

THYROID HYPOFUNCTION IN MALE PARTNERS ATTENDING INFERTILITY CLINIC AND ITS IMPACT ON SEMEN PARAMETERS

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ABSTRACT

BACKGROUND

Thyroid disorders are common in females and their impact on the female reproduction is well established. The role of thyroid hormone on male reproduction received much attention with recognition of thyroid hormone receptor expression on gonadal cells. Studies in humans evaluating the impact of varying severity of thyroid hypofunction on male fertility are limited.

OBJECTIVE

To study the thyroid status and correlation with semen parameters in male partners of couples attending infertility clinic.

MATERIALS AND METHODS

In this retrospective study, data on thyroid hormone levels, anti-TPO antibodies, semen parameters of 125 men attending infertility clinic, after excluding men with known thyroid disorder, on thyroid medication, other drugs and medical conditions which have an influence on thyroid status, were analysed.

RESULTS

Of the total 125 subjects, 84% men were euthyroid, whereas thyroid hypofunction, which included subclinical hypothyroidism and overt hypothyroidism was observed in 14.4% and 1.6% of men respectively. 11% of the subjects had positive anti-TPO antibodies. Normal semen parameters were observed in 82 subjects whereas 43 men had abnormal semen parameters. None of the semen parameters correlated with TSH; however, there was a non-significant increase in spermatozoa with abnormal morphology (95% vs. 90.8%, $p=0.522$), decrease in spermatozoa with normal morphology (5% vs. 7.38, $p=0.273$) and decrease in sperm count (49.24 vs. 37.67 million/mL, $p=0.473$) in subjects with TSH>10 in comparison with subjects with TSH<10.

CONCLUSION

This study found higher prevalence of thyroid hypofunction, and higher positive TPO antibody status among men attending infertility clinic. No correlation was found between thyroid hormones and semen parameters.

KEYWORDS

Thyroid, Hypofunction, Semen, Infertility, Thyroid Deficiency, Male Reproduction.

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BACKGROUND

The impact of thyroid dysfunction on female reproduction has been clearly established. With regard to male reproduction, though few earlier studies were controversial, in the past two decades, the role of thyroid hormones in male reproduction received much attention with identification of thyroid hormone receptors and their expression at different stages of development of germ cells.^(1,2,3,4) Animal studies found the effect of hypothyroidism on immature, and mature testis was different,^(5,6,7) and also reversal of sperm fertility characteristics with T4 administration.⁽⁸⁾ Human studies also found the differential effect of hypothyroidism, depending on whether it occurred prepubertally or postpubertally.^(9,10,11)

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Short-term hypothyroidism has no impact whereas prolonged hypothyroidism may have an impact on male reproduction in adults.⁽¹²⁾ Studies on the impact of hypothyroidism on spermatogenesis and semen parameters are contrast and limited. Hence, an attempt has been made to study the prevalence of thyroid hypofunction and relationship with semen parameters in male partners of couples attending infertility clinic.

MATERIALS AND METHODS

This retrospective study reviewed the medical records of a total of 342 male partners of couples attending infertility clinic of tertiary care teaching hospital between Jan 2016 to May 2016. Data on thyroid hormones and semen analysis was available for 167 men. Out of which, data on 125 men analysed in the present study, remaining 42 men's data excluded. Exclusion criteria included subjects with pre-existing thyroid disease, prior vasectomy, varicocele, cryptorchidism, hyperprolactinaemia, on thyroid medication, steroids, chemotherapy and drugs which can affect thyroid hormone status like amiodarone and lithium. Recorded data on TSH, anti-TPO antibody status, semen parameters were analysed, to know the relationship between thyroid status and semen

parameters. Based on TSH levels, study subjects were categorised into euthyroid (TSH <5 µIU/mL, normal free T4), subclinical hypothyroid (TSH>5.0 µIU/mL, normal free T4) and overt hypothyroid (TSH>10, low free T4). Subjects were categorised into euthyroid group (TSH<5) and thyroid hypofunction group (TSH>5), and were compared. To know the impact of severity of thyroid hypofunction, subjects were categorised, with TSH<10 and >10, and were compared for semen parameters. Normal semen analysis⁽¹³⁾ was considered when 1. Semen volume ≥1.5 mL; 2. Sperm concentration ≥15 million/mL; 3. Sperm count ≥39 million per ejaculate; 4. Total sperm motility≥ 40%(progressive sperm motility>32%); 5. Spermatozoa with normal morphology ≥4%. Based on this, subjects were classified into having normal semen or abnormal semen parameters. Institutional ethical committee clearance was taken to analyse the data.

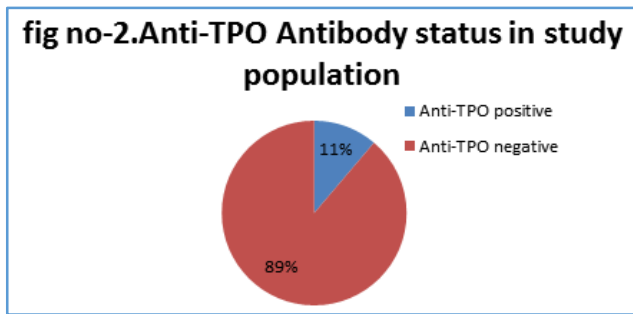
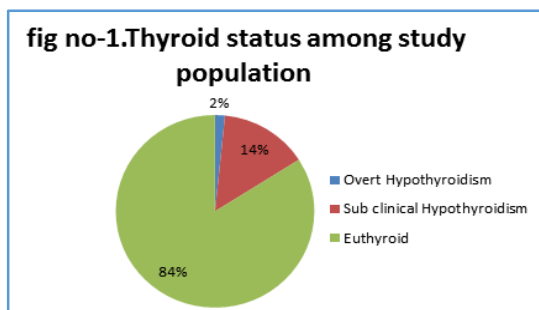
STATISTICAL ANALYSIS

R Programming software (Version 3.0) was used for data analysis. Results were expressed as Mean±SD. Differences between means were analysed by student’s unpaired t test using two tailed tests for significance. P=<0.05 was considered statistically significant. Analysis of the correlation between parameters was performed by using Pearson’s bivariate correlation coefficient.

RESULTS

The age of subjects ranged from 27-54 with a mean age of 34.14±36.23 years, and with mean BMI of 26.39±6.99 kg/m². Of the total subjects, 84% of the subjects (n=105) were euthyroid, whereas 14.4% (n=18), 1.6% (n=2) were having subclinical hypothyroidism and overt hypothyroidism respectively as shown in fig-1. Positive anti-TPO antibodies were observed in 11% of subjects, shown in fig-2. Semen parameters were not significantly different in euthyroid and thyroid hypofunction group as shown in table-1. There was a non-significant increase in spermatozoa with abnormal morphology (95% vs. 90.78%, p=0.522), decrease in spermatozoa with normal morphology (5.0% vs. 7.38%, p=0.273), and decrease in sperm count (37.67 vs. 49.24 million/mL, p=0.473) in subjects with TSH>10 in comparison with subjects with TSH <10, as shown in table-2.

65.6% (n=82) of the subjects had normal semen parameters, whereas 33.6% (n=43) had abnormal semen parameters. TSH and free T4 levels were not significantly different in subjects having normal and abnormal semen parameters, whereas anti-TPO antibody positivity was higher in subjects with abnormal semen than normal group, similarly smokers were more in subjects with abnormal semen, as shown in table-3. No correlation was found between Semen parameters (semen volume, count, motility and morphology) and TSH as shown in table-4.



Parameter	Euthyroid Group (TSH <5) n=105, (Mean±SD)	Thyroid Hypo Function Group (TSH>5) n=20, (Mean±SD)	p-value
Age (years) (Mean±SD)	34.02± 5.86	34.80±5.40	0.581
BMI (kg/m ²) (Mean±SD)	26.70±7.45	24.63±3.00	0.236
TSH(µIU/mL) (Mean±SD)	2.19±0.94	11.49±13.52	<0.001
Free T4 (ng/dL) (Mean±SD)	1.24±0.186	1.303±0.173	0.04
Anti-TPO Antibody Positivity {n, (%)}	5(4.76%)	9(45%)	-
Semen Volume (mL) (Mean±SD)	2.56±1.27	2.44±0.73	0.703
Sperm count (millions/mL) (Mean±SD)	47.47±26.19	57.59±33.51	0.161
Total Motility (%) (Mean±SD)	57.03±15.35	58.06±12.26	0.794
Normal Morphology (%) (Mean±SD)	7.21±3.71	7.88±3.62	0.493

Table 1: Semen Parameters in Euthyroid and Thyroid Hypofunction Group

Parameter	TSH <10 n=121 (mean±SD)	TSH >10 n=4 (mean±SD)	p-value
Semen volume (mL)	2.54±1.22	2.62±0.63	0.887
Sperm count (millions/mL)	49.24±27.72	37.67±8.74	0.473
Total Motility (%)	57.06±15.06	61.67±2.89	0.599
Spermatozoa with normal morphology (%)	7.38±3.69	5.00±3.00	0.273
Spermatozoa with abnormal morphology (%)	90.78±11.34	95.00±3.00	0.522

Table 2: Comparison of Semen Parameters in Subjects with TSH >10 and <10

Parameter	Normal Semen n=82	Abnormal Semen n=43	P value
Free T4 (ng/dL)	1.30±0.17	1.25±0.19	0.04
TSH(μIU/mL)	3.59±6.81	3.55±5.67	0.979
Anti-TPO positive {n, (%)}	4(3.2%)	10(8%)	-
Smoking {n, (%)}	8(6.4%)	11(8.8%)	-

Table 3: Thyroid Status in subjects with Normal and Abnormal Semen

Semen Parameter	TSH
Semen volume	r=-0.0559, p=0.538
Sperm count	r=-0.004, p=0.962
Total Motility	r=0.0607, p=0.519
Sperm Morphology	r=-0.0154, p=0.869

Table 4: Correlation of TSH with Semen Parameters

DISCUSSION

Thyroid disorders are less common in males. The prevalence of hypothyroidism in males in India found to be 5.02% and prevalence of undetected hypothyroidism was 3.47%⁽¹⁴⁾ Anti-TPO antibody positivity in males, in India, reported to be 16.8%.⁽¹⁴⁾

In the present study, 84% of the subjects were euthyroid, whereas 14.4% and 1.6% of the subjects were having subclinical and overt hypothyroidism respectively. TPO antibody positivity was observed in 11% of the subjects.

The published literature in humans reporting the effect of hypothyroidism on semen parameters is limited and contrasting and mostly from western countries. In this study, we found no significant difference in semen parameters in euthyroid males and males having thyroid hypofunction. Similarly, in the Indian context, Manojkumar Sharma et al⁽¹⁵⁾ found no correlation between thyroid hormones and semen parameters. However, earlier studies by Corrales Hernandez et al⁽¹⁶⁾ found hypothyroidism had an adverse impact on sperm quality and progressive motility, and Jayakumar et al⁽¹⁷⁾ reported some improvement in sperm count and motility with levothyroxine treatment.

Morphological abnormalities of sperm with deformed heads greatly reduces its potential to fertilise the mature oocyte. Thyroid hormones does exert their effect on cell cytoskeleton.⁽¹⁸⁾

Krassas GE et al⁽¹⁹⁾ in their prospective controlled study found, morphology is the only sperm parameter, significantly differed in hypothyroid patients in comparison with controls, which improved significantly after treatment. Sperm motility also decreased which improved after treatment, but the difference is not statistically significant. In this study, there was a trend towards having lower counts, reduced normal morphology spermatozoa and increased abnormal spermatozoa in overt hypothyroidism than in subclinical hypothyroidism.

Meeker JD et al⁽²⁰⁾ found an association between free T4 and reduced odds of having sperm motility of less than 50%. We did not find any difference in motility among euthyroid and males with thyroid hypofunction and no correlation with free T4.

Trummer et al⁽²¹⁾ found that presence of abnormal thyroid functions were similar in subjects with normozoospermia and pathozoospermia, whereas prevalence of positive TPO

antibodies was higher in subjects with pathozoospermia, asthenozoospermia in comparison with normozoospermia. In our study, we found higher antibody positivity in males with abnormal semen. In contrast, Poppe K et al found⁽²²⁾ prevalence of abnormal thyroid function and thyroid autoimmunity was not different among men with normal and abnormal semen parameters. Limitation of the study is, thyroid status is based on single TSH value, and single measurement of semen sample, whose reproducibility and variability could not be assessed in view of the retrospective type of the study.

In conclusion, this study found higher prevalence of thyroid hypofunction, and higher positive TPO antibody status among men attending infertility clinic. No correlation was found between thyroid hormones and semen parameters.

More research is needed with large prospective studies evaluating the role of thyroid hypofunction on semen parameters and fertility and if found, response to levothyroxine therapy needs to be evaluated.

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