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NON-NEOPLASTIC THYROID LESIONS: DIAGNOSTIC ACCURACY OF FNAC IN CLINICAL PATHOLOGY

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ABSTRACT

Background: The thyroid gland, named after the Greek word for "shield," is responsible for critical metabolic processes and is frequently affected by various non-neoplastic conditions, including goitres, thyroiditis, and hyperplastic changes. Non-neoplastic thyroid lesions are primarily benign but may mimic malignancy clinically, the challenge lies in differentiating these from malignant cases to avoid unnecessary surgery. Differentiating these lesions is essential, especially in high-prevalence regions like India, where goitre is endemic. This study assesses FNAC as a primary diagnostic tool for such cases, correlating it with histopathological findings. **Methods:** The study involved 220 patients with thyroid swellings who underwent FNAC at a tertiary care centre from August 2016 to August 2018. Patients' clinical histories were recorded, followed by FNAC. Surgical specimens from 78 patients were subsequently evaluated histopathologically to verify FNAC diagnoses. **Results:** FNAC proved to be highly effective, with an accuracy of 94.87% for diagnosing non- neoplastic thyroid lesions. The study found that most cases were benign, with conditions like colloid nodular goitre (40.45%) and Hashimoto's thyroiditis (31.36%) being most prevalent. Notably, only 5-30% of thyroid nodules turned out to be malignant, emphasizing the importance of accurate preoperative diagnosis. Sensitivity, specificity, and predictive values from the FNAC results were high, confirming FNAC as a reliable first-line diagnostic approach for thyroid lesions.**Conclusion:** FNAC is a valuable tool in diagnosing non-neoplastic thyroid lesions, offering high diagnostic accuracy and facilitating appropriate management strategies. The study advocates for its continued use in clinical settings, especially in regions with high thyroid disease prevalence. Further studies could enhance FNAC's accuracy, focusing on minimizing false- negative rates and incorporating advanced imaging techniques.

Keywords: Thyroid, FNAC, Cytology, Histopathology, Goitre, Hashimoto's Thyroiditis, Thyroid Nodules

INTRODUCTION

The thyroid gland, named from the Greek word "thyreos" meaning shield[1], is a vital endocrine organ responsible for producing hormones that regulate metabolism, development, and body temperature. The gland is located in the anterior neck, and thyroid diseases are

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among the most frequently encountered endocrine disorders worldwide. After diabetes mellitus, thyroid issues are the second most common endocrine problems. Thyroid disorders can present as either nodular or diffuse glandular enlargement, which includes both non-neoplastic and neoplastic lesions. The term "goitre" is often used to describe any enlargement of the thyroid, with non-neoplastic thyroid enlargements being significantly more common than malignant ones[2].Non-neoplastic thyroid lesions, such as colloid nodular goiters, hyperplastic nodules, and various forms of thyroiditis (e.g., Hashimoto's thyroiditis and lymphocytic thyroiditis), are typically benign but may still cause clinical concerns due to mass effects, cosmetic issues, and potential hormonal imbalances. Thyroid nodules are palpable in around 4-7% of adults and are found more frequently in females and older individuals[3]. Notably, only 5-30% of palpable nodules turn out to be malignant, emphasizing the importance of accurate differentiation between benign and malignant nodules to avoid unnecessary surgeries[4.]

Fine Needle Aspiration Cytology (FNAC) has emerged as a cornerstone in the initial assessment of thyroid nodules due to its high diagnostic accuracy, minimal invasiveness, and cost-effectiveness which involves a thin needle to collect cells from the thyroid nodule, which are then examined microscopically to identify cytological characteristics. FNAC is often combined with imaging techniques, such as ultrasonography, which enhances the diagnostic yield, particularly for nodules that are small or difficult to palpate. The American Thyroid Association recommends FNAC as the first-line diagnostic tool for thyroid nodules due to its superior diagnostic reliability and cost-efficiency[5]. Despite FNAC's diagnostic accuracy, histopathological examination following surgery remains the definitive standard, particularly for ambiguous cases where FNAC results may not conclusively rule out malignancy. This study investigates the correlation between FNAC and histopathology in diagnosing non-neoplastic thyroid lesions, evaluating the sensitivity, specificity, and accuracy of FNAC as a diagnostic tool.

METHODS

Study Design

This was a prospective study conducted over a two-year period, from August 2016 to August 2018, in the Department of Pathology at a tertiary care centre. The study aimed to assess the accuracy of FNAC in diagnosing non-neoplastic thyroid lesions by comparing FNAC results with postoperative histopathological findings.

Sample Size and Selection

The study included a total of 220 patients who presented with thyroid swellings and were referred for FNAC. All patients were included regardless of age or sex, provided they met the inclusion criteria. Of these, 78 patients later underwent thyroid surgery, allowing for histopathological evaluation of their thyroid tissue to confirm FNAC diagnoses.

Inclusion and Exclusion Criteria

- **Inclusion Criteria:** Patients of any age or sex presenting with thyroid swellings and referred for FNAC were included in the study.
- **Exclusion Criteria:** Patients with known neoplastic thyroid lesions, skin infections at the aspiration site, haemorrhagic diathesis, critical illnesses, or lack of cooperation were excluded from the study to maintain focus on non-neoplastic conditions.

FNAC Procedure:

FNAC was performed as an outpatient procedure after obtaining informed consent .The aspiration site was sterilized, and a 23-gauge sterile needle attached to a 5ml syringe was

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used to collect samples. For adequate sampling, two to five passes were performed per nodule, as recommended for optimal cellular yield. In cystic nodules, fluid was aspirated until the lesion was fully evacuated, and residual material was then collected for cytology.

Sample Processing and Staining:

The aspirate samples were prepared on glass slides. Fixation was achieved using 95% ethanol for slides designated for Papanicolaou staining, while air-dried smears were stained with May-Grünwald-Giemsa stain. Hematoxylin and eosin (H&E) staining was also used for additional cytological detail. Each stained slide was examined microscopically for cellular and non-cellular elements, including colloid, follicular cells, and inflammatory cells, to establish a cytological diagnosis.

Histopathological Analysis:

Out of the 220 patients who underwent FNAC, 78 proceeded to thyroidectomy or other thyroid surgeries. The excised thyroid tissues were fixed in 10% formalin, processed, and embedded in paraffin. Thin sections were stained with H&E for histopathological examination. Cytological diagnoses from FNAC were compared with histopathological findings to evaluate FNAC's diagnostic accuracy.

Statistical Analysis:

The diagnostic accuracy of FNAC was calculated using sensitivity, specificity, Positive predictive value (PPV), Negative predictive value (NPV) and Diagnsotics accuracy. statistical metrics: Data analysis was performed using IBM SPSS Statistics and Microsoft Excel software, ensuring robust statistical evaluation.

RESULTS

In this study, 220 patients presenting with thyroid swellings underwent Fine Needle Aspiration Cytology (FNAC) over two years, with ages ranging from 10 to 75 years. The majority of the patients (90.9%) were female, resulting in a female-to-male ratio of 10:1, reflecting the higher prevalence of thyroid disorders among women.

Age and Type of Lesions

The age group with the highest incidence of thyroid nodules was 31-40 years for females and 41-50 years for males, consistent with the pattern that thyroid nodules often become more common with age. The most prevalent non-neoplastic conditions included simple and nodular colloid goiters, accounting for 40.45% of cases, followed closely by Hashimoto’s thyroiditis at 31.36%. Other non-neoplastic conditions observed were colloid nodular goitre with cystic degeneration (15%), hyperplastic goitres (3.18%), and lymphocytic thyroiditis (1.84%)(table 1).

Table 1: Distribution of Non-neoplastic lesions of thyroid in the study population(n=220)

Cytology Diagnosis	Number	Percentage
Simple and Nodular colloidgoiters	89	40.45%
Hyperplasticgoiters	7	3.18%
Colloid nodular goiters with cystic degeneration	33	15%
Hashimoto’s thyroiditis	69	31.36%
Lymphocytic thyroiditis	4	1.84%
Colloid cyst	13	5.90%
Inadequate	5	2.27%

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Nature of Aspirate and TSH Levels

The aspirate samples from FNAC procedures revealed that 66.81% were hemorrhagic, while 27.74% were colloid, and the remaining 5.45% were a mix of blood and colloid. The high incidence of hemorrhagic aspirates highlights the vascular nature of the thyroid, which often leads to blood-tinged samples(table 2). Additionally, Thyroid-Stimulating Hormone (TSH) levels were tested in 195 of the 220 patients, with normal levels in 68.73%, increased levels in 21.02%, and decreased levels in 10.25%. Most patients (75.46%) were euthyroid (normal thyroid function), followed by 15% with hypothyroidism and 9.54% with hyperthyroidism.

Table 2: Distribution of 220 cases according to the Nature of aspirate

	Number	**Percentage**
Colloid	61	27.74%
Haemorrhagic	147	66.81%
Colloidmixedhaemorrhage	12	5.45%

FNAC vs. Histopathology Findings

Of the 220 patients, 78 subsequently underwent thyroid surgery, and their histopathology results were compared with the preoperative FNAC diagnoses. Among these, 71 cases (91.02%) were confirmed as benign on histopathology, consistent with the FNAC diagnosis, while 7 cases (8.97%) were identified as malignant(table 3). Notably, these malignant cases were misdiagnosed as benign on FNAC, indicating the FNAC's limitations in detecting malignancies in certain cases. The false-negative cases included three cases each of papillary carcinoma and follicular variant of papillary carcinoma, and one case of follicular carcinoma.

Table 3: Correlation of Cytological diagnosis with final Histopathological diagnosis in 78 cases

	Cytology diagnosis (No)	Percentage	Histopathology diagnosis(No)	Percentage
Simple and nodular colloid goiters	46	58.99	45	57.69
Colloid nodular goiter with cystic degeneration	17	21.79	15	19.25
Hyperplastic goiter	1	1.28	1	1.28
Hashimotos thyroiditis	7	8.97	8	10.29
Colloid cyst	2	2.58	2	2.58
Papillary carcinoma thyroid	00	00	3	3.84
Follicular variant of	00		3	3.84

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papillary carcinoma		00		
Follicular carcinoma	00	00	1	1.28
Inadequate	5	6.41	00	00
Total	78	100	78	100

The diagnostic performance of FNAC was evaluated based on several key metrics:

- **Sensitivity:** 98.59%, showing FNAC's high ability to correctly identify benign lesions.
- **Specificity:** 59.14%, which reflects its lower accuracy in ruling out malignancies among patients diagnosed with benign lesions on FNAC.
- **Positive Predictive Value (PPV):** 95.89%, indicating the high likelihood that patients diagnosed with benign lesions indeed had benign pathology.
- **Negative Predictive Value (NPV):** 84%, demonstrating that most patients without benign FNAC results were likely to have neoplastic conditions on histopathology.
- **Diagnostic Accuracy:** 94.87%, reflecting the overall reliability of FNAC as a diagnostic tool for non-neoplastic thyroid lesions.

Cytological and Histopathological Concordance

The correlation between FNAC and histopathological diagnoses was high, with a 91.02% concordance rate for benign lesions. Simple and nodular colloid goitres showed the highest concordance, as 45 out of 46 cases diagnosed by FNAC were confirmed by histopathology(fig 1,2). However, cytological misclassification occurred in some cases: benign FNAC results in 7 cases later revealed malignancies on histopathology, underscoring the importance of histological examination, especially for nodules with suspicious clinical or ultrasound findings.

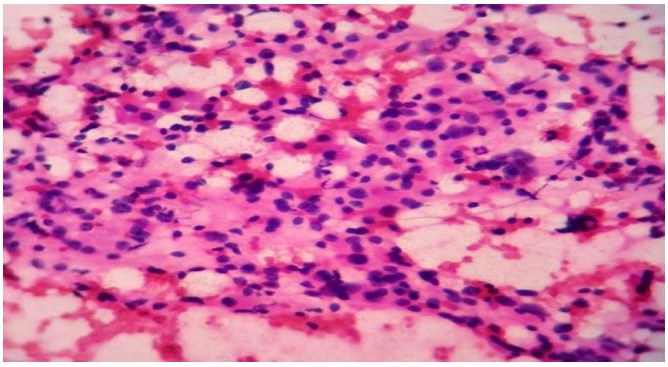

Figure 1: HASHIMOTOS THYROIDITIS: FNAC showing infiltration of follicular epithelial cells by lymphocytes.

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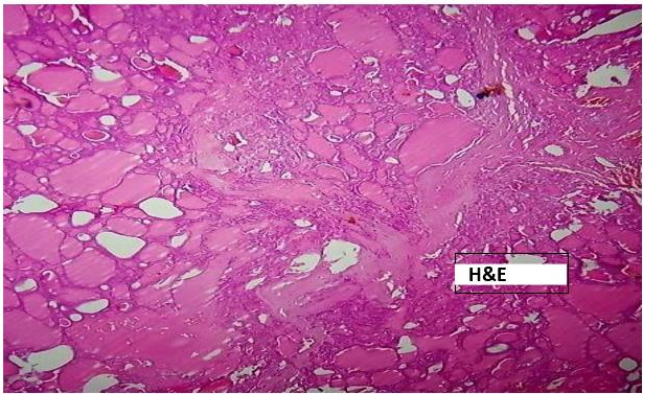

Figure2: FOLLICULARCARCINOMA: Tissue section showing tumor with capsularinvasion.

DISCUSSION:

The diagnosis and management of thyroid nodules remain a significant concern in endocrinology and pathology due to the high prevalence of thyroid disorders and the potential for malignancy, albeit in a small percentage of cases. This study supports Fine Needle Aspiration Cytology (FNAC) as an efficient, accurate, and minimally invasive diagnostic tool for identifying non-neoplastic thyroid lesions, allowing clinicians to triage cases effectively without the need for immediate surgery. Here, we discuss the role of FNAC compared to other diagnostic methods, the study's findings on prevalence and diagnostic accuracy, and how this aligns with findings in existing literature.

FNAC is widely recognized as the first-line diagnostic approach for evaluating thyroid swellings and nodules due to its high diagnostic accuracy, minimal invasiveness, and cost-effectiveness[6]. According to guidelines from the American Thyroid Association, FNAC should be the initial diagnostic test for thyroid nodules, with ultrasound guidance enhancing the accuracy for smaller or non-palpable nodules[7]. This recommendation is particularly relevant given the high vascularity of the thyroid, which can sometimes lead to hemorrhagic aspirates. In our study, 66.81% of FNAC samples contained hemorrhagic fluid, echoing similar observations by Panchal et al., who found hemorrhagic aspirates in 51.33% of cases[8].

The study findings show that simple and nodular colloid goitres and Hashimoto's thyroiditis were the most commonly encountered non-neoplastic lesions, representing 40.45% and 31.36% of cases, respectively. This distribution aligns with the known epidemiology of thyroid conditions, particularly in areas where goitre is endemic due to iodine deficiency. Notably, the prevalence of non-neoplastic thyroid conditions is significantly higher among females than males, with a female-to-male ratio of 10:1 observed in this study. This gender discrepancy is consistent with previous studies, which have documented a higher incidence of thyroid disorders in women, possibly due to hormonal and autoimmune factors[9,10].

Several studies have corroborated the high sensitivity and specificity of FNAC in diagnosing thyroid lesions. For instance, a study by Handa et al[11] found FNAC to be an accurate diagnostic tool with a diagnostic accuracy rate similar to the 94.87% observed in our study. Moreover, this study's FNAC sensitivity of 98.59% demonstrates FNAC's utility in distinguishing benign from malignant lesions preoperatively. However, it is essential to recognize that FNAC is not infallible, as reflected by the few false-negative cases observed in our study, where some benign diagnoses were later identified as malignant on

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histopathological examination. This limitation is shared by other studies, suggesting that although FNAC is valuable, histopathology remains essential, especially when FNAC results are ambiguous or suggest benignity in clinically suspicious cases[12-15].

The need for histopathological confirmation is further highlighted by cases of follicular and papillary carcinomas, where cytological features can sometimes overlap with benign conditions[16,17]. These findings align with previous studies indicating that while FNAC is effective, its diagnostic accuracy is influenced by factors such as the operator's experience, sampling techniques, and the lesion's characteristics[18]. For example, Mandal et al. demonstrated that multiple sampling and ultrasound guidance improved FNAC's diagnostic yield, particularly in cystic or non-palpable nodules[19].

Our study also emphasizes the importance of integrating FNAC with other diagnostic modalities such as ultrasonography and thyroid function tests for comprehensive thyroid lesion evaluation. Ultrasound-guided FNAC has been shown to reduce non-diagnostic rates and increase malignancy detection, especially in nodules with suspicious ultrasound features like microcalcifications and irregular margins[20-22]. Similarly, thyroid function tests provide valuable insights into nodule functionality, as hyperthyroidism and hypothyroidism can correlate with different types of thyroid lesions[23-25]. In this study, normal TSH levels were observed in 68.73% of patients, reinforcing that functional thyroid tests alone are insufficient for nodule characterization, although they provide useful adjunct information.

CONCLUSION

In conclusion, the findings reaffirm FNAC's role as an essential diagnostic procedure for non-neoplastic thyroid lesions. While highly effective, FNAC's limitations in certain cases reinforce the need for a multi-modal approach, incorporating clinical, cytological, and histopathological data to ensure accurate diagnosis and optimal management strategies for thyroid nodules. As FNAC continues to evolve with the integration of advanced imaging techniques, it promises even greater accuracy and utility in clinical practice.

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