

Assessment of Thyroid Functions and its Relationship With Semen Quality in Men

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Abstract

Introduction: In recent years, a partial relationship has been discovered between thyroid hormones and the formation of germ cells and the process of spermatogenesis. The current study aimed to assess thyroid hormone levels and the relationship between those levels and semen quality.

Methods: Forty-seven infertile males, as the treatment group, and 25 healthy individuals, as the control group, were enrolled in this study. Thyroid-stimulating hormone (TSH), triiodothyronine (T3) hormone, and tetraiodothyronine (T4) hormone were calculated, and the parameters of seminal fluid (count, motility, and morphology) were assessed for semen quality.

Results: The results demonstrated that sperm counts, sperm motility%, and normal morphology% were significantly lower in the infertile male group compared with the healthy group. The results further represented a highly significant level of TSH and total T3, while the total T4 was negligible in the infertile male group in comparison with the healthy group. The infertile male group was divided into subgroups based on sperm abnormalities, including asthenozoospermia, oligozoospermia, and azoospermia. Based on the findings, there was a significant reduction in TSH, T3, and T4 levels in oligozoospermia compared with the other groups. However, the levels of TSH, T3, and T4 were significantly higher in asthenozoospermia compared with the other groups, demonstrating the existence of a relationship between thyroid indicators and Asthenozoospermia.

Conclusion: Overall, the mean serum levels of TSH, T3, and T4 were significantly lower in the infertile male group compared with the healthy group. Thus, they were negatively associated with sperm counts, motility%, and normal morphology%. Hence, these negative impacts on thyroid hormones were associated with different sperm abnormalities and semen quality in the infertile males group.

Keywords: Thyroid hormones, Asthenozoospermia, Oligozoospermia, Azoospermia

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Introduction

Based on estimations, 48.5 million couples or 15% of couples worldwide struggle with infertility. Approximately 20%-30% of infertility cases were primarily from males, contributing to 50% of all instances overall, although the world as a whole is not fairly represented by this statistic. In fact, this is because information regarding the rates of male infertility is acutely scarce, and has not been reported accurately.¹ On the other hand, according to earlier studies, men's levels of particular reproductive hormones have been related to the indicators of semen quality.^{2,3} The testosterone, follicle-stimulating hormone (FSH), and luteinizing hormone (LH) all play significant roles in the regulation of male reproductive function by sustaining

the spermatogenesis process. In addition, the balance of endocrine activity for the hypothalamus, pituitary, and testicular axis is necessary for the complete completion of male germ cell development. Therefore, the endocrine gland over- or under-secretion affects the operation of several organs and their function.^{4,5}

Furthermore, in recent years, a partial relationship has been found between thyroid hormones and the formation of germ cells and the process of spermatogenesis. Thyroid hormones may affect central (LH/FSH) and peripheral gonadal activities by binding with the sex hormone protein, which, in turn, may have an impact on the quality of the semen.⁶ Thus, thyroid hormones play a crucial physiological role in regulating semen quality by altering testosterone levels, as well as different seminal parameters,



including sperm motility, viability, and semen volume.⁷ Further, these hormones have a variety of effects on the testis and other cell types, including Leydig and Sertoli and germ cells. Thus, changes in testis function are caused by the excess or deficiency of thyroid hormones.⁸

A recent study revealed that there are numerous in-depth examinations into the general role of thyroid hormones in controlling male reproductive functioning because these hormones use multiple mechanisms to affect male reproductive functioning. To aid a proper understanding of the association between thyroid hormones and male infertility, studies evaluating the relationship between thyroid disorders with that of the altered states in semen quality are barely available.⁹

Thus, the current study sought to assess thyroid hormone levels and the relationship between those levels and semen quality by utilizing practical clinical data from the present study.

Methods

Seminal Fluid Collection

Semen specimens were collected from 47 infertile males enrolled in this study and 25 healthy individuals as the control group after at least 3 days of sexual abstinence. The infertile male group and healthy individuals were asked to bring semen samples by masturbation in the room beside the laboratory. Hence, the samples were collected in sterile, clean, wide-mouthed and plastic labeled, and disposable containers. Then, the containers were closed and labeled by name, age, time of ejaculation, and duration of abstinence. The specimens were placed in an incubator at 37°C for 15-30 minutes to allow for liquefaction. After liquefaction and immediate processing, the following routine parameters for seminal fluids were evaluated according to the methods described in the World Health Organization (WHO).¹⁰ Next, according to the guidelines of the WHO, the infertile male group was divided into three categories, including azoospermia, oligozoospermia, and asthenozoospermia.^{11,12}

The parameters included the volume, pH, viscosity, and appearance of the semen/sperm (count, motility, and morphology).¹² After recording abnormal semen findings, the examinations were performed for a thyroid function evaluation, including thyroid-stimulating hormone (TSH), Triiodothyronine (T3) hormone, and Tetraiodothyronine (T4) hormone. The samples were collected from the participants between September 15, 2021, and August 20, 2022.

Collection of Samples

The samples were collected from different regions of Diyala province from the healthy individuals and the infertile males from the auditors to specialized laboratories and consulting clinics in Baqubah /Diyala province, Iraq, for a purpose of diagnosis and treatment.

The participants were in the age range of 29-46 years.

Informed consent was obtained from the participant after they were informed of the study. Therefore, the entire processes conducted in the study were based on agreed consent by the participants. In addition to recording measurements, the weight and height of all participants were obtained to measure the body mass index (BMI) according to the following equation = weight/(height)².¹³

Then, 6 mL of venous blood was drawn from the healthy and infertile groups, and the blood was then placed in a special tube. Once the blood was coagulated, the serum was extracted from the clotted blood cells using a centrifuge at 5000 rpm for ten minutes. Next, the serum was kept in an Eppendorf tube at -20°C. TSH, T3, and T4 serum levels were determined using a fully automated immune analyzer (Cobas e-C411Roche Diagnostics Ltd., Mannheim, Germany)

Statistical Analysis

The statistical analysis was performed to assess statistical differences in parameter results using of the Statistical Package for Social Sciences Software (SPSS) version 17.01. An independent samples *t* test was utilized to analyze the data from the raw data to compare the parameters of the two groups, as well as determining the mean and standard deviations (SD). Fishers' chi-square test was applied to compare various groups of sperm abnormalities. Moreover, LSD test and analysis of variance (ANOVA) were employed to compare thyroid hormones between aberrant sperm groups. The threshold for the statistical significance was set at $P < 0.01$ or 0.05.

Results

Based on the results (Table 1), the mean age (\pm SD) of the infertile group was 34.36 ± 4.15 years, whereas that of the healthy group was 32.28 ± 2.13 years ($P < 0.05$). Regarding the average BMI, there were no statistically significant

Table 1. Comparison of the Study Parameters for Thyroid Hormones and Semen for the Group of Infertile Males and the Healthy Group

Parameters	Infertile Male Group (Mean \pm SD) n=47	Healthy Group (Mean \pm SD) n=25	P Value
Age (y)	34.36 \pm 4.15	32.28 \pm 2.13	< 0.05*
BMI (kg/m ²)	22.32 \pm 3.62	21.26 \pm 2.95	0.212 ^{NS}
Sperm counts (million/mL)	34.61 \pm 10.92	77.20 \pm 12.69	< 0.001**
Sperm motility (%)	39.34 \pm 10.21	73.84 \pm 10.71	< 0.001**
Normal morphology (%)	48.20 \pm 16.02	81.32 \pm 6.17	< 0.001**
TSH (μ U/mL)	2.12 \pm 0.70	1.77 \pm 0.44	< 0.05*
Total T3 (ng/mL)	2.01 \pm 1.13	1.31 \pm 0.30	< 0.001**
Total T4 (mcg/dL)	8.26 \pm 2.16	7.49 \pm 1.62	0.124 ^{NS}

Note. BMI: Body mass index; TSH: Thyroid-stimulating hormone; T3: Triiodothyronine; T4: Tetraiodothyronine; SD: Standard deviation; NS: Non-significant; ** ($P < 0.01$), * ($P < 0.05$).

differences between both groups, and the infertile group's average BMI was relatively close to that of the healthy group ($P=0.212$). Similarly, the parameters of semen quality were significant decrease in the infertile male group than in the healthy group ($P<0.001$). The results showed that sperm counts, sperm motility%, and normal morphology% represented significant decreases in the mean \pm SD, ($P<0.001$; 34.61 ± 10.92 vs. 77.20 ± 12.69 , 39.34 ± 10.21 vs. 73.84 ± 10.71 , and 48.20 ± 16.02 vs. 81.32 ± 6.17 , respectively). On the other hand, the results demonstrated a highly significant difference in TSH and total T3 (2.12 ± 0.70 vs. 1.77 ± 0.44 and 2.01 ± 1.13 vs. 1.31 ± 0.30 , respectively). However, there was no significant difference ($P=0.124$) in total T4 (8.26 ± 2.16 vs. 7.49 ± 1.62 , respectively).

According to data in Table 2, males with asthenozoospermia, oligospermia, and azoospermia were discovered in each of the 47 abnormal patients, with a total of 25 (53.19%), 15 (31.92%), and 7 (14.89%) men, respectively.

Table 2. Distribution of Sperm Abnormalities in the Infertile Male Group (n=47)

Sperm Abnormality	No. (%) (n=47)	P Value
Asthenozoospermia	25 (53.19)	<0.001**
Oligozoospermia	15 (31.92)	
Azoospermia	7 (14.89)	

Note. ** ($P<0.01$).

Table 3. Comparing Thyroid Levels in Healthy and Infertile Male Groups With Different Sperm Abnormalities

Parameters	Asthenozoospermia (n=25)	Oligozoospermia (n=15)	Azoospermia (n=7)	Healthy (n=25)
TSH (μ IU/mL)	2.26 ± 0.62 **a	1.88 ± 0.79	2.16 ± 0.74	1.77 ± 0.44
Total T3 (ng/mL)	2.06 ± 1.50 **a	1.94 ± 0.50 ^b	1.99 ± 0.53	1.31 ± 0.30
Total T4 (mcg/dL)	8.96 ± 2.00 **a	7.26 ± 2.44 **c	7.91 ± 1.47	7.49 ± 1.62

^a Comparison between asthenozoospermia and healthy groups.

^b Comparison between oligozoospermia and healthy groups.

^c Comparison between asthenozoospermia and oligozoospermia groups.

** $P<0.001$, * $P<0.05$.

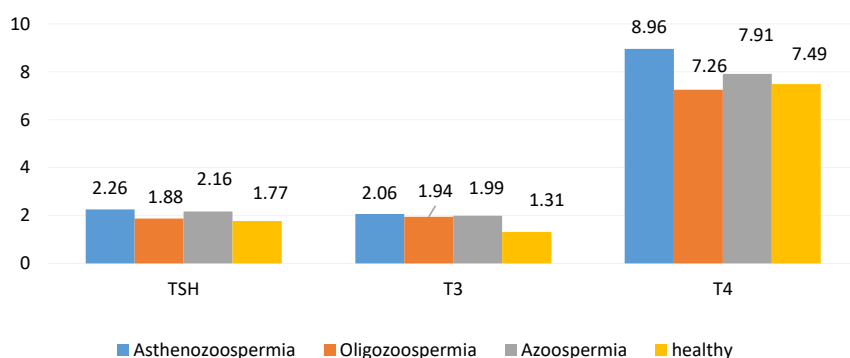


Figure 1. Thyroid Levels in Healthy and Infertile Male Groups With Different Sperm Abnormalities

Table 3 provides the mean \pm SD value of thyroid hormone levels in the three categories of infertile males (i.e., asthenozoospermia, oligozoospermia, and Azoospermia) in comparison to the healthy group (Figure 1). A significant decrease in TSH was observed in oligozoospermia (1.88 ± 0.79 μ IU/mL) in comparison with the healthy group and the other groups, including the healthy group (1.77 ± 0.44 μ IU/mL), azoospermia (2.16 ± 0.74 μ IU/mL), and asthenozoospermia (2.26 ± 0.62 μ IU/mL), respectively. Additionally, a significant decline in total T3 was found in Oligozoospermia (1.94 ± 0.50 ng/mL) compared with the healthy group and other groups, including the healthy group (1.31 ± 0.30 ng/mL), azoospermia (1.99 ± 0.53 ng/mL), and asthenozoospermia (2.06 ± 1.50 ng/mL), respectively. In addition, there was a significant reduction in total T4 in oligozoospermia (7.26 ± 2.44 mcg/dL) compared with the healthy group and other groups, including the healthy group (7.49 ± 1.62 mcg/dL), azoospermia (7.91 ± 1.47 mcg/dL), and asthenozoospermia (8.96 ± 2.00 mcg/dL), respectively. On the other hand, a significantly higher level of TSH, total T3, and total T4 was observed in asthenozoospermia ($P<0.001$) in comparison with the healthy group and the other groups. However, none of the hormones were found to be significantly different in participants with a normal semen profile.

Discussion

The findings of the current study indicated that both groups' ages were comparable ($P<0.05$, Table 1), which

is consistent with the findings of another study¹⁴; most infertile patients were found to be between the ages of 25 and 50, whereas, there was no significant difference in the BMI between the two groups ($P=0.212$). Further, semen analysis parameters revealed a significant decrease in the sperm count, sperm motility, and normal sperm morphology in the infertile male group as compared with the healthy group. This finding is in line with the results of previous studies.^{15,16} According to earlier studies, 90% of male infertility issues are related to sperm count, and abnormal sperm parameters are positively correlated with sperm count. The cause of the issue of sperm count, motility, and morphology stems from disturbances in unorganized control mechanisms, including pre-testicular, testicular, and post-testicular factors.^{17,18} These factors have a negative impact on sperm quality, including varicocele, accessory gland infection, immunological variables, congenital abnormalities, and iatrogenic systemic and endocrine causes such as diabetes mellitus, obesity, and smoking, as well as the possible roles of oxidative stress and low testosterone. As a result, spermatogenesis, loss of sperm motility, and abnormal sperm morphology decrease in the testicular microenvironment.¹⁹ Thus, semen analysis continues to be the single most useful, important, and fundamental investigation with a sensitivity of 89.6%, and it can help in identifying 9 out of 10 men who actually have a problem with male infertility.²⁰

Additionally, the infertile male group experienced manifested thyroid dysfunction. All forms of thyroid dysfunction were clinically significant and were categorized as latent thyroid dysfunction when compared to the healthy group. As a result of an excess or deficiency of thyroid hormones, testis function is altered, including abnormalities in the semen. Reduced sperm density, motility, and morphology have all been linked to hyperthyroidism more commonly than hypothyroidism, which is linked to decreased sperm morphology. Therefore, the diagnostic process for the infertile man should include thyroid function tests as part of the diagnostic workup of the infertile.⁸ The results of another study indicated that thyroid hormones essentially regulate the quality of sperm by changing the quantity of serum testosterone. Additionally, the other mechanisms of thyroid hormones in the regulation of semen quality are mediated by the regulation of the seminal plasma components (calcium, fructose, magnesium, zinc, and the like). By preserving these elements, thyroid hormones control many seminal characteristics such as sperm motility, viability, and semen volume.^{21,22} Recent studies discovered that patients with an unbalanced thyroid profile exhibited lower sperm counts, lower sperm motility, and lower sperm density. Based on the findings of a similar study, thyroid dysfunction conditions had a negative impact on sperm quality, particularly sperm

progressive motility and sperm volume,⁴ which is also supported by the current study.

According to the analysis of the semen (Table 2), 14.89%, 31.92%, and 53.19% of males had azoospermia, oligozoospermia, and asthenozoospermia, respectively, which conforms to the findings of another study.²³ This outcome could be related to a problem with the proper function of a complex system of organs, as well as a local androgen-estrogen balance that is crucial for spermatogenesis.²⁴ Male reproductive function is under the control of both gonadotropins and androgens' effects through a negative feedback loop involving the hypothalamus, pituitary, and testis known as the hypothalamic-pituitary-gonadal axis. Estrogen is thought to have a regulatory role in the testis because estrogen biosynthesis takes place in testicular cells, and the absence of an estrogen receptor has negative consequences on spermatogenesis.²⁵ According to recent research, the testis contains normal germ cells and somatic cells that express estrogen receptors, and it is involved in mediating the estrogen action in spermatogenesis, along with being involved in modulating gonadotropin-releasing hormone release and gonadotropins secretion.²⁶

In the present study, TSH, total T3, and total T4 levels were significantly increased in men with abnormal semen parameters, and it was observed that TSH, total T3, and total T4 levels were greater in men with asthenozoospermia compared with both groups and the healthy group. Thyroid hormones are currently known to play a significant role in the development of the male gonadal tissue and in male reproductive function. Although the underlying mechanisms are not fully understood, they probably influence several important male reproductive system cells through genomic and non-genomic mechanisms and regulate the testicular secretion of testosterone and the concentration of seminal plasma components (calcium, fructose, magnesium, zinc, and the like).²⁷ A previous study reported that thyroid hormones have a direct stimulatory impact on Leydig cells. T3 appeared to increase LH receptors and steroidogenesis in Leydig cells, in addition to being involved in directly boosting the production of basal testosterone, which may be due to its impact on Leydig cells.²⁸ Therefore, thyroid function can be an aspect of good sperm quality,²⁹ which is supported by the results of the present study.

Moreover, increased T4 levels and altered LH and FSH responsiveness led to disruption of the endocrine system's regulation of the development of male reproductive organs and germ cells, which can result in slowed or delayed spermatogenesis. Sperm count and semen volume are consequently adversely impacted by them. Thus, reduced sperm vitality, motility, and count all point to a deterioration in semen quality which could be due to hyperthyroidism,⁹ which corroborates with the results of the current study. However, low levels of T3 and T4 can

affect spermatogenesis by lowering serum testosterone levels which could be due to hypothyroidism, which affects decreased semen quality in terms of sperm count, motility, and low ejaculate volume.²⁹

In conclusion, abnormal thyroid dysfunction may decrease sperm quality which could lead to infertility. According to the findings of the current study, significantly lower serum levels of TSH, T3, and T4 were observed in the infertile male group compared with the healthy group. Thus, it had negative impacts on sperm counts, sperm motility (%), and normal morphology (%) which were associated, in thyroid hormones, with different sperm abnormalities and semen quality in the infertile males group. However, more research and testing are required to understand how the thyroid influences testicular growth and spermatogenesis, which could lead to the discovery of a link between thyroid and sperm quality in male infertility.

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Competing Interests

There is no conflict of interests.

Ethical Approval

The study received approval from the Local Ethics Committee at the Council College of Education for the Pure Sciences/University of Diyala.

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