

## PAPILLARY THYROID CARCINOMA WITH COEXISTENCE OF HASHIMOTO AND TUMOR-ASSOCIATED LYMPHOCYTES

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### ABSTRACT

**Background:** Papillary thyroid carcinoma represents the most common thyroid cancer. The co-existence of Hashimoto thyroiditis and papillary thyroid carcinoma has long been described in clinical research; however, the relationship is still debatable. This study aimed to estimate the coexistence of Hashimoto's thyroiditis and papillary thyroid carcinoma and to correlate these two conditions with the expression of immunological markers, including CD19 and IgG4, and with clinicopathological factors.

**Methods:** The research conducted a retrospective investigation evaluating thyroid tissue obtained from papillary thyroid carcinoma patients with Hashimoto thyroiditis or tumor-associated lymphocytes coexistence. The examination determined B-cell and plasma cell infiltration using CD19 and immunoglobulin G4 markers to correlate them statistically with demographic and clinicopathological variables.

**Results:** Showed coexistence of Hashimoto thyroiditis and tumor-associated lymphocytes with papillary thyroid carcinoma in 74%. A significant association between immunoglobulin G4-related disease and age was detected in patients below 45 years, particularly among those with Hashimoto thyroiditis ( $P=0.039$ ), and with the histological subtypes in patients with classic variant (66.7% in Hashimoto thyroiditis and 20% in tumor-associated lymphocytes) ( $P=0.049$ ). In contrast, other clinicopathological findings showed no correlation to Hashimoto thyroiditis and immunological markers.

**Conclusions:** The high percentage of the coexistence of Hashimoto thyroiditis with papillary thyroid carcinoma, together with the predominance of immunoglobulin G4-related disease in young age patients, draws attention to immunobiological mechanisms behind this cancer, which might help in the development of modern-immune-based diagnostic and therapeutic approaches.

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**Keywords:** Papillary thyroid carcinoma, Hashimoto, Thyroiditis, IgG4-related disease, CD19, Clinicopathological factors.

**P**apillary thyroid carcinoma (PTC) represents 90% of all cases of thyroid cancer. Its incidence has risen over the past four decades. However, PTC has the best overall prognosis of all thyroid cancer types, with high long-term survival rates<sup>[1]</sup>. The diagnosis of PTC depends mainly on the histological features, including papillae and abnormally shaped follicles. In addition, a set of nuclear features is crucial for the diagnosis<sup>[2]</sup>. The latest WHO

classification distinguishes numerous subtypes of PTC according to their microscopic appearance and distinct prognostic traits. It is essential to comprehend the different PTC subtypes to make accurate diagnoses and develop specialized treatment plans<sup>[1]</sup>. Nevertheless, there is an overlap in the morphological and molecular profile between PTC and the common autoimmune disease, Hashimoto's thyroiditis (HT). Typically, women are

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more affected by both PTC and HT than men<sup>[3]</sup>. The frequency of HT in the overall population is believed to be 5–10%, whereas the incidence ranges from 0.3 to 1.5 cases per 1,000 individuals<sup>[4,5]</sup>.

Since its initial identification in 1955, HT has been thought to be potentially linked to the development and progression of PTC. Because it is related to less invasive disease at presentation and a lower recurrence rate, most researchers indicate it may be a protective factor for PTC [6]. In contrast, other research showed that HT is considered an independent risk factor for PTC<sup>[7]</sup>.

The production of autoantibodies and abnormal cellular responses to the thyroid autoantigens characterize the pathogenesis. This leads to lymphocytic infiltration, progressive destruction of thyroid follicles, and oncocytic metaplasia of follicular cells, eventually reducing thyroid hormone production [8,9]. Based on the prevalence of immunoglobulin G4 (IgG4)-positive plasma cells in the thyroid tissue, HT is a heterogeneous disease that can be divided into two subtypes: IgG4-related and non-IgG4-related<sup>[10,11]</sup>. On the other hand, thyroid cancer, particularly PTC, might be surrounded by a significant number of reactive immune cells, mainly lymphocytes. The nature of these cells that called tumor-associated lymphocytes (TAL), is not well understood<sup>[12]</sup>.

The debate on the coexistence of PTC, HT, and the inflammatory cells, including the TAL, may support a hypothesis on the role of the inflammatory cells. Multiple markers are important to specify the lymphocytic infiltration, including the cluster of differentiation 19 (CD19), a type-I transmembrane glycoprotein of 95 kDa that is a member of the immunoglobulin superfamily, which is broadly expressed in B cells throughout most B-cell differentiation stages<sup>[12]</sup>. Another player in this debate is the plasma cell and its IgG4 antibody, specifically the IgG4/IgG (total) antibody ratio, which is a measure of

tolerance induction<sup>[13]</sup>. This research aims to estimate the HT and TAL coexisting with PTC and to assess their relation to the immunological cell markers, including IgG4 and CD19, in the microenvironment in this combination by immunohistochemistry (IHC).

## PATIENTS AND METHODS

### Study Design

Fifty biopsies of patients who underwent thyroidectomy from January 2020 to October 2024 were selected from the Vin Private Laboratory Hospital archive with histologically confirmed PTC-alone and PTC with coexistence of HT or TAL. A retrospective and comparative cross-sectional analysis study was conducted in the Anatomy, Biology, and Histology Department, College of Medicine, University of Duhok. The study was approved by the Ethics Committee of the Duhok Health Directorate as recommended by the Scientific Committee of the College of Medicine (reference number: 30102024-9-13).

### Data Collection

Variables like general information (patient's age, gender, and date of service), clinical details, histopathological findings, and relevant prognostic information, including histologic type, tumor site, tumor size, lymphovascular invasion (LVI), extrathyroidal extension (ETE), lymph node (LN) involvement, pathologic stage classification, and the presence of other thyroid pathology like HT or other TAL [12] were obtained from the patient reports and histopathology records archived in Vin Laboratory.

### Histopathological Analysis

The histological examination of hematoxylin and eosin (H&E) and IHC slides was carried out in the Anatomy, Biology, and Histology Department, College of Medicine, University of Duhok, to confirm the findings in the pathological sheets and to assess special histopathological variables. Formalin-

fixed, paraffin-embedded (FFPE) tissue blocks were sectioned into 3-4  $\mu\text{m}$  thick slices using a microtome, and then tissue sections were mounted on glass slides using a water bath at 45°C for 15-20 mins. The prepared slides were dried and deparaffinized in an oven. Staining was done using an automated technique.

#### Immunohistochemical Study

The Autostainer Link instrument utilizes procedures based on various principles to achieve suitable staining results. The slides were also analyzed to identify the proper malignant region for IHC. FFPE tissue sections were placed on positively charged slides and then subjected to deparaffinization and hydration, followed by heat-induced epitope retrieval (HIER), to unmask antigenic sites, in the Dako PT Link device after being dried in an oven for 15- 20 minutes at 65°C. Dako FLEX Ready-to-Use Primary Antibodies were used with the EnVision FLEX visualization system and applied to FFPE tissue sections. When the staining procedure is completed, the specimens are mounted. Dehydration, clearing, and permanent mounting were performed.

#### Antibodies

Immunohistochemistry was performed using Monoclonal Mouse Anti-Human CD19 (Clone LE-CD19; Dako, Denmark) at 1:50-1:100. In addition, tissue sections were immunostained with Rabbit Anti-Human IgG4 Monoclonal Antibody (Clone EP138; Vitro, Spain) at 1:50. The 2012 international consensus statement provided an overview of the diagnostic criteria for IgG4-RD [14]. The pathological diagnosis of IgG4-RD requires IgG4 immunostaining as a fundamental tool because this simple procedure produces strong diagnostic evidence through reliable results. Study researchers employed IHC staining methods to establish the diagnostic protocol by measuring IgG4-positive plasma cells relative to total IgG-producing plasma cells through the diagnostic tool. The researchers established diagnostic criteria for IgG4-

related thyroiditis that use  $>20$  IgG4+ plasma cells per high-power field combined with IgG4+/IgG+ plasma cells ratios above 30% [10,15].

#### Statistical Analyses

Statistical Package for the Social Sciences (IBM SPSS) Statistics version 27 served as the platform for conducting statistical analysis. The data for categorical variables appeared as both percentages and frequencies. Samples were divided into two age groups, which included patients  $<45$  years and  $>45$  years old [16]. A cross-tabulation analysis examined relationships between age group, gender, tumor size, histological subtype, LVI, LN metastasis, ETE, together with IgG4 and CD19 Immunohistological expressions. A suitable statistical approach involved the chi-square test or Fisher's exact test. Results indicated statistical significance when the p-value reached  $<0.05$ .

## RESULTS

The age of the 50 PTC patients ranged from 19 to 70 years old, with a mean of 39.30 ( $\pm$  12.097 SD). 38 (76%) patients were  $<45$  years old, and 12 (24%) patients were  $>45$  years old. The females were affected more than the males, with 42 (84%) females and 8 (16%) males, and a male-to-female ratio of 1:5.25.

A large percentage of the PTC patients (74%) had thyroiditis, either HT (52%) or tumor-associated lymphocytes (TAL) (22%). Interestingly, in younger patients (below 45), the HT was detected in 57.9%, yet TAL appeared in 18.4%, while in 23.7% there was no inflammation. However, there were equal proportions at 33.3% ( $n=12$ ) among patients aged  $>45$  years old. The analysis showed no significant statistical difference ( $P=0.340$ ) between age and inflammation.

The results also showed that among the female patients, 52.4% presented with HT, while 23.8% exhibited TAL, and 23.8% showed no inflammation. Similarly, the statistics showed no significant difference

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(P=0.775) in inflammation between male and female patients only if the HT cases were added to the TAL, as shown in

Demographic factors	Inflammation N=37 %=(74)		No Inflammation N=13 Gender %=(26)		Total N=50 %=(100)	P Value
	HT	TAL	Female	Male		
	26 (52)	11 (22)	22 (57.9)	7 (18.4)	9 (23.7)	38 (76)
			4 (33.3)	4 (33.3)	4 (33.3)	12 (24)
			22 (52.4)	10 (23.8)	10 (23.8)	42 (84)
			4 (50)	1 (12.5)	3 (37.5)	8 (16)

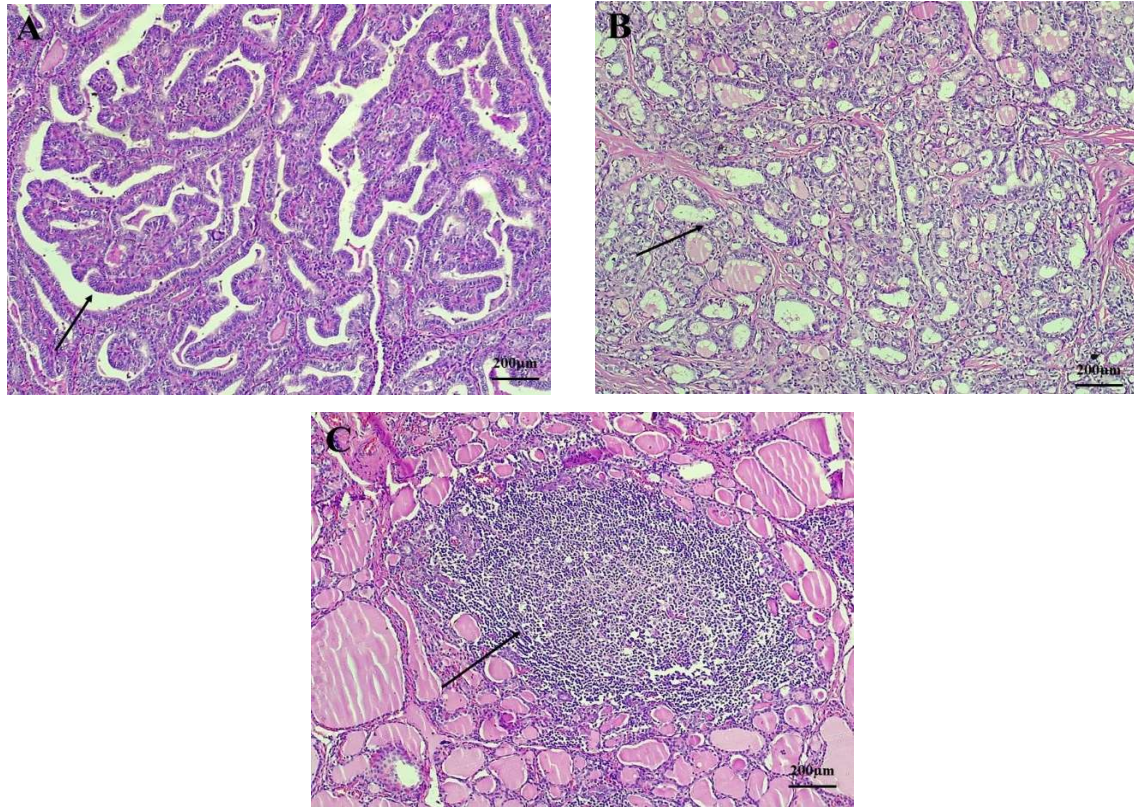
**Table 1: Relationship between age and gender with types of inflammation in PTC patients**

Demographic factors		Inflammation N=37 %=(74)		No Inflammation N=13 %=(26)		Total N=50 %=(100)	P Value
		HT	TAL	Female	Male		
	<45	22 (57.9)	7 (18.4)	9 (23.7)		38 (76)	0.340
	>45	4 (33.3)	4 (33.3)	4 (33.3)		12 (24)	
	Female	22 (52.4)	10 (23.8)	10 (23.8)		42 (84)	0.775
	Male	4 (50)	1 (12.5)	3 (37.5)		8 (16)	

Results are expressed by N= number of patients and %= percentage.

The histological re-examination confirmed 5 histological subtypes: classic PTC, microcarcinoma, follicular variant (FV)-PTC, tall-columnar variant-PTC, and classic-invasive with area of Warthin-like PTC. Across these subtypes, the classic

PTC variants displayed a higher HT inflammation proportion (61.1%) than microcarcinoma and FV-PTC. Figure 1 shows the two most common variants, the classical PTC and microcarcinoma. In addition to HT.



**Figure 1** Papillary thyroid cancer. A; Classic PTC with syncytial-like flat sheets. B; Microcarcinoma papillary thyroid. C; Hashimoto thyroiditis with germinal center (H&E, original magnification 10x).

Statistical analysis showed that age displayed a significant relationship with IgG4-related disease (IgG4-RD) ( $P=0.039$ )

found in HT individuals (41.4%), then in the TAL group (17.2%). Data showed that the number of patients aged over 45 years ( $n=8$ ) exhibited lower rates of IgG-RD

Clinicopathological variables	HT N=26 %=(70.2)		TAL N=11 %=(29.7)
	IgG-R	Not R	
	15 (40.5)	11 (29.7)	5 (13.5)
Age	<45	12 (41.4)	10 (29.7)
	>45	3 (37.5)	1 (12.5)
Gender	Female	11 (34.4)	11 (34.4)
	Male	4 (80)	0 (20)

). The majority of patients under 45 years ( $n=29$ ) presented with IgG-RD, mainly

(17.5%) in the HT group, and none of the patients were in the TAL group, while in non-IgG-related disease (non-IgG4-RD), 50% of patients were in the TAL group, with 12.5% HT group. These results indicated that IgG-related thyroiditis manifests primarily in patients below 45 years, particularly among those with HT. In contrast, gender differences between patients showed no significant differences according to statistical analysis ( $P=0.165$ ) with IgG-RD. The data showed that 34.4% of women had IgG-RD in the HT group, while the TAL group contained 12.5% of patients.

**Table 2: The association of age and gender with IgG-related disease**

Clinicopathological variables	HT N=26 %=(70.2)	TAL N=11 %=(29.7)	Total N=37 %=(100)	P Value
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		IgG-R 15 (40.5)	Not R 11 (29.7)	IgG-R 5 (13.5)	Not R 6 (16.2)		
<b>Age</b>	<45	12 (41.4)	10 (34.5)	5 (17.2)	2 (6.9)	29 (78.4)	0.039
	>45	3 (37.5)	1 (12.5)	0	4 (50)	8 (21.6)	
<b>Gender</b>	Female	11 (34.4)	11 (34.4)	4 (12.5)	6 (18.8)	32 (86.5)	0.165
	Male	4 (80)	0	1 (20)	0	5 (13.5)	

IgG4-R= IgG4-related cases, Not R= IgG4-non related cases.

For the histological subtypes, the classic variant was the most common subtype that made a statistically significant association with IgG-RD (66.7% in HT, 20% in TAL) (P=0.049). The FV-PTC primarily occurred in non-IgG-RD cases (66.7% in HT). The distribution of microcarcinoma was equal

between individuals from IgG-related and non-IgG-related groups. Non-IgG-related HT patients exclusively developed the uncommon PTC variants, such as tall-columnar PTC and Warthin-like PTC, as seen in

across all groups. Moreover, the results evaluated 32 CD19-positive cases and IgG4-related HT in 12 patients (37.5%) but IgG4-non-related HT in 11 (34.4%). Five CD19-negative cases analyzed showed three cases (60%) of IgG4-related HT, while two (40%) demonstrated IgG4-related thyroiditis. The statistical data did not prove a significant association between CD19 expression and IgG4-RD, based on the P=0.096.

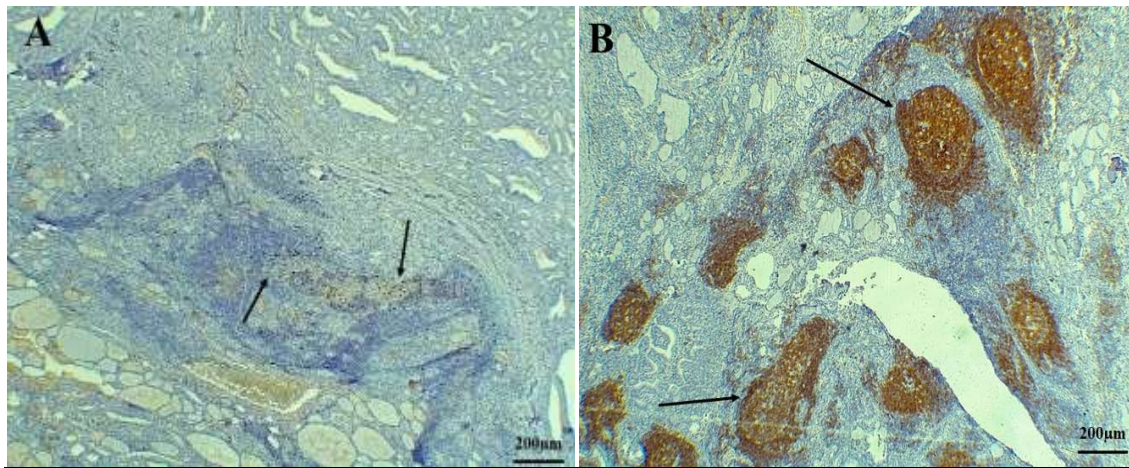
**Table 3.** The LVI-negative cases occurred in both IgG-related and non-IgG-related subgroups. For LN evaluation, 33.3% demonstrated LN positivity, while 66.7% presented LN negativity. The analysis showed that LN metastasis did not significantly correlate (P=0.894) since both positive and negative findings existed

**Table 3: Clinicopathological characteristics of PTC patients based on inflammation and IgG4**

Clinicopathological variables		HT N=26 %=(70.2)		TAL N=11 %=(29.7)		Total N=37 %=(100)	P Value
		IgG-R 15 (40.5)	Not R 11 (29.7)	IgG-R 5 (13.5)	Not R 6 (16.2)		
Histological Subtypes of PTC	Classic	10 (66.7)	1 (6.7)	3 (20)	1 (6.7)	15 (40.5)	0.049
	Microcarcinoma	4 (28.)	4 (28.6)	2 (14.3)	4 (28.6)	14 (37.9)	
	FV-PTC	1 (16.7)	4 (66.7)	0	1 (16.7)	6 (16.2)	

	Tall-Columnar Variant-PTC	0	1 (100)	0	0	1 (2.7)	
	Classic-Invasive with Area of Warthin-like PTC	0	1 (100)	0	0	1 (2.7)	
CD19	Positive	12 (37.5)	11 (34.4)	3 (9.4)	6 (18.8)	32 (86.5)	0.096
	Negative	3 (60)	0	2 (40)	0	5 (13.5)	

The cases of IgG4 expression in IgG4-RD, as well as the expression of CD19 in the tissue, are shown in Figure .



**Figure 2 Immunohistochemical markers. A; IgG4 expression in IgG4-RD reveals more than 20 IgG4-producing plasma cells per high-power field. B; CD19 expression in tissue. (IHC, original magnification 4x).**

The analysis of 29 patients aged <45 years demonstrated that CD19 positivity affected 69% in the HT group, and only 6.9% were CD19-negative. The TAL group had 17.2% of patients with CD19-positive and 6.9% with CD19-negative. The age group >45 of (n=8) demonstrated diverse CD19 expression levels, where HT had 37.5% positive, along with 50% positive within TAL. A statistical comparison revealed no association (P=0.189) between CD19

expression and patient age. In female patients (n=32), 62.5% of HT patients showed CD19 positivity, whereas TAL group patients showed 28.1% positivity. The number of CD19-negative patients remained low for both female groups. The evaluation results showed higher CD19 expression existed in female patients with HT, but statistical analysis revealed no significant relationship (P=0.125), as seen in

**Table 4 The association of Age and Gender with CD19 Expression**

		HT N=26 %=(70.3)		TAL N=11 %=(29.7)		Total N=37 %=(100)	P Value
Demographic factors		CD19+ve	CD19-ve	CD19+ve	CD19-ve		
		23 (62.2)	3 (8.1)	9 (24.3)	2 (5.4)		
Age	<45	20 (69)	2 (6.9)	5 (17.2)	2 (6.9)	29 (78.4)	0.189

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	>45	3 (37.5)	1 (12.5)	4 (50)	0	8 (21.6)	
Gender	Female	20 (62.5)	2 (6.3)	9 (28.1)	1 (3.1)	32 (86.5)	0.125
	Male	3 (60)	1 (20)	0	1 (20)	5 (13.5)	

A comparison of clinicopathological data from PTC patients who had HT and TAL between the CD19-positive and CD19-negative groups was shown in **Error! Reference source not found.** The most common histological subtype observed was classic PTC (n=15), microcarcinoma (n=14), and FV-PTC (n=6). The evaluation showed CD19 expression existed in 60% of classic PTC, 57.1% of microcarcinoma, and 66.7% of FV-PTC among HT patients. In

the TAL group, CD19 expression was demonstrated in 20% of classic PTC and 35.7% of microcarcinoma. The evaluation of PTC subtypes and CD19 expression revealed no significant statistical relationship (P=0.917). Data regarding LN metastasis results demonstrated CD19-positivity in all patients with HT and TAL, but without any significant association with ETE.

**Table 5 Clinicopathological characteristics of PTC patients based on CD19 expression**

Clinicopathological variables	HT N=26 %=(70.3)		TAL N=11 %=(29.7)		Total N=37 %=(100)	P Value	
	CD19+ve 23 (62.2)	CD19-ve 3 (8.1)	CD19+ve 9 (24.3)	CD19-ve 2 (5.4)			
Histological Subtypes of PTC	Classic	9 (60)	2 (13.3)	3 (20)	1 (6.7)	15 (40.5)	0.917
	Microcarcinoma	8 (57.1)	0	5 (35.7)	1 (7.1)	14 (37.9)	
	FV-PTC	4 (66.7)	1 (16.7)	1 (16.7)	0	6 (16.2)	
	Tall-Columnar Variant-PTC	1 (100)	0	0	0	1 (2.7)	
	Classic-Invasive with Area of Warthin-like PTC	1 (100)	0	0	0	1 (2.7)	
LN metastasis	Not-Submitted	13 (59.1)	1 (4.5)	7 (31.8)	1 (4.5)	22 (59.5)	0.389
	Positive	3 (60)	1 (20)	0	1 (20)	5 (13.5)	
	Negative	7 (70)	1 (10)	2 (20)	0	10 (27)	
ETE	Present	1 (33.3)	1 (33.3)	0	1 (33.3)	3 (8.1)	0.076
	Absent	22 (64.7)	2 (5.9)	9 (26.5)	1 (2.9)	34 (91.9)	

## DISCUSSION

Hashimoto thyroiditis, sometimes referred to as autoimmune thyroiditis, is one of the major causes of hypothyroidism and is thought to be a condition in which autoimmune tissue destroys epithelial cells [18]. It is well recognized that PTC on top of HT is a less aggressive condition. The

existence of HT is directly linked to several markers indicating a favorable prognosis for PTC [19]. In the current study, we identified a large incidence (52%) of HT with PTC compared to another research, which recognized a 21.5% incidence only [20]. In patients with HT, the current study found that papillary carcinoma tends to be a

disease of younger age, which is similar to data found by other researchers that found the middle years are most frequently diagnosed with his combination [3,21]. Lee and colleagues declare in their data that females were significantly associated with the presence of HT in PTC [8]. The classification of HT consists of IgG4-thyroiditis, which contains abundant IgG4-positive plasma cells, and non-IgG4-thyroiditis, which lacks IgG4-positive plasma cells. Most patients with IgG4-RD experience a subacute disease course alongside low levels of constitutional symptoms, yet IgG4-thyroiditis demonstrates more progressive disease. The demographic patterns showed a female bias in this thyroid condition, but at a lower proportion than normally seen in thyroid disorders. The disease occurs more frequently in younger patients compared to patients with non-IgG4 type [15]. This is corroborated by our result in which IgG4-RD manifests in younger patients compared to older patients ( $p=0.039$ ). Classic PTC showed the highest IgG4 expression in the HT group compared to other subtypes, including microcarcinoma and FV-PTC, with a significant association difference. On the other hand, there were no significant differences in gender, LVI, ETE, and LN metastasis concerning IgG4 expression. Moreover, this study showed that CD19+ B-cells occurred in both HT and TAL cases of PTC patients, indicating that B-cells play an active role in autoimmune thyroid disease, regardless of histological subtype. Yet, there were no correlations with age, gender, or aggressive tumor features (LVI/ETE) and LN metastasis. The main limitations of this study were the relatively small sample size, which might affect the analysis and results, and the lack of additional tests, for example, the serum antibodies to autoimmune disease, which are difficult to obtain in a retrospective study.

## CONCLUSION

Thyroiditis, particularly HT, is not only detected in a large percentage of the PTC patients but also is reported more in younger patients (below 45), in females, notably the young ones, and classic PTC variants. Furthermore, the majority of patients under 45 years presented with IgG-RD, mainly found in HT patients. The classic variant had a statistically significant association with IgG-RD. On the other hand, despite the female patients of HT showing CD19 positivity, more than the TAL, no association between CD19 expression and patient age was seen. Lastly, PTC cases presenting with HT alongside IgG4 expression and, to a lesser extent, for CD19 expression demonstrate a specific immunological subtype that needs further analysis for its prognostic value and to increase the insights into the immunobiological mechanisms behind thyroid cancer, which might help in the development of modern-immune-based treatment approaches.

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## CONFLICT OF INTEREST

The authors declared that they have no conflict of interest.

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## پوخته

## شیرپه‌نجا پاپیلاری تایرودی دگهل پیکفده‌رکفتنا هاشیموتو تایرودایتس و تایرودا نه‌دیاری کری

**پیش‌هکی و نارمانج:** شیرپه‌نجا پاپیلاری تایرودی نوین‌ه‌راتیا به‌ر به‌لافتترین شیرپه‌نجا تایرودی دکهت. پیکفده‌رکفتنا شیرپه‌نجا پاپیلاری تایرودی و هاشیموتو تایرودایتس ده‌مکئی در یژه دق‌ه‌کولینین کلینیکیدا هاتیه به‌حسکرن؛ بلی، هاتا نوکه ئەف پیوه‌ندیه دبارئ فەکولینئ دایه. نارمانج ژ نه‌جامدانا فی فەکولینئ پیکفده‌رکفتنا هاشیموتو تایرودایتس و شیرپه‌نجا پاپیلاری تایرودی و پیوه‌ندیا وان دگهل دهر برینا مارکهرین به‌رگیرئی، وهکی CD19 ، IgG4 ، و دگهل هوکارین کلینیکا پاتولوجی.

**ریکن کاری:** ئەف فەکولینه هاته نه‌جامدان کو هه‌لسه‌نگاندنا شانمیین تایرودیدی بهینه وهرگرتن ژ نه‌خوشین شیرپه‌نجا پاپیلاری تایرودی دگهل پیکفده‌رکفتنا هاشیموتو تایرودایتس یان لیمفوسایدین پیویست ب وهرم. مارکهرین CD19 و IgG4 هاتنه بکارئینان بو پشکنینا دیارکرنا خانه‌یین B و پلازما دا ژ لایی ئاماریقه پیوه‌ندیا وان یا دیموگرافی و نه‌خوشین کلینیکی بهینه دیارکرن.

**نه‌جام:** نه‌جامین فەکولینئ دیارکرن ریژا ۷۴٪ ژ پیکفده‌رکفتنا هاشیموتو تایرودایتس یان لیمفوسایدین پیویست ب وهرم دگهل شیرپه‌نجا پاپیلاری تایرودی. پیوه‌ندیه‌کا به‌رچاڤ دناقهره نه‌خوشین گریدای IgG4 و نه‌خوشین دین ژبی ۴۵ سالیی دا هاته دهرکفتن، تاییهت ئەو نه‌خوشین هاوکرنا هاشیموتو تایرودایتس هه‌ی (P=0.039)، و دگهل جورین هستولوجی ل نه‌خوشین توشی جورئ کلاسیک (۶۶.۷٪ ل هاوکرنا هاشیموتو تایرودایتس و ۲۰٪ ل لیمفوسایدین پیویست ب وهرم) (P=0.049). دهرامبه‌ر دا، هه‌چ پیوه‌ندیه‌ک نه‌بوو دناقهره هوکارین دی و هاودان و مارکهرین به‌رگیرئی.

**ده‌ستکه‌فتین فەکولینئ:** ریژا زیدابونا شیرپه‌نجا پاپیلاری تایرودی دگهل پیکفده‌رکفتنا هاشیموتو تایرودایتس، دگهل نه‌خوشیا گریدای IgG4 ل نه‌خوشین د ژیه‌کئ بچیک دا، به‌ر هف میکانیزمه‌کا بارگیریا زانستی رادکیشیت پشت ئەفی شیرپه‌نچی، کو رهنکه هاریکاربیت ل پهرمیدانا ریکن ده‌ستنیشانکرئی و چارمه‌سهریکرن لسه‌ر بنه‌مایین به‌رگیریا پیشکەفتی.

## الخلاصة

### سرطان الغدة الدرقية الحليمي مع وجود التهاب الغدة الدرقية هاشيموتو وغير النوعي

**الخلفية والأهداف:** يعد سرطان الغدة الدرقية الحليمي أكثر أنواع سرطان الغدة الدرقية شيوعاً. وقد وُصف وجود التهاب الغدة الدرقية هاشيموتو وسرطان الغدة الدرقية الحليمي معاً في الأبحاث السريرية منذ فترة طويلة، إلا أن العلاقة بينهما لا تزال محل جدل. وقد أظهرت البيانات الحديثة أن التهاب الغدة الدرقية الموجود مسبقاً يؤثر إيجاباً على تطور سرطان الغدة الدرقية الحليمي وتطوره. هدفت هذه الدراسة إلى دراسة وجود التهاب الغدة الدرقية هاشيموتو وسرطان الغدة الدرقية الحليمي معاً، وارتباطهما بالتعبير عن العلامات المناعية، بما في ذلك CD19 و IgG4، وبالعوامل السريرية والمرضية.

**طرق العمل:** أجرى البحث دراسةً استرجاعية لتقييم أنسجة الغدة الدرقية المأخوذة من مرضى سرطان الغدة الدرقية الحليمي المصابين بالتهاب الغدة الدرقية هاشيموتو أو المصابين بالتهاب الغدة الدرقية غير النوعي. وحدد الفحص تسلل الخلايا البائية والبلازما باستخدام تحليل علامات CD19 و IgG4 لربطها إحصائياً بالعوامل الديموغرافية والسريرية المرضية.

**النتائج:** أظهرت النتائج وجود التهاب الغدة الدرقية هاشيموتو مع سرطان الغدة الدرقية الحليمي بنسبة 74%، مع وجود ارتباط كبير بين المرض المرتبط بالغلوبيولين المناعي IgG4 والعمر لدى المرضى الذين تقل أعمارهم عن 45 عاماً، وخاصةً المصابين بالتهاب الغدة الدرقية هاشيموتو (قيمة الاحتمال = 0.039)، ومع الأنماط الفرعية النسيجية لدى المرضى المصابين بالمتغير الكلاسيكي (66.7% في التهاب الغدة الدرقية هاشيموتو و 20% في الخلايا الليمفاوية المرتبطة بالورم) (قيمة الاحتمال = 0.049). في المقابل، لم تُظهر النتائج السريرية المرضية الأخرى أي ارتباط بين التهاب الغدة الدرقية هاشيموتو والعلامات المناعية.

**الاستنتاجات:** إن النسبة العالية من الوجود المتزامن بين التهاب الغدة الدرقية هاشيموتو وسرطان الغدة الدرقية الحليمي مع هيمنة مرض مرتبط بـ IgG4 في المرضى في سن مبكرة تلفت الانتباه إلى الآليات المناعية الحيوية وراء هذا السرطان، والتي قد تساعد في تطوير أساليب التشخيص والعلاج الحديثة القائمة على المناعة.