Original Article

Thyroid Cancer and its Relationship with pre-existing Thyroid Disease and Nodule Size: A retrospective study from a Tertiary Care Centre in Pakistan

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ABSTRACT

Objective: To determine the prevalence of thyroid cancer in patients with pre-existing thyroid diseases (particularly autoimmune thyroid disorders such as Graves' disease) and to explore the association between nodule size and malignancy type among patients treated at a tertiary care centre in Pakistan.

Methodology: A retrospective descriptive analysis of 62 patients diagnosed with thyroid cancer between January 2015 and August 2024 was conducted. Variables included were cancer type, pre-existing thyroid condition, confirmatory diagnostic method, nodule size, recurrence, metastasis, and surgical intervention. Percentages and frequencies were calculated to identify associations and trends.

Results: Out of 62 patients, 59 (95.2%) had valid data on thyroid cancer type. Papillary thyroid carcinoma (PTC) was the most common (76.3%) followed by anaplastic carcinoma (11.9%) medullary carcinoma (6.8%) and follicular carcinoma (5.1%). Thyroid cancer was only identified in 8.1% of patients with thyroid disorder (hypothyroidism or hyperthyroidism), while 91.9% had no prior thyroid condition. Nodules between 1–3 cm accounted for nearly half of all malignancies. Recurrence and metastasis occurred in 4.8% and 19.4% patients respectively. Surgery was performed in 71% of patients.

Conclusion: This study did not find any strong association between thyroid cancer and pre-existing thyroid disease. Most malignant nodules were between 1–3 cm, highlighting the need for early and thorough evaluation of all thyroid nodules irrespective of thyroid disease history or nodule size.

KEYWORDS: Pakistan, Thyroid nodule, Graves' disease, Pre-existing thyroid disease.

INTRODUCTION

Thyroid cancer is the most common type of cancer in the endocrine system, making up to 3.4% of all cancer cases reported annually all over the world.[1] With over 62000 cases, thyroid cancer has become 5th most common cancer in the USA and data suggests that incidence continues to increase.[2] The World Health Organization classifies five primary types of thyroid cancers based on their histological differences: Papillary thyroid carcinoma (PTC), Follicular thyroid carcinoma, poorly differentiated thyroid carcinoma, Medullary thyroid carcinoma and Anaplastic thyroid carcinoma. Papillary thyroid cancer is the most common type, making up to 80% of all thyroid cancer cases.[3]Although

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international data on thyroid cancer is extensive, evidence from Pakistan remains limited. Moreover, the relationship between pre-existing thyroid disease, such as hypothyroidism, hyperthyroidism, goitre, or autoimmune thyroiditis and subsequent carcinoma remains under-documented. Globally, autoimmune thyroid disease has been associated with a modest increase in thyroid cancer risk (odds ratio 1.5–2.0),[4] yet this relationship has not been well-established in Pakistani populations.

The aim of this study was to analyse the clinicopathological profile of thyroid cancer patients at a tertiary care centre in Islamabad, with special focus on pre-existing thyroid disease, nodule characteristics, diagnostic approaches and management outcomes.

METHODOLOGY

This descriptive cross-sectional study was conducted at Shifa International Hospital, Islamabad, Pakistan, a major tertiary care referral centre that serves patients from all over the country. The primary objective of this study was to determine the clinicopathological profile of thyroid cancer patients and to assess any correlation between pre-existing thyroid disease and the development of thyroid malignancy.

Retrospective data were collected using hospital medical and pathology records. All patients with age above 18 and confirmed histological diagnosis of thyroid carcinoma between 1 January 2015 and 31 July 2024 were included. Consecutive sampling method was used. Patients were excluded if they had missing documentations, secondary thyroid involvement from other primary malignancies, or inconclusive histopathological reports, to ensure diagnostic accuracy.

A total of 62 patients met the inclusion criteria and were analysed. Median age of cohort was 50 years (range 18-87 years). Gender information was not recorded. For every patient, data obtained included histopathological subtype of thyroid carcinoma (papillary, follicular, medullary, or anaplastic), presence of pre-existing thyroid disease (such as hypothyroidism, hyperthyroidism, or other thyroid disorders). Additional variables included nodule size on imaging, presence or absence of metastasis, disease recurrence, and whether surgical intervention was performed. Pre –operative FNAC data were not consistently documented for all patients. In this study, thyroid cancer diagnosis was confirmed mainly by post-surgical histopathology.

All collected data were entered and analysed using the Statistical Package for the Social Sciences (SPSS) version 26. Descriptive statistics were applied, and results for categorical variables were expressed as frequencies and percentages. No inferential statistics were performed due to the descriptive nature of the study.

Ethical approval for this study was obtained from the Institutional Review Board (IRB) of Shifa International Hospital, Islamabad. (IRB # 233-24) Throughout the study, patient confidentiality was strictly maintained by anonymizing all data, and no personal identifiers were recorded.

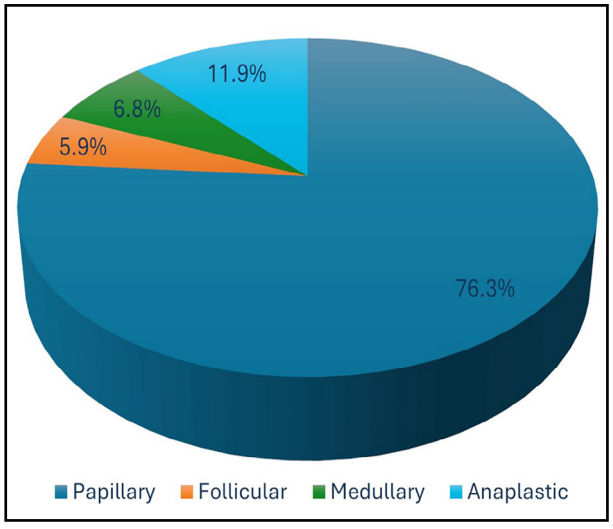

Fig.1: Frequency of Thyroid Cancer Types (n = 59 valid cases).

RESULTS

A total of 62 patients with histologically confirmed thyroid carcinoma were included in the study.

Histopathological Subtypes: Among the 59 cases, papillary thyroid carcinoma was the most frequent subtype, accounting for 76.3% (n=45) of cases. This was succeeded by anaplastic carcinoma in 11.9% (n=7), medullary carcinoma in 6.8% (n=4), and follicular carcinoma in 5.1% (n=3). Three cases (4.8%) were excluded from analysis mainly due to missing data (Fig.1).

Pre-Existing Thyroid Disease: Most patients, 91.9% (n=57), had no pre-existing thyroid disease before cancer diagnosis. Only a small proportion reported hypothyroidism (3.2%), hyperthyroidism (3.2%) or other thyroid-related conditions (1.6%). (Table-I).

Nodule Size, Metastasis, and Recurrence: The median nodule size was 3cm (range: 1-6 cm). Most malignant nodules were between 1-3 cm, accounting for 44 % of cases. In 12.9% of patient's nodule side was

Table-I: Pre-existing Thyroid Conditions (n = 62).

Condition	*Frequency*	*Percentage (%)*
None	57	91.9
Hypothyroidism	2	3.2
Hyperthyroidism	2	3.2
Other	1	1.6

Table-II: Nodule Size on Imaging (n = 62).

Nodule Size	*Frequency*	*Percentage (%)*
<1 cm	4	6.5
1.1–2 cm	15	24.2
2.1–3 cm	12	19.4
3.1–4 cm	10	16.1
4.1–5 cm	7	11.3
>5 cm	5	8.1
Not Known	8	12.9
Total	62	100.

not documented due to missing or incomplete pre op imaging. Details of nodule size distribution are presented in Table-II.

Metastasis was found in 19.4% (n=12) of cases, while recurrence of disease was observed in 4.8% (n=3). The majority, 79.0% (n=49) showed no evidence of metastasis.

Surgical Management: Surgical intervention was performed in 71.0% (n=44) of patients, whereas 25.8% (n=16) did not undergo any surgical procedure. Overall, the results showed that papillary thyroid carcinoma was the predominant histological type and that most cases were found in patients without any known pre-existing thyroid condition. Although not pre-calculated statistically, the sample reflects the institutional frequency of thyroid cancer presentations and provides significant insights into local trends and disease characteristics.

DISCUSSION

This study provides present-day data on thyroid cancer presentation, diagnostic patterns, and outcomes at a major tertiary care centre in Pakistan. Papillary thyroid carcinoma (PTC) was the most common subtype, in keeping with both national and international literature.[5-7]

Several previous studies and reviews have proposed that autoimmune thyroid disorders (Graves' disease, autoimmune thyroiditis) may increase the risk of thyroid cancer. One published meta-analysis demonstrated that patients with Hashimoto's thyroiditis carry an increased risk of developing papillary thyroid carcinoma, with pooled odds ratios around 2.1 (OR: 2.12, 95 % CI: 1.78-2.52) from 27 studies.[8] In contrast, our data demonstrated that 8.1 % of patients had documented pre-existing thyroid disease (3.2 % hypothyroidism, 3.2 % hyperthyroidism, 1.6 % other), while 91.9 % showed no known prior thyroid dysfunction. This suggests that there is no significant association between pre-existing thyroid disease and thyroid cancer in our constitutional cohort. The absence of this association in our cohort may be explained by several factors. Firstly, autoimmune thyroid diseases such as Graves' Disease or Hashimoto's thyroiditis are underdiagnosed in Pakistan due to limited availability of antibody testing and infrequent screening in euthyroid individuals, which may cause underreporting of pre-existing conditions. Also in Pakistan, healthcare-seeking behaviour is usually delayed, with patients presenting primarily when a palpable nodule or compressive symptoms develop, further minimizing the chance of identifying autoimmune thyroid disease before malignancy diagnosis.[9] Secondly, population-based differences in iodine intake, genetics, and environmental factors could modulate the link between thyroid cancer risk and autoimmunity.[10] Thirdly, because this study was done retrospectively, based on hospital records, and conducted in a surgical referral setting, there is potential for selection bias. Patients with overt thyroid disease may have been treated earlier or followed up separately, resulting in fewer cases reaching surgical intervention. Despite these limitations, the study highlights an important observation: thyroid cancer, particularly papillary subtype, can develop in patients without prior thyroid dysfunction, and nodule size rather than disease history seems to be a more relevant predictor in this population.

In our cohort, the most frequently observed malignant nodule sizes were in the 1.1–2.0 cm (24.2 %) and 2.1–3.0 cm (19.4 %) ranges, together comprising nearly 44 % of all thyroid cancers. This indicates that a substantial proportion of thyroid cancers present at a moderate nodule size, rather than as micro carcinomas (< 1 cm) or very large nodules (> 5 cm). The predominance of malignancies within this mid-size range highlights an important diagnostic consideration: thyroid nodules that are small or moderately sized can still foster malignancy, and their clinical significance must not be underestimated. International evidence reinforces this observation. In one of large Korean study of 5,043 patients with thyroid nodules, PTC was observed to be most common in nodules between 1 and 2 cm, while larger nodules (> 4 cm) were more often linked with follicular carcinoma and higher rates of extra thyroidal extension.[11] These similar trends were reported by Durante et al (2018) as well, who observed that the probability of malignancy does not increase linearly with size; instead, intermediate-sized nodules (1–3 cm) manifest the highest malignancy yield on fine-needle aspiration cytology (FNAC).[12] Thus, size thresholds for biopsy or further work-up in our setting may need to be guided by local epidemiological data and resource considerations.

The histological subtype distribution in our cohort 76.3% papillary carcinoma, 5.1% follicular carcinoma, 6.8% medullary carcinoma, and 11.9% anaplastic carcinoma is also broadly in keeping with global epidemiological data.[13] However, our cohort

exhibited a notably higher proportion of anaplastic carcinoma (11.9%) when compared to the global average of 1-2%.[14] This discrepancy can be explained by many context-specific factors. Firstly, our data was collected from a tertiary referral centre, which is likely receiving a higher proportion of advanced or complicated cases referred from other facilities. Such referral bias is very well-documented in studies done at tertiary hospitals and often overinflates the relative frequency of aggressive histology's such as anaplastic thyroid carcinoma (ATC).[15] Secondly, late presentation remains a common concern in low- and middle-income countries (LMICs), including Pakistan, where delays in seeking medical care, limited availability of specialized diagnostic facilities, and inadequate awareness about thyroid disorders contribute to diagnosis at advanced stages.[16,17] A study published from India presented similarly a higher proportion of anaplastic carcinoma (7.6%) in tertiary-care-based data, attributing this to delayed referral and underutilization of early diagnostic modalities such as fine-needle aspiration cytology.[18]In Summary, in Pakistan's tertiary-care settings, all thyroid nodules regardless of thyroid function should undergo early and thorough evaluation to prevent missed malignancies. Given that many cancers arise in nodules measuring 1–3 cm, clinicians should exercise caution with size thresholds and ensure that even small but suspicious nodules are assessed using FNAC. Strengthening diagnostic and referral pathways from primary and secondary care can help reduce delays in presentation due to limited access to imaging and cytology services. Enhancing public and physician awareness regarding thyroid nodule assessment, imaging criteria, and FNAC indications is also essential to minimize diagnostic delays. Furthermore, establishing a national thyroid registry for systematic documentation of disease history, imaging, cytology, and outcomes would support research, improve reporting accuracy, and facilitate the development of locally relevant guidelines.

Limitations and strengths: Several limitations deserve mentioning. Being retrospective, our study was based on accuracy and completeness of medical records; benign thyroid disease may have been undocumented or diagnosed outside our institution. The sample size is small (62 patients) and from a single tertiary-care centre, which may limit generalisability to non-referral settings or less advanced disease. We did not perform multivariate statistical modelling of risk factors (e.g., adjusting for age, sex, TSH, ultrasound features), which limits inference about independent predictors of malignancy or metastasis.

Nonetheless, the study has notable strengths: it provides descriptive data sets from Pakistan on thyroid carcinoma sub-types, pre-existing thyroid disease status and nodule size distribution in a tertiary-care context. The data reflects real-world institutional experience.

CONCLUSION

In summary, our study found that most thyroid carcinomas at our centre occurred in patients without known thyroid disease. Nodule size in the 1–3 cm range represented a substantial proportion of malignancies, underlining the need for rigorous evaluation of such nodules. Further multicentre, prospective studies in Pakistan are required to refine risk-stratification and management guidelines for thyroid nodules and carcinoma.

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Conflict of Interest: The authors declare no conflict of interest.

Ethical Approval: Approved by Institutional Review Board, Shifa International Hospital, Islamabad (IRB #233-24).

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Patient Consent: Not applicable (retrospective study, anonymized data).

Data Availability: Data available upon reasonable request.

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