

# Evaluation of FNAC Thyroid Smears using Bethesda System for Reporting Thyroid Cytopathology Nomenclature with Clinicopathological Correlation

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**Abstract:** ***Background:** The study aimed to interpret thyroid cytology by the Bethesda System for reporting thyroid cytology (TBSRTC) and to analyze the distribution of lesions under various diagnostic categories and subcategories. **Methodology:** This study was conducted as an observational study at tertiary care centre on patients with thyroid lesions. After history taking and detailed local, general and systemic examination, thyroid function tests were conducted. Apart from this, ultrasonography of lesion was done. Patients were subjected to FNAC and after fixation smears were stained with Papanicolaou stain. **Results:** About 53% thyroid lesions were hemorrhagic, followed by 17% blood mixed colloid and 4% colorless serous fluid. Sample adequacy was noted in 93.5% cases in our study. According to Bethesda system of classification, majority of lesions were benign (81.5%) whereas 6.5% lesions were unsatisfactory. Only 6% lesions were categorized as malignant. **Conclusion:** FNAC is widely accepted as the most accurate, sensitive, specific, and cost - effective diagnostic procedure in the preoperative assessment of thyroid nodules. It is the first line of investigation and can differentiate benign nodules from malignant nodules of the thyroid in 95% cases. Applying a standard reporting system for thyroid cytology may enhance the communication between pathologists and clinicians, assists them to find out the rate of malignancy in each cytological group, and facilitating a more reliable approach for patient management.*

**Keywords:** FNAC, Bethesda, thyroid nodules, thyroid cytopathology, neoplastic thyroid nodules, thyroid cytology reporting.

## 1. Introduction

The thyroid is the largest endocrine gland situated superficially in the neck. The main function of this gland is to regulate various metabolic activities by Thyroxin which is mediated by the Pituitary and Hypothalamus by TSH and TRH. Diseases of the thyroid are common and associated with excess release of thyroid hormone (Hyperthyroidism), hormone deficiency (Hypothyroidism), and mass lesions of the thyroid. <sup>[1]</sup> Thyroid nodules are common and it is estimated that around 67 % of people may have one or more thyroid nodules that are otherwise no palpable or asymptomatic. <sup>[2]</sup> Risk factors include iodine - deficient areas, elder age groups, women and patients with a history of neck irradiation. Most nodules are asymptomatic and may present with symptoms ranging from swelling (goiter) to hoarseness of voice, dysphagia, and pain in the neck when their size grows and starts to compress regional structures in the throat and neck. <sup>[3]</sup>

Thyroid nodules are mostly benign and very few of them are malignant. Neoplastic lesions are relatively uncommon and constitute only 0.7% in females and 0.2% in males. But in recent times there has been an increase in the incidence of thyroid neoplasm worldwide and India. <sup>[4]</sup> Thorough clinical history and examinations, ultrasonography, biochemical profile (T3, T4, TSH), Radioisotope scan, thyroid antibodies, FNAC, histopathology, and IHC studies are helpful in establishing etiological diagnosis. FNAC has proven the most cost - effective, safe, simple, and minimally

invasive procedure for the evaluation of thyroid nodules. <sup>[5]</sup> In FNA cytology approx.60% of nodules are classified as benign, <10% are malignant and 30% are not fitted in both the category and termed 'indeterminate', 'atypical', 'rule out', or 'cannot exclude malignancy'. Lack of uniform reporting systems among various laboratories leads to diagnostic confusion among pathologists and clinicians for risk management. <sup>[6]</sup>

A uniform nomenclature system was proposed at the NCI conference which was subsequently known as 'The Bethesda system for reporting thyroid cytopathology' (TBSRTC). <sup>[6]</sup> TBSRTC is recognized as a standardized, category - based reporting system for thyroid fine - needle aspiration (FNA) specimens. Every thyroid FNA report should begin with one of six diagnostic categories. Every diagnostic category consists of implied cancer risk that ranges from 0% to 3% for the "benign" category to virtually 100% for the "malignant" category. This six - tiered Bethesda system provides a standardized system for thyroid smears reporting and facilitates better communication between clinicians and pathologists. The advantage of this approach is that each category has an implicit risk of malignancy which helps clinicians to plan appropriate therapy for the patient. <sup>[6]</sup> The present study aimed to interpret thyroid cytology by the Bethesda System for reporting thyroid cytology (TBSRTC) and to analyze the distribution of lesions under various diagnostic categories and subcategories.

## 2. Methodology

This study was conducted as an observational study in the Department of Pathology, Gandhi Medical College and JawaharLal Nehru Cancer hospital Bhopal during the two years from October 2018 to 30th June 2020. All those patients having thyroid lesions, irrespective of their age and sex, referred for FNAC from Surgery and ENT OPD/ ward were included whereas patients with a skin infection at the site of aspiration; patients with hemorrhagic diathesis; critically ill or anxious patients and non - cooperative patients were excluded from the study. The study was approved by Institute’s ethical committee and written consent was obtained from all the study participants after explaining them nature and purpose of study.

Sociodemographic details such as age, gender, education, occupation and residence was obtained from all the patients and entered in questionnaire. Clinical history in detail was obtained from all the study participants regarding presenting complaints, duration of illness, history of dysphagia, dysphonia, hoarseness of voice. Menstrual history was obtained in females. Family history, drug history was also obtained from all the patients and documented.

Further, all the patients were subjected to local and general examination. Site, size, shape and type of thyroid nodule was observed. Presence of tenderness, consistency, mobility and lymphadenopathy were assessed and findings were documented. All the patients were then subjected to detailed systemic examination. Thyroid function tests were conducted when required. Ultrasonography of thyroid was done to establish USG diagnosis. All the patients were then subjected to FNAC of thyroid nodule. Aspirations were done by one of the following techniques - Orell SR and Vielh; [7] Sanchez MA and Stahl RE. [8] Manual pressure was applied at the site of puncture for at least five minutes. Nature of aspirate was observed and tongue shaped smears were prepared on clean glass slides with the help of another glass slide on the middle third of the slide. After the procedure slides was fixed in isopropyl alcohol for 15 minutes. After fixation smears were stained with Papanicolaou stain. [9] After staining the smears were examined and cytological diagnosis is made and interpreted according to the Bethesda reporting system. [6]

**Statistical analysis:** Data was compiled using MsExcel and analysed using IBM SPSS software version 20. Data was categorized and expressed as frequency and proportions whereas continuous variables were expressed as mean and standard deviation.

## 3. Results

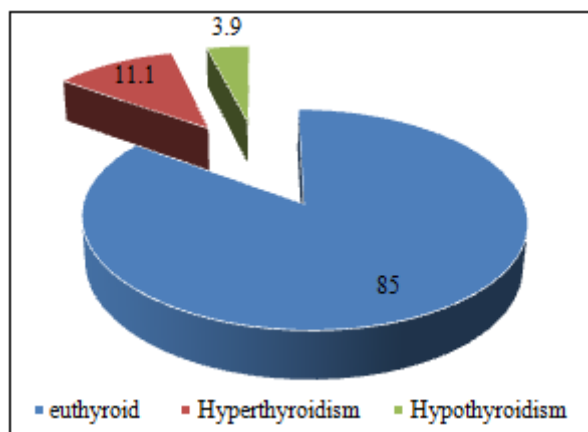
A total of 200 cases with thyroid nodules fulfilling the inclusion criteria were included in our study with mean age of 39.96±15.37 (Range - 8 to 84 years). Female preponderance for thyroid nodule was observed with Female to male ratio 5.67: 1 and 85% (n=170) cases were females. Most common clinical Symptom observed in these patients was swelling in the neck which was present in a total of 198 cases i. e., 99% of cases followed by dysphagia in 20 cases (10 %) in which 4 of them turned out to be malignant.

Cervical lymph nodes were palpable in 5 cases in which two of which turned out to be Papillary thyroid carcinoma. No thyroid swelling palpated in two cases. Duration of symptoms was less than 6 months in 45% cases whereas 55% cases presented with duration of symptoms of more than 6 months.

**Table 1:** Distribution according to thyroid nodule characteristics

Characteristics of thyroid nodules		No. of cases (n=200)	Percentage
Site of lesion	Right lobe	131	65.5%
	Left lobe	38	19%
	Bilateral (diffuse)	13	6.5%
	Mid thyroid (Isthmus)	18	9%
Size	≤1cm	10	5%
	1 - 3 cms	129	64.5%
	4 - 5 cms	50	25%
	>5 cms	8	4%
Consistency	Soft	100	50%
	Firm	81	40.5%
	Mixed	8	4%
	Hard	11	5.5%
Mobility	Mobile	187	93.5%
	Non - Mobile	13	6.5%
Tenderness	Tender	23	11.5%
	Non - tender	177	88.5%
Nodularity	Single nodule	173	86.5 %
	Multiple nodules	12	6%
	Diffuse	15	7.5%

Right lobe involvements was most common (65.5%) and size of nodule ranged between 1 and 3 cms in majority i. e.64.5% cases. Consistency was soft in 50% cases and nodule was mobile in 93.5% cases. Only 13 cases were fixed on palpation in which 10 cases turned out to be malignant. Majority of cases (88.5%) were not associated with tenderness. Most common type of presentation was solitary thyroid nodule (86.5%).



**Figure 1:** Distribution according to thyroid function tests

Thyroid function tests were done in 127 cases, of them, 85% cases were euthyroid and 11.1% and 3.9% cases were hyperthyroid and hypothyroid respectively.

**Table 2:** Distribution according to USG and cytological diagnosis

USG Diagnosis and FNAC characteristics		No. of cases (n=200)	Percentage
USG	Colloid goiter	92	46%
	Multinodular goiter	16	8%
	Thyroiditis	24	12%
	Hyperplastic nodule	02	1%
	Thyroglossal cyst	04	2%
	Solitary thyroid nodule	02	1%
	Neoplasm (adenoma and malignancy)	23	11.5%
	Cystic lesion	04	2%
Nature of aspirate	Other non - specific (bulky mass, hyperechoic lesion, hypoechoic lesion)	33	16.5%
	Hemorrhagic aspirate	106	53%
	Blood mixed colloid	34	17%
	Frank colloid	52	26%
Sample adequacy	Serous fluid	08	4%
	Satisfactory	187	93.5%
	Unsatisfactory	13	6.5%

Maximum number of thyroid cases were diagnosed as Colloid goiter (46%) on USG. Thyroiditis was diagnosed in 12% of cases. About 53% thyroid lesions were hemorrhagic, followed by 17% blood mixed colloid and 4% colorless

serous fluid. Sample adequacy was noted in 93.5% cases in our study. The Fine needle aspiration smears which were adequate for evaluation were categorized into non - neoplastic and neoplastic lesions. The non - neoplastic lesions constituted a major proportion (96.37%).

**Table 3:** Distribution of lesions according to the Bethesda system

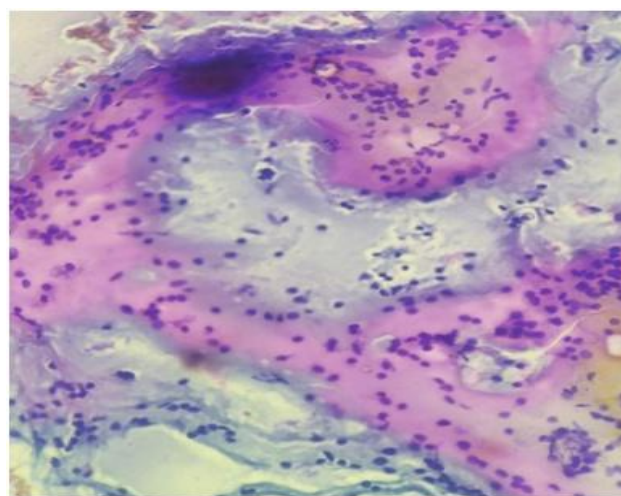
Group	Diagnostic categories	No of cases (n=200)	Percentage
I	“Non - diagnostic or unsatisfactory”	13	6.50
II	“Benign”	163	81.5
III	“Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance”	0	0
IV	“Follicular Neoplasm or Suspicious for a Follicular Neoplasm”: Specified whether Hurthle cell variant	12	6.0
V	“Suspicious for Malignancy”:	0	0
VI	“Malignant”	12	6.0

According to Bethesda system of classification, majority of lesions were benign (81.5%) whereas 6.5% lesions were unsatisfactory. Only 6% lesions were categorised as malignant.

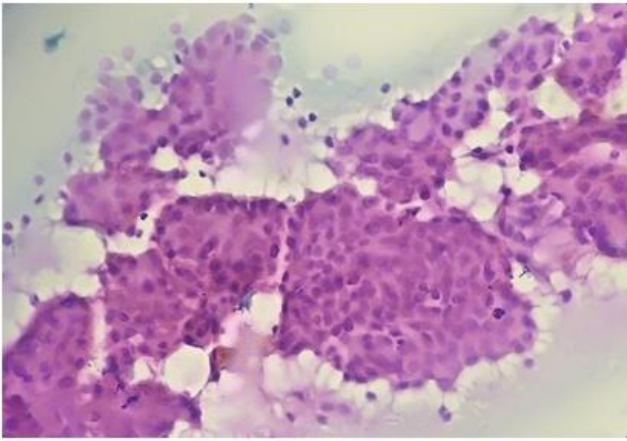
**Table 4:** Distribution of lesions according to various categories of Bethesda

Group	Lesions	No of cases	Percentage
I (n=13)	Hemorrhagic smears	04	30.77
	Cystic lesion	09	69.23
II (n=163)	Colloid goiter	52	31.90
	Colloid goiter with cystic degeneration	42	25.76
	Hyperplastic nodule	37	22.67
	Lymphocytic Thyroiditis including Hashimoto’s thyroiditis	20	12.26
	Subacute Thyroiditis	07	4.29
	Thyroglossal cyst	03	1.84
	Grave’s Disease	01	0.61
	Acute Thyroiditis	01	0.61
IV (n=12)	FN/SFN	12	50
VI (n=12)	Papillary carcinoma	08	66.7
	Medullary carcinoma	02	16.7
	Anaplastic carcinoma	02	16.7

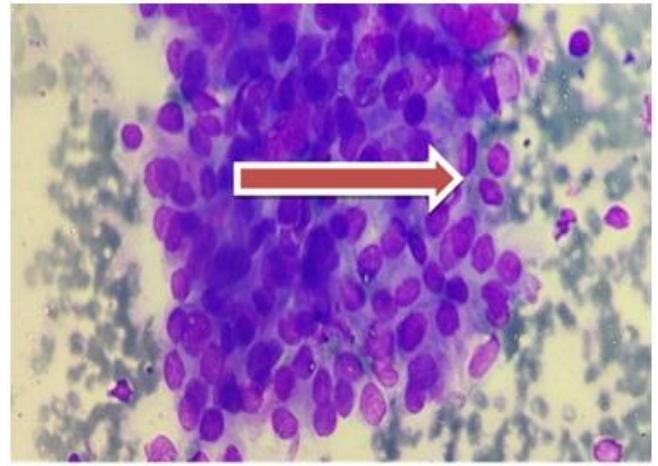
Cystic lesion comprises a major proportion in category - I cases (69.23%). Among category II cases, colloid goiter was maximum with 52 cases followed by colloid goiter with cystic degeneration 42 cases. Among malignant lesions, 66.7% were papillary carcinoma.



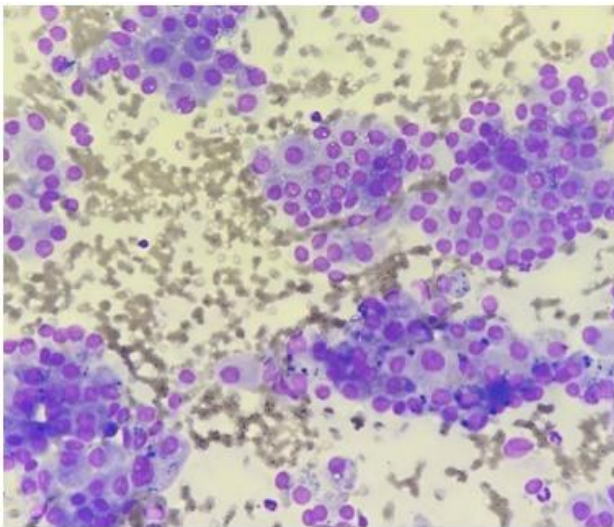
**Figure 2:** Bethesda category - II, Nodular Colloid goitre: - Thyroid follicles with background of abundant colloid.



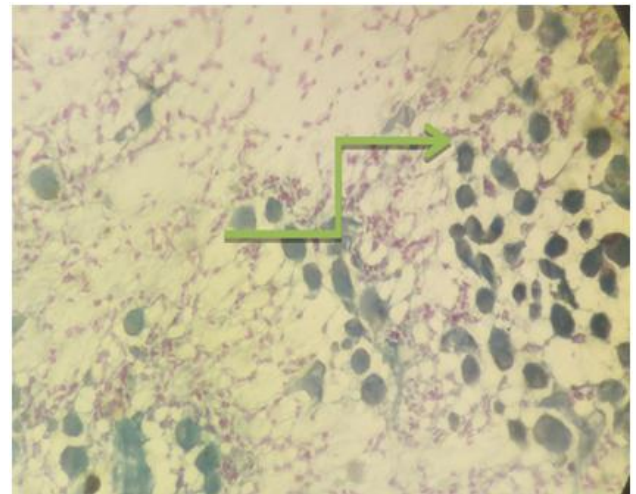
**Figure 3:** Follicular neoplasm: - Microfollicles demonstrate nuclear overlap. Some are loosely cohesive clusters, and there are dispersed, isolated cells (40x)



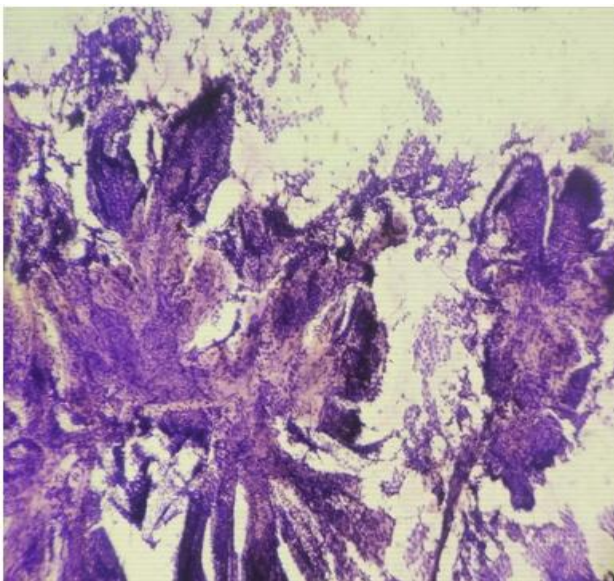
**Figure 6:** Papillary thyroid carcinoma: - Arrow shows nuclear groove



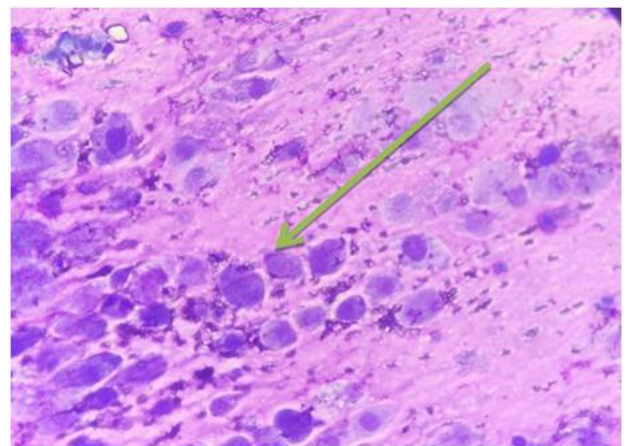
**Figure 4:** Follicular Neoplasm: - The aspirate consists of numerous variably sized groups of crowded Hürthle cells with prominent anisonucleosis. (40x Pap)



**Figure 7:** Medullary carcinoma of thyroid: - Aspirate from 65 year female shows polygonal, plasmacytoid, and spindle shaped noncohesive population of tumor cells



**Figure 5:** Bethesda category - VI: - Papillary thyroid carcinoma. Aspirate from thyroid mass of 58 year female shows true papillary tissue fragments, comprised of fibrovascular cores lined by neoplastic cells



**Figure 8:** Anaplastic thyroid carcinoma. Aspirate from 53 Y/F shows widespread tumor necrosis and associated inflammation. Neoplastic cells are medium - to giant - sized, round to polygonal and spindle - shaped appearance.

#### 4. Discussions

In this study, fine needle aspirations of the thyroid were analyzed and interpreted according to the six - tier category system of Bethesda classification. The Bethesda System for

Reporting Thyroid Cytopathology was modified in 2017 and included a six diagnostic categories. This system was incorporated to maintain uniformity in categorization of thyroid nodular swellings.<sup>[6]</sup> In our study, 200 cases with thyroid nodules were enrolled. Mean age of patients with thyroid nodules was 39.96 years in our study. It is a well-known fact that thyroid lesions are prevalent in females as in our study (5.6 times more as compared to males). In our study, nodular swelling involving right lobe of thyroid were the predominant one (65.5%). Liechty et al<sup>[10]</sup> noticed that there was a predilection for benign and malignant nodules to occur in the right lobe compared to the left lobe. The present study like Sengupta et al<sup>[11]</sup> shows that the right lobe involvement of thyroid lesions was observed maximum in 65.5% cases. The nodule detection by palpation depends on its location within the thyroid gland, on the patient's neck, and early detection yields a better outcome. Hence, we followed the clinical examination by palpation. In our study, the majority of the patients had nodular swelling ranging 1 to 3 cms. The size of the smallest thyroid swelling was 0.5 x 0.5 cms and the largest swelling was 9x 8 cms. We observed that greater the size of nodule higher was the risk of malignancy. In agreement with our result, Kamran et al<sup>[12]</sup> reported that greater nodule size influences cancer risk, although the increase in absolute risk between small (1.0–1.9 cm) and large (4.0 cm) nodules is modest. Notably, a threshold effect is detected at ~2.0 cm in nodule diameter. Thereafter, larger nodule size imparts no further malignant risk, even if 4.0 cm or larger.<sup>[12]</sup> Smith - Bindman et al<sup>[13]</sup> reported that malignancy is more common in thyroid nodules with a diameter of more than 2 cm.

The consistency of normal thyroid is rubbery. In our study, 50% cases had soft consistency of the swelling which is comparable with Kirdak et al.<sup>[14]</sup> In total 24 neoplastic lesions categorized under the Bethesda system (Cat II & Cat IV), 8 cases (33%) had hard thyroid swelling. Here hardness is not conclusive but an important indicator for malignancy. It is supported by various authors.<sup>[15, 16]</sup> The reason for the upward mobility of the neck swellings like thyroid lumps with deglutition is due to the relation of neck swellings to the trachea. If swelling is fixed to the trachea then it will move when the trachea moves. The process of swallowing elevates the trachea. One must observe the neck lump as the patient swallows.<sup>[17]</sup> In our study, 93.5 % of thyroid swelling was mobile with deglutition. Only 13 (6.5%) cases were fixed on palpation in which 10 cases turned out to be malignant.

FNAC will help to avoid unnecessary surgery in patients with benign lesions and to reduce the cost of care, thereby improving the overall quality of life for patients with thyroid nodules. FNAC cannot differentiate follicular adenoma from follicular carcinoma, which is a major limitation of this procedure. In the present study, the majority of patients (85%) have euthyroid status irrespective of the Bethesda category however all cases showing hyperthyroid status were from Category - II and also all hypothyroid cases. All neoplastic lesions were presented as euthyroid status. No significant correlation was found. Aspirate obtained most of the time from thyroid sampling in our study was hemorrhagic (53 %), followed by frank colloid (17%). Jayaram G et al<sup>[18]</sup> suggested that the average number of

needle passes recommended for adequate a sampling of thyroid lumps is two to five. As the thyroid gland is a highly vascular organ, with each impending trauma the chances of aspirating hemorrhagic fluid rises each time, so they advised to keep the number of aspirates to a minimum. Table 5 represents the comparison of Bethesda system with various studies.

**Table 5:** Percentage Comparison of various studies with Bethesda (%)

Studies	I	II	III	IV	V	VI
Yassa et al <sup>[19]</sup>	7	66	4	9	9	5
Nayar et al <sup>[20]</sup>	5	64	18	6	2	5
Mondal et al <sup>[21]</sup>	1.2	87.5	1	4.2	1.4	4.7
Present study	6.50	81.5	0	6	0	6

Histopathological and IHC data were not available of our cases. So Cyto - Histo correlation has not done. It was the major limiting factor of this study.

## 5. Conclusion

FNAC is widely accepted as the most accurate, sensitive, specific, and cost-effective diagnostic procedure in the preoperative assessment of thyroid nodules. It is the first line of investigation and can differentiate benign nodules from malignant nodules of the thyroid in 95% cases. Applying a standard reporting system for thyroid cytology may enhance the communication between pathologists and clinicians, assists them to find out the rate of malignancy in each cytological group, and facilitating a more reliable approach for patient management.

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