Medical Journal of Bakırköy

Med J Bakirkoy 2025;21:19-23
DOI: 10.4274/BMJ.galenos.2024.2023.10-9

Research

# Clinicopathological Reflections of Hashimoto's Thyroiditis and Papillary Thyroid Carcinoma Coexistence

## Hashimoto Tiroiditi - Papiller Tiroid Karsinomu Birlikteliğinin Klinikopatolojik Yansımaları

Can Akcura[1], Samet Alkan[1], Sedat Can Güney[1], Gamze Gelir Çavdar[2], Emel Şenol[3], Ayça Tan[4], Nilüfer Özdemir[1], Hasan Aydede[5], Zeliha Hekimsoy[1]

[1]Manisa Celal Bayar University Faculty of Medicine, Department of Endocrinology and Metabolism, Manisa, Türkiye

[2]University of Health Sciences Türkiye, İzmir Bozyaka Training and Research Hospital, Department of Endocrinology and Metabolism, İzmir, Türkiye

[3]University of Health Sciences Türkiye, Mersin State Hospital, Department of Endocrinology and Metabolism, Mersin, Türkiye

[4]Manisa Celal Bayar University Faculty of Medicine, Department of Pathology, Manisa, Türkiye

[5]Manisa Celal Bayar University Faculty of Medicine, Department of General Surgery, Manisa, Türkiye

## ABSTRACT

**Objective:** Papillary thyroid carcinoma (PTC) is the most common subtype of thyroid cancer. Hashimoto's thyroiditis (HT), a chronic inflammation of the thyroid gland, is one of the most common autoimmune diseases worldwide. In this study, we aimed to determine the relationship between PTC and HT and the clinicopathological effects of the combination of HT and PTC on the course of PTC.

**Methods:** In this cross-sectional retrospective study, PTC cases who underwent surgery and were followed up at our institution's endocrinology outpatient clinic between 2014 and 2022 were divided into two groups according to the presence of HT. Demographic data of both groups, pathological features of the tumor, and preoperative laboratory findings were examined.

**Results:** A total of 42.4% (n=118) of 278 cases were accompanied by HT. The mean age of the patients was 46.44±12.2 years. The majority of patients were female (80.6%, n=224). Multifocality was significantly less common in the HT group (p=0.037).

**Conclusion:** Although multifocality was significantly less common in the HT group, no other statistically significant parameter was discovered in other clinicopathological findings. In light of these findings, the effect of HT on the course of PTC cannot be clearly determined. Considering the conflicting results regarding the effect of HT-PTC coexistence on the course of PTC in the literature, a comprehensive prospective study on this subject is necessary.

**Keywords:** Clinicopathology, Hashimoto's thyroiditis, multifocality, papillary thyroid carcinoma

## ÖZ

**Amaç:** Papiller tiroid karsinomu (PTC), tiroid kanserinin en sık görülen alt tipidir. Tiroid bezinin kronik enflamasyonu ile karakterize Hashimoto tiroiditi (HT), dünya çapında en yaygın otoimmün hastalıklardan biridir. Bu çalışmada PTC ile HT arasındaki ilişkiyi ve HT ile PTC birlikteliğinin PTC seyri üzerindeki klinikopatolojik etkilerini belirlemeyi amaçladık.

**Gereç ve Yöntem:** Bu kesitsel retrospektif çalışmada 2014-2022 yılları arasında kurumumuzda opere olup sonrasında endokrinoloji kliniğimizce takip edilen PTC olguları HT varlığına göre iki gruba ayrıldı. Her iki grubun demografik verileri, tümörün patolojik özellikleri ve hastaların ameliyat öncesi laboratuvar bulguları incelendi.

**Bulgular:** Toplam 278 olgunun %42,4'üne (n=118) HT'nin eşlik ettiği görüldü. Hastaların yaş ortalaması 46,44±12,2 yıldı. Hastaların çoğunluğu kadındı (%80,6 n=224). Multifokalitenin HT grubunda anlamlı derecede daha az olduğu görüldü (p=0,037).

**Sonuç:** Multifokalite HT grubunda anlamlı olarak daha az görülmesine rağmen diğer klinikopatolojik bulgularda istatistiksel olarak anlamlı başka bir parametre saptanmadı. Bu bulgular ışığında HT'nin PTK'nin seyrine etkisini net olarak ortaya koymak mümkün değildir. Literatürde HT-PTC birlikteliğinin PTC seyrine etkisine ilişkin çelişkili sonuçların olduğu göz önüne alındığında bu konuda kapsamlı prospektif çalışmalara ihtiyaç olduğu açıktır.

**Anahtar Kelimeler:** Klinikopatoloji, Hashimoto tiroiditi, multifokalite, papiller tiroid karsinomu

**Address for Correspondence:** Can Akcura MD, Manisa Celal Bayar University Faculty of Medicine, Department of Endocrinology and Metabolism, Manisa, Türkiye
**E-mail:** can.akcura@hotmail.com **ORCID ID:** orcid.org/0000-0003-4182-9002

**Cite as:** Akcura C, Alkana S, Güney SC, Gelir Çavdar G, Şenol E, Tan A, et al. Clinicopathological reflections of hashimoto's thyroiditis and papillary thyroid carcinoma coexistence. Med J Bakirkoy. 2025;21:19-23

**Received:** 02.11.2023
**Accepted:** 23.07.2024
**Publication Date:** 25.03.2025

## INTRODUCTION

Thyroid carcinoma is the most common cancer of the endocrine system, accounting for 3.4% of all cancer types diagnosed annually (1). Papillary thyroid carcinoma (PTC), a differentiated thyroid cancer, is the most common subtype.

Hashimoto's thyroiditis (HT), a chronic inflammation of the thyroid gland, is one of the most common autoimmune diseases worldwide. It has a prevalence rate of 5-10% and is characterized by hypothyroidism, positivity of serum anti-thyroid peroxidase and/or anti-thyroglobulin antibodies, and lymphocyte infiltration with destruction of thyroid follicle cells (2).The relationship between PTC and HT is a long-standing issue. This subject has biomolecular and clinicopathological aspects, and many related studies have been carried out. As a result of these studies, many biomolecular properties in common were found. These findings include *RET/PTC* oncogene rearrangement, BRAF (V600E) mutation partnership, phosphatidylinositol 3-kinase/Akt pathway, *CD98* and *P63* gene expression, and *human 8-oxoguanine DNA glycosylase* gene mutations (3).

From a clinicopathological point of view, HT was investigated to determine if it increased the risk of PTC development. In addition, the pathological features and clinical course of PTC based on HT were also studied. The results of the studies conducted in these areas do not fully overlap with each other, and there are serious contradictions at some points. In this study, we aimed to reveal the clinicopathological effect of HT-PTC coexistence on the course of PTC by screening patients diagnosed with PTC who were followed up in our clinic. We categorized the patients into groups according to HT association and examined the clinical, pathological, and laboratory findings of the patients in each group.

## METHODS

In this study, we included patients with a diagnosis of PTC who were followed up in the endocrinology outpatient clinic of our institution between 2014 and 2022 and whose surgical pathology results were available in the hospital data processing system. The patients were divided into two groups according to the diagnosis of HT in addition to the diagnosis of PTC based on the surgical pathology results and were categorized as the PTC and HT group (group 1) and the PTC-only group (group 2). Demographic data (age, gender) of the patients in both groups, tumor size in the pathology result, number of tumor foci, presence of lymphovascular invasion, presence of extrathyroidal invasion, surgical margin positivity, serum free triiodothyronine (fT3), free thyroxine (fT4), thyroid stimulating hormone (TSH) levels, and thyroid autoantibody (anti-TPO, anti-TG) levels were studied. The study was approved by the Ethics Committee of Manisa Celal Bayar University Faculty of Medicine on 21.06.2023 (approval number: 20.478.486).

### Statistical Analysis

The analysis of the obtained data was performed using statistical package for the social sciences 22.0 software. The concordance of quantitative data with normal distribution was examined using the Kolmogorov-Smirnov test. In the comparison of normally distributed variables between groups, an independent samples t-test was used, and descriptive statistics were presented as mean ± standard deviation. Intergroup comparisons of non-normally distributed variables were made using the Mann-Whitney U test, and descriptive statistics were presented as median (minimum-maximum). In the qualitative variables analysis, chi-square tests were used according to the groups, and the results were presented as frequencies (%). A p-value of $<0.05$ were considered statistically significant.

## RESULTS

As a result of our study, data from 278 patients with PTC were obtained. It was observed that in 42.4% (n=118) of these 278 cases, PTC was accompanied by HT. The mean age of the patients was 46.4412.2± years. The majority of patients were female (80.6%, n=224). In the subgroup analyses, the incidence of HT was significantly higher in female patients, and the patients with PTC coexisting with HT were significantly younger. The demographic information about the patients is presented in Table 1.

Regarding clinicopathological findings, multifocality was significantly less common in group 1 (p=0.037). Extrathyroidal extension (2.5% in group 1 vs. 0.6% in group 2) and surgical margin positivity (9.3% in group 1 vs. 6.9% in group 2) were proportionally higher in group 1. However, lymphovascular invasion was proportionally lower in group 1 (1.7% in group 1 vs. 3.1% in group 2). None of these three findings were statistically significant (Table 2).

The mean tumor size was found to be smaller (13.13 mm in group 2 compared to 11.99 mm in group 1) in group 1, but this difference was not statistically significant. The majority of tumor subtypes in both groups were classical and follicular subtypes. Although the prevalence of the classical subtype was proportionally higher in group 1 (32.2% in group 1 vs. 22.5% in group 2), this rate was not statistically significant (Table 3).

When the preoperative laboratory findings of both groups (fT3, fT4, TSH, anti-TPO, and anti-TG) were examined,

thyroid autoantibody levels were significantly higher in group 1. In terms of thyroid function tests, although the mean TSH level was higher in group 1 (1.72 uU/mL in group 1 compared to 1.37 uU/mL in group 2), this correlation was not statistically significant (p=0.076). fT3 and fT4 levels were similar in both groups. The laboratory findings are detailed in Table 4.

## DISCUSSION

The relationship between PTC and HT has long been a popular topic. The presence of common biomolecular pathways in both clinical settings requires further research to reveal the effect of HT on the development and prognosis of PTC. The literature on this subject has conflicting results. Age, gender, tumor size, tumor subtype, tumor foci number (multifocality), lymphovascular invasion, and extrathyroidal extension, which we analyzed in this study, are all prognostic factors of PTC (4). In addition, thyroid function tests and thyroid autoantibody levels, which are among the laboratory findings, have also been shown to play a role in the prognosis of PTC (5). In our study, we aimed to reveal the clinicopathological effects of HT on the course of PTC by dividing the PTC cases in our clinic

**Table 1.** Demographic data of the patients

| | Group 1 (n=118) | Group 2 (n=160) | p-value* |
|---|---|---|---|
| **Female** | 103 (87.3%) | 121 (75.6%) | **0.015** |
| **Male** | 15 (12.7%) | 39 (24.4%) | **0.015** |
| **Mean age (years)** | 44.64±11.46 | 47.68±12.62 | **0.037** |

Group 1: Hashimoto's thyroiditis+papillary thyroid carcinoma, group 2: Papillary thyroid carcinoma only,
*Independent sample t-test

**Table 2.** Clinicopathological properties of the patients

| | Group 1 (n=118) | Group 2 (n=160) | p-value* |
|---|---|---|---|
| **Multifocality** | 50 (42.4%) | 88 (55%) | **0.037** |
| **Lymphovascular invasion** | 2 (1.7%) | 5 (3.1%) | 0.452 |
| **Surgical margin positivity** | 11 (9.3%) | 11 (6.9%) | 0.455 |
| **Extrathyroidal extension** | 3 (2.5%) | 1 (0.6%) | 0.185 |
| **Mean tumor size (mm)** | 11.99±11.66 | 13.13±14.91 | 0.473 |

Group 1: Hashimoto's thyroiditis + papillary thyroid carcinoma, Group 2: Papillary thyroid carcinoma only,
*Chi-square analysis

**Table 3.** Pathological subtyping of the patients

| Tumor subtype | Group 1 (n=118) | Group 2 (n=160) | Total (n=278) |
|---|---|---|---|
| **Classic** | 38 (32.2%) | 36 (22.5%) | 74 (26.6%) |
| **Follicular** | 47 (39.8%) | 68 (42.5%) | 115 (41.4%) |
| **Classic+follicular** | 13 (11.0%) | 25 (15.6%) | 38 (13.7%) |
| **Oncocytic** | 16 (13.6%) | 24 (15.0%) | 40 (14.4%) |
| **Solid** | 4 (3.4%) | 7 (4.4%) | 11 (3.9%) |

Group 1: Hashimoto's thyroiditis+papillary thyroid carcinoma, group 2: Papillary thyroid carcinoma only

**Table 4.** Preoperative laboratory findings

| | Group 1 (n=118) | Group 2 (n=160) | p-value |
|---|---|---|---|
| **TSH** | 1.72±1.44 | 1.37±1.08 | 0.076* |
| **fT4** | 0.876±0.199 | 0.881±0.146 | 0.876* |
| **fT3** | 3.74±0.65 | 3.68±0.55 | 0.422** |
| **Anti-TPO** | 8.5 (0.2-1300) | 0.5 (0.1-55.5) | **0.0001**** |
| **Anti-TG** | 3.94 (0.01-800.13) | 0.30 (0.02-101.36) | **0.0001**** |

Group 1: Hashimoto's thyroiditis+papillary thyroid carcinoma, group 2: Papillary thyroid carcinoma only,
*Independent sample t-test, **Mann-Whitney U test, TSH: Thyroid stimulating hormone, fT4: Free thyroxine, fT3: Free triiodothyronine, anti-TPO and anti-TG: Thyroid autoantibody

into two groups according to the coexistence of HT and by examining the clinical and pathological features of these two groups.

The demographic analysis revealed that the patients in group 1 were significantly younger (p=0.037). Moreover, the incidence of HT with PTC was significantly higher in women than in men (p=0.015). Both findings are similar to those of previous studies in the literature.

When the HT-PTC coexistence was examined in terms of tumor size, we found that the tumor size was smaller in group 1 (mean 11.99 mm in group 1 vs. mean 13.13 mm in group 2). Although not statistically significant, this result is in line with the literature. In the study of Cappellacci et al. (6), the mean tumor size was found to be 13.711.9± mm in patients with PTC and 17.616.5± mm in patients without Hashimoto's thyroiditis, and this difference was found to be statistically significant (p=0.007). In our study, the evaluation of the histopathological data of the cases revealed contradictory results, consistent with the literature. When both groups were analyzed in terms of the number of tumor foci (multifocality), multifocality was found to be less common in group 1 compared with the other group, and this result was statistically significant (p=0.037). When methodologically similar studies were examined, findings contradicting our results regarding multifocality were found. Tang et al. (2), Molnár et al. (7), and Hanege et al. (8) found a higher rate of multifocality in patients with HT-PTC coexistence. When the two groups were evaluated in terms of lymphovascular invasion, no statistically significant difference was found, but lymphovascular invasion was found to be proportionally lower in group 1 (1.7% in group 1 compared to 3.1% in group 2). When the literature was examined, some studies, similar to ours, revealed that vascular invasion and lymph node metastasis were at a lower rate in patients with HT-PTC coexistence (2,7). However, Konturek et al. (9) found a fourfold increase in the risk factor of level VI lymph nodes in patients with PTC accompanied by HT.In our study, the surgical margin positivity was slightly higher in group 1 (6.9% group 2 vs. 9.3% group 1). However, this rate was not statistically significant. According to the 2015 guidelines of the American Thyroid Society, microscopic tumor invasion is categorized as an intermediate-risk group. However, a more recent study reported that microscopic surgical margin in patients with PTC was not an independent prognostic factor for recurrence-free survival (10,11).

In a meta-analysis by Tang et al. (2), extrathyroidal extension was found at a lower rate in patients with HT-PTC coexistence. In our study, a higher rate of extrathyroidal extension was observed in group 1 (2.5% in group 1 vs. 0.6% in group 2), but this result was not statistically significant.

When both groups were analyzed in terms of tumor subtypes, no statistically significant difference was found in terms of subtype distribution. The most common subtypes in both groups were classical and follicular subtypes. The rates of the oncocytic variant, a less common form, were similar in both groups (13.6% in group 1, 15% in group 2).

There are many studies in the literature on how the coexistence of HT with PTC affects the course of PTC; unfortunately, they do not conclude whether these effects are good or bad prognostic factors. In our study, multifocality was found to be statistically significantly low in group 1, but the absence of a significant correlation in other parameters prevented us from making a definite assumption about the effect of HT-PTC coexistence on the course of PTC.

### Limitation

Because our study was a retrospective cross-sectional study, the patients analyzed were already diagnosed with PTC. For this reason, no information could be obtained regarding the effect of the presence of HT on the development of PTC. This is a major limitation of our study.

## CONCLUSION

It is clear that the association between HT-PTC and HT-PTC has been a matter of curiosity for a long time, and many studies have been conducted on this topic. Our study, like most of the studies in the literature, could not clearly identify this association as an indicator of good or poor prognosis, and some contradictory results were obtained for some of the histological parameters. As a result, more comprehensive, multicenter prospective studies on this subject are needed.

### ETHICS

**Ethics Committee Approval:** The study was approved by the Ethics Committee of Manisa Celal Bayar University Faculty of Medicine on 21.06.2023 (approval number 20.478.486).

**Informed Consent:** Retrospective study.

## FOOTNOTES

### Authorship Contributions

Surgical and Medical Practices: A.T., H.A., Concept: C.A., N.Ö., H.A., Z.H., Design: C.A., N.Ö., Z.H., Data Collection or Processing: C.A., S.A., G.G.Ç., E.Ş., Analysis or Interpretation: S.C.G., A.T., N.Ö., Literature Search: C.A., S.A., S.C.G., G.G.Ç., Writing: C.A., S.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

## REFERENCES

1. Prete A, Borges de Souza P, Censi S, Muzza M, Nucci N, Sponziello M. Update on Fundamental Mechanisms of Thyroid Cancer. Front Endocrinol (Lausanne). 2020;11:102.
2. Tang Q, Pan W, Peng L. Association between Hashimoto thyroiditis and clinical outcomes of papillary thyroid carcinoma: A meta-analysis. PLoS One. 2022;17:e0269995.
3. Noureldine SI, Tufano RP. Association of Hashimoto's thyroiditis and thyroid cancer. Curr Opin Oncol. 2015;27:21-5.
4. Ito Y, Miyauchi A. Prognostic factors of papillary and follicular carcinomas in Japan based on data of kuma hospital. J Thyroid Res. 2012;2012:973497.
5. Lee IS, Hsieh AT, Lee TW, Lee TI, Chien YM. The association of thyrotropin and autoimmune thyroid disease in developing papillary thyroid cancer. Int J Endocrinol. 2017;2017:5940367.
6. Cappellacci F, Canu GL, Lai ML, Lori E, Biancu M, Boi F, et al. Association between hashimoto thyroiditis and differentiated thyroid cancer: A single-center experience. Front Oncol. 2022;12:959595.
7. Molnár C, Molnár S, Bedekovics J, Mokánszki A, Győry F, Nagy E, et al. Thyroid carcinoma coexisting with Hashimoto's thyreoiditis: clinicopathological and molecular characteristics clue up pathogenesis. Pathol Oncol Res. 2019;25:1191-7.
8. Hanege FM, Tuysuz O, Celik S, Sakallıoglu O, Arslan Solmaz O. Hashimoto's thyroiditis in papillary thyroid carcinoma: a 22-year study. Acta Otorhinolaryngol Ital. 2021;41:142-5.
9. Konturek A, Barczyński M, Wierzchowski W, Stopa M, Nowak W. Coexistence of papillary thyroid cancer with Hashimoto thyroiditis. Langenbecks Arch Surg. 2013;398:389-94.
10. Back K, Kim SK, Chai YJ, Kim JH, Choe JH, Kim JS. Does microscopic positive tumor margin in papillary thyroid cancer really matter? Surgery. 2019;166:1160-7.
11. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 Americanthyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016;26:1-133.