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Are Autoimmune Thyroid Diseases a Risk Factor for Thyroid Cancers?

Otoimmün Tiroid Hastalıkları Tiroid Kanserleri için Bir Risk Faktörü müdür?

Şahin BEDİR[1], Mehmet ERDOĞAN[2], Murat ÖZDEMİR[3], Banu SARER YÜREKLİ[2], Yeşim ERTAN[4], Özer MAKAY[3]

[1]*Ege University Faculty of Medicine, Department of Internal Medicine, İzmir, Turkey*
[2]*Ege University Faculty of Medicine, Department of Endocrinology and Metabolic Diseases, İzmir, Turkey*
[3]*Ege University Faculty of Medicine, Department of General Surgery, Division of Endocrine Surgery, İzmir, Turkey*
[4]*Ege University Faculty of Medicine, Department of Pathology, İzmir, Turkey*

ABSTRACT

Aim: Autoimmune thyroid diseases are common in the general population. Thyroid cancer (TC) is the most common endocrine malignancy. The aim of this study was to evaluate the risk of thyroid carcinoma in patients with Basedow-Graves (BG) and Hashimoto's thyroiditis (HT).

Materials and Methods: 1,668 patients underwent thyroid surgery at our institution. Of these, 138 patients were diagnosed with HT (126 women, 12 men) and 78 patients were diagnosed with BG (61 women, 17 men). HT and BG patients diagnosed with TC were identified.

Results: TC was seen in 23.1% of BG patients, 52.2% of HT patients, and 38.7% of nodular goiter (NG) patients. In the comparison of BG patients with HT patients, TC was observed to be more common in HT patients (p<0.001). Moreover, BG patients were compared with NG patients, and TC was detected to be less common in BG patients (p=0.008). The comparison of HT patients (average age: 46.53 years) with NG patients (average age: 51.02 years) revealed that TC was seen more often (p=0.003) and in the earlier age (p=0.019) in HT patients. It was found that, in patients with BG, the frequency of papillary microcarcinoma was higher (p=0.004) and tumor size was smaller, compared to HT and NG patients.

Conclusion: HT is associated with an increased risk of developing TC. Nevertheless, a pathogenesis linking these diseases remains unclear. Therefore, more studies on the subject are needed.

Keywords: Thyroid cancer, Hashimoto's thyroiditis, Basedow-Graves disease, nodular goiter

ÖZ

Amaç: Otoimmün tiroid hastalıkları genel popülasyonda sıkça görülmektedir. Tiroid kanseri (TC) en sık görülen endokrin malignitedir. Bu çalışmanın amacı, Basedow-Graves (BG) ve Hashimoto tiroiditi (HT) hastalarında TC riskini değerlendirmektir.

Gereç ve Yöntem: Kurumumuzda 1.668 hastaya tiroid cerrahisi uygulandı. Bunlardan 138 hastaya HT (126 kadın, 12 erkek) ve 78 hastaya BG (61 kadın, 17 erkek) tanısı konuldu. TC tanısı alan HT ve BG hastaları saptandı.

Bulgular: TK BG hastalarının %23,1'inde, HT hastalarının %52,2'sinde ve nodüler guatr (NG) hastalarının %38,7'sinde vardı. BG hastaları HT hastaları ile karşılaştırıldı ve HT hastalarında TC daha sık görüldü (p<0,001). BG hastaları NG hastaları ile karşılaştırıldı ve BG hastalarında TC daha az görüldü (p=0,008). HT hastaları (yaş ortalaması: 46,53 yıl) ile NG hastalarının (yaş ortalaması: 51,02 yıl) karşılaştırılmasında, HT hastalarında TC'nin daha sık (p=0,003) ve daha erken yaşta (p=0,019) görüldüğü belirlendi. BG'li hastalarda papiller mikrokarsinom sıklığının HT ve NG hastalarına göre daha yüksek olduğu (p=0,004), tümör boyutunun daha küçük olduğu görüldü.

Sonuç: HT, artan TK geliştirme riski ile ilişkilidir. Bununla birlikte, bu hastalıkları birbirine bağlayan patogenez belirsizliğini korumaktadır. Bu yüzden konu hakkında daha fazla çalışma yapılmasına ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Tiroid kanseri, Hashimoto tiroiditi, Basedow-Graves hastalığı, nodüler guatr

Address for Correspondence: Şahin BEDİR MD, Ege University Faculty of Medicine, Department of Internal Medicine, İzmir, Turkey
Phone: +90 532 168 50 55 **E-mail:** sahinbedir7786@hotmail.com **ORCID ID:** orcid.org/0000-0002-5797-0804
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INTRODUCTION

The frequency of autoimmune illnesses is significant in the general population. One of the most prevalent examples is autoimmune thyroid disease (AITD)[1]. Thyroid cancer (TC) is the most common endocrine malignancy[2]. The most frequent factor contributing to hypothyroidism is Hashimoto's thyroiditis (HT). Compared to men, women are seven times more likely to have HT and 2.5 times more likely to develop papillary TC (PTC), which is the most common kind of TC[3]. HT is usually treated medically; however, thyroidectomy is sometimes indicated [4].

The relationship between cancer and inflammation is quite well recognized but that between HT and TC pathogenesis remains unclear[5,6]. The combination of high levels of anti-thyroid peroxidase antibody (anti-TPO), anti-Tg, and thyroid-stimulating hormone (TSH) were discovered to be a risk factor for differentiated TC (DTC)[7]. There are several theories as to why HT arises. It is likely that HT is chronic thyroid inflammation, which damages the thyroid gland's structural integrity and interferes with the synthesis of thyroid hormones in a way that stimulates the release of TSH. In the goiter, sustained high doses of TSH stimulation may also activate TC[8]. Thyroid autoantibodies (TAb) have been linked to an increased risk of TC in several studies; however, the relationship between TAb and TC is still unclear[9].

The association of Graves' disease (GD) with thyroid nodules (TN) and TC is rarely reported. The incidence seems to be increasing according to recent literature[10,11]. It was previously reported that DTC had higher aggressiveness and a poorer prognosis in patients with GD than DTC in euthyroid control patients. Many studies have found controversial results. This may be due to genetic and environmental factors and inadequate patient follow-up[10,12,13]. Thyroid-stimulating antibodies in GD patients can play a role in detecting the high aggression level of TC[14]. Extensive evidence indicates that thyrotropin stimulates the growth and function of DTC. These responses indicate the existence of thyrotropin receptors in the cells of TC[15].

There is an ongoing discussion on the possibility of developing DTC after AITD. The aim of this research was to analyze patients who had surgery for GD and HT associated with TN, and to evaluate the risk of TC.

MATERIALS AND METHODS

In a single university facility, 1668 patients with various thyroid diseases underwent thyroid surgery. It was determined that 78 patients had Basedow-Graves (BG), 138 patients had HT and 1452 had nodular goiter (NG). The study protocol, numbered 15-8/8, was approved by the Ethics Committee of the Ege University Faculty of Medicine where the study was conducted on September 29, 2015. The Helsinki Declaration was followed during the study's execution.

When a preoperative diagnosis was available, total thyroidectomy was the primary surgical therapy. Each patient had their central compartment lymph nodes dissected. Lateral neck lymph node dissection was conducted in the presence of metastasis.

Indications for thyroidectomy for GD were the presence of suspicious cytology and large volume goiters (>90 mL). Patients with suspicious nodules and lymph nodes underwent ultrasound examination and biopsy.

Surgery was performed in HT patients when at least 5 mm TNs, perinodular halo, and a strong anechoic lesion on the posterior wall were detected on ultrasound. Patients analyzed as HT met the following criteria: (1) Ultrasonographic lesions having a perinodular hypoechogenic or hyperechogenic halo, an anechoic lesion with a strengthened posterior wall, and a hypoechoic or hyperechoic nodular pattern of at least 5 mm in diameter; (2) High thyroglobulin antibody (TgAb) or anti-TPO titers; (3) Considering histology, the thyroid parenchyma and stroma having a widespread lymphocytic infiltration with response foci and lymphatic follicles, as well as tiny follicles with a reduced colloid volume, foci of fibrosis, and cells with oxyphilic cytoplasm. Being positive for thyrotrophin receptor antibodies (TRAb), having records of GD, and the lack of clinical, ultrasonography, and morphological evidence of HT were included in the exclusion criteria.

Suspicious lesions found by fine needle aspiration biopsy; [Bethesda grades III and IV: III-atypia of undetermined significance or follicular lesion of undetermined significance; IV-follicular neoplasm or suspicious for follicular neoplasm (Hurthle cell)] and symptoms of tracheal compression were among the indications for surgical treatment in the NG group.

We excluded patients under 18 years of age, with *de novo* metastatic TC, recurrent TC, and significant prior exposure to radiation.

Physical examination, thyroid ultrasonography, thyroid auto-antibody tests and thyroid biopsy were performed on the patients who were going to be operated. The data were analyzed retrospectively.

Statistical Analysis

Statistical Package for the Social Sciences 20.0 (IBM, Turkey) packed software was used to perform statistical analyses. The chi-square test, Student's t-tests, Mann-Whitney U, Kruskal-Wallis test, Post-hoc test, and univariate variance analysis were applied for the examination of the relationships between the variables. P values of <0.05 were considered as statistically significant.

RESULTS

In our research, it was observed that 78 individuals with BG included 61 female and 17 male patients and the mean age was 39.42 (19-73) years. It was determined that, of 138 individuals with HT, 12 female and 12 were male, and the mean age was 49.24 (22-77) years. Of 1452 individuals with NG, 1094 were female, 358 were male, and their mean age was 53.34 (18-83) years.

Malignancy was present in 18 out of 78 patients included in the BG (23.1%) group, in 72 out of 138 patients included in the HT (52.2%) group, and in 562 out of 1452 patients included in the NG (38.7%) group. Malignancy data of the patients with TC in the BG, HT and NG groups are shown in Table 1.

The difference in malignancy was observed to be statistically significant (p<0.001) between the HT and BG groups, between the HT and NG groups (p=0.003), and between the NG and BG groups (p=0.008) (Table 2).

There was a statistically significant difference for HT (p=0.007) and for NG (p<0.001) between malignancy positive and malignancy negative groups in terms of age (Table 3). On the other hand, no significant difference for GD was found between malignancy positive and malignancy negative groups in terms of age (p=0.79) (Table 3). Considering age, there was also no statistically significant difference between GD malignancy positive and HT malignancy positive groups (p=1.000) and between GD malignancy positive and NG malignancy positive groups (p=0.110) (Table 2). A statistically significant difference between NG malignancy positive and HT malignancy positive groups was detected in terms of age (p=0.019) (Table 2).

In our study, the frequency of malignancy was 43.4% (168/387) in the male group and 37.8% (484/1281) in the female group;

Table 1. Malignancy data of the patients with thyroid cancer in Basedow-Graves, Hashimoto's thyroiditis and nodular goiter groups

	Basedow-Graves (n=78)	Hashimoto's thyroiditis (n=138)	Nodular goiter (n=1452)
Malignancy	n=18 (23%)	n=72 (52%)	n=562 (38%)
Papillary microcarcinoma	n=15 (83.3%)	n=34 (47.2%)	n=238 (42.3%)
Papillary carcinoma classic variant	n=2 (11.1%)	n=17 (23.6%)	n=112 (19.9%)
Papillary carcinoma follicular variant	n=0 (0%)	n=9 (12.5%)	n=146 (25.9%)
Papillary carcinoma other type	n=1 (5.5%)	n=9 (12.5%)	n=42 (7.4%)
Follicular carcinoma	n=0 (0%)	n=1 (1.3%)	n=11 (1.9%)
Medullary carcinoma	n=0 (0%)	n=2 (2.7%)	n=11 (1.9%)
Anaplastic carcinoma	n=0 (0%)	n=0 (0%)	n=2 (0.3%)

Table 2. The relationship of prognostic factors and malignancy in patients with Basedow-Graves, Hashimoto's thyroiditis and nodular goiter

	Basedow-Graves	Hashimoto's thyroiditis	Nodular goiter	p
Malignancy (+)	n=18 (23%)	n=72 (52.2%)		<0.001**
	n=18 (23%)		n=562 (38.7%)	0.008*
		n=72 (52.2%)	n=562 (38.7%)	0.003*
Age	44.44±11	46.53±12		1.000
	44.44±11		51.02±13	0.110
		46.53±12	51.02±13	0.019*
Tumor size	0.7±0.6	1.26±1.04		0.048*
	0.7±0.6		1.4±1.3	0.01*
		1.26±1.04	1.4±1.3	0.311
Papillary microcarcinoma	n=15 (83.3%)	n=34 (49.3%)	n=238 (44.2%)	0.004*
Macrocarcinoma	n=3 (16.7%)	n=35 (50.7%)	n=300 (55.8%)	
Multifocality	n =7 (38.9%)	n=30 (41.7%)	n=172 (30.7%)	0.140
Capsular invasion	n=1 (5.6%)	n=7 (9.7%)	n=72 (12.8%)	0.509
Vascular invasion	n=0 (0%)	n=0 (0%)	n=15 (2.6%)	0.317
Lymph node metastases	n=3 (16.7%)	n=10 (13.9%)	n =75 (13.4%)	0.918
Distant metastases	n=0 (0%)	n=0 (0%)	n=15 (3.3%)	0.304

and the difference between these groups was not statistically significant (p=0.054). The frequency of malignancy in NG was 43.6% in the male group and 37.1% in the female group; and the difference between these groups was statistically significant (p=0.034) (Table 4). On the other hand, malignancy frequency in BG was 29.4% in the male group and 21.3% in the female group; and the difference between these groups was not statistically significant (p=0.522) (Table 4). In HT, the frequency of malignancy was found to be 58.3% in the male group and 51.6% in the female group; and the difference was not statistically significant (p=0.885) (Table 4).

In terms of the dominant nodule size, there was no statistically significant difference between GD malignancy positive and GD malignancy negative groups (p=0.596) and between HT malignancy positive and HT malignancy negative groups (p=0.064) (Table 5). However, there was a statistically significant difference for NG between malignancy positive and malignancy negative groups (p<0.001) (Table 5).

In our study, tumor size was 0.75 cm [minimum (min): 0.1 cm - maximum (max): 2.60 cm] in the BG group, 1.26 cm (min: 0.1 cm - max: 5 cm) in the HT group, and 1.48 cm (min: 0.1 cm-11 cm) in the NG group. There was a statistically significant difference between GD and HT malignancy positive groups (p=0.048) and between GD and NG malignancy positive groups (p=0.010) in terms of tumor size (Table 2). On the other hand, there was no statistically significant difference between HT and NG malignancy positive groups in terms of tumor size (p=0.311) (Table 2).

In our study, the frequencies of microcarcinoma and macrocarcinoma were 83.3% (n=15) and 16.7% (n=3) in the BG group; 49.3% (n=34) and 50.7% (n=35) in the HT group; and 44.2% (n=238) and 55.8% (n=300) in the NG group. There was a statistically significant difference between the GD group and other groups in terms of microcarcinoma (p=0.004) (Table 2).

In our study, multifocal TC was observed in GD, HT and NG patients at the rates of 38.9% (n=7), 41.7% (n=30), and 30,7% (n=172), respectively (p=0.140) (Table 2). There was capsular invasion in GD, HT and NG patients with TC at the rates of 5.6% (n=1), 9.7% (n=7), and 12.8% (n=72), respectively (p=0.509) (Table 2). There was no statistically significant difference for GD, HT and NG (0%, 0%, and %2.6, respectively) in terms of vascular invasion (n=15) (p=0.317) (Table 2). There was no statistically significant difference between GD, HT and NG in terms of lymph node metastases '16.7% (n=3), 13.9% (n=10),

Table 3. The relationship of age and thyroid cancer in patients with Basedow-Graves, Hashimoto's thyroiditis and nodular goiter

	Age		p
	Malignancy (+)	Malignancy (-)	
Basedow-Graves	44.44±11 (min: 29 - max: 67)	38.42±12 (min: 19 - max: 73)	0.79
Hashimoto's thyroiditis	46.53±12 (min: 22 - max: 77)	52.20±11 (min: 27 - max: 76)	0.007*
Nodular goiter	51.02±13 (min: 18 - max: 81)	54.81±12 (min: 22 - max: 83)	<0.001**

*p<0.05, **p<0.001.
min: Minimum, max: Maximum

Table 4. The relationship of sex and thyroid cancer in patients with Basedow-Graves, Hashimoto's thyroiditis and nodular goiter

Malignancy +			p
	Male	Female	
Basedow-Graves (n=18)	29.4% (n=5/17)	21.3% (n=13/61)	0.522
Hashimoto's thyroiditis (n=72)	58.3% (n=7/12)	51.6% (n=65/126)	0.885
Nodular goiter (n=562)	43.6% (n=156/358)	37.1% (n=406/1094)	0.034*

*p<0.05,**p<0.001

Table 5. The relationship of dominant nodule and malignancy in patients with Basedow-Graves, Hashimoto's thyroiditis and nodular goiter

	Dominant nodule size (cm)		p
	Malignancy (+)	Malignancy (-)	
Basedow-Graves	1.1±0.7 (min: 0.5 cm-max: 3 cm)	1±0.7 (min: 0.2 cm-max: 4 cm)	0.596
Hashimoto's thyroiditis	1.5±1 (min: 0.3 cm-max: 5 cm)	2±1.3 (min: 0.2 cm-max: 7.5 cm)	0.064
Nodular goiter	2±1.5 (min: 0.2 cm-max: 11 cm)	2.5±1.7 (min: 0.1 cm-max: 26 cm)	<0.001**

min: Minimum, max: Maximum

and 13.4% (n=75), respectively] (p=0.918) and in terms of distant metastases (0%, 0%, and 3.3%, respectively) (n=15) (p=0.304) (Table 2).

In addition, no statistically significant difference in terms of thyroid hormones was revealed between the malignancy-positive and malignancy-negative groups with GD and between the malignancy-positive and malignancy-negative groups with HT. With regard to TSH, there was a statistically significant difference between malignancy positive (1.18 mIU/L) and malignancy negative (0.8 mIU/L) groups with NG (p<0.001). There was no statistically significant difference in terms of TAb between malignancy-positive groups with GD, HT and NG. For TRAb, there was a statistically significant difference between the malignancy-positive (1.4 IU/L) and malignancy-negative (5.2 IU/L) groups with only GD (p=0.031).

DISCUSSION

The study's goal was to find out how frequently TC and AITD coexisted in surgical pathology samples. The study on 1668 patients who underwent surgery between 2005 and 2014 with the diagnosis of pathological GD, HT and ND was retrospectively reviewed. The possibility of developing TC in individuals with HT-associated TN is a controversial issue in the evaluation of the current literature[16,17]. Anil et al.[17] evaluated the true aggression rate of TC in individuals with HT, by using fine needle aspiration cytology. It was discovered that TNs in patients with HT were not more likely to be malignant than those without HT. On the other hand, Larson et al.[18] carried out a study and found that patients were three times more likely to have TC if they had HT. In this study, PI3K/Akt expression was elevated in both HT and well-DTC. This circumstance indicated a significant connection between chronic inflammation and the development of cancer. The association between TC and GD is questionable. The coexistence of TN and GD is widely described, but its significance is uncertain with regard to the potential risk of malignancy[19]. Terzioğlu et al.[20] evaluated concurrent hyperthyroidism and TC and they found that the rate of concurrent carcinoma with GD was 6%. On the other hand, Chen et al.[21] found that the GD group's cancer incidence was 1.37 times higher (p<0.001).

In our study, the prevalence of malignancy in the NG group was 38.7%. The frequency of malignancy in the GD and HT groups was determined to be 23.1% and 52.2%, respectively. Thus, the incidence of malignancy in NG was higher than in GD (p=0.008). The incidence of malignancy in HT was higher than in NG (p=0.003). On the other hand, the incidence of malignancy in HT was higher than in GD (p<0.01). This result has given rise to thought that HT presence may be a risk factor for the development of malignancy (PTC).

Women are 2.5 times more likely than males to acquire PTC, which is the most common kind of TC. Because these diseases are common in women, to ascertain whether there was a connection between PTC and HT in women, Repplinger et al.[3] and associates examined data from their institution. Their data demonstrated that HT was linked to a higher chance of getting PTC. Also, in our study, the most frequent malignancy type was PTC in HT, which was similar with the literature. On the other hand, Wei et al.[22] studied GD patients who had thyroid resection for GD or TN lesions. According to the statistics, low-risk papillary thyroid microcarcinomas with no lymph node metastases or extrathyroidal lymphovascular invasion make up the majority of cancers. In our study, similar with the literature, the most frequent malignancy type was PTC in GD. There was no statistically significant difference between GD, HT and NG in terms of PTC.

Azizi et al.[23] evaluated the association of HT with TC. Their data demonstrated a correlation between both TC and higher serum TgAb concentration and age under 45 years. Also, in our study, there was a statistically significant difference between HT malignancy positive and NG malignancy positive groups in terms of age (46.53, 51.02, respectively), which was similar with the literature (p=0.019). At the same time, in our study, there was a statistically significant difference in age between the malignancy-positive and malignancy-negative HT groups (p=0.007). The mean age of the malignancy-positive group was younger. In the literature, it is debatable if TC and GD are related in terms of age[24,25]. On the other hand, in our study, no statistically significant difference was found between GD and NG patients with malignancy in terms of age. Similarly, there was no statistically significant difference in age between patients with malignant GD and HT.

In the literature, the association between TC and HT is controversial in terms of the gender[23]. Mazokopakis et al.[26] did not find a statistically significant difference in HT with TC in terms of gender. Similarly, in our study, there was no statistically significant difference in HT malignancy groups in terms of the gender. In the literature, the malignancy frequency of GD for women is as high as that for male[27]. In our study, we did not find a statistically significant difference in GD thyroid carcinoma with regard to gender. Consistent with the literature, there was no statistically significant difference between GD malignancy positive and GD malignancy negative groups in terms of dominant nodule size. Similarly, in our study, there was no statistically significant difference between the malignancy-positive and malignancy-negative HT groups in terms of dominant nodule size. In the literature, the size of tumors in the patients with GD was significantly smaller than in the euthyroid group[28]. In our study, similar with the literature, the size of tumors in the patients with GD was significantly smaller than in the HT group (p=0.048). Similarly, in our study, the size of tumors in the patients with GD was significantly smaller than in the NG group (p=0.01). On the other hand, in our study,

there was no statistically significant difference between HT and NG malignancy positive groups in terms of tumor size. In the literature, the microcarcinoma in the patients with GD was significantly more prevalent than in those with NG[25-27]. Our study demonstrated that microcarcinoma in GD was significantly more prevalent than in the HT and ND groups, which was similar with the literature (p=0.004). Azizi et al.[23] found an association of TC with increased serum TgAb concentration in the HT group. On the other hand, in our study, there was no statistically significant difference in neither HT nor BG malignancy positive groups in terms of serum TgAb and TPOAb. Moreover, Azizi et al.[23] found an association of TC with elevated serum concentration of TSH ≥1 µIU/mL in the HT group. Similarly, in the literature, Haymart et al.[29] reported that the incidence of TC was correlated with higher TSH. In our study, there was no statistically significant difference between HT malignancy groups in terms of high serum concentrations of TSH, calcitonin and other TFT. On the other hand, in our study, there was no statistical difference between malignancy positive and malignancy negative groups with GD in terms of TSH, FT3, FT4, TSH and calcitonin. However, a statistical difference was seen between malignancy positive and malignancy negative groups with NG in terms of TSH (p<0.001). There was a statistically significant difference between malignancy positive and malignancy negative groups with GD in terms of TRAb (p=0.031). TRAb level was significantly higher in the malignant group. Yano et al.[30] reported that the TRAb levels in the GD group did not significantly correlate with multifocality or the existence of lymph node metastases. According to these data, TC is not more severe in individuals suffering from GD than in euthyroid ones. These results have made us think that high TRAb level has no effect on the development of malignancy in patients with GD. In our study, similar with the literature, there was no statistically significant difference between GD, HT and NG in terms of multifocality. Konturek et al.[31] found LNM risk to be elevated in people with HT who had multifocal PTC. However, another study conducted by Konturek et al.[32] revealed that the spread of PTC to level VI lymph nodes was four times more common in HT than in patients without HT. As shown in this study, it was determined that multifocality adversely affected the prognosis, but AITD did not increase multifocality. Demircioglu et al.[33] found a relationship between TSH elevation and lymphovascular invasion and extrathyroidal spread in TC. However, in our study, there was no statistically significant difference between GD, HT and NG in terms of capsular invasion and also, in terms of vascular invasion. Similarly, in our study, considering lymph node metastases, there was no statistically significant difference between GD, HT, and NG. However, lymphocytic infiltration around or inside the tumor in PTC may be useful for predicting a good prognosis in HT[34]. This is consistent with the idea that lymphocytic infiltration is an immune response that inhibits the development and multiplication of tumors[35]. Patients with PTC, who have chronic thyroiditis in their non-cancerous thyroids, have a significantly improved prognosis for both relapse-free and overall survival[36]. In the literature, the association between TC and GD is controversial in terms of distant metastases. Cappelli et al.[37] found that cancers associated with GD seemed to be more aggressive than those associated with multinodular toxic goiter or uninodular toxic goiter. Kikuchi et al.[38] demonstrated that patients with small TC in GD had an excellent prognosis. In our study, there was no statistical difference between GD, HT and NG in terms of distant metastases.

Study Limitations

There were some limitations regarding our study. The most important limitation of our study was that it was conducted in a single center. In addition, patients with *de novo* metastatic TC were not included in the study.

CONCLUSION

In conclusion, we examined the clinico-pathological correlations between HT and GD in terms of TC in our region in the western part of Turkey. TC was shown to be more prevalent in HT patients when BG patients were compared with HT patients. It was discovered that TC was less common in BG patients, compared to NG patients. TC was more frequently observed in HT patients compared to NG patients. It was discovered that TC was observed in HT patients at a younger age than in NG individuals. In contrast to HT and NG patients, it was shown that patients with BG had a greater probability of papillary microcarcinoma. TRAb was shown to be lower in BG patients who had TC. Thyroid antibodies and TSH were shown to have no effect on TC risk in AITD.

These data demonstrate that HT is associated with an increased risk of developing PTC. Nevertheless, a pathogenesis linking these diseases remains unclear. More studies are needed on this subject.

Ethics

Ethics Committee Approval: The study protocol, numbered 15-8/8, was approved by the Ethics Committee of the Ege University Faculty of Medicine where the study was conducted on September 29, 2015.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Ş.B., M.E., M.Ö., B.S.Y., Design: Ş.B., M.E., M.Ö., Ö.M., Data Collection or Processing: Ş.B., M.E., M.Ö., B.S.Y., Y.E., Ö.M., Analysis or Interpretation: Ş.B., Y.E., Ö.M., Literature Search: Ş.B., B.S.Y., Writing: Ş.B.

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