, is proposed as to be involved as a causative agent with respect to altered platelet morphology and function. The higher the MPV, the larger and younger the platelets are and more is the risk for thrombosis and are associated with increased risk for hyperglycemic complications. Mean platelet volume (MPV) is an important, simple, effortless, and cost-effective tool measured by hematology analyzer to assess the volume and function of platelets and thus has potential to be used as indicator of presence of vascular complications.

AIMS AND OBJECTIVES

To determine the association between Mean platelet volume and type 2 diabetes mellitus.To compare the values of Mean Platelet Volume in type 2 diabetic subjects on insulin therapy and those on oral hypoglycaemic agents. To determine the association of microvascular complications with Mean platelet volume.

MATERIALS AND METHODS

This study was performed at MAHATMA GANDHI MEMORIAL HOSPITAL, Warangal from November 2018 to May 2020.

STUDY DESIGN AND PATIENT SELECTION

This is a cross sectional , comparative study performed by selecting 100 patients attending the medical OPD and IP patients in MAHATMA GANDHI MEMORIAL HOSPITAL, WARANGAL. Patients with type 2 diabetes (confirmed by the ADA criteria) for more than a year and with good compliance to treatment for a minimum duration of 6 months were selected by simple random sampling technique :

INCLUSION CRITERIA

Confirmed cases of type 2 diabetes on insulin therapy for minimum of 6 months

Confirmed cases of type 2 diabetes on treatment with oral hypoglycaemic agents for a minimum of 6 months

EXCLUSION CRITERIA

Patients with type 1 diabetes. Patients with abnormal platelet counts. Patients taking anti-platelet medications. Patients with chronic kidney disease. Patients with diagnosed malignancy. Patients with Urinary tract infections, cardiac failure. Gestational diabetes. After obtaining informed consent from the study subjects, a detailed history was elicited including history about the duration of diabetes , affected family members and treatment history .All the members were then subjected to a thorough clinical examination by obtaining height, weight, systemic examination along with the examination of fundus.

STANDARDIZED MEAL TEST

A standardized mixed meal was given to all the patients after an overnight fast. The meal consisted of three idlis and a standard serving of sambar and a standard serving of coconut chutney. The total energy content of the standard meal was 9 Kcal/kg, with 60% of the total energy from carbohydrates, 20% of the energy from fat and 20 % of the energy from proteins. Blood glucose levels were then measured. Complete hemogram and Mean platelet volume was performed by cellenium 19 cell counter method. Data analysis was performed by SPSS using Student's t test and Pearson Correlation.

OBSERVATION AND RESULTS

The study population of 100 analysed and the results were tabulated as follows.

The Distribution Of Study Population According To Age And Correlation With Mpv

Age (yrs)	Number	Mean MPV (fl)	Std. Deviation	P value
<= 40	4	10.800	0.0000	0.715
41-55	56	10.886	0.5038	
> 55	40	10.770	0.4692	

In the study population of 100 the mean age was 52.56 years. 40 subjects were above 55 yrs of age and had a mean MPV of 10.770 fl. 56 of them were in the age group of 41- 55 years and the mean MPV of this age group was 10.886 fl and standard deviation of ± 0.5038. and 4 subjects were below 40 years of age and the mean MPV in this age group was 10.80 fl.

The Disrtibution Of Study Population According To Bmi And Its Correlation With Mpv

BMI(Asianpopulation) (Kg/ m2)	Number	Mean MPV (fl)	Std. deviation	P value
Normal(<24.9)	32	10.668	0.393	0.539
Over weight(24-29.9)	60	10.943	0.513	
Obese (> 30)	8	10.789	0.239	

In the study population 32 were classified as having normal BMI (for the Asian population) and the mean MPV of this group was 10.668 ± 0.393 fl. 60 people in the study population were found to be overweight . the mean MPV value of this group was 10.943 ± 0.513 fl. 8 of the study subjects were classified under the obese group and their mean MPV was 10.789 ± 0.239 fl. There was no significant statistical correlation between the mean platelet volume values and BMI.(p value = 0.539). Distribution Of The Study Population According To Duration Of Diabetes And Its Correlation With Mpv In the study population 22 people are found to have DM for less than 3 years and the mean MPV of this group is 10.690 ± 0.4355 fl. • And 40 persons come under the 3-5 year group and the mean MPV of them is 10.760 ± 0.4297 fl. 26 persons come under 5-10 year group and mean MPV of them is 11.046 ± 0.5038 fl.

• 12 persons come under more than 10 years group and mean MPV of them is 10.900 9 ± 0.4938 fl There was no statistical correlation between Mean Platelet Volume and the duration of diabetes mellitus.(p value = 0.180)

Distribution Of Study Population According To Fasting Blood Glucose And Its Correlation With Mpv.

20 among the 1000 in the study population had a Fasting Blood Glucose <100 mg/dl. And the mean MPV of this group was 10.4 ± 0.393 fl. 38 of them had

a Fasting Blood Glucose in the range of 100-126 mg/dl and the mean MPV was 10.784 ± 0.4902 fl. 42 persons in the study population had a Fasting Blood Glucose >126 mg /dl and the mean MPV was 11.09 ± 0.3472 fl.

Distribution Of The Study Population According To Postprandial Blood Glucose And Its Correlation With Mpv.

Among the 100 members of study population only 2 had a post prandial blood glucose <140 mg /dl and the MPV was 9.9 fl. 50 members had postprandial blood glucose ranging from 140-200 mg/dl and the mean MPV of this group was 10.668 ± 0.4711 fl. The remaining 48 persons had postprandial blood glucose values >200 mg /dl and the mean MPV of this group was 11.05 ± 3457 fl.

DISCUSSION

DM is a complex metabolic syndrome characterized by chronic hyperglycemia resulting in complications affecting the peripheral nerves, kidneys, eyes, and micro- and macrovascular structures. Diabetes and its vascular complications can cause a financial havoc, becoming a burden to a country's national economy and dent its growth. India having the highest number of diabetics faces such issues. MPV can be used as a simple economical test in the monitoring of DM and thereby help curb the morbidity and mortality Type 2 DM is characterized mainly by impaired insulin secretion and increased tissue insulin resistance. Sustained hyperglycemia leads to a series of interrelated alterations that can cause endothelial dysfunction and vascular lesions in diabetic complications .Formation of advanced glycation end products, activation of protein kinase C and disturbances in polyol pathways are the possible mechanisms by which increased glucose induces vascular abnormalities. Platelets are small discoid blood cells that circulate and participate in hemostasis. Primary plug formation due to platelets seals the vascular defects and provides the required phospholipid surface for the recruited and activated coagulation factors. In response to stimuli generated by the endothelium of blood vessels, platelets change shape, adhere to subendothelial surfaces, secrete the contents of intracellular organelles, and aggregate to form a thrombus. These pro-aggregatory stimuli include thrombin, collagen, epinephrine, ADP (dense storage granules), and thromboxane A2 (activated platelets).Thus, platelets may assume an important role in signaling of the development of advanced atherosclerosis in diabetes. Platelet hyper-reactivity and increased baseline activation in patients with diabetes is multifactorial . It is associated with biochemical factors such as hyperglycemia and hyperlipidemia, insulin resistance, inflammatory and oxidant state and also with increased expression of glycoprotein receptors and growth factors. Hyperglycemia can increase platelet reactivity by inducing nonenzymatic glycation of proteins on the surface of the platelet, by the osmotic effect of glucose and activation of proteinkinase C. Such glycation decreases membrane fluidity and increases the propensity of platelets to activate. Platelet function is directly regulated by insulin via a functional insulin receptor found on human platelets. Insulin inhibits platelet interaction with collagen and attenuates the platelet aggregation effect of agonists in healthy nonobese individuals. In inflammation, superoxide increases intraplatelet release of calcium after their activation and thus enhancing platelet reactivity. Further more, superoxide limits the biologic activity of nitric oxide (NO) because the oxidative stress impairs endothelial function that reduces production of NO and prostacyclin. Decreasing the effect of NO brings about increased platelet reactivity. Platelets from patients with diabetes express more surface P-selectin and glycoprotein (GP) IIb/IIIa receptors and are more sensitive to agonist stimulation than platelets from patients without diabetes. Larger platelets are also more reactive and aggregable. They contain denser granules, secrete more serotonin and β- thromboglobulin, and produce more thromboxane A2 than smaller platelets, have more adhesion molecules like P-selectin and GP IIb/IIIa. CD62 (P-selectin),CD63, GP IIb/IIIa, platelet factor 4, and β- thromboglobulin are used as markers of platelet activation. Measurements of those markers cannot be used routinely because these methods are costly and time consuming and need specialized equipment. Thus measurement of MPV is a cost-effective and easy method to evaluate platelet function and activity and also correlates with platelet function and activation. A definitive proof showing that a reduction in chronic hyperglycaemia can lead to prevention of many early complications of type 1 DM was obtained from the diabetes control and complications trial (DCCT). This was a large multicentre clinical trial which randomised 1,400 type 1 diabetics to either conventional or intensive diabetes management and evaluated prospectively for the development of nephropathy, retinopathy and neuropathy. A substantially lower HbA1c (7.3%) was achieved by the intensive group rather than the conventionally managed group (9.1%). DCCT also showed that a reduction in microalbuminuria by 39% and clinical nephropathy by 54%, non-proliferative and proliferative retinopathy by 47% and neuropathy by 60% resulted from improvement of glycemic control. The benefit of the improved glycaemic control achieved during the DCCT persisted even after the study concluded and the glycaemic control worsened. The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that a 35% reduction in microvascular

complications was achieved with each percent point decrease in HbA1c. Improvement in lipoprotein risk profiles such as increased HDL and reduced triglycerides resulted with improved glycaemic control. A significant finding of this study was that strict blood pressure control considerably reduced both macrovascular and microvascular complications. The favourable effects of blood pressure control were found to be greater than those of control of glycaemic status. A trial on 4065 type 2 diabetics from 77 centres over Canada and US; Action to control cardiovascular risk in diabetes eye subgroup (ACCORD-Eye) trial showed with intensive glycaemic control and lipid control especially with fenofibrate lead to a 40% reduction in retinopathy within a short period of 4 years. Another large randomised-controlled trial was conducted at 215 centres in 20 countries in Asia, Europe, Australia and US; The Action in Diabetes and Vascular Disease: Preterax and Diamicron modified release-controlled evaluation (ADVANCE) trial. This involved 11140 type2 diabetics and they were studied over 5 years. This study demonstrated a 21% reduction in new onset microalbuminuria and reduction in occurrence of new or worsening nephropathy, with intensive glycaemic control (HbA1c 6.5%) as opposed to standard glycaemic control (HbA1c 7.3%). These two large trials also prove the importance of control of glycaemic status in the prevention of microvascular disease among diabetics. The mean MPV value of the study population of 100 diabetic individuals was 10.836 fl and this is higher than that of the normal healthy population. This is in accordance to the study published by Kodiatte et al, Hekimsoy et al., Demirtunc et al., Zuberi et al., Atea et al., Jindal et al., and Papanas et al. where the mean MPV was 8.27 ±0.74 fl. The mean age of the study population was 52.56 years, and the study by Pradeep et al had a mean age of 56.9 years, and the study by Kodiatte et al had a mean age of 55.19 years. The body mass index on this study did not have any correlation with MPV , his again is in accordance to the study by Coban et al who showed that there was no correlation between the two. The mean BMI of the study population was 25.97 kg/m2. The mean fasting blood glucose values of the study population was 131.42 ± 45.4 mg/dl. In the study by Kodiatte et al the mean fasting blood was 151.5 ± 71.7 mg/dl. There was positive correlation between the fasting blood sugar values and Mean plaetelet volume. This outcome is reiterated by the study results of Kodiatte et al also having similar outcome. zhe postprandial blood glucose values in the study by Kodiatte et al had a mean of 252.9 ±94.85 mg/dl. While in our study group the mean PPBS values were 219.72 ±74.6 mg/dl, and there was a positive correlation between PPBS values and mean platelet volume similar to that in the former. The HbA1C values in our study population was 7.762 ± 1.83while that of the study by Kodiatte et al was 9.13 ±2.53 .Our study done in MGMH revealed a positive correlation between HbA1C levels and mean platelet volume, this is in accordance to the former publication of Kodiatte et al. There was a significant association between HbA1c and MPV, which was also seen in the study done by Demirtunc *et al.* Therefore, it may be concluded that glycemic control decreases the hyperactivity of the platelet function and thus may prevent or delay possible diabetic vascular complications. The mean platelet volume values of subjects in the study population was not found to correlate with the blood urea and serum creatinine values. The values of mean platelet volume was higher in diabetics with proteinuria than in those who lacked it. And there was a significant positive correlation between proteinuria and MPV,thus indicating a correlation existing between MPV and diabetic nephropathy. Likewise the MPV values were higher in subjects with diabetic retinopathy and there was a definite positive correlation between the two. In our study the MPV was significantly high in patients on oral hypoglycaemic agents rather than those on insulin therapy. The mean MPV of the group with insulin therapy was 10.505 ±0.3535fl and the mean MPV in the OHA group was 11.039 ± 0.4318 fl. This derivation was statistically significant (p value 0.000), and it is in accordance to the outcome of the study by Pradeep. V et al. This indicates that a strict glycaemic control with early initiation of insulin can reduce platelet hyperactivity.

CONCLUSION

Mean platelet volume values were significantly lower in diabetic people on insulin therapy than those on oral hypoglycaemic agents. There was a positive correlation between Mean platelet volume and microvascular complication indicating a higher platelet activity in this subgroup. Emphasis should be laid on a strict glycemic control and early initiation of insulin therapy in order to prevent the vascular complications associated with diabetes. Mean platelet volume can serve as a cost effective marker of a the rothrombosis and helps monitor platelet activity.

REFERENCES

1. Kasper, Dennis L. Harrison's manual of medicine. New York, NY, USA: McGraw-Hill, 2005.Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications.
2. Betteridge D, Zahavi J. Jones NAG, Shine B, Kakar VV, Galton DJ. Platelet function in diabetes mellitus in relationship to complications, glycosylated hemoglobin and serum lipoproteins. Eur J Clin Invest 1981; 11: 273–277.
3. Mitchell RN. Haemodynamic Disorders, Thrombo-embolic Disease and Shock.In :Kumar, Vinay, et al.

Robbins and Cotran pathologic basis of disease. Elsevier Health Sciences, 2014.

4. . Schneider DJ. Factors Contributing to Increased Platelet Reactivity in People with Diabetes. Diabetes Care. 2009;32(4):525-527. doi:10.2337/dc08-1865.
5. . Demirtunc, Refik, et al. "The relationship between glycemic control and platelet activity in type 2 diabetes mellitus." Journal of Diabetes and its Complications 23.2 (2009): 89-94.
6. Kodiatte TA, Manikyam UK, Rao SB, et al. Mean Platelet Volume in Type 2 Diabetes Mellitus. Journal of Laboratory Physicians. 2012;4(1):5-9. doi:10.4103/0974-2727.98662.
7. Zuberi, B. F., N. Akhtar, and S. A fsar. "Comparison of mean platelet volume in patients with diabetes mellitus, impaired fasting glucose and non-diabetic subjects." Singapore medical journal 49.2 (2008): 114.
8. Jindal, Sonali, et al. "Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications." Hematology 16.2 (2011): 86-89.