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Association of Hashimoto thyroiditis with papillary thyroid carcinoma and its clinical features – A retrospective study in a tertiary care hospital

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ABSTRACT

Background: Papillary thyroid carcinoma (PTC) is the most widespread endocrine malignancy. Among the several risk factors, Hashimoto thyroiditis (HT) is one of the factors associated with increased incidence of PTC. Both HT and PTC share several epidemiologic features including high prevalence, female predominance, and increased incidence in iodine-sufficient areas. **Aims and Objectives:** The aim of the study was to assess the incidence of HT and PTC coexistent in endemic population. The study also aimed to determine the association of various prognostic parameters of PTC in patients with coexistent HT. **Materials and Methods:** This was a retrospective study done from May 2019 to May 2024 over a period of 5 years in a tertiary care hospital of West Bengal. A total of 54 patients with primary PTC who underwent total thyroidectomy with cervical lymph node dissection (LND) were studied. Patients with primary PTC with neck LND and complete medical history were included in this study. Patients with previous thyroidectomy surgery or patients with incidental PTC diagnosed in thyroidectomy specimens done for a benign neoplasm (without LND) were excluded from the study. **Results:** A total of 54 cases of PTC were studied out of which 23 cases were PTC associated with HT and 31 cases were PTC without HT constituting 42.59% and 57.4%, respectively. PTC associated with HT had a greater incidence in females. In this study, our results showed that PTC with HT had a greater tendency of tumor multifocality, greater mean lymph node size, and increase rate of extranodal tumor extension. At the same time, patients of PTC associated with HT had smaller tumor size and low clinical stage. **Conclusion:** PTC associated with HT had a female preponderance, larger metastatic lymph node, a tendency for multifocality, and extranodal extension. At the same, they also had smaller tumor size and low clinical stage indicating a complex and controversial effect of HT on PTC.

Key words: Hashimoto thyroiditis; Papillary thyroid carcinoma; Thyroid histopathology

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INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most widespread endocrine malignancy.[1] Out of all the thyroid malignancies, PTC is the most common form of differentiated thyroid cancer with the most favorable prognosis and its incidence is gradually increasing.[2] Among the several risk factors, Hashimoto thyroiditis (HT) is one of the factors associated with increased incidence of PTC. Various previous studies demonstrated that HT was significantly associated with the prevalence.[3-6]

Wu et al.,[7] analyzed the association between lymphocytic thyroiditis (LT) and PTC. Their findings demonstrated

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that PTC concomitant with LT was associated with the female sex, a lower capsular invasion rate, larger metastatic lymph node and tendency for multifocality indicating the complexity of the effect of LT on PTC prognosis. Danis et al.,[8] demonstrated that HT is an independent risk factor for PTC development. Osborne et al.,[9] studied the effect of HT on PTC outcomes and demonstrated elaborately both the protective and detrimental effects of HT on PTC. Hussein et al.,[10] studied thyroid cancer associated with HT. Effect of chronic LT on clinicopathological features of PTC was demonstrated by Babli et al.[11]

HT also known as chronic LT is responsible for most cases of hypothyroidism in iodine-sufficient areas.[12] HT similar to PTC also has been steadily on the rise.[13] Both HT and PTC share several epidemiologic features including high prevalence, female predominance, and increased incidence in iodine-sufficient areas.[14] In addition to this, both HT and PTC show some dysregulated non-immune linked genes involved in cell cycle, apoptosis, DNA damage and repair, reactive oxygen species production, and oxidative stress.[15] Amplification of rearranged during transfection oncogene has been described in HT similar to PT.[6,16] Irrespective of all the above features described, the exact causal relationship between PTC and HT is controversial and has a debatable explanation. The aim of the study was to assess the incidence of coexistent HT and PTC in endemic population. The study also aimed to determine the association of various prognostic parameters of PTC in patients with coexistent HT.

Aims and objectives

The aims and objectives of the study is to assess the incidence of coexistent HT and PTC in endemic population. The study also aims to determine the association of various prognostic parameters of PTC in patients with coexistent HT.

MATERIALS AND METHODS

Study design and duration

This was a retrospective study done from May 2019 to May 2024 over a period of 5 years in a tertiary care hospital of West Bengal.

Inclusion and exclusion criteria

Patients with cytological diagnosis of malignant thyroid lesion (Bethesda V) who had undergone thyroidectomy surgery with neck lymph node dissection (Radical thyroidectomy) and have complete medical history available with them were included in this study. Only those cases which were diagnosed as PTC on histopathological examination were included and cases with other thyroid malignancies were excluded from the study.

Patient selection

A total of 54 patients were studied. All the patients with abnormal findings (suspicious/highly suspicious of tumors) on thyroid ultrasonography (TIRADS) were evaluated by fine needle aspiration cytology to further confirm the radiological diagnosis. The patients with cytological diagnosis of a malignant thyroid lesion (Bethesda V) then underwent total thyroidectomy with neck node dissection and the specimens (Figure 1) were received in our pathology department for histopathological study. All the specimens were subjected to routine tissue processing method and hematoxylin and eosin-stained slides were prepared. In addition to this blood tests including thyroid hormone assay (FT_3, FT_4, thyroid stimulating hormone), Calcitonin, parathyroid hormone were evaluated simultaneously. Serological tests for autoantibody detection of Antithyroglobulin antibody (Ab) and thyroid peroxidase Ab were also evaluated.

All the relevant clinical information such as age, sex, and thyroid involvement (diffuse/nodular) were collected from the clinical records.

Histopathological analysis

All the cases of PTC after histopathological evaluation were categorized into two groups, that is, PTC with HT and PTC without HT. The tumor grading and staging were done according to the 8th edition of the American Joint Committee on cancer tumor Node metastasis.[17] (AJCC 8th edition).

Ethical consideration

The study was approved by the Institutional Ethics Committee. Since this was a retrospective study, there was no link between patients and the researchers. Confidentiality regarding the patient's identity was maintained.

Statistics

All the data were represented by number and percentage and expressed in MS Excel sheet using software version IBM SPSS 20.0. $P<0.05$ was considered statistically significant.

RESULTS

A total of 54 cases of PTC were studied out of which 23 cases were PTC associated with HT (Figure 1b and c) and 31 cases were PTC without HT constituting 42.59% and 57.4%, respectively. PTC with HT had a greater incidence in females. Twenty-one out of 23 (91.30%) cases of PTC with HT were female whereas 23 out of 31 (74.19%) cases of PTC without HT were females (Table 1). PTC with HT had a predominant clinical presentation of diffuse thyroid swelling (17 out of 21,

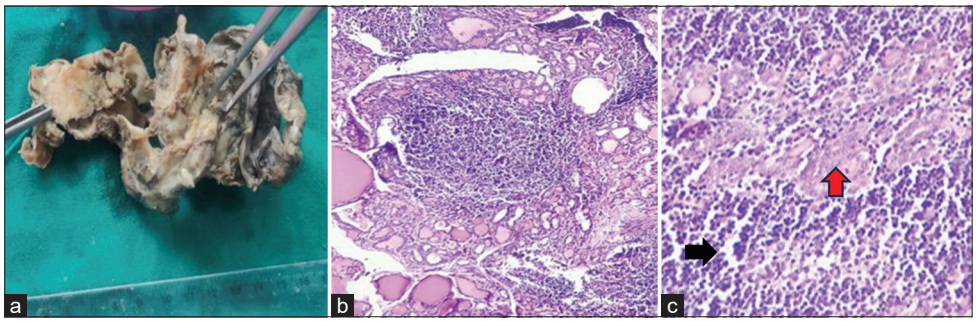

Figure 1: Gross photograph of thyroidectomy specimen (a), microphotograph of Hashimoto thyroiditis (HT) (b) and papillary thyroid carcinoma (Red arrow) within the vicinity of HT (Black arrow) (c) (H&E, ×100)

Table 1: Clinicopathological features of patient having PTC with HT (n=23) and without HT (n=31)

Parameters		PTC with HT (n=23) (%)	PTC without HT (n=31) (%)
A	Sex		
	Female	21 (91.3)	23 (74.19)
	Male	02 (8.69)	06 (19.35)
B	Age in years		
	31–40	09 (39.13)	13 (41.93)
	41–50	07 (30.43)	09 (29.02)
	51–60	04 (17.39)	07 (22.58)
	>60	03 (12.04)	02 (6.45)
C	Thyroid swelling		
	Diffuse thyroid swelling	17 (73.91)	04 (12.9)
	Nodular thyroid swelling	06 (26.09)	27 (87.1)
D	Thyroid selling involving		
	One lobe	06 (26.09)	28 (90.32)
	Both lobes	17 (73.91)	03 (9.68)
E	Unifocal tumor	05 (21.74)	23 (74.2)
	Multifocal tumor	18 (78.26)	08 (25.8)

PTC: Papillary thyroid carcinoma, HT: Hashimoto thyroiditis

80.95%) in comparison to PTC without HT which had predominant nodular thyroid lesion (27 out 31, 87.09%) (Table 1). Multifocality of the tumor was more commonly seen in patients of PTC with HT (n=18, 78.26%) (Table 1). The mean size of the metastatic lymph node was greater (0.66 cm) in patients of PTC with HT than in patients without HT (0.47 cm) (Table 2).

Both the tumor size (T) and central lymph node metastasis were less in patients of PTC with HT than in patients of PTC without HT. Small tumor size (T1) (Figure 1a) was more commonly seen in 78.26% and 38.7% cases in PTC with HT and PTC without HT, respectively (Table 2). Microscopically majority of the PTC were of classic subtype (Figure 2a). Central lymph node metastasis (Figure 2b) was less (56.5%) in PTC with HT than in PTC without HT (80.6%) (Table 3).

In this study, our results showed that PTC patients with HT had a greater tendency of tumor multifocality, greater mean lymph node size, and increase rate of extranodal tumor extension. At the same time, patients of PTC with HT had smaller tumor size and low clinical stage.

DISCUSSION

PTC ([ICD-0: 8260/3-Papillary Carcinoma of thyroid], [ICD-10: C73-malignant neoplasm of thyroid gland])[18] is the most common type of differentiated thyroid cancer.[2] According to GLOBOCAN 2020, the age-standardized incidence rates of thyroid cancer were 10.1/100,000 women and 3.1/100,000 men.[19] Recent World Health Organization classification (5th edition) of thyroid tumors[20] described various variants of PTC including the classic type basing on the combined features of Cytology, architecture/pattern, size, and encapsulation. PTC has a female predominance with F: M ratio of ~3:1.[21] Among various risk factors associated with the development of PTC exposure to ionizing radiation before age 20 is the most important factor.[22]

The association of PTC with HT having a causal (risk factor) relationship is a highly debatable topic.

Coexistence of PTC with HT and their association was first described by Dailey et al.,[23] since then the association between the two diseases remains controversial. Although the exact pathogenic mechanism indicating why PTC and HT develop concurrently is not clear several theories have been proposed. One theory is that HT may represent the host's immune response to preexisting PTC. On the contrary, another possibility suggested is that PTC may be induced or triggered by preexisting HT. Other theories, suggested both diseases may result from an imbalance between apoptotic and antiapoptotic pathways.[24]

Various previous studies suggested that HT had protective effects on PTC. Rye and Yoon[25] demonstrated that HT patients had smaller tumor size, decreased risk of extrathyroidal extension and central lymph node extension, and central lymph node metastasis. Molnár et al.,[26] stated that in HT patients due to continuous immune activation

Table 2: Gross and microscopic features of metastatic cervical lymph nodes in patients of PTC with HT (n=23) and without HT (n=31)

Parameters		PTC with HT (n=23) (%)	PTC without HT (n=31) (%)	P-value
A	Gross findings			
(i)	Number of cases with lymph node metastasis	13 (56.5)	25 (80.6)	<0.001
(ii)	Size of the metastatic LN (mean size in cm)	0.66	0.47	<0.001
B	Microscopic findings (extranodal extension)			
	Yes	19 (82.6)	22 (70.96)	<0.001
	No	04 (17.39)	09 (29.03)	<0.001

PTC: Papillary thyroid carcinoma, HT: Hashimoto thyroiditis, LN: Lymph node

Table 3: Comparison of tumor size (T) and lymph nodal status (N) between patients of PTC with HT (n=23) and PTC without HT (n=31)

Parameters		PTC with HT (n=23) (%)	PTC without HT (n=31) (%)	P-value
A	Tumor size			
	T_1	18 (78.26)	12 (38.7)	<0.001
	T_2	4 (17.39)	06 (19.35)	<0.001
	T_3	5 (21.7)	04 (12.9)	<0.001
	T_4	4 (17.39)	01 (3.2)	<0.001
B	N (lymph node)			
	N_0	10 (43.47)	06 (19.35)	<0.001
	N_1	13 (56.5)	25 (80.6)	<0.001
C	AJCC (8^{th} ed..ition) stage			
	I	19 (82.6)	22 (70.9)	<0.001
	II	01 (4.34)	03 (9.6)	<0.001
	III	02 (8.69)	05 (16.12)	<0.001
	IV	01 (4.34)	01 (3.2)	<0.001

PTC: Papillary thyroid carcinoma, HT: Hashimoto thyroiditis

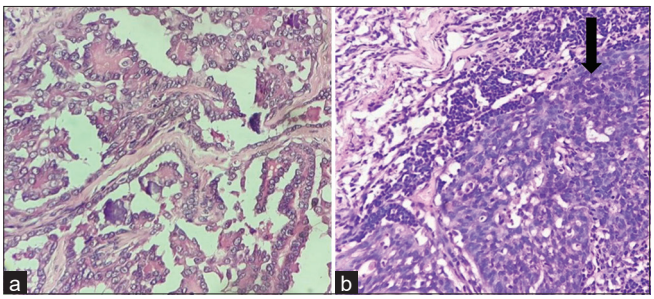

Figure 2: Features of papillary thyroid carcinoma (a) and metastatic deposit in cervical lymph node (black arrow) (b) (H&E, ×400)

and lymphatic hyperplasia lead to lymphadenopathy for which they are closely monitored. This leads to more timely detection and treatment of PTC which ultimately leads to a decrease in central lymph node metastasis. In our study, central lymph node metastasis (Figure 2b) was less (56.5%) in PTC with HT than in PTC without HT (80.6%) (Table 3) similar to the study by Ryu and Yoon.[25]

Marotta et al.,[27] observed increased remission rates and disease-free survival in HT patients.

A number of studies showed detrimental effects of HT on PTC leading to poor prognosis. Lee et al.,[28] Babli et al.,[11] found there was an increased incidence of both multifocality and extrathyroidal extension in HT patients. Zhu et al.,[29] observed that HT patients associated with PTC had increased capsular infiltration and multifocality. De Alcântara-Jones et al.,[30] showed that there was no association between HT and PTC leading to the understanding of causal relationship between HT and PTC even more contentious.

Out of the total 54 cases of PTC studied, 23 cases were associated with HT (n=23, 42.5%) and 31 cases were without HT (n=31, 57.4%) (Table 1). In our study, PTC with HT had a greater female association 21 out of 23 (91.3%) in comparison to the PTC cases without HT, 23 out of 31 cases (74.19%) (Table 1) similar to the study by Siegel et al.,[21] Most patients of PTC with HT presented mostly diffuse thyroid swelling (17 cases out of 23 cases of PTC with HT) (73%) whereas patients of PTC without HT mostly presented with nodular thyroid swelling (27 cases out of 31 cases of PT without HT) (87%). In this study, we found that PTC patients with HT had a greater tendency of multifocality (18 cases out of 23 cases) (78.26%) which was similar to the study by Lee et al.,[28] and Babli et al.[11]

In our study, the mean size of the enlarged lymph nodes was 0.66 cm in patients of PTC with HT whereas it was 0.47 cm in patients of PTC without HT. The enlarged mean size of the lymph nodes might be due to the continuous immune activation and lymphatic hyperplasia in cases of

HT patients as stated by Marotta et al.[27] Extra nodal tumor extension was seen in 82.6% cases of PTC with HT and in 70.96% cases of PTC without HT. In our study, PTC patients with HT had a smaller tumor size (n=18, 78.26%), that is, T_1 was seen in 18 cases out of 23 cases of PTC with HT and in 82.6% cases the AJCC tumor stage was Stage I. The smaller tumor size and tumor stage in patients of PTC with HT were similar to the study by Ryu and Yoon.[25]

Limitations of the study

The major limitation of the study was the small sample size. Prospective studies with larger sample size are needed for a better representation of the association of HT with PTC in endemic population.

CONCLUSION

The present study provided an analysis of the association between HT and PTC. Our findings demonstrated that PTC with concomitant HT was associated with female sex, larger metastatic lymph node, a tendency for multifocality and extranodal extension as well as smaller tumor size and low clinical stage, thus indicating a complex and controversial effect of HT on PTC.

FUTURE PERSPECTIVE

Despite the controversial causal relationship between PTC and HT, harnessing the immunological link between PTC and HT will guide future efforts in clinical research which will broader the horizons of immunotherapy in patients of PTC with coexistent HT.[31]

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REFERENCES

1. Abdullah MI, Junit SM, Ng KL, Jayapalan JJ, Karikalan B and Hashim OH. Papillary thyroid cancer: Genetic alterations and molecular biomarker investigations. Int J Med Sci. 2019;16(3):450-460.
   https://doi.org/10.7150/ijms.29935
2. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American thyroid 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):1-133.
   https://doi.org/10.1089/thy.2015.0020
3. Selek A, Cetinarslan B, Tarkun I, Canturk Z, Ustuner B and Akyay Z. Thyroid autoimmunity: Is really associated with papillary thyroid carcinoma? Eur Arch Otorhinol. 2017;274(3):1677-1681.
   https://doi.org/10.1007/s00405-016-4414-6
4. Anand A, Singh KR, Kushwaha JK, Hussain N and Sonkar AA. Papillary thyroid cancer and Hashimoto's thyroiditis: An association less understood. Indian J Surg Oncol. 2014;5(3):199-204.
   https://doi.org/10.1007/s13193-014-0325-4
5. Zhu Y, Zheng K, Zhang H, Chen L, Xue J, Ding M, et al. The clinicopathologic differences of central lymph node metastasis in predicting lateral lymph node metastasis and prognosis in papillary thyroid cancer associated with or without Hashimoto's thyroiditis. Tumour Biol. 2015;37(6):8037-8045.
   https://doi.org/10.1007/s13277-015-4706-2
6. Ma H, Yan J, Zhang C, Qin S, Qin L, Liu L, et al. Expression of papillary thyroid carcinoma-associated molecular markers and their significance in follicular epithelial dysplasia with papillary thyroid carcinoma-like nuclear alterations in Hashimoto's thyroiditis. Int J Clin Exp Pathol. 2014;7(11):7999-8007.
7. Wu K, Shi L, Wang J and Xie L. Association between papillary thyroid carcinoma and lymphocytic thyroiditis: A retrospective study. Oncol Lett. 2023;25(4):148.
   https://doi.org/10.3892/ol.2023.13734
8. Danis N, Comlekci A, Yener S, Durak M, Calan M, Solmaz D, et al. Association between hashimoto's thyroiditis and papillary thyroid cancer: A single center experience. Acta Endocrinol (Bucharest). 2022;18(1):74-78.
   https://doi.org/10.4183/aeb.2022.74
9. Osborne D, Choudhary R, Vyas A, Kampa P, Abbas LF, Chigurupati HD, et al. Hashimoto's thyroiditis effects on papillary thyroid carcinoma outcomes: A systematic review. Cureus. 2022;14(8):e28054.
   https://doi.org/10.7759/cureus.28054
10. Hussein O, Abdelwahab K, Hamdy O, Awny S, Megahed NA, Hafez MT, et al. Thyroid cancer associated with Hashimoto thyroiditis: Similarities and differences in an endemic area. J Egypt Natl Canc Inst. 2020;32(1):7.
    https://doi.org/10.1186/s43046-020-0017-9
11. Babli S, Payne Richard J, Mitmaker E and Rivera J. Effects of chronic lymphocytic thyroiditis on the clinicopathological features of papillary thyroid cancer. Eur Thyroid J. 2018;7(2):95-101.
    https://doi.org/10.1159/000486367
12. Fiore E, Rago T, Latrofa F, Provenzale MA, Piaggi P, Delitala A, et al. Hashimoto's thyroiditis is associated with papillary thyroid carcinoma: Role of TSH and of treatment with l-thyroxine. Endocr Relat Cancer. 2011;18(4):429-437.
    https://doi.org/10.1530/ERC-11-0028
13. Borowczyk M, Janicki A, Dworacki G, Szczepanek-Parulska E, Danieluk M, Barnett J, et al. Decreased staging of differentiated thyroid cancer in patients with chronic lymphocytic thyroiditis. J Endocrinol Invest. 2018;42(1):45-52.
    https://doi.org/10.1007/s40618-018-0882-4
14. Lekha BS, Chakravarthy R and Kalyan K. Clinical study of HT. IOSR J Denta Med Sci. 2017;16:20-25.
    https://doi.org/10.9790/0853-1603042025
15. Subhi O, Schulten HJ, Bagatian N, Al-Dayini R, Karim S, Bakhashab S, et al. Genetic relationship between Hashimoto`s thyroiditis and papillary thyroid carcinoma with coexisting Hashimoto`s thyroiditis. PLoS One. 2020;15(6):e0234566.
    https://doi.org/10.1371/journal.pone.0234566
16. Resende de Paiva C, Grønhøj C, Feldt-Rasmussen U and Von Buchwald C. Association between Hashimoto's thyroiditis and thyroid cancer in 64,628 patients. Front Oncol. 2017;7:53.

https://doi.org/10.3389/fonc.2017.00053

17. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, et al. The eighth edition AJCC cancer staging manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017;67(2):93-99.
https://doi.org/10.3322/caac.21388
18. Xu B. Papillary Thyroid Carcinoma Overview; 2021. Available from: https://www.pathologyoutlines.com/topic/thyroidpapillary.html [Last accessed on 2024 Jul 15].
19. Pizzato M, Li M, Vignat J, Laversanne M, Singh D, La Vecchia C, et al. The epidemiological landscape of thyroid cancer worldwide: GLOBOCAN estimates for incidence and mortality rates in 2020. Lancet Diabetes Endocrinol. 2022;10(4):264-272.
https://doi.org/10.1016/S2213-8587(22)00035-3
20. Jung CK, Bychkov A and Kakudo K. Update from the 2022 world health organization classification of thyroid tumors: A standardized diagnostic approach. Endocrinol Metab (Seoul). 2022;37(5):703-718.
https://doi.org/10.3803/EnM.2022.1553
21. Siegel RL, Miller KD and Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68(1):7-30.
https://doi.org/10.3322/caac.21442
22. Vladimir S and Norisato M. Radiation-related thyroid cancer. Endocr Rev. 2023;45(1):1-29.
https://doi.org/10.1210/endrev/bnad022
23. Dailey ME, Lindsay S and Skahen R. Relation of thyroid neoplasms to hashimoto disease of the thyroid gland. AMA Arch Surg. 1955;70(2):291.
https://doi.org/10.1001/archsurg.1955.01270080137023
24. Antonaci A, Consorti F, Mardente S and Giovannone G. Clinical and biological relationship between chronic lymphocytic thyroiditis and papillary thyroid carcinoma. Oncol Res. 2009;17(10):495-503.
https://doi.org/10.3727/096504009789735431
25. Ryu YJ and Yoon JH. Chronic lymphocytic thyroiditis protects against recurrence in patients with cN0 papillary thyroid cancer. Surg Oncol. 2020;34:67-73.
https://doi.org/10.1016/j.suronc.2020.03.008
26. 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(3):1191-1197.
https://doi.org/10.1007/s12253-019-00580-w
27. Marotta V, Sciammarella C, Chiofalo MG, Gambardella C, Bellevicine C, Grasso M, et al. Hashimoto's thyroiditis predicts outcome in intrathyroidal papillary thyroid cancer. Endocr Relat Cancer. 2017;24(9):485-493.
https://doi.org/10.1530/ERC-17-0085
28. Lee I, Kim HK, Soh EY and Lee J. The association between chronic lymphocytic thyroiditis and the progress of papillary thyroid cancer. World J Surg. 2020;44(5):1506-1513.
https://doi.org/10.1007/s00268-019-05337-9
29. Zhu F, Shen YB, Li FQ, Fang Y, Hu L and Wu YJ. The effects of hashimoto thyroiditis on lymph node metastases in unifocal and multifocal papillary thyroid carcinoma. Medicine (Baltimore). 2016;95(6):e2674-e2674.
https://doi.org/10.1097/MD.0000000000002674
30. De Alcântara-Jones DM, De Alcântara-Nunes TF, Rocha BO, De Oliveira RD, Santana AC, De Alcântara FT, et al. Is there any association between Hashimoto's thyroiditis and thyroid cancer? A retrospective data analysis. Radiol Bras. 2015;48(3):148-153.
https://doi.org/10.1590/0100-3984.2014.0072
31. Pan J, Ye F, Yu C, Zhu Q, Li J, Zhang Y, et al. Papillary thyroid carcinoma landscape and its immunological link with hashimoto thyroiditis at single-cell resolution. Front Cell Dev Biol. 2021;9:758339.
https://doi.org/10.3389/fcell.2021.758339

Authors' Contribution:
RP- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, manuscript preparation; **CG-** Concept, design, manuscript preparation, editing, and manuscript revision; **MS-** Design of study, statistical analysis and interpretation- final editing of manuscript, editing and submission of article; **SM-** Data analysis, manuscript preparation, statistical analysis; **UM-** Preparation of final draft, editing and corresponding author.

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