

# Association of Lymphocytic Thyroiditis and Thyroid Papillary Cancer

Nassim Essabah Haraj<sup>1,\*</sup>, Soukaina El Aidi<sup>1</sup>, Karima Zine<sup>2</sup>, Siham El Aziz<sup>1</sup>, Samira Nani<sup>2</sup> and Asma Chadli<sup>1</sup>

<sup>1</sup>Endocrinology Department of CHU Ibn Rochd of Casablanca, Faculty of Medicine and Pharmacy of Casablanca, University Hassan II, Morocco

<sup>2</sup>Epidemiology Laboratory, Faculty of Medicine and Pharmacy, Hassan II University, Casablanca

**Abstract:** *Introduction:* The association between the papillary thyroid carcinoma (PTC) and the lymphocytic thyroiditis (LT) is common and remains controversial.

*Objectives:* Define the prevalence of the association of LT with PTC and the characteristics of patients who suffer from PTC with LT compared to those without LT.

*Methods:* This is a retrospective cross-sectional study of patients followed for PTC within the Department of Endocrinology of Casablanca between 1986 and 2015. The statistical analysis was performed using SPSS 16.

*Results:* Among 348 files of patients who suffer from PTC, 49 patients had associated LT, giving a frequency of about 14.1%. The patients were divided into two groups: group with PTC + LT and group with PTC without LT. A female predominance was noticed in both groups. The tumor size was lower in the group with PTC + LT: 0.6cm vs 1.4cm in patients without LT ( $p = 0.001$ ). TNM1 class was predominant in the LT group ( $p = 0.004$ ). There was no difference in recurrence rates in both groups.

*Conclusions:* The association of PTC with LT is common; patients with LT typically present with smaller tumor size and lower TNM stage and have a generally good prognosis.

**Keywords:** Lymphocytic thyroiditis, papillary carcinoma, thyroid, autoimmunity, Thyroid Neoplasms.

## INTRODUCTION

The association between papillary thyroid carcinoma (PTC) and lymphocytic thyroiditis (LT) was described for the first time in 1955 by Dailey *et al.* [1].

This is an association that remains controversial.

Its prevalence varies in different published studies [2]. Several hypotheses have been proposed to explain this association [3-5].

The purpose of this work is to study the characteristics of the association between lymphocytic thyroiditis and papillary thyroid carcinoma.

## PATIENTS AND METHODS

This is a retrospective cross-sectional study of patient files supervised for differentiated thyroid carcinoma at the department of Endocrinology, Diabetology and Metabolic Diseases, University Hospital Center Ibn Rochd Casablanca between 1986 and 2015.

The data collection was based on operating cards, which included demographic and clinical patient characteristics, staging, treatment, and clinical course.

The study included only patients with histologically confirmed PTC who had follow-up.

Lymphocytic thyroiditis is defined by the presence of lymphoplasmacytic infiltrate of the entire gland and may be organized into lymphoid follicles provided with germinal centers.

Patients followed-up for an additional type of thyroid cancer were excluded.

Comparison of means of continuous variables in the 2 groups was accomplished by paired t-test. All statistical analyses were performed on SPSS 16.0.

## RESULTS

Our study included 348 patients with histologically confirmed PTC, followed-up in the Department of Endocrinology and Metabolic Diseases in University Hospital Centre Ibn Rochd. Among these patients, we found 49 cases of associated lymphocytic thyroiditis with prevalence about 14.1%.

The following table summarizes the characteristics of patients followed-up for the papillary thyroid carcinoma (Table 1).

\*Address correspondence to this author at the Department of Endocrinology Diabetology, Metabolic Diseases and Nutrition, Casablanca, Morocco; Tel: 212 (0) 6 67 52 71 12; E-mail: haraj.nassim@gmail.com

**Table 1: Characteristics of the Patients in the Cohort**

CHARACTERISTICS	348 Patients
AVERAGE AGE	43.02 ± 12.17
GENDER RATIO	24 ♀ / 1 ♂ (334 ♀ / 14 ♂)
<b>TYPE OF SURGERY</b>	
Total thyroidectomy	(223) 64.6%
Lobo-isthmectomy + totalization	(122) 35.4%
<b>TNM CLASSIFICATION</b>	
TNM1	(159) 52.1%
TNM2	(77) 25.2%
TNM3	(65) 21.3%
TNM4	(4) 1.3%
RADIOIODINE TREATMENT	(245) 72.7%

### Characteristics of the Thyroid Papillary Carcinoma and the Lymphocytic Thyroiditis

Table 2 compares the two groups PTC with LT and PTC without LT. Patients with lymphocytic thyroiditis

were older (non-significant trend) and had lower mean tumor size ( $p < 0.001$ ). We don't find considerable difference in the other parameters. The evolution was favorable in all the patients with recovery after the end of the treatment.

### DISCUSSION

The prevalence of the lymphocytic thyroiditis and papillary association varies between 4.7% and 84.5% depending on the studies [2] (Table 3).

In contrast with other studies [10,16,18,27,29,30,33,34], we didn't find any female predominance in the group with lymphocytic thyroiditis compared to the group without LT. As in the studies cited, we noted a trend toward a higher mean age in the LT group [10,13,16,19,22,23,25,27,30,33,34].

That said, according to numerous studies, we can find a significantly lower age in the LT group [15,28,30], although some studies disagree with this result [13,15,32,33].

**Table 2: Comparison between PC with LT Group and Group of PC without LT**

	Group 1 CPT without LT	Group 2 CPT with LT	P
Sex			
Female	(277) 95,5%	(48) 98%	0.702
Male	(13) 4.5%	(1) 2%	
Average age ± SD	42.38 ± 12.13	45.9 ± 11.28	0.059
Average size of carcinomas	1.4887 cm	0.6888 cm	0.001
TNM classification			
TNM1	(124) 47.9%	(35) 76.1%	0.004
TNM2	(73) 28.2%	(4) 8.7%	
TNM3	(58) 22.4%	(7) 15.2%	
TNM4	(4) 1.5%	0%	
Microcarcinoma	(73) 25.2%	(13) 26.5%	0.84
Multifocality	(67) 24.6%	(17) 36.2%	0.097
Extrathyroidal extension	(45) 16.1%	(8) 16.3%	0.972
Locoregional recurrence	(8) 3.3%	2.6%	1
Lymph node recurrence	(10) 4.2%	(3) 7.7%	0.403
Positive thyroglobulins			
3 mois	(109) 37.5%	(17) 34.7%	0.51
6-12 mois	(62) 21.4%	(6) 12.2%	0.109
12-24 mois	(19) 6.5%	(3) 6.1%	1
Positive antithyroglobulins			
3 mois	(18) 6.2 %	(9) 18.4%	0.056
6-12 mois	(16) 5.5%	(3) 6.1%	1
12-24 mois	(7) 2.4%	(1) 2%	1

**Table 3: Various Studies Analyzing the Association of LT and PC**

	Years	Country	Association LT/CPT (%)
Matsubayashi S <i>et al.</i> [6]	1995	JAPAN	36/95 (37.9)
Gomez Saez JM <i>et al.</i> [7]	1997	Spain	6/129 (4.7)
Asanuma K <i>et al.</i> [8]	1998	JAPAN	15/69 (21.7)
Singh B <i>et al.</i> [9]	1999	USA	57/388 (14.7)
Loh KC <i>et al.</i> [10]	1999	USA	125/564 (22.2)
Neuhold N <i>et al.</i> [11]	2001	AUSTRALIA	6/10 (60.0)
Tamimi DM <i>et al.</i> [12]	2002	SAUDI ARABIA	34/59 (57.6)
Ohmori N <i>et al.</i> [13]	2007	JAPAN	29/83 (34.9)
Kurukahvecioglu <i>et al.</i> [14]	2007	TURKEY	37/199 (18.6)
Del Rio P <i>et al.</i> [15]	2008	ITALY	72/189 (38.1)
Replinger D <i>et al.</i> [16]	2008	USA	63/292 (21.6)
Fiore E <i>et al.</i> [17]	2009	ITALY	257/304 (84.5)
Kim EY <i>et al.</i> [18]	2009	KOREA	214/1441 (14.9)
Bruland O <i>et al.</i> [19]	2009	NORWAY	7/18 (38.9)
Kim HS <i>et al.</i> [20]	2010	KOREA	105/323 (32.5)
French JD <i>et al.</i> [21]	2010	USA	37/100 (37.0)
Mazokopakis EE <i>et al.</i> [22]	2010	GREECE	12/32 (37.5)
Consorti F <i>et al.</i> [23]	2010	ITALY	25/101 (24.8)
Gul K <i>et al.</i> [24]	2010	TURKEY	40/171 (23.4)
Kim KW <i>et al.</i> [25]	2011	KOREA	307/1028 (29.9)
Ahn D <i>et al.</i> [26]	2011	KOREA	58/269 (21.6)
Huang BY <i>et al.</i> [27]	2011	TAIWAN	85/1788 (4.8)
YYoon YH <i>et al.</i> [28]	2012	KOREA	56/195 (28.7)
Zhang L <i>et al.</i> [29]	2012	CHINA	358/2821 (12)
Jeong JS <i>et al.</i> [30]	2012	KOREA	359/1357 (26)
Zhang Y <i>et al.</i> [31]	2014	CHINA	41/134 (30)
Konturek A <i>et al.</i> [32]	2014	POLAND	130/773 (16)
Park JY <i>et al.</i> [33]	2015	KOREA	169/653(25)
Girardi FM <i>et al.</i> [34]	2015	BRAZIL	148/417(35.4)
Our study	2015	MOROCCO	49/348(14.1)

For the TNM stage, the lowest stages are usually associated with the thyroiditis [10,18,34].

Although we and several other groups did not find significant differences between the 2 groups in the prevalence of microcarcinoma, multifocality, or extrathyroidal extension [18,25,27,29,30], some studies [10,31] reported significantly more multifocality and extrathyroidal extension in the group without LT as well as a higher recurrence rate in this group [10]. Literature review suggests that, despite some conflicting reports, women with PTC and LT are younger than those without LT and have a generally good prognosis.

The frequent association reported between LT and PTC suggests several etiopathogenic hypotheses:

- Some authors consider the association to be fortuitous [35,36].
- Other authors [4,5,37-40] feel that mutations occurring in LT patients in RET/PTC or altered expression of the p63 gene may predispose to PTC.
- Still others [41] suggest that an immunologic response induced by antigens from the PTC are the cause of the lymphocytic infiltration.

- Other groups [42-45] have pointed to the elevated TSH levels often encountered in patients with LT, many of whom are hypothyroid, as a possible tumor growth promoting factor. This is consistent with the observation that patients with Graves' disease who have elevated TSIG acting through agonist binding to the TSH receptor, as well as chronic low grade thyroid inflammation, also have a reportedly higher incidence of PTC [46].

## CONCLUSION

The PTC/LT association is not rare. In our study LT patients had generally smaller tumors and lower TNM scores compared with non-LT patients; both groups had a similar evolution and prognosis. The smaller tumor size and lower TNM stage in LT patients could be partially due to more frequent surveillance in known LT patients. Studies are necessary to elucidate probable etiopathogenic associations between these two entities.

The authors declare that there is no conflict of interest regarding the publication of this paper.

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