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RESEARCH ARTICLE

# Thyroid dysfunction and semen quality among males investigated for infertility in Southern Nigeria

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## Abstract

The relationship between thyroid and testis is well understood, and the association between changes in thyroid function and male infertility has been reported. However, the contribution of thyroid dysfunction to male infertility is not sufficiently addressed in our setting. This study aims to assess the thyroid hormones level among males undergoing investigation for infertility and to establish correlations between thyroid hormones and sperm indices. Thyroid hormones were determined in 150 infertile males and 50 fertile male controls. Semen analysis was done according to the World Health Organization criteria while thyroid hormones were determined using Enzyme linked Immunosorbent assay technique. The measured anthropometric data, sperm indices and thyroid hormone levels were compared using appropriate statistical tools. Serum triiodothyronine, and thyroxine levels were significantly lower ($p < 0.001$), while thyroid stimulating hormone was higher among infertile males than control subjects. The body mass index of the infertile subjects was significantly higher ($p < 0.011$) than control subjects. Of the 150 subjects, 41.33% (62/150) were euthyroid, 7.33% (11/150) had subclinical hypothyroidism while 51.34% (77/150) had overt hypothyroidism. Among the 88 altered thyroid function, 6.82% (6/88) had normozoospermia, 44.32% (39/88) had oligozoospermia while 48.86% (43/88) were azoospermia. The area Under the Curve of T3 (0.858), T4 (0.765) and sperm count (0.875) were able to differentiate fertile men from infertile subjects. Thyroid disorders are prevalent among infertile men and should be considered in the laboratory assessment of male infertility cases. Including thyroid function tests in the investigative panel can help identify and manage potential thyroid-related factors contributing to infertility. This comprehensive approach ensures thorough evaluation and targeted treatment for better reproductive outcomes in affected individuals.

## 1. INTRODUCTION

Altered thyroid function may significantly contribute to the increasing incidence of male infertility (1), especially in the so-called infertility belt of sub-Saharan Africa. Studies in experimental animals have linked thyroid dysfunction with poor semen quality and quantity. for instance, induction of thyroid hypo-function in rats using 6-n propyl 2-thiouracil resulted in decreased semen volume, spermatogenic arrest, reduced number and constriction of seminiferous tubules, as well as diminished testicular and accessory gland weight (1). In Nigeria,

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the prevalence of male infertility ranges from 40 to 50% of all infertility cases, even though it varies across different regions (2). Male infertility may be due to deficiencies in the semen quality which is used as a surrogate to measure male fecundity (3).

The declining trend of semen quality all over the world may be due to several factors. The need to carefully examine these factors and bring about effective therapeutic and preventive measures cannot be over emphasized. Environmental and lifestyle habits are increasingly recognized as significant influencers of infertility (4). These factors disrupt the normal endocrine environment including thyroid hormone levels, that exert influence on semen quality and male infertility (5). Although studies have been conducted on the roles of thyroid hormone in the control of male reproduction (6,7), reports disclosing the association between thyroid disorders and abnormal semen quality are scarce (8). Thyroid hormones regulate the functions of testicular tissues such as leydig cells, Sertoli cells and germ cells, but thyroid hormone status is rarely investigated during laboratory workup among infertile males (2,9). Intriguingly, both excess and deficiency of thyroid hormone can impact testicular functions, affecting semen quality and quantity. Evidence has associated thyroid hyper-function with decreased sperm count, volume, motility and morphology, while hypo-function was associated with reduced sperm morphology (9).

Iodine, an essential nutrient for the human body, is crucial for the synthesis of thyroxine by the endocrine system (10-12). Inadequate intake (deficit or excess) can have a strong influence on the synthesis of thyroid hormone and thus leading to several thyroid dysfunctions and disorders including male infertility. Iodine deficiency increases the chances of male infertility by under producing the required levels of thyroid hormones. Some authors have highlighted Nigeria's susceptibility to iodine deficiency disorders, due to the country's location close to the equator and extended periods of rainfall throughout the year (13). Despite the implementation of some interventions to prevent iodine deficiency disorders, only about 70% households consume salts with adequate iodine content >15 parts per million (ppm) which also vary from one location to another (13,14). Thyroid hormones do not only modulate testis function by genomic and non-genomic effects, but also control the redox status of testis by depending on the antioxidant systems (15).

Studies have suggested a strong correlation between body mass index (BMI) and iodine status, which can influence the epidemiological assessment of nutritional iodine levels. Urinary iodine concentration was reported to be positively correlated with median of BMI and negatively associated with stunting prevalence in a population (16). Evidence has implicated work-place exposures to toxic substances in the pathogenesis of male infertility (17,18). It is plausible to imagine the effects of an altered thyroid function on spermatogenesis and semen quality indices. Therefore, this study was designed to assess thyroid hormones levels among males undergoing infertility investigations and their correlation with sperm indices.

## 2. MATERIALS AND METHODS

### 2.1. Study Design

This cross-sectional study involved male partners of infertile couples presenting at the fertility clinic with a confirmed diagnosis of infertility, as determined by the clinician. Fertile males served as controls.

### 2.2. Study Site

Samples were collected from infertile males attending the Human Reproduction and Research Programme (HRRP) unit at the University of Benin Teaching Hospital. Controls were sourced from fertile males residing in the same locality.

### 2.3. Sample Size

The minimum sample size was determined using the formula described by Alonzo et al. (8); with a 11.0% prevalence of thyroid abnormalities among infertile males as reported in previous study (9).

$$n = \frac{Z^2pq}{I^2} \quad \ldots\ldots (1)$$

Where; n - minimum sample size, P – estimated prevalence, Z-Standard normal deviate that corresponds to 95% confidence limit (1.96), I is the alpha level of significance (5%) and q is (1-p).

$$n = \frac{(1.96)^2 \times 0.11 \times (1-0.11)}{0.05 \times 0.05} = 150 \quad \ldots\ldots (2)$$

A total of 150 infertile males were enrolled into the study, and 50 men of proven fertility served as controls.

## 2.4. Inclusion and Exclusion Criteria

Male subjects diagnosed with infertility by a clinician, without chronic illnesses and physical abnormality that may affect reproduction, were included in the study. Additionally, men with proven fertility served as controls. Exclusion criteria comprised individuals with specific genital and systemic diseases such as genital infection, undescended testis, hepatic, renal, endocrine, autoimmune that may impair the reproductive capacity, as well as those taking thyroid hormones medications or other drugs that could influence the results.

## 2.2. Ethical Consideration

Ethical approval was obtained from the Ethical Committee of the University of Benin Teaching Hospital (UBTH) (Protocol Number: ADM/E 22/A/VOL. VII/14831269, dated 18th February, 2022). Informed consent was obtained from all the participants before commenceing sample collection.

## 2.3. Anthropometric and Demographic Measurements

Clinical and anthropometric measurements including sex, age, weight and height were recorded for each participant. Body mass index (BMI) was calculated using the formula: BMI = weight (kg)/height squared ($m^2$). Structured questionnaires were administered to collect socio-demographic characteristics.

## 2.4. Definition of Terms/Classification of Subjects

Subjects were classified according to the number of sperm cell count; normospermia - sperm count of ≥$15.0\times10^6$cells/mL, oligospermia - sperm count $15.0\times10^6$ cells/mL, and azoospermia, absence of sperm cells in the ejaculates. Hypothyroidism was defined as under-secretion of T4 and T3, hyperthyroidism as over-secretion of triiodothyronine (T3) and thyroxine (T4), and subclinical thyroid dysfunction as elevated or low Thyroid-stimulating hormone (TSH) with normal thyroid hormone levels. Overt thyroid disease was defined by abnormal thyroid hormone levels accompanied by low or high TSH.

## 2.5. Sample Collection

All participants were instructed to collect semen samples by masturbation into sterile containers after three to five days of sexual abstinence. The semen samples were labeled with time of collection and number code and brought to the laboratory within one hour of collection. Five millilitres of venous blood was collected from each individual into non-anticoagulated container in the morning and the blood was spun at 3000 rpm for 10 minutes, and serum was separated into clean container and stored at -20°C prior to hormonal analysis.

## 2.6. Seminal Fluid Analysis

Freshly collected semen samples were examined for colour and liquefaction at room temperature. Semen volume was measured and sperm count, motility, morphology and viability were determined microscopically using World Health Organization (WHO) standard procedure (10).

## 2.7. Biochemical Analysis

The thyroid hormone levels were determined using enzyme linked-immunoborbent assay (ELISA) methods with reagents supplied by Elabscience. The principle of T3 and T4 test method is as follows: This is a competitive enzyme immunoassay. This involved the addition of immobilized antibody, enzyme-antigen conjugate and serum containing the native antigen in the wells of the microplate. Upon mixing of the immobilized antibody with the enzyme-antigen conjugate and serum containing the native antigen, a competitive reaction results between the native antigen in the serum and the enzyme-antigen conjugate for a limited number of insolubilized binding sites. Then, the antibody-bound fraction is separated from unbound antigen by decantation. The enzyme activity in the antibody-bound fraction is inversely proportional to the native antigen concentration in the serum.

For the TSH, the immunoenzymometric assay was employed. The surface of the microplate wells was first immobilized by the interaction of the streptavidin coated on the wells with biotinylated monoclonal anti-TSH antibody added to the wells. Upon the addition of the serum containing the native antigen on the coated wells, there is a reaction between the native antigen and the antibodies without competition or steric hindrance to form a soluble sandwich complex. This complex is deposited to the well due to the high affinity reaction of the streptavidin and biotinylated antibody. At equilibrium, the antibody-bound fraction was separated from the unbound antigen by decantation. The enzyme activity in the antibody-bound fraction is directly proportional to

the native antigen concentration. A the concentration of native antigen in the serum increases, the activity of the enzyme bound to the antibody decreases, and vice versa (18).

### 2.8. Statistical Analysis

The data were analyzed using the statistical package for Social and Science Pprogram (SPSS) version 20 (SPSS Inc. Chicago, IL, USA). Mean±Standard Eror of the Mean (SEM) values were calculated for both tests and controls, and Student's t-test was employed to compare the means. The relationships between the values were explored using Pearson correlation coefficient. A significant level of $p<0.05$ was considered statistically significant.

## 3. RESULTS AND DISCUSSION

The socio-demographic characteristics of the 200 subjects in the study reveal that a majority, 67.5%, are between the ages of 35-40years, with smaller proportions in older age groups: 8.5% between 41-46years, 16.0% between 47-52 years, 2.0% between 53-58years, and 12.0% are 59 year and above. The mean age of the study participants is 42.31 ± 0.51years. Of the total subjects, 9.0% had a primary level of education, 27.0% secondary level of education and 64.0% tertiary level of education.

Regarding BIM, 1.0% of participants were underweight with a mean BMI of 18.0 ± 0.00kg/m$^2$, 38.5% had a healthy mean BMI of 22.42 ± 1.50kg/m$^2$, 16.5% were overweight with a mean BMI of 27.30 ± 1.51 kg/m$^2$, 35.0% wereobese class I with a mean BMI of 31.11 ± 1.45 kg/m$^2$ and 9.0% were obese class II, with a mean BMI of 35.00 ± 0.00kg/m$^2$.

Occupationally, 32.5% of participants were civil servants, with 84.61% of them being infertile subjects and 15.39% being controls. Additionally, 17.5% were farmers, with 71.43% being infertile subjects and 28.57% being controls. Furthermore, 25.0% were drivers, with 80.0% being infertile subjects and 20.0% being controls and 25.0.0% were traders, with 60.0% being infertile subjects and 40.0%) being controls. The differencein coccupation distribution between controls and infertile subjects was statistically significant (p=0.029).

Regarding awareness of the adverse effects of increased BMI on fertility, 65.0% of participants were aware, with 69.23% of them being subjects and 30.77% being controls. Conversely, 35.0% were not aware, with 85.71% of them being subjects and 14.29% being controls. The difference in awareness between the control group and subjects was statistically significant ($p < 0.001$). Tables 1 provide further details on these socio-demographic variables.

Table 2 shows the levels of thyroid hormones (T3, T4), thyroid stimulating hormone and BMI among infertile and control groups. It was observed that the mean levels of T3 and T4 were significantly lower ($p < 0.001$) among the infertile males than control group, while mean TSH ($p < 0.001$) and BMI ($p < 0.011$) were significantly higher among the infertile males when compared with controls.

Table 3 shows level of seminal indices among infertile and control groups. It indicated that the mean levels of sperm count, total motility, progressive motility viable sperm cells normal morphology and volume among the infertile group were significantly lower ($p < 0.001$) compare to control subjects.

Table 4 shows the seminal indices among the classes of thyroid disorders. The pattern of thyroid function observed were euthyroid 62/150 (41.3%), subclinical hypothyroidism 11/150 (7.3%) overt or clinical hypothyroidism 77/150 (51.3%) among infertile males. It was observed that the mean sperm count, total motility, progressive motility, viable sperm cells and normal morphology of euthyroid infertile subjects were significantly higher $p < 0.05$) when compared with subclinical hypothyroidism and overt or clinical hypothyroidism infertile subjects. There was no significant different in mean semen volume between the groups.

Table 5 shows level of thyroid hormones (T3 and T4), TSH and BMI among infertile euthyroid subjects, subclinical hypothyroidism subjects and overt or clinical hypothyroidism subjects. Mean BMI of euthyroid infertile males was significantly lower ($p < 0.01$) when compared with subclinical hypothyroidism and overt or clinical hypothyroidism.

Table 6 shows the correlation between thyroid hormones, BMI and seminal indices. It was observed that thyroid hormones correlated positively with seminal indices and negatively with BMI ($p < 0.001$), while TSH correlated inversely with seminal indices and positively with BMI ($p < 0.001$). In addition, BMI correlated negatively with seminal indices ($p < 0.001$).

Table 7 shows Area Under Curve of Receiver Operating Characteristics, it was observed that AUC of the diagnostic tests shows a good measure of discriminating ability between fertile and infertile subjects. The AUC of T3 (0.858), T4 (0.765) and sperm count (0.875), $p<0.001$ appear to separate infertility from fertility (Figure 1).

**Table 1.** Socio demographic characteristics of respondents

| Variablkes | Total (n=200) | Infertile group (n=150) | Fertile group (n=50) | $X^2$ | p-value |
|---|---|---|---|---|---|
| **Age (years)** | | | | | |
| 35-40 | 135 (67.5%) | 115 (85.18%) | 20 (14.81%) | 337.6 | P<0.001 |
| 41-46 | 17 (8.5%) | 10 (58.82%) | 7 (41.17%) | | |
| 47-52 | 32 (16.0%) | 25 (78.12%) | 7 (21.8%) | | |
| 53-58 | 4 (2.0%) | 0 (0.0%) | 4 (100.0%) | | |
| 59-Above | 12 (6.0%) | 0 (0.0%) | 12 (100.0%) | | |
| **Occupation Status** | | | | | |
| Civil Servant | 65 (32.5%) | 55 (84.61%) | 10 (15.39%) | 9.00 | P=0.029 |
| Trader | 50 (25.0%) | 30 (60.00%) | 20 (40.0%) | | |
| Driver | 50 (25.0%) | 40 (80.0%) | 10 (20.0%) | | |
| Farmer | 35 (17.5%) | 25 (71.43%) | 10 (28.57%) | | |
| **Classification of seminal parameter** | | | | | |
| Normospermic | 91 (45.5%) | 41 (45.0%) | 50 (54.9%) | 14.23 | P<0.001 |
| Oligospermic | 61 (30.5%) | 61 (100.0%) | 0 (0.0%) | | |
| Azoospermic | 48 (24.0%) | 48 (100.0%) | 0 (0.0%) | | |
| **Educational status** | | | | | |
| Primary | 18(9.0%) | 11(61.11%) | 7(38.89%) | 94.36 | P<0.001 |
| Secondary | 54(27.0%) | 40(74.07%) | 14(25.93%) | | |
| Tertiary | 128(64.0%) | 99(77.34%) | 29(22.66%) | | |
| **Body mass index (kg/m$^2$)** | | | | | |
| Underweight | 2(1.0%) | 1(50.0%) | 1(50.0%) | 108.4 | P<0.001 |
| Normal | 77(38.5%) | 28(36.36%) | 49(63.63%) | | |
| Overweight | 33(16.5%) | 33(100.0%) | 0(0.0%) | | |
| Obese I | 70(35.0%) | 70(100.0%) | 0(0.0%) | | |
| Obese II | 18(9.0%) | 18(100.0%) | 0(0.0%) | | |

P<0.05= Significant, P>0.05= Non significant, BMI= Body mass index

**Table 2.** Level of Thyroid hormones and BMI among study groups

| Parameters | Infertile group N=150 | Fertile Groups N=50 | P-Value |
|---|---|---|---|
| T3 (ng/mL) (Ref Range: 0.52-1.85) | 0.52±0.04 | 1.19±0.03 | P<0.001 |
| T4 (ng/mL) (Ref Range: 4.4-10.8) | 4.01±0.19 | 5.86±0.16 | P<0.001 |
| TSH (mIU/mL) (Ref Range: 0.39-6.16) | 5.29±0.28 | 3.98±0.20 | P<0.001 |
| BM I(kg/m$^2$) (Ref Range: 18.5-24.5) | 28.99±0.34 | 22.46±0.26 | P<0.011 |

Value are expressed in Mean±SEM. P<0.05- Significant, P>0.05- Non significant, T3- Triiodothyronine, T4-Thyroxine, TSH-Thyroid stimulating hormone, BMI-Body mass index, Ref.- Reference.

**Table 3.** Seminal indices among study groups

| Parameter | Infertile Group N=150 | Fertile Group N=50 | P-Value |
|---|---|---|---|
| Sperm Count (X10$^6$) (Ref Range: 12-16) | 8.31±0.72 | 22.36±0.90 | P<0.001 |
| Total Motility (%) (Ref Range: 38-42) | 30.44±2.60 | 80.24±1.64 | P<0.001 |
| Prog.Motility (%) (Ref Range: 31-34) | 18.08±1.96 | 54.10±2.72 | P<0.001 |
| Viable Sperm Cell (%) (Ref Range: 55-63) | 32.64±2.64 | 80.04±1.65 | P<0.001 |
| Non-Viable Sperm Cell (%) | 35.28±2.74 | 19.96±1.65 | P<0.001 |
| Normal Form (%) (Ref Range: 3.0-4.0) | 5.69±0.59 | 16.12±1.06 | P<0.001 |
| Abnormal Form (%) | 83.64±1.08 | 61.67±3.55 | P<0.001 |
| Volume (mL) (Ref Range: 1.4-1.7) | 2.48±0.05 | 2.91±0.06 | P<0.001 |

Value are expressed in Mean±SEM. P<0.05- Significant, P>0.05- Non significant, Prog-Progressive, Ref.- Reference.

**Table 4.** Seminal indices among euthyroid, subclinical and overt (clinical) hypothyroid infertile males

| Parameters | Euthyroid N=62 | Subclinical Hypothyroid N=11 | Overt (Clinical) Hypothyroid N=77 | P-Value |
|---|---|---|---|---|
| Sperm Count ($X10^6$) (Ref Range: 12-16) | 14.04±1.16 | 6.91±2.77 | 3.90±0.63 | P<0.000 |
| Total Motility (%) (Ref Range: 38-42) | 40.00±3.86 | 30.00±10.08 | 22.81±3.56 | P<0.006 |
| Prog.Motility (%) (Ref Range: 31-34) | 25.60±3.43 | 17.45±7.64 | 12.12±2.22 | P<0.004 |
| Viable Sperm Cell (%) (Ref Range: 55-63) | 43.76±3.69 | 31.36±10.16 | 23.88±3.69 | P<0.001 |
| Normal Form (%) (Ref Range: 3.0-4.0) | 10.29±1.08 | 3.09±1.44 | 2.36±0.42 | P<0.000 |
| Volume (ML) (Ref Range: 1.4-1.7) | 2.44±0.09 | 2.45±0.20 | 2.53±0.09 | P=0.765 |

Values are expressed in Mean±SEM. P<0.05- Significant, P>0.05- Non significant; PROG-Progressive, Ref- Reference.

**Table 5.** Level of thyroid hormones, TSH and BMI among euthyroid, subclinical and overt (clinical) hypothyroid infertile males

| Parameters | Euthyroid N=62 | Subclinical Hypothyroid N=11 | Overt (Clinical) Hypothyroid N=77 | P-Value |
|---|---|---|---|---|
| T3 (ng/dL) (Ref. Range: 0.52-1.85) | 0.98±0.05 | 0.55±0.09 | 0.18±0.01 | P<0.000 |
| T4 (ug/mL) (Ref. Range: 4.4-10.8) | 6.25±0.23 | 4.85±0.31 | 2.24±0.08 | P<0.000 |
| TSH (mIU/mL) (Ref Range: 0.39-6.16) | 2.03±0.18 | 6.37±0.06 | 8.43±0.14 | P<0.000 |
| BMI ($Kg/m^2$) (Ref Range: 18.5-24.5) | 28.02±0.54 | 28.55±1.80 | 29.83±0.44 | P=0.041 |

Value are expressed in Mean±SEM. P<0.05- Significant, P>0.05- Non significant, T3-Triiodothyroxine, T4- Thyroxine, TSH-Thyroid stimulating hormone, BMI-Body mass index, Ref-Reference.

**Table 6.** Correlation of thyroid hormones, thyroid stimulating hormones, BMI and seminal indices among study groups

| Parameters | R-Value | P-Value |
|---|---|---|
| T3/Sperm count | 0.554 | P<0.001 |
| T4/Sperm count | 0.564 | P<0.001 |
| TSH/Sperm count | -0.529 | P<0.001 |
| T3/Total motility | 0.414 | P<0.001 |
| T4/Total motility | 0.407 | P<0.001 |
| TSH/ Total motility | -0.344 | P<0.001 |
| T3/Progressive motility | 0.353 | P<0.001 |
| T4/Progressive motility | 0.336 | P<0.001 |
| TSH/Progressive motility | -0.328 | P<0.001 |
| T3/Normal morphology | 0.462 | P<0.001 |
| T4/Normal morphology | 0.506 | P<0.001 |
| TSH/Normal morphology | -0.457 | P<0.001 |
| T3/Viable sperm cell | 0.451 | P<0.001 |
| T4/Viable sperm cell | 0.434 | P<0.001 |
| TSH/Viable sperm cell | -0.366 | P<0.001 |
| BMI/Sperm count | -0.621 | P<0.001 |
| BMI/Total motility | -0.550 | P<0.001 |
| BMI/Prog Motility | -0.503 | P<0.001 |
| BMI/Viable sperm cell | -0.542 | P<0.001 |
| BMI/Normal form | -0.584 | P<0.001 |

T3=triiodothyronine; T4=thyroxine; TSH=thyroid stimulating hormone

**Table 7.** Area under ROC urve

| Test Result Variable(s) | Area | P-value | Asymptotic 95% Confidence Interval | |
|---|---|---|---|---|
| | | | Lower Bound | Upper Bound |
| T3(ng/ml) | 0.858 | 0.001 | 0.807 | 0.908 |
| T4(ug/dl) | 0.765 | 0.001 | 0.702 | 0.828 |
| Sperm Count (Million) | 0.875 | 0.001 | 0.828 | 0.921 |

P<0.05- Significant, P>0.05-Non significant, T3-Triiodothyroxine, T4- Thyroxine.

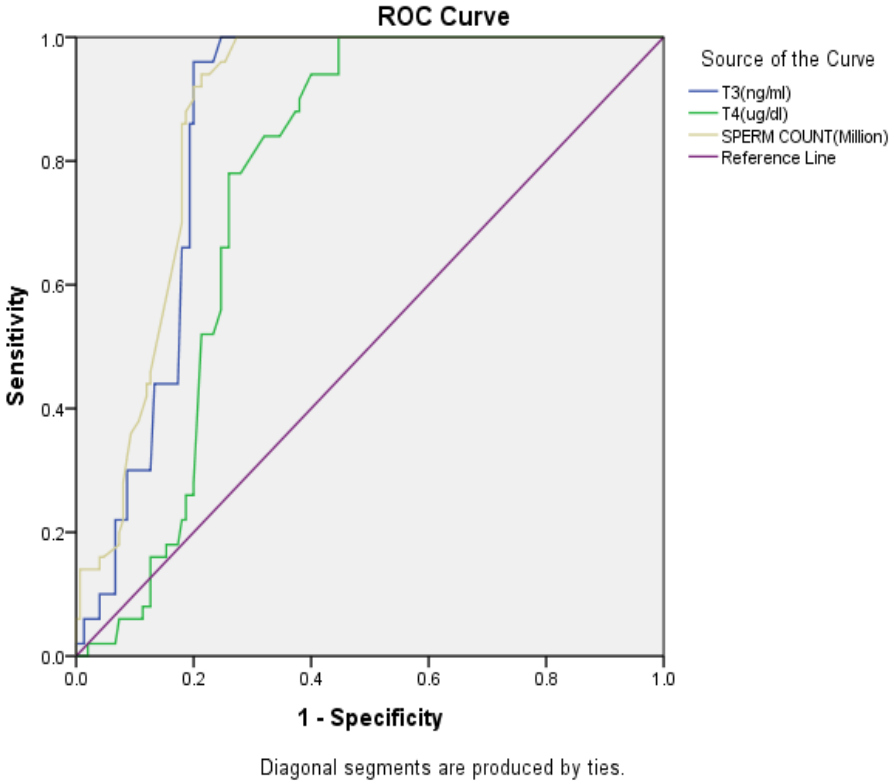


**Figure 1.** Receiver operating characteristics (ROC) curve

Male infertility may be due to several factors ranging from endocrine disorder, immunological, (21,22), genetic and chromosomal defects (23) as well as unknown causes (24). The first line of medical investigation to identify males with infertility is to carry-out seminal fluid analysis (2,21). The involvement of thyroid hormone abnormalities in male infertility among Nigerians in most cases is underestimated. Given that Nigeria is prone to iodine deficiency disorders because of its landscape and heavy rainfall couple with insufficient iodinated salt intake in several households, it is important to pay attention to thyroid dysfunction in the investigation of male infertility. Thyroid dysfunction can affect physiological functions of leydig cells, Sertoli cells, and sperm cells production. Therefore, this study was designed to evaluate the levels of thyroid hormones in males investigated for infertility and correlate thyroid function parameters with sperm indices.

A large proportion of infertile males had thyroid abnormalities. Of the 150 subjects, 58.7% had either sub-clinical hypothyroidism or clinical hypothyroidism, while only 41.33% were euthyroid. The sperm parameters of subjects with thyroid disorders were of poorer quality and quantity indicating the impact of thyroid dysfunction on male infertility. Another interesting finding is the association between thyroid hormone levels, TSH, and sperm characteristics among the infertile subjects. This might be as a result of the role thyroid hormones play in sperm quality and quantity modulation. As reported, hypothyroidism can affect spermatogenic process, thereby leading to the production of poor sperm quality and quantity (22). It was observed that the infertile males had sperm indices which were significantly lower except non-viable form and abnormal form that were increased compare with control group. Several studies have reported abnormalities of sperm indices among infertile males (22,24), this could result in the inability of males with semen abnormities to fertilize a fertile female partner.

Thyroid hormones affect the male reproductive organs via genomic and non-genomic pathways. It was reported that Genomic effects result from the coming together of T3 to thyroid hormone receptor (TR) in the nucleus of Sertoli and Leydig cells. Here, the hormone–receptor complex switch-on gene transcription and protein biosynthesis (26-28). TRα1 is the main isoform present in germ cells during the developmental stages of spermatozoa (from intermediate spermatogonia to pachytene spermatocyte) and in Sertoli cells. T3 also acts on non-germ cells by controlling their multiplication and differentiation (8). Specifically, T3 is reported to have a double effect on Leydig cell, it acutely activates luteinizing hormone (LH) synthesis and chronically inhibits it (28). T3 terminates Sertoli cell multiplication, and changes the closeness between them as well as hampering the expression of the neural cell adhesion molecule (29).

The binding of thyroid hormone to non-nuclear receptors presents in the cytoplasm and mitochondria of spermatozoon, upregulate cyclic adenosine monophosphate (cAMP) production, and the release of calcium ions required for motility. Some authors have demonstrated that T4 enhance the rapid increase of flagella movements, and increase number of spermatozoa. Thyroid hormones are also involved in the maintenance of redox balance in the testis (8). The predominant mitochondria proteins found in the mid-piece of spermatozoa are glutathione peroxidase which act in conjunction with other selenium-containing proteins to maintain redox balance. The ideal redox status is necessary for the improvement of sperm motility and thyroid autoimmunity (29).

It was earlier suggested that hypothyroidism can impair spermatogenesis and male infertility. This may be due to the ability of the hypothyroid subjects to cause a reduction in Steroid hormone binding globulin (SHBG) and Androgen binding protein (ABP) synthesis, which can lead to a decrease in LH, FSH and total testosterone levels (30). Luteinizing hormone (LH) is known to act on leydig cells to produce testosterone, this hormone together with follicle stimulating hormone (FSH) and ABP play important roles in spermatogenesis (27). Most of the infertile males with hypothyroidism were either subclinical hypothyroid or overt or clinical hypothyroid. Hypothyroidism can affect sperm motility through various mechanism like increase in the levels of reactive oxygen species (ROS) that can alter the sperm cell membrane, changes in the pH of the sperm, abnormal activity of Na+ K+ ATPases, altered transmembrane transport of calcium in the sperm cell membrane, mitochondrial number, expression of mitochondrial genes which can cause a reduction in sperm motility thereby reducing fertility (24,30).

It was also observed that the infertile euthyroid males had significantly higher levels of sperm indices compared with hypothyroid infertile males except semen volume that was not significant increased. This aligned with previous study (31), where it was reported that the sperm indices of hypothyroid patients were poorer than those of euthyroid counterparts. They observed that sperm count, sperm motility and sperm morphology were greatly reduced in hypothyroid group than the euthyroid subjects. Hypothyroidism has more negative effect on sperm morphology than other semen parameters (31).

## 4. CONCLUSIONS

Thyroid gland dysfunction was common among infertile men in this study. The thyroid disorders observed were subclinical hypothyroidism, overt or clinical hypothyroidism, and less than half of the study participants were euthyroid. The sperm parameters of the infertile subjects with thyroid dysfunction were poorer in quality and quantity than euthyroid infertile subjects. Thyroid gland dysfunction may have harmful impacted on sperm indices. Thyroid dysfunction should not be ignored when evaluating men with infertility.

**Author contributions:** This study was conducted and approved by all authors. MAE: Designed the study. MAE, IA: Wrote the protocol. IA: Sourced for the funds. MAE, AI, JAO: Contributed to the literature search, conducted the data gathering, laboratory analysis, statistical analysis. MAE, IA: Drafted the manuscript. MAE: supervised the study. MAE, IA, JOA: Review the draft and proofread the final manuscript.

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**Ethics statement:** This research was reviewed and approved by the institutional review board of the University of Benin Teaching Hospital (UBTH) ((Protocol/registration Number: ADM/E 22/A/VOL. VII/14831269 dated 18th February, 2022). Informed consent was obtained from all participants.

**Conflict of interest:** The authors declare that they have no conflict of interest.

## REFERENCES


1. Choudhury S, Chainy GBN, Mishro MM. Experimentally induced hypo- and hyper-thyroidism influence on the antioxidant defence system in adult rat testis. Andrologia. 2003;35(3):131–140. https://doi.org/10.1046/j.1439-0272.2003.00548.x
2. Uadia PO, Emokpae AM. Male infertility in Nigeria: A neglected reproductive health issue requiring attention. J Basic Clin Reprod Sci. 2015;4(2):45–53. http://doi.org/10.4103/2278-960X.161042
3. Boitrelle F, Shah R, Saleh R, Henkel R, Kandil H, Chung E, Vogiatzi P, Zini A, Arafa M, Agarwal A. The sixth edition of the WHO manual for human semen analysis: A critical review and SWOT analysis. Life (Basel). 2021;11(12):1368. https://doi.org/10.3390/life11121368
4. Emokpae MA, Brown SI. Effects of lifestyle factors on fertility: practical recommendations for modification. Reprod Fertil. 2021;2(1):R13-R26. https://doi.org/10.1530%2FRAF-20-0046
5. Anelli V, Gatta E, Pirola I, Delbarba A, Rotondi M, Cappelli C. Thyroid impairment and male fertility: a narrative review of literature. The Aging Male. 2024;27(1):2310303. https://doi.org/10.1080/13685538.2024.2310303
6. Hussain T, Metwally E, Murtaza G, Kalhoro DH, Chughtai MI, Tan B, Omur AD, Tunio SA, Akbar MS, Kalhoro MS. Redox mechanisms of environmental toxicants on male reproductive function. Front Cell Dev Biol. 2024;12:1333845. https://doi.org/10.3389/fcell.2024.1333845
7. Sengupta P. Current trends of male reproductive health disorders and the changing semen quality. Int J Prev Med. 2014;5:1-5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3915461/
8. Sengupta P, Dutta S. Thyroid disorders and semen quality. Biomed Pharm J. 2018;11(1):1–10. https://dx.doi.org/10.13005/bpj/1342
9. La Vignera S, Vita R. Thyroid dysfunction and semen quality. Int J Immunopathol Pharmacol. 2018;32:2058738418775241. https://doi.org/10.1177%2F2058738418775241
10. Andersson M, Braegger CP. The role of iodine for thyroid function in lactating women and infants. Endocr Rev. 2022;43:469–506. https://doi.org/10.1210/endrev/bnab029
11. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. Nat Rev Dis Primers. 2022;8:30. https://doi.org/10.1038/s41572-022-00357-7
12. Yuan S, Liu C, Liu Z, Wang J, Xu Y, Shi J. Correlation between thyroid function indices and urine iodine levels in patients with nodular goiter. Am J Transl Res. 2023;15(6):4147-4154. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10331665/
13. Kareem YO, Ameyaw EK, Amoah RM, Adegboye OA, Yaya S. An assessment of Individual, community and state-level factors associated with inadequate iodised salt consumption among pregnant and lactating women in Nigeria. BMC Preg Childbirth, 2023;23(1):524. https://doi.org/10.1186/s12884-023-05833-w
14. Moyib OK. Iodine content of branded iodized Nigerian table salt: Ten years after USI Certification. Nigerian J Chem Res. 2018;23(1):10–20. https://www.ajol.info/index.php/njcr/article/view/179010
15. Sengupta P, Dutta S. Thyroid disorders and semen quality. Biomed Pharm J. 2018;11(1):1–10. https://doi.org/10.1177%2F2058738418775241
16. Moleti M, Di Mauro M, Paola G, Olivieri A, Vermiglio F. Nutritional iodine status and obesity. Thyroid Res. 2021;14(1):25. https://doi.org/10.1186/s13044-021-00116-y
17. Leso V, Vetrani I, De Cicco L, Cardelia A, Fontana L, Buonocore G, Iavicoli I. The Impact of thyroid diseases on the working life of patients: A systematic review. Int J Environ Res Public Health. 2020;17(12):4295. https://doi.org/10.3390%2Fijerph17124295
18. Moronkeji MA, Emokpae MA, Ojo TA, Moronkeji RE, Ogundoju LT. The patterns and occupational distribution of hormonal abnormalities among men investigated for infertility in some centers in the Southwest, Nigeria. J Clin Transl Res. 2021;7(2):221-228. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8177851/
19. Alonzo TA, Pepe MS and Moskowitz CS. Sample size calculations for comparative studies of medical tests for detecting presence of disease. Stat Med 2002; 21(6): 835-852. https://doi.org/10.1002/sim.1058
20. Alahmar A, Dutta S, Sengupta P. Thyroid hormones in male reproduction and infertility. Asian Pac J Reprod, 2019;8(5):203-210. https://doi.org/10.4103/2305-0500
21. World Health Organization. WHO laboratory manual for the examination and processing of human semen 6th edition. Cambridge 2021; Cambridge University Press. https://www.who.int/publications/i/item/9789240030787
22. Mazzilli R, Medenica S, Di Tommaso AM, Fabozzi V, Zamponi D, Cimadomo L et al. The role of thyroid function in female and male infertility: a narrative review. J Endocrinol Invest. 2023;46:15–26. https://doi.org/10.1007/s40618-022-01883-7
23. Ferlin A, Foresta C. Infertility: practical clinical issues for routine investigation of the male partner. J Clin Med. 2020;9(6):1644. https://doi.org/10.3390%2Fjcm9061644
24. Dosiou C. Thyroid and fertility: recent advances. Thyroid, 2020;30(4):479–486. https://doi.org/10.1089/thy.2019.0382
25. Vander BM, Wyns C. Fertility and infertility: definition and epidemiology. Clin Biochem. 2018;62:2–10. https://doi.org/10.1016/j.clinbiochem.2018.03.012
26. Mahdi BM. Semen Analysis and Insight into male infertility. Open Access Maced J Med Sci. 2021;9(A):252-256. https://doi.org/10.3889/oamjms.2021.5911

27. Condorelli RA, La Vignera S, Mongioì LM, Alamo A, Giacone F, Cannarella R, Calogero AE. Thyroid hormones and spermatozoa: in vitro effects on sperm mitochondria, viability and DNA integrity. J Clin Med, 2019;8(5):756. https://doi.org/10.3390/jcm8050756

28. Rehman R, Zafar A, Fatima SS, Mohib A, Sheikh A. Altered sperm parameters and subclinical hypothyroidism; A cross sectional study in Karachi, Pakistan. Int J Clin Pract, 2020;74(9):e13555. https://doi.org/10.1111/ijcp.13555

29. Kakoulidis I, Ilias I, Stergiotis S, Togias S, Michou A, Lekkou A, Mastrodimou V, Pappa A, Milionis C, Venaki E, Koukkou E. Study on the interaction between serum thyrotropin and semen parameters in men. Med Scis. 2022;10(2):22. https://doi.org/10.3390%2Fmedsci10020022

30. Chaker L, Razvi S, Bensenor IM, Azizi F, Pearce EN, Peeters RP. Hypothyroidism. Nat Rev Dis Primers. 2022;8:30. https://doi.org/10.1038/s41572-022-00357-7

31. Khourdaji I, Lee H, Smith RP. Frontiers in hormone therapy for male infertility. Transl Androl Urol 2018;7(Suppl 3):S353-S366. https://doi.org/10.21037%2Ftau.2018.04.03