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Original Article

Can long-term treatment of hashimoto's thyroiditis effectively improve sexual dysfunction in women?

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ABSTRACT

Aims: Numerous studies have identified thyroid diseases as a significant risk factor for women's sexual health. This study aimed to evaluate how treatment of women diagnosed with Hashimoto's thyroiditis affected their sexual function and psychological well-being, comparing them with a control group.

Methods: In this study, 61 sexually active women with permanent primary hypothyroidism, diagnosed for at least one year and treated for at least 6 months between January 2022 and December 2023, were included. The inclusion criteria for group 1 were as follows: participants had to have overt hypothyroidism with a thyroid stimulating hormone level >10 IU/ml and a serum free T4 level <0.86 ng/dl. The control group comprised 31 sexually active, age-matched, healthy women.

Results: Response to treatment was assessed using the Female Sexual Function Index questionnaire and the Beck Depression Inventory by interview. No significant difference was found between the two groups in terms of Female sexual function index parameters and Beck depression scores (p: 0.198 and p:0.353 respectively) except in TSH levels (p: 0.016).

Conclusion: Long-term (at least 6 months) treatment of hypothyroidism may be able to improve sexual dysfunction in women. Further studies of larger series and longer treatment follow-up are needed to confirm the present findings.

Keywords: Hashimoto's thyroiditis, female sexual dysfunction, hypothyroidism

INTRODUCTION

The interaction between the neurological, endocrine, and circulatory systems plays a critical role in human sexuality, as it is a complex physiological process. Additionally, diverse sexual orientations and behaviors may have associations with mental health.[1] Due to the less defined parameters of female sexual dysfunction (FSD) compared to those of male sexual dysfunction, accurately determining the prevalence of sexual dysfunction in women poses a significant challenge. Sexual dysfunction refers to a condition that occurs during the sexual response cycle, hindering an individual from obtaining satisfaction from their sexual activities.[2]

In recent years, there has been increased awareness of FSD. This condition includes a range of issues and can significantly affect a woman's quality of life. Therefore, it is important to conduct thorough patient screening and diagnosis before starting appropriate treatment.[3]

Arousal, desire, orgasm, lubrication, pain/discomfort, and satisfaction are the key categories used to define FSD.[4] Studies have revealed that FSD affects a substantial proportion of women, with estimates ranging from 40% to 60%.[5] Importantly, sexual dysfunction can be associated with endocrine pathologies and may serve as an indicator of more severe endocrine disorders.[6]

Hashimoto's thyroiditis is a leading cause of hypothyroidism in regions with sufficient iodine intake. It is an autoimmune disorder initiated by environmental triggers in individuals with a genetic predisposition.[7] The condition predominantly affects young and middle-aged women, with its prevalence increasing with age. The annual incidence is estimated at 0.3 to 1.5 cases per 1,000 individuals, with a female-to-male ratio of approximately 7:1.

Patients with Hashimoto's thyroiditis typically present with lymphocytic infiltration of the thyroid gland and elevated serum levels of thyroid autoantibodies, including anti-thyroglobulin (anti-Tg) and anti-thyroid peroxidase (anti-TPO).[8] Although irregular menstruation and infertility are frequently associated with hyperthyroidism, female sexual dysfunction, menstrual irregularities, anovulation, and impaired fertility can also occur in both overt and subclinical hypothyroidism.[9,10]

While thyroid gland hyperactivity and hypoactivity are more prevalent in women of all ages than in men, there have been limited studies utilizing the Female Sexual Function Index (FSFI) to assess the impact of thyroid disorders on women's sexual function. Most of these studies have been based on small, randomized, population-based samples and selected

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patient populations. However, many of them have indicated a connection between thyroid disease and sexual dysfunction, particularly in women.[11] The incidence of sexual dysfunction (SD) in women with hypothyroidism ranges from 22% to 46%. Numerous studies indicate a significant correlation between hypothyroidism and SD, demonstrating a notable decrease in FSFI scores among women with hypothyroidism compared to control groups.[6,10,12-14] Nevertheless, some studies in the literature have reported contradictory results.[15,16]

To date, no studies have specifically evaluated the effects of long-term treatment on changes in thyroid function among women with permanent hypothyroidism secondary to Hashimoto's thyroiditis. The present study aimed to investigate the impact of long-term treatment on sexual function and psychological well-being in female patients diagnosed with Hashimoto's thyroiditis, by comparing outcomes with those of a matched control group.

METHODS

The study received approval from the Fırat University Non-interventional Researches Ethics Committee (Date: 18.02.2022, Decision No: 2022/02-10). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Before the study, we obtained informed consent from all patients and women in the control group. In this study, 61 sexually active women with permanent primary hypothyroidism, diagnosed for at least one year and treated for at least 6 months between January 2022 and December 2023 were included (group 1). The inclusion criteria for group 1 were as follows; participants had to have overt hypothyroidism with a thyroid stimulating hormone (TSH) level >10 IU/ml and a serum free T4 level <0.86 ng/dl. Additionally, they needed to exhibit diffuse fibrous bands and/or a lobular appearance and/or pseudonodule appearance on thyroid ultrasonography, have anti thyroid peroxidase (TPO) and anti thyroglobulin (TG) antibodies before treatment, and have received levothyroxine treatment at a dose of 1.2-1.8 µg/kg/day for at least 6 months. The target posttreatment TSH level was considered to be 0.4-4.5 mU/L on average.[8] The control group comprised 31 sexually active, age-matched, healthy women (group 2). All patients in group 1 were monitored and treated at the endocrinology outpatient clinic of Fırat University Hospital. We assessed demographic characteristics such as age, education level (primary, high school, or university graduate), smoking, alcohol use, income status, number of births, and occupational status (whether they had an occupation or not) for all women. Participants with neurological disease, cardiovascular disease, a history of previous pelvic surgery, major psychiatric illness, premature ovarian failure, diabetes and those who have not engaged in sexual activity in the last month, as well as individuals diagnosed with secondary or subclinical hypothyroidism with abnormal TSH levels outside of the post-treatment target, pregnant or breastfeeding women, and participants using any medication other than levothyroxine that may affect thyroid function or sexual response were excluded from the study. The study included women who were in stable heterosexual relationships and were sexually active.

The Female Sexual Function Index questionnaire was completed using a mutual interview method. This questionnaire is comprised of 19 questions, validated in Turkish, and assesses 6 parameters including arousal, orgasm, sexual desire, lubrication, pain, and satisfaction. It aims to evaluate sexual functioning and any associated issues within the past 4 weeks. The questionnaire includes 19 questions, each with a specific scoring range. 1. Questions 1 and 2 focus on sexual desire and are scored between 1 and 5 points. 2. Questions 3, 4, 5, and 6 assess sexual arousal, with a scoring range of 0-5 points. 3. Questions 7, 8, 9, and 10 pertain to vaginal lubrication and are also scored on a scale of 0-5 points. 4. Questions 11, 12, and 13 are about orgasm and carry a scoring range of 0-5 points. 5. Questions 14, 15, and 16 analyze sexual satisfaction and are rated between 1 and 5 points. 6. The last three questions, 17, 18, and 19, evaluate pain during intercourse and are scored between 0-5. The following coefficients are used to assess female sexual function: 0.6 for desire, 0.3 for arousal and lubrication, and 0.4 for orgasm, satisfaction, and pain. If the total score is less than 26.55, it is considered indicative of female sexual dysfunction.[17]

The Beck Depression Inventory (BDI) is a self-reported inventory consisting of 21 items, previously adapted for the Turkish population.[18,19] Each of the 21 questions is rated on a scale of 0 to 3 (none to severe), with the highest possible total score being 63. Psychiatric evaluation was conducted using the BDI, and a diagnosis of depression was made when the BDI score was 17 or higher.

Statistical Analysis

We conducted statistical analysis using the SPSS (Statistical Package for Social Sciences for Windows 22) software package (IBM Corp. Armonk, NY). Mean values were reported as median (minimum-maximum) for descriptive continuous variables. Categorical variables were presented as frequency and percentage. We used the Pearson chi-square test to compare categorical variables between groups and the non-parametric Mann-Whitney U test to compare continuous variables between two independent groups. A significance level of $\alpha=0.05$ was set for all statistical tests conducted.

RESULTS

Post Hoc power analysis was performed for our study. The calculated power (1-beta) based on this test is 0.852, considering type I error (alfa) of 0.05, sample size of 30, effect size of 0.79 and two-sided alternative hypothesis (H1). The average age of the 61 hypothyroid patients participating in the study was 39.25 (±8.04) years, while it was 35.73 (±6.17) years in the control group. The average duration of treatment was 263.8 days (181-328). The two groups did not differ significantly in terms of age (p: 0.106). Demographic details for both groups can be found in **Table 1**.

Apart from TSH levels, there were no other significant differences between the two groups in terms of variables (**Table 2, Figure a, b**).

In the control and hypothyroidism groups, there was no correlation between the parameters within the groups (**Table 3**).

DISCUSSION

Numerous studies have identified thyroid diseases as a significant risk factor for women's sexual health. Despite considerable research, the precise mechanisms through which thyroid diseases trigger FSD remain incompletely understood. Notably, investigations in women have highlighted the crucial

Table 1. Demographic characteristics of the groups

Categories	Group 1 (n: 61, %)	Group 2 (n: 31, %)
Education level		
No literacy	1 (1.63%)	0 (0%)
Primary school	1 (1.63%)	0 (0%)
Middle school	25 (40.98%)	0 (23.3%)
High school	20 (32.78%)	4 (12.90%)
University	14 (22.98%)	27 (37.20%)
Economic status		
Low	24 (39.34%)	0 (0%)
Middle	16 (26.23%)	0 (0%)
High	21 (34.43%)	31 (100%)
Occupation		
Housewife	47 (77.09%)	0 (0%)
Retired	1 (1.63%)	0 (0%)
Worker	1 (1.63%)	7 (22.58%)
Officer	12 (19.68%)	23 (74.19%)
Self-employed	0 (0%)	1 (3.23%)
Other	0 (0%)	0 (0%)
Smoking status		
Yes	9 (14.75%)	9 (29.03%)
No	52 (85.25%)	22 (70.97%)
Alcohol use		
Yes	0 (0%)	2 (6.45%)
No	61 (100%)	29 (93.55%)
Number of children		
None	8 (13.12%)	2 (6.45%)
1	9 (14.75%)	11 (35.50%)
2	28 (45.90%)	10 (32.25%)
3 or more	16 (26.23%)	8 (25.80%)

Table 2. The median values of the hypothyroid and control groups, respectively, and the p-values in the comparison between the groups

	Group 1 (hypothyroid)	Group 2 (control)	p
BMI	27.42 (±5.77)	25.50 (±3.35)	0.094
Waist circumference	89.52 (±12.92)	85.00 (±10.74)	0.157
Total cholesterol	180.14 (±43.28)	165.72 (±49.64)	0.164
LDL	120.58 (±36.96)	108.32 (±42.21)	0.161
Triglyceride	130.97 (±67.32)	120.05 (±60.76)	0.455
HDL	53.02 (±12.34)	53.96 (±14.61)	0.752
FSH	10.95 (±13.44)	8.92 (±9.72)	0.970
LH	9.16 (±9.68)	6.74 (±7.22)	0.242
Prolactin	12.47 (±9.93)	14.07 (±20.03)	0.882
Fasting blood glucose	90.51 (±13.29)	86.35 (±10.98)	0.138
fT3	2.96 (±0.47)	3.09 (±0.50)	0.187
fT4	1.20 (±0.25)	1.12 (±0.13)	0.112
TSH	4.49 (±4.88)	2.30 (±1.09)	0.016
Desire	3.18 (±1.06)	3.01 (±1.30)	0.546
Arousal	2.90 (±1.16)	2.28 (±1.44)	0.052
Satisfaction	3.52 (±1.32)	3.52 (±1.13)	0.995
Lubrication	2.55 (±1.05)	2.29 (±1.19)	0.668
Orgasm	2.56 (±1.20)	2.48 (±0.93)	0.365
Pain	2.19 (±2.01)	2.03 (±1.72)	0.827
Total FSFI	17.51 (±5.00)	16.00 (±5.36)	0.198
Beck depression score	15.77 (±9.43)	14.01 (±6.34)	0.353

BMI: Body-mass index, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, FSH: Follicle-stimulating hormone, LH: Luteinizing hormone, fT3: Free triiodothyronine, fT4: Free thyroxine, TSH: Thyroid stimulating hormone, FSFI: Female Sexual Function Index

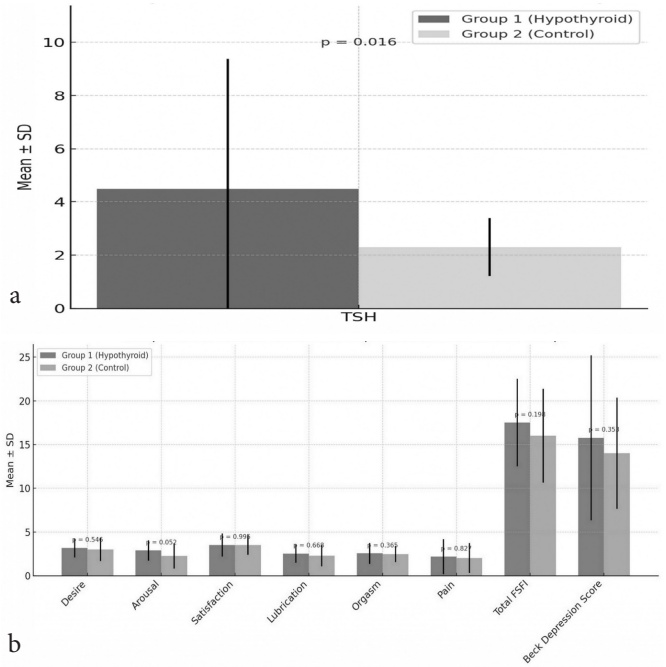

Figure. a) Comparison of TSH levels between groups, b) Comparison of sexual function and depression scores between groups

TSH: Thyroid stimulating hormone

Table 3. p and r values in comparison of parameters within the control and hypothyroidism groups

Group 1 (hypothyroid)	FSFI	Beck score
Beck score	0.232 (0.158)	
T3	0.135 (-0.254)	0.713 (-0.063)
T4	0.325 (-0.130)	0.411 (-0.108)
TSH	0.955 (-0.008)	0.614 (-0.067)
Group 2 (control)		
Beck score	0.260 (-0.216)	
T3	0.596 (-0.103)	0.401 (0.156)
T4	0.728 (-0.067)	0.638 (-0.088)
TSH	0.555 (0.114)	0.110 (0.293)

FSFI: Female Sexual Function Index, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid stimulating hormone

role of low circulating levels of thyroid hormone as one of the primary factors influencing the development of FSD. This suggests a complex interplay between thyroid function and sexual health that warrants further investigation. The study conducted by Oppo et al.[14] revealed a compelling link between the circulating levels of TSH, free thyroxine (fT4) and the degree of FSD in women with hypothyroidism. Changes in the functioning of the hypothalamic thyroid axis can lead to disruptions in prolactin levels, while variations in circulating thyroid hormone levels can impact the genitals due to the presence of thyroid hormone receptors. These physiological conditions are particularly important to consider. The increased levels of prolactin due to hyperprolactinemia have inhibitory effects on the pulsatile release of gonadotropin-releasing hormone. This, in turn, leads to a decrease in the production of dehydroepiandrosterone (DHEA), estrogen and testosterone. It has been claimed that symptoms such as mood disorders, fatigue and depression may also indirectly lead to FSD.[14,20]

In studies conducted in women with hypothyroidism undergoing FSFI, statistically significant decrease was found in the subdomain scores of FSFI in a way inversely

proportional to TSH towards fT4 when comparing women with clinical hypothyroidism with healthy controls.[14]

In their study, Atis et al.[7] demonstrated that the FSD levels were notably elevated in women diagnosed with subclinical hypothyroidism and clinical hypothyroidism, particularly when their TSH levels exceeded 10 mU/L, in comparison to women in the healthy control group. In a recent study including 104 women diagnosed with clinical hypothyroidism (Hashimoto's thyroiditis, nodular goiter, idiopathic hypothyroidism,), significant decreases in parameters such as, arousal, lubrication and desire were observed compared to the control group. However, no significant differences were found in subdomains such as overall FSFI score, satisfaction, sexual pain or orgasmic function.[6] Veronelli et al.[21] indicated that there was a negative correlation between the presence of antithyroid antibodies and the FSFI score. The results of the study by Krysiak et al.[12] involving 50 women with hypothyroidism indicated that women with hypothyroidism caused by inflammatory infiltration of the thyroid gland had lower rates of FSD compared to those with hypothyroidism caused by other factors such as radiotherapy, iodine deficiency, radioiodine therapy, thyroid hypoplasia or thyroid surgery. In a comparative study involving 16 euthyroid women with Hashimoto's thyroiditis and 18 controls, it was observed that the rate of FSD, as determined by the FSFI score, was notably lower in patients with subclinical autoimmune hypothyroidism, yet comparatively higher than in the control group. The authors suggested that this situation could potentially result in thyroid dysfunction due to the combined impact of autoantibodies and hormonal dysregulation. They found an inverse relationship between TPO antibody levels and total FSFI scores, lubrication, sexual satisfaction and sexual desire in individuals with euthyroid Hashimoto's thyroiditis and autoimmune subclinical hypothyroidism.

Thyroid autoimmunity was found to be significantly linked to hypoactive sexual desire disorder (HSDD) regardless of thyroid function. No significant differences were observed in other parameters compared to the control group, and there was no discernible relationship between FSFI scores and TSH or T4 levels ($p>0.05$).[14]

Pasquali et al.[6] discovered that women with Hashimoto's thyroiditis had a lower total FSFI score than the established cut-off value. However, there was no significant difference compared to the control group. The existing data regarding the impact of euthyroid hormone therapy on sexual function in women is conflicting. Nevertheless, similar to hypothyroidism in women, it is believed that the existence of autoantibodies may contribute to the development of sexual dysfunction in this specific patient population. In studies conducted in women with hypothyroidism undergoing FSFI, statistically significant reductions were found in the subdomain scores of FSFI inversely proportional to TSH and propotional to fT4.[14]

Contradictory results have been found in studies on subclinical hypothyroidism. One study involved 25 untreated women with subclinical hypothyroidism, 20 women with clinical hypothyroidism, and 25 age-matched healthy women. The findings indicated that 56% of the women with clinical hypothyroidism, 54.6% of those with subclinical hypothyroidism, and only 14.6% of the control group experienced FSD.[10] In a comprehensive study by Luo et al.,[15] 1,119 Chinese women were surveyed, with 168 diagnosed with subclinical hypothyroidism and 951 healthy controls. The results revealed no significant variance in FSD rates between the two groups. Furthermore, detailed subgroup analysis showed no noteworthy differences in the occurrence of low arousal, low desire, decreased orgasm, poor lubrication, sexual pain and low satisfaction between the two groups. A similar conclusion has been speculated by Hong et al.[16]

Correction of hypothyroidism in women has been associated with improvements in sexual function. Administration of L-thyroxine is known to normalize prolactin levels in the majority of patients with hypothyroidism. This reduction in prolactin levels has been proposed as a potential mechanism for decreasing the incidence of female sexual dysfunction (FSD) in this population.[22] As a matter of fact, Oppo et al.[14] showed that after 3 months of treatment, the desire, satisfaction and pain areas of FSFI were completely normalized, while the arousal and orgasm areas were largely unchanged in hypothyroid patients, and that this partial response was probably due to the short period of time, and that full normalization of the sexual function was possible after a longer treatment. The strong connection found between serum fT4 and TSH and FSFI in both treated and untreated hypothyroid women suggests that reduced levels of circulating thyroid hormones play a significant role in FSD associated with hypothyroidism.

In another study, Pasqueli et al.[6] found that 33% of women with hypothyroidism who were receiving treatment for Hashimoto's thyroiditis showed no significant difference in FSD or FSFI scores compared to the control group.

Gomez et al.[23] definitively established that hypothyroid women experience a significantly higher prevalence of desire, penetration pain, and sexual dysfunction during intercourse, even when effectively treated with levothyroxine. They confidently asserted that this phenomenon is a result of hypothyroidism causing dysfunction in sexual response.

These studies suggest that some aspects of sexual dysfunction in women with thyroid disorders are reversible. In our study, improvement was found in all aspects of FSFI scores of Hypothyroid patients. We may conclude the improvement of all parameters to the longer duration of treatment and long-term regulation of the circulating thyroid hormone level.

In our study, only TSH values showed a significant difference between the groups, and this can be explained by the fact that despite the improvement in free T3 and T4 in the treatment groups, fluctuations in TSH levels are quite frequent and this may be considered as a clinically expected result.

Non-thyroid factors (cardiovascular, endothelial, neurological (somatic/autonomic) and mood changes) have been reported to contribute to the development of FSD in association with hypothyroidism. It has been well known that marked thyroid dysfunction may be associated with reversible mental dysfunctions that may mimic almost every psychiatric symptom profile.[14] As a matter of fact, it has been suggested that thyroid autoimmunity may also be associated with mood disorders, which are mainly represented by refractory depression and anxiety, independent of thyroid function.[24] The fact that the patients we treated also had positive Beck depression scores suggests the positive effects of medical treatment on mood. Therefore, we think that the normal mood of our patients due to the improved active thyroid hormone level also contributes to the improvement of the FSFI results.

Limitations

This study has several limitations, including the low number of cases and the absence of baseline FSFI and BDI data in the hypothyroidism group before treatment. To address this, we implemented a control group to mitigate these limitations.

CONCLUSION

As a result, long-term treatment of hypothyroidism (defined as a minimum duration of six months) may contribute to improvements in sexual dysfunction among women. However, further studies involving larger cohorts and extended follow-up periods are necessary to validate these findings and establish definitive clinical recommendations.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Fırat University Non-interventional Researches Ethics Committee (Date: 18.02.2022, Decision No: 2022/02-10).

Informed Consent

Before the study, we obtained informed consent from all patients and women in the control group.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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