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Serum Level of Vitamin D, Testosterone, Estrogen in Females with Sexual Dysfunction: A meta-analysis

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Abstract:

Introduction: One of the most important fat-soluble vitamins is vitamin D. Hypovitaminosis D has been linked to dysfunction in sexual activity in both healthy females and males with erectile dysfunction. Detecting the impact of vitamin D on female sexual activity via the estrogen and testosterone hormones was an intriguing research topic.

Aim of the study: The target of this research is to examine role of Vitamin D on female sexual dysfunction and in what way.

Subjects and methods: This meta-analysis follows the PRISMA flow diagram. This research aims to detect the impact of vitamin D on female sexual function by measuring vitamin D, testosterone, and estrogen serum levels in cases with FSD compared with normal females.

Results: After the search and screening, one study was eligible for inclusion in our meta-analysis. Results of the meta-analysis show that the quantity of serum vitamin D3 was decreased in females with FSD compared with controls, and the domain scores were also connected with the amounts of vitamin D3. There was a statistically significant negative relationship between the BDI and the whole FSFI scale. There is no statistically significant relationship between hormone levels and the Female Sexual Function Index.

Conclusion: Our findings show that there is an association between vitamin D insufficiency and female sexual dysfunction. FSD was also associated with depression symptoms.

Key words: Vitamin D; Estrogen; Testosterone; Female Sexual Dysfunction; Male Sexual Dysfunction; Alopecia Areata; Vitiligo.

1. Introduction

Female sexual dysfunction (FSD) is known as problems observed by a female during any stage of normal sexual engagement, including physical pleasure, orgasm, interest, preference, and arousal [1]. FSD is a widespread issue that affects about 40% of women; however, there are some treatment options. It is a growing and widespread issue. Common symptoms of FSD include decreased vaginal lubrication, soreness and discomfort during intercourse, a decreased sense of desire, and orgasm problems [2].

Vitamin D has paracrine, endocrine, and autocrine activities. Sunlight, nutrition, and vitamin D supplementation are all sources of vitamin D [3]. Hypovitaminosis D is linked to sexual dysfunction in healthy women and erectile dysfunction in males when other diseases are present [4]. The primary sex hormone in males is testosterone. In men, testosterone is important in the formation of male reproductive tissues such as the testes and prostate, in addition to the development of secondary sexual features like body hair growth and increased muscle and bone mass [5]. Androgens may have a role in the regulation of vaginal tissue physiology and female genital sexual arousal [6]. Estrogen, or estrogen, is the predominant female hormone. In both males and females, estrogen levels are lower than androgen levels [7]. Although estrogen levels in men are significantly lower than in women, estrogen plays important physiological roles in men [8]. Estradiol and testosterone are both important steroid hormones for controlling female sexual desire [9].

Vitamin D deficiency affects other sexual disorders, like erectile dysfunction in male sexual dysfunction [10]. Also, it was found by other studies that some dermatological diseases are exaggerated by vitamin D deficiency, as in alopecia areata [11] and vitiligo [12].

2. Subjects and methods

2.1. Subjects

This meta-analysis follows the PRISMA flow diagram and the guidelines of the Cochrane Handbook.

Eligibility Criteria

Inclusion criteria included:

- Adult females aged between 20 and 45 years.
- Females suffering from sexual dysfunction according to FSFI score.

Exclusion criteria included:

- Patients with depression and diseases affecting Vitamin D level.
- Cases on antidepressant drugs.
- Cases that are not sexually active.

2.2. Information Sources

We searched PubMed, Scopus, Web of Science, and Cochrane CENTRAL databases till April 2021 for related records. The research involves the following 4 articles: Vitamin D3 deficiency is associated with female sexual dysfunction in premenopausal women, Vitamin D and Male Erectile Function, Vitamin D insufficiency alopecia areata patients, Decreased circulatory levels of Vitamin D in Vitiligo.

2.3. Search and Study Selection

Interventional and observational studies included peoples with sexual dysfunction and depression disorders. There are three steps. The initial stage entailed transferring the results of electronic databases to a Microsoft Excel [4] sheet via EndNote Software [13]. The second phase was carried out by two different authors and includes title and abstract screening as well as full-text examination of the articles put into the Excel sheet. Step 3 of the involved citations from step 2. In addition, we personally checked the references of the involved papers for any potential missing research.

2.4. Data Collection

We collected data regarding:

- The baseline demographics of included participants.
- Outcome endpoints which included Vitamin D level in the serum
- The third category involved data for assessing the likelihood of bias. The data collection process was conducted utilizing Microsoft Excel [14].

2.5. Risk of bias Assessment

Two authors utilized Cochrane's risk of bias tool for clinical trials to assess the risk of bias in the included papers [15]. The tool evaluates patient randomization, allocation concealment & sufficient blinding across seven domains [16]. Each domain is put to either “low”, “unclear”, or “high” risk of bias.

2.5. Main outcome and measures

All outcomes, including decreased vitamin D levels in female sexual dysfunction cases, decreased vitamin D levels in other sexual disorders such as erectile dysfunction in male sexual disorder, and decreased vitamin D levels

in many dermatological diseases, such as vitiligo and alopecia areata, were formulated prior to data collection.

2.6. Analysis

We used Review Manager Software to do the meta-analysis for this study, which included both continuous and dichotomous outcomes. We used mean difference (MD) and 95% confidence interval (CI) to analyse continuous data. While dichotomous data were analysed using risk ratio (RR) and 95% CI, all data from different independent experiments were displayed as mean standard deviation [11]. The students t-test method was used to compare two groups, and a one-analysis of variance (ANOVA) approach was utilised to compare the variance among at least three groups. Statistical significance is described as a p value less than 0.05.

3. Results

A systematic review of one article discovered that hypovitaminosis D is involved in female sexual dysfunction; this meta-analysis revealed that vitamin D is significantly reduced in female sexual dysfunction cases compared to the control group, as well as in other sexual disorders such as erectile dysfunction in male sexual disorders and many dermatological diseases such as alopecia areata and vitiligo (**Figure 1**).

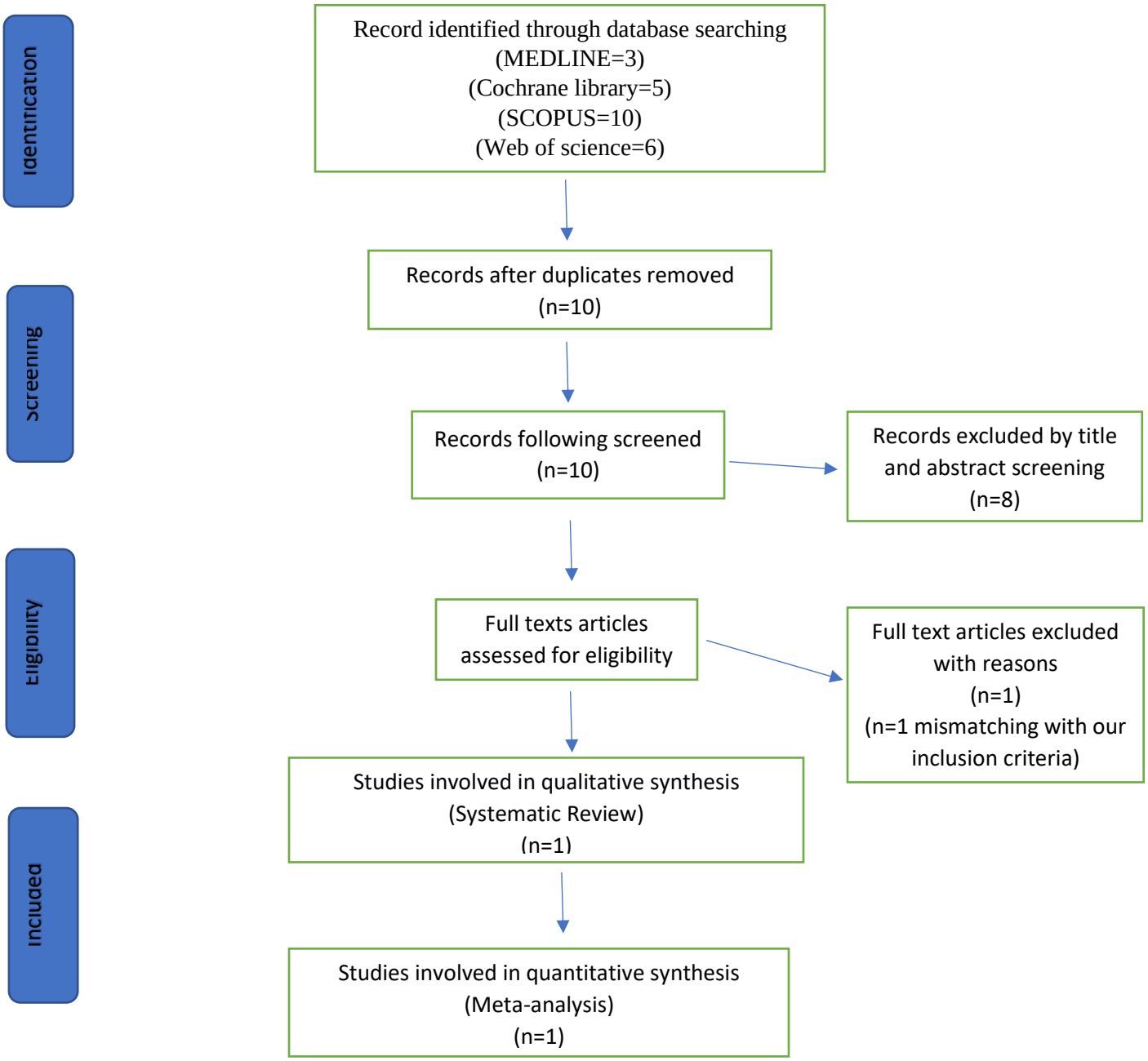

Figure1: The PRISMA flow diagram of our literature search.

3.1. Conclusions and relevance

This systematic review and meta-analysis discovered that hypovitaminosis D plays a part in the etiology of female sexual

dysfunction and other sexual and dermatological disorders. Vitamin D supplements will be very important in the management plan for female sexual dysfunction (**Table 1**).

Table 1. The relationship of Vitamin D3 and BDI score with FSFI score between the groups.

Variables	Group 1 (FSFI score > 26.55)	Group 2 (FSFI score ≤ 26.55)	P-value.
Vitamin D3	26.3 ± 11.7 nmol/L	15.9 ± 8.4 nmol/L	0.0001
BDI score	9.5 ± 4.9	15.4 ± 8.2	0.0001

Vitamin D levels were significantly diminished in the FSD group compared to the control group, which shows that FSD has more depression symptoms than the control group (**Table 2**).

Table 2: Correlation between FSFI and Vitamin D3, BDI score according to Spearman correlation coefficient.

		FSFI score	Desire	Arousal	Lubrication	Orgasm	Satisfaction	Pain
Vitamin D3	R	0.388	0.334	0.377	0.297	0.340	0.228	0.248
	P	0.0001	0.0001	0.0001	0.002	0.0001	0.018	0.010
BDI b score	R	-0.492	-0.322	-0.408	-0.437	-0.398	-0.309	-0.435
	P	0.001	0.001	0.0001	0.0001	0.0001	0.001	0.0001

In a summary, the meta-analysis of this study revealed a significant decrease in vitamin D level in female sexual dysfunction cases as compared to control, depression score is higher in female sexual dysfunction cases as compared to control, significant diminish in vitamin D level in erectile dysfunction in males, significant diminish in Vitamin D level in alopecia areata disease, and significant diminish in Vitamin D level in vitiligo disease.

4. Discussion

FSD can have a significant impact on the quality of life of many women. It has been discovered that 40% of females in the United States experience sexual issues, which are frequently misunderstood and ignored. Female sexual dysfunction is difficult to diagnose since it is multifaceted [17]. Calciferol is another term for vitamin D3, a fat-soluble vitamin found in a variety of foods and as a dietary supplement. It is also created endogenously from ultraviolet (UV) rays when they enter the skin and promote the process of its synthesis. Testosterone is the primary male sex hormone, produced mostly by the testes [18]. It's carried into the bloodstream by the protein sex-hormone-binding globulin (SHBG), and testosterone is a significant but mysterious female hormone [18]. It operates directly as an androgen and also as an important precursor for the creation of estradiol; nevertheless, the management of testosterone production in women is unknown due to the lack of a feedback loop covering its production. In females, testosterone has physiological effects in both reproductive and non-reproductive tissues [14]. Estrogen is the most important female sex hormone, and it plays important roles in both reproductive and non-reproductive tissues. Estrogen can be produced in non-reproductive tissues, for example, the liver, brain, bone, heart, and muscle, and this is consistent with the range of estrogen activities [7].

In the present research, A total of 4 articles searching for vitamin D's function in the pathogenesis of female sexual dysfunction and other sexual and dermatological diseases found a significant relationship between vitamin D deficiency and female sexual dysfunction, erectile dysfunction, vitiligo, and alopecia areata. There was highly statistically significant variance between the control and case groups regarding vitamin D levels. Our findings are in accordance with Canat and his colleagues, as they found that there is a link between FSD and a deficiency of vitamin D3 [17]. Annweiler and his colleagues revealed that severe cognitive impairment is associated with hypovitaminosis D. A lack of vitamin D3 may affect female sexual dysfunction through impaired cognitive processes [17]. In our study, there was no statistical variance among cases and control groups concerning age, and this comes in line with a study by Hayes and his colleagues, who

reported that given the age-related decrease in female sexual function, one could suggest that sexual disorders or dysfunctions would elevate with age. Most sexual disorders or dysfunctions appear to decline with age, and sexual pain disorders seem to decrease; an age-related decrease in sexually associated personal suffering may help explain this. As a result, the significance of sex appears to diminish with age [1].

Also, in this study, we found that there is no statistically significant correlation or relation between serum testosterone and serum estrogen levels, age, depression score, or FSFI score with serum vitamin D level. In this research, we discovered that there is a negative impact of vitamin D that is not related to estrogen nor testosterone hormones in developing female sexual dysfunction, as there was no relation nor correlation between estrogen and testosterone with vitamin D and the FSFI score. This comes in line with a study by Basson in which he concluded that there is no evidence of low androgen activity in females with low sexual libido [19].

Limitations

This study has numerous limitations, including the fact that it is a case-control study, which may be related to a retrospective nature and does not indicate causation.

Conclusion

This systematic review and meta-analysis propose that vitamin D plays a major role in the etiology of FSD and other sexual and dermatological diseases. Understanding the possible factors and biological pathways involved in the etiology of female sexual dysfunction will help us develop effective treatments.

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Conflicts of Interest: The authors declare no conflicts of interest.

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