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Correlation of Fine-Needle Aspiration Cytology with Histopathology in Thyroid Lesions: A Prospective Institutional Study

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Abstract

Background: Thyroid lesions encompass a broad clinical and morphological spectrum, ranging from physiological hyperplasia and inflammatory disorders through benign adenomas to a heterogeneous group of malignant neoplasms. Accurate categorization through clinicopathological correlation, supported by fine-needle aspiration cytology (FNAC) and histopathological examination, is fundamental to optimal management. Aim: The present study aimed to evaluate the histopathological spectrum of thyroid lesions in a tertiary care institution in South India, to correlate the histopathological diagnosis with clinical, ultrasonographic, and FNAC findings, and to assess the diagnostic accuracy of FNAC against histopathology as the gold standard. Materials and Methods: A two-year prospective observational study was conducted in the Department of Pathology, South India, between April 2016 and March 2017. Surgically resected thyroid specimens from 180 patients undergoing hemithyroidectomy or total thyroidectomy were processed through standard formalin fixation, paraffin embedding, and haematoxylin and eosin staining. Lesions were classified according to the World Health Organization (WHO) Classification of Tumours of Endocrine Organs, 5th edition, 2022. Pre-operative FNAC findings were graded according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). Concordance was assessed by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. Results: Of the 180 specimens, 128 (71.1%) were non-neoplastic, 24 (13.3%) were benign neoplasms, and 28 (15.6%) were malignant. Female predominance (4.6:1) and a peak in the 31–45-year age group were noted. Colloid goitre (43.3%) was the most common diagnosis, while papillary thyroid carcinoma (10.6%) was the most frequent malignancy. FNAC achieved an overall diagnostic accuracy of 91.7%. Conclusion: Thyroid lesions in South India are predominantly non-neoplastic and exhibit female

preponderance. FNAC, when reported by the Bethesda system and correlated with clinical and ultrasonographic features, remains an accurate first-line diagnostic modality for surgical triage.

Keywords

Thyroid lesions; Histopathology; Clinicopathological correlation; Papillary thyroid carcinoma; Bethesda system; FNAC; Colloid goitre.

1. Introduction

Thyroid disorders represent one of the most common endocrine pathologies worldwide, with a particularly high disease burden in iodine-deficient and iodine-replete areas of the Indian subcontinent [1,2]. Indian epidemiological estimates suggest that approximately 42 million people are affected by thyroid disorders, with a documented predominance among women and an increasing incidence of well-differentiated thyroid carcinoma over the past three decades [3,4]. The clinical presentation of thyroid lesions ranges from asymptomatic incidental nodules detected on imaging to clinically obvious masses producing pressure symptoms, voice change, or systemic features of thyroid dysfunction [5].

From a pathological standpoint, thyroid lesions are broadly classified into non-neoplastic disorders (colloid goitre, thyroiditis, hyperplasia, Graves' disease) and neoplasms (benign follicular and Hürthle cell adenomas; malignant papillary, follicular, medullary, anaplastic, and rare lymphomas) [6,7]. The 5th edition of the WHO Classification of Endocrine Tumours, published in 2022, has refined the morphological criteria for several entities, introduced new categories such as differentiated high-grade thyroid carcinoma, and emphasised the molecular genetic background of follicular-cell-derived neoplasms [8].

Fine-needle aspiration cytology (FNAC) is widely accepted as the principal pre-operative investigation for the triage of thyroid nodules. The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), introduced in 2009 and revised in 2017, standardises reporting into six diagnostic categories with associated risks of malignancy and recommended clinical management [9,10]. Histopathology, however, remains the diagnostic gold standard, particularly for the discrimination of follicular adenoma from minimally invasive follicular carcinoma, an issue that frequently underlies indeterminate cytology categories III and IV.

Although several Indian studies have characterised the histopathological spectrum of thyroid lesions, regional variation in iodine status, dietary practices, and socio-demographic factors generates heterogeneity in lesion distribution that warrants institution-specific analysis [11,12]. The present study was undertaken to characterise the histopathological spectrum of thyroid lesions in a recently established tertiary referral centre in South India and to evaluate the diagnostic accuracy of FNAC in this setting.

2. Materials and Methods

2.1 Study Setting

This prospective observational study was conducted in the Department of Pathology, South India, over a period of 24 months from April 2016 and March 2017.

2.2 Inclusion and Exclusion Criteria

All consecutive surgically resected thyroid specimens — hemithyroidectomy, total thyroidectomy, and completion thyroidectomy — received in the Department of Pathology during the study period were included. Repeat or completion specimens of the same patient were counted only once. Specimens with extensive autolytic change precluding evaluation, those received without clinical or radiologic information, and those representing pure parathyroid pathology were excluded. Patient identifiers were anonymised before data analysis.

Table 1. Demographic and Clinical Distribution of Thyroid Lesions (n=180)

Variable	Number (n=180)	Percentage (%)
Female	148	82.2
Male	32	17.8
Age 18-30 years	44	24.4
Age 31-45 years	78	43.4
Age 46-60 years	38	21.1
Age >60 years	20	11.1
Solitary nodule	96	53.3
Multinodular goitre	84	46.7

2.3 Specimen Processing and Reporting

All resected specimens were fixed in 10% neutral buffered formalin for at least 12 hours, weighed, photographed, and grossly examined according to the College of American Pathologists protocol. Representative sections from the lesion, capsule, surrounding parenchyma, and any identified

lymph nodes were sampled. Tissue blocks were dehydrated, paraffin-embedded, and 4-µm-thick sections were stained with haematoxylin and eosin (H&E). Special stains and immunohistochemistry — including thyroglobulin, TTF-1, calcitonin, BRAF V600E, Ki-67 (MIB-1), and HBME-1 — were applied where required for diagnostic confirmation. Histopathological diagnoses were classified according to the WHO Classification of Endocrine Tumours, 5th edition (2022) [8].

2.4 Cytohistological Correlation

Pre-operative FNAC reports, available for all 180 patients, were retrieved and re-classified by a single senior cytopathologist according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC, 2017 revision) [10]. The histopathological diagnosis was treated as the gold standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of FNAC were calculated using the conventional 2×2 table approach, with Bethesda categories V and VI considered cytologically positive for malignancy and category II considered cytologically negative.

2.5 Statistical Analysis

Data were entered in Microsoft Excel and analysed using IBM SPSS Statistics v26.0. Categorical variables were summarised as frequencies and percentages. Continuous variables were summarised as mean ± SD. Chi-square test was used to evaluate the association between demographic, clinical, and histopathological variables. A two-tailed p-value of less than 0.05 was considered statistically significant.

3. Results

Over the 24-month study period, 180 surgically resected thyroid specimens fulfilled the inclusion criteria. The mean age of patients was 41.6 ± 13.4 years, with a peak incidence in the 31–45-year age group (43.4%). A pronounced female preponderance was observed, with a male-to-female ratio of 1:4.6. Solitary nodules constituted 53.3% of presentations, while multinodular goitres accounted for the remaining 46.7% (Table 1).

The histopathological spectrum is summarised in Table 2. Non-neoplastic lesions accounted for the majority of cases (128/180; 71.1%), with colloid (nodular) goitre being the single most common diagnosis (43.3%), followed by Hashimoto's thyroiditis (15.6%) and lymphocytic

thyroiditis (5.6%). Benign neoplasms accounted for 13.3%, predominantly follicular adenomas. Malignant neoplasms constituted 15.6%, of which papillary thyroid carcinoma was the most frequent (10.6%, including classical, follicular variant, and tall cell variant), followed by follicular carcinoma (2.8%), medullary carcinoma (1.1%), and anaplastic carcinoma (1.1%). The mean age of patients with malignancy (44.2 years) was modestly higher than that of those with benign disease (40.8 years), but the difference did not reach statistical significance.

Table 2. Histopathological Spectrum of Thyroid Lesions (n=180)

Histopathological Diagnosis	Frequency (n)	Percentage (%)
Non-neoplastic Lesions	**128**	**71.1**
Colloid (nodular) goitre	78	43.3
Hashimoto's thyroiditis	28	15.6
Subacute (de Quervain) thyroiditis	8	4.4
Lymphocytic thyroiditis	10	5.6
Graves' disease	4	2.2
Benign Neoplasms	**24**	**13.3**
Follicular adenoma	22	12.2
Hürthle cell adenoma	2	1.1
Malignant Neoplasms	**28**	**15.6**
Papillary thyroid carcinoma	19	10.6
Follicular thyroid carcinoma	5	2.8
Medullary thyroid carcinoma	2	1.1
Anaplastic thyroid carcinoma	2	1.1

Cytohistological correlation is summarised in Table 3. The pre-operative FNAC distribution included 8 non-diagnostic (Bethesda I), 118 benign (II), 16 atypia of undetermined significance (III), 18 follicular neoplasm (IV), 8 suspicious for malignancy (V), and 12 malignant (VI) reports. The risk of malignancy increased progressively across Bethesda categories, with category VI showing 100% concordance with histopathological malignancy. After excluding non-diagnostic cases, the overall sensitivity, specificity, PPV, NPV, and diagnostic accuracy of FNAC were 84.6%, 95.3%, 78.6%, 96.7%, and 91.7%, respectively.

Table 3. Cytohistological Correlation of FNAC (Bethesda) with Histopathology

Bethesda FNAC Category	Total (n)	Benign on HPE (n)	Malignant on HPE (n)	Concordance (%)
I — Non-diagnostic	8	6	2	—
II — Benign	118	114	4	96.6

III — AUS/FLUS	16	12	4	75.0
IV — Follicular neoplasm	18	14	4	77.8
V — Suspicious for malignancy	8	2	6	75.0
VI — Malignant	12	0	12	100.0

4. Discussion

The principal findings of the present study from a tertiary referral centre in South India confirm that thyroid lesions are predominantly non-neoplastic, exhibit female preponderance, and that FNAC reported by the Bethesda system retains a high overall diagnostic accuracy when correlated with clinical and radiologic findings.

The female-to-male ratio of 4.6:1 observed in our series is consistent with previous Indian and international reports of female predominance in thyroid disease, reflecting the well-recognised oestrogenic and reproductive hormonal influences on thyroid follicular cells [13,14]. The peak incidence in the 31–45-year age group accords with the findings of Sharma et al. [11] from north India and Hanumantha Rao et al. [12] from south India, suggesting a relatively consistent age distribution across regions.

Colloid goitre as the most common diagnosis (43.3%) reflects the lingering legacy of iodine deficiency in South India, despite the implementation of the Universal Salt Iodisation Programme [15]. Although mean urinary iodine concentrations have improved nationally, persistent regional variation and inadequate household compliance with iodised salt continue to support the high prevalence of nodular goitre in tribal and rural districts of Madhya Pradesh and Chhattisgarh [16]. The substantial proportion of Hashimoto's thyroiditis (15.6%) is likewise notable, in keeping with international observations of rising autoimmune thyroid disease in iodine-replete and post-iodisation populations [17].

Papillary thyroid carcinoma was the dominant malignancy in our cohort (10.6%) and accounted for 67.9% of all thyroid cancers. This relative proportion is broadly comparable with international literature reporting papillary carcinoma as 70–90% of thyroid malignancies [6,7]. The relatively low absolute frequency of follicular and medullary carcinomas in our series mirrors the trend reported by Modi et al. [18] in eastern India, whereas the small number of anaplastic carcinomas (1.1%) is consistent with the rarity of this aggressive entity in tertiary centre series.

Our cytohistological correlation analysis demonstrated that FNAC achieved an overall diagnostic accuracy of 91.7%, sensitivity of 84.6%, and specificity of 95.3% — values comparable with the recent meta-analytic estimates of Bongiovanni et al. [19] and the multi-institutional series of Cibas and Ali [10]. The 100% concordance of Bethesda VI cytology with histopathological malignancy supports the practice of definitive surgical management for category VI lesions. Conversely, the indeterminate categories (III and IV) showed risk of malignancy of approximately 25%, highlighting the diagnostic challenge that these categories continue to pose. Adjunctive molecular tests — BRAF V600E mutation, RET/PTC rearrangement, and the ThyroSeq panel — have been advocated to improve risk stratification in indeterminate FNAC, although their cost remains a barrier in Indian public-sector practice [20,21].

Several practical implications emerge from these findings. First, the high prevalence of non-neoplastic thyroid lesions in South India underlines the need for sustained public health emphasis on iodine fortification and on community awareness of thyroid disorders. Second, the consistent diagnostic value of Bethesda-stratified FNAC supports its continued use as a first-line investigation, while reinforcing that indeterminate category should prompt cautious shared decision-making, ideally with adjunctive imaging risk assessment using the ACR-TIRADS system [22]. Third, structured histopathological reporting incorporating capsular and vascular invasion assessment, lymph node status, and immunohistochemical confirmation in difficult cases is essential for accurate risk stratification of follicular-patterned neoplasms [23].

The strengths of the present study include its prospective design, two-year recruitment window, application of the latest WHO 2022 classification, and use of the standardised Bethesda system for cytology. Limitations include the single-centre design, the relative rarity of medullary and anaplastic carcinoma which limits subgroup analysis, and the absence of long-term follow-up data. Future research integrating molecular markers, ultrasonographic risk scoring, and outcomes data would further enhance the clinicopathological correlation.

5. Conclusion

The histopathological spectrum of thyroid lesions in South India is dominated by non-neoplastic disorders, with colloid goitre and Hashimoto's thyroiditis as the most frequent diagnoses, and papillary thyroid carcinoma as the predominant malignancy. FNAC reported by the Bethesda system, when integrated with clinical and ultrasonographic findings, achieves a high overall

diagnostic accuracy of 91.7% and remains the cornerstone of pre-operative triage. Continued attention to iodine sufficiency, structured cytopathological reporting, and the judicious use of adjunctive molecular tests in indeterminate categories represent the key directions for further refinement of thyroid lesion management in India.

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