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Correlation of Platelet Distribution Width [PDW], Mean Platelet Volume [MPV] and Red Cell Distribution Width [RDW] with Serum Blood Sugar Levels: A Case- control Study in the West Luck Now Population

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Authors' contributions

This work was carried out in collaboration between all authors. Authors NT, SS and RK designed the study. Author NT wrote the protocol and wrote the first draft of the manuscript. Authors HJ and FA managed the literature searches and analyses of the study performed. Authors RK and ST helped in guiding and conceptualizing the study. Authors NRG and AK helped by referring patients for the study to the lab. All authors read and approved the final manuscript.

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ABSTRACT

Background: Diabetes itself is known to have long standing complications of both micro-vascular as well as macro vascular type. One of the life threatening complications that diabetes gives rise to is stroke and Ischemic heart disease Altered thrombocyte morphology and function have been reported in patients with diabetes mellitus. Few researches have been conducted on complete blood count parameters like Platelet-Crit [Pct], Platelet distribution width [PDW], Mean Platelet Volume [MPV] and Red Cell Distribution width [RDW-SD, CV].

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Aim: The aim of the present study was to determine the associations between platelet morphology markers like PDW, MPV and RDW with Fasting glucose (FBG), Post- prandial blood glucose [PPBG] and Random blood sugar[RBS] in long standing diabetics.
Materials and Methods: Analyses were performed in 2 groups, one for cases and another for controls. A total of 240 patients, with 150 cases and 90 controls were analyzed over a period of 6 months. The data was collected from the hospital registry. Patient's blood had been collected in Fluoride vials for sugar estimation [FBG, RBS, PPBS] and CBC for platelet parameters and RDW of the same patients was done. The identity of the patient was not disclosed and ethical approval was taken.
Results: No significant correlation could be achieved between the tested parameters and the increased blood sugar level [p-value>0.05]. RDW-SD was seen to be an important diagnostic tool for interpretation if the sample size would have been adequate [ROC curve analysis]. Also in blood sugar level estimation, FBS, PPBS &RBS were found to be significantly increased.
Conclusion: The FBS, RBS, PPBS were seen to be significantly increased in the case group as compared to the control group. There was no significant correlation seen between the platelet parameters, the RDW and Blood sugar parameters [p-value>0.05] .RDW was seen to be a good tool for investigation when ROC cure for RDW-SD was analyzed.

Keywords: Diabetes; mellitus; complication; platelet; parameters; RDW.

1. INTRODUCTION

Diabetes mellitus is one of the most common diseases affecting a large part of the Indian population, both young and old. Diabetes itself is known to have long standing complications of both micro-vascular as well as macro vascular type. One of the life threatening complications that diabetes gives rise to is stroke and Ischemic heart disease. However it's unfortunate that there is a want for standardized lab diagnostic modalities to diagnose the long term complication at an early stage so as to lessen the cardiovascular morbidity and mortality. Hyper viscosity of blood and thickening of vascular wall is a known to occur in long standing diabetes. Hence new researches are being targeted to identify simple and easily available lab parameters which could act as red flags or markers in detecting these pathologies. Few such researches have been conducted on complete blood count parameters like Platelet-Crit [Pct], Platelet distribution width [PDW], Mean Platelet Volume[MPV] and Red Cell Distribution width[RDW-SD,CV], a simple and easily available parametric analysis which has not gained much popularity as yet. Altered thrombocyte morphology and function have been reported in patients with diabetes mellitus (DM) specially the type 2 DM [1]. Thrombo-embolic diseases are among the major cause of mortality in developed and developing countries. Early diagnosis of progressive activation of coagulation can help manage these diseases successfully. A list of markers being investigated are pro-thrombin fragment 1+2, thrombin-anti thrombin complex (TAT), and platelet activation, such as β-thromboglobulin (β-TG) or soluble platelet P-selectin [2]. However, laboratory measurement of these indices is laborious and expensive. Additionally, the above mentioned indices cannot be included in routine laboratory tests [2–3]. The aim of the present study was to determine the associations between platelet morphology markers [MPV&PDW] and RDW-SD, RDW-CV with fasting glucose (FBG), Post- prandial blood glucose [PPBG] and Random blood sugar [RBS] in long standing diabetics.

2. MATERIALS AND METHODS

Analyses were performed in 2 groups,one for cases and another for controls. A total of 240 patients, with 150 cases and 90 controls were analyzed over a period of 6 months. The data was collected from the hospital registry. Patients blood had been collected in Fluoride vials for sugar estimation [FBG, RBS, PPBS] and CBC of the same patients was done,by collecting the blood in ethylenediaminetetraacetate EDTA vials and running the tests on Sysmex 5 part counter, which gave us the values of RDW-SD,RDW-CV, MPV and PDW. These values were recorded and analyzed. The identity of the patient was not disclosed and ethical approval was taken. Subjects included in the study were newly diagnosed cases or cases not on medication while subjects excluded were those on medications, those having co morbid conditions, subjects with active infections and those on any hormonal therapy.

Data were analyzed using SPSS 16 software for Windows. All continuous data following normal

distribution are presented as mean (SD, standard deviation). Independent- samples were examined with students' t-test, One- Way ANOVA, and paired-samples t-test were used .A two tailed P value <0.05 was considered statistically significant for all comparisons.

3. RESULTS

Table 1 reveals the independent T-test to test the significance difference between two groups for different variables. The Table 2 shows that there is no significant difference in red cell distribution width (RDW) between cases and control (t=0.616,p>0.05 for SD & t=0.673,p>0.05 for CV).The level of random blood sugar (RBS) is found to be significantly high in case group compare to control group (t=5.701,p <0.001). Table 2 also revealed that the level of fasting blood sugar (FBS) is also significantly high in case group (t=3.880,p<0.01).Statistical test also shows that the post-prandial blood sugar (PPBS) is also found to be higher in case group compare than control group (t=2.556,p=<0.05). The amount of mean platelet volume (MPV) and platelet distribution width (PDW) is almost same in both groups (p>0.05).This lack of significance could be due to the small sample size in our study which is refuted by studies done by other authors where the correlation came out to be significant between platelet parameters and diabetes mellitus of long standing duration.

From Figs. 1 to 7, the different ROC curves for different tests are being represented. A good diagnostic test is one that has small false positive and false negative rates across a reasonable range of cut off values. A bad diagnostic test is one where the only cut offs that make the false positive rate low have a high false negative rate and vice versa. [Fig. 1, Table 3] represents ROC curve for red cell distribution width (RDW) SD. The area under the curve is 0.44 under the null hypothesis that H_0: True area =0.5.The criterion of this test being as a good diagnostic tool is statistically not significant due to very poor area under the curve (p>0.05). Similarly Fig. 2, Table 4. represents ROC curve for red cell distribution width (RDW) CV and the area under the curve for this test is 0.534 which is statistically assumed to be poor (p>0.05). This test cannot be good diagnostic marker. Similarly the area under the curve for RBS is 0.985, for FBS it is 1.00 and for PPBS it is 0.952 and these all areas are assumed to be excellent (p<0.05) so these tests may be good indicators .Where as area under the curve for MPV and PDW are 0.598 and 0.585 respectively which are supposed to be the very poor so these tests can be indicators. [Figs. 3-7. Tables 5-9].

Table 1. T-test group statistics

	Group	N	Mean	Std. deviation	Std. error mean
RDW-SD	Control	90	187.84	12.0799	1.7
	Case	150	195.82	11.6905	1.0
RDW-CV	Control	90	62.1	2.3240	.51
	Case	150	64.05	2.7869	.44
RBS mg/dl	Control	56	378.28	18.674	2.9
	Case	84	819.6	70.455	6.3
FBS	Control	24	348.68	21.160	3.6
	Case	48	649.68	44.557	5.8
PPBS	Control	12	494.68	25.697	5.8
	Case	64	1025.4	87.061	8.2
MPV[fl]	Control	90	47.9	1.1285	.25
	Case	150	53.052	3.1378	.49
PDW	Control	90	62.36	3.493	.781
	Case	150	65.6	3.538	.559

Table 2. Independent samples student's t test

		t	p-value
RDW-SD	Equal variances assumed	-.616	.540
RDW-CV	Equal variances assumed	-.673	.503
RBS mg/dl	Equal variances assumed	-5.701	**<0.001**
FBS	Equal variances assumed	-3.880	**.001**
PPBS	Equal variances assumed	-2.556	**.022**
MPV[fl]	Equal variances assumed	-1.772	.082
PDW	Equal variances assumed	-.834	.408

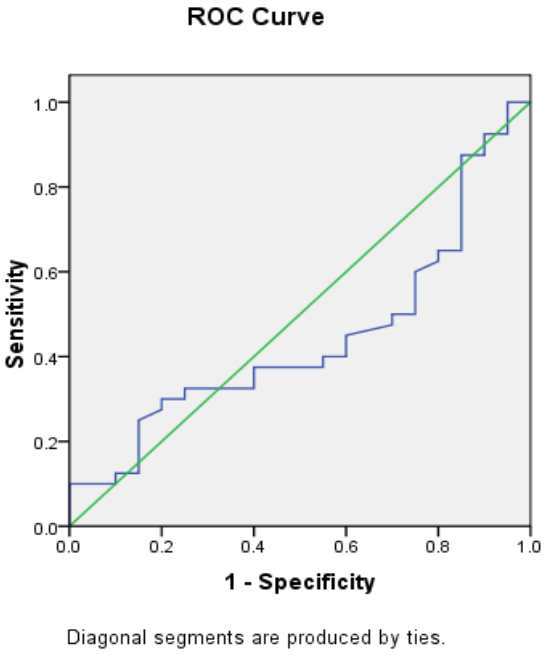

Fig. 1. ROC curve - RDW SD

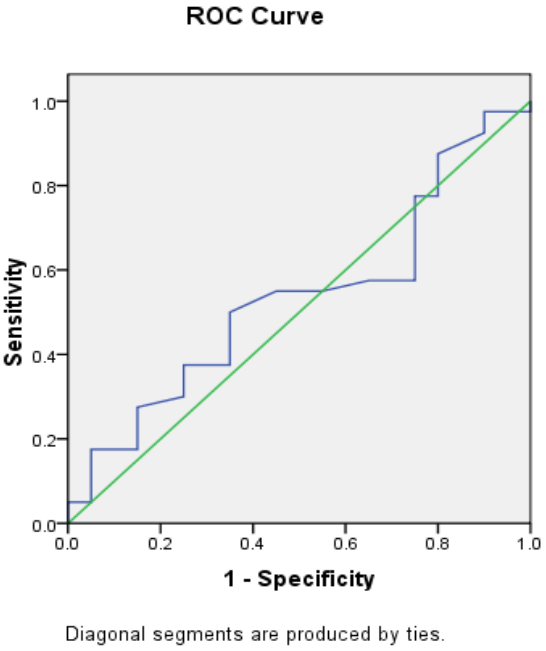

Fig. 2. ROC curve - RDW CV
a. The positive actual state is case

4. DISCUSSION

Our findings do not match with the studies done till now and the most probable reason for this is the small sample size of the study which is also a limitation of the study. Several investigators have used a series of platelet indices measured by hematology analyzers, given the fact that platelet activation causes morphologic changes in platelets while the thickened vascular walls lead to injury of RBC membranes. The mean platelet volume (MPV) is probably the most extensively studied platelet activation marker [4–9]. Recently, novel platelet indices such as mean platelet component (MPC) and platelet component distribution width (PCDW) have been investigated as prospective platelet activation markers [10–11].

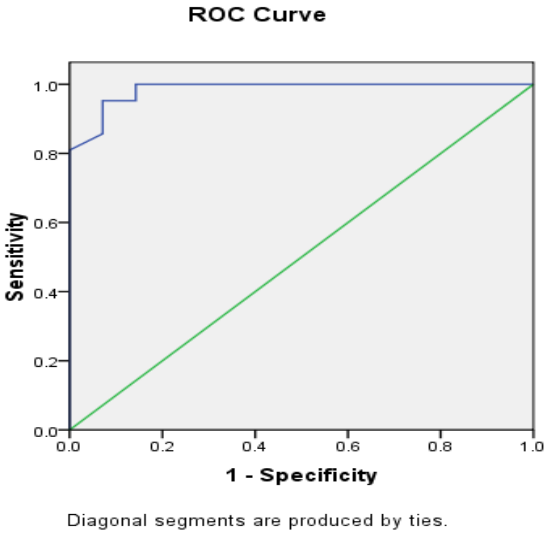

Fig. 3. ROC curve – RBS
a. The positive actual state is case

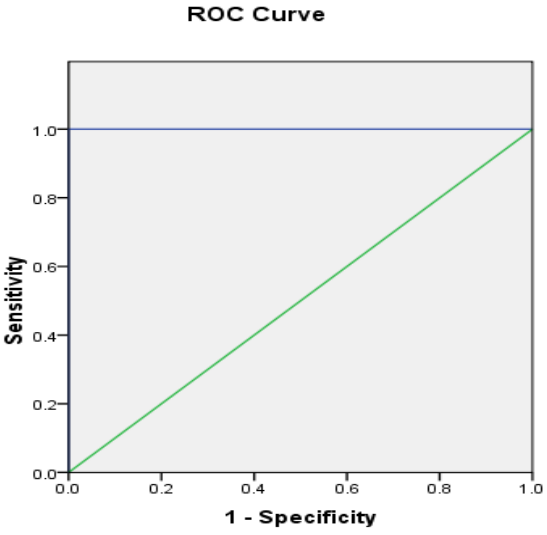

Fig. 4. ROC curve – FBS
a. The positive actual state is case

Table 3. Area under the curve

Test result variable (s): RDW-SD				
Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
.444	.077	.480	.292	.596

The test result variable(s): RDW-SD has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased

a. Under the nonparametric assumption; b. Null hypothesis: true area = 0.5

Table 4. Area under the curve

Test result variable (s):RDW-CV				
Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
.534	.078	.672	.381	.687

The test result variable(s): RDW-CV has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption; b. Null hypothesis: true area = 0.5

Table 5. Area under the curve

Test result variable (s): RBS mg/dl				
Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
.985	.015	.000	.000	1.000

The test result variable(s): RBS mg/dl has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption; b. Null hypothesis: true area = 0.5

Table 6. Area under the curve

Test result variable (s): FBS				
Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
1.000	.000	.001	.000	1.000

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Table 7. Area under the curve

Test result variable (s): PPBS				
Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
.952	.056	.017	.000	1.000

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Table 8. Area under the curve

Test result variable (s): MPV[fl]				
Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
.598	.075	.221	.451	.744

The test result variable(s): MPV [fl] has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption; b. Null hypothesis: true area = 0.5

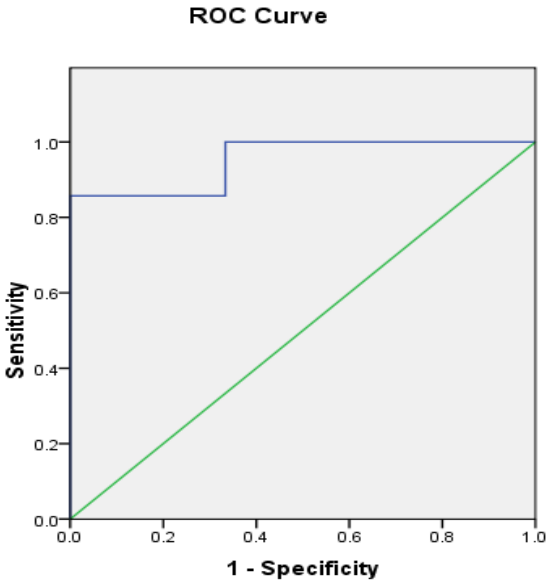

Fig. 5. ROC curve – PPBS
a. The positive actual state is case

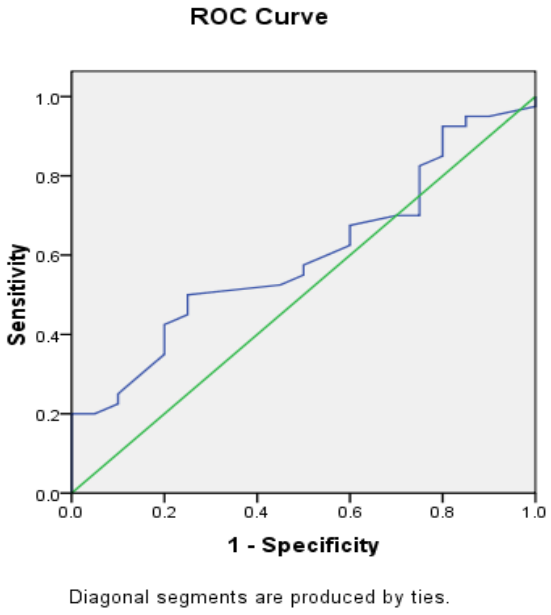

Fig. 6. ROC curve – MPV

Our study was conducted bearing in mind the fact that platelet activation causes morphologic changes of platelets, including both the spherical shape and pseudopodia formation while the thickened blood vessels may play some role in destruction or injury to RBC's which will in turn lead to altered RDW-SD,CV. Platelets with increased number and size of pseudopodia differ in size, possibly affecting platelet distribution width (PDW).It was intriguing to investigate whether pseudopodia formation could cause specific changes, supporting the differential diagnosis between platelet activation and other causes of platelet swelling.

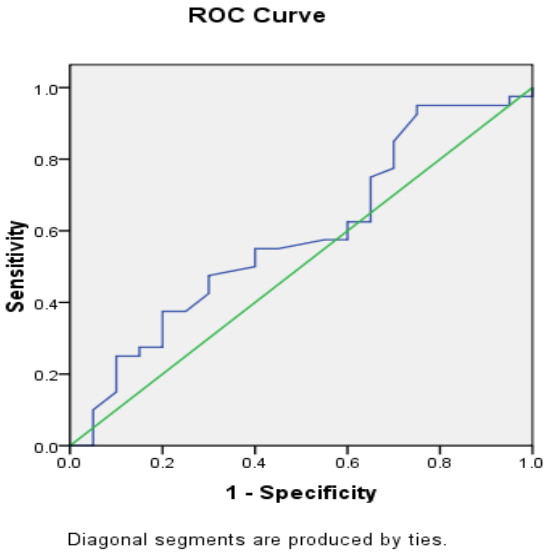

Fig. 7. ROC curve – PDW
a. The positive actual state is case

This phenomenon is being thought to be instrumental in pathogenesis of coronary lesions. Several hypotheses have been proposed, including inflammation, endothelial dysfunction, changes in blood rheological properties, increased uric acid, and conditions associated with increased platelet volume [12-15]. The cellular components of the blood in patients with long standing DM at risk for coronary diseases have not been evaluated comprehensively as yet. Our study was an attempt to do just that. Previous studies have shown, that the MPV is higher in the blood of those long standing diabetics who suffer from atherosclerosis, than in the normal subjects [16,17]. Platelets play a critical role in inflammation, thrombosis, and cardiovascular physiopathology. Additionally, increased MPV is associated with acute coronary syndrome, carotid artery disease, sepsis, deep vein thrombosis, pulmonary embolism, and coronary artery disease [18-22] Only MPV and platelet count have been evaluated in earlier investigations while PDW and PCT have been ignored. PCT has been assumed to indicate the number of circulating platelets in a unit volume of blood, analogous to the hemato-Crit for erythrocytes [23]. Not many authors have paid attention to the damage of red cells by thickened occluding vessels hence leading to altered RDW-SD, CV.

Table 9. Area under the curve

Test result variable (s): PDW				
Area	Std. error[a]	Asymptotic sig.[b]	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
.585	.079	.286	.430	.740

The test result variable(s): PDW has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption; b. Null hypothesis: true area = 0.5

Some authors have demonstrated that platelet-Crit correlates with C-reactive protein (CRP) levels in patients with chronic inflammatory diseases such as tuberculosis [24]. In addition to an increased RDW value; PDW was significantly higher in long standing diabetics as compared to non diabetics as seen in one study [25]. Some studies have suggested that PDW is more specific than MPV for indicating platelet activation and that it is a simple, practical, and specific activation marker for coagulation [26]. However, insufficient data on the clinical significance of PDW are available. Increased distribution width of red and white blood cells may be associated with impaired deformability of these cells and thus increased micro vascular resistance [27-29].

RDW is a marker of the variation in erythrocyte shape and morphology. Hemolysis and various nutritional deficiencies, such as iron, vitamin B12, and folate deficiencies, may increase the value of RDW. Regardless of the hemoglobin level, an increased RDW has predictive importance for mortality and morbidity in terms of atherosclerotic disease and heart failure [30,31]. The relationship between RDW and atherosclerosis in long term DM has been shown in only 2 studies till now [25,32]. The presence of a significant correlation between increased RDW and high-sensitivity CRP levels suggests that RDW may be a useful marker associated within flammation [33,34]. One of the major limitations of this study is its sample size. A small sample size and loss to follow-up limits the proper study of the progression of the disease. Hence a more comprehensive study with follow-up is the need of the hour.

5. CONCLUSIONS

To the best of our knowledge, our study is the first in Lucknow, Uttar Pradesh India that investigates the predictive value of Platelet and Red Cell parameters in long standing diabetics. It is important to study these parameters as they can act as red flags in diagnosing micro and macro vesicular complications of diabetes mellitus of long standing duration. Although our findings were not very conclusive, which could be attributed to small sample size it was seen that RDW-SD could be an important indicator for diagnosing these complications early. Further large-scale and comprehensive studies are needed to bring out better results, as in areas like the west Lucknow population such cheap tests could be life saving for the poor rural population.

CONSENT

No direct patient contact was needed for our study we took CBC slip readings of diabetics sent to lab for routine investigations.

ETHICAL CLEARANCE

It has been received from the institutional ethical committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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