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Biochemical Study of Gender Effect on Thyroid Cancer in the Egyptian Population

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Method Article

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ABSTRACT

Background and Objective: Thyroid is one of the largest glands; its hormones affect almost every cell in the body, the incidence of thyroid cancer has raised in recent years, About 52,070 new cases of thyroid cancer in the United States in 2018 only. This study was undertaken to determine if gender was associated with susceptibility of thyroid cancer.
Materials and Methods: This study was carried out on 174 cases divided into 108 thyroid patients and 66 healthy as controls. The mean age of cases was (40.58±1.46) they include 48 female and 18 males. All participants were subjected to an estimation of thyroid stimulating hormone (TSH), free thyroxine (FT4), total antioxidant capacity (TAC), in addition to malondialdehyde (MDA).
Results: For TSH results that was an obvious effect of gender on TC, while for FT4 there was an effect of gender on thyroiditis and TC, for TAC there was a biting effect on thyroiditis and TC, for MDA there was an effect also on thyroiditis and TC, for tissue TAC (TTAC) that was a clear effect of gender on both thyroiditis and TC, and for TMDA there was a little effect.
Conclusion: Gender of TC patients effects on biochemical investigations of the thyroid.

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Keywords: Thyroid cancer; gender; thyroid hormones; thyroiditis; total antioxidant capacity; malondialdehyde.

ABBREVIATIONS

Thyroid cancer (TC); Thyroid stimulating hormone (TSH); Free thyroxine (FT4); Total antioxidant capacity (TAC); Malondialdehyde (MDA); Oxidative stress (OS); Reactive oxygen species (ROS); Tissue TAC (TTAC); and Tissue MDA (TMDA).

1. INTRODUCTION

The incidence of thyroid cancer has increased by 50% in the United States during the past 25 years [1]. Thyroid cancer is cancer originating from Oxidative stress, caused by the imbalance in reactive oxygen species (ROS) produced during normal cell metabolism and /or efficiency scavenger antioxidant defence, is implicated in the pathogenesis of many chronic diseases [2]. In hypermetabolic state, the tissue oxidative injury was associated with hyperthyroidism. Available data indicate that hyperthyroidism tissue exhibit and increased (ROS) production when hyperthyroid tissues increase their metabolic capacity, mitochondrial ROS generation is increased as a side effect of enhanced electron carrier level. Investigations of antioxidant defense system have returned controversial results [3]. Tissue susceptibility to the oxidative challenge was increased with any thyroid hormone-linked biochemical changes. This may explain the injury and dysfunction of the tissue suffer under stressful conditions. Mitochondria, as a primary target for oxidative stress, might account for hyperthyroidism linked tissue dysfunction [4]; there are four types of thyroid cancer Papillary, Follicular, medullary and the Anaplastic thyroid cancer [5].

2. MATERIALS AND METHODS

Study group: To conduct this study; 174 volunteers were divided into 3 groups healthy (n=66; 18 males and 48 female) thyroiditis (thyroid inflammation) (n=56; 8 males and 48 female) and TC patients (n=52; 14 males and 38 female) underwent surgical thyroidectomy. This study was approved by Mansoura University's Ethical Committee and informed, written consent was obtained from all patients' volunteer participants.

Assessment of thyroid function: Thyroid stimulating hormone (TSH) and free thyroxine (FT4) were determined in plasma samples by ELISA (IMMUNOSPEC, CA, USA) following the manufacturer's instructions. Normal thyroid function (euthyroidism) was defined as normal TSH levels (0.4-4.5 u IU / mL) and FT4 (0.7-1.9 ng / dL)

Evaluation of oxidative stress: Total antioxidant capacity (TAC) and lipid peroxidation products, malondialdehyde (MDA) were determined both in plasma samples as well as tissue homogenate of thyroid using the corresponding diagnostic kit (Biodiagnostic, Egypt) following manufacturer's instructions. TAC and the pink chromogen produced by the reaction of thiobarbituric acid with MDA were measured spectrophotometrically (SpectraMax M5, Molecular Devices) at 520 nm and 532 nm, respectively. Tissue oxidation was assessed by measuring both TTAC and TMDA in thyroid tissue homogenate for diseased groups only. The thyroid tissue homogenised in 10% (w /v) PBS (pH 7.4) using mini hand held homogenizer. The homogenates were centrifuged at 14000 rpm, 4°C, for 15 minutes, and the supernatants obtained were collected and stored at 80°C for further analysis, TAC unit was mM/L and MDA unit was nmol/ml.

2.1 Statistical Analysis

Statistical analysis of data was performed using the software statistical package (SPSS program version17.0). The Student t-test was used to compare the numerical values, a minimum of 50 participants was found to be adequate, thus the study population (n =52) was readily in the correct power. A P=0.05 was defined to be statistically significant.

3. RESULTS

There was a significant increase in TSH level in male thyroiditis and male thyroid cancer groups when compared to male control group (p=0.001& 0.012) respectively. On the other hand, there was no significant change in TSH level in male thyroiditis when compared to male thyroid cancer group (P=0.33) (Table 1 and Fig. 1). For the

female, there was a significant increase in TSH level in female thyroiditis and female thyroid cancer groups when compared to female control group (p=0.001). Also, there was a significant increase in mean TSH level in female thyroiditis when compared to female thyroid cancer group (P=0.001) (Table 1 and Fig. 1).

There was a significant increase in FT4 level in male thyroiditis and male thyroid cancer groups when compared to male control group (p=0.001) for both. On the other hand, there was no significant change in FT4 level in male thyroiditis when compared to male thyroid cancer group (P=0.33) (Table 2 and Fig. 2). For the female, there was a significant increase in FT4 level in female thyroiditis and female thyroid cancer groups when compared to female control group (p=0.001) (Fig. 2). Also, there was a significant increase in FT4 level in female thyroiditis when compared to female thyroid cancer group (P=0.04).

Association of TAC Level and MDA Level to Different Gender in Different Studied Groups:

There was a significant decrease in TAC level in male thyroiditis and male thyroid cancer groups when compared to male control group (p=0.001) for both. While, there was a significant increase in TAC level in male thyroiditis when compared to male thyroid cancer group (P=0.001) (Table 3 and Fig. 3), for female; there was a significant decrease in mean TAC level in female thyroiditis and female thyroid cancer groups when compared to female control group (p=0.001) for both (Fig. 3). There was a significant increase in mean TAC level in female thyroiditis when compared to female thyroid cancer group (P=0.001).

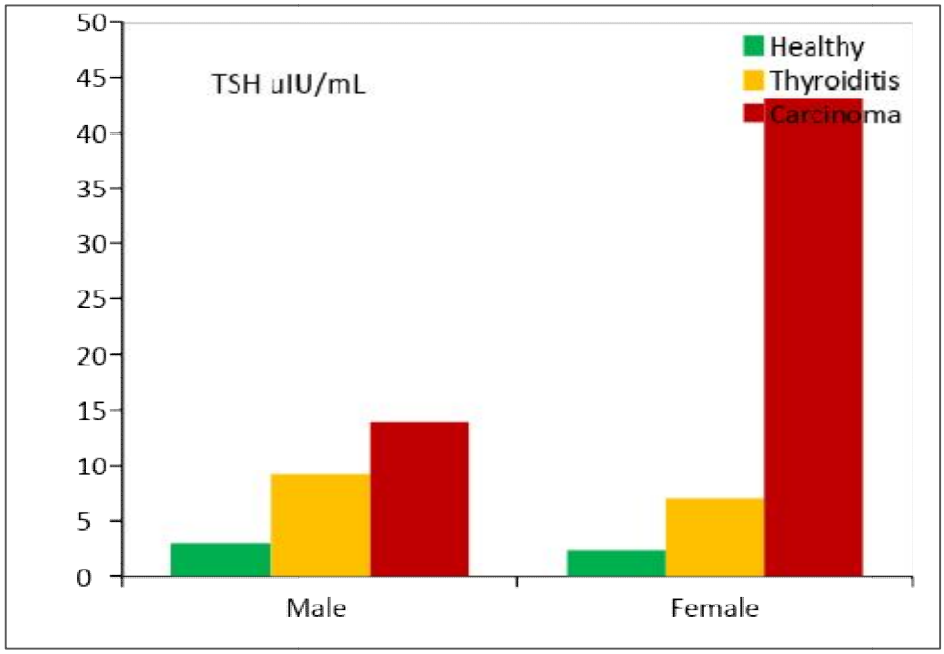

Fig. 1. Effect of gender on TSH level in different studied groups

Table 1. Effect of gender on TSH level in different studied groups

	Male	SD	P	P1	Female	SD	P	P1
Healthy	18	0.46			48	0.69		
Thyroiditis	8	2.60	0.001		48	4.57	0.001	
Carcinoma	14	17.39	0.012	0.33	38	30.45	0.001	0.001

N: Number of cases in each group, SD= Standard Deviation, P: significance of diseased groups against the healthy group, P1: Significance between diseased groups

Table 2. Effect of gender on FT4 level in different studied groups

	Male	SD	P	P1	Female	SD	P	P1
Healthy	18	0.33			48	0.41		
Thyroiditis	8	1.89	0.001		48	1.66	0.001	
Carcinoma	14	0.67	0.001	0.33	38	0.92	0.001	0.04

N: Number of cases in each group, SD= Standard Deviation, P: significance of diseased groups against the healthy group, P1: Significance between diseased groups

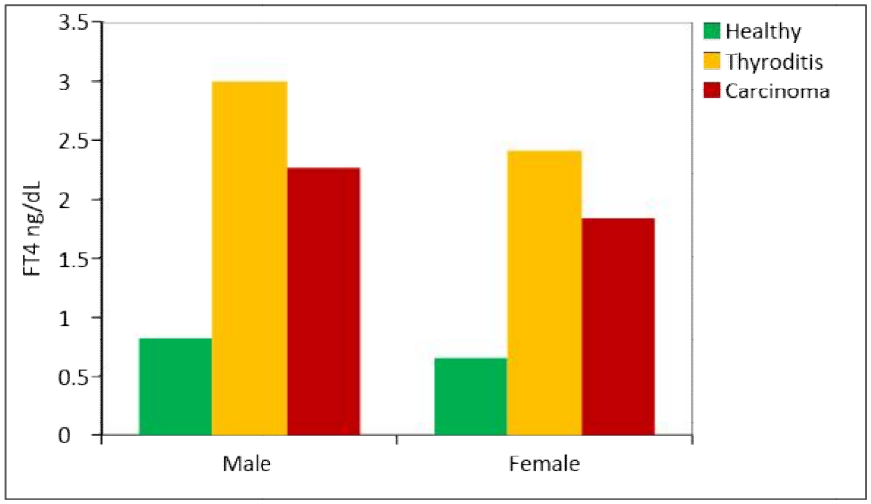

Fig. 2. Effect of gender on FT4 level in different studied groups

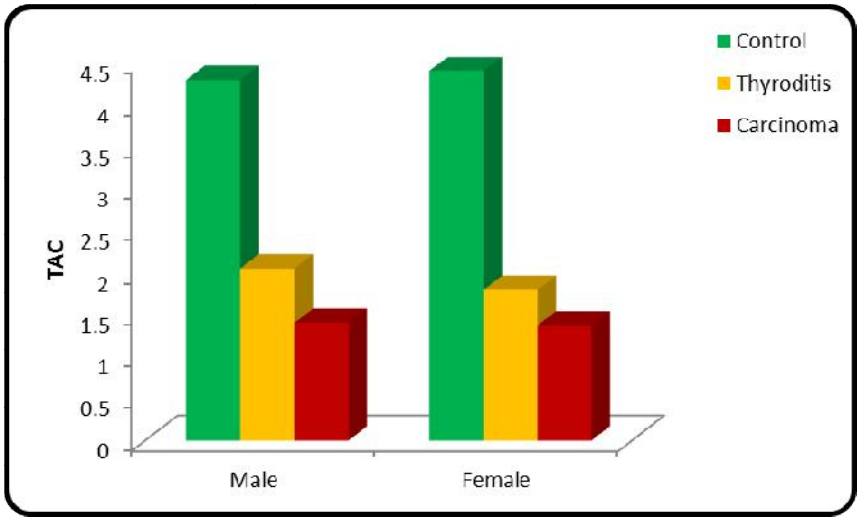

Fig. 3. Effect of gender on TAC level in different studied groups

Table 3. Effect of gender on TAC level in different studied groups

	Male	SD	P	P1	Female	SD	P	P1
Healthy	18	1.61			48	1.52		
Thyroiditis	8	0.11	0.001		48	0.34	0.001	
Carcinoma	14	0.07	0.001	0.001	38	0.31	0.001	0.001

N: Number of cases in each group, SD= Standard Deviation, P: significance of diseased groups against the healthy group, P1: Significance between diseased groups

There was a significant increase in MDA level in male thyroiditis and male thyroid cancer groups when compared to the male control group (p=0.001) for both. While there was no significant difference in MDA level in male thyroiditis when compared to male thyroid cancer group (P=0.57) (Table 4 and Fig. 4). For the female, there was a significant increase in MDA level in female thyroiditis and female thyroid cancer groups when compared to female control group (p=0.001) for both (Fig. 4). While there was a significant decrease in MDA level in female thyroiditis when compared to female thyroid cancer group (P=0.003).

Tissue TAC and Tissue MDA (TTAC & TMDA): No significant difference in male TTAC level in thyroiditis was observed when compared to thyroid cancer groups (p1=0.48). As well as, for female TTAC level there was no significant difference in TTAC level in thyroiditis when compared to thyroid cancer groups (p1=0.06) (Table 5 and Fig. 5).

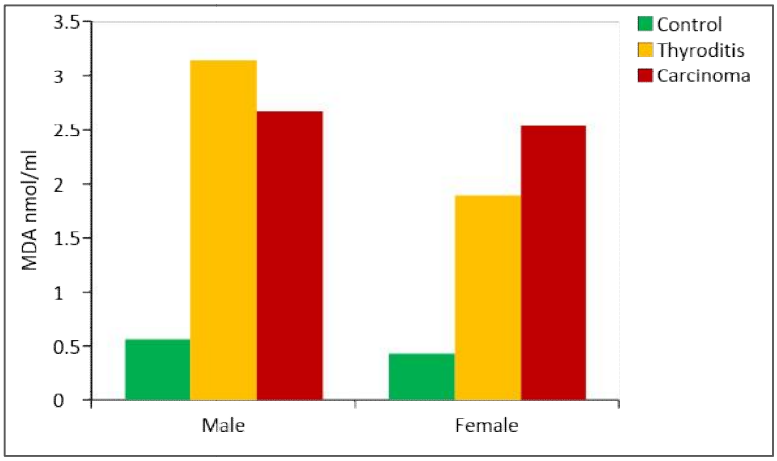

Fig. 4. Effect of gender on MDA level in different studied groups

Table 4. Effect of gender on MDA level in different studied groups

	Male	SD	P	P1	Female	SD	P	P1
Healthy	18	0.42			48	0.27		
Thyroiditis	8	2.77	0.001		48	1.04	0.001	
Carcinoma	14	0.97	0.001	0.57	38	0.92	0.001	0.003

N: Number of cases in each group, SD= Standard Deviation, P: significance of diseased groups against the healthy group, P1: Significance between diseased groups

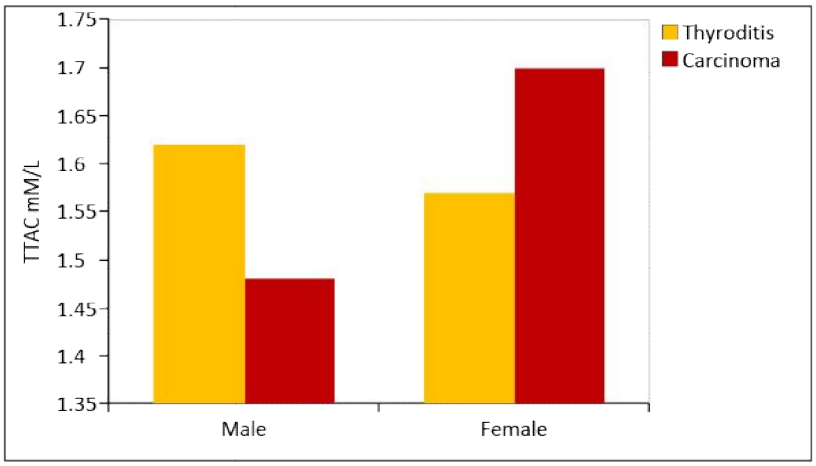

Fig. 5. Effect of gender on TTAC level in different studied groups

Table 5. Effect of gender on Tissue TAC & Tissue MDA level in different studied groups

		Male	SD	P1	Female	SD	P1
TTAC	Thyroiditis	8	0.42		48	0.34	
	Carcinoma	14	0.41	0.48	38	0.24	0.06
TMDA	Thyroiditis	8	0.31		48	0.76	
	Carcinoma	14	1.16	0.03	38	1.91	0.001

N: Number of cases in each group, SD= Standard Deviation, P: significance of diseased groups against the healthy group, P1: Significance between diseased groups

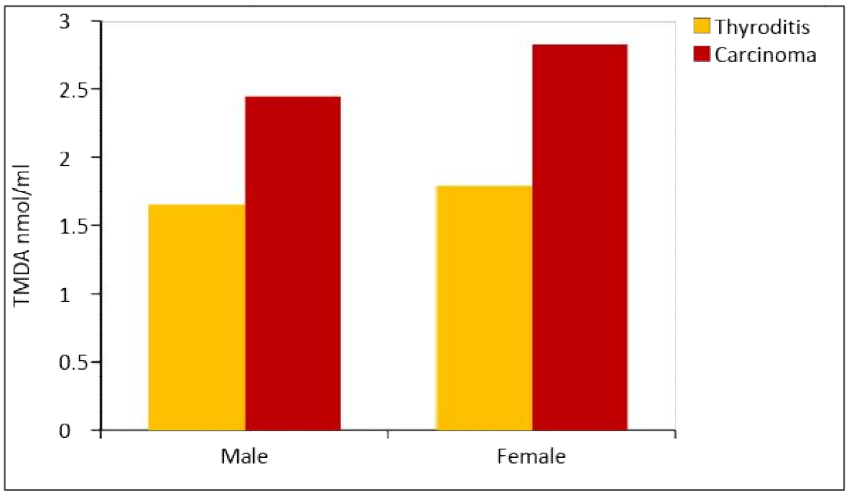

Fig. 6. Effect of gender on TMDA level in different studied groups

There was a significant decrease in male TMDA level in thyroiditis when compared to thyroid cancer groups (p1=0.03). As well as, for female TMDA level there was a significant decrease in the TTAC level in thyroiditis when compared to thyroid cancer groups (p1=0.001) (Table 5 and Fig. 6).

4. DISCUSSION

Thyroid cancer had been the most common type of endocrine malignancy, and its incidence has been continuously growing over the last several decades [6]. However, most of these approaches still have not reached the highest possible accuracy for the detection of all the main types of thyroid cancer, and they might have limited performance in the populations with a high pretest probability of cancer [7].

This study included (174) subjects, divided into (108) thyroid patients (22 male, and 86 female) and 66 matched healthy controls in age and sex (18male, and 48 female). The patients were divided into two subgroups into thyroiditis (56) and thyroid Carcinoma patients (52). Cases and controls did not differ with regard to age and sex. Women found to be the majority of subjects in both case and control groups (79.5% and 72.7% respectively).

The current study showed a significant high increase in serum TSH obtained from thyroiditis and thyroid cancer groups as compared to control group (P=0.001&0.001) respectively. Moreover, the level of Thyroid-stimulating hormone (TSH) obtained from the thyroiditis group was significantly reduced as compared with thyroid cancer.

This finding was in agreement with those of several authors [8,9]. The later demonstrated that Higher TSH levels were associated with Thyroid malignancy and the risk of malignancy rises in parallel with serum TSH within the normal range, and high levels of serum TSH concentrations were associated with advanced stage of thyroid cancer.

In the current study, there was a highly significant increase in FT4 obtained from thyroiditis and thyroid cancer groups as compared to control group (P=0.001&0.001) respectively. Also, there was a highly significant

increase in FT4 obtained from thyroiditis group as compared to thyroid cancer group (p=0.04). This result was confirmed by data obtained by several authors [10,11].

This result was not compatible with the observations of Lin-zheng He Who reported that FT4 were also compared between patients with thyroid cancer and patients with thyroiditis, but neither of them showed a significant difference, with or without the inclusion of the values out of the normal range [12].

Results from the current study did not show any significant increase in FT4 from male thyroiditis as compared to male thyroid cancer group (P=0.33). While there was a significant increase in mean FT4 from female thyroiditis as compared to female thyroid cancer group (P=0.04). There was a significant decrease in TSH from male thyroiditis as compared to male thyroid cancer group (P=0.001). Moreover, there was a significant increase in mean TSH from female thyroiditis as compared to female thyroid cancer group (P=0.001). This result was in agreement with Suzuki [13]. In Melville study, thyroid-stimulating hormone (TSH) levels show a significant association with the risk of papillary thyroid cancer (PTC) that appears gender-based, with lower than normal serum TSH levels years before a cancer diagnosis linked to an increased risk of PTC in women, while in contrast a higher than normal pre-diagnostic level was linked to a greater risk in men [14].

In this study, a highly significant decrease in TAC obtained from thyroiditis and thyroid cancer groups as compared to control group (P=0.001&0.001) respectively. This was in harmony with Lassoued S. who found that increased oxidative stress in thyroid cancer and thyroiditis has been revealed [15], and Wang D. who showed that TAC values were decreased in thyroid disease patients. Thus, TAC levels were lower in patients with thyroid cancer than in those with thyroiditis disease, which were, in turn, lower than those in healthy subjects [16].

The findings form the study showed that MDA levels were increased, while serum TAC was decreased in thyroid cancer and thyroiditis patients as compared with control. These preliminary findings indicate that an oxidant/antioxidant imbalance associated with thyroid cancer and thyroiditis. Free radicals and ROS participate in the physiological and pathological process in the thyroid gland. This result was in agreement with SM Hosseini-Zijoud who detected that the MDA levels were increased, while serum TAC was decreased in thyroid cancer and thyroiditis patients. These preliminary findings suggest that oxidant/antioxidant imbalance may be associated with or possibly indicate an increased risk to medullary thyroid carcinoma [17].

In this current study, there was no significant difference in TTAC from thyroiditis as compared to thyroid cancer groups (P1=0.25), while, there was a significant decrease in TMDA from thyroiditis as compared to thyroid cancer groups (P1=0.001).

According to Sagharchian, Oxidative stress had been shown to be the most significant influential factor in cancer pathogenesis. Follicular cells were affected in papillary thyroid carcinoma (PTC), which was the most prevalent thyroid cancer associated with oxidative stress. Thyroid cancer patients had oxidant/antioxidant imbalance, which could increase the risk of thyroid cancer. Thyroid hormones exerted a key role in the modulation of antioxidant systems and oxidative stress was demonstrated both in hyper- and hypothyroidism. In the field of hypothyroidism [18].

To the best of knowledge, this was the first study to evaluate MDA and TAC in association with thyroiditis and TC. In this study, the most important findings were the patients with thyroiditis and TC have elevated MDA levels and low TAC levels which when compared to healthy ones. These two parameters were playing a role on OS. No reports were available in the literature to comment on the simultaneous measurement of these parameters in TC. Thyroid hormones were associated with the oxidant and antioxidant status of the human organism. The findings obtained from in vitro and in vivo studies showed that thyroid hormones had a strong impact on OS [19]. Thyroiditis or TC was associated with an increase of parameters of OS in either tissue /plasma compared with control subjects including lipid peroxides. In conclusion, some important differences in the OS parameters and lipids profile between the patients and healthy controls were observed in this study. Increased MDA levels in both patients groups represent increased lipid peroxidation which might play an important role in the pathogenesis of the TC patients .also, MDA could be used as a reliable marker of OS and oxidative damage in studied groups.

As OS played a role in the pathogenesis of many chronic diseases including thyroid diseases. previous studies indicated that patients with either hyperthyroidism or hypothyroidism had increased the risk for the presence of oxidative stress [19,2]. In this study, oxidative stress was found to be increased in both patients.

5. CONCLUSIONS

This study found that the gender of TC patients may effect on biochemical investigations of the thyroid. Thus additional studies were required to examine the possible relation between gender effects with environmental epidemiology, genetic mutations, diet, hobbies and other hormones involved in the development of thyroid cancer were warranted.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Pelizzo MR, Boschin IM, Bernante P, Toniato A, Piotto A, Pagetta C, Nibale O, Rampin L, Muzzio PC, Rubello D. Natural history, diagnosis, treatment and outcome of medullary thyroid cancer: 37 years experience on 157 patients. EJSO. 2007;33:493e497.
2. Izmedu P, Hormona T, Markera LI, Stresa OU, Hipotireozi S. Association between thyroid hormones, lipids and oxidative stress markers in subclinical hypothyroidism. J Med Biochem. 2015;34:323-331.
3. Venditti P, Di Meo S. Thyroid hormone-induced oxidative stress. Cell. Mol. Life Sci. 2006;63:414–434.
4. Antonio Mancini, Chantal Di Segni, Sebastiano Raimondo, Giulio Olivieri, Andrea Silvestrini, Elisabitta Meucci, Diego Currò. Thyroid hormones, oxidative stress, and inflammation. mediators of inflammation. 2016;3.
5. LiVolsi VA. Pathology of thyroid disease. In: Falk SA: Thyroid Disease: Endocrinology, Surgery, Nuclear Medicine, and Radiotherapy. Philadelphia, Pa: Lippincott-Raven. 1997;127-175.
6. Nikiforov Y. Role of molecular markers in thyroid nodule management: Then and now. Endocr Pract. 2017;23:979-988.
7. Nikiforova MN, Mercurio S, Wald Al, Barbi de Moura MB, Callenberg K, Santana-Santos L, et al. Analytical performance of the ThyroSeq v3 genomic classifier for cancer diagnosis in thyroid nodules. Cancer. 2018;1682-1690.
8. Resende de Paiva C, Grønhøj C, Feldt-Rasmussen U, von Buchwald C. Association between Hashimoto's thyroiditis and thyroid cancer in 64,628 patients. Frontiers in Oncology. 2017;53:1-10.
9. Prasad C, Supreet Kumar, Tej Kumar Y. Comparative study on association between serum TSH concentration and thyroid cancer. Int Surg J. 2017;4(8):2800-2805.
10. Antonelli A, Ferri C, Ferrari SM, Di Domenicantonio A, Giuggioli D, Galleri D, et al. Increased risk of papillary thyroid cancer in systemic sclerosis associated with autoimmune thyroiditis. Rheumatology. 2016;55(3):480–484.
11. Kammoun-Krichen M, Bougacha-Elleuch N, Mnif M, Bougacha F, Charffedine I, Rebuffat S, et al. IL-1β a potential factor for discriminating between thyroid carcinoma and atrophic thyroiditis. European Cytokine Network. 2012;23(3).
12. Lin-Zheng He, Tian-Shu Zeng, Lin Pu, Shi-Xiu Pan, Wen-Fang Xia, Lu-Lu Chen. Thyroid hormones, autoantibodies, ultrasonography, and clinical parameters

for predicting thyroid cancer. International Journal of Endocrinology; 2016.
13. Satoru Suzuki, Shin-Ichi Nishio, Teiji Takeda, Mitsuhisa Komatsu. Gender-specific regulation of response to thyroid hormone in aging. Thyroid Res. 2012;5:1.
14. Nancy A. Melville. TSH levels linked to papillary thyroid cancer, with sex differences. Medscape Medical News; 2017.
15. Lassoued S, Mseddi M, Mnif F, Abid M, Guermazi F, Masmoudi H, El Feki A, Attia H. A comparative study of the oxidative profile in Graves' disease, Hashimoto's thyroiditis, and papillary thyroid cancer. Biological Trace Element Research. 2010;138:107–115.
16. Wang D, Feng JF, Zeng P, Yang YH, Luo J, Yang YW. Total oxidant/antioxidant status in sera of patients with thyroid cancers. Endocrine-Related Cancer. 2011;18:773–782.
17. Seyed-Mostafa Hosseini-Zijoud, Seyed Alireza Ebadi, Mohammad Taghi Goodarzi, Mehdi Hedayati, Roghayeh Abbasalipourkabir, Mohammad Parsa Mahjoob, Jalal Poorolajalal, Fabio Zicker, Nasrin Sheikh. Lipid peroxidation and antioxidant status in patients with medullary thyroid carcinoma: A case-control study. Journal of Clinical and Diagnostic Research. 2016;10(2):BC04-BC07.
18. Samaneh Famil Sagharchian, Mahdi Hedayati, Faranak Kazerouni, Ali Rahimipour, Mehrnoosh Shanaki. Salivary lipid peroxidation and antioxidant status in the patients with papillary thyroid carcinoma: A case-control study. 2018; 11(3):e9941.
19. Erem C, Suleyman AK, Civan N, Mentese A, Nuhoglu I, Uzun A, Ersoz HO, Deger O. Ischemia-modified albümin and malondiaaldehyde levels in patients with overt and subclinical hyperthyroidism: Effect of treatment on oxidative stress. Endocine Journal. 2015;62(6):493-501.

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