e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(7); 1118-1125

Original Research Article

Association between Platelet Lymphocyte Ratio and Erectile Dysfunction in Diabetic Patients

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Received: 20-05-2023 / Revised: 11-06-2023 / Accepted: 08-07-2023
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Conflict of interest: Nil

Abstract:

Erectile dysfunction (ED) is a prevalent condition that commonly affects middle-aged and older men, with diabetes serving as a significant risk factor. The purpose of this study was to examine the relationship between platelet lymphocyte ratio (PLR) in ED and non-ED diabetic male patients. A total of 105 adult males were included and detailed medical history, IIEF-5 score, age and various hematological and biochemical parameters were assessed. The prevalence of ED in diabetic patients was determined to be 63.6%, with 11.4% experiencing severe ED. PLR was significantly elevated in ED patients, with the mean value of 155.3±85.3 in compare to control i.e. 130.7±25. However, significant differences were not found in the PLR values between the ED subgroups. A negative correlation was identified between PLR and the IIEF-5 score. Serum testosterone levels were lower in ED patients and exhibited a positive correlation with the IIEF-5 score. Age and diabetes duration exhibited significant associations with ED, with higher prevalence observed in older age groups and longer durations of diabetes. Glycemic control, evaluated through measures such as fasting blood sugar, postprandial sugar, random blood sugar, and glycated hemoglobin, displayed a notable negative correlation with the International Index of Erectile Function-5 (IIEF-5) score. Lipid profiles exhibited elevated triglycerides and very low-density lipoprotein (VLDL) levels, along with decreased high-density lipoprotein (HDL) levels in ED patients. The findings underscore the potential role of PLR as independent predictors of ED in individuals with diabetes. Further research involving different demographic locations with association of molecular and genomics aspects is recommended to enhance the diagnosis and treatment of ED.

Keywords: Erectile dysfunction, Diabetes and Platelet-lymphocyte ratio.

Introduction

Erectile dysfunction (ED) is a pathophysiological condition that adversely affects sexual and reproductive activity of middle-aged and older men1. It may be a side effect of some drugs as well as associated with psychosocial, neurological, hormonal, and vascular factors [1]. A review of all population-based research in the United States in 2009 showed that ED is the most frequent endocrine condition in males [2]. According to a European poll, approximately 30% of men suffer with ED [3].

Around the world, 320 million men will have ED by 2025, up from an estimated 150 million in 1994. Epidemiological studies have shown that age, depression, anxiety, chronic illness, cardiovascular disease such as hypercholesterolemia, benign prostatic hyperplasia (BPH), lower urinary tract symptoms, hyperlipidaemia, lack of exercise, diabetes, obesity and smoking are important risk factors in erectile dysfunction [1,4]. Among these Diabetes-related erectile dysfunction is one of the most underdiagnosed long-term consequences. Diabetes mellitus (DM) is a chronic metabolic condition that causes severe morbidity and death including libido difficulties, ejaculatory issues, and erectile dysfunction (ED). ED develops at a younger age in the diabetic population than in the general population, in addition to being more common [5, 6] with a frequency ranging from 35 to 80%. [7].

The relationship between erectile dysfunction (ED), depression, and poor glycaemic control [8, 9] is a vicious cycle that is linked to both type 1 and type 2 diabetes. Despite evidence suggesting that ED is

a significant problem in men with type 2 diabetes mellitus (T2DM), it is frequently overlooked in routine clinical practice [10].

There are several Haematological parameters such as white blood count (WBC), mean platelet volume (MPV), platelet distribution width (PDW), platelet count (PCT), platelet to lymphocyte ratio (PLR), and neutrophil to lymphocyte ratio (NLR) and some markers and mediators (interleukin (IL)-1β, TNF-β, IL-6, CRP, IL-10,) and endothelial/prothrombotic factors of the systemic inflammatory response have received renewed attention in recent years as predictors of endothelial dysfunction and inflammation [11, 12]. Furthermore, data have emphasised the predictive significance of platelet lymphocyte ratio (PLR) as potential markers to determine inflammation in cardiac, various oncological diseases, and especially in acute coronary syndromes [13] but little to be known about their role in ED patients. Thus, present work was designed to study an association of platelet lymphocyte ratio and other parameters in diabetic male patients with erectile dysfunction.

Materials and Methods

Ethics committee:

This prospectively designed study complies with the rules of the Declaration of Helsinki, regulations involving patient's rights and ethical guidelines and was approved by the Institutional Ethical Committee (approval number: 1704/Acad-III/MCA/2020).

Study groups:

This shall be a prospective study comprising adult male population of more than 18 years attending OPD clinics in psychiatry and urology department of JLN medical college and hospital in duration from 29/06/2022 to 15/02/2023. A total of 105 male patients between 18 and 80 years old diabetic with complaints of ED and non-ED which were defined by an International Index of Erectile Function-5 (IIEF-5) score lower than 21 points and who met the inclusion criteria were enrolled in this study as subject group and greater than 21 points were enrolled as control group. The degree of ED was assessed through IIEF-5 form on the basis of erectile function. A score between 1 and 7 was defined as severe, a score between 8 and 16 was considered moderate, and a score between 17 and 21 was defined as mild and above 21 was considered as normal.

The exclusion criteria were as follows:

Patients with pelvis bone fracture & spine injury in past history; erectile dysfunction due to genitourinary tract pathology-any stricture; inflammatory pathology; any abnormal anatomy of the genitourinary tract; any psychiatric illness like stress, anxiety, depression, neurosis, or patients taking medication for the above disorders like – SSRI, TCA; having medications for psychological disorders like Stress, Anxiety, Depression; patients with cerebral disorders like- cerebrovascular accidents, multiple sclerosis, CNS malignancy; not engaged in any sexual relationship over a period of last one year; Patients with autonomic neuropathy due to long term complication of diabetes. All participants provided detailed anamnesis, and a thorough physical examination was conducted for each individual. Fasting blood samples (12 h) were obtained in the morning between 8 and 10 a.m. from all the subjects.

Method of collection of data:

The blood samples were collected and analyzed for complete blood count, fasting blood glucose (FBG), Random blood sugar (RBS), Post prandial sugar, aspartate transaminase, alanine transaminase, Glycosylated haemoglobin A1c (HbA1c), triglyceride, high-density lipoprotein, low density lipoprotein, very low-density lipoprotein, total cholesterol, Platelet count, serum testosterone level in aid with radiological Investigation. The serum testosterone level was evaluated through KRISHGEN, GENLISA-Testosterone ELISA kit (Ref. KBD378). Further, PLR was calculated as the absolute thrombocyte count divided by the absolute lymphocyte count.

Special Investigation: - Arterial colour doppler (pudendal artery).

Statistical Analysis: Statistical analysis was done using SPSS package software V.29. The independent T-test was used to compare biochemical and hematological parameters in ED and Non-ED groups. The association of ED prevalence with respect to age and duration of diabetes was analyzed using Chi-square test. Furthermore, a positive and negative correlation was established between IIEF-5 score and the other measured parameters. The statistical level of significance was accepted as $\alpha = 0.05$.

Results

A total of 250 diabetic patients were enrolled in the study, and 140 patients were found eligible after applying the exclusion criteria. Out of them, 105 patients were screened for the ED, whereas 35 patients did not give the consent or incomplete the questionnaire. This study included 105 diabetic male patients, out of them 70 (ED group) were found to have ED, and 35 subjects with no ED (Control group). Therefore, the prevalence of ED in male diabetic patients was found to be 63.6%. Among the 70 ED patients, 22 (31.4%) were found with mild ED, 40 (57.1%) with moderate ED and 8 (11.4%) with severe ED.

In this current study the mean age was 43.4±6.0 years in the control group and 52.6±10 years in the

patient group was found significant (p-value, <.001) (Table 1). On the basis of biochemical and hematological parameters, the comparison between ED and non-ED groups was depicted in the Table no. 1. The mean value of Platelet lymphocyte ratio, random blood sugar, fasting sugar, post prandial sugar, triglyceride, VLDL and HBA1C in control and patient group was 130.7±25 and 155.3±85.3, 188.1±31.4 and 238.5±125, 126.2±18.5 and 152.9±71.1, 178.2±34.1 and 208.5±55.9, 88.8±35.1 and 160.6±107, 20.4±7.3 and 30.5±12.5 and 7.4±0.7 and 8.4±1.5, respectively. These values were found with significant increase in the patient group in compare to control group (Table 1). However, the mean value of lymphocyte count, HDL and serum testosterone was detected with significant decrease in the patient group in compare to control group i.e. 33.8±7.5 and 28.3±12.0, 52.7±21.5 and 44±16.8, 8.2±8.5 and 2.7±5.8, respectively. In remaining parameters significance differences were not found between control and patient group (Table 1).

The incidence of ED in different age groups was depicted in Table no. 2. The maximum number of ED patients, i.e. 26 (37.1%) was found in the age range of 51-60 years and in the non-ED group, maximum number i.e. 17 (48.6%) was detected in the age range of 41-50 years. However, maximum prevalence (100%) of ED was found in >60 age group followed by 83.8% in 51-60 age group, 56.4% in 41-50 age group and minimum (38.09%) was detected in ≤40 year age group. A significant association (P value, 0.001) was observed between the prevalence of ED and the age group, where ED prevalence gradually increasing with the age (Graph1). Moreover, according to duration of diabetes, the highest prevalence of ED i.e. 88.4% was found in >10 years of diabetes patients followed by in 5-10 years (82.7%) and <5 years (46%) duration. However, in non-ED group maximum numbers 27 (77.1%) were found in short history of diabetes i.e. <5 years. A statistical significance (P value, 0.003) association was also observed between duration of diabetes and ED prevalence. A sudden increase of ED prevalence was observed in 5-10 years duration of diabetes, depicted in graph 2.

Based on the IIEF-5 scores, the patient group (n=70) was further divided into four subgroups according to the degree of ED as follows: “severe” (IIEF-5 score: 1–7), “moderate” (IIEF- 5 score: 8–16), and “mild” (IIEF-5 score: 17–21). These subgroups were statistically analyzed and compared using matched pairs to determine any significant differences regarding PLR parameter. However, no significant differences were found among the ED subgroups regarding the PLR (P=0.59).The correlations analysis between IIEF-5 score and all the measured parameters were depicted in Table 4.

A significant negative correlation was found between the IIEF -5 score and age, platelet count, platelet lymphocyte ratio, fasting sugar, post prandial sugar, VLDL and HBA1C. Whereas, two parameters such as SGPT and serum testosterone was found positively correlated with the IIEF-5 score. The remaining parameters were not shown significant correlation in this study (Table 4).

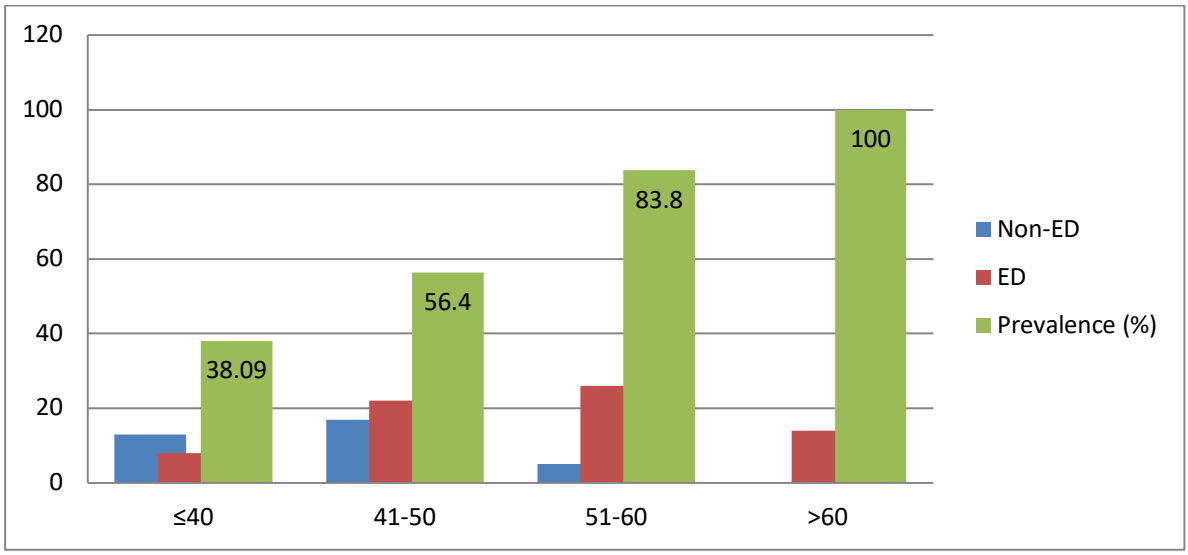
Table 1: Comparison on the basis of Biochemical and Hematological parameters

S.N.	Parameters	Control Group (Non-ED), N=35, Mean±SD	Patient Group (ED group), N= 70, Mean±SD	P value
1.	AGE	43.4±6.0	52.6±10	<.001 **
2.	Platelet Count(In Lacs)	2.8±0.5	2.9±1.0	0.305
3.	Lymphocyte Count (In %)	33.8±7.5	28.3±12.0	0.004 *
4.	Platelet Lymphocyte Ratio	130.7±25	155.3±85.3	0.028 *
5.	Random Blood Sugar (Mg %)	188.1±31.4	238.5±125	0.047 *
6.	Fasting Blood Sugar (Mg %)	126.2±18.5	152.9±71.1	0.004 *
7.	Post Prandial Sugar (Mg %)	178.2±34.1	208.5±55.9	0.001 **
8.	Total Cholestrol (Mg %)	168.1±25.2	166.6±39.1	0.816
9.	Triglyceride (Mg %)	88.8±35.1	160.6±107	0.000 **
10.	HDL (Mg %)	52.7±21.5	44±16.8	0.042 *
11.	VLDL (Mg %)	20.4±7.3	30.5±12.5	0.000 **
12.	LDL (Mg %)	102.3±24	95.5±30.3	0.226
13.	SGOT	41.8±20.7	44.3±41.3	0.684
14.	SGPT	51.3±41.6	42.1±43.8	0.302
15.	S.BILLIRUBIN (T) (Mg %)	0.8±0.4	1.0±2.2	0.355
16.	S. BILLIRUBIN (D) (Mg %)	0.2±0.08	0.2±0.2	0.437
17.	S.Total Protein (Gm %)	6.8±1.0	7.1±0.9	0.149
18.	S. ALBUMIN (Gm %)	4.0±0.7	4.0±0.7	0.826
19.	ALP (U/L)	81.9±21.7	78.8±31	0.558
20.	HbA1C (%)	7.4±0.7	8.4±1.5	0.000 **
21.	Serum Testosteron (conc.)	8.2±8.5	2.7±5.8	0.001 **

* Significant at the level of p< 0.05, ** Significant at the level of p<=0.001. HDL= high density lipoprotein, VLDL= very low density lipoprotein, LDL= low density lipoprotein, SGOT= serum glutamic-oxaloacetic transaminase, SGPT= Serum Glutamic Pyruvic Transaminase, ALP= alkaline phosphatase, HbA1C= haemoglobin A1cl.

Table 2: Distribution of ED with respect to age

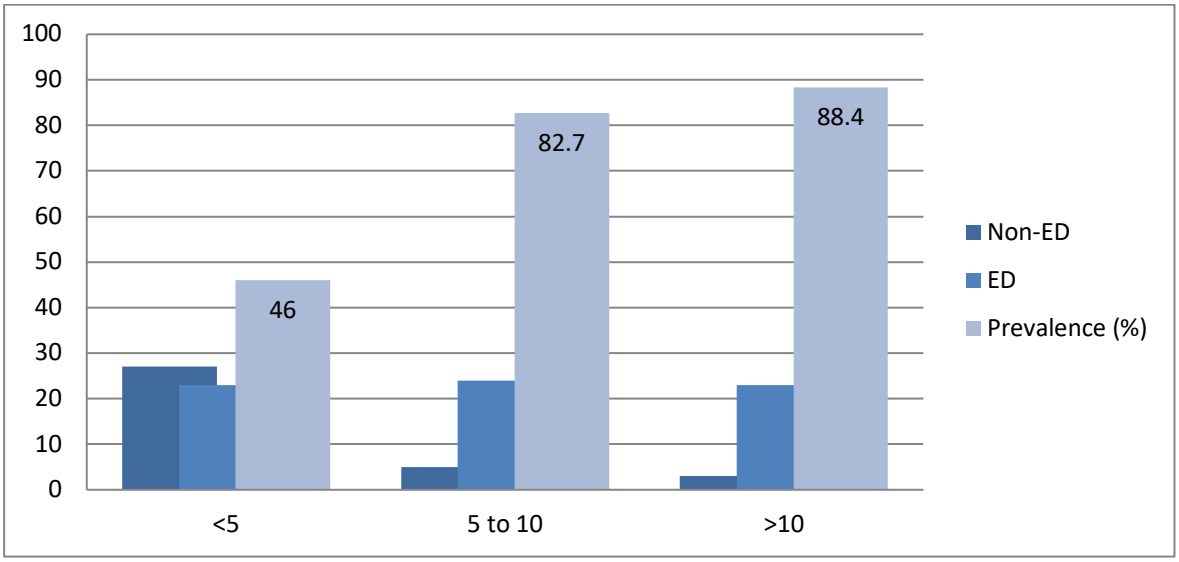
S.N.	Age	Non-ED	ED	Total	Prevalence (%)
1	≤40	13	8	21	38.09
2	41-50	17	22	39	56.4
3	51-60	5	26	31	83.8
4	>60	0	14	14	100
5	Total	35	70	105	66.6
6	P- value				<0.001



Graph 1: Distribution of ED and non-ED patient with respect to age

Table 3: Distribution of groups according to duration of Diabetes

SN	Duration of Diabetes	Non-ED	ED	TOTAL	Prevalence (%)
1	<5	27	23	50	46
2	5-10	5	24	29	82.7
3	>10	3	23	26	88.4
4	Total	35	70	105	
5	P-value			0.003	



Graph 2: Distribution of ED and non-ED according to duration of diabetes

Table 4: Correlation analysis between IIEF-5 score and other parameters for all the participants included in the study (n=105)

S.N.	Parameters	Correlation with IIEF-5 score (R)	P value
1.	Age	-0.575	<0.001**
2.	Platelet Count (in lacs)	-0.218	0.048*
3.	Lymphocyte Count (in %)	0.037	0.704
4.	Platelet Lymphocyte Ratio	-0.193	0.048*
5.	Random Blood Sugar (Mg %)	-0.162	0.287
6.	Fasting Sugar (Mg %)	-0.346	<0.001**
7.	Post Prandial Sugar (Mg %)	-0.293	0.004 *
8.	Total Cholestrol (Mg %)	0.027	0.785
9.	Triglycerid (Mg %)	-0.129	0.199
10.	HDL (Mg %)	0.135	0.182
11.	VLDL (Mg %)	-0.260	0.009*
12.	LDL (Mg %)	0.008	0.938
13.	SGOT	0.064	0.522
14.	SGPT	0.213	0.031*
15.	S.BILLIRUBIN (T) (Mg %)	0.062	0.538
16.	S. BILLIRUBIN (D) (Mg %)	0.05	0.687
17.	S.TOTAL PROTEIN (Gm %)	-0.14	0.162
18.	S. ALBUMIN (Gm %)	0.091	0.364
19.	ALP (U/L)	0.005	0.962
20.	HBA1C (%)	-0.466	<0.001**
21.	Serum Testosterone (conc.)	0.389	<0.001**

* Significant association at the level of p< 0.05, ** Significant association at the level of p<=0.001.
HDL= high density lipoprotein, VLDL= very low density lipoprotein, LDL= low density lipoprotein, SGOT= serum glutamic-oxaloacetic transaminase, SGPT= Serum Glutamic Pyruvic Transaminase, ALP= alkaline phosphatase, HbA1C= haemoglobin A1c

Discussion

Erectile dysfunction (ED) is a significant condition that is becoming more prevalent and impacts both the affected individual and their partner. Currently, it affects over 140 million middle-aged or older men globally, and projections suggest that this number will escalate to approx. 300 million by the year 2025 [14]. It is a prominent complication of type 2 diabetes mellitus (T2DM), but it often goes unnoticed in routine clinical practice [15]. According to the current study, around 63.6% of patients diagnosed with type 2 diabetes mellitus (T2DM) were found to have erectile dysfunction (ED), while 11.4% had severe ED. The prevalence of ED among T2DM patients varies significantly across different studies conducted in various countries, with reported rates ranging from 32% to 77%. A recent cross-sectional study carried out in Nepal reported an exceptionally high prevalence of erectile dysfunction (ED) among diabetes patients, reaching 76.87% [16]. However, previous studies conducted in Lucknow, Uttar Pradesh, and Jaipur, Rajasthan, India, revealed comparatively lower rates of ED, ranging from 32% to 59.38% [15 and17]. Futhermore, similar prevalence of current work was observed in a cross-sectional study conducted in Sri Lanka and Jammu, North India [18 and 19].

In above mentioned data the varying rates of erectile dysfunction (ED) among diabetic patients might be due to various factors such as sample sizes, demographic traits, age distribution, study settings, duration of type 2 diabetes mellitus (T2DM), severity and the presence of additional medical conditions. The current investigation revealed a significant association between age and the prevalence of ED. The occurrence of ED in diabetic individuals escalated as they grew older, with the highest prevalence found among those aged over 60 years (100%), while the lowest prevalence was observed in the age group below or equal to 40 years (38.09%).

In a separate study conducted in India, the prevalence of ED was found to be 48.1% among individuals aged over 60 years, whereas the lowest prevalence (0.00%) was observed in the age group below or equal to 30 years, which was comparatively lower to the current study [15]. Garg et. al., [20] also documented a similar pattern, where the prevalence of ED was as minimal as 20% among individuals below the age of 40 years, but escalated to 100% in those aged over 60 years. Langer et. al., [1] also found a significant association between age and the prevalence of ED, with a majority of ED cases observed in the age group of 40 to 60 years, resembling the findings of the present study. The impact of age on prevalence and severity of disease could be attributed to physiological changes that may occur with growing age. Additionally, the presence of Type 2 diabetes

mellitus (T2DM) further elevates the risk of developing ED [21].

The current study also demonstrated the prevalence of ED to be significantly associated with the duration of diabetes; as the longer duration of diabetes, higher the prevalence of ED. In this study, the highest prevalence of ED (88.4%) was observed in >10 years duration of diabetes patient and lowest prevalence (46%) was found in short duration of diabetes. Similarly, various studies also documented a longer duration of T2DM as an independent risk factor for ED [21, 22, 18, 19, 1, 20, 23 and 24]. Our data also demonstrated that duration of diabetes increases the risk of ED in diabetes patients. In the previous studies, ED has been linked with many inflammatory markers and mediators [25, 26]. The PLR is one of the inflammatory markers which have been extensively studied and used in the prognosis of various health conditions such as; adverse cardiovascular outcomes and atherosclerosis, cancer, critical extremity ischemia [12, 27, 28, 29 and 30]. In recent years, PLR has been suggested as a biomarker used for the diagnosis of ED [31]. Similarly, other biochemical parameters can also use to identify the differences in the patient and control group for the prognosis and diagnosis of the diseases. Considering this information, we aimed to examine the association and correlation of ED with the PLR and other biochemical parameters.

In the current study glycemic control, which evaluated by fasting blood sugar (FBS), postprandial blood sugar (PPBS), random blood sugar (RBS) and glycated hemoglobin (HbA1c) level was found increased and significantly associated with ED in men with diabetes. They all showed a significant negative correlation with the IIEF-5 score in the diabetes patient except RBS. As the value of IIEF-5 score decreases, the value of glycemic control increases in the studied population. Similarly, Cho et. al., [32] were reported the significant association of these parameters in the studied population. However, Dave et. al., [33] were not found these values significantly associated with ED in their study. Various studies have found a positive correlation between poor glycemic control and the prevalence of ED [21, 22, 19, 20, and 23].

The mean value of triglycerides and VLDL was found with significant increase in ED patient. On the other hand, significant decrease was detected in the mean value of HDL in ED patient group as compare to the control group. The significant increase in the lipid profile, Garg et. al., [20] reported in their study in patients with ED as compared to those without ED. Whereas, serum triglyceride and HDL showed no significant association with ED in study conducted by Parmar et. al.,[17]. Among all the lipid profiles in the studied population, VLDL was found significantly negative correlated with the IIEF-5 score. However, triglycerides and HDL was not detected with the significant correlation. Dave et. al., [33] also reported the no correlation between dyslipidemia and ED patients.

Among the biochemical parameters, statistically significant negative correlation was found in platelet count and platelet lymphocyte ratio (PLR) with the IIEF-5 score. Mean PLR value was found significant high in patient group in compare to the control group. The significant increase in the PLR value also reported in various studies of ED patients in diabetes and non-diabetes populations [31 and 34]. Based on a subgroup analysis in the erectile dysfunction group (n=70), there were no significant differences across the groups regarding the PLR values (p=0.59 for PLR).The other parameter i.e. serum testosterone, which was evaluated through Elisa reader, reported significant positive correlation with IIEF-5 score. Where, mean serum testosterone level was found lower in the ED patient in compare to the control group. The significant decrease in the serum testosterone level also reported by the finding of Parmar et. al., [17] and Shi et. al.,[35]. Further, vascular insufficiency was found 82% in the ED patients, however the comparison between color Doppler ultrasonography and the PLR values did not performed in this study.

Conclusion

These findings emphasize the potential role of PLR as a predictor of erectile dysfunction in diabetic patients which is significantly higher as compare to non-ED patient. Erectile dysfunction is found to be associated with higher age, longer duration of diabetes and lower serum testosterone levels. Additionally, this study highlights the importance of achieving better glycemic control to mitigate the prevalence of ED in individuals with diabetes. Molecular and genomic association studies could be used in near future to further enhance the diagnosis and treatment of ED patients. Overall, this study significantly contributes to our understanding of the intricate relationship between PLR, diabetes, and ED, opening new avenues for early detection, effective management, and targeted interventions for diabetic patients experiencing ED.

Acknowledgement: The authors are thankful to and Principal, JLN Medical College and Multi-Disciplinary Research Unit Ajmer, Rajasthan, India for providing facilities and their support.

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