

Early Detection of Vasculogenic ED in Diabetic Patients by Assessment of Platelet Indices

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Received for publication October 27,2020;Accepted January 4, 2021;
Published online January 4, 2021.

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doi: 10.21608/aimj.2021.46652.1336

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INTRODUCTION

Failure to obtain or sustain a satisfactory erection of the penile for sexual intercourse is erectile dysfunction (ED).¹ Average prevalence of up to 10 % in men aged less than 50 years; ED is a common global issue. In males aged 60-70 years, the incidence rises to 20 %-40 %. The largest prevalence of men older than 70 years is 50 %-100 %.²

Diabetes mellitus (DM) has been shown to be substantially and independently related to erectile dysfunction.³ ED prevalence in patients with diabetes varies from 20% to 70%, irrespective of the severity or length of the disease or the regulation of hyperglycaemia.⁴

Its etiology can be organic, psychogenic, or most commonly, derived from a combination of the two.⁵

In diabetic patients, ED aetiopathogenesis is complex and influenced by several psychological or organic factors.⁶ It is also recognised that age plays a part in

the ED pathogenesis in DM.⁷ Hyperglycaemia that is involved in most complications of diabetes may be directly linked to these causes.⁸

It is recognized that platelets play a major part in the pathogenesis of atherothrombosis.⁹

Markers of platelet activities are platelet indices (PIs). With low research expenses, they can assist to diagnose and predict several illnesses and conditions.¹⁰ Concurrent and frequent PIs measurements can assist with the prediction and diagnosis of some diseases and can assist with the treatment plan.¹¹

In automatic full blood count, platelet count (PC), mean platelet volume (MPV) and platelet distribution width (PDW) are regularly calculated PIs. They are linked to platelet morphology and kinetics of proliferation.¹²

In patients with unregulated DM, the mean platelet volume was reported to be greater than in those with

ABSTRACT

Background: The permanent incompetence to attain or preserve an erection is erectile dysfunction (ED). ED impacts a lot of men all over the world. Vasculogenic, hormonal, neurogenic, anatomical, drug-induced and psychogenic factors are included in ED pathophysiology. A significant pathophysiological factor underlying vasculogenic erectile dysfunction is endothelial dysfunction (EDys). Platelet Indices are significant biomarkers for platelet activation and pathophysiology of atherothrombosis, including average volume of platelets, width of platelet distribution and count of platelets. Measurement of Platelet indexes in diabetic males can detect erectile dysfunction early on.

Objective: The purpose of this research is to measure the PIs with ED in diabetic men and to associate among PIs and ED and also to associate among PIs and vasculogenic ED.

Patients and methods: The research was performed on 90 persons who were split into 3 groups: Group A: 30 diabetic male patients with ED, Group B: 30 diabetic male patients without ED, Group C: 30 healthy individuals as control.

Results: A significant relationship among platelet indices, ED, and DM was shown in the present research. A statistically substantial increase was found in PIs (MPV, PDW) and HbA1C in ED with DM than DM and control groups. A statistically substantial decrease in PIs (PC) was also found in ED with DM than DM without and control groups.

Conclusion: A substantial correlation in DM among platelet indices and ED. In patients with diabetes with ED, particularly those with vasculogenic pathology, PIs have increased.

Keywords: Platelet Indices; Early Detection; Erectile Dysfunction; Diabetic Patients.

Disclosure: The authors have no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the authors.

Authorship: All authors have a substantial contribution to the article.

regulated disease and in healthy non-diabetic people.¹³

In recent years, there have been some studies which report that mean platelet volume (MPV) increases in patients with vasculogenic ED.¹⁴ MPV is a platelet size marker that is readily measured and routinely accessible at relatively low prices by automated blood counters and reflects indirectly platelet activity. Since large platelets are metabolically and enzymatically more active than small platelets and generate more thromboxane, recognised as the most powerful vasoconstrictor agent, increasing the production of large platelets can lead to the pathogenesis of atherothrombosis. Increased platelet activity therefore plays a significant role in the development of atherosclerosis via mechanisms such as thrombocyte collection, synthesis of thromboxane, and expression of adhesion molecules.¹⁵

Subjects AND METHODS

This research was performed on 90 persons divided into three groups (Group A) 30 diabetic male patients with ED were attended to Dermatology and Venerology department at Al-Azhar University Hospitals, (Group B) 30 diabetic male patients without ED and (Group C) 30 healthy individuals as control.

Patient with the following criteria was included in the study: heterosexual males below 75 years of age, existence of ED estimated by the International Index of Erectile Function (IIEF), ED patients investigated by penile dynamic Doppler, patients with diabetes mellitus. We excluded patients with the following criteria from the study: significant cardiac diseases, neurological diseases, major psychiatric disorders, pelvic trauma and operations, penile trauma and operations, hormonal disturbances affecting the sexual functions, using medicines which influence sexual function or sexual desire.

All patients have undergone a Full History including Sexual History, clinical examinations including genital examination and laboratory investigations: venous blood sample was taken for measurement of CBC, HbA1c, and platelet indices.

In patients have ED with DM (group A) investigated by Pharmaco-penile duplex ultrasonography (PPUD). It done to assess the grade of erection following intracorporal injection (ICI) of prostaglandin E1 in one corpora cavernosa. Before and after ICI, the cavernous artery diameter was measured. Peak systolic flow velocity (PSV), end diastolic velocity (EDV) and resistance index (RI) were measured after ICI at 5, 10, and 15 minutes. The PSV has been graded as less than 25 cm/s, 25–35 cm/s and more than 35 cm/s. The EDV has been graded as 5 cm/s or less and larger than 5 cm/s. The RI has been graded as 0.8 cm/s or less and larger than 0.8 cm/s. Patients were divided into four groups according to the PPUD study: diabetic with arteriogenic ED, diabetic with venogenic ED, diabetic with mixed arterio-venogenic ED and diabetic with psychogenic ED.

Statistical analysis:

The data was analyzed using version 18.0 of the Statistical Program for Social Science (SPSS). Mean \pm standard deviation (SD) was the quantitative data expressed. Qualitative data were represented in terms of frequency and percentage. P-value $<$ 0.05 was deemed significant (S), P-value $>$ 0.05 was deemed non-significant (NS).

RESULTS

The next table indicates that a statistically substantial differences between the three studied groups in term of age, weight and BMI with p-value = 0.006, 0.001 and $<$ 0.001 respectively while no statistically substantial differences were found between the three studied groups in terms of height with p-value = 0.775. The platelet count was statistically substantially decreased and increase in PDW, MPV, HbA1c and IIEF in ED with DM and DM without ED.

Table 1: Comparison among the three groups studied for demographic data and the laboratory for the cases

		ED with DM group	DM without ED group	Control group	Test value	P-value	Sig.
		No. = 30	No. = 30	No. = 30			
Age	Mean \pm SD	55.10 \pm 8.32	52.73 \pm 9.82	46.67 \pm 12.15	5.433	0.006	HS
	Range	41 – 78	36 – 72	30 – 81			
Height	Mean \pm SD	168.13 \pm 6.22	168.03 \pm 7.85	166.97 \pm 6.87	0.255	0.775	NS
	Range	156 – 178	155 – 180	157 – 178			
Weight	Mean \pm SD	76.07 \pm 6.67	78.83 \pm 9.55	70.40 \pm 9.67	7.259	0.001	HS
	Range	67 – 93	59 – 98	56 – 93			
BMI	Mean \pm SD	26.89 \pm 1.47	27.83 \pm 1.69	25.22 \pm 2.81	12.185	0.000	HS
	Range	24.4 – 29.6	24.2 – 32	18.7 – 29.4			
Platelet	Mean \pm SD	295.43 \pm 58.71	332.17 \pm 62.34	350.23 \pm 57.07	6.628	0.002	HS
	Range	198 – 475	197 – 419	255 – 499			
PDW	Mean \pm SD	17.14 \pm 1.02	14.83 \pm 0.98	13.75 \pm 1.51	62.717	0.000	HS
	Range	15 – 18.7	12.9 – 17.2	11 – 16.4			
MPV	Mean \pm SD	10.72 \pm 0.84	9.19 \pm 0.89	7.89 \pm 0.97	73.941	0.000	HS
	Range	9 – 12.1	7.1 – 11.4	5.7 – 10			
HbA1C	Mean \pm SD	9.08 \pm 1.56	7.28 \pm 1.35	5.47 \pm 0.82	59.223	0.000	HS
	Range	6.6 – 14.2	5.2 – 10.7	4.3 – 7.4			
IIEF	Mean \pm SD	12.13 \pm 4.12	–	22.78 \pm 2.23	12.451	$<$ 0.001	HS
	Range	4.83 – 20.43	–	18.30 – 25.16			

studied.

The next table indicates that a statistically substantial reduction in platelet count and an increase in PDW, MPV and HbA1c in ED with DM than control group.

Table 2: Comparison of laboratory data among ED

		ED with DM group	Control Group	Test value	P-value	Sig.
		No. = 30	No. = 30			
Platelet	Mean \pm SD	295.43 \pm 58.71	350.23 \pm 57.07	-	0.001	HS
	Range	198 – 475	255 – 499			
PDW	Mean \pm SD	17.14 \pm 1.02	13.75 \pm 1.51	10.16	0.000	HS
	Range	15 – 18.7	11 – 16.4			
MPV	Mean \pm SD	10.72 \pm 0.84	7.89 \pm 0.97	12.08	0.000	HS
	Range	9 – 12.1	5.7 – 10			
HbA1C	Mean \pm SD	9.08 \pm 1.56	5.47 \pm 0.82	11.20	0.000	HS
	Range	6.6 – 14.2	4.3 – 7.4			

with DM group and control group

The next table indicates that a statistically substantial reduction in platelet count and an increase in PDW, MPV, and HbA1c in ED with DM group than DM without ED group.

		ED with DM group	DM without ED group	Test value*	P-value	Sig.
		No. = 30	No. = 30			
Platelet	Mean ± SD	295.43 ± 58.71	332.17 ± 62.34	-2.350	0.022	S
	Range	198 – 475	197 – 419			
PDW	Mean ± SD	17.14 ± 1.02	14.83 ± 0.98	8.912	0.000	HS
	Range	15 – 18.7	12.9 – 17.2			
MPV	Mean ± SD	10.72 ± 0.84	9.19 ± 0.89	6.837	0.000	HS
	Range	9 – 12.1	7.1 – 11.4			
HbA1C	Mean ± SD	9.08 ± 1.56	7.28 ± 1.35	4.756	0.000	HS
	Range	6.6 – 14.2	5.2 – 10.7			

Table 3: Comparison among ED with DM group and DM without ED group regarding laboratory data

The next table indicates that a statistically substantial correlation observed among HbA1c and platelet count while the negative association among HbA1c and IIEF was statistically substantial, a statistically substantial positive association among HbA1c, PDW and MPV.

ED with DM group	HbA1C	
	R	P-value
IIEF	-0.451	0.012
Platelet	0.027	0.889
PDW	0.475	0.008
MPV	0.448	0.013

Table 4: Correlation of HbA1c level and laboratory data in ED with DM group

The next table indicates that a statistically substantial negative correlation observed among IIEF and PDW and MPV and positive association with Platelet count.

ED with DM group	IIEF	
	R	P-value
Platelet	0.505	0.004
PDW	-0.402	0.027
MPV	-0.391	0.033

Table 5: Correlation of IIEF level with laboratory data in ED with DM group

The next table indicates that a statistically substantial positive correlation observed among PSV and PDW and MPV and no statistically significant correlation with Platelet count.

ED with DM group (Arteriogenic)	PSV	
	R	P-value
Platelet	-0.101	0.700
PDW	0.556	0.021
MPV	0.564	0.018

Table 6: Correlation between vasculogenic changes (PSV) by PPUD and Platelet Indices

DISCUSSION

Erection is a complicated event in which the vascular endothelium, smooth muscle bundles, autonomic nerves and extracellular matrix participate simultaneously.¹⁶

ED is predominant in patients with diabetes mellitus and those with disseminated vascular diseases, such as coronary and peripheral atherosclerosis; EDs may also be present in other vascular beds in men with penile vascular damage.¹⁷

The pathogenesis of endothelial dysfunction and ED is linked with reduced endothelial nitric oxide synthase (NOS) expression and activation, which is responsible for the production of Nitric Oxide (NO). Nitric oxide (NO) is a calming factor that plays a significant part in stimulating the erection process and sustaining it.¹⁸

Diabetic vasculopathy, which include micro- and macro-angiopathy and endothelial dysfunction, has an important part in having caused ED in DM by triggering atherosclerotic changes with a reduction in the flow of penile blood, a main factor in vascular ED.⁸

PPDU is the most commonly used examination for the diagnosis of vascular induced ED, but it is invasive and costly.¹⁹

Previous studies assumed that platelet and leukocyte adhesion has an adverse impact on erection through the release of vasoconstrictor substances and reactive oxygen species, and this could also play a part in the ED progress.²⁰

PIs are popular indicators that are used to evaluate the activity and function of platelets.²¹

This study was conducted to measure the PIs of men with diabetes who have ED and to associate among PIs and ED and also to associate among PIs and vasculogenic ED

As regard the relation between three studies groups, showed a significant relation between platelet indices, ED and DM.

A statistically substantial increase was found in PIs (MPV, PDW) and HbA1c in group A (ED with DM) than group B (DM with out ED) and group C (control group). A statistically substantial decrease was also reported in PIs (PC) in group A (ED with DM) than group B (DM with out ED) and group C (control group).

A statistically substantial difference was found among group A (ED with DM), group B (DM without ED) and group C (control group) regarding age, weight and BMI

As regard PIs (MPV and PDW), there was a statistically substantial negative association among IIEF-5 score in group A (ED with DM) when compared with group C (control), so there has been a substantial increase in MPV and PDW with increased ED severity (decreased IIEF-5 score). A statistically substantial association was also found among PIs (MPV and PDW) with HbA1c.

A statistically substantial association was also found among PIs (MPV and PDW) and vasculogenic alteration as measured by the PPDU and nonsignificant within PIs (PC) that means increased of PIs (MPV and PDW) in vasculogenic ED. As regard HbA1c, a statistically substantial negative relationship among HbA1c which represent

glycaemic regulation and ED severity as per to the IIEF-5 score that means uncontrolled diabetic patients have more severe ED.

As regard diabetes, there has been a statistically substantial rise in the PDW, MPV and HbA1c levels in DM without ED than control group.

In this research, a significant increase in PIs (MPV and PDW) in group A (ED with DM) than group B (DM without ED) and group C (control). A substantial association among ED and PIs (MPV and PDW) levels was found in patients, particularly in arterial, venous or mixed vasculogenic ED. Nevertheless, among PIs (PC) and vasculogenic ED, no substantial relationship was found. This implies that in diabetic men, levels of PIs (PC, MPV and PDW) rise with the intensity of ED.

The findings of the current study are in line with the research from El Taieb that was study the relationship among platelet indices and erectile dysfunction among men with diabetes and showed that platelet indices levels were substantially greater in ED patients with DM than in healthy men.²²

In patients with vasculogenic ED, Ciftci and his colleagues found higher than normal levels of PC and MPV. They proposed that platelets can play a role in vascular complications pathogenesis, and MPV can assist in the assessment of disease progression.²³

Bayraktar and his colleagues detected significantly higher MPV levels in ED than controls.²⁴

As regard PIs in relation between group B (DM without ED) and group C (control), the findings of the current study are in line with the study of Jindal that was done on 75 patients with type 2 DM as the 'research group' and 50 non-diabetic patients as controls to evaluate diabetic versus non-diabetic platelet indices and to evaluate their usefulness as measures of the existence of complications in DM patients. They found that Platelet indices, particularly PDW, vary among diabetics and controls, and among diabetics with and without microvascular complications.²⁵

Senturk and his colleagues detect non substantial difference in MPV values among patients and controls in their latest research (Can the early biomarkers for erectile dysfunction be platelets?).²⁶

With regard to the association among HbA1c and the ED severity, as per the IIEF-5 score, the findings of the present research were consistent with the Giugliano research, which evaluated the prevalence and correlations of ED in a population of males with diabetes in a total of 1290 patients (611 males and 659 females) and evaluated their utility as indicators of the glycemic regulation, as evaluated by HbA1c level, was a danger factor for ED in males with diabetes.²⁷

Lu found that HbA1c levels were an important and independent danger factor for extreme ED relative to non- or mild-to-moderate ED in the Chinese population of 792 diabetic males. Guo and his colleagues proposed that to assess the intensity of ED, PDW could be used as a marker. A study on 358 ED patients demonstrated a relation among ED and

platelet function, and PDW could possibly be monitored as a helpful marker for predicting the ED severity even when normal platelet counts and MPV values are noticed.²⁸

CONCLUSION

A significant association between platelet indices and ED in patients with diabetes with ED particularly those with vasculogenic pathology, PIs have increased. Our results suggest that PIs might as a marker for early ED diagnosis in men with diabetes. In the future, PIs may have an important role for early diagnosis of ED especially vasculogenic ED.

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