Journal of Medicine, Physiology and Biophysics
ISSN 2422-8427 An International Peer-reviewed Journal
Vol.46, 2018

The Association Between Subclinical Hypothyroidism and Erectile Dysfunction

Dr Noman Aslam[1] Dr Waheed ur Rehman[2] Dr Qazi Muhammad Ibrahim[3]
1.House Officer Holy Family Hospital, Rawalpindi
2.House Officer Lahore General Hospital, Lahore
3.House Officer Services Institute Of Medical Sciences, Lahore

Abstract
Objective: To assess the association between subclinical hypothyroidism and erectile dysfunction**Study Design**: cross sectional study.**Study Place and Duration**: department of General Medicine at Lahore General Hospital Lahore, Services Hospital Lahore and Holy Family Hospital Rawalpindi from January 2018 to June 2018**Material and methods:** A total number of 180 subjects were involved in this study. The study patients were categorized into three groups' i.e. erectile dysfunction with sub clinical hypothyroidism, erectile dysfunction with euthyroidism and controls with euthyroidism. Data was subjected statistical analysis with the help of computer software SPSS version 23. Mean±S.D was calculated for quantitative variables. For qualitative variables, frequency and percentages were calculated. Independent t test and Chi square was applied to assess the statistical difference. P value of less than or equal to 0.05 was considered as statistically significant.**Results:** The difference between the ED with SCH group and the ED with euthyroidism group was statistically insignificant for FT3 (p=0.135) and E2 (p=0.318). The difference between the ED with SCH group and the controls with euthyroidism group was statistically significant except FT3 (p=0.098).**Conclusion:** Patients with erectile dysfunction commonly present with subclinical hypothyroidism and it can be concluded that subclinical hypothyroidism is associated with erectile dysfunction. However severity of erectile dysfunction is not associated to subclinical hypothyroidism. From the results of this study, recommendations regarding the need of thyroid function screening for men presenting with erectile dysfunction can be made.
Keywords: Subclinical Hypothyroidism, Erectile Dysfunction, Euthyroidism, Thyroid, thyroxine, triiodothyronine

Introduction

Recurrent or consistent inability to maintain or attain erection of the penis for proper sexual intercourse is termed as erectile dysfunction [1]. In US 30 million or more males suffer from erectile dysfunction as shown by many epidemiological studies [2]. Similarly in three major cities of China Beijing, Guangzhou and Chongqing prevalence of erectile dysfunction is reported to be 26.1% [3]. Erection of penis involves hormonal as well as psychogenic input and is considered a very complex process [4]. Risk factors associated with erectile dysfunction include hypogonadism, endocrine disorders, thyroid diseases and hyperprolactinemia [5, 6]. Thyroid function failure is very largely associated with erectile dysfunction; ratio of erectile dysfunction is reported to be 52.1% in hypothyroidism [7, 8].

Mild thyroid failure is known as subclinical hypothyroidism and its diagnosis is based upon elevation of thyroid stimulating hormone in serum along with normal concentrations of free thyroxine or FT4. This mild form of hypothyroidism has the capacity to advance towards overt hypothyroidism. Studies on the epidemiology of hypothyroidism show that prevalence of subclinical hypothyroidism is much more as compared to the prevalence of overt hypothyroidism. Prevalence of subclinical hypothyroidism ranges from 3.4% to 5.8% while prevalence of overt hypothyroidism ranges from 0.03% to 0.7% [9]. In this study association of subclinical hypothyroidism with erectile dysfunction was assessed. Not many studies provide such data in this region of the world. Therefore there is a need to find the association between subclinical hypothyroidism and erectile dysfunction.

Material and Method

This study was performed at department of General Medicine at Lahore General Hospital Lahore, Services Hospital Lahore and Holy Family Hospital Rawalpindi from January 2018 to June 2018. This was a cross sectional study. Ethical approval was obtained from the Hospital Ethics Committee. Inclusion was based upon the following criteria; patients with erectile dysfunction, in the age group of 18-65 years and having normal sexual hormones. Exclusion from this study was based upon the following criteria; patients with the history of previous over hypothyroidism, patients currently suffering from overt hypothyroidism, patient with previous or current hyperthyroidism, patient who undergone neck surgery previously, patients who had radioactive iodine therapy or thyroidectomy, patients with diabetes mellitus, patients suffering from any chronic illnesses like renal insufficiency, liver failure or any other systemic disease, patients treated with PDE5 inhibitors or sexual hormones within last three months patients with chronic wasting disease.

Control group consisted of males belonging to the age group of 18-65 years and having normal thyroid

homes in their serum. Members of the control group were excluded on the basis of the same criteria that have been mentioned above. Written informed consent was taken from all the participants of the study. A total number of 180 subjects were involved in this study. Sample size was calculated from the reference study conducted by Dawei Chen et al 10. Non probability consecutive type of sampling technique was used to collect the sample. Baseline measurements involved, FT3 (free triiodothyronine) FT4 (free thyroxine), PRL (prolactin), TSH (thyroid stimulating hormone), TT (total testosterone) and E2 (estradiol). The study patients were categorized into three groups i.e. erectile dysfunction with sub clinical hypothyroidism, erectile dysfunction with euthyroidism and controls with euthyroidism. Measurements were carried out with the help of electrochem-iluminescence immunoassay. Normal range of thyroid stimulating hormone was 0.27-4.7 mU\L, free thyroxine 12.0-22.0 pmol\L, free triiodothyronine 3.60-7.50 pmol\L, prolactin 4.6-31.4 ng\ml, and total testosterone 2.49 to 8.36 ng per ml and estradiol 7.63 to 42.59 pg per ml. Patients with concentration of thyroid stimulating hormone greater than 4.2 mU\L and normal concentrations of free thyroxine and triiodothyronine were diagnosed with sub clinical hypothyroidism. Control group patients had normal thyroxine concentrations, normal triiodothyronine and normal thyroid stimulating hormone levels in their serum and were termed as euthyroid. Diagnosis of erectile dysfunction was carried out with the help of IIEF-5 questionnaire (International Index of Erectile Function). Data thus obtained from all measurements and questionnaire was then subjected statistical analysis with the help of computer software SPSS version 23 Mean±S.D was calculated for quantitative variables. For qualitative variables, frequency and percentages were calculated. Independent t test and Chi square was applied to assess the statistical difference between groups. P value ≤0.05 was considered as significant.

Results

One hundred and eighty patients were included in this study. The study patients were categorized into three groups i.e. erectile dysfunction with sub clinical hypothyroidism, erectile dysfunction with euthyroidism and controls with euthyroidism. The mean age and BMI of the ED with SCH group was 30.61±3.68 years and 23.70±2.11 kg/m^{2}respectively.n=25 (56.8%) were previous smokers and n=19 (43.2%) were current smokers. While, the mean age and BMI of the ED with euthyroidism group was 32.67±3.11 years and 24.11±2.71 kg/m^{2}respectively. n=52 (56.5%) were previous smokers and n=40 (43.5%) were current smokers. The difference was statistically insignificant except age (p=0.001). (Table I)

The mean IIEF-5 scores, TSH, FT3, FT4, TT, E2 and PRL of the ED with SCH group was10.23±3.04, 5.68±2.01(mU/l), 5.34±0.94 (pmol/I), 16.16±1.80 (PMOL/I), 5.31±1.49 (ng/ml), 31.52±7.20 (pg/ml) and 11.71±3.60(ng/ml) respectively. While, the mean IIEF-5 scores, TSH, FT3, FT4, TT, E2 and PRL of the ED with euthyroidism group was 11.42±4.20,2.18±0.92(mU/l),5.53±0.54(pmol/I), 16.98±1.67(PMOL/I), 4.71±1.17(ng/ml), 32.45±3.66 (pg/ml) and 9.01±2.75(ng/ml) respectively. The difference was statistically insignificant for FT3 (p=0.135) and E2 (p=0.318). (Table II)

The mean age and BMI of the ED with SCH group was 30.61±3.68 years and 23.70±2.11 kg/m^{2}respectively.n=25 (56.8%)were previous smokers and n=19 (43.2%)were current smokers. While, the mean age and BMI of the controls with euthyroidism group was 33.50±4.04 years and 24.56±1.91 kg/m^{2}respectively. n=27 (61.4%) were previous smokers and n=17 (38.6%) were current smokers. The difference was statistically significant except (p=0.664). (Table III)

The mean IIEF-5 scores, TSH, FT3, FT4, TT, E2 and PRL of the ED with SCH group was 10.23±3.04, 5.68±2.01 (mU/l), 5.34±0.94 (pmol/I), 16.16±1.80 (PMOL/I), 5.31±1.49 (ng/ml), 31.52±7.20 (pg/ml) and 11.71±3.60 (ng/ml) respectively. While, the mean IIEF-5 scores, TSH, FT3, FT4, TT, E2 and PRL of the controls with euthyroidism group was 22.75±0.62, 2.36±0.99(mU/l), 5.61±0.53(pmol/I), 18.18±1.41(PMOL/I), 4.36±1.16(ng/ml), 35.54±5.71 (pg/ml) and 8.79±2.08(ng/ml) respectively. The difference was statistically significant except FT3 (p=0.098). (Table IV).

Table I
Demographic Characteristics

Variable	Erectile Dysfunction with Subclinical hypothyroidism n=44	Erectile dysfunction with Euthyroidism n=92	P-value
Age (yrs)	30.61±3.68	32.67±3.11	0.001
BMI	23.70±2.11	24.11±2.71	0.387
Smoking			
Current	n=19 (43.2%)	n=40 (43.5%)	0.246
Previous	n=25 (56.8%)	n=52 (56.5%)	

Table II

Variable	Erectile Dysfunction with Subclinical hypothyroidism n=44	Erectile dysfunction with Euthyroidism n=92	P-value
IIEF-5 scores	10.23±3.04	11.42±4.20	0.000
Thyroid Stimulating Hormone (mU/l)	5.68±2.01	2.18±0.92	0.000
FT3(pmol/I)	5.34±0.94	5.53±0.54	0.135
FT4(PMOL/I)	16.16±1.80	16.98±1.67	0.009
TT(ng/ml)	5.31±1.49	4.71±1.17	0.010
E2(pg/ml)	31.52±7.20	32.45±3.66	0.318
Prolactin(ng/ml)	11.71±3.60	9.01±2.75	0.000

Table III
Demographic Characteristics

Variable	Erectile Dysfunction with Subclinical hypothyroidism n=44	Controls with Euthyroidism n=44	P-value
Age (Yrs)	30.61±3.68	33.50±4.04	0.000
BMI	23.70±2.11	24.56±1.91	0.047
Smoking			
Current	n=19 (43.2%)	n=17 (38.6%)	0.664
Previous	n=25 (56.8%)	n=27 (61.4%)	

Table. IV

Variable	Erectile Dysfunction with Subclinical hypothyroidism n=44	Controls with Euthyroidism n=44	P-value
IIEF-5 scores	10.23±3.04	22.75±0.62	0.000
Thyroid Stimulating Hormone (mU/l)	5.68±2.01	2.36±0.99	0.000
FT3(pmol/I)	5.34±0.94	5.61±0.53	0.098
FT4(PMOL/I)	16.16±1.80	18.18±1.41	0.000
TT(ng/ml)	5.31±1.49	4.36±1.16	0.001
E2(pg/ml)	31.52±7.20	35.54±5.71	0.005
Prolactin(ng/ml)	11.71±3.60	8.79±2.08	0.000

Discussion

After the exclusion of the subjects who had normal concentrations of sex hormones, the frequency of patients with subclinical hypothyroidism presenting with erectile dysfunction was reported to be around 24.44%. This ratio is much more as compared to the prevalence of subclinical hypothyroidism among men with erectile dysfunction reported in previous epidemiological studies [11]. Thyroid failure is largely associated with erectile dysfunction [12]. Studies have reported that prevalence of erectile dysfunction among patients with subclinical hypothyroidism is much more as compared to ratio of erectile dysfunction in healthy euthyroid males [13]. Current study has the same results showing that IIEF-5 scores were much lower in patients with subclinical hypothyroidism as compared to the males with euthyroidism. Thus it can be established that mild thyroid failure is commonly associated with erectile dysfunction in males with normal sex hormone concentrations. However exact mechanism of this relation between erectile dysfunction and subclinical hypothyroidism is still unknown.

On the other hand it has also stated that sub clinical hypothyroidism along with the evidence of elevated thyroid stimulating hormone is also related to the erectile dysfunction. The mechanism behind this is that elevated thyroid stimulating hormone results in reduction of biological activity of Luteinizing Hormone and also inhibit the secretion of Gonadotropin releasing hormone, which play an important role in human sexual intercourse [14]. Moreover elevated levels of thyroid stimulating hormone also result in endothelial dysfunction resulting in reduced formation and availability of nitric oxide and it's a fact that nitric oxide plays a vital role in vascular system and relaxation of corporal muscle to sustain and attain the penile erection [15, 16, 17 and 18].

Studies have showed that receptors for thyroid hormone are also present in smooth muscles and

endothelium of corporal cavernosa of the penis and that treatment with thyroid hormone replacement i.e. L thyroxine is associated with the restoration of penile erection by improving the function of smooth muscles and endothelial tissue [19, 20].

Prolactin levels are directly associated with the concentrations of thyroid stimulating hormone [21]. In this study even though prolactin levels were within reference range, but were slightly higher among the males of subclinical hypothyroidism with erectile dysfunction as compared to the healthy males. This increase can be attributed thyroid function failure and thereby the compensatory increase of thyrotropin releasing hormone in subclinical hypothyroidism [22]. Prolactin has a role in Gonadotropin releasing hormone pulsatility and the functioning of hypothalamic-pituitary-gonad axis [23]. Increase in the prolactin concentration has been associated with abnormal sexual activity and erectile dysfunction [24].

Multiple previous studies have provided the evidence of the fact that reduced levels of thyroxine in serum are largely associated with abnormal penile erection and lower scores of erectile dysfunction and that administration of L thyroxine can prove helpful in restoration of normal functioning of penile erection among the patients with overt hypothyroidism [25]. Therefore extent of thyroid failure might be directly associated with the severity of impotence. That is why subclinical hypothyroidism is evidently associated with erectile dysfunction but it does not affect the severity of erectile dysfunction. Further studies are required to elaborate this statement. Nevertheless high prevalence of subclinical hypothyroidism in patients with erectile dysfunction suggests the enhancement of screening of thyroid function in males presenting with erectile dysfunction.

Conclusion

Patients with erectile dysfunction commonly present with subclinical hypothyroidism and it can be concluded that subclinical hypothyroidism is associated with erectile dysfunction. However severity of erectile dysfunction is not associated to subclinical hypothyroidism. From the results of this study, recommendations regarding the need of thyroid function screening for men presenting with erectile dysfunction can be made.

Conflict of interest: No
Funding Source: No

References

1- Erasmus LJ, Potgieter MJ, Semenya SS. Erectile dysfunction: Definition and materia medica of Bapedi traditional healers in Limpopo province, South Africa. Journal of Medicinal Plants Research. 2015 Jan 17;9(3):71-7.
2- Goldstein I, Goren A, Li V, Tang WY, Hassan TA. Erectile dysfunction prevalence, patient characteristics, and health outcomes globally. The Journal of Sexual Medicine. 2017 May 1;14(5):e298.
3- Zhang X, Yang B, Li N, Li H. Prevalence and risk factors for erectile dysfunction in Chinese adult males. The journal of sexual medicine. 2017 Oct 1;14(10):1201-8.
4- Yafi FA, Jenkins L, Albersen M, Corona G, Isidori AM, Goldfarb S, Maggi M, Nelson CJ, Parish S, Salonia A, Tan R. Erectile dysfunction. Nature Reviews Disease Primers. 2016 Feb 4;2:16003.
5- McCabe MP, Sharlip ID, Lewis R, Atalla E, Balon R, Fisher AD, Laumann E, Lee SW, Segraves RT. Risk factors for sexual dysfunction among women and men: a consensus statement from the Fourth International Consultation on Sexual Medicine 2015. The journal of sexual medicine. 2016 Feb 1;13(2):153-67.
6- Maseroli E, Corona G, Rastrelli G, Lotti F, Cipriani S, Forti G, et al. Prevalence of Endocrine and Metabolic Disorders in Subjects with Erectile Dysfunction: A Comparative Study. J Sex Med. 2015;12:956-965.
7- Papagiannopoulos D, Khare N, Nehra A. Evaluation of young men with organic erectile dysfunction. Asian journal of andrology. 2015 Jan;17(1):11.
8- Nikoobakht MR, Aloosh M, Nikoobakht N, Mehrsay AR, Biniaz F, Karjalian MA. The role of hypothyroidism in male infertility and erectile dysfunction. Urol J. 2012;9:405-409.
9- Mao YS, Liu ZM, Chen CX, Zhu ZW, Hong ZL. Ningbo thyroid dysfunction prevalence study: a cross-sectional survey in an employees-cohort. Chin Med J (Engl). 2010;123:1673-1678.
10- Chen D, Yan Y, Huang H, Dong Q, Tian H. The association between subclinical hypothyroidism and erectile dysfunction.
11- Yan YR, Liu Y, Huang H, Lv QG, Gao XL, Jiang J, et al. Iodine nutrition and thyroid diseases in Chengdu, China: An epidemiological study. QJM. 2015;108:379-385.
12- Krassas GE, Tziomalos K, Papadopoulou F, Pontikides N, Perros P. Erectile dysfunction in patients with hyper- and hypothyroidism: how common and should we treat? J Clin Endocrinol Metab. 2008; 93:1815-1819.
13- Krysiak R, Szkróbka W, Okopień B. The effect of l-thyroxine treatment on sexual function and depressive symptoms in men with autoimmune hypothyroidism. Pharmacol Rep.2017 Jun;69(3):432-437.
14- Onal ED, Saglam F, Sacikara M, Ersoy R, Cakir B. Thyroid autoimmunity in patients with hyperprolactinemia: an observational study. Arq Bras Endocrinol Metabol.2014;58:48-52.

15- Taddei S, Caraccio N, Virdis A, Dardano A, Versari D, Ghiadoni L, et al. Impaired endothelium-dependent vasodilatation in subclinical hypothyroidism: beneficial effect of levothyroxine therapy. J Clin Endocrinol Metab.2003; 88:3731-3737.
16- Guay AT. ED2: erectile dysfunction = endothelial dysfunction. Endocrinol Metab Clin North Am. 2007;36:453-463.
17- Sarac B, Yildirim MK, Bagcivan I, Kaya K, Kilicarslan H, Yildirim S. Effect of hypothyroidism on the nitrergic relaxant responses of corpus cavernosal smooth muscle in rabbits. Int J Urol. 2006;13:58-63.
18- McMahon CG. Erectile dysfunction. Intern Med J. 2014;44:18-26.
19- Carosa E, Di Sante S, Rossi S, Castri A, D'Adamo F, Gravina GL, et al. Ontogenetic profile of the expression of thyroid hormone receptors in rat and human corpora cavernosa of the penis. J Sex Med. 2010;7:1381-1390.
20- Razvi S, Ingoe L, Keeka G, Oates C, McMillan C, Weaver JU. The beneficial effect of L- thyroxine on cardiovascular risk factors, endothelial function, and quality of life in subclinical hypothyroidism: randomized, crossover trial. J Clin Endocrinol Metab. 2007;92:1715-1723.
21- Hekimsoy Z, Kafesciler S, Guclu F, Ozmen B. The prevalence of hyperprolactinaemia in overt and subclinical hypothyroidism. Endocr J. 2010;57:1011-1015.
22- Demssie YN, Davis JR. Hyperprolactinaemia. Clin Med. 2008;8:216-219.
23- Corona G, Mannucci E, Petrone L, Giommi R, Mansani R, Fei L, et al. Psycho-biological correlates of hypoactive sexual desire in patients with erectile dysfunction. Int J Impot Res.2004;16:275-281.
24- De Rosa M, Zarrilli S, Di Sarno A, Milano N, Gaccione M, Boggia B, et al. Hyperprolactinemia in men: clinical and biochemical features and response to treatment. Endocrine.2003;20:75-82.
25- Carani C, Isidori AM, Granata A, Carosa E, Maggi M, Lenzi A, et al. Multicenter study on the prevalence of sexual symptoms in male hypo- and hyperthyroid patients. J Clin Endocrinol Metab. 2005; 90:6472-6479.