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The Physiological Association Between Mean Platelet Volume and Diabetes Mellitus Type 2; Correlation Between HbA1c Score and MPV Index

Syed Farhan Uddin[1], Shabnam Rani[2], Nudrat Zeba[3], Gordhan[4], Nadeem Memon[5], Mohammad Khalid Nizaman[6]

[1]Associate Professor, Department of Physiology, Muhammad Medical College MirpurKhas
[2]Assistant Professor, Department of Medicine, Muhammad Medical & Dental College, Mirpur Khas
[3]Associate Professor Community Medicine, Bilawal Medical College,
[4]Associate Professor, Medicine department, Muhammad medical college MirpurKhas
[5]Associate Professor, Department of Medicine, Muhammad Medical & Dental College MirpurKhas.
[6]Senior Registrar Internal medicine Indus medical college Tando Muhammad khan

A B S T R A C T

Objective: To evaluate difference in mean platelet volume between non-diabetics and diabetics individual and to find the relationship between Hba1c level and MPV among type 2 diabetic individuals.

Methodology: This was a retrospective study conducted from December 2022 to November 2023 in Muhammad Medical College and Hospital with prior approval from ethical committee via letter No: Physiol dated 10-03-20. By random sampling 370 participants were selected in which 214 were diabetics and 156 were non-diabetics. Their blood pressure, BMI, Hba1c level, fasting and post prandial glucose level was measured. For evaluation of complete blood picture and MPV an automatic (Beckman coulter) machine was used. Statistical analysis was done by Graph Pad Prism 9.

Results: it was noted that both male and female show significant association between raised MPV and increased serum glycemic level (P value less than 0.05). In male MPV increased in 21.89% patients (x2 =33.96, df=3 and P value= 0.0001). In female MPV increased in 17.29% patients (Odd ratio3.07 and P value= 0.0006).

Conclusion: Mean platelet volume in diabetics was found to be higher as compared to non-diabetic subjects. In diabetic patients with Hba1c less than 6.5% had less raised MPV as compare to diabetics with Hba1c level greater than 6.5%.

Key words: MPV, DM type 2, HbA1c score, MPV index, correlation

Introduction

Diabetes mellitus (DM) is a widely prevailing endocrine disorder, which slowly and gradually affects multiple organs in the human body. The characteristic sign of DM is an increased serum glucose level and decrease intracellular glycemic level.[1]World Health Organization describes Diabetes mellitus as a metabolic disorder which is cause by defect in insulin release or production, or mechanism of action. Globally 171 million people get affected by this disease and according to an estimate by the end of 2030; 366 million people will suffer from DM type 2.[2]

Diabetes mellitus effect different systems of body leading to cerebrovascular accidents, altered kidney functions and neuropathies. Most of these disorders are produced by the thrombotic and embolic complications of diabetes mellitus. Platelets activation in diabetes is the mechanism behind these thrombo embolic complications. Mean platelet volume is the indicator which measures the level of platelet activation.[3] Because of increase platelet

activation diabetic patients are on increased risk of atherosclerosis and cardiovascular complications.[4]

Persistent hyperglycemia for prolong period of time stimulate neutrophils in liver to release thrombopoetin, which increases the production of platelets in bone marrow causing release of immature platelets with raised mean platelet volume in blood.[5] Uncontrolled hyperglycemia promotes glycation of platelets surface proteins which not only make them more reactive but also reduce the fluid content of its plasma membrane. Therefore type 2 diabetic patients have increase expression of glycoprotein Ib and IIb/IIIa at cell surface. All these changes make platelets stickier and more prone to stimulate coagulation and thrombus formation.[6]

Platelets with increased volume have concentrated granules in the cytoplasm which releases excessive thromboxane A2 making platelets more sensitive and susceptible to aggregate together on exposure to collagen and Adenosine di phosphate (ADP).[7]

Insulin controls the action of platelets by some regulatory mechanisms. It inhibits excessive activation and aggregation of platelets following an injury or inflammation. It stimulate release of nitrous oxide synthetase which increases the production of Nitrous oxide in blood leading to vasodilation and lastly it increases intracellular concentration of a second messenger called cAMP (cyclic adenosine monophosphate) which signals to reduce the activation and clamping of platelets together. Thereby inhibits abnormal clotting in blood vessels.[8] Worldwide these three tests are preferred for diagnosis of Diabetes mellitus type 2. Measurement of fasting blood glucose, 2 hours post glucose ingestion results of oral glucose tolerance test and value of Hemoglobin A1c.[9]

The Normal Glycemic index in a healthy individual is about 72 to 108 mg/dL. In pre diabetics, the plasma fasting glucose is about 100 to 125 mg/dL and value for oral glucose tolerance is about 140 to 199 mg/dL. Whereas in diabetics the random blood sugar is more than 200mg/dl, fasting blood sugar is more than 126mg/dl and oral glucose tolerance test is more than 200mg/dl.[10] In Diabetics individuals the recommended maintenance range of HBA1c score from 6.5 to 7% is considered to safer in long run as the risk for development of diabetes related complications get reduce.[11] A Diabetic Association of America (ADA) in 2013 gives criteria for controlled diabetes vs uncontrolled diabetes. It says diabetics with HBA1c lesser then 7% have a controlled glycemic level, whereas HBA1c greater than 7% have an uncontrolled glycemic level. Which 50 times increases the risk for micro and macro vascular complications.[12]

Mean platelet volume (MPV) is a routinely done test as it is an inflammatory marker of different pathologies. Increase MPV indicates larger platelets with more aggressive and reactive behavior. Many researches globally found an increase in MPV in DM type 2.[13] The reference range for MPV is 7.5 to 12 fl. MPV have an inverse relationship with platelet count i.e., volume of platelets get decreased as the production rate of platelets increases. Platelets of more than 15fl are considered to be young and more energetic as compared to platelets with standard MPV.[14] MPV are a low coast, easily available and feasible to interpret test which worldwide attracts the attention of many researchers and medical practitioners globally.[15] The aims and objective of the study was to evaluate the relationship between serum glycemic level and mean platelet volume (MPV)

Methodology

This was a cross sectional study conducted from December 2022 to November 2023.The setting of the study was Mohammad Medical College/Hospital of Mirpurkhas. Total 370 patients were recruited for this study. The inclusion criteria included age range between 30 to 50 years, suffering from type 2 diabetes mellitus. All those patients suffering from hypertension, anemia, chronic kidney disease, chronic obstructive pulmonary disease, alcohol and drug use were excluded from the study. A prior permission was taken from the Ethical committee of Mohammad medical College Mirpurkhas by ethical latter No: Physiol dated 10-03-20. The study was carried out according to rules of Helsinki's declaration. The total data (n=370) was divided in two groups. 214 patients were in the study group who were diagnosed with diabetes mellitus type 2 and 156 were in control group (with HbA1c level less than 6.5%) who were non-diabetics healthy individuals. In study group (n=214), 128 were males and 86 were females. Whereas in control group n=156 (with HbA1c level less than 6.5%), 74 were males and 82 were females. All subjects were provided with both verbal explanation about the procedure of the study and a written consent form. A detailed history and clinical evaluation was conducted on all the patients to find out any possible pathology or complication of Diabetes. Blood pressure and BMI were measured of all subjects. For the evaluation of complete blood picture and mean platelet volume, the blood sample was taken from anterior cubital vein to a test tube containing anticoagulant EDTA at room temperature

then send to an automated blood analyzer machine (BECKMEN COULTER ACT 5diff) in laboratory. For the evaluation of plasma glucose level, blood sample was collected in a sodium fluoride containing test tube and was placed in (Johnson vitors 250) auto analyzer, which work on the principle of glucose oxidation method whereas for HbA1c level an EDTA containing test tube is used which was subjected to a high performance liquid chromatography (HPLC).

The Graph Pad Prism 9 was used as a tool to statistically evaluate the results of the study. The column option was operated to evaluate the mean, median, mode and error of mean. Chi square and Fischer's exact test was applied to determine the P value which was considered significant at > 0.05.

Results

The total data (n=370) was divided in two groups. 214 patients were in the study group (128=male and 86= female). Whereas in control group (n=156), 74 were males and 82 were females.

Table I Describes the demographic and basic clinical evaluation data of the participants. The mean values of male and female participants are shown separately. The mean age of females was 38.59±7.3 and 39.68±6.1 of males. The systolic BP in males was 123.4±8.7 and diastolic was 79.23±5.6 while in female systolic was 113.4±13.4 and diastolic was 77.4±6.5. HbA1c level in males was 7.03±0.6 and in female 7.08±0.6.

Table 1: examines the basic clinical parameters of participants.

Variables	Mean±SD	Min	Max	STD Error of Mean
Age (Females)	38.59±7.3	24.0	50.0	0.56
Age (Males)	39.68±6.1	30.0	50.0	0.42
BMI (Males)	20.3±2.4	17.14	25.8	0.17
BMI (Females)	19.9±2.8	17.5	27.4	0.21
Systolic (males)	123.4±8.7	100	140	0.61
Systolic (females)	113.4±13.4	90	139	1.03
Diastolic (males)	79.23±5.6	70.0	89.0	0.39
Diastolic (Females)	77.4±6.5	67.0	89.0	0.50
Fasting blood sugar (Non-Diabetic Males)	85.8±9.0	70.0	100.0	1.05
Fasting blood sugar (Diabetic Males)	115.5±16.0	70.0	135.0	1.41
Fasting blood sugar (Non-Diabetic Females)	83.16±9.0	70.0	100.0	0.9
Fasting blood sugar (Diabetic Females)	111.6±17.0	70.0	132.0	1.8
Hba1c (Non-Diabetic Males)	4.95±0.5	4.1	6.0	0.06
Hba1c (Diabetic Males)	7.03±0.6	6.1	8.3	0.05
Hba1c (Non-Diabetic Females)	4.99±0.59	4.1	6.0	0.06
Hba1c (Diabetic Females)	7.08±0.6	6.1	8.1	0.06

Table II discusses that female showed significant association between raised MPV and increased serum glycemic level. 64(17.29%) females expressed increased MPV (Odd ratio3.07 and P value= 0.0006)

Table II: association of MPV in females of control and test groups

Hba1c % (Females)	MPV (7-12fl).	MPV more than 12fl	Odd ratio	P value
Hba1c less than 6.5%	51(13.78%)	31(8.37%)	3.07	0.0006
Hba1c more than 6.5%	22(5.94%)	64(17.29%)		

Table III discusses that Male showed significant association between raised MPV and increased serum glycemic level. 81(21.89%) males expressed increased MPV (X^2/df=33.95/3 and P value=0.0001)

Table III: Discusses the mean platelet volume in male patients with HbA1c level less than 6.5 versus more than 6.5.

Hba1c % (Males)	MPV (7-12fl)	MPV more than 12fl	X^2/df	P value
Hba1c less than 6.5%	45(12.16%)	29(7.83%)	33.95/3	0.0001
Hba1c more than 6.5%	47(12.70%)	81(21.89%)		

Discussion

Diabetes mellitus is a syndrome which involve multiple system in the body e.g. eyes, kidney and cerebrovascular disease. In the Countries where the DM is most prevalent, including Unites States of America, China and India. To prevent complications of DM it is essential to monitor the severity of disease. Mean platelet volume is a latest indicator which predict the severity of diseases.[16]

The present study shows a significant correlation between MPV and Diabetes mellitus in male type 2, 81(21.89%) male expressed increased MPV (X^2/df=33.95/3 and P value=0.0001) while female also signifies a strong

association (64(17.29%) female expressed increased MPV (Odd ratio 3.07 and P value= 0.0006). The male association was slightly more than females. We found that diabetic participants, who had their Hba1c levels above 6.5%, were having a considerable higher level of MPV as compared to controlled diabetics having Hba1c level below 6.5%. The similar results were concluded by Adnan M etal [17] in 2020 who found Raised MPV in diabetics males were greater than diabetic females. In the current study it was noted that in male more significant rise in MPV was noted in male gender. In another study by Ding et al [18] in 2021 found similar results as of present study.

He concluded that MPV is increased in patients of type 2 diabetes as compared to healthy subjects. Kodiatte T et al In 2012 [16] found a directly proportional relationship between Hba1c score and MPV values. They found a 2 fold increase in MPV in diabetics with HbA1c greater than 6.5% as compared to diabetics with HbA1c less than 6.5%. This is in favor of present study. A contradictory result was found by Adanan etal[19] in 2020 found increase MPV in diabetic female pregnant subjects as compared to non-diabetic pregnant females. It was opposite to result of present study but the study conducted by Zhobwei Z was mainly of pregnant women and not on normal female gender. Güngör et al. In 2016 [20] found contradicting results as of present study. He found no any significant correlation between MPV and glycemic control. Sertbas in 2017[21] found increase MPV in diabetics as compared to normal healthy subjects. Erhanin [22] in 2019 found no significant relation between diabetes type 2 and mean platelet volume but in the study conducted by Avarna et al [23] in 2023 found more raised MPV in patients of diabetes with HBA1c greater than 7% as compared to HBA1c less than 7%. This is in favor of present study. Oshima etal[24] in 2018 evaluated that MPV in uncontrolled diabetes is highly raised as compared to controlled diabetes. They followed the criteria of Hba1c distribution in two groups (less than 6.5 and greater than 6.5). a similar type of result was deduced by Essawi K[25] in 2023 who discovered that hyperglycemia for a prolong duration produces oxidative stress which affects the physiology, morphology and metabolism of cells , it also damages the endothelial limning of blood vessels leading to wide spread state of coagulation and thrombosis in blood. The study conveyed by Lemchukwu etal.in 2023 presents no any significant correlation between MPV and Hba1c score.

This discussion provides an insight of the relationship between mean platelet volume and diabetes mellitus. Most of the studies are in favor of the results deduced in the current study i.e. mean platelet volume increases in diabetes mellitus but few results are contradictory to results of current study.

LIMITATIONS: the first limitation of present study is its small sample size, second the result of present study cannot be impose on a wide variant of population because the participants were from a single district and health care institute of Mirpurkhas and lastly the study design was cross sectional which shows the correlation between Hba1c and MPV but cannot tell which one was the causing factor of other.

Conclusion

It was found that DM type2 have altering effects on platelet volume which make them highly active and more susceptible for thrombus formation. More researches globally are required to further elaborate and find the effects of DM type 2 on the morphology and physiology of Platelets. This will help to create new strategies for controlling diabetes up to Hba1c level 6.5 which is crucial to limit the drastic effects of DM type 2 on Blood parameters.

RECOMMENDATIONS: The hematological parameters especially mean platelet volume should be considered as a marker to estimate the glycemic control in patients of diabetes mellitus. More research is necessary in different regions of the globe to verify the association between MPV and serum glycemic level.

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