Original Article

ISSN (0): 2347-3398; ISSN (P): 2277-7253

Is Thyroid Dysfunction Affecting Oxidative Stress Index in Semen

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Abstract

Background: Declining trend of semen quality has become a major public health problem. Oxidative stress is playing major role in the current scenario of poor male fertility potential. Thyroid hormones have a pivotal role to play in that context as it potentially alters the oxidative status of the semen. Thus, in present study effect of thyroid abnormalities on oxidative status of semen quality is explored. **Objective:** This study aimed to determine the relationship between Thyroid dysfunction and Oxidative stress in semen of infertile couple. **Subjects and Methods:** The study included 100 Semen samples from the males of infertile couple attending the infertility clinic JNMCH AMU in the year 2016-2018. TSH levels were determined and simultaneously Total Antioxidant Capacity and Oxidative stress status of semen samples was evaluated by colorimetric method. The effect of thyroid dysfunction on Oxidative stress of semen was assessed using Pearson moment correlation test. **Results and Conclusion:** Higher values of TSH caused significant reduction in TAC and elevation of oxidative stress Index. Thereby showing that Thyroid dysfunction adversely affects the oxidative status and compromises male reproductive function.

Keywords: Oxidative stress, Male infertility, Total Antioxidant capacity, Thyroid, Semen parameters.

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Received: October 2019
Accepted: December 2019

Introduction

Infertility is considered as major health as well as social problem in India. Infertility refers to the condition where an infertile couple is not able to conceive after 12 months of unprotected sexual intercourse. [1] Approximately 5-15% of all married couples in country are facing this problem. [2]
Generally, the social stigma is attached to female partner but around 50 % males are also contributing to infertility. About 50 % of male partners experiencing infertility do not seek professional help and up to 25% of couples seeking infertility treatment do not complete a male factor evaluation,[3] Rate of fertility has been decreasing during the last few decades which is a serious concern.
Recent evidences have pointed to the presence of elevated oxidative stress in abnormal semen samples.[4] Oxidative stress is defined as an imbalance between the generation of reactive oxygen species (ROS) and the protective action of antioxidant systems responsible for their neutralization and removal.[5]
Testis have a substantial amount of unsaturated fatty acids, which is potent substrate to generate ROS reactive oxygen species along with limited antioxidant capacity. Thus, there is much higher susceptibility towards oxidative damage in testis as compared to another cells.[6]
Hyperthyroidism appears to make tissue more vulnerable to oxidative damage. As thyroid hormone revitalizes physiological functions, it is quite inevitable that elevated level of thyroid hormone would overstimulate metabolic state, and increase free radical formation
resulting in oxidative damage and generation of free radicals in different tissues.[7]
Hypothyroidism also leads to alterations in testicular redox status, oxidant production, and testicular oxidant capacity due to hypometabolism. Both transient and persistent decrease in thyroid hormone levels have been demonstrated changes in antioxidant defense mechanism during gonadal development and maturation.[8]
Therefore, in in order to explore the impact of thyroid dysfunction on oxidative stress levels, the study was conducted so as to find out effective ways to reduce oxidative by optimizing thyroid status and thereby improving male reproductive health through improvement of semen parameters.

Subjects and Methods

This was a Prospective cohort study between June 2016 to June 2018. All the males of infertile couple attending infertility clinic outpatient department (OPD) of Jawaharlal Nehru Medical College and Hospital, Aligarh, Uttar Pradesh, India were taken as subjects. Ethical clearance from the Institutional Ethics Committee (IEC) of Jawaharlal Nehru Medical College and hospital was taken in order to

conduct this study. Patients were enrolled after taking written informed consent and satisfying inclusion and exclusion criteria.

Inclusion Criteria

All the males of infertile couple attending infertility clinic for couple infertility in reproductive age group

Exclusion Criteria

Males having systemic diseases (such as diabetes, hypertension, cancer), Endocrinal abnormalities which may affect male reproductive function. Subjects diagnosed with any sexually transmitted diseases, Males undergoing therapies such as radiotherapy and chemotherapy, urogenital problems or any other serious chronic diseases that might have an impact on reproductive system were not included.

Methodology

We recruited 100 men who attended infertility clinic at JNMCH after fulfilling the inclusion criteria. Detailed history was taken and physical examination performed. Baseline physical and sociodemographic characteristics were documented such as age, BMI (WHO classification 2014), alcohol addiction, [9] smoking Index, [10] educational qualification, and religious status.

Blood investigations and semen samples were collected. Blood samples were taken from patients using aseptic precautions and was evaluated for Hemogram and Serum TSH, and T4 levels were assessed using CLIA Kit (Chemiluminescence Immunoassay. American Thyroid Association was considered as the standard body of reference.

ATA reference range

I. Euthyroid: 0.4-4.0 milliunits per litre [m U/L]
II. Hyperthyroid :<0.4 milliunits per litre [m U/L]
III. Hypothyroid: >5.5 milliunits per litre [m U/L]

Oxidative Stress Index (OSI) and Total antioxidant capacity (TAC)

The semen samples were collected from the subjects, centrifuged for separation of plasma, and stored at -80°C until further analysis was done for oxidative stress index (OSI) and total antioxidant capacity (TAC).

From this sample, semen plasma OSI and TAC was measured by colorimetric method and expressed as millimole (mM).

Total Oxidative Status (TOS)

Oxidants present in the semen sample oxidize the ferrous ion-o-dianisidine complex to ferric ion. The oxidation reaction was enhanced by glycerol molecules, which were abundantly present in the reaction medium used in the test. The ferric ion made a colored complex with xylenol orange in an acidic medium. The color intensity was measured spectrophotometrically, and was proportional to the total amount of oxidant molecules present in the sample. The assay was calibrated with hydrogen peroxide and the results were expressed in terms of micromolar hydrogen peroxide equivalent per litre (μmol H202 Equiv./L)

Total Antioxidant Capacity (TAC)

The 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS•+) radical cation-based assays are among the most abundant antioxidant capacity assays. Measurement methods were based on the decolorization of ABTS radical by the presence of antioxidants in the sample in acetate buffer. (ABTS) is incubated with meth myoglobin and hydrogen peroxide to produce ABTS+. These species were blue-green. Antioxidants present in the sample cause a reduction in absorption proportional to their concentration.

This reaction was monitored spectrophotometrically and the bleaching rate was inversely related to the TAC of the sample. The reaction was calibrated with Trolox, which is widely used as a traditional standard for TAC measurement assays, and the assay results are expressed in mmol Trolox equivalent/L.

Automated Calibration-After manual spectrophotometric optimization processes, the assay kits were applied to an automated analyzer (Aeroset) and final TOS and TAC is estimated. Followed by calculation of Oxidative Stress Index through Formula for each semen sample.

Oxidative Stress Index (OSI) = TOS/TAC x 100

Methodology: Correlation between TSH levels and Oxidative stress was evaluated using Moment Pearson Correlation Test. Chi square and unpaired t-test was used to analyze Qualitative and quantitative data. SPSS 25 was used to assess the data.

Results

In present study, mean age distribution of the study subjects(N=100) was 34.27+5.3 yrs. Mean BMI was 25.99+2.97. Majority of the population followed religion Islam. Primary infertility was the major concern of the study population.

Of 100 subjects, 22(22.00%) were smokers10 where 15 were moderate,6 light and 1heavy smoker and 8(8.00%) were alcoholics9 where 7 were mild and 1 moderate drinker respectively. Gutka was consumed by 32 % of the population.

The number of Euthyroid cases were 73(73.00%), whereas 24(24.00%) and 3(3.00%) were hypothyroid and hyperthyroid respectively, diagnosed on the basis of serum TSH and T4 levels. No cases of subclinical hypothyroidism were reported. The Mean value of serum TSH (mU/L) in study subjects was 3.39 ± 2.57 with median (25th-75th percentile) of 2.6(2.05-3.92).

Oxidative stress status was documented for each sample, using standard methods as described and similarly Total Antioxidant Capacity was obtained for each sample. Mean TAC was calibrated to be 4.253+1.297 and Mean Oxidative Stress Index was estimated to be 0.1688+0.067. as shown in Table 1. [Table 1]

Correlation of TAC with TSH

In our study, mean of serum TSH was 3.39137+2.571 and mean TAC was 4.253+1.297. Pearson correlation test showed that there is significant negative correlation between serum TSH

and TAC (r-value -0.39 and p-value <0.001). It therefore suggests that higher values of TSH can decrease Total antioxidant capacity which may prevent oxidative stress which is responsible for deteriorated semen quality.

Above table shows that in our study, mean of S.TSH was 3.391+2.571 and mean OSI was 0.1688+0.067. Pearson correlation test showed that there is significant positive correlation between S. TSH and OSI (r-value 0.579 and p-value <0.001). Thus it shows that as TSH level increases it result in increase in Oxidative stress levels and therefore may result in impaired reproductive function as shown in Table 2. [Table 2]

Table 1: Patient Charachteristics

Patient characteristics	Frequency/Mean value	Percentage
Age	34.27+5.3 yrs	
BMI	25.99+2.97	
Alcohol	8	8.00%
Tobacco consumption	32	32.00%
Smoking	22	22.00%
Serum TSH(mU/L)		
Euthyroid	73	73.00%
Hyperthyroid	3	3.00%
Hypothyroid	24	24.00%
Mean ± SD	3.36 ± 2.5	
Median(25th-75th percentile)	2.6(2.05-3.92)	
Oxidative stress Index TotalAntioxidant Capacity	0.1688+0.067 4.253+1.297	

Table 2

	Mean	SD	r-value	P- value
S. TSH	**3.39137**	**2.571**		
TAC	4.253	1.297	-0.39	<0.001
OSI	0.1688	0.067	0.579	<0.001

Discussion

The mean Age group of the study population was 34.27+5.3 years and similarly multiple studies quoted the same age group,[11,12,13] as the couple is keen for conception and reports promptly when they are unable to conceive due to social pressure.

Mean BMI of the group was 25.99+2.97, most were in overweight category and correlation with Oxidative stress Index was assessed using Pearson Correlation was obtained which showed positive but insignificant correlation (BMI-r=0.362 and p- 0.405).Studies have reported that oxidative stress did increase with an increase in BMI, primarily due to an increase in seminal macrophage activation.[14] Others have demonstrated that oxidative stress increases with increasing BMI and age, as a sequel to an impaired antioxidant status.[15] The difference may be due to patients falling in to overweight category rather than obese which majority of the studies have reported

Further we found that 22% were smokers. The means of OSI was compared in smokers and non-smokers using unpaired t-test and no significant difference was found (t-value=.612; p value=.432) showing thereby that smoking did not affect Oxidative stress levels in subjects. Others have reported that Infertile men who smoke cigarettes have higher levels of seminal Oxidative stress than infertile nonsmokers.[16,17] The difference may be due to the levels of smoking, as in our study most were light to moderate smokers as opposed to the studies where smokers were heavy.

Our study reported that there was positive and significant correlation between OSI and TSH which suggests that as TSH rises Oxidative stress increases, and as TSH increases the capacity to fight oxidative stress decreases so Hypothyroidism can significantly alter the oxidative stress levels which is known to affect semen quality. [5]. Oxidative stress causes an imbalance between the antioxidant defense systems and the rate of production of reactive oxygen species (ROS). It leads to lipid peroxidation and oxidatively damaged DNA. [18] Hypothyroidism-associated ROS is the consequence of both increased production of free radicals and reduced capacity of the antioxidative defense. Elevated thyroid-stimulating hormone (TSH) alters oxidative stress processes. Lipid peroxidation is reported to be high in hyperlipidemia, which is a consistent biochemical feature in hypothyroidism. [19] Thus, majority of the studies report that Hypothyroidism adversely affect oxidative stress level which eventually affect semen parameters

Conclusion

In the light of the present study it is proposed that, thyroid dysfunction exaggerates oxidative stress levels in the semen and thereby impairs semen quality which is also supported by various studies, so efforts should be put to optimize thyroid levels for improving male reproductive health. Presently thyroid assessment is not a part of infertility evaluation but with the growing evidence of thyroid affecting oxidative stress levels, we may encounter that semen parameters might not be majorly affected but oxidative stress could be high which may lead to infertility with subtle semen abnormalities.

Therefore, thyroid assessment may be done even when the semen parameters are normal. Further large-scale studies are required as supporting evidence to assess the role of thyroid hormones in optimizing oxidative stress index and thereby improvising male fertility.

References

1. Lindsay TJ, Vitrikas KR. Evaluation and treatment of infertility. Am Fam Physician 91(5):308-14.
2. Lo KC, Lamb DJ. The testis and male accessory organs. In: Strauss JF, Barbieri RL, eds. Yen and Jaffe's Reproductive Endocrinology: Physiology, Pathophysiology, and Clinical Management. 5th ed. Philadelphia, Pa: Elsevier, Inc. 2004; 1: 367–387.
3. Schlegel PN, Sigman M, Collura B, De CJ, Eisenberg ML, Lamb DJ, Sokol RZ, Spandorfer SD, Tanrikut C. Diagnosis and Treatment of Infertility in Men: AUA/ARM Guideline. Male Infertil. 2015 Oct;53.
4. Walczak-Jedrzejowska R., Wolski J. K., Slowikowska-Hilczer J. (2013). The role of oxidative stress and antioxidants in male fertility. Central European Journal of Urology, 66(1), 60–67
5. Sikka S. (2001). Relative impact of oxidative stress on male reproductive function. Current Medicinal Chemistry, 8(7), 851–862
6. Wagner MS, Wajner SM, Maia AL. The role of thyroid hormone in testicular development and function. J Endocrinol 2008; 199(3):351-365.
7. Krassas GE, Pontikides N, Deligianni V, Miras K. A prospective controlled study of the impact of hyperthyroidism on reproductive function in males. J Clin Endocrinol Metab 2002; 87(8): 3667-3671.
8. Anbalagan J, Sashi AM, Vengatesh G, Stanley JA, Neelamohan R,Aruldhas MM. Mechanism underlying transient gestational-onset hypothyroidism-induced impairment of posttesticular sperm maturation in adult rats. Fertil Steril 2010; 93(8): 2491-2497
9. Drinking histories of fatally injured drivers - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Classification-of-drinking-level-by-quantity-and-frequency-of-alcohol-consumption_tbl1_11163758
10. Garretsen, HFL. Probleemdrinken: Prevalentiebepaling, beinvloedende factoren en preventiemogelijkheden: Theoretische overwegingen en onderzoek in Rotterdam. Lisse: Swets & Zeitlinger; 1983 (in Dutch) .
11. Peter AO, Temi AP, Olufemi AP, Simidele OM, Adeniran AS, et al. (2016) Pattern of Semen Parameters and Factors Associated with Infertility in Male Partners of Infertile Couples in Nigeria. Andrology (Los Angel) 5: 161. doi:10.4172/2167-0250.1000161
12. Sangisapu S, Karunakaran S, Pillai ak. Effectiveness of double wash swim-up versus double density gradient swim-up technique of sperm preparation in in vitro fertilization.
13. Oguz Y, Guler I, Erdem A, Mutlu MF, Gumuslu Oktem M.Bozkurt N, Erdem M. The effect of swim-up and gradient sperm preparation techniques on deoxyribonucleic acid (DNA)fragmentation in subfertile patients. Journal of assistedreproduction and genetics. 2017 Jun;35(6):1083-9.
14. O. Tunc, H. W. Bakos, K. Tremellen Impact of body mass index on seminal oxidative stress First published: 29 December 2010 https://doi.org/10.1111/j.1439-0272.2009.01032.x
15. Willibald Wonisch et al Oxidative stress increases continuously with BMI and age withunfavourable profiles in malesThe Aging Male, 2012; 15(3): 159–165© 2012 Informa UK, Ltd.ISSN 1368-5538 print/ISSN 1473-0790 onlineDOI: 10.3109/13685538.2012.
16. Saleh RA, Agarwal A, Sharma RK, Nelson DR, Thomas AJ Jr. Effect of cigarette smoking on levels of seminal oxidative stress in infertile men: a prospective study. Fertil Steril. 2002 Sep;78(3):491-9. doi: 10.1016/s0015-0282(02)03294-6. PMID: 12215323.
17. Dai JB, Wang ZX, Qiao ZD. The hazardous effects of tobacco smoking on male fertility. Asian J Androl. 2015 Nov-Dec;17(6):954-60. doi: 10.4103/1008-682X.150847. PMID: 25851659; PMCID: PMC4814952.
18. Yoshikawa T, Naito Y. What is oxidative stress? JMAJ. 2002;45:271–6.
19. Nanda N, Bobby Z, Hamide A. Association of thyroid stimulating hormone and coronary lipid risk factors with lipid peroxidation in hypothyroidism. Clin Chem Lab Med. 2008;46:674–9.

How to cite this article: Khanam D, Shaheen. Is Thyroid dysfunction affecting Oxidative Stress Index in Semen. Asian J. Med. Res. 2019;8(4): OG06-OG09.

DOI: dx.doi.org/10.21276/ajmr.2019.8.4.OG3

Source of Support: Nil, **Conflict of Interest:** None declared.