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Is Hashimoto Thyroiditis a risk factor in male infertility?

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Abstract

Hashimoto's thyroiditis is known as thyroid dysfunction and is one of the most common endocrine diseases worldwide. This study seeks to investigate thyroid dysfunction in the male reproductive system. Normal thyroid function is crucial for male reproduction. Semen quality parameters are among the most critical factors affecting male fertility. The main aim of this research was to investigate the effect of thyroid dysfunction on semen quality parameters such as sperm motility, number, and morphology. This cross-sectional retrospective case-control study was conducted between December 2021 and May 2022 in Bahcesehir University Göztepe Medicalpark Hospital Invitro Fertilization center. Patients with Hashimoto's thyroiditis (n=52) were included in the study as the case group. The control group was selected from age and body mass index (BMI)-matched patients who underwent semen analysis (n=57). The participants' age and BMI were 30.90±4.45 and 24.49±1.46, respectively. When we evaluated semen analysis results, we found the number of sperms ($p<0.001$), motility ($p<0.01$), and morphology ($p<0.001$) were significantly better in the controls than in the patients with Hashimoto's thyroiditis. Oligozoospermia, asthenozoospermia, and oligo-asthenozoospermia as sperm abnormalities were observed in patients with Hashimoto's thyroiditis. Hashimoto's thyroiditis has a negative effect on semen quality parameters such as sperm motility, number, and morphology. Evaluation of infertile men is recommended in terms of thyroid dysfunction.

Keywords: male infertility, Hashimoto's thyroiditis, semen quality, sperm abnormality

1. Introduction

Male infertility affects at least 7% of men worldwide as a common condition (1). Male infertility responds poorly to the initial treatments and is mostly cured with secondary treatments (2). About 30 to 50% of male infertility cases are known as idiopathic due to low-quality of spermatozoa (3). The main causes of male infertility in the world are defective spermatozoa due to reduced sperm counts, abnormal structure/morphology, and poor motility which have been reported in several publications (4, 5).There has been a global decline in the semen quality in the past few decades (6).

The thyroid gland is the most important gland affecting the body's metabolism and actions. Although thyroid dysfunction is more common in women than men, these disorders also occur in men, affecting their physical and sexual health (7). The most significant adverse effects include a decrease in the number and motility of sperm, which reduces male fertility. Male sexual function is affected by thyroid function, and men with thyroid disorders experience varying degrees of sexual disorders, including delayed ejaculation, erectile dysfunction, premature ejaculation, and reduced sexual desire (8, 9).

Hashimoto's thyroiditis as thyroid dysfunction is one of the prevalent diseases worldwide (8). Hashimoto thyroiditis is characterized by tertiary lymphoid follicles development, chronic inflammation, and higher concentrations of circulating autoantibodies against thyroglobulin (anti-TG) and thyroid peroxidase (anti-TPO) as an organ-specific autoimmune disease (9). Measuring serum anti-TG and anti-TPO levels enables the diagnosis of chronic autoimmune thyroiditis. Since anti-TG will be found to be high in almost all patients with autoimmune thyroid disease and anti-TPO positivity, this antibody has no significant effect on the diagnosis. The frequency of autoimmune thyroid disease with low anti-TPO and high anti-TG levels is around 5%. Anti-TPO and anti-TG are positive at a rate of 95-100% in Hashimoto's thyroiditis (10).

Although male infertility has been increasing and difficult

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to treat, limited studies on risk factors and the main causes of male infertility (11). Considering the sustainable effects of thyroid dysfunction on male fertility and sexual function, timely screening and treatment of thyroid diseases in men with sperm abnormalities and erectile dysfunction should be considered to keep and improve men's health. The present study was conducted to study the impact of Hashimoto's thyroiditis on men's sexual function and fertility.

2. Materials and Methods

The Ethics Committee of Medeniyet University approved this cross-sectional case-control study (Decision no: 2021/0009 Date: 27.01.2021). One hundred nineteen men aged between 25 and 40 were included in this study during December 2021 - May 2022. Out of this group, 57 men were included in the control group, and 52 men with Hashimoto's thyroiditis were included in the case group. A man with fewer than 15 million sperm per ml of semen was accepted as oligozoospermia. Asthenospermia is defined as a less than 40% sperm motility or less than 32% progressive motility (12).

ELISA (BioVendor, Heidelberg, Germany) was used to measure serum Anti-TG, Anti-TPO, fT4, and TSH concentrations. DIAPLUS kit (Toronto, Canada) protocol was followed to perform this hormone assay. The reference ranges of T4 and TSH were 4.4-10.8 µg/dl and 0.39-5.95 µg/dl, respectively. The anti-TG measurement range is 10–4000 IU/mL, and the anti-TPO measurement range is 5–600 IU/mL. Anti-TPO< 35 IU/mL, and anti-Tg< 115 IU/mL were accepted as negative.

Semen samples were collected through masturbation after a 3-4-day sexual abstinence based on the WHO guidelines of 2010 (12). Complete semen analyses were done after liquefaction for 15 to 30 min at room temperature. Once liquefaction was performed, motility of each sample was evaluated at room temperature and its heated microscope stage was standardized for our laboratory.

2.1. Statistical analysis

The normality was checked based on the Kolmogorov-Smirnov test, and the nonparametric tests were conducted considering the non-normality of the groups before the statistical analyses. Mean and standard deviations (SD) measured to check each continuous variable, including age, BMI, FSH, LH, FT4, TSH, Testosterone, Prolactin (ng/ml), volume, number (Millions), motility (%), and morphology. The Mann-Whitney U test performed to study the difference between the two groups. SPSS v22 used for statistical analyses. $p < 0.05$ was regarded as statistically significant.

To calculate the sample size with the GPower 3.1 program, two groups' total mean was measured based on the Mann-Whitney test with the power of 95%, effect size of 50%, and 0.05 type 1 error for at least 92 patients (13).

3. Results

This study included one hundred nine age-matched (30.90 ± 4.45) and BMI-matched (24.49±1.46) men. Table 1 shows descriptive statistics of study parameters.

Table 1. Descriptive statistics of study parameters in the all group (n=119)

Study parameters	median (range)	mean ± SD
Age	32 (25-39)	30.90 ± 4.45
BMI	24.6 (21-29.21)	24.49 ± 1.46
FSH	6 (3.44-9)	6.09 ± 1.11
LH	5 (3.28-8)	5.34 ± 1.08
FT4	1 (0.9-1.41)	1.08 ± 0.11
TSH	2 (1.5-3.2)	2.24 ± 0.39
Testosterone	4.45 (2.44-7.28)	4.49 ± 0.73
Prolactin (ng/ml)	14.8(4.23-19.67)	14.96 ± 2.82
Anti-TPO	11 (3-65)	29.22 ± 24.55
Anti-TG	2.1 (1.5-5)	21.47 ± 25.21
Volume	3 (1.5-5)	3.44 ± 0.74
Number (10^6/ml)	32 (12-95)	35.63 ± 17.31
Motility (%)	56 (19-81)	54.11 ± 13.21
Morphology	5 (2-10)	4.43 ± 1.73

SD, standard deviation

Table 2 shows comparison of case and control groups on the study parameters.

Table 2. Comparison of case and control groups

Study parameters	Case (n=52) M±SD	Control (n=57) M±SD	*p*
Age	30.84±4.27	30.96±4.65	0.907
BMI	24.51±1.49	24.47±1.45	0.442
FSH	6.60±1.13	5.99±0.88	0.058
LH	5.43±1.30	5.27±0.83	0.822
FT4	1.06±0.10	1.09±0.12	0.303
TSH	2.22±0.34	2.26±0.43	0.981
Testosterone	4.48±0.67	4.50±0.78	0.400
Prolactin (ng/ml)	14.98±2.42	14.95±3.16	0.496
Anti-TPO	54.65±3.21	6.03±2.32	**<0.001**
Anti-TG	43.46±1.41	20.10±0.31	**<0.001**
Volume	3.46±0.65	3.42±0.82	0.987
Number (Millions)	28.38±15.71	42.24±16.13	**<0.001**
Motility (%)	46.46±13.26	61.10±8.51	**<0.001**
Morphology	3.34±1.54	5.42±1.23	**<0.001**

M: Mean; N: Number of subjects; BMI: Body mass index; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; FT4: Free T4; TSH: Thyroid-stimulating hormone; T4: Thyroxine; *All variables tested by a Mann-Whitney U test

As stated in Table 2, a Mann-Whitney test did not find a statistically significant association between case and control in regard to age and BMI (*p*-value>0.05).

There was not a statistically significant difference between case group and controls in regard to FSH(*p*-value=0.058), LH (*p*-value=0.822), FT4 (*p*-value=0.303), TSH (*p*-value=0.981), Total Testosterone (P-value=0.400), Prolactin (*p*-value=0.496) and Volume (*p*-value=0.987). Case group and controls showed a statistically significant difference in terms of number of sperm (*p*-value<0.001). The case group had significantly lower count than the controls (M=28.38; SD=15.71 vs. M=42.24; SD=16.13).

Case group and controls showed a statistically significant difference between in regard to Anti-TPO and Anti-TG (*p*-value<0.001).

The group with thyroid dysfunction (M=46.46; SD=13.26) and the healthy group (M=61.10; SD=8.51) showed a significant difference in terms of Motility (p-value <0.001). There was a statistically significant difference between case group and controls in terms of morphology (p-value<0.001). The case group had significantly lower morphology score than the controls (M=3.34; SD=1.54 vs. M=5.42; SD=1.23).

Table 3. Comparison of various sperm abnormalities in case and control groups

Sperm Abnormality	Normal (n=87)	Oligozoospermia (n=8)	Asthenozoospermia (n=14)	Oligo-asthenozoospermia (n=4)
Case	30 (34.5%)	8 (100%)	14 (100%)	4 (100%)
Control	57 (65.5%)	0 (0%)	0 (0%)	0 (0%)

Oligozoospermia was observed in 7.3% (n=8) of our patients (all in thyroid dysfunction group). Also, asthenozoospermia was seen in 12.8% (n=14) of our participants (all in thyroid dysfunction group). Four patients (3.6%) in this study suffered from two (Oligozoospermia and asthenozoospermia). Fig. 1 clearly shows that sperm abnormalities were more common in patients with thyroid dysfunction.

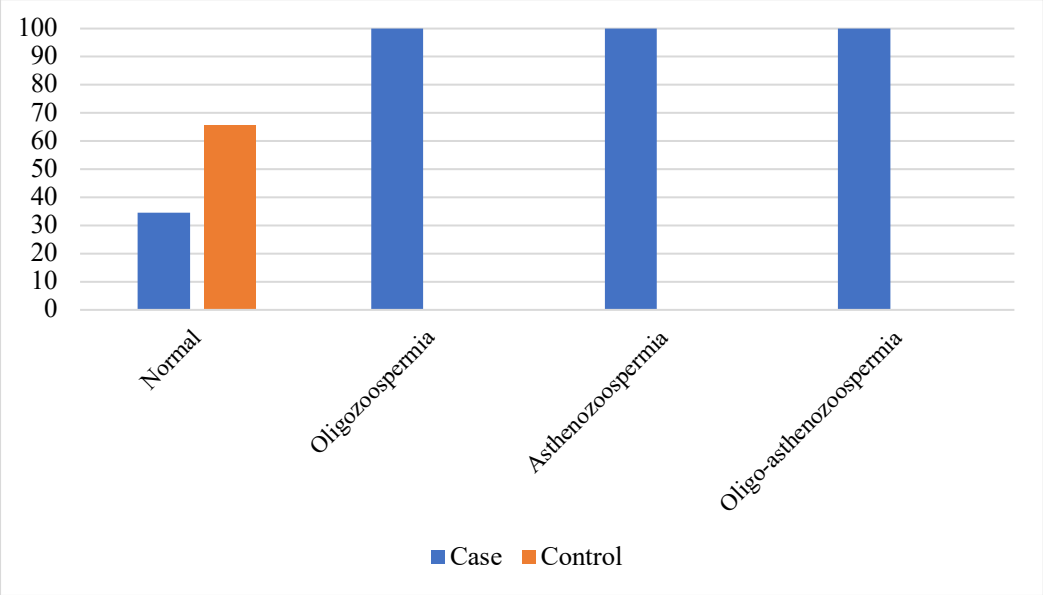

Fig. 1. Frequency of sperm abnormalities in case and control groups

4. Discussion

In this study, the effect of Hashimoto's thyroiditis on semen quality was analyzed. Based on the obtained results, Hashimoto's thyroiditis have significant effects on sperm motility, sperm count, and sperm morphology. These parameters in Hashimoto patients had much lower values than ordinary individuals in the control group. Oligozoospermia, asthenozoospermia, and oligo-asthenozoospermia were observed in the case group. In this regard, Hashimoto's thyroiditis significantly affect the men's reproductive system, and this effect includes reduced sperm motility, reduced sperm count, and a negative impact on morphology.

According to WHO, the quality of semen in men is decreasing (6, 14). Several studies have been conducted in recent years on the factors affecting the quality of semen (15-17). These studies are important because they can provide effective treatment by identifying the factors that reduce the quality. Semen quality is affected by nutritional, socioeconomic and environmental factors, such as rurality (18), phthalate levels (19), air pollution, harmful chemicals, and excessive heat (20). In addition to these factors, autoimmune diseases also affect the quality of semen (21). In the current study, thyroid dysfunction was also identified as a factor in reducing the quality of semen. Abalovich et al.(22) found a significant relationship between thyroid dysfunction and semen quality. Among the semen quality parameters, Hyperthyroidism had the most negative effect on the motility parameter. Krassas et al. (23) reported adverse effects of thyroid dysfunction on sperm morphology and sperm motility. Li et al. (24) reported the negative effect of Triiodothyronine levels on semen measures. Krassas et al. (25) recognized thyroid dysfunction as the cause of reduced sperm motility. These results were in line with studies by, Sengupta (26) and Clyde (27). Kidd et al.(28) reported reduced sperm counts in hyperthyroid men. Lisovskaya et al. (29) observed more thyroid dysfunction in men with sperm abnormalities. Niroomand et al. (30) studied 28 patients with Hyperthyroidism and Hypothyroidism regarding sperm abnormalities. Normozoospermia was seen in 68.75%, pathozoospermia was observed in 32.14%, and asthenospermia in 17.85%.

This study has several limitations. One of the important

limitations is that this is a retrospective design. Another limitation is that the sample size, which is relatively small due to financial constraints. Semen quality is affected by abstinence time for semen analysis, smoking habits, season, and time of sample collection. It is suggested that the samples of semen be collected considering the above-mentioned cases. Therefore, more samples should be studied to show the effect of thyroid disorders on the men's reproductive system.

As a result, Hashimoto's thyroiditis negatively affects the semen quality. Sperm motility and sperm count are lower in men with thyroid dysfunction. Sperm morphology is also negatively affected by Hashimoto's thyroiditis. Evaluation of thyroid antibodies to rule out Hashimoto's thyroiditis, is recommended in all infertile men.

Conflict of interest

The authors have no conflict of interest.

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None to declare.

Authors' contributions

Concept: M.Ö., M.A., Design: M.A., A.A.E., K.G., Data Collection or Processing: A.A.E., K.G., Analysis or Interpretation: M.Ö., M.A., Literature Search: M.Ö., M.A., A.A.E., KG., Writing: M.A., M.Ö.

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