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ARTICLE

Full Length Research Paper

Role of mean platelet volume in individuals with type II diabetes mellitus

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Diabetes mellitus (DM) is a global pandemic. Large platelets are highly thrombotic and thus put the patient at a higher risk. Mean platelet volume (MPV) is a determinant of platelet functionality and increased MPV are associated with increased risk for hyperglycemic complications. We aimed to investigate the association of MPV, a marker for platelet size and activity with fasting blood glucose (FBS), postprandial blood glucose (PPBS), glycosylated hemoglobin (HbA1c) and duration of diabetes. We also compared MPV in diabetics and healthy controls. This is a case control study carried out in both individuals with type II diabetes mellitus and healthy controls. All the patients who attended our hospital during September 2012 to march 2013 were included in the study, taking inclusion and exclusion criteria into consideration. In 171 individuals with type II DM and 37 healthy controls, MPV and platelet counts were analyzed by fully automated hematology analyzer SEIMENS ADVIA 2120. Samples were also subjected for FBS, PPBS and HbA1c. The control and test groups were compared with Z test; difference between two means. Pearson's coefficient of correlation (r value) was calculated to know the relationship between two variables. t Test was done to test the significance of r value obtained and p value was calculated. p Value < 0.05 is considered significant. The analysis was done by Microsoft excel sheet. MPV was significantly higher in diabetics when compared to healthy controls (7.91 + 0.87 > 6.91 + 0.71). There was also a statistically significant positive correlation between HbA1c and MPV (r value - 0.5, p value - 0.4). Though FBS and PPBS showed a negative correlation with MPV but were not statistically significant. MPV, a simple, reliable and cost effective tool can be used in diabetes mellitus as an accessory marker for monitoring vascular complications and glycemic control.

Key words: Mean platelet volume, diabetes mellitus, glycosylated hemoglobin.

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share a phenotype of hyperglycemia (Alvin et al., 2011) Platelets play a major role in maintaining normal homeostasis (Mitchell, 2010). Increased activation of platelets has been implicated in the pathogenesis of vascular complications (Papanas et

al., 2004). Mean platelet volume (MPV), an important, simple, effortless, and cost-effective tool measured by hematology analyzer assess the volume and function of platelets. The higher the MPV, the larger and younger the platelets are and more is the risk factor for thrombosis. Diabetes mellitus 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 (Maitra, 2010). The world wide prevalence of DM has risen dramatically in the past two decades from 30 million cases in 1985 to 185 millions in 2010 (Alvin et al., 2011) Countries with the highest absolute number of diabetics are in India (19 million), China (16 million), and the United States (14 million) (King, 1998).

With an increasing incidence worldwide, diabetes will be the leading cause of morbidity and mortality in the foreseeable future (Alvin et al., 2011). As excess mortality in diabetes is predominantly due to the vascular complications of the disease, (Brand, 1989) the vascular complications of DM should be prevented in order to reduce the incidence of mortality and morbidity. The cause of these complications is poorly understood but may be related to platelet changes, as they play a major role both in thrombosis and atherosclerosis (Wincour, 1992). Several clinical studies have shown that patients with diabetes have an altered population of circulating platelets compared with non diabetics (Preston et al 1978). Type II DM is caused by a combination of peripheral resistance to insulin action and relative insulin deficiency. Sustained hyperglycemia leads to formation of advanced glycation end products, activation of protein kinase C and disturbance in polyol pathway resulting in damage of endothelium and vascular smooth muscles (Maitra, 2010).This probably explains increased prevalence of diabetic micro vascular complications in individuals with poor glycemic control and longer duration of DM (Zuberi et al., 2008).Blood platelets are highly complex, discoid, anucleate cells derived from bone marrow megakaryocytes that participate in critical reactions central to homeostasis and thrombosis (Jonathan, 2001). In response to stimuli generated by the endothelium of blood vessels, platelets change shape, adhere to sub endothelial 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) (Mitchell, 2010).Thus, platelets may assume an important role in signaling of the development of advanced atherosclerosis in diabetes (Angiolillo et al., 2005).

Functional and morphological abnormalities of platelets in diabetes mellitus are reported. 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 (Corash et al., 1977), thus playing an important role in intracoronary thrombus formation and acute thrombotic events (Smith et al., 1999).This suggests a relationship between platelet size and function with diabetic vascular complications and thus changes in MPV reflect the state of thrombogenesis. Mean platelet volume is expected as a possible marker for platelet size and function; hence individuals with higher MPV are more thrombotic. It is also shown that MPV values are high in patients with diabetes mellitus (Hekimsoy et al., 2004, Erikçi et al., 2008).

Thus in our study, we determined the platelet activity with MPV in individuals with type II DM and compared with healthy controls and also studied to see if MPV was influenced in relation to the duration of the disease. We also evaluated the correlation of FBS, PPBS and HbA1c with MPV and total platelet count.

MATERIALS AND METHODS

The present study was a case control study conducted between September 2012 and March 2013 in a tertiary care rural hospital. The sample size was determined by the number of patients attending our hospital during the above mentioned period after taking inclusion and exclusion criteria into consideration. This study was carried out in 171 patients who were already diagnosed to have type II diabetes mellitus and 37 healthy controls. The diabetic group consisted of subjects recently diagnosed, those on regular treatment and individuals with irregular medication. This group included individuals with both vascular complications and without complications. Healthy controls included who were not diabetic and without any vascular complications. Males with hemoglobin (Hb) less than 12 gm/dl and females with Hb less than 11 gm/dl in both test and control groups along with suspected or confirmed cases of malignancies, individuals with history of anti thrombotic medication and individuals with gestational diabetes were excluded from the study.

Venous blood samples were analyzed from both the groups for complete blood count, FBS, PPBS and HbA1c. Under aseptic conditions, 2 ml of venous blood was collected in EDTA vials for complete blood counts and HbA1c. The FBS and PPBS were analyzed in samples collected in sodium fluoride. Early morning samples were drawn for estimating fasting blood glucose levels. Postprandial glucose levels were estimated in samples collected within 2 h of taking food. Samples were maintained at room temperature and analyzed within one hour of collection. MPV and platelet counts were analyzed in fully automated hematology analyzer SEIMENS ADVIA 2120. HbA1c was calculated by high performance liquid chromatography while FBS and PPBS were estimated by hexokinase method in fully automated D-10 and Dade dimensions analyzers, respectively. The tests were explained to the subjects and consent taken. The procedures are in accordance with the ethical committee. Complete clinical evaluation was done in both diabetic and healthy controls to look for any associated micro or macro vascular complications. All the data were documented and subjected for statistical analysis. MPV and platelet counts were evaluated with FBS, PPBS and HbA1c to assess possible trend or correlation.

Table 1. Age and sex distribution in diabetics and healthy controls.

	Diabetics	Healthy controls
Number	171	37
Age (mean in years)	54.44 ± 12.16	43.27 ± 14.74
Female (%)	32.16	48.65
Male (%)	67.84	51.35
Mean duration of diabetes (years)	5.20 ± 2.37	-
Complications (%)	18.71	-

Table 2. Comparison of various parameters in diabetics and healthy controls.

Parameter	Diabetics	Healthy controls	Z value NR/DR	p value
FBS	192.76 ± 64.99	99.86 ± 11.95	17.38	$< 0.01 \times 10^{-8}$
PPBS	245.60 ± 76.10	116.83 ± 15.86	20.18	$< 0.01 \times 10^{-10}$
HbA1c	8.81 ± 2.04	5.50 ± 0.33	19.94	$< 0.01 \times 10^{-9}$
Hemoglobin	12.69 ± 1.43	13.10 ± 1.54	-1.49	Not significant
Platelet count	2.50 ± 0.95	2.54 ± 0.95	-0.22	Not significant
MPV	7.91 ± 0.87	6.91 ± 0.71	7.41	< 0.00001

Statistical analysis

Statistical evaluation was performed by Microsoft excel sheet. The data was expressed as mean ± SD in both control and test groups. The parameters were compared with Z test; difference between two means. Pearson's coefficient of correlation (r value) was calculated to know the relationship between two variables. t Ttest was done to test the significance of r value obtained and p value calculated (p value < 0.05 is considered significant, r of 0 to 1 is considered as positive, correlation with > 0.5 as strong correlation, r < 0 indicates negative correlation).

RESULTS

In this study, samples from 171 diabetics and 37 healthy controls were analyzed for MPV, platelet counts, HbA1c, FBS and PPBS. There were 116 males and 55 females in diabetic individuals with male to female ratio of 2.01:1. In control group (healthy, non diabetics) 19 males and 18 females were included. Samples of varying ages with a minimum age of 40 years and maximum age of 81 years were included in the present study. Out of 171 diabetics, micro vascular complications like peripheral neuropathy, diabetic foot, microalbuminuria, and retinopathy were observed in 32 individuals. The various parameters were compared in diabetics and healthy controls. The mean age in diabetics was 54.44 + 12.16 when compared to 43.27 + 14.74 in healthy controls as shown in Table 1. The mean FBS levels were 192.76 ± 64.99 in diabetics while 99.86 ± 11.95 in controls. There was significant difference of mean PPBS levels in diabetics (245.60 ± 76.10) and controls (116.83 ± 15.86). The mean HbA1c

were higher in tests (8.81 ± 2.04) than the controls (5.50 ± 0.33). We noticed a strong statistical difference in the means of FBS, PPBS and HbA1c. MPV values were 7.91 ± 0.87 in diabetic individuals whereas 6.91 ± 0.71 in controls. The mean of total platelet counts in test and control groups were 2.50 ± 0.95 and 2.54 ± 0.95, respectively which were not statistically significant as depicted in Table 2.

The parameters were compared with Z test which is difference between two means, Pearson's coefficient of correlation (r value) was calculated to know the relationship between two variables. t Test was done to test the significance of r value obtained and p value calculated. p Value < 0.05 is considered significant. MPV and total platelet counts were analyzed with HbA1c, FBS, PPBS and duration of the disease by Pearson's coefficient of correlation. MPV showed a statistically significant strong positive correlation with HbA1c (r - 0.5; p value - 0.04), positive but, statistically not significant correlation with duration of the disease and negative and statistically not significant correlation with FBS and PPBS as shown in Table 3. Total platelet counts showed positive; statistically not significant correlation with HbA1c, FBS, PPBS and duration of the disease as tabulated in Table 4.

DISCUSSION

In our study MPV was higher in diabetics than in controls. There was significant statistical difference between the

Table 3. Correlation of MPV with various parameters.

Characteristic	Parameter	r value	p value
MPV	FBS	-0.12	Negative NS
MPV	PPBS	-0.12	Negative NS
MPV	HbA1c	0.5	0.04 SS
MPV	Duration	0.012	Positive NS

NS: Not significant; SS: Statistically significant.

Table 4. Correlation of total platelet count with various parameters.

Characteristic	Parameter	r value	p value
Platelet count	FBS	0.19	Positive NS
Platelet count	PPBS	0.21	Positive NS
Platelet count	HbA1c	0.21	Positive NS
Platelet count	Duration	0.092	Positive NS

NS: not significant.

two groups. This was in correlation with the studies done by Zuberi et al. (2008); Jindal et al. (2011); Papanas et al. (2004); Kodiatte et al. (2012). Studies done by Kodiatte et al. (2012) showed higher MPV values in individuals with diabetic micro vascular complications than those without complications. Thus, it proves the role of platelet hyperactivity in pathogenesis of micro vascular complications. However in our study, MPV was not significantly different in diabetic individuals with and without micro vascular complications. This was also observed in studies by Hekimsoy et al. (2004). This can be explained by rapid consumption of platelets in diabetics with complications.

In this study we demonstrated a statistically significant positive correlation of MPV with HbA1c in diabetic population. These observations were similar to the studies done by Kodiatte et al. (2012). This proves that hyperglycemic states lead to increase in platelet volume and activity. However fasting blood glucose and postprandial glucose levels showed negative but statistically not significant correlation with MPV. The negative correlation of plasma glucose levels can be due to different dietary consumption. It suggests that HbA1C is a reliable parameter than FBS and PPBS for assessment of glycemic control.

In this study the mean of total platelet count was not statistically different in diabetics and healthy controls. The counts were slightly lower in diabetics. This was similar to studies done by Hekimsoy et al. (2004) but opposite findings that is higher values in diabetics than non diabetics were observed by Zuberi et al. (2008); Kodiatte et al. (2012). Decrease in platelet count can be due to

participation of platelets in thrombotic process (Mathur et al., 2001). There was positive but statistically not significant correlation of FBS, PPBS and HbA1c with total platelet count suggesting a minor role of platelet count in diabetes mellitus. As the platelet counts are dependent on several variables, that is, mean platelet survival, platelet production rate, and turnover rate in DM, it cannot be considered as an important parameter in DM. There are several factors like hyperglycemia, hyperlipidemia, and insulin resistance, an inflammatory state and increased expression of glycoprotein receptors and growth factors which influence platelet hyper-reactivity and increased baseline activation in patients with diabetes. Platelets in DM have deregulated signaling pathways that lead to an increased activation and aggregation in response to a given stimulus (platelet hyper-reactivity).

Platelet activation contributes to the pathology by triggering thrombus formation and causing micro capillary embolization with the release of constrictive, oxidative, and mitogenic substances such as platelet-derived growth factor (PDGF) and vascular endothelial growth factor (VEGF) that accelerate progression of local vascular lesions like the neovascularization of lens in diabetic retinopathies (Kodiatte et al., 2012). If increased number of large and reactive platelets alone was responsible for vascular damage, then the rate of damage would have been constant for the duration of disease and independent of diabetic control. Thus the progression of vascular complications in DM cannot be explained by platelet reactivity alone. There are other vascular risk factors that may be influenced by the

degree of control of diabetes (Hekimsoy et al., 2004).Our study supports this by a low positive statistically not significant correlation between MPV and duration of diabetes. A direct relation between platelet dysfunction and the development of diabetic complications has yet to be firmly established (Hekimsoy et al., 2004).No correlation was observed with MPV and presence of complications. Similar findings were noted by (Hekimsoy et al., 2004)

Thus it can be concluded that glycemic control decreases the hyperactivity of platelets and may prevent or delay the diabetic micro vascular complications. This indicates that elevated MPV could be either the cause for or due to the effect of the vascular complications. Hence, platelets may play a role and MPV can be used as a simple parameter to assess the vascular events in diabetes. However, further studies are required to know whether increased MPV is the cause or the end result of vascular complications. However, our data needs to be confirmed by larger studies. The limitations of this study were non assessment of body mass index (BMI) and qualitative defects of platelets.

CONCLUSION

In our study we demonstrated a strong positive correlation of MPV with HbA1c and higher values of MPV in diabetics when compared to non diabetic healthy individuals. Thus in DM, platelets are large, hyperactive and aggregable leading to increased risk of atherosclerosis and associated vascular complications. However, the increased MPV as the cause or the end result of vascular complications needs to be further explored. Thus, we propose MPV as a simple, reliable, cost effective accessory tool to monitor the progression of DM and its complications.

Key message

Mean platelet volume is comparatively higher in individuals with type II DM than healthy controls suggesting its possible role in progression of the disease.

Conflict of interests

The authors declare that they have no competing interests.

Authors contribution

Dr V. Tejeswini: Conceived the study, participated in its

design, statistical analysis and drafted manuscript; Dr. P. Premalatha. PAV Krishnama charyulu Sequence alignment and helped to draft manuscript.

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