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PlateletIndices:As BiomarkersofVascularComplicationsin T2Diabetes Mellitus

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I. Introduction

In the modern world, diabetes mellitus (DM) has become a global health problem.[1]World Health Organization (WHO) defines diabetes mellitus (OM) as achronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads to damage to the heart, blood vessels, eyes, kidneys, and nerves.Four hundred twenty-two million people suffering from it, and its incidence is rapidly rising in the middle- and low-income countries.[2]There is a globally aimed to halt the rise in diabetes by 2025.[2]The hyperglycemia,dyslipidemia,and insulin resistancein diabetes causes endothelial and pericyte injury, making it a prothrombotic state.

Platelets are known to play a vital role in thrombosis. Platelets with altered morphology are found in diabetics.[3]Meanplateletvolume(MPV)is abloodparameterusedformeasuringplateletsize.[4]Hence increasedmean plateletvolume (MPV) and plateletdistributionwidth (POW) might be associatedwith increased thrombotic potential.[5]Diabetic patients have shown significantly higher MPV than the nondiabetic subjects.[6]The newer hematological analyzers can give us various platelet parameters which help in early detection of the prothrombotic state of the platelets.

Platelet indices, namely PC (Platelet Count), mean platelet indices that are MPV, platelet distribution width (PDW) plays a prominent role in atherosclerosis and thrombosis.In myocardialinfarction,[7]coronary artery disease,[8] as well as DM[9-12]MPV has been found to increase.

Platelet indices may serve as useful tools, being simple, quick, effective and routinely available at a relatively low cost; thus they can act as an alarm for diagnosis, initiation, or progression of diabetic complications. Hence,becauseofthis,we aimedto study plateletparametersintype 2 diabetesandits relation to complications.

II. Materialandmethods

Thepresent study was conducted in Department of General Medicine inSri Venkateswara Ramnarayan RUIA Government General Hospital,Tirupathi. Written informedconsentwas taken from all the patients.

This was a cross-sectional study comprising 80 DM (type 2) patients admitted in medical wards and AMC , and 80 nondiabetic controls. Based on complications study group is divided into diabetes with complicationsandwithout complicationsand based on HbA1clevel study group is dividedinto two groups those with $HbA1_c$<7and $HbA1_c$>7.The study was conducted over 6 months from February 2019 toJuly 2019. All the patients who met the inclusion criteria and those who gave consent were included in the study. The demographicinformationand clinical details of the patientswere recorded,includingdurationof diabetes, family history of diabetics, hypertension, drug history, particular reference to any complications, or comorbidities. Otherbiochemicalparameterslikefastingbloodglucose,postprandialbloodglucose,$HbAl_c$were obtained.

Inclusioncriteria:

1. Age>18years.
2. Allnoninsulin-dependentOM(type2DM)patientsonadmittedinmedicalwardsandAMC.

Exclusioncriteria:

1. Malepatientswith hemoglobin(Hb)<13g%andfemalepatientswithHb<12g%.
2. Controlgroup-Nondiabeticswithcoronaryarterydiseasewerenottakenascontrols.
3. PeoplewithdiabetesonantI-plateletdrugssuchasAspirinandClopidogrel.

4. Patients with any diagnosedmalignancy/ thrombocytopenia/thrombocytosis, chronic renal failure, cyanoticheart disease.

Samplecollection:

Venous blood samples for estimationof glucose, serum creatinine,and lipid profile were collected in the sodium fluoride tube, and for platelet indices were collected in tri-potassium ethylene diamine tetra acetic-acidvacutainers.Sampleswereteste dwithin 1h of collectionto minimizevariations.Completebloodcount was performed on 5-part hematology analyzer. Blood glucose and $HbAl_c$ were estimated using fully automated biochemistryanalyzer. 2 mlvenousbloodwascollectedin each tube under strict aseptic precautions.

Statisticalanalysis:

The statisticalanalysiswas doneusingMicrosoft Excelin2013.Analysisofvariance(ANOVA) is used to compare the variables. Data are expressed as mean. The p-value <0.05 is considered statistically significant.ANOVAtest was used for makingthe comparisonbetweentwo variablesnamely $HbAl_c$<7 v/s $HbAl_c\geq$7 and diabetics with vascular complications v/s without vascular complications. Bar diagram and Pie charts were used for graphical representation of this data.

III. **Observation andResults**

The study group is divided into three groups. Group I.Normal controls (non-diabetics) (n=80), Group 2.Diabetics without complications (n=30), Group 3.Diabetics with complications (n=50). In Group 3 (DM with complications), 29 patients had retinopathy, 18 had neuropathy, and 8 had nephropathy with many patients sufferingfrommorethanonecomplication.BasedonHbAlclevels,thereweretwogroups:DMwithHbAlc <7%(*n*=22) andDMwithHbAlc>7%(*n*=58). The distributionofthe study groups is shownin**Figures1 and 2.**

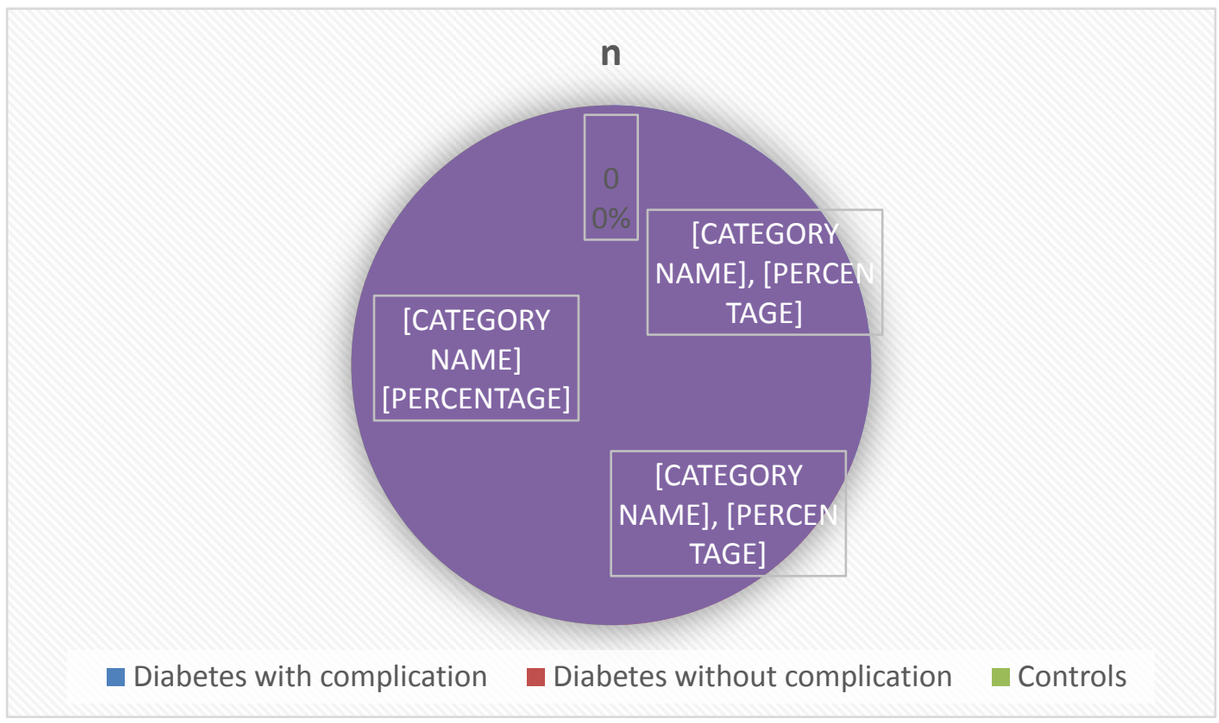

Figure 1: Distributionofthestudypopulationintothreegroups.

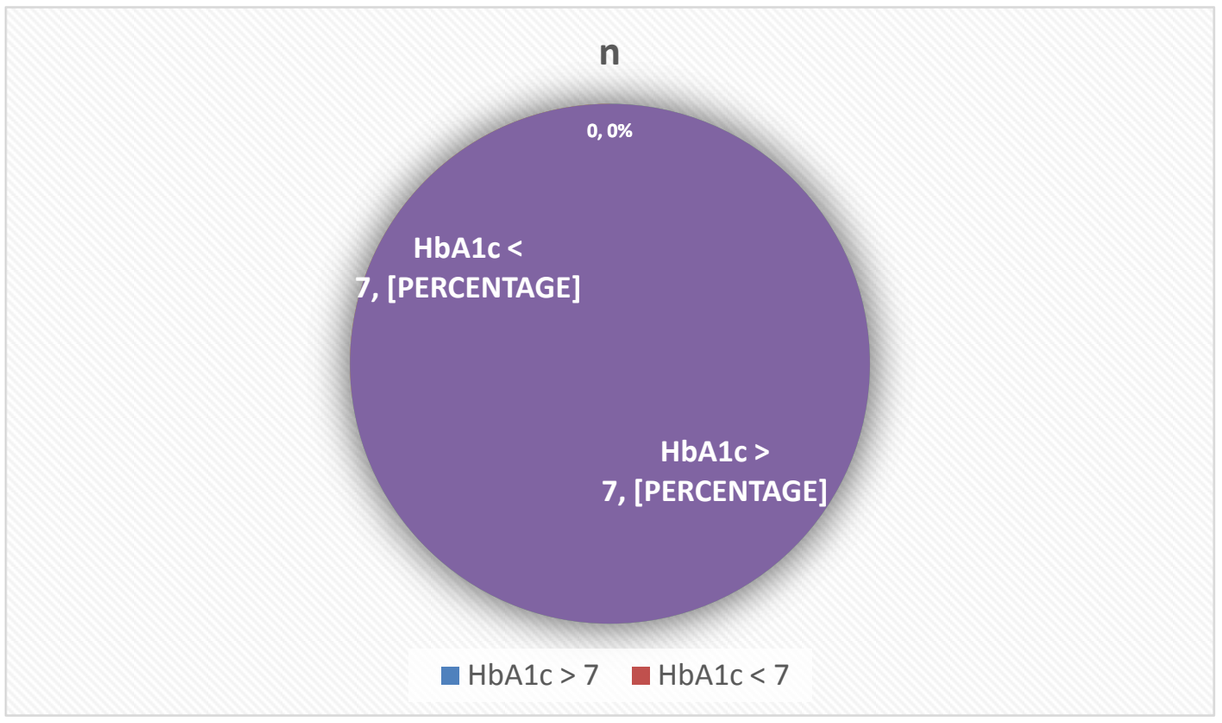

Figure2: DistributionofDiabeticpatientsintotwogroupsbasedonHbAlcvalues.
HbAlc-Glycatedhemoglobin

On comparisonofdemographic,clinicalandbiochemicalparametersbetweenOM without complications and OM with complications **(Table 1and Figure 3),** Patients having diabetes with complication had a highermean age as comparedto patients having diabeteswithout complication(51.27 vs 56.21), andthis was found to be statistically significant *(P* <0.05). The mean duration of diabetes (in years) in patients without complicationswaslowercomparedto thosewithcomplicationsthedifferencebeingstatisticallysignificant. BMI, Creatinine, and HbAlc were found to be higher among patients with complication as compared to patients without complication, and thiswas foundto be statisticallysignificant.

Table1: Comparisonofclinicalandbiochemicalparametersbetween DiabetesMellituswithoutcomplications and Diabetes Mellitus with Complications expressed as mean.

Variable	**Diabeteswithoutcomplications(n=30)**	**Diabeteswithcomplications(n=50)**
Age(years)	51.27	56.21
BMl(kg/m2)	21.22	22.12
Durationofdiabetes(years)	2.681	8.281
HbAlc(%)	7.264	8.916
fastingbloodsugar(mg/dl)	158.421	174.281
postprandialbloodsugar(mg/dl)	226.745	283.723
Totalcholesterol(mg/dl)	179.29	190.672
HDL(mg/di)	45.234	40.641
Creatinine(mg/di)	0.81	1.175

BMI-BodyMassIndex,HbAlc-Glycatedhemoglobin,HDL-High-DensityLipoprotein

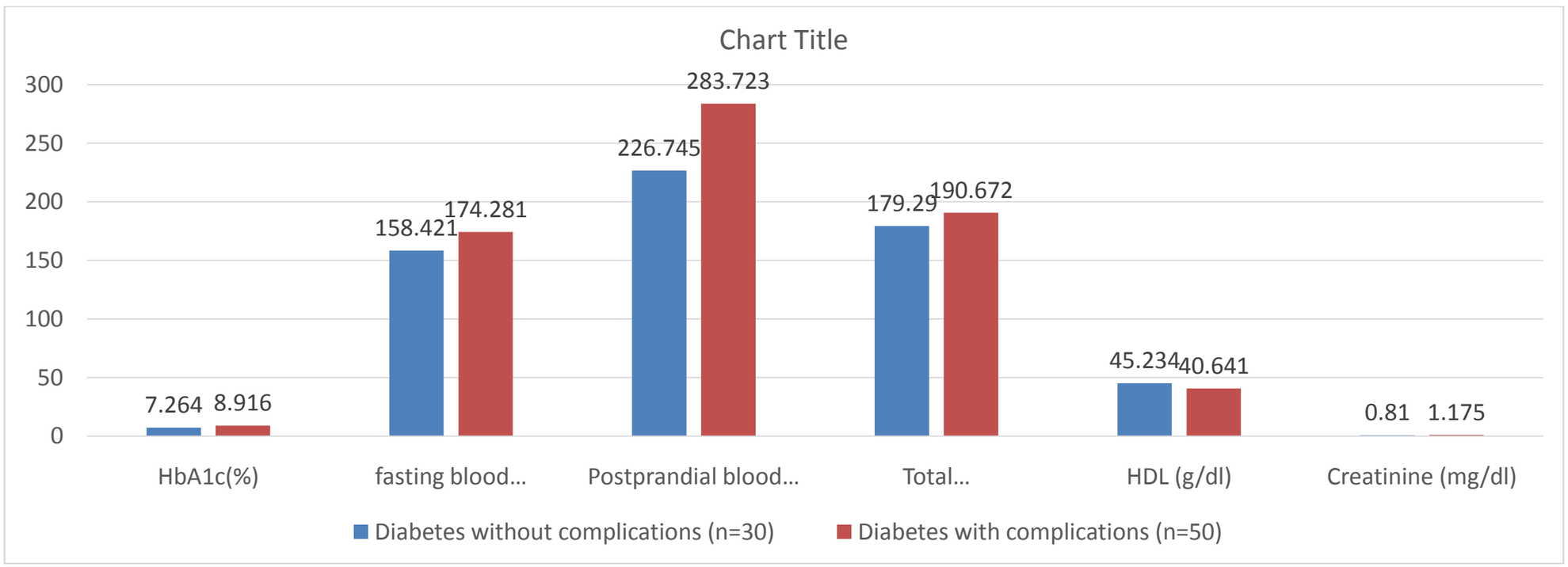

Figure 3: Bardiagram showing the comparison of biochemical parametersbetween diabetes mellituswith and withoutcomplications. HbAlc-Glycatedhemoglobin,HDL-High-DensityLipoprotein

On comparisonofhaematological parametersbetweencontrols, Diabeteswith complicationsandDiabetes withoutcomplications**(Table 2 and Figure4**)Hbwas foundtobehigheramongpatientswithout complication and controls as compared to patients with complications *(P* <0.05). All the platelet parameters including PC, MPV, PDWwere found to be higher among OM with complication as compared to OM without complication,and this was foundto be statistically significant.

Table 2: Comparison of haematological parameters among controls, OM with complications andOM without complications

variable	**control (n=80)**	**DM without complications (n=30)**	**Diabeteswithcomplications (n= 50)**	**p**
Hb(2/dl)	13.824	12.68	11.023	**<0.05**
TLC(cumm)	8368.12	8004.66	7264.78	**>0.05**
Pitcount(xl0^{6}/cumm)	2.85	2.56	3.245	**<0.05**
MPV(fl)	12.123	13.133	14.14	**<0.05**
PDW(fl)	17.02	18.34	19.94	**<0.05**

Hb-Haemoglobin, TLC- Total Leucocyte Count, Pit count- Platelet count, MPV-Mean Platelet Volume, POW-Platelet Distribution Width

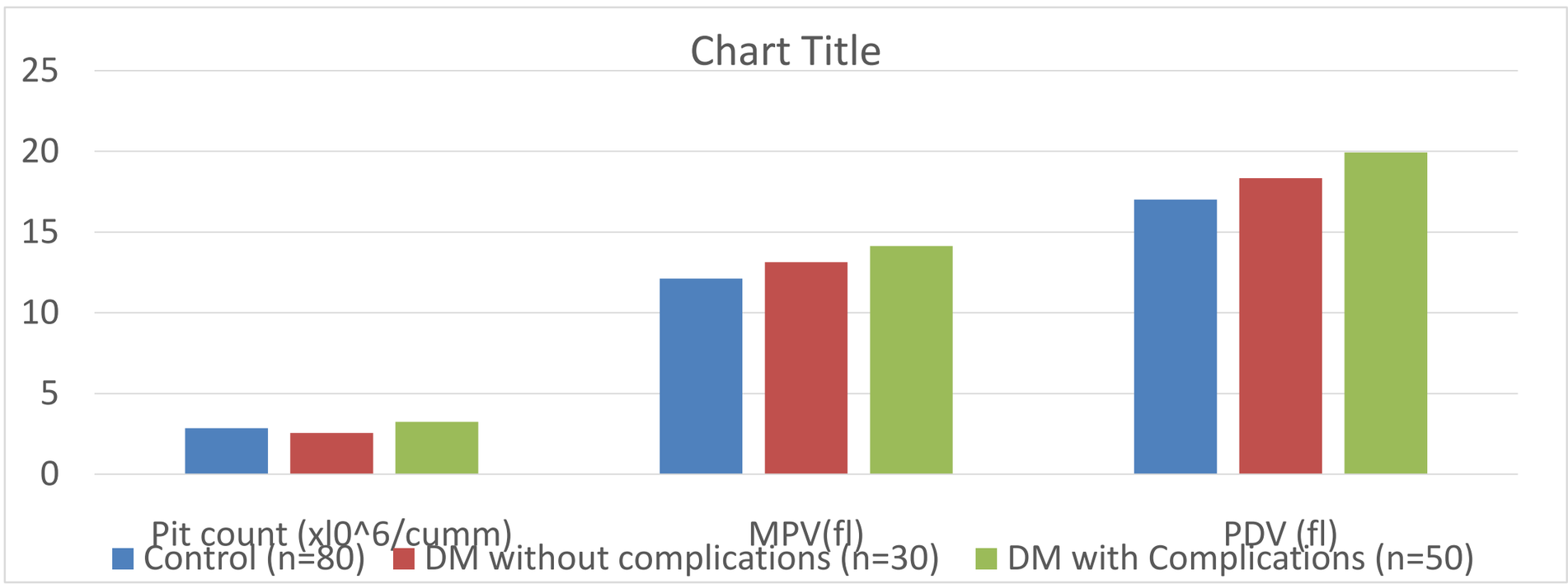

Figure 4: Bar diagram showing the comparisonof platelet parameters among controls, DM without complications and DM with complications.Pltcount- Platelet count, MPV-Mean Platelet Volume, POW-Platelet Distribution Width

On comparisonofbiochemicalandhaematological parametersamongDMwith HbAlc <7%(n=22) and DM with HbAlc >7% (n=58) fasting blood sugar, postprandial blood sugar, total cholesterol, and serum creatinine were found to be higher among DM with HbAlc **>7% (Table 3, figure 5).** Among the platelet parametersplateletcount,MPV,PDWwasfoundto be higheramongDMwith HbAlc >7%**(table 4, figure6).**

Table 3:comparisonof biochemical parameters among among DM with HbAlc <7%(n=22) and DM with HbAlc >7% (n=58)

Variable	HbAlc<7%(n:::22) Mean	HbAlc>7%(n:::58) Mean
fastingbloodsugar(mg/dl)	141.21	186.121
postprandial bloodsugar(mg/dl)	198.245	261.123
Totalcholesterol(mg/dl)	161.242	180.715
HDL(mg/di)	46.285	39.611
Creatinine(mg/di)	0.78	1.163

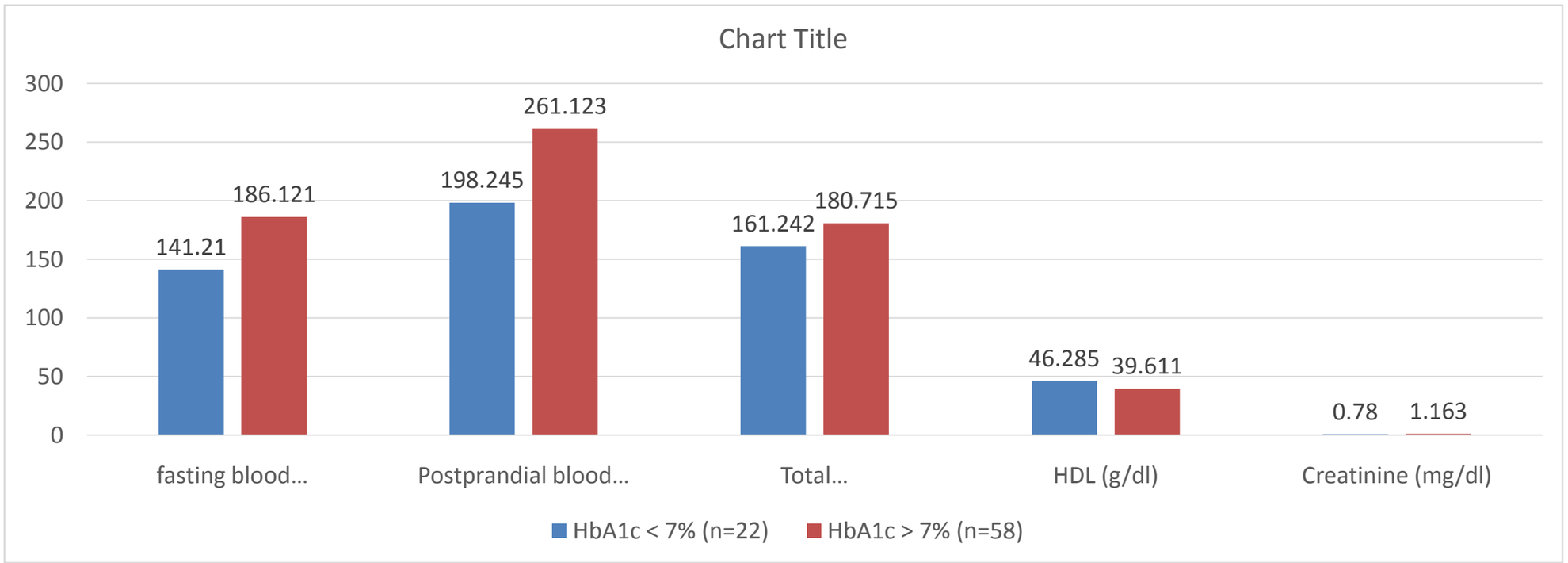

Figure 5: Barchart depicting comparision of biochemicalparameters among among DM with HbAlc <7% (n=22) and DM with HbAlc >7% (n=58)

Table 4: Comparisonof haematologicalparameters among among DM with HbAlc <7%(n=22) and DM with HbAlc >7% (n=58)

variable	HbAlc<7%(n=22) Mean	HbAlc>7%(n=58) Mean	p value
Pitcou.nt(xl0^6/cumm)	2.47	3.65	**<0.05**
MPV(fl)	10.163	12.36	**<0.05**
PDW(fl)	14.644	15.964	**<0.05**

Pitcount-Plateletcount,MPV-MeanPlateletVolume,POW-PlateletDistributionWidth

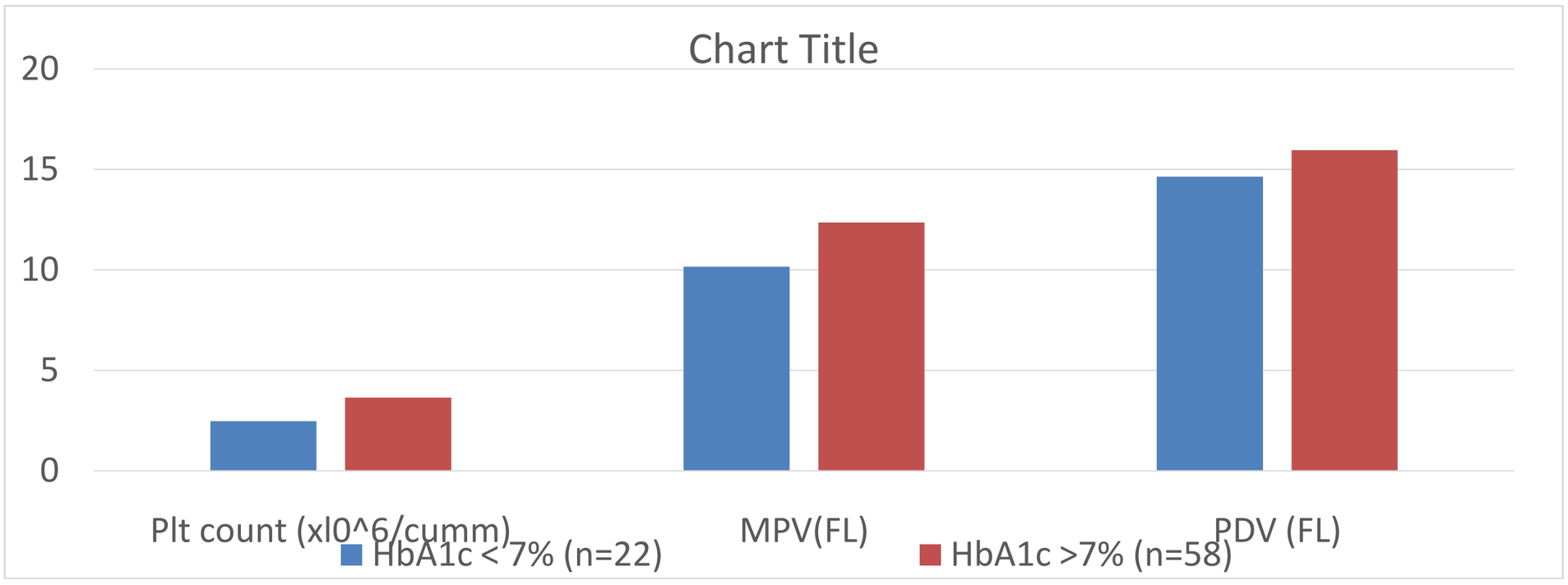

Figure6: BarchartdepictingComparisonofhaematologicalparametersamongamongOMwithHbAlc<7% (n=22)andOMwithHbAlc>7%(n=58).Pitcount-Plateletcount,MPV-MeanPlateletVolume,POW-Platelet Distribution Width

IV. Discussion

DM is characterized by a prothrombotic state comprising increased platelet activation, elevated circulating levels of C-reactive protein (CRP), PAI-1 and fibrinogen. An increased platelet activity has been reportedinpeoplewithdiabetesasdemonstratedbyanincreaseinGPIIb/Illa,lb-IXandla/Illa.16CD62and CD 63 with increase in platelet count, platelet distribution width / and mean platelet volume, the most commonlyused measureof plateletsizeisapotential marker ofplateletreactivity.[13-15]Platelet sizeseemstobe related totheirfunction asMPVishigher inpeople withdiabetes withcomplications.[16-21]Thisisfollowedbyan increase inthedevelopment of cardiovascularand atherosclerоticcomplications associated with DM.Inpeople with diabetes with poor glycemic control, longer duration of the disease, associated hypertension, and obesity theprevalenceof microvascular complications ishigher.[22]Thepresent study was conducted tostudy theroleof platelet parameters inOMinterms of glycemic control anddevelopment of complications.

All the platelet parameters like platelet count, MPV, POW were found to be higher in OM with complicationsgroup andin $HbAl_C \geq 7$group and is foundto be statisticallysignificant. **Buch *et al.*[23]**found a positiveassociationofMPV,POWwithOMbutnotwithPLCRandPC.IshanDubey*et al.*,[24]observedthat MPV is significantly higher in patients with type -2 diabetes mellitus with HbA1C ≥7 and those with vascular complications. **Rajas S. Walinjkar *et al.'*** [25]observed that MPV, PDW, and P/LCRwas higher and more significant in diabetic subjects with microvascular complications. Platelet dysfunction also showed a positive association with HbAlC

V. Conclusion

Platelet parameterslike PC, MPV, PDWwere higher amongpeoplewith diabetes comparedto controls and OMwith complicationsgroupandHbAlc>7group. ThusPlatelet indicesmayserveas useful,simple,and cost-effective markersforthe developmentofcomplicationsin diabeticpatientsandtherebymayplaya crucial roleinthemonitoringof**DM**therebydecreasingmorbidityandmortality.

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