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Lower MPV Can Independently Predict Erectile Dysfunction in T2DM

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Abstract

Objectives: To find out the frequency of erectile dysfunction in diabetic patients and the association between erectile dysfunction and various clinical and laboratory parameters such as diabetic neuropathy, diabetes control, and cardiovascular risk factors.

Subjects and methods: 91 type 2 diabetic patients were screened for erectile dysfunction. Clinical data were collected and included body mass index (BMI, blood pressure (BP, heart rate, duration of diabetes and diabetes complications mainly peripheral diabetic neuropathy (PDN. Laboratory data included testosterone, pituitary gonadotropins, fasting plasma glucose (FPG, HbA1c, complete blood count (CBC, serum creatinine and lipid profile. Associations of testosterone and erectile dysfunction with various clinical and biochemical parameters were studied.

Results: Erectile dysfunction (ED) was present in 56% of our patients. No significant difference in total testosterone level, LH, FSH or Prolactin level between patients with and those without erectile dysfunction. Patients with peripheral diabetic Neuropathy were significantly at higher risk for erectile dysfunction (ED) [p=0.008]. High HbA1c, Low MPV and low MCH were significant and independent predictors for ED (p= 0.033, 0.033, 0.004 respectively, OR= 1.651, 5.562, 9.524 respectively). Testosterone level was negatively and significantly associated with BMI, heart rate and RDW (p= <0.005, 0.047, 0.028 respectively).

Conclusion: Erectile dysfunction is very common among type 2 diabetic patients. It is strongly and directly associated with peripheral diabetic neuropathy (PDN) so, questionnaire and patient examination for PDN and further interrogation of patients complaining of PDN for erectile dysfunction (ED) is of utmost significance. This disorder can be easily predicted by the low MPV and low MCV which are found to be independent predictors in our study population. ED in T2DM is not related to serum testosterone level. Proper control of blood glucose and reaching the target HbA1c can protect diabetic patients from development of such disorder as HbA1c is also found to be a significant independent predictor of it.

Keywords: Diabetes; Erectile dysfunction; MPV; MCH; Neuropathy; Testosterone

Introduction

Erectile dysfunction (ED is a difficulty in achieving and maintaining adequate erection for a satisfactory sexual performance and the stability of this condition more than 25% of sexual attempts [1]. It is the most common problem, affecting 80 to 85% of the patients seeking medical help for sexual dysfunction and its prevalence is expected to reach 322 million people worldwide in 2025 [2]. It occurs due to the complicated interaction between neural, vascular, endocrine, medical and pharmacological factors [3]. Most of these causes affect the intrapenile vasculogenic mechanisms, whether arterial or venous. A common finding is a decrease in local nitric oxide, which is considered as the main neurotransmitter involved in initiation of erection. Fibrosis may also be present within the corpora cavernosa, which limits their expandability, prevents the venules from compressing against the tunica albuginea, and thereby allows venous leakage from the penis [4]. There is an increasing evidence identifying ED as an early finding for atherosclerotic cardiovascular disease and its associated stroke and mortality [1,5].

Materials and Methods

The study was approved by the Research and Ethics Committee of King Fahd Hospital, Asir Province, Saudi Arabia and informed consent was obtained from each participant. Ninety-one male type 2 diabetic patients were recruited from the out-patient endocrinology clinics from January to June, 2018. Patients were excluded if they had been hospitalized for acute illness such as infection or inflammation within the recent month and if they were already receiving testosterone replacement therapy or medication that can affect the blood test results such as iron therapy. Cardiovascular and peripheral

arterial disease, kidney disease, thyroid or other endocrine disorder, smoking and anemia were also exclusion criteria.

Detailed history and complete physical examination were done for all participants. Data regarding age, duration of diabetes, presence of diabetes complications and medication were collected. Laboratory investigations included complete blood count (CBC), fasting plasma glucose, HbA1c, lipid profile, serum creatinine, prolactin, total testosterone and pituitary gonadotropins (LH, FSH).

Blood pressure and pulse rate were measured using automatic blood pressure (BP) machine after 5 minutes of rest. Body mass index was also calculated using the formula: BMI = weight (kg)/height (m2). The International Index of Erectile Function (IIEF) was applied for diagnosis of ED [6] and the revised NDS clinical scoring system was used for diagnosis of peripheral diabetic neuropathy (PDN) [7].

After an overnight fasting venous blood samples were taken into tripotassium ethylene diamine tetraacetic acid, using a Roche Minos cell counter and automatic blood counter (Avid CELL-DYN 3500; Abbot Laboratories, Abbot Park, IL, USA) immediately after sample collection for platelet indices, WBC count, and RBC indices. Standardiza¬tion, calibration of instrument, and processing of samples were done according to the manufacturer's instructions. Fasting blood glucose was measured using the glucose oxidase method (Spinreact, Girona, Spain). Total Hb was measured colorimetrically. HbA1c was determined immunoturbidimetrically. The final result was expressed as percent HbA1c and is calculated from the HbA1c/Hb ratio, including a conversion equation to match a HPLC reference method. HbA1c (%) = HbA1c/Hb) x 175.8 + 1.73 [8].

Hormonal assay, FSH, LH, prolactin and total testosterone, TSH, FT4, FT3, in serum were determined by electrochemiluminescent immunoassay on a Roche Modular E170 autoanalyser. Total cholesterol, HDL, cholesterol, and TG were measured by BioMerieux Laboratory, Marcy l'Etoile, France; LDL cholesterol was calculated as follows: LDL-C = TC – HDL-C – TG/5 according to the method used by Friedewald [9]. Creatinine was measured by kinetic colorimetric assay based on the Jaffé method on Cobas c701 (Roche Diagnostics, Mannheim) according to the manufacturer's instructions.

Our laboratory reference ranges

Testosterone: 6.7-29 nmol/l, LH: 1.5-12.4 mol/l, FSH: 1.5-12.4 nmol/l, prolactin 65.2-539.1 nmol/l. TSH: 0.35-4.9 uIU/ml, FT4: 7.5-21.1 pmol/l, FT3: 3.8-7.8 pmol/l. FPG mmol/l, HbA1c as % of total hemoglobin. RBC 4.5-6.3 10^9/L, WBC 4-11 10^9/L, MCH 26-36 pg, MCHC 32-36 gm/dL, HCT 38-52%, Hb 14-18 gm/dL, Platelets 140-440 10^9/L, RDW 11-14%, MPV 7-13 fL, TC: 3-5.2 mmol/l, LDL-C: 3-5.2 mmol/l, HDL-C: 1.04-1.55 mmol/l, TG: 0.34-1.95 mmol/l, creatinine 80-115 µmol/l.

Statistical analysis

Sample size was calculated by PASS software version 11.0.8 Hintze J. PASS 11. NCSS, LLC. Kaysville, Utah, USA. www.ncss.com.). Calculation relied upon a previous study by Ugwu. In this study HbA1c was 6.8 ± 0.8 in those without ED and 8.0 ± 1.9 in those with ED. Group sample sizes of 40 patients with ED and 40 without achieve 95% power to detect a difference of 1.2 between the null hypothesis that both group means are 6.8 and the alternative hypothesis that the mean of group 2 is 8.0 with estimated group standard deviations of 0.8 and 1.9 and with a significance level (alpha of 0.05000 using a two-sided two-sample t-test.

Data were entered and analyzed using SPSS software (version 21. Categorical data were presented as frequencies and percentages while quantitative data were presented as mean ± SD if normally distributed (Kolmogorov-Smirnov test $p > 0.050$) or median and interquartile range (IQR) if skewed (Kolmogorov-Smirnov test $p \leq 0.050$). Comparing categorical data for two groups was performed by Chi-square test while comparing quantitative data for two groups was performed by Independent-Samples t-test for normally distributed data or Mann-Whitney U test for skewed data. Correlation of a continuous data with binomial data was done by point bi-serial correlation while its correlation with ordinal/continuous data was done by Spearman's correlation. A diagnostic cut off value of a test to discriminate diseased cases from non-diseased cases was evaluated using Receiver Operating Characteristic (ROC) curve analysis. Predictors were initially tested at univariate level then those with rather significant result were entered into a prediction model using binary logistic regression analysis to detect the independent predictors with their odds ratios (95% CI). Results were considered significant if p value < 0.050 and graphs were used when appropriate.

Results

Fifty-one patients of the study group (56% of total number of patients) had erectile dysfunction. These were older in age and had more prevalence of peripheral diabetic neuropathy (p=0.039, 0.008 respectively). There was a clear trend towards higher HbA1c in ED patients (p=0.05. They also had significantly higher hematocrit (HCT [0.034], and on the other hand, they had significantly lower MCH (p=0.036 and lower MPV (p=0.017.

A binomial logistic regression was performed to ascertain the effects of presence of PDN, age (years, HbA1C, low MCH (<34 *versus* ≥ 34, non-low MCV (≥ 80 *versus* <80 and low MPV (≤ 9.35 *versus*>9.35 on the likelihood that participants have ED. Cut off values of 34 for MCH and 80 for MCV were drawn from the normal reference ranges while a cutoff of 9.35 for MPV was drawn from a ROC curve analysis of our data. The diagnostic accuracy of this cutoff value showed 82.4% sensitivity, 55% specificity, 70% PPV and 71% NPV (AUC=0.707, p value=0.001) **(Figures 1,2).**

High HbA1c proved to be an independent risk factor of erectile dysfunction (p=0.033) meanwhile low MPV and low MCH were independent predictors for this disorder (p=0.036, 0.034 respectively, OR= 5.562, 9.524 respectively). Peripheral diabetic neuropathy was a significant risk factor for ED (p=0.009) but it did not prove to be an independent predictor. (**Tables 1-4, Figures1-3**)

Testosterone did not correlate with erectile dysfunction and was not significantly different between both groups of patients (p= 0.645, 0.642 respectively). Testosterone correlated positively and significantly with TC, RBC, Hb, HCT, FSH (p= 0.037, 0.043, 0.01, 0.046, 0.045 respectively). Testosterone correlated negatively with BMI values and class, pulse rate, serum creatinine, WBC, RDW and platelet count (p= <0.0005, <0.0005, 0.047, 0.028, 0.032, 0.028, 0.021 respectively). (**Tables 2,5**)

Table 1: Clinical data of patients with and without erectile dysfunction.

Variable	Group		P1	Crude OR	P2
	With ED (n=51)	Without ED (n=40)			
Age (years)	60 (47-64)	51 (42.25-61)	*0.039	1.038	0.060
BMI class: Count (Percent) Ideal (18.5-24.9 kg/m²) Overweight (25-29.9 kg/m²) Class I obesity (30-34.9 kg/m²) Class II obesity (35-39.9 kg/m²) Class III obesity (>40 kg/ m²)	3 (5.9%) 15 29.4%) 24 (47.1% 7 (13.7%) 2 (3.9%)	3 (7.5%) 9 (22.5%) 16 (40%) 9 (22.5%) 3 (7.5%)	***0.689	0.805	0.333
BMI kg/m²	30.8 (28.7-33.9)	31.5 (27.9-35.6)	*0.349	0.975	0.574
SBP mmHg	130 (120.5-141)	134 (120-140)	*0.956	0.992	0.582
DBP mmHg	77 (69-80)	78 (69-84)	*.421	0.977	0.338
Mean BP	94 (88.2-99.8)	93.3 (88.3-103.3)	*.548	0.977	0.333
Pulse (Mean ± SD) bpm	77.8 ± 9.4	81.3 ± 10.5	**0.098	0.964	0.101
Presence of Diabetic neuropathy Count (Percent)	38 (74.5%)	19 (47.5%)	***0.008	3.231	0.009
Duration of DM (years)	12 (6-16)	8 (2.5-15)	*0.085	1.047	0.152

Data are presented as Median (IQR) unless otherwise stated. P1 by *Mann-Whitney U test,

**Independent Samples t-Test, ***Chi-Square test and ****Fisher's Exact Test. P2 by Binary Logistic Regression.

OR=Odds Ratio, BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BP: Blood pressure.

Table 2: Laboratory variables of patients with and without erectile dysfunction.

Variable	Group		P1	Crude OR	P2
	With ED (n=51)	Without ED (n=40)			
Serum total testosterone nmol/l	11.25 (9.2-17.9)	14.1 (8.7-16.9)	*0.642	0.982	0.660
LH nmol/l	4.06 (3.26-5.17)	3.35 (2.77-5.27)	*0.217	0.934	0.357
FSH nmol/l	4.25 (3.53-6.65)	5.05 (2.95-7.83)	*0.636	0.911	0.219
Prolactin nmol/l	134.9 (121.8-152.9)	136 (90.6-154.1)	*0.301	0.999	0.595
TSH uIU/ml	1.91 (1.31-3.21)	2.39 (1.72-3.595)	*0.334	0.840	0.331
FT4 pmol/l	14.9 ± 3.3	14.6 ± 2.3	**0.741	1.041	0.733
FT3 pmol/l	4.6 ± 0.66	4.8 ± 0.47	**0.536	0.528	0.512
FPG mmol/l	7.6 (6.05-11.9)	8.3 (6.73-11.0)	*0.713	1.017	0.766
HbA1C %	8.66 ± 1.4	8.08 ± 1.3	**0.053	1.381	0.058

TC mmol/l	4.12 ± 1.05	4.17 ± 1.13	**0.816	0.953	0.813
LDL-C mmol/l	2.1 (1.6-2.9)	2.2 (1.55-3.0)	*0.620	0.935	0.708
HDL-C mmol/l	1.025 (0.89-1.15)	1.04 (0.855-1.2)	*0.833	0.904	0.907
TG mmol/l	1.42 (1.06-1.88)	1.48 (1.1-1.9)	*0.724	1.125	0.644
S cr µmol/l	80.5 (70-94.25)	78 (69-88)	*0.412	1.005	0.578
WBCs 10/L	7.00 (6.35-8.075)	6.3 (5.55-7.675)	*0.143	1.152	0.331
RBCs 10/L	5.62 (5.12-6.048)	5.505 (5.2-6.3)	*0.693	0.862	0.493
Hb gm/dL	15.95 (14.4-16.9)	15.65 (14. 816.6)	*0.767	1.103	0.442
HCT %	47.8 (34.2-51.2)	42.1 (33.4-46.6)	*0.034	1.073	0.055
MCV fL	84.3 (29.2-88.4)	77.75 (31.2-86.7)	*0.247	1.010	0.312
MCH pg	29.9 (28.6-41.6)	45.3 (29.5-48.5)	*0.036	0.943	0.034
MCHC gm/dL	33.3 (32.6-71.5)	33.8 (30.3-79.7)	*0.935	0.994	0.588
RDW %	14.05 (13.4-14.7)	13.9 (13.5-14.6)	*0.755	1.175	0.487
PC 10/L	212.5 ± 75.5	210.6 ± 47	**0.754	1.001	0.749
MPV fL	8.75 (8.2-9.3)	9.4 (8.6-10.2)	*0.017	0.543	0.036

Data are presented as Median (IQR) unless otherwise stated. P1 by

*Mann-Whitney U test, **Independent Samples t-Test. P2 by Binary Logistic Regression. OR=Odds Ratio.

LH: luteinizing hormone, FSH: follicle stimulating hormone, TSH: thyroid stimulating hormone, FT4: free tetraiodothyronine, FT3: Triiodothyronine,

FPG: Fasting plasma glucose, HbA1c: glycosylated hemoglobin, LDL-C: low density lipoprotein cholesterol, HDL-c: high density lipoprotein cholesterol, TG: triglycerides, S cr: serum creatinine

WBC: White blood cell count, RBC: Red blood cell count, Hb: hemoglobin, HCT: Hematocrete, MCV: Mean corpuscular volume, MCH: Mean

corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, PC: platelet count, MPV: Mean platelet volume.

Predictors of the likelihood of occurrence of ED

Table 3 is showing the difference between those with and without ED as regard to these three parameters. There were two studentized residuals with values of -2.988 and -3.494 standard deviations which were kept in the analysis. The logistic regression model was statistically significant ($\chi 2$ (6)=33.553, p<0.0005). The model explained 43.4% (Nagelkerke R^2) of the variance in ED and correctly classified 72.1% of cases. Sensitivity and positive predictive value were 75.5%, while specificity and negative predictive value were 67.6%. Of the 6 predictor variables, HbA1C, MCH and MPV were statistically significant as shown in **Table 4**. Patients had 1.65 times higher odds to exhibit ED for every 1% rise in HbA1C, had 9.5 times higher odds to exhibit ED for those with MCH<34, and had 5.56 times higher odds to exhibit ED for those with MPV ≤ 9.35.

Table 3: MCV, MCH and MPV in the two study groups.

Parameter	ED group		χ2	P1	Crude OR (95% CI)	P2
	With ED (n=51)	Without ED (n=40)				
Low MCH pg	36 (70.6%)	13 (32.5%)	13.086	<0.0005	4.99 (2-12.2)	<0.0005
Non-low MCV fL	37 (72.5%)	20 (50%)	4.870	0.027	2.6 (1.1-6.3)	0.029
Low MPV fL	42 (82.4%)	18 (45%)	13.925	<0.0005	5.7 (2.2-14.8)	<0.0005

Data are presented as count (%). P1 value by Chi-square. OR=Odds ratio, CI=confidence interval. P2 value by simple logistic regression.

This table is showing that the frequency of low MCH (<34), non-low MCV (≥80) and low MPV (≤9.35) are statistically and significantly higher in those with ED as compared to those without ED.

Table 4: Independent predictors of ED.

Predictor	B	S.E.	Wald	P value	OR	95% CI for OR	
						Lower	Upper
PDN Absent Present	0.194	0.651	0.089	0.766	R 1.214	0.339	4. 352
MCV fL <80 ≥ 80	-0.908	0.780	1.357	0.244	R 0.403	0.087	1.858
MCH pg ≥ 34 <34	2.254	0.783	8.296	0.004	R 9.524	2.055	44.146
Age (years)	0.044	0.027	2.592	0.107	1.045	0.990	1.103
HbA1C (%)	0.501	0.236	4.529	0.033	1.651	1.040	2.620
MPV fL >9.35 ≤ 9.35	1.716	0.577	8.835	0.003	R 5.562	1.794	17.244
Constant	-8.100						

Table 5: Correlation of total serum testosterone with clinical and laboratory variables.

Variable	Correlation coefficient	P
Erectile dysfunction	-0.049	*0.645
Age (years)	-0.074	0.485
BMI class	-0.491	<0.0005
BMI kg/m²	-0.509	<0.0005
SBP mmHg	0.125	0.250
DBP mmHg	0.181	0.091
MBP mmHg	0.198	0.066
Pulse bpm	-0.212	0.047
Presence of Diabetic neuropathy	0.044	*0.681
Duration of DM (yrs)	0.028	0.793
FPG mmol/l	-0.124	0.252
HbA1C %	-0.047	0.665
TC mmol/l	0.229	0.037
LDL-C mmol/l	0.194	0.079
HDL-C mmol/l	0.168	0.129
TG mmol/l	-0.097	0.381

S cr µmol/l	-0.241	0.028
TSH uIU/ml	0.042	0.731
T4 pmol/l	0.293	0.078
T3 pmol/l	-0.058	0.825
LH nmol/l	0.186	0.080
FSH nmol/l	0.244	0.045
Prolactin nmol/l	0.052	0.696
WBC 10/L	-0.288	0.032
RBC 10/L	0.271	0.043
Hb gm/dL	0.340	0.010
HCT %	0.270	0.046
MCV fL	0.224	0.098
MCH pg	-0.086	0.529
MCHC gm/dL	-0.223	0.098
RDW %	-0.294	0.028
PC 10/L	-0.311	0.021
MPV fL	0.143	0.294

p value by Spearman's Correlation and *Point Bi-serial Correlation.

LH: luteinizing hormone, FSH: follicle stimulating hormone, TSH: thyroid stimulating hormone, FT4: free tetraiodothyronine,

FT3: Triiodothyronine, FBG: Fasting blood glucose, HbA1c: glycosylated hemoglobin, LDL-C: low density lipoprotein cholesterol,

HDL-c: high density lipoprotein cholesterol, BUN: Blood urea nitrogen, WBC: White blood cell count, RBC: Red blood cell count,

HCT: Hematocrete, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin,

MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, MPV: Mean platelet volume.

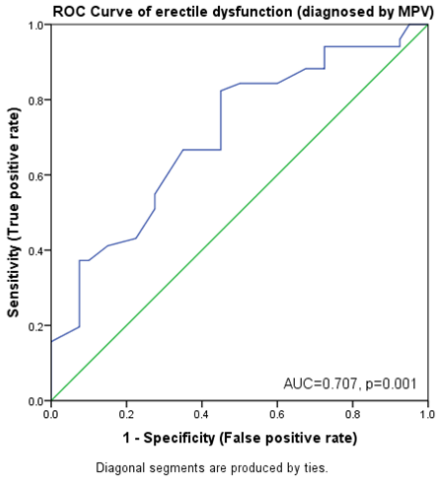

Figure 1: This ROC curve shows that area under the ROC curve (AUC) of diagnosing ED by MPV cutoff value was 0.707 (p=0.001)

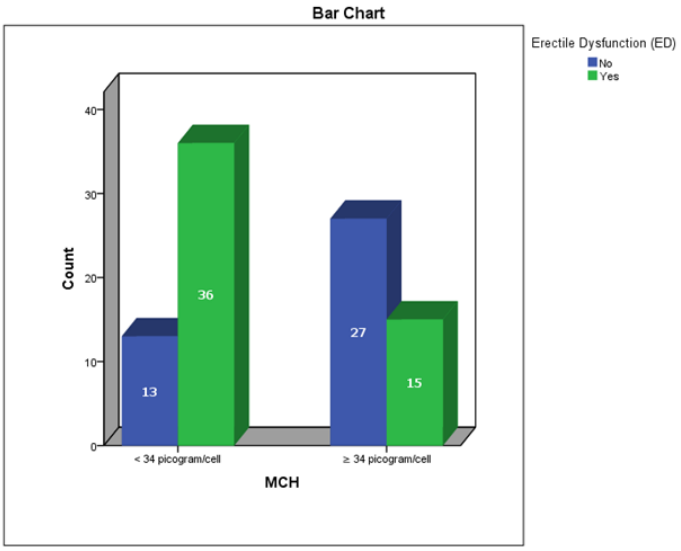

Figure 2: This figure shows that low MCH is more frequently encountered in those with ED while higher MCH was more in those without ED

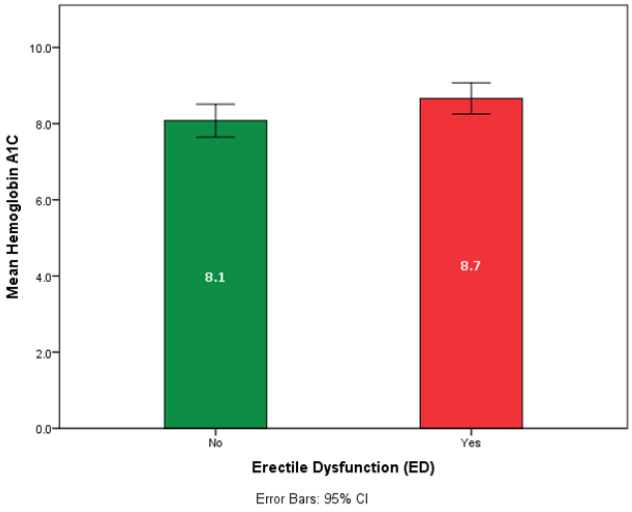

Figure 3: This graph shows that HbA1c is higher in those with ED (p=0.053)

Discussion

Several researchers reported a high prevalence of ED in diabetic patients ranging from 20 to 90% with more affection at an earlier age than non -diabetic population. The differences in prevalence may be attributed to different criteria of the studied groups [10-12]. For example, in Lal Meena's study the prevalence was 78%and was associated with higher cardiovascular risk [13] and increased with increasing age. The prevalence increased from 20% in the age group less than 40 to 100% in the age group more than 60 years.

In the Massachusetts male ageing study, men with treated diabetes had a 28% prevalence of complete ED, about three times higher than the prevalence in the entire study (10%). It also showed the extremely deleterious epidemiologic link between coronary artery disease, diabetes and ED [14]. In our study, ED was present in 56% of the study group who were older in age (p= 0.039) than those without ED.

The effect of age on prevalence and severity of the disease might be due to age-related changes occurring in the body and various other complications that may coexist in diabetic patients, but ultimately the accelerated atherosclerosis is the common factor for increased prevalence of ED and cardiovascular disease in aging population [14].

Although Romeo [12] declared peripheral neuropathy as an independent predictor of ED (p= 0.023), in our study, diabetic peripheral neuropathy was significantly associated with ED (p=0.008), and it was a significant risk (0.009), however, not an independent predictor.

In a study of 90 patients, Spanish researchers [15] uncovered clear links between erectile dysfunction and peripheral neuropathy. They found strong association between the severity of neuropathy symptoms and ED (p=0.009).

Similarly, in another study of Japanese, diabetic neuropathy was positively associated with severe erectile dysfunction among diabetic patients aged less than 65 years [16]. In Ugwu's study, autonomic neuropathy was significant only when duration of diabetes was removed from the model [17].

Our patients suffering from ED showed a significant trend towards higher HbA1c (p=0.05) and high HbA1c proved to be an independent predictor of erectile dysfunction (p=0.033). Similar to our observation, HbA1c was also reported by Romeo and Ugwu and others as an independent predictor of ED in diabetic patients [12,17].

Available studies indicate that increased MPV triggers arterial atherosclerotic processes and thrombosis including penile arteries. Sensitivity of high MPV in detection of arteriogenic ED was mentioned in some reports reaching 54% with a specificity of 88% and 82% positive predictive value [18,19].

In contrast to most literature reports, our study demonstrated statistically significant association of ED with low MPV and accuracy of cut off value ≤9.35 fL was shown by an AUC of 0.707 (p value = 0.001) with sensitivity, specificity, positive predictive value and negative predictive value of 82.4%, 55%, 70% and 71% respectively. Lower MPV had shown to be an independent predictor of erectile dysfunction (p=0.003, OR=5.562).

However, our observation is in agreement with a recent interesting study that was published in 2018, demonstrating the strong association between low MPV and high risk for critical limb ischemia in patients with peripheral arterial atherosclerotic disease. In that study, diabetes was one of the criteria to define critical limb ischemia and ROC analysis revealed a cut-off of ≤ 10.2 fL for MPV to best predict critical limb ischemia (sensitivity: 65%, specificity: 42%, positive predictive value: 71%, negative predictive value: 36%). MPV was not associated with myocardial infarction or stroke in the same study [20].

Decreased MPV could be regarded as an enhanced consumption of large platelets in inflammatory states [21].

Atherosclerosis affects all vascular beds, so, the earliest symptom development is expected in the artery with the narrowest lumen such as the penile artery. The negative impact of ED on coronary arteries has been published [22].

In our study low MCH was also an independent predictor of ED (p= 0.004, OR=9.524). This is a new observation that is, up to our knowledge, documented for the first time.

In this study, there was no significant difference between both groups of patients in testosterone level indicating that erectile dysfunction in diabetic patient is mostly due to factors other than hypogonadism. Although erections are clearly androgen-dependent, as evidenced by the marked reduction in the frequency, amplitude, and rigidity of erections in marked hypogonadism, the level of androgens required to induce ED is debatable. It is believed that there is a level of testosterone that is required for normal erection in adults and once this threshold is achieved, additional amounts do not further affect the frequency, amplitude, or rigidity of erections [23].

Total testosterone correlated negatively with BMI value and class in our study population. Similarly, Chuang reported inverse correlation between testosterone level and BMI. It is believed that this inverse correlation is responsible for the modulation of the lean body mass, fat mass and body composition [24].

In agreement with our results is the positive correlation between serum total cholesterol (TC) and testosterone observed by Chuang [24].We did not find significant associations between testosterone and other lipids that may be explained by the fact that most of our patients were receiving hypolipidemic drugs according to the American Diabetes Association clinical practice guidelines 2017.

Al-Chalabi [25] found a significant negative correlation between testosterone and diastolic blood pressure. She also reported a significant negative correlation between testosterone and TC and LDL-C. In our study we did not find such association between testosterone and blood pressure. However, testosterone level correlated negatively with heart rate. The higher the testosterone, the lower the heart rate that may indicate more cardiac fitness and decreased work of the heart. In Poliwczak's study, testosterone therapy reduced heart rate Variability in the treated group of patients [26].

It is noteworthy mentioning that in the present study higher testosterone level was associated with lower serum creatinine level (p=0.028). Effect of testosterone on kidney function was previously demonstrated by Goel who reported a significant delay in the progression of chronic kidney disease in patients who received testosterone replacement. The treated men had a 24% decreased risk of end stage renal disease and 25% decreased risk of death [27].

Some reports indicate that testosterone increases the biological activity of erythropoietin, alters iron metabolism and stimulates red blood cell production thus increasing

hemoglobin level [28]. This can explain our observation of the direct and strong correlation between serum testosterone and red cell count, hematocrit and haemoglobin level (p=0.043, 0.046, 0.01 respectively).

The relation between atherosclerotic and cardiovascular diseases and white blood cell count was evoked by several authors. Judith [29] demonstrated inverse correlation between total testosterone and total WBC in males 40 to 78 years of age who did not have history of coronary artery disease. We found the same correlation in our study population. These results support a link between hormonal status and low-grade inflammation and consequently the higher risk to atherosclerotic cardiovascular disease.

RDW has shown its significance as a predictive and risk factor for cardiovascular and overall mortality in the general population and in various conditions such as obesity, malignancies, and chronic kidney diseases [30]. In our study it is inversely associated with testosterone level (p=0.028). This may indirectly reflect the link between testosterone level and cardiovascular disease.

Conclusion

Erectile dysfunction in diabetic patients is strongly associated with peripheral neuropathy, not serum total testosterone level, so sexual history should not be missed in diabetic patients having PDN. This dysfunction can be also easily predicted by the uncontrolled diabetic state and simple CBC. Achieving target HbA1c in diabetic patients is of utmost significance to avoid ED. Requesting simple inexpensive CBC can significantly reflect the presence of an underlying complication such as ED with its widely known association with coronary atherosclerosis. Erectile dysfunction in diabetic patients is multifactorial as shown by its association with variable clinical and laboratory parameters. We believe that management of diabetes is an art that can has its effect on improving patient's health and quality of life by simple basic and cost-effective clinical practice.

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