CORRELATION OF GLYCOSYLATED HEMOGLOBIN AND MEAN PLATELET VOLUME IN PATIENTS WITH TYPE II DIABETES MELLITUS

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ABSTRACT

Objective: To determine the correlation between glycosylated hemoglobin (HBA1c) and mean platelet volume (MPV) among the patients suffering from type II diabetes mellitus.

Study Design: Correlational study.

Place and Duration of Study: Pak Emirates Military Hospital Rawalpindi, from Jun 2018 to Dec 2018.

Methodology: A total of two hundred patients with type II diabetes mellitus reporting for the routine follow-up were recruited. They were divided into two groups on the basis of HBA1c levels. Group A had patients with HBA1c level <7% and group B had patients with HBA1c levels >7%. Mean platelet volume and routine socio-demographic factors were measured and compared in both the groups.

Results: Mean duration of diabetes among the patients was 4.28 ± 5.128 years. A total of 163 (81.5%) patients were using the oral hypoglycemic while 37 (18.5%) were on the insulin. Mean platelet volume of patients in group A was 8.16 ± 0.39 while mean platelet volume of patients in group B was 9.34 ± 0.81. There was strong correlation of mean platelet volume and glycosylated hemoglobin among the patients in this study (*p*-value <0.001). Long duration of illness also was significantly different among two groups upon application of regression analysis.

Conclusion: This study showed a strong link between glycemic control i.e. glycosylated hemoglobin levels and mean platelet volume among the patients suffering from type II diabetes patients. Patients with poorly controlled DM and high levels of glycosylated hemoglobin should be routinely screened for this erythrocyte index in order to early recognize and prevent the vascular complications.

Keywords: Diabetes mellitus type 2, Erythrocyte indices, Glycated hemoglobin A.

INTRODUCTION

Diabetes mellitus (DM) is one of the commonest metabolic disorders. Patients from both developed and developing countries have been affected in number of ways by this multi-system disease[1]. Though a metabolic disorder, it has a variety of complications and manifestations including hematological, micro-vascular, macro-vascular, immunological and other physiological manifestations involving all most all the systems of the body[2].

Normal platelet count, size and activity has been linked with their optimal functioning and playing a role in maintaining hemostasis[3]. Increase in the size of platelets is usually marker of increased functioning capacity. Various chemicals released from platelets responsible for thrombus formation are also produced in excess when size of platelets is increase making this condition pathological[4]. Increased in the size of platelets has been linked with various chronic illnesses including DM, hypertension (HTN), ischemic heart disease (IHD) and chronic infections[5].

Relationship of mean platelet volume (MPV) and diabetes control has been an area of interest for the researchers around the world. Radha *et al* concluded that MPV was significantly higher among the patients with uncontrolled diabetes as compared to the patients with controlled diabetes. Vascular complications were also found more in the diabetics with raised MPV[6]. Another study done on diabetics revealed that better glycemic control has been associated with a decrease in MPV regardless to the type of

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hypoglycemic used for the control of DM[7]. A study done in India involving comparison of diabetic and non-diabetic population concluded that MPV was significantly raised among the diabetics and could be used to predict the presence of vascular complications among them[8]. One recent Turkish study is also important in this regard which concluded that there is a clear increase in MPV among the diabetic patients and is also associated with the cardiovascular complications among these patients[9].

Mechanism by which hyperglycemia is linked with platelet volume is complex and multi-dimensional. Some researchers have been unable to clarify that MPV is cause or effect of the vascular damage that takes place in the diabetic patients. In the diabetics various mechanisms could prone the individual towards the thrombotic phenomenon. Some of these include increased platelet activity, dysfunction of endothelial lining and activation of pathways of coagulation. In particular, diabetic platelets are characterized by dysregulation of several signaling pathways leading to enhanced adhesion, activation and aggregation. These alterations result from the interaction among hyperglycemia, insulin resistance, inflammation and oxidative stress. All these factors lead to the increased MPV which may serve as a precursor for other complications among these diabetic patients[4-6].

A study with small sample size has been done in the past in Khyber province regarding this aspect[10] but no population based study has so far been undertaken on type II diabetic patients in Pakistan to identify the change in MPV among the patients with well controlled and poorly controlled patients. This study aims to determine the correlation between glycosylated hemoglobin (HBA1c) and mean platelet volume (MPV) among the patients suffering from type II diabetes mellitus being treated at our tertiary care teaching hospital.

METHODOLOGY

This correlational study was conducted at a tertiary care hospital of Rawalpindi between June 2018 to December 2018. Screening was performed on the type II diabetic patients diagnosed by consultant medical specialist for more than one year reporting for routine follow up visit at diabetic clinic of a tertiary care teaching hospital. Type II diabetic patients with ages between 18 and 60 and diagnosed for more than one year were included. Exclusion criteria were females who did not consent to or those with a past or current history of any other chronic physical illness other than diabetes (IHD, HTN, CRF, RA or other diseases of chronic nature) or with hematological autoimmune or malignant disease prior to the diagnosis of type II DM were also not included in the study. Patients with history of repeated transfusions in past one year were also part of the exclusion criteria. Patients with hemoglobin level less than 12mg/dl and those who were on antiplatelet drugs were also not included in the analysis.

Approval for the study was taken from ethical review board committee of Pak Emirates Military Hospital. Patients were provided with a detailed description of the study and were inducted into the study after written informed consent. Subjects with confounding variables like presence of chronic physical illness other than DM and hematological or oncological problems prior to the diagnosis of DM were identified by detailed history taking and excluded from the study. Five milliliter of venous blood was drawn and secured in two separate K2-EDTA filled plastic vacutainer tubes by venipuncture under aseptic precautions for the measurement of HBA1c and MPV. Technique of high performance liquid chromatography was used to measure the levels of glycosylated hemoglobin the sample[11]. Seven percent was used as cut off value for the division of patients into two groups. Group A had patients with HBA1c less than 7% while group B had patients with HBA1c more than 7 percent[12]. Mean platelet volume was analyzed with an automated whole blood counter. Quality controls in our laboratory documented good reproducibility of MPV measures, with intra assay and intera assay coefficients of variation of

≤2% on commercial controls. We used reference range of MPV as 7.4–10.4 fL[13]. We calculated the BMI of the study participants by using the recent WHO calculator for BMI[14]. A proforma was specially designed for this study before the start to incorporate all the relevant social and demographic factors in addition to the main study variable. Those proformas were filled for each patient participating in the study.

All statistical analyses was performed using Statistics Package for Social Sciences version 24. Data are presented as mean ± SD for the variable like age, duration of diabetes. Frequency and percentage was calculated for the gender, BMI classes and mode of treatment (oral hypogly-cemic or insulin). Student's t-test was used to compare the mean platelet volume in both the groups. The $p≤0.05$ was considered statistically significant.

RESULTS

A total of 125 (62.5%) patients were males while 75 (37.5) were females. Mean duration of diabetes among the patients included in the study was 4.28 (± 5.128). One hundred & sixty three patients were using oral hypoglycemics while 37 were on the insulin. Table-I shows the general characteristics of the study participants. MPV of patients in group A was 8.16 ± 0.39 while MPV of patients in group B was 9.34 ± 0.81. Statistical comparison of both the groups revealed that

DISCUSSION

Diabetes is a chronic illness with lifelong treatment. Despite treatment it poses the individual to various complications involving almost all the systems[3]. Ours is a developing country

Table-I: Characteristics of study participants (n=200).

Age (years)	
Mean ± SD	43.53 ± 3.105
Range (min-max)	20 - 59 years
Gender	
Male	125 (62.5%)
Female	75 (37.5%)
Duration of Diabetes mellitus	4.28 ± 5.128 12 months - 15 years
Mode of Treatment	
Oral hypoglycemic	163 (81.5%)
Insulin	37 (18.5%)
Body Mass Index	
Normal	101 (50.5%)
Obese and over weight	99 (49.5%)

Table-II: Comparison of mean platelet volume of both groups.

	Group A	Group B	*p*-value
Mean Platelet Volume	8.16 ± 0.39	9.34 ± 0.81	<0.001

with most relatively low literacy rate[15]. This and many other factors have been responsible for poor or partial compliance of most of the patients in our country. Noncompliance is always counter therapeutic and predisposes the individual towards complication of the underlying illness[16].

Table-III: The correlated factors relating to the difference in Mean Platelets Volume and glycemic control in both the groups: the binary logistic regression analysis.

	p-value	Odds ratio	95% Confidence Interval	
			Lower	Upper
Age (ref. is <25-40 years)	0.387	1.359	0.678	2.722
Duration of illness (reference is <5 years)	0.000	17.432	6.325	48.042
Gender (ref. is male)	0.070	0.513	0.249	1.057
BMI (ref. is normal BMI)	0.444	1.330	0.641	2.761
Mode of treatment (ref. is insulin use)	0.705	0.853	0.376	1.937

there was significant difference between the mean platelet volumes of both the groups (table-II). Long duration of illness also was significantly different among two groups upon application of regression analysis (table-III).

Our study was designed with the aim to look for the hematovascular component among the patients of diabetes and see its relationship with the poor control of illness. Glycosylated hemo-globin was used as marker of poorly controlled

illness in our study population and mean platelet volume was related to the levels of HBA1c.

Mean platelet volume has been linked with the poorly controlled chronic illness including the diabetes in the studies done in the past[6-9]. Results in our analysis supported this association and mean platelet volume was strongly linked with the levels of HBA1c. Radha *et al* and Sarbeta *et al* produced similar results were MCV was linked strongly with levels of HBA1c[6,7]. There have been multiple pathways postulated for this causation. It has been studied that platelet function is some-times directly proportional to the size of platelets. If this is true than patients with poor glycemic control are at a higher risk of developing compli-cations related to the increased platelet function. These may include the hypercoagulable state and alteration in the signaling pathways predisposing the individuals towards various micro and macro vascular complications[4-6]. Tajarernmuang *et al* showed clear link between MCV and vascular complications[6]. Therefore early screening of this parameter may be helpful in early detection and prevention of the complications. This study also highlights the fact that control of diabetes and proper medications has not been linked with raised MPV so it can be concluded that risk of developing the complications among these individuals has been less as compared to the patients with poor control of the illness.

Most of the patients in our analysis were males. These results were similar to the studies done in the past among local and foreign populations[10,17,18]. Harreiter *et al* and Muhammad *et al* also had male predominance in their analysis[10,18]. Reason for this finding may be either more risk of males for developing the diabetes or sampling problem as our study sample was from a Military Hospital which increases the chance of male patients to be recruited more. Further studies on public hospitals may show more realistic findings.

Mean duration of diabetes in our sample population was around 4.5 years. Similar results have been generated by other studies done in the past[9,10]. Harreiter *et al* also produced results with mean duration of DM similar to ours[10]. Long duration of illness had significant association with MPV in our study. Our study criteria was narrow and we did not include the patients which were more than 60 years of age, which might be the reason for slightly less mean duration of illness in our target population. More sophisticated design may add some more convincing evidence to our findings.

Most of our patients were on oral hypo-glycemic drugs instead of insulin. Only around 27 percent were using insulin for the control of diabetes. Studies in the past have also supported these findings[10,19]. Chahudry *et al*, in their study also concluded that oral hypoglycemic agents were more commonly used than insulin[19]. Future studies might look into the relationship of use of insulin and control of DM and MPV. It can be an interesting finding, results of which may alter the treatment model of this devastating illness.

Another interesting finding was the high BMI in almost half of the target population. This should be seen with a lot of concern as the link of high BMI and complications of DM has already been established[20]. Various studies have proven the relationship of high BMI with raised MPV among the diabetics[21,22]. Therefore high body mass index can directly or indirectly affect the patients suffering from type II DM. this is also interesting from the point of view of socioecono-mic profile. Pakistan has been classed as low and middle income country. In the perspective this is an astonishing finding that most patients of lower and middle socioeconomic status have been either overweight or obese. Longitudinal studies in public sector hospitals exploring this finding will be really interesting and fruitful.

Despite strict inclusion and exclusion criteria and strengths, this analysis had few limitations as well which need to be kept in account for proper understanding of the results. The major limitation of our study is the use of laboratory method to check the MPV without having baseline results of the study population prior to the diagnosis of

DM. As study was not prospective so we cannot hypothesize that raised mean platelet volume was a consequence of DM or raised HBA1c. The sample size and the target population selected for the study pose methodological issues as well. The findings cannot be generalized as this was not a population based study. A specific group of patients in a tertiary care hospital was targeted instead of a randomized sample of all type II diabetic patients reporting for routine checkup at various hospitals of Pakistan. Another limitation is the chance that the subject may have different reading from another laboratory, so standardization or cross check from other source would have been generated more accurate results. We suggest further studies on a broader based and a more representative sample size using sophisticated methodology in order to generalize the results.

CONCLUSION

This study showed a strong link between glycemic control i.e. HBA1c levels and mean platelet volume among the patients suffering from type II DM. Patients with poorly controlled DM and high levels of glycosylated hemoglobin should be routinely screened for this erythrocyte Indices in order to early recognize and prevent the vascular complications.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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