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ORIGINAL ARTICLE

RELATIONSHIP BETWEEN THYROID PROFILE AND SEMEN QUALITY

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ABSTRACT

Background: Endogenous hormones are critical to spermatogenesis and maintenance of male reproductive function. Follicle stimulating hormone (FSH), luteinizing hormone (LH), inhibin B and testosterone all serve important and well-known functions in the male hypothalamopituitary-gonadal axis and male reproduction. However, the potential relationship between other hormones, including thyroid hormones, and semen quality are still not completely understood. Thus in the present study an attempt has been made to report the degree of associations between thyroid hormones and semen quality.
Methods: Fifty-five men were recruited from an infertility clinic between August 2010 to May 2011. Fresh semen samples were assessed for quality (concentration, motility and morphology) and the serum levels of Tetraiodothyronine (T_4), Triiodothyronine (T_3), and Thyroid stimulation hormone (TSH) were measured.
Result & Conclusion: We have found that though men with abnormal semen profile had higher total T_3, T_4 concentrations and lower TSH concentrations compared to those with normal semen profile, only T_4 showed significant increase and further it was found that only total T_4 was significantly associated with asthenozoospermia. Further studies and observation are needed on a larger number of patients, to validate the correlation with Thyroid status and to justify the trial of a small dose of anti-thyroid drug in asthenozoospermic patients.

Key words: Male infertility, Thyroid hormones, Oligozoospermia, Asthenozoospermia

INTRODUCTION

Infertility is a major problem affecting approximately 5-15% of all married couples[1]. In a country like India, infertility implies great psychological and social stigma mostly directed against female partners, in spite of the fact that usual causes of infertility includes a male factor (30%), a female factor (35%), a combination of both (20%) and finally unexplained or idiopathic infertility (15%)[1]. Previous studies[2,3] have reported that circulating levels of specific reproductive hormones in men are associated with semen quality parameters. However, the potential relationship between other hormones, including thyroid hormones, and semen quality are still not completely understood. Although the effects of hyperthyroidism[4] and hypothyroidism[4] on female reproduction are well established, the effects of thyroid disorders on male infertility are not studied extensively, probably because in thyrotoxic male, attention is usually focused on other manifestations of the disease, and fertility status is frequently not evaluated. However few studies[5,6] suggest that

thyroid dysfunction can impair the quality of semen, and lower the sperm motility and/or count, Thus in the present study, the relationship between thyroid hormone levels and semen quality was explored in a population that included men recruited from an infertility clinic to detect associations between thyroid hormone levels and semen quality.

MATERIAL AND METHOD

This study was designed to determine the relationship between thyroid profile and semen quality. Fifty-five men (age 26 to 37 years) of infertile couple were enrolled from August 2010 to May 2011. Causes of infertility in female partner of all these men were excluded by gynaecologist. Exclusionary criteria included prior vasectomy or current use of exogenous hormones, Cryptorchidism, Hyperprolactinemia, subject with pre-existing thyroid disease or taking drugs (antihypertensive, antipsychotic, steroids, and chemotherapy), lack of approval by physician and subjects showing disinterest. All subjects were studied as outpatient. Participant's examination included interviews for medical and nutritional history. Present and past history of each case was recorded in detail regarding their general information i.e. name, age, sex, address, religion, occupation, economic status, nutritional and personal habits, education, medication and history suggestive of any systemic illness. Each subject was then examined for various anthropometric parameters: Weight (Kg) and height (meters) were measured (using Omron digital body weight scale HN-286 and SECA 206 wall mounted metal tapes respectively). Body Mass Index (BMI) was calculated by Weight (Kg) / height squared (m^2). All anthropomorphic measures reflect the average of 2 measurements (measured by same person on same instrument to avoid inter-instrument and inter personal variation). All subjects were asked to collect semen by masturbation into a sterile plastic specimen cup at the hospital. Subjects were instructed to abstain from ejaculation for at least 72 hours prior to providing the semen sample. The sample was liquefied for at least 20 minutes, but no longer than 1 hour prior to performing a routine semen analysis, which included measurements of volume, pH, sperm concentration, sperm motility, progressive motility, and sperm morphology. Semen samples were analyzed for sperm concentration and motion parameters using a computer aided semen analyzer. Motile sperm were defined according to the World Health Organization (WHO) grade as 'A' grade sperm (rapidly progressive with a velocity $\geq$25 µm/s at 37°C) and 'B' grade sperm (slow/sluggish progressive with a velocity $\geq$5 µm/s but <25 µm/s)[7]. For morphology, two slides were prepared from each fresh semen sample. The resulting thin smear was allowed to air dry before staining with the Diff-Quik staining kit (Dade Behring AG, Dudingen, Switzerland). Morphological assessment was performed with an Olympus microscope using an oil immersion 1006 objective. A minimum of 200 sperm cells were counted from the 2 slides for each specimen. Strict scoring criteria were used to classify men as having normal or subnormal morphology[8].

A sample of blood was drawn after overnight fast of 12 hours with an aseptic technique on the same day that the semen sample was collected. Sera were separated from the collected blood samples. Total T_3, T_4 and TSH were measured by Chemiluminescence Immunoassay (CLIA) using Acculite CLIA microwells kit. The interassay CVs for both hormones were less than 9%. For TSH, interassay CVs was less than 8%. The study was approved by Ethical committee, and all subjects signed an informed consent form.

Statistical analysis: Data analyses were performed with the SPSS Version 15 statistical software. The results were expressed as mean ± SD if the variables were continuous, and as percentage, if categorical. All values were within the normal distribution curve. The Chi square test was used for evaluating differences in proportions between groups. The two tailed (unpaired) student's test for independent samples, analysis of variance (ANOVA) was used, in assessment of the significance of difference between group means. The Chi square test was used for evaluating differences in proportions between groups. For all analyses, the nominal level of statistical significance was<0.05.

RESULTS

Fifty-five men (age 26 to 37 years) of infertile couple were divided into two groups on the basis of semen profile as per WHO protocol[7]:

Group A: Comprised of 30 men of age group 26 to 37 years (mean 30.8 ± 2.95 years) having normal semen parameters (Table 1).

Group B: Comprised of 25 men of age group 26 to 36 years (mean 31.24 ± 2.94 years) having abnormal semen parameters (Table 1).

Table 1: Comparison of Semen and thyroid profile of normal and abnormal subjects (Mean ± SD)

Characteristics	Group A (n=30)	Group B (n=25)
Age (Years)	30.8 ± 2.95	31.24 ± 2.94
Sperm counts (million/ml)	67.83 ± 9.95	28.32 ± 14.60
Sperm motility (%)	63.76 ± 6.06	42.09 ± 14.06
Normal morphology (%)	84.12 ± 4.25	80.92 ± 5.27
Total T_3 (ng/ml) (0.52 - 1.90)	1.18 ± 0.33	1.28 ± 0.46
Total T_4 (mcg/dl) (4.40 - 10.80)	7.15 ± 2.24	8.39 ± 1.90*
TSH (µIU/ml) (0.42 - 5.45)	2.07 ± 1.03	1.92 ± 1.10

*p<0.05

Table 1 shows the various semen characteristics of study population. In group A sperm counts varied from 46 to 83 million/ml with mean of 67.83 ± 9.95, percentage of sperm motility ranged from 50 to 76 with mean of 63.76 ± 6.06 and percentage of normal sperm morphology varied from 78 to 92 with mean of 84.10 ± 4.25 , whereas in group B sperm counts varied from 13 to 64 million/ml with mean of 28.32 ± 14.60 , percentage of sperm motility ranged from 15 to 70 with mean of 42.0 ± 14.06 and percentage of normal sperm morphology varied from 70 to 90 with mean of 80.92 ± 5.27 (Table 1). Though men with abnormal semen profile had higher total T_3, T_4 concentrations and lower TSH concentrations than with normal semen profile, but only T_4 showed the significant difference (Table 1).

Table 2: Distribution of sperm abnormalities in group B subjects

Sperm Abnormality	No. of Subjects (n = 25) (%)
Oligozoospermia	8 (32)
Asthenozoospermia	12 (48)
Oligo-asthenozoospermia	5 (20)

Out of 25 abnormal subjects, Oligozoospermia was found in 8 (32%, 95% confidence interval [CI], 28.67% - 34.21%), asthenozoospermia in 12 (48%, 95% confidence interval [CI], 43.4% - 51.9%) and oligo-asthenozo-ospermia in 5 men respectively (20%, 95% confidence interval [CI], 17.34% - 23.34%) (Table 2). Total T_3 (ng/ml) of oligozoospermic men ranged from 0.62 to 1.59 with mean of 1.20 ± 0.35, total T_4 (mcg/dl) varied from 5.6 to 9.26 with the mean of 7.49 ± 1.23 ,and TSH (µIU/ml) ranged from 0.96 to 2.50 with mean of 1.71 ± 0.52 (Table 3) but none of the thyroid profile parameters showed any significant difference when compared with men having normal semen profile, whereas in asthenozoospermic men total T_3 (ng/ml) ranged from 0.74 to 2.63 with mean of 1.33 ± 0.61, total T_4 (mcg/dl) varied from 7.03 to 12.9 with the mean of 9.24 ± 2.01, and TSH (µIU/ml) ranged from 1.09 to 6.80 with mean of 2.09 ± 1.55. Out of the three measured hormones only total T_4 was significantly higher in asthenozoospermic men compared to those with normal semen profile ($P < 0.05$), but still well within the normal limits. Total T_3 (ng/ml) of men with oligoasthenozoospermia ranged from 1.11 to 1.73 with mean of 1.2 ± 0.25 (mean ± SD), total T_4 (mcg/dl) varied from 5.90 to 10.24 with the mean of 7.81 ± 1.91 (mean ± SD), and TSH (µIU/ml) ranged from 1.62 to 2.16 with mean of 1.85 ± 0.20 (mean ± SD), but none of the measured hormones were significantly different compared to subjects with normal semen profile.

Table 3: Comparison of Thyroid profile in normal subjects and men with various sperm abnormalities

	Normal (n=30)	Oligozoospermia (n=8)	Asthenozoospermia (n=12)	Oligo-asthenozoo-spermia (n=5)
Total T_3 (ng/ml)	1.18 ± 0.33	1.20 ± 0.35	1.33 ± 0.61	1.28 ± 0.25
Total T_4 (mcg/dl)	7.15 ± 2.24	7.49 ± 1.23	9.24 ± 2.01*	7.81 ± 1.91
TSH (µIU/ml)	2.07 ± 1.03	1.71 ± 0.52	2.09 ± 1.55	1.85 ± 0.20

*<0.05

DISCUSSION

In the present study none of the subjects suffered from manifested thyroid dysfunction, all kinds of thyroid dysfunction were clinically insignificant and were classified as latent thyroid dysfunction. Sub clinical thyroid dysfunction was not correlated with altered semen density, sperm motility and morphology. This result corresponds with other studies[9].

However over the years, several studies have addressed the effect of excess of thyroid hormone on male reproduction. Clyde et al[10] investigated three young thyrotoxic males and found that two patients had marked Oligozoospermia with decreased motility and third patient had borderline low sperm counts associated with decreased motility. Kidd et al [11] investigated 5 patients of Grave's disease and found 4 of 5 subjects had total sperm counts less than 40 million/ml, whereas only one had sperm density less than 24 million/ml. Abalovich et al[12] investigated the effect of hyperthyroidism on spermatogenesis in 21 patients and reported that 9 patients (43%) had low total sperm counts, whereas 13 (61.9%) had progressive motility problem. Krassas et al[5] reported that male patients with hyperthyroidism have abnormalities in seminal parameters, mainly sperm motility. These abnormalities improve or normalize when patients become euthyroid.

In the current study total T_4 was within normal limits in both the study group, but its level was significantly increased in men with abnormal semen parameters, however T_3 and TSH were not found to be significantly different. These results agree with those of Poppe et al[13]. Further it was observed that total T4 was significantly greater in men with asthenozoospermia, however no relation of T3 and/or TSH was established with oligozoospermia, asthenozoospermia, or Oligo-asthenozoospermia, and this is similar to the observation of Hammami[14].

Nonetheless, this study has few limitations. Firstly, collection of only a single semen sample to assess semen parameters, and the collection of a single blood sample to measure serum hormone levels. However, it is not expected to greatly affect our results, since despite the diurnal and pulsatile fluctuations in serum hormone levels, a single blood sample can be used to provide a reliable measure of hormones over both short and long time periods in population studies[15,16]. Collection of only one semen sample is also not expected to affect our results. Uhler and coworkers[17] collected multiple semen samples (between 2 and 4) from each subject at time intervals that coincided with their partner's menstrual cycles, but found that the subsequent semen samples did not add value compared to using only the first semen sample collected on the same day as the serum hormone measures. In addition, a requirement for multiple blood or semen samples may limit participation rates. Secondly, the design was cross-sectional and therefore, causal relationship cannot be ascertained. Finally, because the present study was conducted among men recruited through an infertility clinic, our ability to generalize the results to the general population may be limited.

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