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ASSOCIATION BETWEEN MALE ERECTILE DYSFUNCTION (MED) AND LEVELS OF VITAMIN D IN INDIVIDUALS WITH DIABETES MELLITUS (TYPE II)

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ABSTRACT

Background: Present investigations have recommended that an association could be present between Vitamin D deficiency and male erectile dysfunction (MED).

Objective: The current investigation assessed the association between vitamin D levels and MED in individuals with type 2 diabetes mellitus (DM).

Methodology: The investigation included 150 participants with type 2 DM aged between 19-75 years. The questionnaire known as the 'International Index of Erectile Function' (IIEF-5) was used. Based on their IIEF-5 score, the participants were divided into three categories: those with 'severe ED' (IIEF-5 score between 5 and 10); 'moderate ED' (IIEF-5 score between 11 and 20); and 'no ED' (IIEF-5 score between 21 and 25). Every individual had their biochemical variables, vitamin D, and hormonal assessment performed. The three categories were evaluated on all characteristics.

Results: Out of 150 participants that were part of the investigation, 38 patients (25.3%) were not diagnosed with erectile dysfunction, whereas 112 patients (74.6%) satisfied the criteria for ED (IIEF-5 < 21). The mean age was 60.25 ± 9.86 years and the average level of vitamin D was 14.78 ± 9.26 ng/ml. Vitamin D levels were quite distinct among all three categories ($p = 0.031$) when the participants were split into three categories based on IIEF-5 assessment. Specifically, there was a significant difference in vitamin D levels between patients who had an IIEF-5 score of 5–10 points and those who had a score of 11–20 points ($p < 0.027$). There were age differences ($p=0.022$) across the three categories.

Conclusion: In conclusion, MED and vitamin D insufficiency are significantly correlated in male patients with diabetes type 2 mellitus. This association is thought to be driven by the increased synthesis of nitric oxide in vascular cells caused by vitamin D through a variety of routes, the repression of apoptosis, and the avoidance of endothelial dysfunction through the suppression of

oxidative stress. In conclusion, there is a correlation between vitamin D levels and ED scores, particularly for males with type 2 diabetes mellitus who are among the ages of 40 and 60.

Keywords: Male Erectile Dysfunction, Vitamin D, Diabetes Mellitus

Introduction

Male erectile dysfunction (MED) is defined as the lack of ability to attain or keep the erection strong enough to perform an effective mating on a daily basis. Men with diabetes that is type 2 are more likely to have this problem [1,2]. According to one's years of age, kind, and length of diabetes, the incidence of diabetics MED ranges from 32% to 90% [3]. Furthermore, in 12–30% of men with diabetes, sexual dysfunction manifests as the initial symptom; yet, in later monitoring, erectile dysfunction is thought to be an indicator of silent cardiovascular disease [4,5].

While dysfunction in endothelial cells is linked to vascular disorders, the pathogenesis of MED in men with diabetes is multifaceted [6]. One early indicator of the onset of atherosclerosis is thought to be impaired endothelial function [7]. Men with genital endothelial malfunction are more inclined to have harm to endothelial cells in the blood vessels of other organs, and it serves a major part in the pathogenesis of MED [8,9].

A correlation among a lack of in vitamin D and an elevated risk of heart disease has been proposed by recently published studies [10]. Via both genetic and non-genetic routes, vitamin D is known to enhance endothelium synthesis of nitric oxide (NO), suppress cell death, and shield them from oxidative damage [11–13]. Because shortage in vitamin D is associated with endothelial cells to malfunction, which is believed to result in erection problems, it follows that deficiencies in vitamin D is associated with erectile dysfunction. The function of endothelial cells is thought to be a crucial role in establishing and sustaining the erection of penile tissue. [14–16]

A majority of individuals who have diabetes have inadequate circulating vitamin D levels and a high blood sugar level, according to recently published prospective research [17]. This result is consistent with how vitamin D affects diabetic individuals' blood sugar levels [18]. Conversely, it has been demonstrated that low levels of vitamin D in the serum are linked to obesity, insulin resistance, inability to tolerate glucose, and hyperglycemia during fasting [19–21]. In the present research, vitamin D levels and MED were compared among individuals with type 2 diabetes.

Methodology

The research comprised 150 successive participants with diabetes type 2 mellitus (DM) who received hospitalization to our hospital's diabetes clinics for outpatient care. The patients' ages ranged from 19 to 75 years old, and they all were having normal functions of liver and kidney (‘alanine aminotransferase <35 U/L’ and ‘glomerular filtration rate >89ml/dk/2.62 m^2’) in addition to leading normal lifestyle with frequent exercising.

Individuals who had undergone crucial surgical procedures on their pelvis, utilized medications that trigger ED (beta-blockers, diuretics, etc.), had a high level of prolactin, prostate tumors, hypogonadism, issues with the thyroid, unusual bleeding from the rectum (suspected in time, lump, attachment, etc.), had previous experience of total or transurethral removing the prostate, severe heart disease and neurological disease, an acute cerebrovascular crisis, an ongoing or recent spread of infection, unrestrained diabetes, individuals with a history of mental illness, and individuals who had been treated or were still receiving vitamin D replacement therapies were not included in the investigation.

The ‘local ethics commission’ gave the study its approval. In compliance with the procedures set forth by the ‘Institutional Review Board and the Declaration of Helsinki’, the patients provided informed and written permission. Every patient provided a thorough medical history and conducted a physical assessment, which included measurements of ‘height’, ‘weight’, ‘waist circumference’, ‘body mass index’, and ‘blood pressure’. The following parameters were measured in the blood: ‘total testosterone’, ‘prolactin’, ‘follicle-stimulating hormone (FSH)’, ‘glycosylated haemoglobin’, ‘total

cholesterol', 'high-density lipoprotein cholesterol', 'triglycerides', 'creatinine', 'calcium', and 'phosphate'; 'vitamin D levels'; and 'prostate specific antigen (PSA)'. The specimens of blood were taken in February and April, taking into account the seasonal changes in vitamin D concentrations. Samples of blood that had been fasted were taken between 9:00 and 12:00 AM. Samples of blood were drawn into tubes labelled 'SST II', 'LH PST II', and 'EDTA', and they were all examined at the same time.

To identify the presence of erectile dysfunction, the International Index of Erectile Function (IIEF-5) questionnaire was given to each participant [22]. A score between '21 and 25' on the IIEF-5 showed no problems with erectile dysfunction, between '11 and 20' points for mild erection disorder, and between '5 and 10' points for extreme problems with erectile dysfunction. These three categories were assessed on all characteristics. Furthermore, an assessment was conducted on the correlation among the IIEF-5 scores and the presence of vitamin D levels.

Employing conventional equipment, enzymatic calorimetry techniques were used to measure the sugar levels in the entire bloodstream. The 'intra- and interassay coefficient variances' were found to be 7 and 9%, respectively. Utilising an 'enzymatic colorimetric test', the levels of 'total cholesterol', 'HDL', 'triglycerides', 'calcium', and 'phosphate' were determined using a 'Hitachi 748 auto-analyser'. The 'Friede-wald formula' was used for determining LDL cholesterol values. Based on the guidelines provided in the 'NHANES Laboratory Procedure Guide': 'Glycohemoglobin', 'HbA1c levels' were determined using 'boronate affinity high-performance liquid chromatography' (HPLC). Using 'automatic immunochemoluminescent' testing, 'total the hormone testosterone', 'prolactin level, and LH level were quantified. Testosterone test had 'coefficients of variation of 4.4%' and '4.2% within runs', accordingly. The 'prolactin', 'LH', and 'vitamin D coefficients of variation' were 3.2 and 2.2%, 2.9 and 2.8%, and 3.3 and 3.0% between the two runs, correspondingly.

The statistical evaluation was carried out using SPSS 23. The following 'descriptive statistics i-e mean, standard deviation, minimum, median, and maximum were utilised to describe continuous factors'; 'analysis of variance (ANOVA) was utilised for contrasting two separate variables with typical distribution; Pearson's correlation coefficient' was used to analyse the association between 'normally distributed two continuous variables'; 'Spearman's Rho correlation coefficient' was calculated to analyse the 'relationship between two continuous variables that are normally distributed'; 'the relationship between categorical variables was evaluated using the chi-square test' and $p<0.05$ was considered as significant.

Results

Of the participants that were part of the investigation, 38 patients (25.3%) were not diagnosed with erectile dysfunction, whereas 112 patients (74.6%) satisfied the criteria for ED (IIEF-5 < 21). Tables 1 and 2 provide a summary of the individuals' medical and biochemical information. 35.8% of the study subjects used oral diabetes medications exclusively, 19.0% used insulin treatment exclusively, and 45.2% used both insulin treatment and oral diabetic drugs.

Among all patients, the average level of vitamin D was 14.78 ± 9.26 ng/ml. 'ARCHITECT vitamin D commercial kit standards' were 8–54 ng/ml for summertime and 5.9–46.2 ng/ml for wintertime. Vitamin D levels were quite distinct among all three categories ($p =0.031$) when the participants were split into three categories based on IIEF-5 assessment (Table 2). Specifically, there was a significant difference in vitamin D levels between patients who had an 'IIEF-5 score of 5–10 points' and those who had a score of '11–20 points' ($p < 0.027$). There were age differences ($p=0.022$) across the three categories.

Participants with IIEF-5 scores of '5–10 points' and those with scores of '21–25 points' showed a significant difference in mean age ($p < 0.038$). Individuals with lower IIEF scores were shown to be elderly than those with greater numbers. Table 1 shows that there were no differences in waist circumference, BMI, or length of diabetes among the three categories.

Among the three categories, there was no difference in the concentrations of prolactin, thyroid-stimulating hormone (TSH), LH, FSH, HbA1c, or testosterone (Table 2). The IIEF-5 score and vitamin D levels showed a somewhat good connection ($p = 0.049$, $r = 0.32$). Following age division

of the patients into three groups (<40 years, 40–60 years, and >60 years), the 40–60 years age group showed a somewhat favourable connection (r = 0.488, p < 0.021) between their vitamin D levels and IIEF-5 score. Vitamin D levels and the IIEF-5 score were not correlated with the levels of hormones such testosterone, LH, FSH, prolactin, and TSH.

Table 1. Comparing Medical, Antropometrical, and Social variables based on IIEF-5 score

	All Patients (n =150)	**No Problem In Erection (N =38)**	**Mild Problem In Erection (N =64)**	**Extreme Problem In Erection (N = 48)**	**p value**
'Age' (years)	60.25 ± 9.86	63.45± 8.48	51.67 ± 8.64	58.32 ± 8.76	.022
'BMI' (kg/m2)	28.15 ± 3.36	27.54 ± 3.45	28.22 ± 3.22	28.09 ± 2.96	.985
'Waist' (cm)	96.92 ± 8.73	96.54 ± 6.33	95.53±8.85	93.45 ± 6.33	.624
'Systolic BP' (mmHg)	125.88 ± 23.77	140.12± 26.23	137.22 ± 24.36	139.54 ± 18.03	.899
'Diastolic BP' (mmHg)	74.68 ± 12.38	76.86 ± 11.43	73.68 ± 12.66	73.88 ± 13.35	.573
Duration of Diabetes mellitus (years)	8.26 ± 6.82	6.06 ± 4.69	8.44 ± 6.88	9.39 ± 7.58	.329
Duration of Erectile dysfunction	4.37 ± 4.86	0.06 ± 0.33	4.35 ± 4.22	6.5 ± 5.4	0.001

Table 2: Assessment of all chemical factors with score of IIEF-5

	All Patients (n =150)	**No Problem In Erection (N =38)**	**Mild Problem In Erection (N =64)**	**Extreme Problem In Erection (N = 48)**	**p value**
High density lipoprotein (36–56 mg/dl)	40.29 ± 8.73	42.73 ± 11.53	41 ± 9.76	37.55 ± 11.73	0.076
Low Density Lipoprotein (<125 mg/dl)	144.38 ± 71.38	130.25 ± 35.87	135.78 ± 59.48	163.5 ± 86.2	0.682
'Cholesterol' (<180 mg/dl)	210.23 ± 52.22	219.89 ± 79.85	198.3 ± 31.44	205.68 ± 50.77	0.983
'Potassium' (3.2–5.3 mEq/L)	4.58 ± 0.54	4.47 ± 0.58	4.63 ± 0.52	4.58 ± 0.5	0.478
'Blood urea nitrogen' (20–40 mg/dl)	36.35 ± 11.1	32.11 ± 10.5	35.22 ± 10.60	37.2 ± 13.49	0.273
'Alanine transaminase' (0–50 U/L)	28.69 ± 19.3	30.97 ± 15.20	29.1 ± 24.60	25.6± 14.14	0.320
'FSH' (1.5–14 mU/mL)	5.68 ± 4.63	5.17 ± 3.58	5.8 ± 3.42	7.01 ± 3.85	0.479

'LH' (6–26 mU/mL)	5.69 ± 2.92	5.21 ± 2.82	5.67 ± 2.1	5.83 ± 2.68	0.285
'Free T3' (1.69–3.68 pg/dL)	3.79 ± 0.53	3.89± 0.48	3.78 ± 0.52	3.76 ± 0.56	0.689
'Free T4' (0.6–1.35 pg/mL)	2.35± 2.44	2.62 ± 3.03	2.06 ± 0.45	2.44 ± 2.74	0.499
'Calcium' (9.3-11.6 mg/dl)	8.66 ± 0.53	8.75 ± 0.57	8.65 ± 0.5	8.58 ± 0.54	0.377
'Phosphorus' (3.1–5 mg/dl)	2.58± 0.59	2.63 ± 0.58	2.52 ± 0.58	2.69 ± 0.58	0.426
'PSA' (0–4.1 ng/mL)	2.37 ± 2.44	2.43± 2.52	2.44 ± 2.69	2.23 ± 0.97	0.956
'Vitamin D' (20–99) ng/ml)	14.78 ± 9.26	15.28 ± 9.84	16.82 ± 8.43	11.62 ± 5.39	0.031
'Glucose' (69–104 mg/dl)	183.5 ± 96.11	175 ± 79.88	172.8 ± 77.8	204.42 ± 109.4	0.442
'Sodium' (133–142 mEq/L)	140.08± 3.8	138.87 ± 3.5	140.5± 3.88	139.9 ± 3.96	0.447
'Creatinine' (0.68–2.2 mg/dl)	0.85 ± 0.35	0.8 ± 0.27	0.83± 0.36	0.88 ± 0.38	0.643
'Aspartate transaminase' (6–36U/L)	22.58 ± 9.42	23.68 ± 8.93	22.42 ± 8.04	21.87 ± 8.63	0.465
Prolactin (1.8–19 mg/L)	8.03 ± 5.06	8.35± 6.58	7.8 ± 3.40	7.84 ± 6.1	0.484
Testosterone (3.1–9.1 nmol/L)	3.38± 0.47	3.06 ± 0.06	3.56 ± 0.68	3.38 ± 0.94	0.981
TSH (0.57–6.94 mU/ml)	2.73 ± 2.45	2.52 ± 1.97	2.92 ± 0.8	2.6 ± 2.02	0.399

Discussion

In individuals with type 2 diabetes, the current investigation discovered a strong correlation between MED and vitamin D deficiency. Furthermore, the group with severe MED had lower vitamin D levels than the groups with moderate MED and no MED. About 50% of males with type 2 diabetes have an increased risk of erectile dysfunction, according to epidemiologic studies [23]. Males with diabetes had a three-fold higher risk of erectile dysfunction than non-diabetic males in the Massachusetts male ageing investigation [4]. Although the pathogenesis of MED in male diabetics is complex, it involves a vascular disease linked to a reduction in endothelial function [6]. Low serum vitamin D levels have been linked to endothelial dysfunction, according to recent research [10]. Remarkably, a majority of diabetic individuals who had inadequate vitamin D concentrations had low blood sugar levels, especially in the for a long time and sustained period of diabetes, according to Al-Tamini and Ali [18].

In the current research, male individuals with diabetes type 2 mellitus had their erectile dysfunction and plasma levels of vitamin D examined for potential correlations. In the end, we discovered that those with lower IIEF-5 score also had reduced vitamin D levels. In the age range of 40 to 60, this link was considerably more noticeable. This research is the initial study to show that male diabetes patients who also have a lack of vitamin D have a greater risk of MED. Obese people with chronic diabetes are reported to have a greater prevalence of erectile dysfunction [3,24]. Additionally, recent research has shown a connection among vitamin D insufficiency and being overweight. The result is thought to be caused by decreased sunlight exposure, decreased vitamin D bioavailability, and decreased vitamin D absorption by fat tissue [25–27]. The current investigation discovered 'a

significant difference' (p =0.036) in the distribution of 'BMI' between the 'vitamin D-deficient' and 'vitamin D-insufficient groups'. Nevertheless, a significant correlation between BMI and IIEF-5 score could not be found in this investigation.

The IIEF-5 score, vitamin D levels, prolactin, TSH, LH, and FSH levels did not significantly correlate with each other. According to a study by Wher et al., there is an association among vitamin D and plasma levels of testosterone, and the two hormones exhibit seasonal changes [28]. It was demonstrated by 'Wehr et al. and Pilz et al' that vitamin D may directly affect gonadal functioning [29–32]. Nevertheless, the current study's findings do not align with theirs.

Hypogonadism can also be caused by type 2 diabetes mellitus and vitamin D insufficiency, so those patients were not included in the present investigation. While the minimal range of total testosterone levels recommended by Lunenfeld et al. was 12.1 nmol/L, we considered total testosterone levels within reference ranges (3.1–9.1 nmol/L) to be acceptable. Considering the decreased testosterone threshold that characterises testosterone insufficiency, opinions differ. Furthermore, we were unable to discover a relationship between vitamin D and levels of testosterone [33].

The present investigation discovered that levels of hormones have no bearing on the association between MED and vitamin D. Thus, it is possible that endothelial dysfunction linked to low vitamin D levels causes erectile dysfunction. In a recent research investigation, 'Canguven et al'. demonstrated that rises in IIEF-5 scores and total testosterone levels might be seen with a 12-month vitamin D treatment. Regarding the impact of vitamin D therapy on erectile dysfunction, we are unable to offer any commentary. We did not follow up with those patients since our goal was to ascertain whether vitamin D and MED are related [34].

In conclusion, MED and vitamin D insufficiency are significantly correlated 'in male patients with diabetes type 2 mellitus'. This association is thought to be driven by the increased synthesis of nitric oxide in vascular cells caused by vitamin D through a variety of routes, the repression of apoptosis, and the avoidance of endothelial dysfunction through the suppression of oxidative stress. In conclusion, 'there is a correlation between vitamin D levels' and MED scores, particularly for males with type 2 diabetes mellitus who are among the ages of 40 and 60.

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