Prediction of Microvascular Complicationswith Meanplatelet Volume Intype 2 Dm

Dr. Prachi Jain, Dr. Ila Pahwa, Dr. Shafali Saluja

I. INTRODUCTION

Diabetesis most commonmetabolic disorder characterizedbychronichypergly cemiaassociatedwith long-termmacro-andmicro-vascularcomplications involving the blood vessels, eyes, kidneys, and nerves.Ithasbecomeaglobalhealthcrisiswith422milli on peoplesufferingfromitanditsincidenceisrapidlyrising in middle- and low-income countries. Diabetes-relatedcomplicationsareresponsiblefor morbidity. Many people have them at the time of diagnosis.DMischaracterizedbyprothromboticstateo fplateletsdue to the persistent hyperglycemia and insulin resistance.

The hyperglycemia, dyslipidemia, and insulin resistance in diabetes causes endothelial and pericyte injury, making it a prothrombotic state.Formationofglycationendproducts,activationof proteinkinaseCanddisturbancesinpolyolpathwaysar e thepossiblemechanismsbywhichincreasedglucose induces vascular abnormalities. Increasedplateletactivationissuggestedtobeinvolved in the pathogenesis of vascular complications. Plateletactivationtriggersthrombusformation thromboembolismwithreleaseofPDGFand VEGFthat accelerate the progression of vascular lesions.

Platelets with altered morphology are found in diabetics.Plateletsarelargerwithdensergranuleswhic hare enzymaticallyandfunctionallyhyperactive.Theysecr ete more pro-aggregatory molecules.

Meanplateletvolume(MPV)isabloodparam eterusedfor measuringplateletsize.LargerplateletshavehigherMP V.It canbedoneeasilyinthelaboratorywithCBC.Itcouldale rt usregardingendothelialdysfunctionandhelppredict microvascular complications.

Microvascular complications, retinal lesions,proteinuriaand microalbuminuria,havebeendescribed asfactorsthatarepredictiveofcardiovascularand cerebrovascularmorbidityandmortalityamongdiabet ic subjects.Hence,ifdetectedearly,microvascularcompl ications would alert us regarding the increased risk of cardiovascularandcerebrovascularcomplications.Th us, microvascularcomplicationswerechosentobestudied in this study.

AIM OF STUDY
This study has been done:
•TocompareMeanPlateletVolumeintype2DiabetesM ellituspatientswithgoodglycaemiccontrolwiththatof poorglycaemic control.
•Tostudytheassociationbetweenmeanplateletvolume and microvascular complications of diabetes.
•Toassesstherelationbetweenmeanplateletvolume,gl ycaemic control, gender, BMI, duration of diabetes and HbA1c.

II. MATERIALS AND METHOD

80diabeticpatientsfromOPDandIPDwerestudied.Ad etailedhistorywastaken.Patientswereevaluatedfor microvascular complications (retinopathy, proteinuria).
MeanPlateletVolume,fastingbloodglucose,Post-prandialbloodglucose,HbA1C,andSr.Creatininewer e obtained.
GlycosylatedHaemoglobin(A1C)≥6.5%orfastingblo odglucose(FBG)≥126mg/dl,fastingshouldbeforatlea st8 hoursor2-hourserumglucose≥200mg/dlduringanoralglucoseto lerancetestorarandomserumglucose≥200 mg/dlwithsymptomsofhyperglycaemiawastakenas diagnosing criteria in this study.
Microalbuminuria,(hallmarkofdiabeticnephropathy) was examined using spot urine albumin creatinine ratio (ACR).PatientswithACRof<20mg/gformenand<30 mg/gfor womenwerecategorizedasmicroalbuminurianegativ eand thosewith>20mg/gand>30mg/grespectivelyas microalbuminuria positive.

DiabeticRetinopathywasdefinedbydirectophthalmoscopy examination.Patientswithatleast2microaneurysmsand/or retinalhemorrhage,and/orothersignsofretinaldamage were diagnosed as having retinopathy.

After baseline evaluation, the patients were divided into 2 groups based on HbA1C levels.
1. Diabeticswithgood control (patients HbA1c<7%)
2. Diabetics with poor glycemic control (patients with HbA1c>7%)

Alltheparameterswerecomparedbetweenboththegroups. Thesegroupswerefurthersubgroupedbasedonthe presenceorabsenceofcomplications.TheMPVineach groupwerecompared.Allparameterswerethensubjected to statistical analysis.

INCLUSION CRITERIA
• Newly detected type II diabetes mellitus patients or Known type II diabetes mellitus patients on treatment withOHA/Insulin andable and willing to participate in the study.
• Male and female patients of age >30 years.

EXCLUSION CRITERIA

•Type I diabetes mellitus •Pregnancy
•Females with (Hb<10g%) and males with (Hb<12g%).
•Patients on antiplatelets, antithrombotics or ondrugs causing bone marrow suppression.
•Patients with diagnosed malignancy.
•Patients with known chronic kidney disease and coronary artery disease.

EXCLUSION CRITERIA
•Patients with UTI,hematologic diseases, hepatic or cardiac failure and chronic illness like RA.
•Patients with cardiac valve replacement,
•Patients with thrombocytosis and thrombocytopenia. •History of blood transfusion in last 14 days.
•Patients with that are on medication altering the platelet function.

RESULTS
•In this study, in good glycemic control group, majority belonged to 51-60 years age class interval with a mean age of 49.09 years andmajority in poor glycemic control group belonged to same age class interval with a mean age of 51.27 years.
•Similarly, in good glycemic control group males and females were equally distributed (50.00%) and majority in poor glycemic control group were females (54.00%)

PARAMETERSOF STUDYPARTICIPANTS

S.NO	PARAMETER	GOODGLYCEMICCONTROLGROUP(n=30)	POORGLYCEMICCONTROLGROUP(n=50)	P-value
1)	AGE (years)	49.09 ± 9.79	51.27±9.12	0.3806
2)	GENDER (M/F)	15/15	23/27	0.6382
3)	BMI (kg/m^2)	27.21 ± 4.74	28.08 ± 3.85	0.3507
4)	MPV (fL)	7.76 ± 0.46	10.18 ± 0.83	<0.0001
5)	FBS (mg/dl)	120.63 ± 22.32	162.20 ± 29.09	<0.0001
6)	PPBS (mg/dl)	169.49 ± 44.09	241.58 ± 51.74	<0.0001

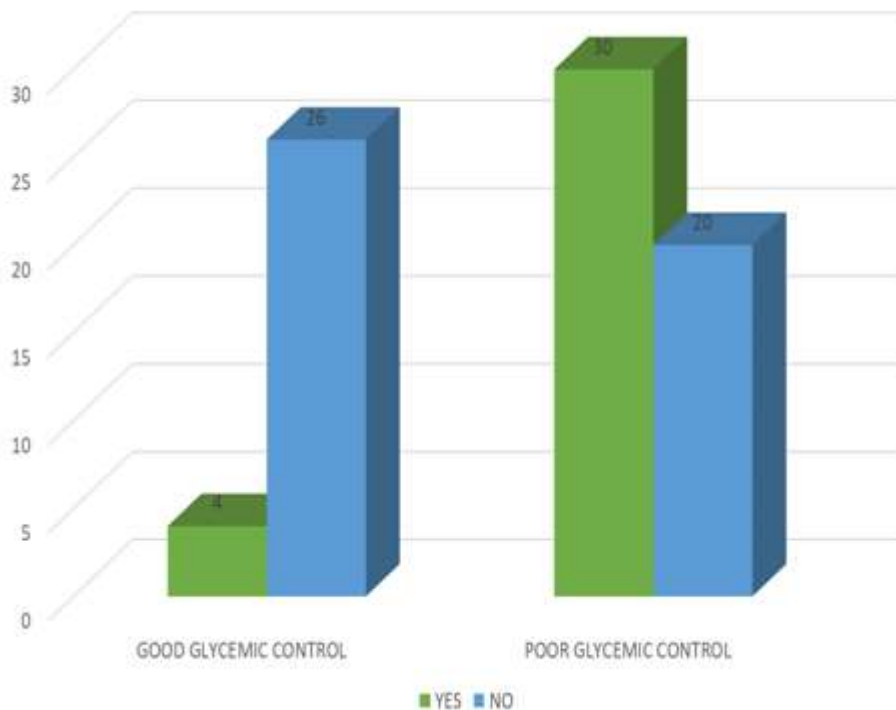| 7)	Duration Of Diabetes (years)	6.63 ± 3.61	7.45 ± 3.50	0.2632

RESULTS
•Majority in good glycemic control group belonged to 101-120 mg/dl FBS class interval (30%) with a mean FBS of 120.63 mg/dl and majority in poor glycemic control group belonged to > 140 mg/dl FBS class interval (82%) with a mean FBS of 162.20 mg/dl.
•Similarly, in good glycemic control group, majority belonged to ≤ 150 mg/dl PPBS class interval (50%) with a mean PPBS of 169.49 mg/dl and majority in poor glycemic control group belonged to 201-250 mg/dl PPBS class interval (38%) with a mean PPBS of 241.48 mg/dl.
•In duration of diabetes distribution, it was observed that, majority in both good and poor glycemic control group belonged to 6-10 years duration of diabetes.

RESULTS
•IncaseofMPVdistribution,itwasobservedthat,ingoodglycemiccontrolgroupandpoorglycemiccontrolgroup,a meanMPVof7.76±0.46fLand10.18±0.83fLwasnotedrespectively(p=<0.0001).Thedatasubjectedtostatistical unpaired t test reveals

RETINOPATHY STATUS

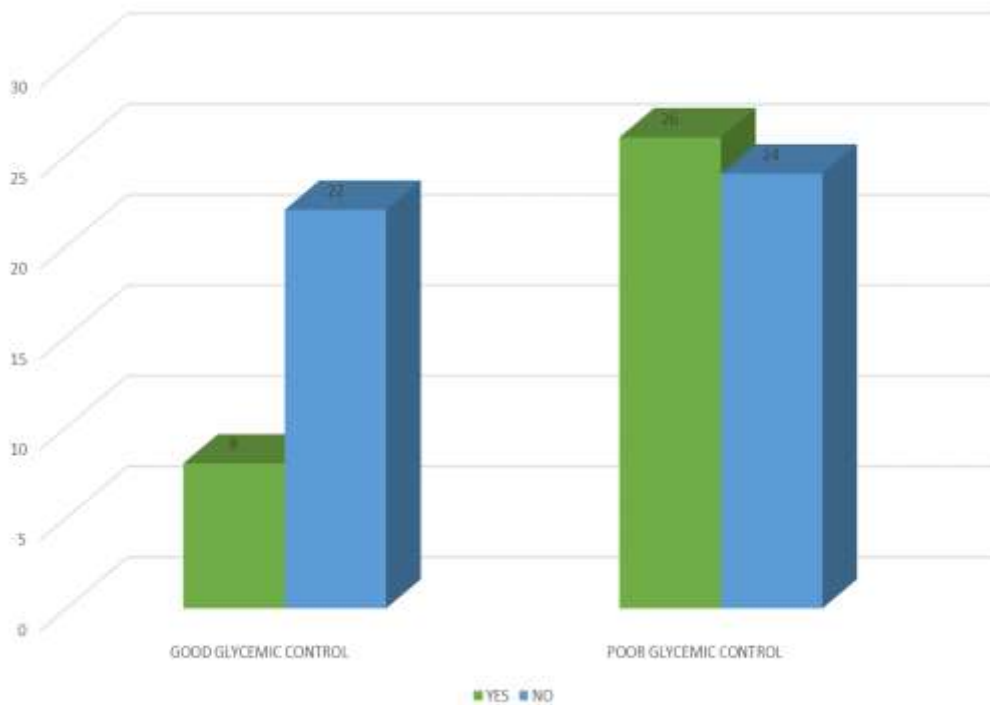| Mean Platelet Volume Vs Retinopathy Distribution	Retinopathy +ve	Retinopathy -ve	P value
Mean	10.46	8.78	<0.0001
SD	0.93	1.17	

PROTEINURIA STATUS

Mean Platelet Volume Vs Proteinuria Distribution	Proteinuria +ve	Proteinuria -ve	P value
Mean	10.16	8.54	<0.0001
SD	1.10	1.17	

RESULTS
•While analyzing MPV distribution, it was observed that in proteinuria +ve group had a mean MPV of 10.26 fL and in proteinuria -ve group, a meanMPV of8.62fL(p=<0.0001) was observed.
•Also, it was observed that, mean MPV in retinopathy +ve group is 10.46 fL ± 0.93 and mean MPV in retinopathy -ve group is 8.78 fL ± 1.18. (p= <0.0001).
•Thisrevealstheexistenceofstatisticallysignificantassociation
betweenMPVdistributionandretinopathystatus(p<0.05)as well as with proteinuria status.
•So,higherMPVvaluesareseenindiabeticpatientswithmicro vascular complications than those without complications.

PEARSON'S CORRELATIONOF MPVWTH FOLLOWINGPARAMETERS

PARAMETERS	MPV	
	Pearson's	P-value
FBS	0.61	<0.0001
PPBS	0.64	<0.0001
HbA1c	0.75	<0.0001
Duration of diabetes	0.23	<0.0001

There is a strongpositive correlationbetweenFBS,PPBS, Hba1c levels,

DISCUSSION

Diabetesanditscomplicationsresultintoaheavyburdenon ourhealth services andeconomy. The microvascular complicationsoccurduetoincreasedprothromboticand atheroscleroticpotentialindiabetesespeciallywhenitis prolonged and / or poorly controlled.

Inthisstudyweaimedtofindouttheplateletindicesintype2 DMandtheirassociationwiththepresenceofmicrovascular complications,andwiththeregulationanddurationof hyperglycemia in patients.

Insulinhasbeenshowntoantagonizetheeffectofplateletagonists likecollagen,adenosinediphosphate,epinephrineand platelet activatingfactor.Plateletshaveinsulinbindingsiteanditisassumed thatinsulinreducesplateletresponsesagainstaggregantfactors includingthrombin,ADPandplateletactivatingfactor. Thusitisfound thatinsulinresistanceresultsinplateletdysfunction.Itis supportedin Westerbacka et al.,2002 and Vinik etal., 2001 study.

Inourstudy,wefoundthatMPVwassignificantlyhigherin diabeticswithpoorglycemiccontrolthanwithgoodglycemic control.Itreinforcedthefactthatpoorglycemiccontroland longer duration may increase the risk of diabetic complications.

Thisissimilartotheobservationofmostofthepreviousother studiesbyKodiatteTAetal.,LeventDemirtasetal.,AlhadasKR etal.,whichindicatesthatlargerandhencehyperactive platelets are due to the chronic hyperglycemia. MPVisanindicatorofaveragesizeandactivityofplatelets. Largerplateletsaremoreactiveenzymaticallyand metabolicallyandhavehigherthromboticabilityascompared to small sized platelets which are depicted by increased MPV.

TherelationshipbetweenthedurationofdiabetesandMPV levelswasalsostatisticallysignificantsincep<0.05.Insimple terms,forevery1-year increaseindurationofdiabetesthereis a9.0flincreaseinMPVamongthestudysubjects.Thisis in contrasttothestudiesdonebyDemirtuncetal.andHeki

msoy etal.,whichshowednosignificantcorrelationbetweenMPVand duration of diabetes.

Also,therelationshipbetweentheFBSandPPBSwith MPV levelswasstatisticallysignificantsincep<0.05.Insimple terms,forevery100mg/dlincreaseinFBSorPPBSthere isa 7.96 fl increase in MPV among the study subjects.

TherelationshipbetweentheHba1clevelsandMPVlevelswasstatisticallysignificantsincep<0.05.Thismeansas Hba1clevelsincreasesMPVlevelsalsoincreasesin adirectandlinearfashioninourstudysubjects.ThisobservationwassimilartothestudiesdonebyKodiatteetal.This provesthatincreasedplateletvolumeand activityresultsfromhyperglycaemicstates.Insimplterms,forevery 1%increase inHba1clevelthereisa5.1flincrease inMPVamongthe study subjects.

AgarwalBKetal.,KhandekarMMetal.,SharmaMetal., andKhodeV et al also observed results similar to this study.TajarernmuangetalshowedclearlinkbetweenMCVandvascular complications.Therefore,earlyscreeningofthisparametermaybe helpful in early detection and prevention of the complications.

III. CONCLUSION

• MPVwassignificantlyhigherindiabeticindividuals havingmicrovascularcomplications.MeanPlatelet Volumechangeisfoundtobestatisticallyassociated withuncontrolleddiabetes i.e.,poorglycemiccontrol andhenceMPVmaybeconsideredasmarkerof platelet activation.

REFERENCES

[1]. •Jindal S, Gupta S, Gupta R. Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. Hematol 2011;16(2):86-9.

[2]. •Kakouros N, Rade JJ, Kourliouros A, Resar JR. Platelet function in patients with diabetes mellitus: from a theoretical to a practical perspective. Int J Endocrinol 2011;2011:742719.

[3]. •Ulutas K, Dokuyucu R, Sefil F. Evaluation of mean platelet volume in patients with type 2 diabetes mellitus and blood glucose regulation: a marker for atherosclerosis?. Int J Clin Exp Med 2014;7(4):955-61.

[4]. •29. Akinsegun A, Akinola Olusola D, Sarah JO, Olajumoke O, Adewumi A, Majeed O, et al. Mean platelet volume and platelet counts in type 2 diabetes: mellitus on

treatment and non-diabetic mellitus controls in Lagos, Nigeria. Pan Afr Med J 2014;18:42.

[5]. •30. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des 2011;17:47–58.

[6]. •Kodiatte TA, Manikyam UK, Rao SB, Jagadish TM, Reddy M, Lingaiah HM, et al. Mean platelet volume in type 2 diabetes mellitus. J Lab Physicians 2012;4:5-9.

[7]. •Levent Demirtas, Husnu Degirmenci, Emin Murat Akbas, Adalet Ozcicek, Aysu Timuroglu, Ali Gurel, et al. Association of hematological indicies with diabetes, impaired glucoseregulation and microvascular complications of diabetes. Int J Clin Exp Med 2015;8(7):11420–7.

[8]. •Alhadas KR, Santos SN, Freitas MM, Viana SM, Ribeiro LC, Costa MB. Are platelet indices useful in the evaluation of type 2 diabetic patients? J Bras Pathol Med Lab 2016;52:96-102.

[9]. •Westerbacka J, Yki-Jarvinen H, Turpeinen A, Rissanen A, Vehkavaara S, Syrjala M, etal., (2002). Inhibition ofplatelet-collagen interaction: anin vivo action ofinsulin abolished by insulinresistance in obesity. ArterosclerThrombVascBiol ;22:167-72.

[10]. •Vinik A. I, Erbas T, Park T. S, Nolan R andPittenger G. L, (2001). Platelet dysfunction in type IIdiabetes. DiabetesCare ;24:14761485.

[11]. •26. Kakouros N, Rade JJ, Kourliouros A, Resar JR. Platelet function in patients with diabetes mellitus: from a theoretical to a practical perspective. Int J Endocrinol 2011;2011:742719.

[12]. •30. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des 2011;17:47–58.

[13]. •Harreiter J, Kautzky-Willer A. Sex and gender differences in prevention of type 2 diabetes. Front Endocrinol (Lausanne) 2018; 9(1): 220-27.

[14]. •Radha RK, Selvam D. MPV in Uncontrolled & Controlled Diabetics-Its Role as an Indicator of Vascular Complication. J ClinDiagn Res 2016; 10(8): EC22-26.

[15]. •Sertbas Y, Sertbas M, Okuroglu N, Ozturk MA, Abacar KY, Ozdemir A. Mean platelet volume changes before and after glycated hemoglobin (HbA1c) improvement in a large study population. Arch Med Sci 2016; 13(4): 711-15.

[16]. Agrawal B, Manchanda B, Garg A et al. Mean platelet volume in acute myocardial infarction: a case-controlled study. Journal of Cardiovascular Research.2015;1:4.

[17]. Sharma M, Narang S, Neema s et al. Study of altered platelet morphology with changes in glycaemic status. Int J Res Med Sci. 2016;4(3):757-761.

[18]. Khode V, Sindhur J, Kanbur D et al. Mean platelet volume and other platelet volume indices in patients with stable coronary artery disease and acute myocardial infarction: A case control study. J Cardiovasc Dis Res. 2012;3:272-5.

[19]. Khandekar MM, Khurana AS, Deshmukh S D et al. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction: an Indian scenario. J Clin Pathol. 2006;59:146–149.