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ORIGINAL ARTICLE

# Histopathological spectrum and frequency of thyroid carcinomas in thyroidectomy Specimens: experience from a tertiary care hospital in Karachi

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## ABSTRACT

**Background:** Thyroid cancer constitutes 92% of all endocrine malignancies, and ranks as the eighth most prevalent cancer in females.

**Methods:** This descriptive cross-sectional study was conducted to determine the frequency and histopathological features of thyroid cancers in thyroidectomy specimens, at the Department of Histopathology, Dow University of Health Sciences, Ojha campus, Karachi. Histopathological data of 350 specimens was collected during the course of research, from June 2021 to June 2022.

**Results:** Of the 350 thyroidectomies, benign thyroid lesions were diagnosed in 281 (80.3%), low-risk neoplasms in 8 (2.3%) and thyroid cancer in 61 (17.4%) cases. Neck swelling was the most common presentation, followed by solitary thyroid nodule. Total thyroidectomy was the preferred type of surgery for malignant cases and benign cases with compressive symptoms. Female-to-male ratio was 6:1. Papillary thyroid carcinoma was the most frequent malignant neoplasm, diagnosed in 42 thyroidectomies (68.9%), followed by follicular and medullary carcinomas, 5 cases each (8.2%). Poorly differentiated thyroid carcinoma was documented in 2 cases and only one case of anaplastic carcinoma was reported. Most of the thyroid cancers were pathological stage T3.

**Conclusion:** Thyroid cancers accounted for 17.4% of all thyroidectomy cases with a strong female predominance. Papillary thyroid carcinoma was the most common type and most cases presented at pT3 stage. This emphasizes the need for thorough clinical and radiological evaluation of neck swellings to enable timely diagnosis.

**Keywords:** Anaplasia, Histopathology, Thyroidectomy, Thyroid Cancer

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## Introduction

Thyroid disorders are among the most frequent causes of anterior neck swellings, encountered in the head and neck outpatient clinics worldwide (1). The spectrum of thyroid diseases includes solitary thyroid nodules, multinodular goiter, and autoimmune thyroiditis, which may present either as hyperthyroidism or hypothyroidism (1). A solitary thyroid nodule is a discrete lesion resulting from abnormal thyroid cell proliferation, and detectable by clinical or

radiological examination. It has a prevalence of 5-7% in the general population, shows a female predominance, and the risk of malignancy ranges from 4 to 6.5%, increasing progressively with age (2).

Evaluation of thyroid nodule begins with the estimation of serum thyroid-stimulating hormone (TSH). In cases of elevated TSH, indicating a hypo-functioning (cold) nodule, a radionucleotide scan [I-123] is preformed, followed by a thyroid ultrasonography and fine needle aspiration cytology (FNAC) (3). Imaging findings are characterized according to the Thyroid Imaging Reporting and Data Systems (TIRADS), and cytology reporting follows the Bethesda system (4,5). Both the systems stratify thyroid nodules according to an increasing risk of malignancy.

Thyroid cancer constitutes 92% of all endocrine malignancies, and ranks as the eighth most prevalent cancer in females, with GLOBOCAN 2020 reporting an age standardized incidence rate (ASIR) of 10.1 per 100,000 for women and 3.0 per 100,000 for men, and notably higher rates in the developed countries (6). In Pakistan, a study from Karachi states an ASIR of 1.7 per 100,000 for females and 0.5 per 100,000 for males (7).

The new World Health Organization (WHO) 5th edition, classifies thyroid neoplasms into tumors of thyroid follicular-cell derivation and tumors of thyroid C-cell derivation (medullary carcinoma) (8). Follicular cell-derived tumors are further characterized into benign, low-risk and malignant neoplasms. Malignant ones include papillary, follicular, high grade, poorly differentiated and anaplastic carcinomas. Thyroid follicular nodular disease, is the revised terminology for multinodular goiter, and is currently categorized as benign neoplasm, reflecting the presence of clonal and non-clonal follicular cell proliferations in the lesion (8). Another update is that the encapsulated follicular variant Papillary thyroid carcinoma (FVPTC) is now a separate entity named as Invasive encapsulated follicular variant of papillary thyroid carcinoma (IEFVPTC), taking into account that these tumors bear molecular and prognostic` similarity to follicular carcinoma (8).

## Methods

This cross-sectional retrospective study was conducted at the Department of Histopathology, DUHS Ojha campus Karachi from June 2021 to June 2022. The study was approved by the Institutional Review Board (IRB-762/DUHS/2021). Patient information was retrieved from the hard copies of histopathology reports stored in the department. Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 23.0. The study included thyroidectomy and lobectomy specimens from patients aged 14-80 years. Trucut thyroid biopsies were excluded, as a definitive diagnosis of follicular carcinoma requires assessment of the capsular and vascular invasion on the resection specimens. All these cases were diagnosed by an expert histopathologist and the challenging cases were discussed in the departmental meeting to establish a consensus diagnosis. The malignant tumors were staged according to the American Joint Committee on Cancer (AJCC 8th edition) (9). The cases in our study were originally diagnosed according to the WHO 4th edition (2017) (10). While analyzing the data for the study, we studied the diagnostic criteria in the WHO 5th edition (2022) and reclassified the cases accordingly (8). Those diagnosed as multinodular goiter were updated to follicular nodular disease, and those as

encapsulated follicular variant PTC were reclassified as invasive encapsulated FVPTC (8, 11). However, as we did not re-evaluate the glass slides, some we could not evaluate the presence of high-grade features in these tumors to classify papillary and follicular carcinomas to differentiated high-grade thyroid carcinoma, which is a limitation of this study.

## Results

During the study period, 370 thyroidectomy specimens were received. Of the 350 specimens that met the inclusion criteria, 190 were total thyroidectomies, 46 were subtotal thyroidectomies and 114 were lobectomies. There were 302 (86.3%) females and 48 (13.7%) males, with a female-to-male ratio of 6:1. Mean age of the patient was 37.25+11.73 years, with the majority (n=189, 54%) between 31 and 50 years. Neck swelling was the most frequent presenting complaint (n=291, 83.1%), followed by a single thyroid nodule and a cold nodule (11 cases each, 3.1%).

Benign lesions accounted for 281 (80.3%) cases, low-risk neoplasms for 8 (2.3%), and carcinomas were diagnosed in 61 thyroidectomies (17.4%) (Table 1).

**Table 1: Frequency of all thyroid lesions**

| Thyroid Lesions | Frequency (n) | Percentage (%) |
|---|---|---|
| Benign | 281 | 80.29 |
| Low-risk | 8 | 2.29 |
| Malignant | 61 | 17.43 |
| Total | 350 | 100 |

In the benign category, follicular nodular disease (multinodular goiter) was the most frequent benign neoplasm, diagnosed in 217 cases (77%). Hashimoto thyroiditis was the most common non-neoplastic benign entity in 17 cases (6.0%) (Table 2). Non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) represented the most frequent low-risk tumor in 7 cases (Table 3).

**Table 2: Frequency of non-neoplastic lesions & benign thyroid neoplasms**

| Category | Benign Thyroid Lesion | Frequency (n) | Percentage (%) |
|---|---|---|---|
| Non-neoplastic lesions | Hashimoto thyroiditis | 17 | 6.0 |
| | Lymphocytic thyroiditis | 9 | 3.2 |
| | Grave's disease | 4 | 1.4 |
| | Colloid cyst | 1 | 0.4 |
| Benign Neoplasms | Follicular Nodular Disease | 217 | 77.2 |
| | Follicular adenoma | 31 | 11.0 |
| | Hurthle cell adenoma | 2 | 0.7 |
| Total | | 281 | 100.0 |

**Table 3: Frequency of low-risk follicular cell-derived thyroid neoplasms**

| Category | Frequency(n) | Percentage (%) |
|---|---|---|
| NIFTP | 7 | 87.5 |
| FTUMP | 1 | 12.5 |
| Total | 8 | 100.0 |

NIFTP: Non-invasive follicular thyroid neoplasm with papillary-like nuclear features
FTUMP: Follicular tumor of uncertain malignant potential

A total of 61 malignant neoplasms were identified, and their distribution is presented in Table 4. Papillary thyroid carcinoma was the most frequent malignancy in 42 thyroidectomies (12.0%) (Image 1 and 2). IEFVPTC was identified in 6 cases (9.8%). Follicular (Image 3 and 4) and medullary thyroid carcinoma were seen in equal frequency (5 each case, 8.2%), while anaplastic thyroid carcinoma (Image 5) and

poorly differentiated thyroid carcinoma were less than 5% (Table 4).

**Table 4: Frequency of malignant thyroid neoplasms**

| Malignant thyroid Neoplasms | Frequency (n) | Percentage (%) |
|---|---|---|
| Papillary thyroid carcinoma (PTC) | 42 | 68.9 |
| Classic subtype<br>Follicular variant,<br>infiltrative<br>Tall cell PTC | 36<br>5<br>1 | 59<br>8.2<br>1.6 |
| Invasive encapsulated follicular variant PTC | 6 | 9.8 |
| Follicular thyroid carcinoma | 5 | 8.2 |
| Minimally invasive<br>Widely invasive | 3<br>2 | 4.9<br>3.3 |
| Anaplastic thyroid carcinoma | 1 | 1.6 |
| Poorly differentiated thyroid carcinoma | 2 | 3.3 |
| Medullary thyroid carcinoma | 5 | 8.2 |
| **Total** | **61** | **100.0** |

The malignant thyroid tumors were staged as: pT1 in16 cases (26%), pT2 in 17 (28%), pT3 in 23 (38%) and pT4 in 5 cases (8%) (Figure 1).

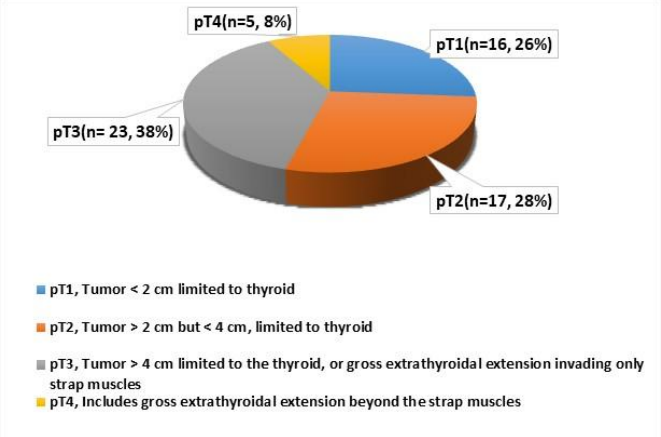



**Figure 1: Thyroid Cancer Staging for primary tumors**

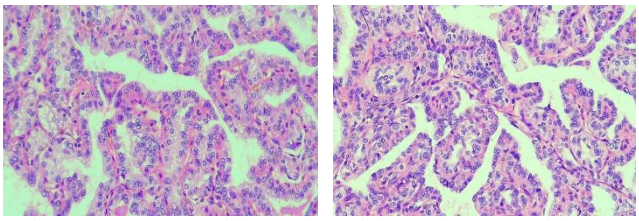


**Figure 2 & 3: Papillary thyroid carcinoma with PTC nuclei exhibiting nuclear enlargement, clearing, overlapping and nuclear grooves.**

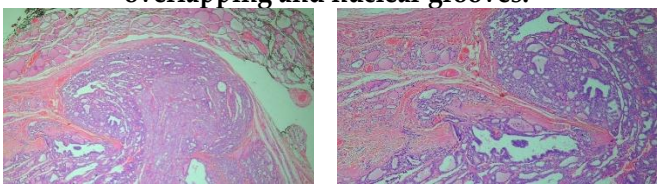
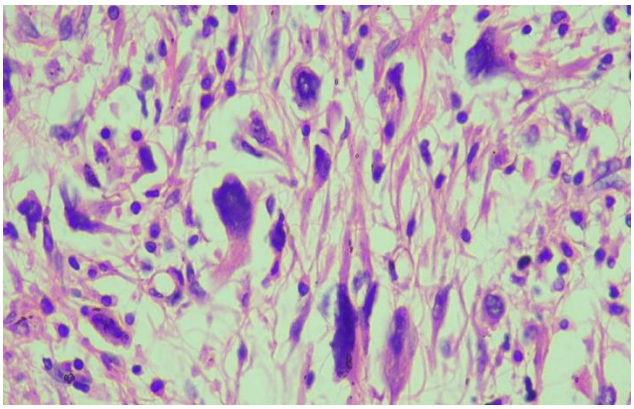


**Figure 4&5: Follicular Thyroid carcinoma with capsular invasion.**



**Anaplastic Thyroid Carcinoma with high grade nuclear pleomorphism**

## Discussion

The results of this study report that benign thyroid lesions were more frequent than the malignant ones, both types showed a strong female predominance, consistent with international and national studies (12, 13, 14, 15). Among the nonneoplastic lesions, we observed higher frequencies of Hashimoto thyroiditis and chronic lymphocytic thyroiditis, in agreement with a recent study conducted in India by Santosh et al (16). Follicular nodular disease (multinodular goiter) was the most common benign neoplasm in our study, as reported in literature (12, 17). Malignant tumors comprised 17.43% of all thyroidectomies, this

rate is higher than 13% reported in a study from Nigeria and 11% from a study by Qureshi et al (17, 18). In the current study, papillary thyroid cancer accounted for 69.8% of cancers, and follicular for 8.2%. Kiran et al. report a very similar frequency of 76.8% for papillary carcinoma and 10% for follicular carcinoma (13). A very high frequency of 90% is reported in a study from Saudia Arabia, and most were microcarcinomas (measuring 1 cm or less) (15). The global incidence of thyroid cancer has increased markedly over the past three decades, and is projected to rise further (19). However, this apparent rise is largely attributed to enhanced detection through widespread application of ultrasonography and other advanced diagnostic modalities (20). Most of these cancers are Papillary thyroid carcinomas, usually microcarcinomas, detected at stage I (67.4%) (GLOBOCAN) (6, 15). In contrast, 38% of the patients in our study were presented as stage III disease. The higher stage at diagnosis may be attributed to delayed diagnosis and limited access to health care facilities. In this research, neck swelling was the most frequent presenting symptom. Thyroid cancer typically presents as an asymptomatic painless nodule or neck swelling, however, in developing countries patients often seek medical advice only when the swelling becomes prominent or symptomatic (14). Other factors which may contribute to an advanced stage may include low public awareness of thyroid cancer especially in long-standing neck swellings, socioeconomic constraints, limited health care access, lack of routine medical checkups and inadequate use or availability of diagnostic modalities.

### Strength & Limitations of Study

The strength of the study lies in the large number of thyroidectomies reported in one year, and the classification of thyroid lesions according to the WHO 5th edition. However, the study has few limitations. We did not re-examine the glass slides of the cases, which may have influenced the final classification of some tumors such as NIFTP, FTUMP and poorly differentiated carcinomas. Additionally, we could not correlate the histopathology with the cytological and radiological findings of the cases.

## Recommendations

Future research avenues should focus on the mutational analyses in benign, low-risk and malignant thyroid tumors, utilizing immunohistochemical, polymerase chain reaction (PCR) and sequencing techniques in our population.

## Conclusion

Our findings highlight the need for timely evaluation of neck swellings or nodules through careful clinical assessment, and appropriate radiological investigations to facilitate earlier diagnosis and management.

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| All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed. | |