Section: Pathology

Original Research Article

INTERPRETATION OF THYROID ASPIRATION SMEARS BY USING BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY AT TERTIARY CARE CENTRE

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ABSTRACT

Background: The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was introduced at the "Thyroid Fine Needle Aspiration State of the Science Conference" held in Bethesda, Maryland, to address inconsistencies in thyroid cytology reporting. Before the development of this system, thyroid FNAC results were often reported in varied and non-standardized terminologies, leading to confusion among clinicians and inconsistencies in patient management. This standardized system categorizes thyroid FNAC results into six diagnostic groups, each associated with a specific risk of malignancy and a corresponding clinical management plan. The aim & objective is to study the demographics, different cytomorphological patterns and distribution of various thyroid lesions by adopting "The Bethesda System for Reporting Thyroid Cytopathology". **Materials and Methods:** The present study is a prospective study of 102 patients with clinically enlarged thyroid gland and referred to Central Laboratory, Department of Pathology, Raichur Institute of medical Sciences(RIMS) Teaching Hospital, Raichur for FNAC between April 2023 to October 2024. FNAC smears were studied and the thyroid diseases were classified according to TBSRTC system. **Result:** Our study revealed female preponderance(88.2%) with mean age of 36.42 years and predominant age group being 3rd and 4th decade(28.4%). In our study, majority of the clinical diagnosis was Goitre(65.7%). Spectrum of thyroid lesions encountered on cytology were follicular nodular disease(52%), lymphocytic thyroiditis (40.1%), 2.9% each of follicular neoplasm and papillary thyroid carcinoma and 2% had suspicious of papillary carcinoma. Most common thyroid lesion according to TBSRTC belonged to Category II(92.2%)
followed by Category IV and Category VI(2.9%) and least common was Category V(2.0%). **Conclusion:** FNAC is a simple, rapid, safe, reliable and cost effective procedure for initial screening of various thyroid pathologies and for therapeutic management.

INTRODUCTION

Thyroid swelling is a commonly encountered clinical condition, particularly in young females, where it often presents with symptoms such as pressure effects and cosmetic deformities.[1] It may also manifest with symptoms related to altered thyroid function, such as hypothyroidism or hyperthyroidism, depending on the underlying pathology. Enlargement of the thyroid gland, whether diffuse or nodular, often prompts medical attention due to its visibility and associated anxiety regarding the possibility of malignancy.

The prevalence of palpable thyroid nodules varies widely, ranging from 4–7% in adults and 0.2–1.5% in children. These rates increase significantly in regions with endemic goitre and when advanced diagnostic modalities like ultrasound(USG) are employed.[2] Although the majority of thyroid nodules are benign, approximately 5–20% may harbour malignancy, making the accurate identification of malignant nodules a critical challenge in routine clinical practice.[3] Malignant thyroid neoplasms, although relatively rare compared to benign conditions, carry significant clinical consequences, emphasizing the need for an efficient

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and accurate preoperative diagnostic protocol. The differentiation between benign and malignant nodules is not always straightforward based solely on clinical evaluation or radiological features, thus underscoring the indispensable role of cytological and histopathological assessments. In clinical practice, the early detection of malignancy has profound implications for prognosis, as most thyroid cancers, particularly papillary carcinoma, have excellent outcomes when diagnosed early and managed appropriately. Understanding the incidence of thyroid lesions, their age and sex distribution, and their cytomorphological characteristics is essential for effective clinical management. In areas where thyroid disorders are highly prevalent, especially among women of reproductive age, public health initiatives focusing on early detection and management can significantly reduce the burden of disease. Thyroid lesions can occur across all age groups, but there is a strong female predominance, often attributed to hormonal factors and genetic predispositions. Analysing the age and sex distribution of thyroid lesions provides valuable insights into their epidemiology and helps identify high-risk populations. For instance, younger individuals with solitary cold nodules, older males with rapidly enlarging neck masses, and individuals with prior radiation exposure constitute higher-risk groups for thyroid malignancy. Such data are crucial in tailoring diagnostic and therapeutic strategies to meet the specific needs of these groups, ultimately improving clinical outcomes.

Fine-needle aspiration cytology (FNAC) has become a cornerstone in the diagnostic evaluation of thyroid swellings. This minimally invasive, cost-effective, and reliable technique allows clinicians to distinguish between neoplastic and non-neoplastic lesions, thereby reducing the frequency of unnecessary surgical interventions.[4] FNAC is especially valuable because it provides rapid preliminary information about the nature of the thyroid lesion, guiding clinicians toward appropriate further investigations or therapeutic decisions. A properly performed FNAC, combined with an experienced cytopathological interpretation, significantly enhances diagnostic yield, reducing the need for diagnostic thyroidectomy, which carries inherent risks and healthcare costs.

As a part of a comprehensive diagnostic approach, FNAC complements other investigations such as thyroid function tests (TFT), USG, and tumor marker studies, enabling a thorough assessment of thyroid nodules.[5] In select cases, molecular testing of FNAC samples, assessing genetic mutations such as BRAF or RAS, can further refine risk stratification and aid in decision-making. The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was introduced at the "Thyroid Fine Needle Aspiration State of the Science Conference" held in Bethesda, Maryland, to address inconsistencies in thyroid cytology reporting.[6] This standardized system categorizes thyroid FNAC results into six diagnostic groups, each associated with a specific risk of malignancy and a corresponding clinical management plan. The categories range from non-diagnostic specimens to definite malignancies, with intermediate categories allowing for a risk-based approach to patient care. Each category is assigned an implied risk of malignancy, typically based on large multi-institutional studies, thus helping clinicians to counsel patients accurately regarding prognosis and treatment options. Importantly, The Bethesda System provides not only standardized terminology but also recommendations for repeat FNAC, lobectomy, total thyroidectomy, or observation based on the cytological category. The Bethesda System has become an internationally recognized framework, improving communication between pathologists and clinicians, enhancing diagnostic accuracy, and facilitating evidence-based management of thyroid lesions. Several studies across different populations and healthcare settings have validated the utility of it, demonstrating improved concordance between cytological diagnosis and histopathological outcomes.

Aims and Objectives

1. To study demographics of thyroid lesions.
2. To study the different cytomorphological patterns and distribution of various thyroid lesions by adopting “The Bethesda System for Reporting Thyroid Cytopathology”.

MATERIALS AND METHODS

A prospective study from April 2023 to October 2024 was done on 102 patients who presented with enlarged thyroid gland attending outpatient clinics and hospitalised inpatients in Ear Nose Throat department and Surgery department of RIMS teaching hospital, Raichur and referred to Central Laboratory, Department of Pathology, RIMS Teaching Hospital, Raichur for FNAC. Patients with skin infection at the site of aspiration, critically ill or anxious patients and patients not willing for FNAC even after explaining the purpose, utility, and consequences of procedure were excluded from the study. The study proposal was approved by the Institutional Ethics Committee, RIMS, Raichur. A written and informed consent of patient for FNAC procedure was obtained. In each patient, a detailed clinical history and local examination was done using case pre-defined proforma. Radiological investigation report was documented wherever done. FNAC was performed using 22-24gauge needle. Smears were prepared; air dried smears were stained with May-Grunwald-Giemsa(MGG) stain and alcohol fixed smears were stained with Haematoxylin and Eosin(H&E) stain and Papanicolaou(PAP) stain. FNAC smears were studied and the thyroid diseases were classified according to TBSRTC system. Statistical analysis was done using the frequency distribution table in Microsoft Excel Office.

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RESULTS

The FNAC smears of a total 102 cases of thyroid swellings were examined. Among 102 patients, female predominance(88.2%) was noted. The age distribution ranged from 12 and 70 years. The average age was 36.42 years with standard deviation 13.63. In this study, we found that most of the patients affected belonged to 3rd and 4th decade(28.4%) [Table 1]. Most of the thyroid lesions were diffuse(46%) followed by right sided lesions (32.3%), left-sided lesions(19.6%) and least were midline lesions(1.96%) [Table 2]. Goitre(65.7%) was the predominant clinical diagnosis among the study patients, followed by solitary thyroid nodule(7.8%), diffuse goitre(6.9%), 4.9% each of multinodular goitre and nodular goitre, thyroiditis(2.9%), 1.0% each for colloid cyst, colloid goitre, hashimoto's thyroiditis, neck swelling, thyroid carcinoma and thyroid nodule [Table 3]. Out of 102 cases, radiological examination was done for 45 patients (44.1%) among which thyroiditis(13.7 %) was the most common radiological diagnosis followed by TIRADS II (7.8%), 3.9 % each showed colloid nodule and multinodular goitre, 2.9% each showed colloid cyst and TIRADS III, 2% each had colloid goitre and solitary thyroid nodule and least common radiological diagnosis were 1 % each for adenoma, benign cyst and benign thyroid nodule. Radiological examination was not available for 57 patients(55.9%) [Table 4]. In the present study, non-neoplastic lesions were more common than neoplastic lesions. The distribution of cytodiagnosis showed 2.9 % each of follicular neoplasm and papillary thyroid carcinoma cases and 2% had suspicious of papillary carcinoma [Table 5]. The distribution of cases across six TBSRTC showed majority of cases constituted Category II (Benign) [Figure 1-3] accounting for 92.2% cases, Category IV(Follicular Neoplasm-FN/Suspicious for a Follicular Neoplasm-SFN) [Figure 4] and Category VI (Malignant) [Figure 6 & 7] comprised 2.9% cases each while Category V(Suspicious for Malignancy) [Figure 5] observed in 2.0% cases. Among the benign cases (Category II), follicular nodular disease [Figure 1&2] was the most frequently diagnosed benign lesion comprising 52% of the cases followed by lymphocytic thyroiditis [Figure 3] in 40.1% cases. No cases of Category III (Atypia of Undetermined Significance-AUS/Follicular Lesion of Undetermined Significance-FLUS) were noted in the present study [Table 6].

Table 1: Distribution of Age

Age (Years)	Frequency	Percent
< =20	11	10.8%
21 – 30	29	28.4%
31 – 40	29	28.4%
41 – 50	20	19.6%
>50	13	12.7%
Total	102	100%

Table 2: Distribution of laterality

Laterality	Frequency	Percent
Right	33	32.3%
Left	20	19.6%
Diffuse	47	46.0%
Midline	2	1.96%
Total	102	100.0%

Table 3: Distribution of Clinical Diagnosis

Clinical Diagnosis	Frequency	Percent
Goitre	67	65.7%
Solitary Thyroid Nodule	8	7.8%
Diffuse Goitre	7	6.9%
Multinodular Goitre	5	4.9%
Nodular Goitre	5	4.9%
Thyroiditis	3	2.9%
Adenoma	1	1.0%
Colloid Cyst	1	1.0%
Colloid Goitre	1	1.0%
Hashimoto's Thyroiditis	1	1.0%
Neck Swelling	1	1.0%
Thyroid Carcinoma	1	1.0%
Thyroid Nodule	1	1.0%
Total	102	100%

Table 4: Distribution of USG Report

USG Report	Frequency	Percent
Not Given	57	55.9%
Thyroiditis	14	13.7%
TIRADS II	8	7.8%

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Colloid Nodule	4	3.9%
Multinodular Goitre	4	3.9%
Colloid Cyst	3	2.9%
TIRADS III	3	2.9%
Colloid Goitre	2	2.0%
Diffuse Goitre	2	2.0%
Solitary Thyroid Nodule	2	2.0%
Adenoma	1	1.0%
Benign Cyst	1	1.0%
Benign Thyroid Nodule	1	1.0%
Total	102	100%

Table 5: Distribution of FNAC Diagnosis

FNAC Diagnosis	Frequency	Percent
Lymphocytic Thyroiditis	27	26.4%
Colloid Goitre	21	20.5%
Nodular Goitre	18	17.64%
Hashimoto's Thyroiditis	15	14.7%
Colloid Cyst	10	9.8%
Adenomatoid Nodule	3	2.9%
Follicular Neoplasm	3	2.9%
Suspicious of Papillary Carcinoma	2	1.9%
Papillary Thyroid Carcinoma	3	2.9%
Total	102	100%

Table 6: Distribution of FNAC Diagnosis by TBSRTC 2023 Category

TBSRTC Category	TBSRTC Category Count (%)	FNAC Diagnosis	Frequency (%)
Category- I Non diagnostic	0 (0%)	Cyst fluid only. Virtually acellular specimen. Other (e.g., obscuring blood, clotting artifact, drying artifact)	0%
Category -II Benign	94 (92.2%)	Follicular Nodular Disease	53 (52.0%)
		Lymphocytic Thyroiditis(Hashimoto's)	41(40.2%)
Category-III AUS/FLUS	0(0%)	Specify if AUS-nuclear atypia or AUS-other	0%
Category-IV FN/SFN	3 (2.9%)	Follicular Neoplasm	3 (2.9%)
Category -V SM	2 (2.0%)	Suspicious of Papillary Carcinoma	2 (2.0%)
Category-VI Malignant	3 (2.9%)	Papillary Thyroid Carcinoma	3 (2.9%)

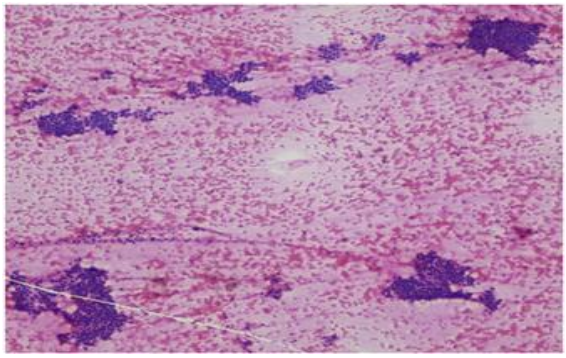

Figure 1: Category II Benign - Follicular nodular disease (H&E, 20X) showing thyroid follicular cells in sheets and macrofollicles against background of colloid and hemorrhage.

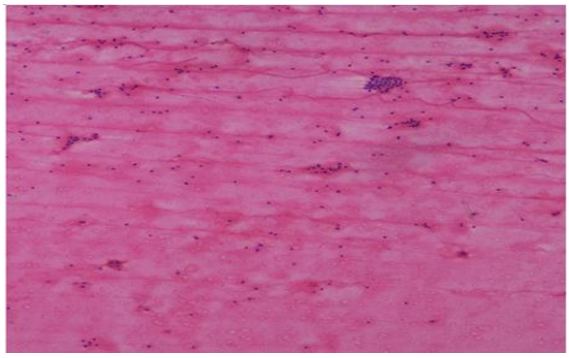

Figure 2: Category II Benign - Follicular nodular disease suggestive of colloid nodule (H&E, 20X) showing few thyroid follicular cells in the background of abundant thin colloid.

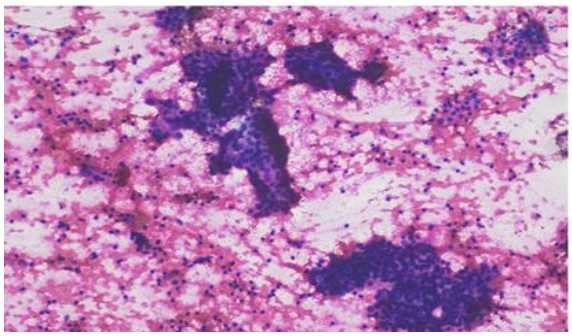

Figure 3: Category II Benign - Lymphocytic thyroiditis (H&E, 20X) showing thyroid follicular cells arranged in sheets and macrofollicles in a background of abundant polymorphous lymphocytes admixed with hurthle cells.

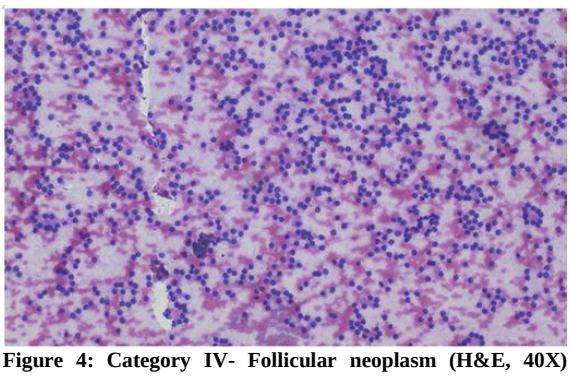

Figure 4: Category IV- Follicular neoplasm (H&E, 40X) showing thyroid follicular cells arranged in repetitive microfollicles with absent papillary nuclear features.

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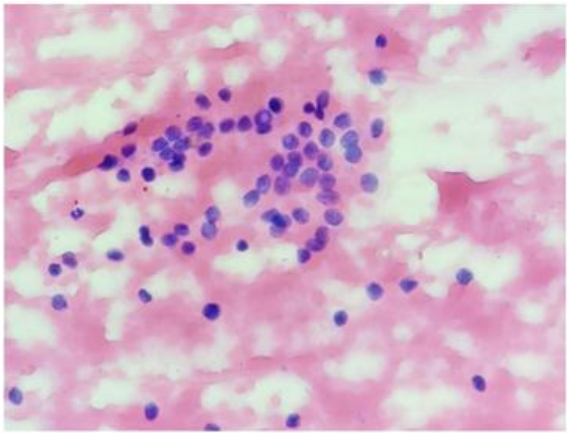

Figure 5: Category V- Suspicious for Papillary thyroid carcinoma (H&E, 40X) showing thyroid follicular cells arranged in macrofollicle and singly scattered with few cells showing enlarged nuclei with powdery chromatin and occasional intranuclear pseudoinclusion.

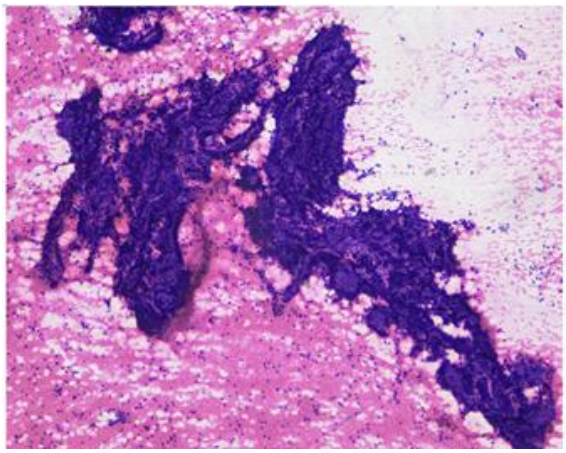

Figure 6: Category VI- Papillary thyroid carcinoma (H&E, 20X) showing thyroid follicular cells arranged in papillary pattern.

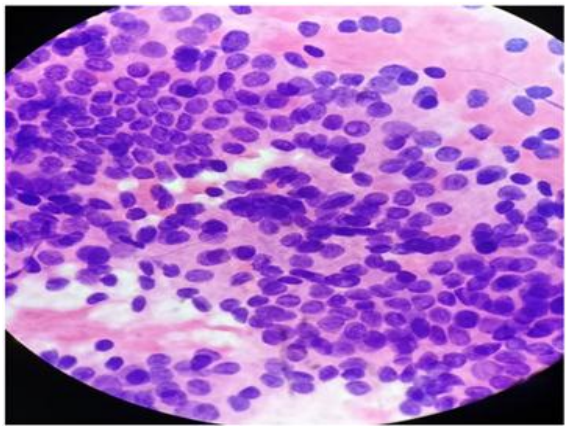

Figure 7: Category VI - Papillary thyroid carcinoma showing (H&E, 40X) showing thyroid follicular cells with enlarged nuclei, overcrowding, powdery chromatin, nuclear groove and intranuclear pseudoinclusions.

DISCUSSION

As a screening technique, cytological assessment of thyroid swellings is a quick, simple, and affordable diagnostic process. It assists in classifying patients as either conservative or surgical candidates. Interobserver and intraobserver variability, particularly in uncertain instances, are the technique's primary drawbacks. Furthermore, there is a lack of consistency in the reporting systems that are employed, which differ not only between nations but also between laboratories and even within employees of the same laboratory. This interferes with the clinician's ability to interpret accurately, which impacts patient care. Therefore, the study was carried out using "The Bethesda System for Reporting Thyroid Cytopathology" in order to investigate the distribution of thyroid lesions by age and sex as well as the various cytomorphological patterns and distribution of thyroid lesions.

A total of 102 patients were included for the study. The mean age of the patients in our study was 36.42 years. The minimum and maximum age was 12 and 70 years, respectively. Most of the patients are between 21 and 40 years. Among 102 patients, female predominance was noted. 88.2% were females and 11.8 % are males. According to Anand et al, a total number of 646 patients were included in their study with complaints of thyroid swelling assessed by FNA. The patients' ages ranged from 7 to 85 years old, with a mean age of 41.78 years. The ratio of men to women was 1: 6.3. In contrast, the age group in our study ranged from 12 to 70 years old, with a mean age of 36.42 years.[6] Similar to the Anand et al. study, female predominance was seen. Of the 150 cases in the Misra et al. study, 90.6%(135) were female and 9.4%(14) were male. Analysis by age showed that thyroid lesions were distributed differently in different age groups. Notably, the age groups of 21–30 and 41–50 years old accounted for the majority of instances, whereas the age group of 61–70 years old was dominated by men.[7] Similar to the Misra et al. study, the present study also revealed that the majority of patients are in the age range of 21 to 40. The current study's findings that thyroid lesions are more common in women and that they are most common in those aged 21 to 40 are in line with research by Cibas et al,[8] and Safirullah et al.[9] As per Mehra et al., the mean age of the patients was 37.1 years with the ratio of men to women was 1: 4.[10]

In the present study, the clinical diagnosis distribution showed majority 65.7%(67 cases) had goitre, followed by solitary thyroid nodule in 7.8%, diffuse goitre in 6.9%, 4.9% had multinodular goitre, 4.9% had nodular goitre, 2.9% had thyroiditis, 1.0% each for colloid cyst, colloid goitre, hashimoto's thyroiditis, neck swelling, thyroid carcinoma and thyroid nodule. Majority of cases were found to have diffuse lesions which was among 47(46%) patients followed by Right sided lesions among 33(32.3%) patients. Left-sided lesions were observed among 20(19.6%) patients and 02(1.96%) patients had midline lesions. Anand et al., study also showed predominance of diffuse lesions(40%).[6] Misra et al., study showed diffuse(30%) followed by right sided lesions.[7]

According to our patients' USG reports, 13.7% of them had thyroiditis, 7.8% had TIRADS II, 3.9% had

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colloid nodule, 3.9% had multinodular goitre, 2.9% had colloid cyst, 2.9% had TIRADS III, 2% had colloid goitre, 2% had STN, and 1% each of adenoma, benign cyst, and benign thyroid nodule were found.

All patients had FNAC diagnosis according to TBSRTC in our study, it showed that 52% has follicular nodular disease, 40.1% had lymphocytic thyroiditis, 2.9 % follicular neoplasm, 2.9% had papillary thyroid carcinoma and 2% had suspicious of papillary carcinoma. Among our patients, 92.2% had TBSRTC category II, 2.9% had category IV, 2.0% had category V, 2.9% category VI. The distribution of cases according to Bethesda system showed that 92.2 % cases are benign, 2.9 % had Follicular Neoplasm, 2% had Suspicious for Malignancy, 2.9% cases are malignant. According to Misra et al.'s study, 88.00% of the 132 cases were classified as benign(Bethesda II). Atypia of Follicular Lesion(Bethesda III) and Follicular Neoplasm(Bethesda IV) each had 2.67%(4 cases), Suspicious for Malignancy(Bethesda V) had 1.33%(2 cases), Unsatisfactory/Nondiagnostic(Bethesda I) had 1.33%(2 cases), and Malignant(Bethesda VI) had 4.00%(6 cases). Similar to the Misra et al. study, ours likewise revealed that 92.2% of the population fell into the benign category. However, none of our patients fall into the nondiagnostic category.[7] This study's case distribution among Bethesda System categories is consistent with findings from earlier investigations. The majority of the lesions were reported as benign in investigations by Cibas et al,[8] and Yang et al,[11] which similarly used the six-tier grading approach.

Benign and malignant lesions are diagnosed cytologically in 92.2% and 7.8% of cases, respectively. Follicular nodular disease and lymphocytic thyroiditis(Hashimoto's thyroiditis) constituted the benign lesions, while papillary thyroid cancer is the malignant lesions. Follicle nodular disease was the most prevalent lesion among all benign cases. Thyroid papillary carcinoma was the most prevalent type of malignancy, accounting for 2.9% of all malignant cases. Our findings are consistent with the study by Kamali et al.[12] Out of the 281 cases examined, 247 (87.90%) were benign, 4 (1.42%) were neoplastic, 5 (1.78%) were suspicious for malignancy, 7 (2.49%) were suspicious for a follicular neoplasm, 11 (3.91%) had atypia of unknown significance, and 7 (2.49%) were inadequate, according to the Ranjan et al. study.[13]

The majority of thyroid lesions (62%), according to a research by Gupta et al. on 60 individuals with clinically palpable thyroid lesions, were found to be benign.[14] According to Akshatha et al., of the 101 cases they examined, 47 (46.5%) were benign, 33 (32.6%) were inflammatory, 09 (8.9%) were follicular neoplasms, 04 (3.9%) were malignant, and 09 (8.9%) were insufficient.[15] 33 (70.2%) cases were diagnosed as colloid nodular goitre on FNAC, 04 (8.5%) as autoimmune thyroiditis, 08 (17.0%) as follicular neoplasm, 01 (2.1%) as suggestive of malignancy, and 01(2.1%) as papillary carcinoma, according to Muppidi et al.[16]

Successfully distinguishing benign from malignant lesions and prioritizing patients in need of surgery are the objectives of thyroid FNA. The six-tired Bethesda method offers standardized terminology for reporting thyroid FNA smears, facilitating improved dialogue and comprehension between pathologists and doctors. The benefit of this methodical approach is that each of the six Bethesda categories has an inferred risk of cancer, which aids clinicians in developing the right course of treatment for the patient.

CONCLUSION

The major screening test for thyroid lesions is Fine-Needle Aspiration Cytology(FNAC), which gives clinicians vital information for patient care. Because of its excellent accuracy, affordability, speed, ease of use, and safety, FNAC is a well recognized diagnostic technique. Thyroid lesions are categorized into six different groups by the Bethesda System, a standardized reporting structure that supports FNAC. In the present research study, the case distribution as per the Bethesda classification, we have higher number of benign cases and the number of Follicular Neoplasm, Suspicious for Malignancy and malignant cases being lower.

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