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# Study of Thyroid Hormones in Male Infertility

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**Original Research Article**

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**Abstract:** Hormones are one of the principal factors in intercellular and inter-organ communication. The thyroid hormones are crucial for normal functioning because of their control over body's basal metabolic rate, as well as growth, development, and differentiation of many cells/organs in the body.The present study was based on a cross-sectional study design carried out at the outpatient department of Maheshwara Medical College & Hospital from January 2017 to July 2018. Serum levels of free thyroxin (FT4), thyroid stimulating hormone (TSH), free testosterone, prolactin (PRL), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) were measured using immunoassay commercial kits in both groups. The normal reference ranges for thyroid hormones were as follows: TSH, 0.3 to 5.0 IU/mL and T4, 4.5 to 12.5 g/dL. Erectile dysfunction was evaluated using International Index of Erectile Function (IIEF-5) questionnaire. The results were averaged as (mean ± standard deviation) for each parameter subgroups separately. Each variable, including age, serum levels of hormones, sperm parameters, and IIEF-5 scores, were assessed by sample *t* test.In our present study, age of hypothyroid subject group and normal control group is found to be non-significantly related ($P$ = .367). Similarly, no significant relation was also noted among the FSH levels ($P$ = .834) of the two groups. There was significant ($P$ < .001) relation among the hypothyroid and normal groups in IIEF-5 scores, Serum PRL level, sperm count, sperm motility and morphology. Abnormal thyroid function resulted in decreased male fertility and/or impaired sexual activity. In hypothyroid subjects, high levels of PRL may affect sexual drive and result in occurance of Erectile Dysfuction. Thyroxin administration can improve fertility and reverses the effects of hormonal abnormalities. These observations show that sexual dysfunctions are almost always multifactorial (physical and psychological factors). In the present study, patients with hypothyroidism had significantly higher level of serum PRL and lower IIEF-5 score; the Serum levels of FSH, LH and free testosterone were not significantly different among the two groups. Overall, hypothyroidism linked with male infertility by adversely resulting in erectile dysfunction and semen quality.
**Keywords:** Thyroid hormones, Male infertility, ED, FSH, LH, Testosterone, IIEF, Semen analysis.

## INTRODUCTION

Hormones are one of the principal factors in intercellular and inter-organ communication. We have several endocrine glands producing chemical messengers to participate in various physiological functions, and the thyroid gland holds a central place in controlling the physiology of human body. The thyroid hormones are widely considered to be indispensible to the human body. Thyroid stimulating hormone (TSH) is secreted by the pituitary gland and stimulates the thyroid gland to secrete two different thyroid hormones: tri-iodo-L-thyronine (T3 or triiodothyronine) and tetraiodo-L-thyronine (T4 or thyroxine). The thyroid hormones are crucial for normal functioning because of their control over body's basal metabolic rate, as well as growth, development, and differentiation of many cells/organs in the body [1]. Given diverse roles of thyroid in the human body, it would be interesting to explore if thyroid affects testes, and consequently the process of spermatogenesis [2]. Spermatogenesis is hormonally controlled by the gonadotropin releasing hormone (GnRH), which in turn stimulates the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), affecting the growth of the Sertoli and Leydig cells [3]. In the last two decades, researchers have identified thyroid hormone receptors

(TRs) directly on cells within the testes, indicating that thyroid hormones greatly affect growth and development of the testes [1]. It is thought that TRs are located on the Sertoli cells of the testes, and it is believed that T3 binds directly to these receptors [4]. Higher free T4 levels have also been associated with greater sperm concentration and a reduced occurrance of having <50% sperm motility [5]. However, T4 levels must be controlled because hyperthyoridism, which could lead to thyrotoxicosis, may compromise sperm motility. Hypothyroidism has been linked to abnormalities in sperm morphology which normalizes after euthyroidism is restored [6]. These finding initiated us for the present study of thyroid hormones in male infertility cases.

## MATERIALS& METHODS

The present study was based on a cross-sectional study design carried out at the Outpatient department of Maheshwara Medical College & Hospital. Subjects referred to infertility clinic from January 2017 to July 2018 were selected, and the data was collected using a structured questionnaire. A total of 54 people have given their consent for participating in the present study. Out of these, 43 were eligible after consideration of the inclusion exclusion criteria. 50 male subjects with no relevant history of infertility are selected as control group. The inclusion criteria were as follows: age range of 25 to 50 years, not being investigated or treated for sexual dysfunction before the onset of thyroid symptoms, and being married for more than 1 year. Patients with diabetes mellitus, cardiovascular diseases, including history of myocardial infarction, coronary angioplasty, or coronary artery bypass grafting, or urological diseases were excluded from the study. Presence of severe complications related to thyroid hormone and other hormones which may be known to effect the fertility are also excluded from the study. The Ethics Committee of the Maheshwara Medical College & Hospital, Sangareddy, and Telangana has approved the study. Written informed consent in the language understandable to the subjects has been obtained from all the participants of the study.

Basic parameters like blood pressure, GRBS are done and clinical data is collected for analysis. A questionnaire is given to the subjects for collection of relevant clinical information on medical history, smoking habits, alcohol consumption, any major accidents or surgeries and the use of medications. Serum levels of free thyroxin (FT4), thyroid stimulating hormone (TSH), free testosterone, prolactin (PRL), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) were measured using immunoassay commercial kits in both groups. The normal reference ranges for thyroid hormones were as follows: TSH, 0.3 to 5.0 IU/mL and T4, 4.5 to 12.5 g/dL.

Erectile dysfunction was evaluated using International Index of Erectile Function (IIEF-5) questionnaire [7]. This is a 5-item version of the 15-item IIEF questionnaire for diagnosing the presence and severity of erectile dysfunction (ED). These items focus on erectile function and intercourse satisfaction. Possible scores for the IIEF-5 range from 5 to 25. This questionnaire was translated into local language for better understanding and response by the subjects. Semen analyses were done according to the World Health Organization guidelines [8]. Semen was obtained by masturbation after 3 to 7 days of sexual abstinence. Semen sample was collected into a sterile container, using no lubricant jelly. Reference limits of semen parameters are as follows: total sperm number, 39 million per ejaculate (range: 33 to 46); sperm concentration: 15 million per mL (range: 2 to 16); vitality: 58% live (range: 55% to 63%); progressive motility: 32% (31% to 34%); total (progressive + nonprogressive) motility: 40% (range: 38% to 42%); and morphologically normal forms: 4.0% (range: 3.0% to 4.0%)[8].

The data was arranged in suitable tables for analysis under the relevant headings. The results were averaged as (mean ± standard deviation) for each parameter subgroups separately. Each variable, including age, serum levels of hormones, sperm parameters, and IIEF-5 scores, were assessed by sample *t* test. Statistical analysis was done using IBM SPSS Statistics 20 package. p-value of <0.05 is considered as statistically significant and p-value of <0.005 is considered as statistically highly significant.

## RESULTS

In our present study, age of hypothyroid subject group and normal control group is found to be non-significantly related ($P$ = .367). Similarly, no significant relation was also noted among the FSH levels ($P$ = .834) of the two groups.

There was significant ($P$ < .001) relation among the hypothyroid and normal groups in IIEF-5 scores, Serum PRL level, sperm count, sperm motility and morphology.

**Table-1: Mean, SD & SE of Characteristics, hormonal, and seminal parameters**

| | | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|
| Age (years) | Hypothyroid | 32.79 | 4.988 | .761 |
| | Normal | 31.79 | 4.713 | .719 |
| IIEF-5 Score | Hypothyroid | 11.60 | 1.966 | .300 |
| | Normal | 18.14 | 3.962 | .604 |
| FSH (mU/mL) | Hypothyroid | 8.56 | 1.031 | .157 |
| | Normal | 8.60 | 1.027 | .157 |
| LH (mU/mL) | Hypothyroid | 8.74 | .978 | .149 |
| | Normal | 8.19 | .958 | .146 |
| Free Testosterone (pg/mL) | Hypothyroid | 8.63 | 1.047 | .160 |
| | Normal | 15.37 | 3.047 | .465 |
| Prolactin (ng/mL) | Hypothyroid | 304.72 | 41.375 | 6.310 |
| | Normal | 259.30 | 41.734 | 6.364 |
| Sperm Count (million/mL) | Hypothyroid | 33.33 | 5.308 | .809 |
| | Normal | 73.37 | 8.389 | 1.279 |
| Sperm motility (%) | Hypothyroid | 33.00 | 5.104 | .778 |
| | Normal | 70.07 | 7.778 | 1.186 |
| Sperm morphology (%) | Hypothyroid | 33.07 | 5.198 | .793 |
| | Normal | 69.95 | 7.958 | 1.214 |

**Table-2: Correlations of Characteristics, hormonal, and seminal parameters**

| Sample *t* test Correlations | | | | |
|---|---|---|---|---|
| | | N | Correlation | Sig. |
| Age (years) | Hypothyroid & Normal | 43 | -.100 | .523 |
| IIEF-5 Score | Hypothyroid & Normal | 43 | -.357 | .019 |
| FSH (mU/mL) | Hypothyroid & Normal | 43 | .011 | .944 |
| LH (mU/mL) | Hypothyroid & Normal | 43 | -.100 | .521 |
| Free Testosterone (pg/mL) | Hypothyroid & Normal | 43 | -.082 | .599 |
| Prolactin (ng/mL) | Hypothyroid & Normal | 43 | -.092 | .557 |
| Sperm Count (million/mL) | Hypothyroid & Normal | 43 | .096 | .540 |
| Sperm motility (%) | Hypothyroid & Normal | 43 | -.227 | .143 |
| Sperm morphology (%) | Hypothyroid & Normal | 43 | -.049 | .756 |

**Table-3: Sample *t* test statistics of Characteristics, hormonal, and seminal parameters**

| **Sample *t* test** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Paired Differences | | | | | t | df | Sig. (2-tailed) |
| | | Mean | Std. Deviation | Std. Error Mean | 95% Confidence Interval of the Difference | | | | |
| | | | | | Lower | Upper | | | |
| Age (years) | Hypothyroid & Normal | 1.000 | 7.198 | 1.098 | -1.215 | 3.215 | .911 | 42 | .367 |
| IIEF-5 Score | Hypothyroid & Normal | -6.535 | 5.011 | .764 | -8.077 | -4.993 | -8.551 | 42 | .000 |
| FSH (mU/mL) | Hypothyroid & Normal | -.047 | 1.447 | .221 | -.492 | .399 | -.211 | 42 | .834 |
| LH (mU/mL) | Hypothyroid & Normal | .558 | 1.436 | .219 | .116 | 1.000 | 2.549 | 42 | .015 |
| Free Testosterone (pg/mL) | Hypothyroid & Normal | -6.744 | 3.303 | .504 | -7.761 | -5.728 | -13.390 | 42 | .000 |
| Prolactin (ng/mL) | Hypothyroid & Normal | 45.419 | 61.412 | 9.365 | 26.519 | 64.318 | 4.850 | 42 | .000 |
| Sperm Count (million/mL) | Hypothyroid & Normal | -40.047 | 9.487 | 1.447 | -42.966 | -37.127 | -27.681 | 42 | .000 |
| Sperm motility (%) | Hypothyroid & Normal | -37.070 | 10.227 | 1.560 | -40.217 | -33.922 | -23.769 | 42 | .000 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Sperm morphology (%) | Hypothyroid & Normal | -36.884 | 9.715 | 1.482 | -39.874 | -33.894 | -24.895 | 42 | .000 |

## DISCUSSION

Abnormal thyroid function resulted in decreased fertility and impaired sexual activity [9, 10]. In animals, if hypothyroidism occurs soon after birth, delay in sexual maturation will be observed [11]. Serum levels of FSH, LH, and free testosterone were not significantly different. In hypothyroid subjects, high levels of PRL may affect sexual drive and result in ED [12, 13]. Thyroxin administration can improve fertility and reverses hormonal abnormalities[14, 15] Not all of the patients with thyroid diseases do experience sexual dysfunction. Moreover, all of the patients with hyper or hypothyroidism reaching euthyroid state do not recover from sexual dysfunction. These observations show that sexual dysfunctions are almost always multifactorial (physical and psychological factors)[16].

In the present study, patients with hypothyroidism had significantly higher level of serum PRL and lower IIEF-5 score, which means more erectile problems. In continuation, the Serum levels of FSH, LH and free testosterone were not significantly different among the two groups. An extensive study can be made with increased number of subjects and control groups over a varied geographical and climate areas. The limitations of the present study, such as less number of subjects, narrow range of age group, and consideration of only males with hypothyroids have to be overcome in the research studies. Overall, it can be concluded that hypothyroidism results in male infertility by adversely resulting in erectile dysfunction and semen quality.

## CONCLUSION

From the present study, it can be concluded hypothyroidism is more related to increased serum PRL levels and decreased IIEF-5 score. It can also be confirmed that there was no correlation found between hypothyroidism and levels of serum FSH, LH and free testosterone. It can be further concluded that in most of the infertility cases, detecting hypothyroidism and treating for the same if found can be of great significance.

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