Research Article

Multivariate Evaluation of Histopathological Prognostic Factors in Thyroid Neoplasm: A Retrospective Study from a Tertiary Care Centre

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Abstract

Background: Thyroid neoplasms comprise a heterogeneous group of lesions with varying biological behavior and prognostic outcomes. Histopathological evaluation remains essential for identifying adverse prognostic features that influence therapeutic decision-making and patient management.

Objectives: To evaluate the histopathological spectrum of thyroid neoplasms and assess the frequency of adverse prognostic factors in a tertiary care center.

Materials and Methods : A retrospective observational study was conducted in the Department of Pathology at a tertiary care center over a period of 18 months. Histopathological records of 34 thyroid neoplasms diagnosed between January 2024 and June 2025 were reviewed. Demographic data, tumor subtype, focality, capsular invasion, lymphovascular invasion, perineural invasion, angioinvasion, extrathyroidal extension, and lymph node status were analyzed. Descriptive statistical analysis was performed.

Results: Thirty-four thyroid neoplasms were evaluated. The mean age at presentation was 47.2 years, with a female predominance (79.4%). Papillary thyroid carcinoma was the most common neoplasm. Multifocality was observed in 35.3% of cases. Capsular invasion and lymphovascular invasion were identified in 5.9% of cases each, while perineural invasion was observed in 2.9%. Angioinvasion was noted in 8.8% of cases, and extrathyroidal extension was present in 2.9%. These adverse histopathological features were predominantly associated with malignant thyroid neoplasms.

Conclusion: Papillary thyroid carcinoma constituted the predominant thyroid neoplasm in the present study and demonstrated a marked female preponderance. Although adverse histopathological features were encountered infrequently, their identification remains critical for risk stratification and individualized patient management.

Keywords: Thyroid neoplasms, Papillary thyroid carcinoma, Histopathology, Prognostic factors, Multifocality, Extrathyroidal extension.

Introduction

Thyroid neoplasms are among the most common endocrine tumors worldwide, with a steadily increasing incidence over the past few decades owing to improved diagnostic techniques, greater surveillance, and heightened awareness. Although the majority of thyroid tumors exhibit an indolent clinical course and favorable prognosis, a subset demonstrates aggressive biological behavior characterized by local invasion, lymph node metastasis, distant dissemination, recurrence, and disease-specific mortality. This heterogeneity underscores the importance of accurate histopathological evaluation for prognostic assessment and optimal patient management.[1–4]

Histopathological examination remains the cornerstone for the diagnosis, classification, staging, and prognostic stratification of thyroid neoplasms. The fifth edition of the World Health Organization (WHO) Classification of Endocrine and Neuroendocrine Tumours has refined the diagnostic criteria for thyroid tumors by incorporating distinctive morphological patterns together with molecular alterations, thereby improving diagnostic precision and facilitating risk-adapted therapeutic strategies.[10] Likewise, advances in the understanding of thyroid tumor biology have led to a more comprehensive classification system that better reflects tumor behavior and clinical outcomes.[12]

Several histopathological parameters have been identified as important determinants of prognosis in thyroid neoplasms. These include tumor size, histological subtype and variant, capsular invasion, vascular invasion, extrathyroidal extension, multifocality, lymph node involvement, surgical margin status, tumor necrosis, mitotic activity, and the presence of distant metastasis.[1,2,4,6,15] These pathological features not only influence tumor staging according to the American Joint Committee on Cancer (AJCC) system but also play a pivotal role in predicting

recurrence risk and disease-specific survival.[17,19]

Among differentiated thyroid carcinomas, papillary thyroid carcinoma (PTC) is the most prevalent subtype and generally carries an excellent prognosis. However, certain histological variants, including tall-cell, hobnail, diffuse sclerosing, columnar cell, and solid variants, have been consistently associated with more aggressive clinical behavior and poorer outcomes.[2] Recent systematic reviews and meta-analyses have further demonstrated that pathological subtype is an independent predictor of recurrence and survival, emphasizing the necessity of meticulous histological evaluation.[2]

Tumor invasiveness represents another critical prognostic determinant. Capsular and vascular invasion are particularly significant in follicular-patterned neoplasms, while microscopic and gross extrathyroidal extension correlate with increased recurrence rates and reduced disease-free survival.[1,15] Multifocality and lymph node metastasis have also been recognized as adverse prognostic indicators, although their independent impact may vary according to patient age, tumor subtype, and extent of disease.[14,16] Comprehensive pathological reporting of these features is therefore essential for individualized postoperative risk stratification and therapeutic planning.[15,17]

Recent evidence has highlighted the growing importance of integrating conventional histopathological parameters with molecular characteristics to improve prognostic accuracy. Molecular alterations involving BRAF, RAS, TERT promoter, TP53, RET, and other oncogenic pathways have demonstrated significant associations with aggressive tumor behavior, recurrence, and disease-specific mortality.[4] Although molecular testing is increasingly incorporated into clinical practice, conventional histopathological evaluation remains the most universally available, cost-effective, and indispensable method for prognostic assessment, particularly in resource-limited healthcare settings.[1,4]

The American Thyroid Association (ATA) risk stratification system emphasizes the integration of histopathological findings with clinical and radiological parameters for predicting recurrence risk and guiding postoperative management.[20] Likewise, contemporary literature recognizes that detailed pathological assessment is fundamental to individualized patient care and serves as the basis for determining the need for radioactive iodine therapy, intensity of follow-up, and long-term surveillance.[3,16,22]

Despite significant advances in the understanding of thyroid tumor biology, considerable variability exists in the prevalence and prognostic significance of individual histopathological parameters across different populations and healthcare settings. Data from developing countries remain comparatively limited, highlighting the need for institution-specific studies to evaluate the clinicopathological profile of thyroid neoplasms and their associated prognostic factors. Such information may contribute to improved pathological reporting, risk stratification, and evidence-based management strategies.

Therefore, the present study was undertaken to evaluate the histopathological prognostic factors in thyroid neoplasms diagnosed at a tertiary care centre and to analyze their distribution and clinicopathological significance in relation to established prognostic parameters.

Materials and Methods

This retrospective observational study was conducted in the Department of Pathology at ASRAM Medical College, Eluru, after obtaining approval from the Institutional Ethics Committee.

Histopathological records of patients diagnosed with thyroid neoplasms between January 2024 and June 2025 were reviewed. A total of 34 cases fulfilling the inclusion criteria were included in the study.

Inclusion Criteria

Patients who underwent total thyroidectomy, hemithyroidectomy, or lobectomy.

Histopathological confirmation of thyroid neoplasm.

Exclusion Criteria

Inadequate tissue specimens.
Cases with prior chemotherapy or radiotherapy.
Cytology-only diagnoses without histopathological confirmation.

Data regarding age, sex, surgical procedure, tumor subtype, focality, capsular invasion, lymphovascular invasion, perineural invasion, angioinvasion, extrathyroidal extension, and lymph node involvement were collected from pathology records.
Descriptive statistical analysis was performed using frequencies, percentages, means, and medians.

Results

A total of 34 histopathologically confirmed thyroid neoplasms were included in the present study. The patients ranged in age from 17 to 84 years, with a mean age of 47.2 years and a median age of 43.5 years, indicating that thyroid neoplasms occurred across a wide age spectrum, with the majority of cases presenting during middle age.
Of the 34 patients, 27 (79.4%) were females and 7 (20.6%) were males, resulting in a female-to-male ratio of 3.9:1. The marked female predominance observed in the present study was consistent across the spectrum of thyroid neoplasms.
Histopathological examination revealed that papillary thyroid carcinoma (PTC) was the most frequently encountered thyroid neoplasm, accounting for the majority of malignant cases. Follicular thyroid carcinoma (FTC) was the second most common histological subtype, followed by medullary thyroid carcinoma (MTC). The predominance of PTC was evident irrespective of patient age and sex, reflecting its well-established status as the most common malignant thyroid tumor.
Evaluation of tumor focality demonstrated that 22 tumors (64.7%) were unifocal, while 12 tumors (35.3%) exhibited multifocality. Multifocal lesions were identified in more than one-third of the study population, indicating the presence of multiple tumor foci within the thyroid gland in a substantial proportion of patients.
Histopathological assessment of adverse prognostic parameters demonstrated that capsular invasion was identified in 2 cases (5.9%). These tumors showed unequivocal penetration of the tumor capsule, a feature considered significant in assessing the biological behavior of follicular-patterned thyroid neoplasms.
Similarly, lymphovascular invasion was observed in 2 cases (5.9%), characterized by the presence of tumor emboli within endothelial-lined lymphatic or vascular channels. Angioinvasion, defined as tumor invasion into blood vessels, was documented in 3 cases (8.8%), representing one of the important histopathological indicators associated with an increased risk of hematogenous dissemination, particularly in follicular-derived thyroid carcinomas.
Perineural invasion was an uncommon finding and was identified in 1 case (2.9%), while extrathyroidal extension (ETE) was also documented in 1 case (2.9%). The case demonstrating ETE showed tumor infiltration beyond the thyroid capsule into adjacent soft tissues, representing a locally advanced pathological feature.
Overall, adverse histopathological prognostic parameters were observed only in a minority of cases. Most tumors lacked evidence of capsular invasion, vascular invasion, perineural invasion, or extrathyroidal extension, suggesting that the majority of thyroid neoplasms included in the present series exhibited relatively favorable pathological characteristics.

Table 1. Demographic Characteristics

Parameter	Value
Total cases	34
Mean age (years)	47.2
Median age (years)	43.5

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Age range (years)	17-84
Female	27 (79.4%)
Male	7 (20.6%)
Female : Male ratio	3.9:1

Table 2. Histological Distribution of Thyroid Neoplasms

Histological Subtype	umber (n)	Percentage (%)
Papillary thyroid carcinoma	26	76.5
Follicular thyroid carcinoma	3	8.8
Medullary thyroid carcinoma	1	2.9
FT-UMP / Borderline lesions	1	2.9
Others	3	8.8

Table 3. Adverse Histopathological Features

Feature	Cases (n)	Percentage (%)
Capsular invasion	2	5.9
Lymphovascular invasion	2	5.9
Perineural invasion	1	2.9
Angioinvasion	3	8.8
Extrathyroidal extension	1	2.9

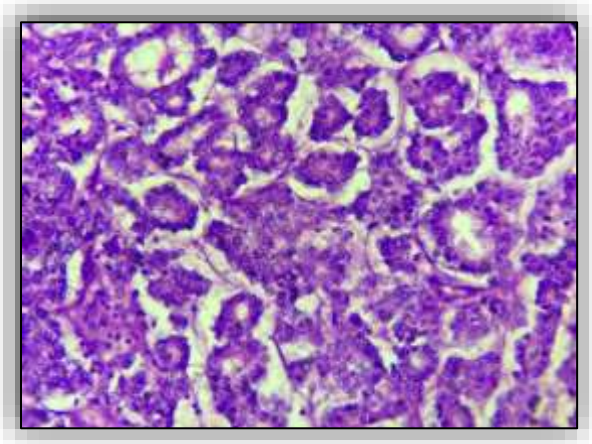


Fig. 1 HPE of Papillary carcinoma thyroid ; H& E stain; 40x

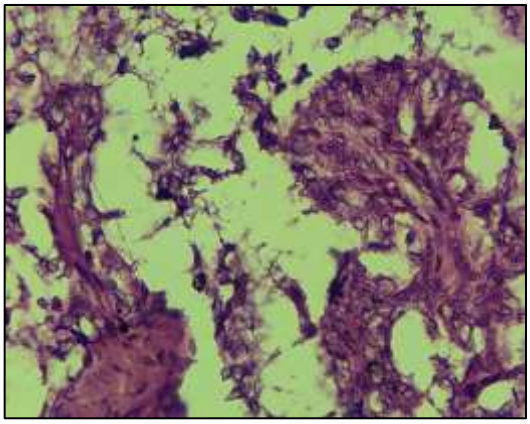


Fig. 2 HPE of Papillary carcinoma thyroid ; H& E stain; 40x

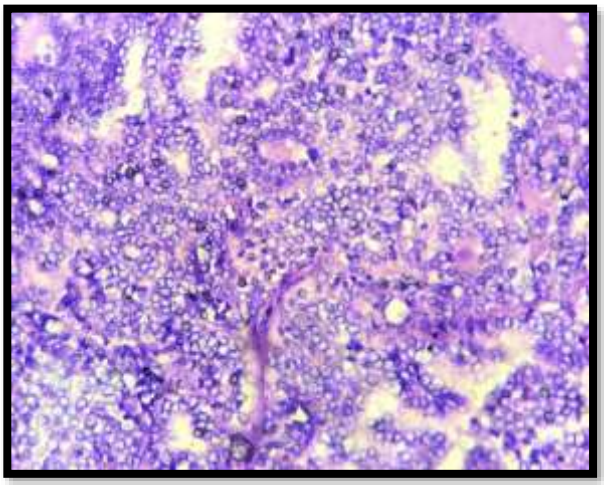


Fig. 3 HPE of Papillary carcinoma thyroid ; H& E stain; 40x

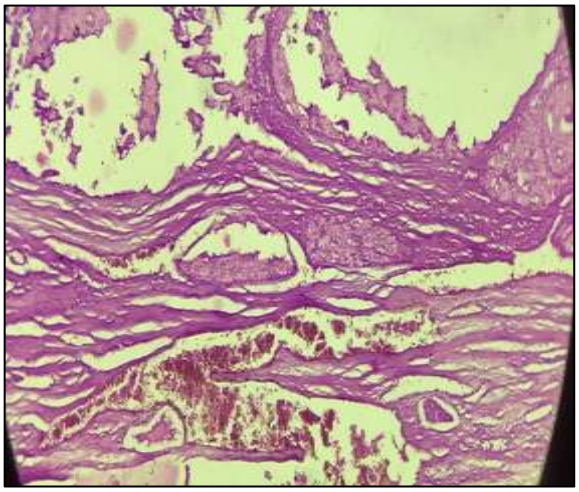


Fig. 4 HPE of Papillary carcinoma thyroid showing capsular invasion ; H& E stain; 40x

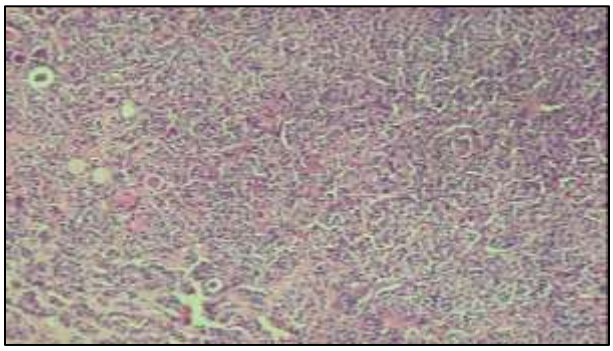


Fig. 5 HPE of Follicular carcinoma thyroid ; H& E stain; 40x

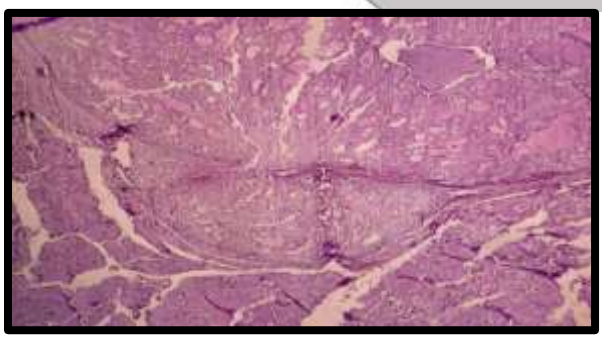


Fig. 6 HPE of Follicular carcinoma thyroid showing capsular invasion; H& E stain; 40x

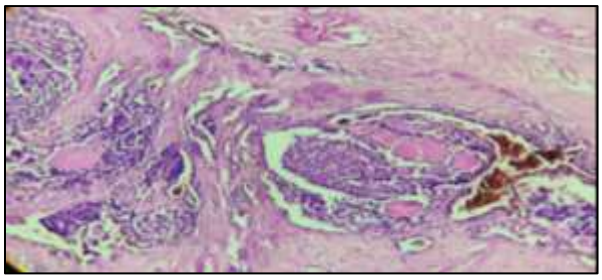


Fig. 7 HPE of Medullary carcinoma thyroid ; H& E stain; 40x

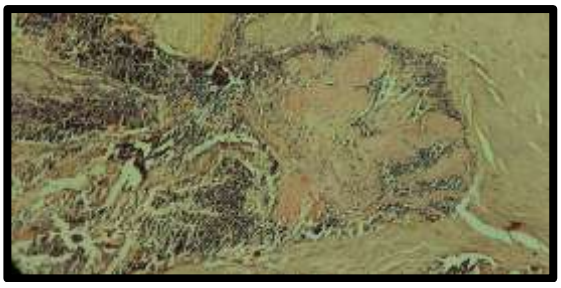


Fig. 8 HPE of Medullary carcinoma thyroid ; Congo red stain; 40x

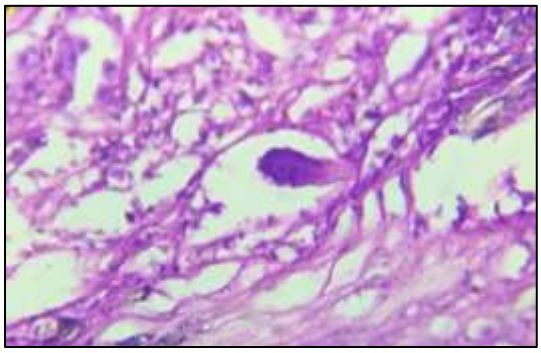


Fig. 9 Tumor emboli

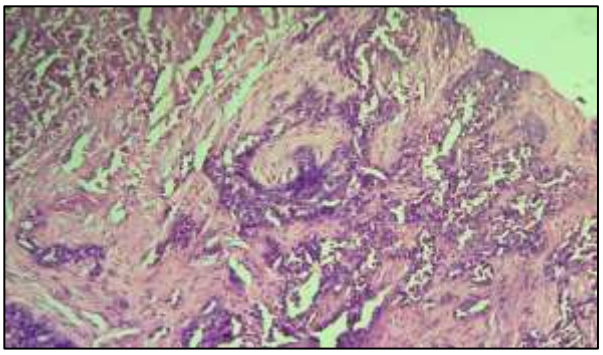


Fig. 10 Perineural invasion

Discussion

The present study evaluated the histopathological prognostic factors in 34 thyroid neoplasms diagnosed at a tertiary care centre. The findings reaffirm the well-established clinicopathological characteristics of thyroid malignancies,

including female predominance, middle-age presentation, the predominance of papillary thyroid carcinoma (PTC), and the relatively infrequent occurrence of adverse histopathological prognostic features such as capsular invasion, lymphovascular invasion, angioinvasion, perineural invasion, and extrathyroidal extension (ETE). Collectively, these observations suggest that most tumors in the present series exhibited favorable pathological characteristics, although a subset demonstrated features associated with more aggressive biological behavior.

The mean age of the study population was 47.2 years, with patients ranging from 17 to 84 years of age. This age distribution is comparable to that reported in previous studies, where differentiated thyroid carcinomas are most commonly diagnosed during the fourth and fifth decades of life.[1],[22] Age remains one of the most important prognostic variables incorporated into the AJCC TNM staging system because increasing age is consistently associated with higher recurrence rates, distant metastasis, and disease-specific mortality.[17],[19] Although age itself was not analyzed as an independent prognostic variable in the present study because of the limited sample size, the predominance of middle-aged patients is in agreement with the established epidemiological profile of thyroid carcinoma.

A marked female predominance was observed, with females accounting for 79.4% of cases and a female-to-male ratio of 3.9:1. This finding closely parallels the global epidemiological trend, where thyroid carcinoma occurs three to four times more frequently in women than in men.[22] Hormonal influences, particularly the interaction between estrogen signaling and thyroid follicular cells, along with autoimmune thyroid disease and environmental factors, have been proposed to contribute to this sex disparity. Despite the higher incidence in women, several studies have demonstrated that thyroid carcinoma in men may exhibit more aggressive clinicopathological characteristics and poorer outcomes, emphasizing the importance of individualized risk assessment.[1],[16]

Papillary thyroid carcinoma was the predominant histological subtype in the present study, followed by follicular thyroid carcinoma and medullary thyroid carcinoma. This distribution is consistent with the current WHO classification and numerous epidemiological studies reporting that PTC constitutes approximately 80–85% of thyroid malignancies.[10],[12] The predominance of PTC reflects its generally indolent biological behavior and excellent long-term survival. However, recent evidence has highlighted that prognosis varies considerably according to histological subtype and variant. A systematic review and network meta-analysis by Zhao et al. demonstrated that aggressive variants such as tall-cell, hobnail, diffuse sclerosing, and columnar cell PTC are associated with significantly higher risks of recurrence and disease-specific mortality than the classical variant.[2] Consequently, precise histopathological subclassification has become increasingly important for accurate prognostic stratification and treatment planning.

Tumor focality represents another important histopathological parameter with potential prognostic significance. In the present study, multifocality was observed in 35.3% of cases, whereas 64.7% were unifocal. The prevalence of multifocality observed in our series falls within the range reported in published literature. Multifocal PTC has traditionally been associated with an increased incidence of cervical lymph node metastasis, local recurrence, and the need for completion thyroidectomy or radioactive iodine therapy.[14] Nevertheless, its role as an independent predictor of survival remains controversial, as several studies suggest that multifocality primarily influences recurrence rather than disease-specific mortality.[14],[16] These findings underscore the importance of carefully documenting tumor focality in pathology reports and incorporating it into postoperative risk stratification.

Capsular invasion was identified in 5.9% of cases. This parameter is particularly relevant in follicular-patterned neoplasms, where definitive evidence of capsular penetration distinguishes minimally invasive follicular thyroid carcinoma from benign follicular adenoma.[10],[13] Accurate recognition of capsular invasion requires meticulous histological sampling and remains one of the most challenging aspects of thyroid pathology. The relatively low frequency observed in the present study may reflect the predominance of papillary thyroid carcinoma, in which capsular invasion has less diagnostic significance than in follicular neoplasms.

Lymphovascular invasion was also observed in 5.9% of tumors, while angioinvasion was present in 8.8%. Vascular invasion is a well-recognized adverse prognostic feature, particularly in follicular thyroid carcinoma, because it facilitates hematogenous dissemination to distant organs such as bone and lung.[13],[15] Several studies have

demonstrated that extensive vascular invasion is associated with significantly increased risks of recurrence, distant metastasis, and reduced disease-free survival.[1],[4] The relatively low incidence of vascular invasion in the present study likely reflects the predominance of differentiated tumors with favorable pathological characteristics.

Perineural invasion was identified in only one case (2.9%). Although uncommon in differentiated thyroid carcinoma, perineural invasion is generally considered a marker of locally aggressive disease and has been associated with higher rates of recurrence in several head and neck malignancies.[15] Its rarity in the present study is consistent with previous reports indicating that perineural invasion is far less frequent than lymphovascular invasion or extrathyroidal extension in thyroid carcinoma.

Extrathyroidal extension was observed in one case (2.9%). ETE remains one of the most clinically significant pathological predictors of recurrence and survival because it reflects direct invasion of surrounding soft tissues beyond the thyroid capsule. Both the AJCC staging system and the American Thyroid Association (ATA) risk stratification model recognize gross ETE as an indicator of advanced disease and an important determinant of postoperative management.[17],[20] Although only a single case demonstrated ETE in the present series, its identification has important therapeutic implications, including consideration of radioactive iodine therapy, closer surveillance, and individualized follow-up.

Overall, adverse histopathological prognostic features were infrequent in the present study. This finding suggests that most tumors were diagnosed at relatively early pathological stages before the development of extensive local invasion or vascular spread. Similar observations have been reported in recent systematic reviews, which indicate that the majority of differentiated thyroid carcinomas exhibit favorable histological characteristics and excellent long-term survival, whereas a relatively small subset demonstrates aggressive pathological features responsible for most disease-related morbidity and mortality.[1],[4],[6]

Recent advances in thyroid pathology have emphasized the integration of conventional histopathological assessment with molecular profiling to improve prognostic accuracy. Alterations involving BRAF, TERT promoter, RAS, TP53, and other oncogenic pathways have been associated with aggressive clinicopathological features, recurrence, and poorer survival.[4] Nevertheless, in many institutions, particularly in resource-limited settings, comprehensive molecular testing is not routinely available. Consequently, careful evaluation and standardized reporting of conventional histopathological parameters remain indispensable for prognostic assessment and clinical decision-making.[3],[10],[15]

Limitations

The present study has certain limitations. The relatively small sample size and the single-centre design may limit the generalizability of the findings. In addition, long-term follow-up data, recurrence rates, disease-free survival, and molecular analyses were not available, precluding correlation of histopathological parameters with clinical outcomes. Despite these limitations, the study provides valuable insight into the distribution of prognostically important histopathological features in thyroid neoplasms encountered at a tertiary care centre.

Conclusion

In conclusion, the present study demonstrates that papillary thyroid carcinoma is the predominant thyroid malignancy and that most tumors exhibit favorable pathological characteristics with a low frequency of adverse prognostic features. Nevertheless, meticulous assessment of tumor focality, capsular invasion, vascular invasion, perineural invasion, and extrathyroidal extension remains essential because these parameters continue to form the basis of pathological reporting, risk stratification, and therapeutic decision-making. Standardized histopathological evaluation, in accordance with current WHO classification, AJCC staging, and ATA guidelines, remains fundamental to optimizing the management of patients with thyroid neoplasms.

Ethical approval: As this study is a retrospecective study, in this type of study formal consent is not required.
Informed Consent Statement: Patient consent was waived since all tissues used in this study were obtained from Laboratory department in our institute, they were de-identified and unlinked to patient information.
Data Availability Statement: The data presented in this study are available on request from the corresponding author.
Funding: This study was not supported by any funding.
Conflicts of interest: The authors declare that they have no conflict of interest.
Consent for preparation: For this type of study informed consent is not required.
Consent for publication: For this type of study consent for publication is not required

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