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Mean Platelet Volume in Type 2 Diabetes Mellitus

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ABSTRACT

To study mean platelet volume (MPV) and its relationship with glycemic control in type 2 Diabetes mellitus. Study Design: Case control study Place and Duration: June to November 2012. One hundred Type 2 DM and forty healthy controls were selected through non-probability purposive sampling according to inclusion and exclusion criteria The subjects were divided into; controls (group I), controlled diabetics (groups II) and uncontrolled diabetics (group III). Blood samples were collected in bottles containing sodium citrate and processed on automated hematoanalyzer. Blood glucose and HbA1c were measured on automated chemistry analyzer. The Data was analyzed on SPSS version 20.0 using one way-ANOVA, Fischer`s LSD and Pearson's correlation (r). A p-value of <0.05 was taken statistically significant. Out of 140 subjects, male and female in groups I, II and III were found as 26 and 14, 34 and 16, and 22 and 28 respectively. The mean ± SD age was noted as 45.18 ± 8.84, 46.36 ± 5.98 and 43.64 ± 9.01 years respectively ($p \geq 0.09$). A highly significant platelet count difference was observed between groups I and III ($p<0.001$). The MPV was found as 9.7±0.68, 9.94±0.69 and 11.28±1.15 fl (femtolitre) in three groups respectively ($p<0.0001$). Significantly higher MPV values were found in uncontrolled diabetic subjects compared with normal healthy controls and controlled diabetics ($p=0.0001$). The MPV was positively correlated with HbA1c ($r=0.540$, $p=0.0001$) and duration of DM ($r=0.410$, $p=0.0001$), negatively correlated with platelet count ($r=-0.6$, $p=0.4$) and correlation was not found with age ($r=0.30$, $p=0.69$) and gender ($r=0.10$, $p=0.20$). Mean platelet volume was found elevated in type 2 DM particularly in those having uncontrolled glycemic control. The MPV was positively correlated with HbA1c and duration of DM but negatively correlated with platelet count.

Introduction

Diabetes mellitus (DM) is a metabolic syndrome characterized by chronic hyperglycemia caused by relative or absolute insulin deficiency.[1] According to International Diabetes Federation (IDF), the number of diabetics older than twenty is going to rise from 285 million in 2010 to 439 million in 2030.[2] The Pakistan ranks at sixth position regarding diabetes burden in the world.[3] According to an estimate of Shera, et al. there are 15% Pakistani's with diagnosed DM and millions more which remain undiagnosed and unaware of having DM.[4,5] The Pakistan National Diabetes Survey (PNDS) declared that for each diagnosed case of DM, there are 2 cases of undiagnosed DM and 3 cases of impaired glucose tolerance approximately.[6,7] The chronic hyperglycemia, in long term, causes damage in target organs like eyes, nerves, kidney, heart and blood vessels.[1,8] A change in platelet morphology and function has been documented in DM.[9] The mean platelet volume (MPV) is a measure of average size and function of platelets.[9] The MPV is related with megakaryocyte ploidy. The rate of fragmentation of megakaryocyte and proplatelet formation are the determinators of great dispersion of MPV. An increase in MPV is mediated through thrombopoietin, interleukins (IL) 6 and 11 in conditions with high platelet consumption like DM.[10] These cytokines affect megakaryocyte ploidy and cause formation of platelets which are larger and more reactive than normal.[11] An increase in MPV in type 2 DM is reported in many studies particularly those having diabetic microvascular complications.[12-14] The diabetic subjects exhibit tendency of thrombogenicity because of circulating larger platelets. The large platelets contain more granules, compared with smaller platelets, hence exhibit thrombogenic potential. Both the size of platelets and their granules are independent to hormonal control. The platelet size does not change in peripheral circulation as they become senescent. The MPV is a newly emerging risk factor for atheroma formation and thromboembolic phenomena. Many studies have documented MPV as an independent risk factor for cardiac events, brain ischemia and albuminuria in diabetic subjects.[10-14] The glycated hemoglobin A (HbA1c) is a validated and a reliable indicator of blood glucose control in DM subjects [8] and has been studied in relation to MPV in many studies.[10-14] The MPV estimation is cost effective, less time consuming, easy to perform and obviates observer bias, by using automated hematology analyzers.[15] The aim of present study is to investigate association of MPV with glycemic control in type 2 DM patients. The present study hypothesizes that a higher MPV would be independently associated with DM and association is modified by level of glycemic control.

Subjects and Methods

A case control study was conducted at Diabetic clinic, Department of Medicine, Isra University Hospital Hyderabad from June-November 2012. The study was approved by Board of Advanced Studies and Research (BASR) and Ethical review

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committee of institute. One hundred Type 2 DM and forty healthy controls were selected through non-probability purposive sampling according to inclusion and exclusion criteria. Diagnosed cases of type 2 DM according to criteria set by the American Diabetes Association[8] of duration ≥5years and age >25 but <60 years were included. Type 2 DM subjects having renal failure, chronic systemic diseases, urinary tract infections, recent major surgery, and a history of antiplatelet or anticoagulant drug therapy were excluded. The study subjects were divided into three groups;

Group I. Normal subjects taken as controls (n=40),

Group II. Diabetic subjects with HbA1c ≤7% (n=50) and

Group III. Diabetic subjects with HbA1c >7% (n=50).

Consent was taken from volunteer participants, followed by enquiry about medical history related to DM, antidiabetic drugs, and symptoms related to the diabetic complications and were recorded on a structured proforma. DM was defined according to criteria set by American Diabetes Associaiton.[8] The HbA1C was used as an indicator of glycemic control. The body mass index (BMI) was calculated from the weight and height by formula; BMI= Weight (kg)/Height (m^2). Systemic BP was recorded with a mercury sphygmomanometer after the patient had taken 5 minutes rest. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg.[16] The Blood samples were collected in bottles containing sodium citrate as anticoagulant and processed on automated hematoanalyzer, Sysmex KX 21. The MPV was defined as an average size of platelet and 8–12 fl was taken as normal range.[9] The blood glucose was detected by glucose oxidase and HbA1c by tetradecyl trimethyl ammonium bromide (TTAB) on automated clinical chemistry analyzer (Hitachi 902, Roche diagnostics, USA). The HbA1c measurement was based on turbidometric Inhibition immunoassay (TINIA) for hemolyzed whole blood.

The Data was analyzed using SPSS version 20.0 for Windows release (Chicago, Illinois, USA). The quantitative variables were presented as mean ± SD and range i.e. age, platelet counts and MPV. Frequencies were presented for categorical variables i.e. gender. Quantitative data between and among groups was analysed by one way-Analysis of Variance (one way-ANOVA) and Post-Hoc Fischer`s LSD test. Pearson's correlation (r) was used to investigate correlation of MPV with platelet counts, HbA1c, age, gender, and duration of DM. A p-value of <0.05 was taken statistically significant.

Results

Out of 140 study subjects, male and female in groups I, II and III were found as 26 and 14, 34 and 16, and 22 and 28 respectively. The mean ± SD age was noted as 45.18 ± 8.84, 46.36 ± 5.98 and 43.64 ± 9.01 years with non-significant p-values (p ≥ 0.09 for all groups). The systolic blood pressure was noted as mean ±SD in three groups as 120.87 ± 6.29, 141.60 ± 20.36 and 128.1± 18.15 mmHg respectively and diastolic blood pressure as 120.87 ± 6.29, 141.60 ± 20.36 and 128.1± 18.15 mmHg respectively. The random blood sugar was noted as 144.7 ± 20.63, 210.5 ± 120.89 and 263.04± 122.57 mg/dl in three groups respectively with highly significant p-values (p < 0.001 for all groups). The BMI calculated for groups I, II and III was found as 26.39±4.36, 25.91±2.37 and 25.98±2.29 kg/m^2 respectively. The overweight and obesity noted in groups I, II and III was 23 (16.2%) and 9 (6.3%), 25 (17.6%) and 5 (3.5%) and 25 (17.6%) and 5 (3.5%) respectively. Mean duration of DM for groups II and III was found as 8.76 ± 3.13 and 11.32 ± 3.69 years respectively. The enquiry about drug therapy revealed that the Diabetics were taking sulfonylureas and metformin alone or in combination.

The platelet counts in controls and diabetic groups were nearly similar in groups I and II (p=0.57), but a significant difference was noted between Group I and III (p=0.031) (Table I). The platelet counts revealed no significant correlation with age (r=0.11, p=0.1), gender (r=0.03, p=0.34), and BMI (r=0.08, p=0.1). However, a negative correlation of platelets was found with MPV (r= –0.6, p=0.4), HbA1c (r= –0.22, p=0.001) and duration of DM (r= –0.1, p=0.2).

The MPV noted in controls (group I) and diabetics (group II and III) was 9.7±0.68, 9.94±0.69 and 11.28±1.15 fl (femtolitre) respectively with a highly significant p-value (p <0.0001 for all groups) (Table II). The MPV was positively correlated with HbA1c (r=0.540, p-value= 0.0001) and duration of DM (r=0.410, p=0.0001). However no correlation was found with age (r=0.30, p=0.69) and gender (r=0.10, p=0.20), and negative correlation was found with platelet count (r= –0.6, p=0.4). Significantly higher MPV values were found in uncontrolled diabetic compared with normal healthy controls and controlled diabetics (p<0.001 for all groups) (Table. II)

The mean ± SD values for HbA1c in Group I, II and III were found as 5.15±0.64%, 5.99±0.53% and 9.99±1.67% respectively, shown in Table III. The HbA1c values as high as 13.9% were found in uncontrolled diabetics. This indicates prevailing bad glycemic control in our diabetic population which remain unaware of the consequences

Table I. Platelet count of controls and Diabetic subjects (x103/µl)

	Group I (Controls)	Group II (HbA1c <7%)	Group III (HbA1c ≥7%)	p-value
Mean ±SD	294 ± 67.41	284 ± 91.59	255 ± 89.93	I vs. (0.57)
Range	119-410	105-569	102-483	I vs.III (0.031) II vs.III (0.089)

Table. II. Mean Platelet Volume (fl*) in controls and Diabetic subjects

	Group I (Controls)	Group II (HbA1c <7%)	Group III (HbA1c ≥7%)	p-value
Mean ±SD	9.7 ± 0.68	10.17 ± 0.86	11.28 ± 1.15	I vs.II (0.019)
Range	8.50-11.00	7.60-11.8	8.20-14.0	I vs.III (0.0001) II vs.III (0.001)

**femto-liter*

Table. III. Glycosylated HbA (HbA1c) in controls and Diabetic subjects (%)

	Group I (Controls)	Group II (HbA1c <7%)	Group III (HbA1c ≥7%)	p-value
Mean ±SD	5.15 ± 0.64	6.0 ± 0.54	9.93 ± 1.68	I vs. (0.01)
Range	4.95 - 5.36	4.80 - 6.90	7.60 -13.90	I vs.III (0.0001) II vs.III (0.001)

Discussion

Morphologic and physiological alterations of platelets have been reported in DM in various studies.[13,14,17,18] The MPV is a newly emerging risk factor for atherothrombosis in Diabetics.

Many studies have shown that increased MPV is a risk factor for myocardial infarction, cerebral ischemia, TIA and diabetic microvascular complications like albuminuria.[19,20] We found significant differences in platelet counts, HbA1c and MPV values in both diabetic groups compared with normal healthy controls. The finding of platelet parameter i.e., MPV of present research work is highly consistent to previous studies.[9-15] Bavbek et al.[21] studied 140 type 2 diabetics and 30 healthy controls and reported elevated MPV and elevated selections on platelet surface, and concluded that platelets having over expressed selectins may play role in the microvascular complications of diabetes mellitus. The Dolasik et al.[22] conducted a study on 60 newly diagnosed diabetic subjects and found a higher MPV values compared with normal controls and MPV values were improved within six month metformin therapy. The findings are comparable to present study. Our study revealed a positive correlation between MPV and HbA1c which is consistent to results of Dalamaga et al.[23] that conducted a prospective study on diabetics, diabetic-myelodysplastic and normal healthy controls and found elevated MPV. One recent study, conducted on controlled and uncontrolled diabetics reported higher MPV values in uncontrolled diabetics and showed a positive correlation between MPV and glycemic status (HbA1c),[24] this also supports finding of present study. The study of Papanas et al.[14] conducted on 265 patients with type 2 DM and 151 healthy controls, reported a positive correlation of MPV with microvascular complications (e.g. microalbuminuria, retinopathy). However correlation was not found between MPV and HbA1c which is contrary to present research work. The finding of significantly elevated MPV in diabetics compared with healthy controls and significant platelet count differences between group I (controls) and uncontrolled diabetics of our present study, is also comparable to previous study of Hekimsoy et al.[13] A study of Muscari et al.[25] reported that blood glucose, body fat and ischemic ECG changes are independently associated with elevated MPV in an elderly population. The present study did not observe any association of MPV with blood sugar and is contrary to the study of Muscari et al.[25] The contradiction might have been introduced by different sample size, study population, medical seeking behavior, health facilities of country and biased statistical analysis.

The Dogan et al.[26] observed a positive correlation of MPV with HbA1c but could not find any association between MPV in patients taking different anti-diabetic drug regimens. The relationship of MPV with glycemic control is a supportive finding related to present research work. The study of Kosus et al. [27] assessed MPV values in patients with gestational DM and found highly significant MPV. Although diabetic population was different but elevated MPV finding is consistent with present study. In a most recent study [28] from Turkey, MPV values were higher in diabetics than normal subjects and tended to increase with progression of diabetic nephropathy. The MPV was found positively correlated with HbA1c, [28] is highly consistent to present work. The Demirtunc et al.[28] conducted study on diabetics and controls and found close relationship of platelet hyperactivity as measured by MPV and poor glycemic control. In his study, the improvement in glycemic control normalized MPV values and reported that platelet hyperactivity may be a risk factor for vascular complications in diabetics. These findings support our present study as diabetic patients with higher HbA1c % were having higher MPV values, rising parallel with each other. The HbA1c values as high as 13.9% were found in uncontrolled diabetics. This indicates prevailing bad glycemic control in our diabetic population and of its complications they remain unaware. As the HbA1c is a validated indicator of glycemic control and has linear relationship with diabetic vascular complications, hence it is concluded that MPV may also be taken as an indicator of glycemic status and diabetic vascular complications beside HbA1c but this needs further large scale, prospective studies to be conducted.

Conclusion:

Mean platelet volume was found elevated in type 2 DM particularly in those having uncontrolled glycemic control. The MPV was positively correlated with HbA1c and duration of DM but negatively correlated with platelet count.

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