Urology Open Access Open Journal

SOAOJ PUBLISHING

Case series

Evaluating Erectile Dysfunction: Don't Forget Hypofunctional Thyroid!

Andrea Fabiani MD[1*], Maria Pia Pavia MD[2], Pompeo Salvatore Nicoli MD[3], Lucilla Servi MD[4]

[1]Urology Unit, Surgery Department, Macerata Civic Hospital, Area Vasta 3 Asur Marche (Italy)
Coordinator Italian Andrology Society (SIA), Section Marche, Emilia Romagna, San Marino (MERS)
[2]Urologic Clinic, Marche Polytechnic University, Ancona (Italy)
[3]Operative Unit Nuclear Medicine, Macerata Civic Hospital, Area Vasta 3 Asur Marche (Italy)
[4]Head of Urology Unit, Surgery Department, Macerata Civic Hospital, Area Vasta 3 Asur Marche (Italy)

***Correspondence to:** Andrea Fabiani, MD, Section Urology, Department Surgery Macerata Civic Hospital, Via Santa Lucia, 62100, Macerata (MC), Italy, Tel: +3907332572507, +393474865381; E-mail : andreadoc1@libero.it

Received: July 13th, 2020; **Accepted:** July 17th, 2020; **Published:** July 18th, 2020

Citation: Fabiani A, Pavia MP, Nicoli PS, and Servi L Evaluating erectile dysfunction : Don't forget hypofunctional thyroid!. *Urology Open A Open J.* 2020; I(1): 5-9.

ABSTRACT

Introduction

Erectile Dysfunction (ED) is a substantial problem in men, both in terms of its prevalence and impact. Endocrine abnormalities increase in prevalence with increasing age as well as ED increases with age. Reports suggested that thyroid disease may contribute to 6% of cases of impotence. In scientific literature there are only a few papers that address the problem of the relationship between hypothyroidism and sexual dysfunctions.

Patients and Methods

We report three cases of men suffering for still undiagnosed hypothyroidism who came to our attention complaining of sexual dysfunctions such as ED, Hypoactive Sexual Desire (HSD) and Premature Ejaculation (PE).

Results

In all three cases, sexual dysfunctions improved with the treatment of the hypothyroidism.

Conclusions

There is a little link between the etiological or co-morbid factors present and the method of management of ED in an individual but, especially in case of certain endocrine conditions, the specific remediation of the abnormality may cure the ED. Reporting these cases, we underlines the need of a thyroid function evaluation in selected cases.

Keywords: *Hypothyroidism; Sexual dysfunction; Levo-thyroxine; Erectile dysfunction.*

INTRODUCTION

Erectile Dysfunction (ED) is a substantial problem in men, both in terms of its prevalence and impact. The incidence and prevalence are increasing in line with several demographic and medical factors such as age, diabetes and metabolic syndrome.[1] ED is currently considered as a multifactorial disease in the majority of cases. In general terms, there is a poor correlation between the etiological and co-morbid factors and the management of ED in an individual.[2] The exception to this rule may be found in some endocrine conditions in which the specific remediation of the endocrine abnormality may cure ED.[3] Endocrine abnormalities increase in prevalence with increasing age as well as ED increases with age. The role of endocrine abnormalities in ED varies from 2% to 23% in the reported literature.[4] Concerning the correlation between endocrine system and ED, we use to think that the only cause of ED is the lack of testosterone, especially when the patient complains of a loss of libido. In fact, data from literature underlines as type 2 diabetes mellitus, central obesity, secondary hypogonadism and hyperprolactinemia are conditions playing a central role in determining consultation for ED[4] or sexual dysfunctions more generally.[5] Although thyroid disease is regu-

larly mentioned as an endocrine cause of ED, there is little documentation to support this topic. Reports suggested that thyroid disease may contribute to 6% of cases of impotence.[6] A clinician should be alert to the possibility, but it is unlikely that untreated thyroid disease will present as ED. Only a few studies have evaluated the relationship between ED and thyroid function, documenting a more frequent association with the hyperthyroidism.[7,8] Conversely, the correlation between ED and hypothyroidism is more discussed.[6,9] Herein, we report three cases of ED complained by two young and one older male patients in which sexual dysfunctions were treated by normalizing thyroid function

CLINICAL SCENARIO 1

A 30-year-old man came for andrologic evaluation complaining ED and Hypoactive Sexual Desire (HSD). At anamnesis, Hodgkin Lymphoma treated with chemotherapy and radiotherapy at the side of the latero-cervical, supraclavicular and mediastinic lymph-nodes was reported. Disease remission was obtained when he was 17-years-old. Ever since then, the patient has never checked thyroid function, despite the radio- and chemo- therapy treatment. The young man was planning his wedding. He was extremely worried about the situation that has become bothersome for about a year. On physical examination, no noteworthy alterations were detected. Testicular sizes were normal. In the left iliac fossa, a surgical scar of the previous varicocelectomy, performed four years earlier, was highlighted. The response to the International Index of the Erectile Function (IIEF 15) questionnaire scored 18. Administering to our patient the structured Interview on Erectile Dysfunction (SIEDY),[10] we obtained for the organic (scale1), relational (scale 2) and intrapsychic (scale 3) component, a score of 5/12, 1/12 and 2/18 respectively. We prescribed laboratory tests including thyroid function without any prescription for sexual dysfunction. Total Cholesterol was 210 mg/dl (<200), Cholesterol LDL 140 mg/dl (<160), Triglycerides 310 mg/dl (40-170), Prolactin (PRL) was normal. Thyroid Stimulating Hormone (TSH) was 8.9 mcU/ml (0.25-4.5), Triiodothyronine (FT3) 1.1 pg/ml (2-4), Thyroxine (FT4) 0.5 ng/dl (0.7-1.7), Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH) and Testosterone were normal. Glycemia and Glycated Hemoglobin (HbA1c) were within the normal range. After laboratory tests evaluation, the patient has been assessed by our consultant for thyroid disease. Ultrasound evaluation revealed the thyroid gland with modestly reduced dimensions, a right lobe with inhomogeneous features and a solid lump in the opposite lobe (8.3 mm in diameter). He diagnosed a severe hypothyroidism and prescribed Levothyroxine 50 mcg oral daily. Two months later, TSH reduced to 2.65 mcU/ml, FT4 0.70 ng/dl, FT3 arose up to 3.78 pg/ml. Thyreoglobulin (TgAb) and Thyroperoxidase (TPOAb) antibodies were negative, confirming the hypothyroidism related to the previous radiotherapy treatment. Considering the appropriate response to the treatment, levothyroxine therapy was continued until the tenth months in which the dose was modulated and rose up to 75 mcg oral daily, when TSH was 4.35 mcU/ml, FT4 8.3ng/dl and FT3 4 pg/ml. At andrological control, IIEF 15 scored 24 and all SIEDY domains were normal.

CLINICAL SCENARIO 2

The patient was a 20-year-old man presenting at our observation complaining about ED and premature ejaculation (PE). The main information obtained was a history of thyroid carcinoma surgically treated when he was 18. IIEF 15 score was 18. SIEDY scale 1, 2 and 3 was 6, 0, 3 respectively. Physical examination was regular. He didn't take any drugs except thyroid replacement therapy. He told that the thyroid specialist had just increased the dosage of Levothyroxine 50 mcg to 75 mcg. We prescribed laboratories tests without any drug for sexual dysfunction. We advised the young man about the possibility that his sexual dysfunction could be related to hypothyroid function. The patient reported that he had not been advised at the time of pre-surgical counselling about the risk to develop any sexual concern after thyroidectomy. Laboratory tests revealed a TSH value of 9 mcU/ml. 8 weeks later than the new Levothyroxine dosage, the young patient declared an improvement of his sexual activity, scoring 25 at IIEF15, no abnormal scales on SIEDY test. The TSH levels were 3 mcU/ml. Ejaculation latency time was declared satisfactory.

CLINICAL SCENARIO 3

The third patient was a 66 years old man. He came to our attention accompanied by his 31-years-old younger partner, complaining of ED and HSD. Previously he underwent to an andrological visit for the same problems and he had taken Testosterone Replacement Therapy (TRT) with daily 60 mg gel formulation for 3 months (testosterone pre-TRT value: 2.27 ng/ml). The actual testosterone value was 3.70 ng/ml and the sexual problems not improved. Total Prostate-specific antigen (PSA) was 2.9 ng/ml. The IIEF 15 score was 10 and SIEDY domains 1,2,3 were 8,1,0, respectively. Physical exam was unremarkable. Current therapy consisted in anti-hypertensive drugs. Consulting previous laboratory results, we noted an increased value of PRL (25.7 ng/ml). Since association of increased PRL-values and hypogonadism may be the result of a thyroid dysfunction, we prescribed specific laboratory tests and an ultrasound study of thyroid. TSH was 8.5 mcU/ml and both FT3 and FT4 within normal range. TgAb and TPOAb were negative. Diagnosis of subclinical hypothyroidism was made (ScH). Therapy with Levothyroxine 25 mcg was started. In 8 weeks, IIEF15 rose up from 10 to 20 points. SIEDY organic component (3/12), TSH (3.5 mcU/ml), PRL (14 ng/ml) and Testosterone (4.5 ng/ml) normalized.

DISCUSSION

Only a few studies have evaluated the relationship between ED and thyroid function, showing a more frequent association with hyperthyroidism.[7,8] Conversely, the correlation between ED and hypothyroidism is more discussed.[6,9] The receptors for thyroid hormones have been identified in the human cavernous body and it seems that hyperthyroidism may compromise penile relaxation mediated by nitrogen monoxide.[11,12] In a recent review, Bates and colleagues described as men with hypo- and hypertiroidism have increased rates of sexual dysfunction, including ED in men with hypothyroidism.[13] In their multicenter study, in 2005, Carani and co-workers underlined as most patients with thyroid hormones disorders experience some sexual dysfunctions which can be reversed by normalizing thyroid hormone levels. Subjects were screened for HSD, ED, PE and Delayed Ejaculation (DE) on presentation and 6 to 8 weeks after recovery from the thyroid hormone disorder. In their 48 adult men, 14 were affected by hypothyroidism. In half of the treated hypothyroid men, DE was improved as revealed by all IIEF subdomains.[7] Krassas, et al. investigated the impact of hyper- and hypothyroidism on men sexual health. In 71 dysthyroid men, they noted an extremely common ED prevalence. Treatment of thyroid dysfunction restored erectile function. The authors concluded that screening for thyroid function in men presenting with ED is recommended, whereas specific treatment of ED should be postponed for at least 6 months after achieving euthyroidism.[14] In effect, Krysiak, et al. revealed as L-thyroxine treatment improved sexual and mood disturbances in 24 hypothyroid patients, both over and subclinical.[15] Similarly, Nikoobakht

and colleagues described an adverse effect of hypothyroidism on erectile function. They noted serum concentration of PRL and seminal parameters, including sperm count, morphology and motility, significantly different between the hypothyroid (24 patients) and the control group (66 normal individuals).[16]

What about our three scenarios? We know that hormonal sources of ED are uncommon, especially in young population. Individuals with endocrine disorders such as diabetes, hyperthyroidism and hypothyroidism have significantly poorer erectile function than disease-free men. Especially for men under 40-years-old with ED, the diversity of etiologies should prompt to psychosocial and relationship history.[17] Though physical examination and laboratory evaluation of most men with ED may not reveal the exact diagnosis, they represent an opportunity to identify critical associated conditions that should not be missed.[18] In fact, we continuously repeat, like a "*mantra*", that physical examination and laboratory evaluation of men complaining of ED are opportunities to identify not only the etiology but also important co-morbidities that can lead to life-threatening conditions.[19] General and local examination for men with ED does not involve the thyroid palpation. The blood pressure and heart rate and rhythm measurement, male secondary sex characters representation, gynecomastia, peripheral pulses, the ruling out obvious abdominal masses, vibratory sensation, waist circumference measurement, the observation of scars from previous surgery or trauma are listed as "*mandatory*".[18] The recommended laboratory routine tests are fasting blood glucose test and a lipid profile. They may uncover potentially serious conditions and diabetes mellitus and dyslipidemia are important co-morbidities for ED. Serum prolactin will reveal a rare prolactin producing pituitary micro-adenoma.[3] Assessment of serum testosterone will document adult onset hypogonadism that can cause both ED and the metabolic syndrome.[18] Serum PSA measurement is indicated in men over 40-years to 45-years, specifically if testosterone replacement therapy is being considered.[20] Thyroid function is considered as an additional laboratory test prescribed at the discretion of the physician based on the medical history and clinical scenario. As in our first two cases, anamnesis leads to a thyroid function evaluation. In both scenarios, the clinical history of young patients has imposed thyroid hormones tests. No attention has been paid to the consequences of treatments that patients underwent at a young age. In case one, radiotherapy in cervical and thoracic districts was the main risk factor to evaluate. From literature we learn that, despite their specific functional consequences, radiotherapy-induced thyroid abnormalities remain underestimated and underreported.[21] The most common radiation-induced thyroid dysfunction is the primary hypothyroidism affecting 20% to 30% of patients administered following curative radiotherapy to the neck region, with approximately half of the events occurring within the first 5-years after therapy.[22] Radiotherapy-induced thyroid dysfunction is caused by damage to small vessels and to the gland capsule. Radiation-induced atherosclerosis of the carotid artery may also result in relative ischemia of the thyroid gland.[23] Other mechanisms include parenchymal cell damage and autoimmune reactions.[24] Analyzing the thyroid function of 177 patients treated for Hodgkin's disease, Bethge and co-workers found 27% to have subclinical (20%) or overt (7%) hypothyroidism in the group of patients underwent combined radiotherapy and chemotherapy. No patients treated with only chemotherapy developed hypothyroidism.[25] Recommended follow-up procedures include at least annual evaluation with a history for symptoms of thyroid dysfunction, clinical examination, and measurement of thyroid hormones and thyrotropin. Management of overt hypothyroidism is based on hormone replacement therapy. Thyroid hormone therapy is also recommended in cases of subclinical hypothyroidism.[25,26] In our clinical scenario, the young patient one was not adequately subjected to an endocrinological follow-up. As referred by the own patient, the first evaluation of thyroid function was prescribed by the andrologist investigating sexual dysfunction. At the diagnosis of hypothyroidism he was reassured in relation to the etiology of the sexual disorders and referred to the specialist for formulate effective therapy that would have normalize sexual function in a short time. In light of previous experience, in the second case scenario reported the development of hypothyroidism is obviously unexpected.[27] Radical thyroidectomy is related to an iatrogenic hypothyroidism requiring substitution therapy but general surgeons do not seem to have knowledge of the possible patho-physiological relationship between the lack of thyroid hormones and the possible onset of symptoms related to the male sexual and reproductive sphere. The possible role of thyroid hormones in the NO-mediated response to sexual stimulation and on prostaglandin E1 and Sildenafil in the treatment of ED was investigated using the corpus cavernosum of the rat model. Hypothyroidism or thyroidectomy was found to cause depletion of Endothelium Derived Relaxant Factor (EDRF) thereby causing very feeble contraction of the cavernosum muscle, in both PGE1 and Sildenafil, oligospermia and less than 45% motile sperm. Thyroxine treatment produced contraction proportionate to the concentration of PGE1 and sildenafil providing evidence that the erectogenic actions of both PGE1 and sildenafil are possible only in the presence of adequate thyroid hormone level.[28] Kilikarsian and colleagues investigated the nitric oxide (NO)/cyclic guanosine monophosphate (cGMP) pathway on hypothyroidism in an experimental rabbit model to found a possible role in ED physiopathology. The hypothyroidism was surgically induced by thyroidectomy for 6 weeks. They described plasma thyroid-stimulating hormone and prolactin levels significantly higher in hypothyroid rabbits. The consequent decrease of released or synthesized NO from nitrergic nerves and endothelium was responsible, in hypothyroid group, for the reduced erective response to nerve and pharmacological stimulation.[29] These data tried to identify the pathophysiological hormonal relationship between hypothyroidism and ED. They impose a reflexion on an important issue to reach during the counselling of the male patient that will undergo radical thyroidectomy. Although thyroid disease is less frequent in men than in women, ED must be considered as possible sequelae of thyroid surgery in both young and old men. In the third clinical case, the relationship between hyperprolactinemia, subclinical hypothyroidism (ScH), hypogonadism and sexual dysfunction was highlighted. Sharma, et al. published data from 2,848 individuals describing the prevalence and predictors of hyperprolactinemia in ScH. They report a 31.61% of male patient with ScH presenting with hyperprolactinemia (defined as a value > 17 ng/ml in men). In ScH males, also serum estradiol was significantly higher, and testosterone significantly lower than euthyroid group. TSH>8.33 mIU/L in males had a sensitivity of about 50% with a very high specificity of >90% in detecting hyperprolactinemia.[30] Chen and co-workers described ScH as common in ED patients and associated with ED, whereas the severity of ED is not related to ScH. They recommended the screening for thyroid dysfunction in men presenting with ED.[31] More recently, Cannarella, et al. revealed as levo-thyroxine (LT4) treatment in ScH patients with an arterial ED (they did not have diabetes mellitus, hypertension, dyslipidemia and did not take any drug) improved sexual function. In the group treated for 6 months, LT4 resolved arterial ED by improving the blood penile flow, possibly inducing smooth muscle cell relaxation and ameliorating the endothelial function.[32] 1n the third reported clinical case, the pa-

tient came to our attention after a failed substitutive testosterone therapy trial without any clinical benefit. Hypogonadism must be considered the consequence of hyperprolactinemia secondary to ScH, not diagnosed at the moment of the first andrological evaluation. Therapy with LT4 improved sexual dysfunctions by reducing prolactin levels and increasing total testosteron blood levels. As least consideration, we would like to pay attention to the usefulness of the structured interview for erectile dysfunction (SIEDY test),[10] especially in the third case, in which the diagnostic value of anamnesis is lower than the first two cases reported. The SIEDY is an important tool for aetiological diagnosis of ED and his use must be improves in the daily clinical practice. In general, our three clinical cases highlight the importance of thyroid hormones on sexual function. The role may be both direct and inderect through an interference to testosterone or endothelial metabolism. All three patients complain of ED and in two cases (case 1 and 3) also HSD. Unexpectately, PE was referred by patient 2 but we could consider that this symptom was complained as a manifestation related to ED. So, in selected cases, we think that sexual dysfunctions may be considered as a mirror of thyroid function. We are not able to demonstrate the need of a screening for thyroid dysfunction in men presenting with sexual dysfunction, but we suggest to consider it in selected cases.

CONCLUSIONS

There is little correlation between etiological or co-morbid factors and the management of ED in an individual, but often sexual issues caused by endocrine conditions resolve once disorders had been treated. Hypothyroidism, both primary and subclinical, should be diagnosed in selected cases and its treatment could solve sexual dysfunction.

AUTHORS' CONTRIBUTIONS

All authors participated in the design and conduct of the study. All authors reviewed and approved the final version of the manuscript.

REFERENCES

1. Heaton JPW, Morales A. Endocrine Causes of Impotence (non-diabetes). *Urol Clin North Am*. 2003; 30(1): 73-81. doi: 10.1016/s0094-0143(02)00115-5.

2. Porst H, Burnett A, Brock G, Ghanem H, Giuliano F, et al. SOP Conservative (medical and mechanical) Treatment of Erectile Dysfunction. *J Sex Med*. 2013; 10(1): 130-171. doi: 10.1111/jsm.12023.

3. Buvat J. Hyperprolactinemia and Sexual Function in Men: A Short Review. *Int J Impot Res*. 2003; 15(5): 373-377. doi: 10.1038/sj.ijir.3901043.

4. Maseroli E, Corona G, Rastrelli G, et al. Prevalence of Endocrine and Metabolic Disorders in Subject with Erectile Dysfunction: A Comparative Study. *J Sex Med*. 2015; 12(4): 956-965. doi: 10.1111/jsm.12832.

5. Corona G. Isidori AM, Aversa A. Endocrinologic Control of Men's Sexual Destre and Arousal/Erection. *J Sex Med*. 2016; 13(3): 317-337. doi: 10.1016/j.jsxm.2016.01.007.

6. Corona G, Wu FC, Forti G, et al. Thyroid Hormones and Male Sexual Function. *Int J Androl*. 2012; 35(5): 668-679. doi: 10.1111/j.1365-2605.2012.01266.x.

7. Carani C, Isidori AM, Granata A, et al. Multicenter Study on the Prevalence of Sexual Symptoms in Male Hypo- and Hyperthyroid Patients. *J Clin Endocrinol Metab*. 2005; 90(12): 6472-6479. doi: 10.1210/jc.2005-1135.

8. Veronelli A, Masu A, Ranieri R, et al. Prevalence of Erectile Dysfunction in Thyroid Disorders: Comparison with Control Subjects and with Obese and Diabetic Patients. *Int J Impot Res*. 2006; 18(1): 111-114. doi: 10.1038/sj.ijir.3901364.

9. Wu FC, Tajar A, Beynon JM, et al. Identification of Late Onset Hypogonadism in Middle Aged and Elderly Men. *N Engl J Med*. 2010; 363(2): 123-135. doi: 10.1056/NEJMoa0911101.

10. Petrone L, Mannucci E, Corona G, et al. Structured Interview on Erectile Dysfunction (SIEDY): A New, Multidimensional Instrument for Quantification of Pathogenetic Issues on Erectile Dysfunction. *Int J Impot Res*. 2003; 15(3): 210-220. doi: 10.1038/sj.ijir.3901006.

11. Carosa E, Di Sante S, Rossi S, 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(4pt1): 1381-1390. doi: 10.1111/j.1743-6109.2009.01701.x

12. Krassas GE, Poppe K, Glinoer D. Thyroid Function and Human Reproductive Health. *Endocr Rev*. 2010; 31(5): 702-755. doi: 10.1210/er.2009-0041.

13. Bates JN, Kohn TP, Pastuszak AW. Effect of Thyroid Hormone Derangements on Sexual Function in Men and Women. *Sex Med Rev*. 2020; 8(2): 217-230. doi: 10.1016/j.sxmr.2018.09.005.

14. Krassas GE, Tziomalos K, Papadopoulou N, Pontikides N, Perros P. Erectile Dysfunction in Patient with Hyper- and Hypothyroidism: How Common and should we Treat?. *J Clin Endocrinol Metab*. 2008; 93(5): 1815-1819. doi: 10.1210/jc.2007-2259.

15. Krysyak R, Szkrobka W, Okopien B. The Effect of L-Thyroxine treatment on Sexual Function and Depressive Symtoms in Men with Autoimmune Hypothyroidism. *Pharmacol Rep*. 2017; 69(3): 432-437. doi: 10.1016/j.pharep.2017.01.005.

16. Nikoobakht MR, Aloosh M, Nikoobakht N, et al. The Role of Hypothyroidism in Male Infertility and Erectile Dysfunction. *Urol J*. 2012; 9(1): 405-409.

17. Ludwig W, Phillips M. Organic Cause of Erectile Dysfunction in Men under 40. *Urol Int*. 2014; 92(1): 1-6.

18. Ghanem HM, Salonia A, Martin-Morales A. SOP: Physical Examination and Laboratory Testing for Men with Erectile Dysfunction. *J Sex Med*. 2013; 10(1): 108-110. doi: 10.1111/j.1743-6109.2012.02734.x.

19. Seftel AD, Sun P, Swindle R. The Prevalence of Hypertension, Hyperlipidemia, Diabetes Mellitus and Depression in Men with Erectile Dysfunction. *J Urol*. 2004; 171(6 Pt 1): 2341-2345. doi: 10.1097/01.ju.0000156766.89773.10.

20. Zohdy W, Kamal EE, Ibrahim Y. Androgen Deficiency and Abnormal Penile Duplex Parameters in Obese Men with Erectile Dysfunction. *J Sex Med*. 2007; 4(3): 797-808. doi: 10.1111/j.1743-6109.2007.00499.x.

21. Jereczek-Fossa BA, Alterio D, Jassem J, et al. Radiotherapy-Induced Thyroid Disorders. *Cancer Treat Rev*. 2004; 30(4): 369-384. doi: 10.1016/j.ctrv.2003.12.003.

22. Costine LS. What Else don't we know about the Late Effects of Radiation in Patients Treated for Head and Neck Cancer?. *Int J Radiat Oncol Biol Phys*. 1995; 31(2): 427-429. doi: 10.1016/0360-3016(94)00584-8.

23. Feehs RS, Mcquirt WT, Bond MG. Irradiation: A Significant Factor for Carotid Atherosclerosis. *Arch Otolaryngol Head Neck Surg*. 1991;

117(10): 1135-1137. doi: 10.1001/archotol.1991.01870220083014.

24. Nishiyama K, Tanaka E, Tarui Y. A Prospective Analysis of Subacute Thyroid Dysfunction after Neck Irradiation. *Int J Radiat Oncol Biol Phys*. 1996; 34(2): 439-444. doi: 10.1016/0360-3016(95)02079-9.

25. Bethge W, Guggenberger D, Bamberg M, Kanz L, Bokemeyer C. Thyroid Toxicity of Treatment for Hodgkin's Disease. Ann Hematol. 2000; 79(3): 114-118. doi: 10.1007/s002770050565.

26. Mercado G, Adelstein DJ, Saxton JP, et al. Hypothyroidism: A Frequent Event after Radiotherapy and after Radiotherapy with Chemotherapy for Patient with Head and Neck Carcinoma. *Cancer*. 2001; 92(11): 2982-2987. doi: 10.1002/1097-0142(20011201)92:11<2892::aid-cncr10134>3.0.co;2-t.

27. Shafer RB, Nuttal FQ, Pollack K. Kuisk H. Thyroid Function after Radiation and Surgery for Head and Neck Cancer. *Arch Intern Med*. 1975; 135(6): 843-846.

28. Amadi K, Sabo MA, Sagay AS. Thyroid Hormone: The Modulator of Erectile Function in the Rabbit. *Niger J of Physiol Sci*. 2006; 21(1-2): 83-89. doi: 10.4314/njps.v21i1-2.53966.

29. Kilicarslan H, Bagcivan I, Yildirim MK, Sarac B, Kaya T. Effect of Hypothiroidism on the NO/cGMP Pathway of Corpus Cavernosum in Rabbits. *J Sex Med*. 2006; 3(5): 830-837.

30. Sharma LK, Sharma N, Gadpayle AK, Dutta D. Prevalence and Predictors of Hyperprolactinemia in Subclinical Hypothyroidism. *Eur J Intern Med*. 2016; 35: 106-110. doi: 10.1016/j.ejim.2016.07.012

31. Chen D, Yan Y, Huang H, Dong Q, Tian H. The Association Between Subclinical Hypothyroidism and Erectile Dysfunction. *Pak J Med Sci*. 2018; 34(3): 621-625. doi: 10.12669/pjms.343.14330.

32. Cannarella R, Calogero AE, Aversa A, Condorelli RA, La Vignera S. Is there A Role for Levo-Thyroxine for the Treatment of Arterial Erectile Dysfunction? The clinical Relevance of the Mean Platelet Volume. *J Clin Med*. 2020; 9(3): 742. doi: 10.3390/jcm9030742.