

View on various clinical determinants of thyroid neoplasms based on their histopathological patterns

By Asaad Albayati

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Abstract

Background: Most thyroid cancers are differentiated, either follicular or papillary, and they respond effectively to radioactive iodine therapy.

Aim of study: To investigate about the histopathological types of thyroid cancer and their relationship to certain demographic and clinical characteristics.

Methods: A retrospective observational study with analytic component conducted during a period of six months from (May to November 2023). It included 120 patients collected from oncology department records and diagnosed with thyroid cancer. The following information were collected (Age, gender, occupation, smoking status, family history of thyroid malignancy, tumor stage according to the 7th edition of the American Joint Committee on Cancer Staging, thyroid status, presentation, ultrasound details, and histopathological report).

Results: In this study, 68.3% were presented as goiter; Lymphadenopathy was noticed in 18.3%; and the most prevalent histologic type was papillary. 80.6% of papillary type were staged T1 (80.6%) compared to 23.5% of follicular type. In papillary type, 38.9% had tumor size $< 1 \text{ cm}^3$ while 76.5% of follicular type had size $> 2 \text{ cm}^3$. Lymphadenopathy was seen in 47.1% of follicular type compared to 11.1% in papillary type. Regarding presentation, goiter was found in 72.2% of papillary type compared to 17.6% in follicular type and these differences were statistically significant.

Conclusion: Thyroid cancer is more common in younger age groups and in females. The papillary form accounts for the majority of patients, indicating that a tiny percentage of the afflicted population has an iodine deficiency. The degree of lymph node metastasis may be predicted by histopathological features.

Keywords: Thyroid, carcinoma, papillary, histopathological, follicular.

INTRODUCTION

The most prevalent type of endocrine and head-and-neck cancer is thyroid cancer, which makes up 0.5% of malignant cancers in men and 1.5% in women. Its incidence is steadily rising, making up around 1% of all malignancies ⁽¹⁾. Papillary (75–85%), follicular (10–20%), medullary (5%), and anaplastic (less than 5%) tumors are all classified as thyroid cancer ⁽²⁾. Most thyroid cancers are differentiated, either follicular or papillary, and they respond effectively to radioactive iodine therapy. These malignancies are also highly curable ⁽³⁾. Over the past few decades, the prevalence of malignant tumors has been steadily rising on a global scale ⁽⁴⁾. This increased prevalence is most likely the result of a mix of factors such as increased radiation exposure in the population, environmental risk factors, changes in lifestyle, and an apparent rise brought on by the frequent use of sensitive diagnostic methods ^(5, 6). This slow-growing tumors nevertheless has a low death rate despite its rising occurrence. Overall, patients with papillary type tumors have a 93% 10-year survival rate, while patients with follicular type tumors have an 85% survival rate ⁽⁷⁾. The genetic foundation of the majority of thyroid malignancies has been linked to mutations and translocations in the genes encoding the mitogen-activated protein kinase cellular signaling pathway ⁽⁸⁾. The other major risk factors are female sex, a family history of thyroid cancer, and thyroid radiation exposure in childhood ⁽⁹⁾. These tumors typically manifest as a single embodied thyroid knob that is degenerating or exerting pressure on the surrounding parenchyma; yet, they can also form in a thyroid organ that has already experienced other diseases. Most often, the patient or doctor finds the thyroid carcinoma by accident—either as a lump in the neck or perhaps as a coincidental finding during a neck ultrasound. It could manifest as a painful, slowly growing mass that is accompanied by hoarseness, dysphagia, or dysphonia, or it could cause breathing difficulties ⁽¹⁰⁾. Surgery is the major treatment for thyroid malignancies, and radioactive iodine therapy is the main adjuvant therapy. Many developing nations lack access to radioactive iodine and surgical facilities ^(11, 12). Therefore, planning and resource utilization in these resource-constrained countries may be aided by an understanding of thyroid cancer trends. The aim of this study is to investigate about the histopathological types of thyroid cancer and their relationship to certain demographic and clinical characteristics.

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PATIENTS AND METHODS

Study design, setting, and time: This was a retrospective observational study with analytic component conducted at Al-Yarmouk Teaching Hospital and private hospital during a period of six months from (May to November 2023).

Study Population and sample size: The study included 120 patients collected from oncology department records and diagnosed with thyroid cancer. Diagnosis of thyroid cancer was confirmed histopathological examination. The hospital's archive was searched for the patient files who admitted from 2017 to 2022, and pertinent data was gathered by completing the structured data sheet.

Data collection: The following information were collected (Age, gender, occupation, smoking status, family history of thyroid malignancy, tumor stage according to the 7th edition of the American Joint Committee on Cancer Staging⁽¹³⁾, thyroid status, presentation, ultrasound details, and histopathological report). Patients who had incomplete records (i.e., patients without cytology or biopsy result) and patients who had secondary thyroid cancer were excluded from this study.

The main histologic types of thyroid carcinoma include the following:

1. Differentiated (including papillary, follicular, hurthle).
2. Medullary.
3. Anaplastic (aggressive undifferentiated tumor).
4. Borderline thyroid tumor

Statistical analysis: The data analyzed using Statistical Package for Social Sciences (SPSS) version 26. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Analysis of Variance (ANOVA) (two tailed) test was used to compare the continuous variables accordingly. Chi square test was used to assess the association between histologic types and certain information, while fisher exact test was used instead when the expected frequency was less than 5. A level of P – value less than 0.05 was considered significant.

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RESULTS

In this study, age was ranging from 26 to 74 years with a mean of 44.51 ± 8.2 years; 51.7% of them were aged < 40 years; 67.5% were females; 45% were housewives; 45% were current smokers; and 14.2% had positive family history of thyroid malignancy. (Table 1).

Table 1: Distribution of study samples by socio-demographic characteristics

Socio-demographic variable	No. (n= 120)	Percentage (%)
Age (Year)		
< 40	62	51.7
40 – 59	41	34.2
≥ 60	17	14.1
Gender		
Male	39	32.5
Female	81	67.5
Occupation		
Employed	31	25.8
Housewife	54	45.0
Retired	12	10.0
Private work	23	19.2
Smoking status		
Current smoker	54	45.0
Nonsmoker	66	55.0
Family history of thyroid cancer		
Positive	17	14.2
Negative	103	85.8

As shown in table (2), most of the patients were in euthyroid status (86.7%); 66% of cases were in stage T1; tumor size was < 1 cm³ in 37.5%; 68.3% were presented as goiter; Lymphadenopathy was noticed in 18.3%; and the most prevalent histologic type was papillary (60%).

3**Table 2: Distribution of study samples by clinico-pathological characteristics**

Clinico-pathological variable	No. (n= 120)	Percentage (%)
Thyroid status		
Euthyroid	104	86.7
Hypothyroidism	7	5.8
Hyperthyroidism	9	7.5
Tumor stage n= 97		
T1	64	66.0
T2	18	18.6
T3	9	9.3
T4	6	6.2
Tumor size (cm³)		
< 1	45	37.5
1 – 2	42	35.0
> 2	33	27.5

Presentation		
Goiter	82	68.3
Nodule	38	31.7
Lymphadenopathy		
Yes	22	18.3
No	98	81.7
Histopathology		
Papillary Carcinoma	72	60.0
Follicular Carcinoma	17	14.2
Borderline thyroid tumor	23	19.2
Medullary Carcinoma	8	6.6

No statistical significant associations ($P \geq 0.05$) between histological type of thyroid CA and all demographic characteristics (Table 3).

Table 3: Association between histological type of thyroid CA and demographic characteristics

Variable	Histological type of thyroid CA				Total (%) n= 120	P- Value
	Papillary (%) n= 72	Follicular (%) n= 17	Borderline (%) n= 23	Medullary (%) n= 8		
Gender						
Male	22 (30.6)	6 (35.3)	9 (39.1)	2 (25.0)	39 (32.5)	0.837
Female	50 (69.4)	11 (64.7)	14 (60.9)	6 (75.0)	81 (67.5)	
Occupation						
Employed	20 (27.8)	3 (17.6)	6 (26.1)	2 (25.0)	31 (25.8)	0.596
Housewife	34 (47.2)	8 (47.1)	8 (34.8)	4 (50.0)	54 (45.0)	
Retired	8 (11.1)	0 (0)	3 (13.0)	1 (12.5)	12 (10.0)	
Private work	10 (13.9)	6 (35.3)	6 (26.1)	1 (12.5)	23 (19.2)	
Smoking status						
Current smoker	31 (43.1)	8 (47.1)	12 (52.2)	3 (37.5)	54 (45.0)	0.849
Nonsmoker	41 (56.9)	9 (52.9)	11 (47.8)	5 (62.5)	66 (55.0)	
Family history of thyroid cancer						
Positive	7 (9.7)	3 (17.6)	5 (21.7)	2 (25.0)	17 (14.2)	0.362
Negative	65 (90.3)	14 (82.4)	18 (78.3)	6 (75.0)	103 (85.8)	
Mean \pm SD						
P - Value						
Age (Year)	43.3 \pm 10.6	45.7 \pm 13.1	42.5 \pm 12.1	47.2 \pm 4.3		0.775

We noticed that 80.6% of papillary type were staged T1 (80.6%) compared to 23.5% of follicular type. In papillary type, 38.9% had tumor size < 1 cm³ while 76.5% of follicular type had size > 2 cm³. Lymphadenopathy was seen in 47.1% of follicular type compared to 11.1% in papillary type. Regarding presentation, goiter was found in 72.2% of papillary type compared to 17.6% in follicular type and these differences were statistically significant (P < 0.05) (Table 4).

Table 4: Association between histological type of thyroid CA and clinic-pathological characteristics

Variable	Histological type of thyroid CA				Total (%) n= 120	P - Value
	Papillary (%) n= 72	Follicular (%) n= 17	Borderlin e (%) n= 23	Medullary (%) n= 8		
Tumor stage n= 97						
T1	58 (80.6)	4 (23.5)	-	2 (25.0)	64 (66.0)	0.001
T2	9 (12.5)	6 (35.3)	-	3 (37.5)	18 (18.6)	
T3	4 (5.6)	3 (17.6)	-	2 (25.0)	9 (9.3)	
T4	1 (1.3)	4 (23.5)	-	1 (12.5)	6 (6.2)	
Tumor size (cm³)						
< 1	28 (38.9)	0 (0)	13 (56.5)	4 (50.0)	45 (37.5)	0.001
1 – 2	25 (34.7)	4 (23.5)	9 (39.1)	4 (50.0)	42 (35.0)	
> 2	19 (26.4)	13 (76.5)	1 (4.3)	0 (0)	33 (27.5)	
Presentation						
Goiter	52 (72.2)	3 (17.6)	19 (82.6)	8 (100.0)	82 (68.3)	0.001
Nodule	20 (29.8)	14 (82.4)	4 (17.4)	0 (0)	38 (31.7)	
Lymphadenopathy						
Yes	8 (11.1)	8 (47.1)	2 (8.7)	4 (50.0)	22 (18.3)	0.001
No	64 (88.9)	9 (52.9)	21 (91.3)	4 (50.0)	98 (81.7)	

DISCUSSION

Thyroid gland disorders represent a significant public health problem, and the prevalence and presence of these disorders within a community are influenced by a number of variables.

In this study, mean age was 44.51 years with more than half of patients aged < 40 years. Similar finding was seen in studies conducted by Shah AA et al in 2018 (mean 39 years)⁽¹⁴⁾, and Al-Wageeh S et al in

2020 (mean 40 years) ⁽¹⁵⁾. This could be because of the likelihood that Iraqis have been exposed to radiation, a significant risk factor, as a result of the country's three decades of repeated wars. This suggests that more researches are necessary to determine the cause of thyroid cancer in younger age group.

Regarding gender, about two thirds of study patients were females. This result agreed with most of studies as those conducted by Tewodros Wubshet MD et al in 2022 ⁽¹⁶⁾, Barasa M et al in 2019 ⁽¹⁷⁾, Ukekwe FI et al in 2017 ⁽¹⁸⁾, and Wali ON et al in 2022 ⁽¹⁹⁾. This result might be explained by either that although the exact association between sex hormones and thyroid is still unknown, it is believed that sex hormones are to blame for the comparatively greater prevalence of thyroid cancer in females, especially during their reproductive years or other possible explanation is that compared to men, women may experience clinical investigation for thyroid disorders more frequently ⁽²⁰⁾.

In the current study, the most common histopathological type of thyroid cancer was papillary (60%) followed by follicular (14.2%). This result is similar to a study conducted by Tewodros Wubshet MD et al in 2022 which shows 77.6% of cases to be papillary thyroid carcinomas ⁽¹⁶⁾. Variable proportions of similar papillary thyroid carcinoma predominances have been found in other literatures ^(14, 15, 17, 19, 21). Other studies show different results with predominance of follicular type as those conducted in Sudan 2023 ⁽³⁾ and Ethiopia 2020 ⁽²²⁾. According to reports, papillary carcinoma accounts for 85–90% of all occurrences of TC worldwide. It is followed in frequency by follicular carcinoma ⁽²³⁾. Follicular type has historically been linked to iodine deficiency ⁽²⁴⁾. So, residence in an endemic goiter region is associated with increased risk of follicular carcinoma ⁽³⁾. The therapeutic approach is determined by the disease classification, which is an important consideration. Sixty-six percent of our patient group were diagnosed in stage I and this is consistent with the results of Tabiti H et al study in 2024 ⁽²⁵⁾ and Zhu J et al study in 2022 ⁽²⁶⁾.

In our study 80.6% of papillary type cases staged I compared to 23.5% of follicular type cases and this in accordance with study conducted by Nixon IJ et al in 2012 ⁽²⁷⁾ which reflects a fact that papillary thyroid cancer patients have a better prognosis than follicular cancer patients. In conclusion, thyroid cancer is more common in younger age groups and in females. The papillary form accounts for the majority of patients, indicating that a tiny percentage of the afflicted population has an iodine deficiency. The degree of lymph node metastasis may be predicted by histopathological features. It is essential to have an early detection strategy and adequate recommendations for thyroid nodules that are adapted to available resources in order to prevent patients from seeking treatment at advanced stages. There are

several restrictions on this study. First, these factors could not be taken into consideration due to the lack of comprehensive information on recurrence and problems associated to surgery. Second, the patients' vascular invasion and other histological features were not evaluated or taken into account. Third, our results were not comprehensive due to the absence of information on the histological subtypes of follicular or papillary thyroid cancer. The lack of information on the site of metastases (lung, bone, etc.) and the timing of distant metastases (synchronous, metachronous) constituted a fourth significant constraint.

References

1. Salari N, Kazeminia M, Mohammadi M. The Prevalence of Thyroid Cancer in Iran: a Systematic Review and Meta-analysis. *Indian journal of surgical oncology*. 2022;13(1):225-34.
2. Du L, Zhao Z, Zheng R, Li H, Zhang S, Li R, et al. Epidemiology of Thyroid Cancer: Incidence and Mortality in China, 2015. *Frontiers in oncology*. 2020;10:1702.
3. Elhassan MMA, Gismalla MDA, Mohamed SAH, Faggad A. Clinicopathological profile and management of thyroid carcinoma: a Sub-Saharan country experience. *Thyroid Research*. 2023;16(1):35.
4. 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.
5. Albi E, Cataldi S, Lazzarini A, Codini M, Beccari T, Ambesi-Impiombato FS, et al. Radiation and thyroid cancer. *International journal of molecular sciences*. 2017;18(5):911.
6. Huo S, Liu Y, Sun A, Zhang B. Environmental and social determinants of thyroid cancer: A spatial analysis based on the Geographical Detector. *Frontiers in Endocrinology*. 2022;13:1052606.
7. Jasim MS, Hussein IH, Alidrisi HA, Mansour AA. Risk Stratification of Differentiated Thyroid Cancer: A Single-Center Study in Basrah. *Cureus*. 2023;15(10):e47990.
8. Singh A, Ham J, Po JW, Niles N, Roberts T, Lee CS. The Genomic Landscape of Thyroid Cancer Tumorigenesis and Implications for Immunotherapy. *Cells*. 2021;10(5):1082.
9. Kalarani IB, Sivamani G, Veerabathiran R. Identification of crucial genes involved in thyroid cancer development. *Journal of the Egyptian National Cancer Institute*. 2023;35(1):15.
10. Mileva M, Stoilovska B, Jovanovska A, Ugrinska A, Petrushevska G, Kostadinova-Kunovska S, et al. Thyroid cancer detection rate and associated risk factors in patients with thyroid nodules classified as Bethesda category III. *Radiology and oncology*. 2018;52(4):370.
11. Fualal J, Ehrenkranz J. Access, availability, and infrastructure deficiency: the current management of thyroid disease in the developing world. *Reviews in Endocrine and Metabolic Disorders*. 2016;17:583-9.
12. Jayarajah U, Fernando A, Prabashani S, Fernando EA, Seneviratne SA. Incidence and histological patterns of thyroid cancer in Sri Lanka 2001-2010: an analysis of national cancer registry data. *BMC Cancer*. 2018;18(1):163.

13. Young JS, Takabe K, Asaoka M, Edge SB. Comparing the American Joint Committee on Cancer (AJCC) breast cancer staging eighth versus seventh edition and breast cancer biology in large databases. *American Society of Clinical Oncology*; 2019.
14. Shah AA, Jain PP, Dubey AS, Panjwani GN, Shah HA. A study of clinicopathological characteristics of thyroid carcinoma at a Tertiary Care Center. *Journal of Cancer Research and Therapeutics*. 2018;14(2):357-60.
15. Al-wageeh S, Ahmed F, Nikbakht H-A, Al-shami E, Askarpour MR, Chowdhury U. An investigation of the histopathological pattern of thyroid in patients undergoing thyroid operations: a cross-sectional study. *Open Access Surgery*. 2020;47-52.
16. Tewodros Wubshet M, Tewodros Deneke M, Eshetu Alemayehu M, Wubshet T. Histopathologic Patterns and Cytohistologic Correlation of Thyroid Lesions among Patients with Thyroid Biopsies in Jimma Medical Centre, South West Ethiopia: A Retrospective Study. 2022.
17. Barasa M, Abdallah A. Cyto-histologic discordancy in patients undergoing thyroidectomy at Aga Khan University Hospital. *Pan African Medical Journal*. 2019;32(1).
18. Ukekwe FI, Olusina DB, Okere PC. Patterns of thyroid cancers in Southeastern Nigeria: A 15 year histopathologic review (2000-2014). *Journal of Clinical and Diagnostic Research: JCDR*. 2017;11(8):EC16.
19. Wali ON, Mraisel AC, Salih AN. Histopathological study of thyroid carcinoma in Misan province. *Journal of Bioscience and Applied Research*. 2022;8(2):93-102.
20. Brown ED, Obeng-Gyasi B, Hall JE, Shekhar S. The Thyroid Hormone Axis and Female Reproduction. *International Journal of Molecular Sciences*. 2023;24(12):9815.
21. AL-SALEEM IAAA, KAREEM WA. Histopathological Study in Patients with Enlarged Thyroid gland. *The Eurasia Proceedings of Science Technology Engineering and Mathematics*. 2020;9:23-30.
22. Mulatu B, Michael Y, Alemu S, Demissie WR. Pattern of Thyroid Cancer and Its Associated Factors Among Thyroid Patients Underwent Thyroidectomy at Jimma Medical Center, Southwest Ethiopia; A Four Years Retrospective Review. 2020.
23. Arrangoiz R, De Llano JG, Mijares MF, Fernandez-Christlieb G, Vasudevan V, Sastry A, et al. Current understanding of papillary thyroid carcinoma. *International Journal of Otolaryngology and Head & Neck Surgery*. 2021;10(3):184-221.

24. Der EM. Follicular Thyroid Carcinoma in a Country of Endemic Iodine Deficiency (1994–2013). *Journal of Thyroid Research*. 2018;2018:6516035.
25. Tabiti H, Guensi A, Bendahhou K, TABITI H. Epidemiological and Histological Characteristics of Differentiated Thyroid Carcinoma: A Case of the Department of Nuclear Medicine at Ibn Rochd Hospital, Casablanca, Morocco. *Cureus*. 2024;16(1).
26. Zhu J, Sun K, Wang J, He Y, Li D, Liu S, et al. Clinicopathological and surgical comparisons of differentiated thyroid cancer between China and the USA: A multicentered hospital-based study. *Frontiers in Public Health*. 2022;10:974359.
27. Nixon IJ, Whitcher MM, Palmer FL, Tuttle RM, Shaha AR, Shah JP, et al. The impact of distant metastases at presentation on prognosis in patients with differentiated carcinoma of the thyroid gland. *Thyroid*. 2012;22(9):884-9.