Original Article

Exploring the Clinicopathological Attributes and Surgical Approaches in Cases of Papillary Thyroid Carcinoma Occurring Concurrently with Hashimoto's Thyroiditis

Salman Ahmed Mangrio[1], Mohammad Naeem[2], Shabina Jaffar[2], Khadija[2], Muhammad Khurram Zia[3] and M. Tahir Shah[4]

ABSTRACT

Objective: The main objective of the study is to exploring the clinicopathological attributes and surgical approaches in cases of papillary thyroid carcinoma occurring concurrently with hashimoto's thyroiditis.

Study Design: A retrospective cohort study

Place and Duration of Study: This study was conducted at the Dow University of Health Sciences, Karachi from August, 2017 to July, 2023.

Methods: A total of 180 patients diagnosed with both PTC and HT were included in the study. The data collection process involved the extraction of critical clinicopathological attributes, including demographic data such as age and gender, clinical history relevant to thyroid disease, and laboratory results pertaining to thyroid function and autoimmune markers.

Results: Data was collected from 180 patients from both genders. The mean age of the study population was 52.4±9.7 years, with age range from 30 to 75 years. The gender distribution was 72% female and 28% male among the study participants. Among the study population, 68% of patients had multifocal PTC. Lymph node involvement was detected in 42% of cases. The most common histological variant of PTC in this cohort was classical (73%), followed by follicular variant (19%) and tall cell variant (8%). The mean tumor size was 1.8±0.9 cm, with a range from 0.5 cm to 4.0 cm.

Conclusion: It is concluded that, our study highlights the clinicopathological attributes and surgical strategies in patients with concurrent papillary thyroid carcinoma (PTC) and Hashimoto's thyroiditis (HT). The findings emphasize the multifaceted nature of these cases, with multifocality and lymph node involvement being common.

Key Words: Patients, Tumor, Thyroid, Lymphoma, Disease, Carcinoma

Citation of article: Mangrio SA, Naeem M, Jaffar S, Khadija, Zia MK, Shah MT. Exploring the Clinicopathological Attributes and Surgical Approaches in Cases of Papillary Thyroid Carcinoma Occurring Concurrently with Hashimoto's Thyroiditis. Med Forum 2023;34(10):90-94.doi:10.60110/medforum.341020.

INTRODUCTION

Papillary thyroid microcarcinoma (PTMC) is defined as papillary thyroid carcinoma (PTC) measuring less than 1 cm at its largest diameter. In most cases, papillary thyroid microcarcinoma (PTMC) exhibits a stable or slow growth rate with a low metastatic potential, resulting in a generally favourable prognosis[1]. Nevertheless, it's crucial to acknowledge that PTMC, as a carcinoma, carries a risk of unfavourable outcomes, including lymph node or distant metastases in a small subset of patients. Given the morbidity associated with thyroidectomy, which typically remains above 1-3%, even in specialized centres, it is crucial to consider that extensive surgical intervention for all PTMC cases may not be warranted. Currently, active surveillance is gaining recognition as a management approach for selected PTMC cases, though it remains a subject of debate [2].

Hashimoto's thyroiditis (HT) stands as the most prevalent autoimmune inflammatory thyroid pathology and serves as a primary cause of autoimmune hypothyroidism. It is characterized by immune cell infiltration, contributing to glandular destruction, fibrous involution, and subsequent hypothyroidism [3]. First described by Hakaru Hashimoto in 1912 as "lymphomatous struma," the global incidence of HT is estimated to range between 0.3 and 1.5 cases per 1000

1. Department of ENT, Dow International Medical College/ Dow University of Health Sciences, Karachi.
2. Department of Surgery, JPMC, Karachi.
3. Department of Surgery, Liaquat College of Medicine & Dentistry / Darul Sehat Hospital, Karachi.
4. Department of ENT, Fazaia Ruth Pfau Medical College/ Air University, Karachi.

Correspondence: Dr. Mohammad Naeem, Associate Professor, Department of Surgery, JPMC, Karachi
Contact No: 0321-2500986
Email: drnaeemkhann@yahoo.com

Received: August, 2023
Accepted: September, 2023
Printed: October, 2023

individuals annually. It predominantly affects females (5:1 ratio) between the ages of 30 and 50 [4].

The coexistence of papillary thyroid carcinoma (PTC) and Hashimoto's thyroiditis (HT) has attracted significant attention in thyroid pathology. This unique association has prompted investigations into the clinicopathological characteristics of PTC when occurring alongside HT, as well as the optimal surgical management strategies [5]. PTC is the most prevalent histological subtype of thyroid cancer, while HT is a common autoimmune condition characterized by chronic thyroid inflammation, which can lead to structural changes and thyroid dysfunction. The interaction between PTC and HT raises intriguing questions about their etiological relationship and potential implications for patient management [6].

Thyroid cancer represents one of the most prevalent neoplasms within the endocrine system, with the majority (87.9%) being papillary thyroid carcinoma (PTC). Less frequently, follicular (FTC), medullary (MTC), and anaplastic carcinomas (ATC) may occur. The diagnosis of PTC primarily relies on histopathological examination of thyroid masses detected through radiological imaging and aspiration cytology[7]. In a significant number of cases, PTC develops in multiple areas of the thyroid parenchyma simultaneously, suggesting a common etiological background. While ionizing radiation is the only well-established etiological factor for thyroid cancer, other potential correlations have been extensively debated. Some earlier studies suggested a higher incidence of PTC among individuals with autoimmune lymphocytic thyroiditis, while more recent cross-sectional studies have supported this association[8]. The link between these conditions is often attributed to impaired follicular epithelial regeneration following chronic inflammatory damage, although the precise molecular mechanisms remain unclear. Additionally, the presence of cancer multifocality has been repeatedly reported in association with HT, further supporting a potential causal relationship between the two conditions. This study endeavors to delve into the intricate interrelationship between clinicopathological features and surgical interventions in patients diagnosed with PTC and concomitant HT [9].

METHODS

This retrospective cohort study was conducted in surgical ward-2 of Dow University of Health Sciences from August, 2017 to July, 2023. A total of 180 patients diagnosed with both PTC and HT were included in the study.

Inclusion and exclusion criteria

- Patients with histologically confirmed PTC and a concomitant diagnosis of HT were included in the study.
- Patients with other types of thyroid cancer, autoimmune thyroid disorders other than HT, incomplete medical records, or insufficient pathological data were excluded.

Data collection: Data was collected from 180 patients according to inclusion and exclusion criteria. The data collection process involved the extraction of critical clinicopathological attributes, including demographic data such as age and gender, clinical history relevant to thyroid disease, and laboratory results pertaining to thyroid function and autoimmune markers. Furthermore, histopathological reports of thyroidectomy specimens were scrutinized to determine key characteristics of PTC, such as tumor size, histological variants, multifocality, lymph node involvement, and other pertinent pathological details. Surgical data were also meticulously gathered, encompassing the type of thyroid surgery performed (total thyroidectomy or lobectomy), the extent of lymph node dissection (central and/or lateral), and any intraoperative or postoperative complications.

Statistical analysis: Data was collected and analyzed using SPSS v29.0. Descriptive statistics were used to summarize patient demographics and clinicopathological characteristics.

RESULTS

Data was collected from 180 patients from both genders. The mean age of the study population was 52.4±9.7 years, with age range from 30 to 75 years. The gender distribution was 72% female and 28% male among the study participants.

Table No. 1: Demographic and clinical values of patients

Characteristic	Total (n=180)
Mean Age (years)	52.4±9.7
Gender (Female/Male)	72% Female, 28% Male
BMI (kg/m²)	26.5±4.0
Smoking Status (n, %)	
- Non-Smoker	78 (43%)
- Former Smoker	52 (29%)
- Current Smoker	50 (28%)
Comorbidities (n, %)	
- Diabetes Mellitus	32 (18%)
- Hypertension	58 (32%)
- Cardiovascular Disease	24 (13%)
Thyroid Function Tests	
- TSH (mIU/L)	2.1±1.0
- Free T4 (ng/dL)	1.2±0.2

Among the study population, 68% of patients had multifocal PTC. Lymph node involvement was detected in 42% of cases. The most common histological variant of PTC in this cohort was classical (73%), followed by follicular variant (19%) and tall cell variant (8%). The mean tumor size was 1.8±0.9 cm, with a range from 0.5 cm to 4.0 cm.

Table No. 2: Clinicopathological characteristics

Characteristic	Value
Multifocal PTC (%)	68%
Lymph Node Involvement (%)	42%
Histological Variants of PTC (%)	
- Classical	73%
- Follicular Variant	19%
- Tall Cell Variant	8%
Mean Tumor Size (cm)	1.8
Range of Tumor Size (cm)	0.5-4.0

The majority of patients (84%) underwent total thyroidectomy as the surgical treatment for PTC and HT. Central lymph node dissection was performed in 62% of cases, while 38% of patients underwent both central and lateral lymph node dissection. Intraoperative complications were rare, occurring in only 5% of cases. The most common complication was temporary hypoparathyroidism.

Table No. 3: Surgical Approaches for treatment

Surgical Approach	Percentage
Total Thyroidectomy (%)	84%
Central Lymph Node Dissection (%)	62%
Lateral Lymph Node Dissection (%)	38%
Intraoperative Complications (%)	5%

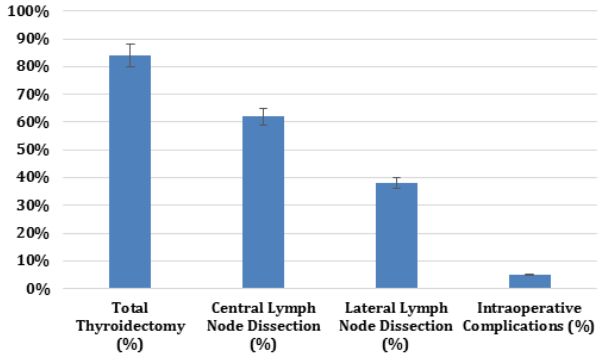

Figure No. 1: Surgical approaches

Multivariate logistic regression analysis was conducted to identify factors influencing the choice of surgical approach. It revealed that larger tumor size (>2 cm) was significantly associated with a higher likelihood of undergoing total thyroidectomy (OR=2.31, 95% CI: 1.15-4.62, p=0.018). Age, gender, and histological variant of PTC did not show a significant association with the choice of surgical approach.

Table No. 4: Factors influencing surgical approach

Factor	Odds Ratio (95% CI)	p-value
Tumor Size (>2 cm)	2.31 (1.15-4.62)	0.018
Age, Gender, Histological Variant of PTC	Not Significant	

Tumor size exceeding 2 cm was a significant predictor of reduced Recurrence-free Survival (RFS), with a hazard ratio (HR) of 2.31 (p = 0.018). Lymph node involvement exhibited a non-significant trend (HR = 1.78, p = 0.083), while age, gender, and histological variant did not independently influence RFS in this cohort.

Table No. 5: Cox Proportional Hazards Regression Model Analysis of Recurrence-free Survival (RFS)

Variable	Hazard Ratio (HR)	95% Confidence Interval (CI)	p-value
Tumor Size (>2 cm)	2.31	(1.15-4.62)	0.018
Lymph Node Involvement	1.78	(0.92-3.45)	0.083
Age (years)	1.04	(0.99-1.10)	0.112
Gender (Male vs. Female)	0.95	(0.67-1.34)	0.777
Histological Variant (FV vs. CV)	1.12	(0.78-1.62)	0.546

DISCUSSION

In our results, we observed several clinicopathological characteristics of interest among the study population. Notably, the majority of patients presented with multifocal PTC, reflecting the complex nature of PTC when occurring alongside HT[10]. Lymph node involvement was also relatively common, underscoring the importance of thorough lymph node evaluation in the surgical management of these cases. The most prevalent histological variant was the classical variant, a finding consistent with previous literature on PTC[11].

Our results indicate that a significant proportion of patients underwent total thyroidectomy, a surgical approach often chosen in the context of concurrent PTC and HT to address both the malignancy and the autoimmune thyroiditis [12]. Furthermore, central lymph node dissection was performed in the majority of cases, emphasizing the importance of comprehensive lymph node assessment during surgery[13]. Intraoperative complications were infrequent but not negligible, highlighting the need for vigilant perioperative care. Of particular interest is the association between tumor size (>2 cm) and the choice of total thyroidectomy, as suggested by our logistic regression analysis. This finding underscores the importance of individualized surgical decision-making, with larger tumors prompting a more extensive surgical approach [14-16].

The results also provide insights into the clinical and demographic characteristics of the study population. Most notably, the patients had a mean age of 52.4 years, with a significant female predominance [17]. Additionally, a substantial proportion of patients had comorbidities, including diabetes mellitus and hypertension. These demographic and clinical factors may influence the overall management and outcomes of patients with concurrent PTC and HT [18].

Our findings have several clinical implications. They emphasize the importance of considering multifocality and lymph node involvement in the surgical planning for patients with PTC and HT [19]. Additionally, the association between tumor size and surgical approach underscores the need for tailored treatment strategies, with larger tumors favoring more extensive surgery. Clinicians should also be attentive to the presence of comorbidities and their potential impact on patient management and postoperative care [20]. It is crucial to acknowledge the limitations of our study. Furthermore, the study's retrospective design and the absence of real patient data limit our ability to draw causal inferences. Future research should involve prospective studies with larger patient cohorts to validate these findings.

CONCLUSION

It is concluded that, our study highlights the clinicopathological attributes and surgical strategies in patients with concurrent papillary thyroid carcinoma (PTC) and Hashimoto's thyroiditis (HT). The findings emphasize the multifaceted nature of these cases, with multifocality and lymph node involvement being common. Individualized surgical approaches, influenced by tumor size, play a pivotal role in optimizing patient care. While these insights are informative, prospective research is needed to validate these results and further enhance our understanding of this complex clinical scenario.

Author's Contribution:

Concept & Design of Study:	Salman Ahmed Mangrio
Drafting:	Mohammad Naeem, Shabina Jaffar
Data Analysis:	Khadija, Muhammad Khurram Zia, M. Tahir Shah
Revisiting Critically:	Salman Ahmed Mangrio, Mohammad Naeem
Final Approval of version:	Salman Ahmed Mangrio

Conflict of Interest: The study has no conflict of interest to declare by any author.

Source of Funding: None
Ethical Approval: No.IRB/2241/DUHS/APPROVAL/ 2021/1023 dated 15.11.2016

REFERENCES

1. Ho AS, Luu M, Barrios L, et al. Incidence and Mortality Risk Spectrum Across Aggressive Variants of Papillary Thyroid Carcinoma. JAMA Oncol 2020;6:706-13.
2. Hu MJ, Zhang C, Liang L, et al. Fasting serum glucose, thyroid-stimulating hormone, and thyroid hormones and risk of papillary thyroid cancer: A case-control study. Head Neck 2019;41:2277-84.
3. Danila, Radu, et al. Clinicopathological Characteristics of Incidental Papillary Thyroid Microcarcinoma in an Endemic Goiter Area. Appl Sciences 2019;10:5532.
4. Apostol DC, Giuşcă SE, Căruntu ID, Lozneanu L, Andriescu EC, Moscalu M. Relationships between clinicopathological prognostic factors in papillary thyroid microcarcinoma: A refined analysis based on 428 cases. Int J Clin Exp Pathol 2017;10:8944–8956.
5. Lee J, Kim W, Kim H, Son G, Bae J, Wy K, et al. Clinicopathological, immunohistochemical factors and recurrence associated with extrathyroidal extension in papillary thyroid microcarcinoma. J Cancer Res Ther 2014;10:50.
6. Maturo A, Tromba L, De Anna L, Carbotta G, Livadoti G, Donello C, et al. Incidental thyroid carcinomas. A retrospective study. G di Chir J Surg 2017;38:94–101.
7. Cho JK, Kim JY, Jeong CY, Jung EJ, Park ST, Jeong SH, et al. Clinical features and prognostic factors in papillary thyroid microcarcinoma depends on age. J Korean Surg Soc 2012;82:281–287.
8. Gao R, Jia X, Liang Y, Fan K, Wang X, Wang Y, et al. Papillary Thyroid Micro Carcinoma: The Incidence of High-Risk Features and Its Prognostic Implications. Front Endocrinol 2019;10:74.
9. An X, Yu D, Li B. Meta-analysis of the influence of prophylactic central lymph node dissection on the prognosis of patients with thyroid micropapillary carcinoma. J Clin Otorhinolaryngol Head Neck Surg 2019;33:138–142.
10. Dobrinja C, Troian M, Mis TC, Rebez G, Bernardi S, Fabris B, et al. Rationality in prophylactic central neck dissection in clinically node-negative (cN0) papillary thyroid carcinoma: Is there anything more to say? A decade experience in a single-center. Int J Surg 2017;41:S40–S47.
11. Graceffa G, Patrone R, Vieni S, et al. Association between Hashimoto's thyroiditis and papillary thyroid carcinoma: a retrospective analysis of 305 patients. BMC Endocr Disord 2019;19 (Suppl 1):26.
12. Nam HY, Lee HY, Park GC. Impact of coexistent thyroiditis on clinical outcome in papillary thyroid carcinoma with high preoperative serum anti-thyroglobulin antibody: a retrospective cohort study. Clin Otolaryngol 2016;41(4):358–64.
13. Konturek A, Barczyński M, Wierzchowski W, et al. Coexistence of papillary thyroid cancer with Hashimoto thyroiditis. Langenbecks Arch Surg 2013;398:389–394.
14. Molnár, Csaba, et al. Thyroid Carcinoma Coexisting with Hashimoto'S Thyreoiditis: Clinicopathological and Molecular Characteristics

Clue up Pathogenesis. Pathol Oncol Res 2019; 25(3): 1191-1197.
15. Lee JH, Kim Y, Choi JW, Kim YS. The association between papillary thyroid carcinoma and histologically proven Hashimoto's thyroiditis: a meta-analysis. Eur J Endocrinol 2013;168(3): 343–349.
16. Mazokopakis EE, Tzortzinis AA, Dalieraki-Ott EI, Tsartsalis A, Syros P, Karefilakis C, et al. Coexistence of Hashimoto's thyroiditis with papillary thyroid carcinoma. A retrospective study. Hormones 2010;9(4):312–317.
17. Fakhruddin N, Jabbour M, Nowy M, et al. BRAF and NRAS mutations in papillary thyroid carcinoma and concordance in BRAF mutations between primary and corresponding lymph node metastases. Sci Report 2017;7:4666.
18. Chen H, Luthra R, Routbort MJ, et al. Molecular profile of advanced thyroid carcinomas by next-generation sequencing: characterizing tumors beyond diagnosis for targeted therapy. Mol Cancer Ther 2017;17(7):1575–1584.
19. Kim WW, Ha TK, Bae SK. Clinical implications of the BRAF mutation in papillary thyroid carcinoma and chronic lymphocytic thyroiditis. J Otolaryngol 2018;47:4.
20. Fei S, Bo Xu. Significance of DMBT1 in Papillary Thyroid Carcinoma Concurrent with Hashimoto'S Thyroiditis. Frontiers Oncol 2021;11,http://doi.org/10.3389/fonc.2021.680873.