Vitamin D is an independent predictor of sexual dysfunction in females

Original Article

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ABSTRACT

Background: Sexual functions are complex in physiology, and there are several elements that influence them. Female sexual dysfunction is an overlooked condition that is seldom addressed and discussed, especially in Eastern countries.
Aim: To assess serum levels of 25(OH) vitamin D3 and sex hormones in females suffering from sexual dysfunction.
Patients and Methods: One hundred participants were included in this case-control study. They were divided into two groups: 50 females with sexual dysfunction and 50 age-matched, healthy, sexually active females. They provided comprehensive medical and drug history and answered the arabic form of Female Sexual Function Index. In addition, serum vitamin D3, estradiol, and total testosterone levels were measured using ELISA.
Results: Serum vitamin D3 was significantly lower in cases compared to controls (16.53 ± 8.41 and 26.1 ± 13.93 ng/ml, respectively, p <0.001), but there was no significant difference in estradiol (366.51 ± 154.75 and 338.75 ± 150.86 pg/ml, respectively, p = 0.4) or total testosterone (0.97 ± 0.88 and 0.82 ± 0.39 ng/ml, respectively; p = 0.3). Substantial positive correlations have been observed between vitamin D3 and sexual desire, arousal, and full-scale scores (p < 0.001, = 0.006, = 0.008, respectively), but not with lubrication, orgasm, or satisfaction (p > 0.05 for each).
Conclusion: Low serum vitamin D3 level may lead to female sexual dysfunction, while estradiol and total testosterone have minimal impacts.

Key Words: Estradiol, Female sexual dysfunction, Vitamin D3, FSFI, Testosterone.

Received: 07 July 2024**, Accepted:** 24 December 2024

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ISSN: 2090-6048, 2024

INTRODUCTION

Sexual dysfunction is a disorder that happens during sex cycle and prevents satisfaction with sexual engagement. These illnesses encompass irregularities in women's desire, lubrication, arousal, orgasm, satisfaction, and pain. It is difficult to predict the prevalence of sexual dysfunction in women[1].

Vitamin D3 has been reported to be involved in the control of sexual function[2]. In animal studies, vitamin D3 deficiency was linked to delayed maturation of the vagina during puberty[3]. Expression of vitamin D3 receptors has been found in female reproductive organs such as the ovarian tissue[4]. Gonadal aromatase expression has been shown to be controlled with vitamin D3[5]. Moreover, women who have deficiency of vitamin D3, may suffer from anomalies in reproductive physiology and sexual function[6].

Estradiol and testosterone hormones may help regulate female sexual function[8]. Estrogen is the primary feminine hormone. However, androgens may be involved in the control of vaginal tissue physiology and female genital sexual arousal[7].

The study aimed to determine serum levels of 25-OH vitamin D3, total testosterone, and estradiol in females with sexual dysfunction.

PATIENTS AND METHODS

Study population and design

This case-control study included female visitors to the Outpatient Clinic of Dermatology, Venereology, and Andrology Department, Faculty of Medicine, Benha University Hospital, Egypt. Participants were assigned into 2 groups: 50 females with sexual dysfunction (cases)

DOI: 10.21608/HA.2024.301632.1109

and 50 healthy, age-matched females without sexual dysfunction (controls).

Inclusion criteria

• Married women with sexual dysfunction after at least a year of normal sexual activity.

• Their age ranges from above 18 years to 45 years.

Exclusion criteria

Postmenopausal women, those who had bilateral oophorectomy, hormonal replacement therapy, or oral contraceptive pills in the six weeks preceding the study, those who were not sexually active, patients with chronic systemic diseases such as hepatic, diabetic, renal, and neoplastic, and pshychiatric patients, as well as pregnant and lactating women, were not able to participate in the study.

Methods

Each participant underwent careful history-taking, including the age, age of onset of menarche, number of pregnancies, educational status, age of the partner, medical history, and drug history. A full history of sexual function in the last year was taken (onset, course, duration of the complaint), and a clinical examination was performed to exclude systemic diseases. Assessment of different aspects and domains of sexual function was done with the validated arabic form of Female Sexual Function Index (FSFI)[9]. The cutoff score < 26.55 has been used to diagnose FSD.

On the third day of menstruation, blood samples were collected for laboratory investigations, which included measuring serum 25(OH) vitamin D3 utilizing the Human ELISA kit (catalogue No. 201-12-1538, catalogue No. 201-12-1538, SunRed, China), serum levels of total testosterone with the GmbH Testosterone ELISA kit (catalogue No. BDTT37-BA, made in China), and serum levels of estradiol with the E2 ELISA kit (ZEUS Diagnostic, Inc., USA). The Benha Faculty of Medicine's Clinical and Chemical Pathology Department carried out laboratory work.

Ethical approval

The Ethics Committee for Human Research of the Faculty of Medicine, Benha University, Egypt approved this study (MS 5-8-2021). Before enrolling in this study, each individual provided written informed consent. The Declaration of Helsinki's ethical requirements for humans were upheld.

Statistical analysis

The data were analyzed with SPSS (Statistical Package for Social Science) version 26 (Armonk, NY: IBM Corp). The used statistical methods included mean and Standard deviation, Student's t-test for parametric data, MannWhitney U- test for nonparametric data, Pearson correlation coefficient, logistic regression analysis and receiver operating characteristic (ROC) curve analysis. A *P* value of <0.05 was judged significant.

RESULTS

The mean age of the studied cases was 36.5±5.07 years with no statistically significant difference compared with the controls (p =0.3). Vitamin D3 was significantly lower in cases than the controls (16.53±8.41, 26.1±13.93 ng/ml, respectively, p <0.001), while there was no significant difference regarding estradiol and total testosterone (p =0.4, 0.3, respectively) (Table 1, Figure 1).

Table 1: Charateristics of the study groups

	Cases		Controls		*t*	*p*
	mean	±S.D	mean	±S.D		
Age (year)	36.50	5.07	35.27	5.91	1.1	0.3
Age of menarche (year)	13.02	1.39	13.04	1.09	0.1	0.9
BMI (kg/m_2)	26.2	3.6	25.7	3.9	0.7	0.5
Vitamin D3 (ng\ml)	16.53	8.41	26.1	13.93	4.1	<0.001*
Estradiol (pg\ml)	366.51	154.75	338.75	150.86	0.9	0.4
Total testosterone (ng\ml)	0.97	0.88	0.82	0.39	1.1	0.3

*Significant, BMI (body mass index)

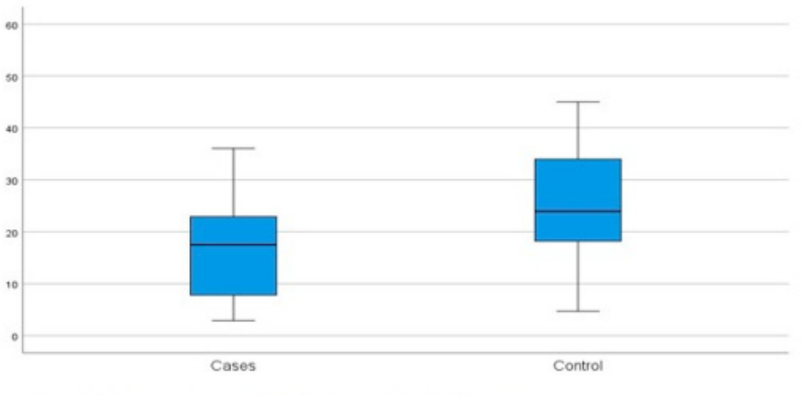

Fig. 1: Study groups regarding vitamin D3 (ng/ml)

There was significant positive correlation between vitamin D3 and desire, arousal and the full-scale score *(p* <0.001, =0.006, =0.008, respectively). However, no significant correlation was detected regarding other domains of FSFI ($p > 0.05$ for each) (Table 2).

A vitamin D3 level of 20.8 pg/mL was found to be a cutoff point for predicting sexual dysfunction in females, as proved by ROC curve analysis (AUC = 0.72; 60% sensitivity; 58% specificity; 95% CI: 0.62–0.82) (Figure 2)

Table 2: Correlation between vitamin D3 and FSFI domain scores

	r	*P*
Desire	0.359	<0.001*
Arousal	0.270	0.006*
Lubrication	0.058	0.568
Orgasm	0.071	0.483
Satisfaction	0.042	0.676
Pain	0.129	0.202
Full Scale Score	0.264	0.008*

*Significant

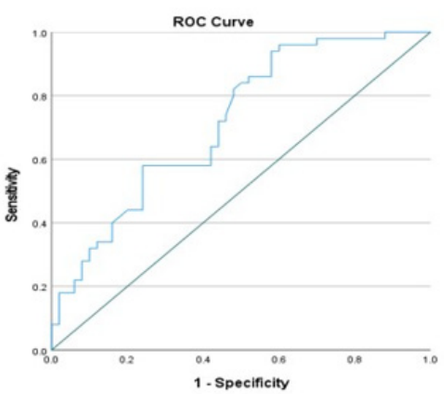

Fig. 2: Reciever operating characteristics (ROC) curve analysis of vitamin D3 for prediction of female sexual dysfunction

There was statistically significant negative correlation between vitamin D3 and number of pregnancies, estradiole level ($p = 0.044, 0.001$, respectively) (Table 3). Multivariate logistic regression analysis revealed that vitamin D3 level was the only significant independent predictor of FSD (OR=0.923; 95%CI =0.878-0.971; p =0.002) (Table 4).

Table 3: Correlation between vitamin D3 and other variables

	r	*P*
Age	-0.125	0.217
Age of menarche	-0.007	0.948
Duration of marriage	-0.154	0.126
Age of the partner	-0.176	0.079
Number of pregnancies	-0.202	0.044*
Estradiol (pg\ml)	-0.317	0.001*
Total testosterone (ng\ml)	-0.129	0.2

Table 4: Logistic regression analyses of various variables for prediction of sexual dysfunction

	Univariate analysis				Multivariate analysis			
	p	OR	95%	CI	*p*	OR	95%	CI
Age	0.006*	1.113	1.031	1.200	0.827	1.021	0.849	1.227
Age of menarche	0.936	0.987	0.719	1.355				
Duration of marriage	0.002*	1.131	1.047	1.222	0.144	1.126	0.960	1.320
Age of partner	0.012*	1.083	1.018	1.152	0.715	0.975	0.853	1.115
Number of pregnancies	0.016*	1.569	1.088	2.264	0.521	1.152	0.748	1.773
Vit. D3	<0.001*	0.915	0.872	0.960	0.002*	0.923	0.878	0.971
Estradiol	0.364	1.001	0.999	1.004				
Total Testosterone	0.290	1.455	0.726	2.914				

*Significant

DISCUSSION

Sexual dysfunction (SD) is a complex illness that affects people of all ages. Vitamin D3, either deficiency or insufficiency, has been linked to sexual dysfunction, according to some studies; thus, this study examined vitamin D3 levels in a sample of Egyptian women who reported SD.

The current study found that vitamin D3 levels were considerably lower in cases compared to controls. There was a strong positive relationship between vitamin D3 and desire, arousal, and the full-scale score. Furthermore, multivariate logistic regression analysis identified vitamin D as an independent risk factor in female sexual dysfunction.

According to Krysiak *et al.*[10] , Inal *et al.*[11] and Canat *et al.*[12], women with vitamin D insufficiency had lower total FSFI scores as well as scores in all three domains (sexual desire, orgasm, and satisfaction) than women with normal vitamin D. These findings are consistent with our own. Moreover, vitamin D supplementation improved libido and overall FSFI scores in women with vitamin D deficiency ($p < 0.05$)[10].

Similarly, Jalali-Chimeh *et al.*[13] found that administering 300,000 units of vitamin D intramuscularly resulted in significantly higher FSFI scores at 4 and 8 weeks ($p = 0.002, < 0.001$, respectively).

Several hypotheses have been proposed to clarify the influence of vitamin D on sexual function. Endothelial cells may be directly buffered from oxidative stress by vitamin D, which also affects endothelial stability[14]. Furthermore, vitamin D3 activates endothelial nitric oxide synthase, increasing nitric oxide synthesis, which is essential for cardiovascular system function. Women with low 25 (OH) vitamin D3 levels may have reduced blood flow to their pelvic genital organs, which might impair sexual performance[15].

In this line, Rad *et al.*[17] and Riazi *et al.*[16] demonstrated that vitamin D treatment promotes development and proliferation of genital epithelial cells, controls pH of the vagina, and reduces genital dryness in postmenopausal

females. Consequently, the local genital significance of vitamin D for sexual intimacy cannot be overlooked.

In regards to sex hormones and female sexual function, the levels of estradiol and total testosterone were not significantly different between patients and controls. Rosen *et al.*[18] reported similar results.

Nevertheless, Cipriani *et al.*[19] found that testosterone systemic treatment for 6 months directly altered clitoral blood flow while simultaneously improving sexual function as measured by FSFI.

Furthermore, the current study demonstrated a significant negative correlation between vitamin D3 and estradiol but a non-significant negative association between vitamin D3 and total testosterone.

In the same context, mice exhibiting mutations in the vitamin D receptor gene also displayed decreased expression of the aromatase gene, abnormal synthesis of estradiol, uterine hypoplasia, and follicular damage. Therefore, for the gonads to function normally in both sexes, appropriate quantities of vitamin D are required[20].

LIMITATIONS OF THE STUDY

The small size of the study groups and being single-center study are the main drawbacks of the present study.

CONCLUSION

The current study indicated that women with sexual dysfunction had a low vitamin D3 level.Vitamin D3 deficiency, not testosterone or estradiol, was found to have a substantial impact on arousal and the full FSFI Score.

CONFLICT OF INTEREST

There are no conflicts of interest.

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