Original Article

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Pathology Section

# Cytomorphological Spectrum of Thyroid Lesions Based on Bethesda Reporting System: Diagnostic Utility and Pitfalls

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## ABSTRACT

**Introduction:** Fine Needle Aspiration Cytology (FNAC) is the frontline diagnostic tool in assessing Thyroid enlargement. FNAC is simple, easy to perform, cost effective procedure with rapid diagnosis. Other diagnostic tests like Ultrasound, radionucleotide scanning, Thyroid profile are adjuvant to FNAC which is more reliable.

**Aim:** To categorise the spectrum of Thyroid lesions on FNAC according to the Bethesda system for Reporting Thyroid Cytopathology (TBSRTC) and study its utility and pitfalls.

**Materials and Methods:** This was a retrospective observational study carried out in the Department of Pathology at Government Medical College/Government General Hospital, Mahabubnagar, Telangana, India, from January 2019 to December 2021. The analysis of the data was done from January 2022 to June 2022. FNAC and fine needling was performed in cases of enlarged Thyroid gland, the smears were prepared and fixed in 95% ethyl alcohol, stained with Hematoxylin and Eosin and Papanicolaou stain. Cytohistopathological concordance was done wherever was possible. Sensitivity, Specificity, Positive Predictive value, Negative Predictive value were calculated.

**Results:** Out of 155 cytology cases, 8 cases (5.16%) were unsatisfactory/nondiagnostic, 133 cases (85.80%) were Benign lesions, 8 cases (5.16%) were follicular neoplasm/suspicious for follicular neoplasm, No cases were reported as Atypia of undetermined significance, 3 cases (1.93%) were suspicious for malignancy and 3 cases (1.93%) were malignant. Cytohistopathological concordance was studied in 19 cases. One of the case reported on cytology as Anaplastic carcinoma was referred to higher center for further management.

**Conclusions:** FNAC plays a pivotal role in diagnosis of Thyroid Swellings. The Bethesda system for reporting Thyroid Cytopathology effectively categorises the Thyroid lesions into various sub groups which facilitates better communication between the pathologist and clinician resulting in proper management of the patient. In this study, the number of Benign cases predominated and occurred in females. Cases presenting with nodular lesions, suspicious for malignancy and malignant lesions are advised surgical resection for further evaluation. The Bethesda system was found useful in categorisation of lesions and in advising medical or surgical management, urgency of treatment and the extent of surgery.

**Keywords:** Bethesda system for thyroid cytology, Cytohistological concordance, Fine-needle aspiration cytology

## INTRODUCTION

Enlarged Thyroid gland is one of the routinely encountered condition in the Outpatient Department. The spectrum of Thyroid swellings range from developmental, inflammatory, benign neoplastic to malignant lesions [1]. It is observed that 67% of people with Thyroid nodules are asymptomatic and non-palpable [2]. Various diagnostic modalities employed for assessment of Thyroid swellings include Fine Needle Aspiration Cytology (FNAC), Ultrasound examination, Radionucleotide imaging and Thyroid hormone studies [3]. Various studies conducted reveal that about 42 million people in India suffer from Thyroid diseases comprising about 3.2% of general population as per Unnikrishnan AG and Menon UV, [4]. Thyromegaly is commonly seen in females and various factors contributing to Thyromegaly include iodine deficiency, radiation exposure, goitrogenic diet. Various diagnostic modalities employed for Thyroid assessment like Physical examination, ultrasound examination are not very reliable due to pitfalls [5]. Thyroid FNAC is a commonly used first line investigation in assessment of Thyroid swellings as it is a simple, quick, safe, cost effective and minimally painless technique with a quick turn around time. FNAC of Thyroid swellings has a sensitivity of 89 to 98% and Specificity of 92% in the diagnosis of Thyromegaly [6]. FNAC of Thyroid swellings has both therapeutic and diagnostic utility [7].One of the biggest advantages of FNAC is that by rendering a diagnosis as benign or malignant on FNAC unnecessary surgery can be spared in benign patients and appropriate management can be advised preventing considerable morbidity [8]. FNAC of Thyroid when used as an adjunct with ultrasound helps in detection and aspiration of smaller and deep seated Thyroid lesions which leads to early diagnosis of Thyroid cancers [9]. It is observed that the incidence of Thyroid malignancy is relatively low and only 1 in 20 clinically identified nodules are malignant, hence Thyroid Fine Needle Aspiration Cytology (FNAC) can help to reduce the rate of surgery for benign Thyroid disease [10]. It has been observed that in Thyroid cytopathology, there is an area of obscurity or a grey zone where a proper categorisation of lesion is difficult. There is a considerable disparity in the terminologies used for reporting Thyroid cytopathology in various institutes which has lead to confusion at times and difficulty in data sharing among cytopathologists working in various institutes [11,12]. This led to the introduction of "The Bethesda System for Reporting Thyroid Cytopathology" (TBSRTC) to improve communication between Pathologists and clinicians [13,14]. The Bethesda System for Reporting Thyroid Cytopathology" (TBSRTC) comprises of definitions, diagnostic criteria, explanatory notes, and a management proposition for each diagnostic category [14].

The aim of the present study was to study the spectrum of Thyroid lesions in our institute and categorise them according to The Bethesda System for Reporting Thyroid Cytopathology, to study its utility and pitfalls, to do Cytohistopathological Concordance and calculate sensitivity, specificity, positive predictive value and negative predictive value.

## MATERIALS AND METHODS

The present study was a retrospective study done at Government Medical College/Government General Hospital, Mahabubnagr, Telangana, India. All Cytological Cytopathology reports of Fine Needle Aspiration Cytology of Thyroid cases issued from January 2019 to December 2021 were retrieved and reviewed from Cytology archives.The duration of study was for a period of six months from January 2022 to June 2022. The study was approved by Institutional Ethical Committee (RcNo:GMCMBNR/IECBMR/AP/1/6/22).

**Inclusion criteria:** All cases with Thyroid enlargement moving with deglutition in the thyroid region, irrespective of the cellularity, T3, T4, TSH findings, lateral aberrant thyroid, those cases with repeat aspirations and aspiration under guidance were included in the study.

**Exclusion criteria:** All palpable swellings in neck other than Thyroidal region and those cases of Histopathology where corresponding cytology is not available or not done were excluded from the study.

### Procedure

A brief clinical history followed by physical examination was carried out in all the cases presenting with Thyroid swelling. The site of Thyroid swelling was first cleaned with a spirit swab and FNAC was performed by aspiration and non aspiration technique or fine needle sampling technique.The aspirated material was blown on a clean glass slides and with the help of spreader slide Smears were prepared. Out of a total of 155 cases of cytology 19 cases had histopathology.

The smears were fixed in 95% ethanol, stained with Hematoxylin, Eosin and Papanicolaou stain. Slides were throughly examined for celluarity, background, nuclear and cytoplasmic features.In clinically nodular lesions,diffuse lesions and in multinodular lesions aspiration was done from different sites. In cystic lesions, fluid was evacuated and re-aspiration was done. Any fluid obtained was centrifuged and smears were made. Ultrasound guided aspiration was done whenever required. All the Thyroid lesions were categorised according to The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) which includes:

- Category I-Non-diagnostic or Unsatisfactory
- Category II-Benign
- Category III-Atypia of undetermined significance/Follicular lesion of undetermined significance (AUS/FLUS)
- Category IV-Follicular neoplasm/Suspicious for follicular neoplasm (SFN)
- Category V-Suspicious for malignancy (SFM)
- Category VI-Malignant

## STATISTICAL ANALYSIS

The results were analysed using descriptive statistics and Sensitivity, Specificity, Positive Predictive value, Negative Predictive value were calculated using open source epidemiologic statistics for public health, open Epi software version 3.01.

## RESULTS

The spectrum of Thyroid lesions in all the categories are described in [Table/Fig-1]. A total of 155 Thyroid lesions were studied and categorised as per The Bethesda System for Reporting Thyroid Cytopathology. Out of the 155 cases, 145 were females and 10 were males with a female to male ratio of 14.5:1. The youngest patient was female child of 9 years with Hashimoto Thyroiditis. The oldest patient was 76 years female patient with Anaplastic carcinoma. Most common age group affected with Thyroid lesions was 2nd to 3rd decade [Table/Fig-2]. The most common Thyroid lesion was Hashimotos Thyroiditis which was most commonly seen in 3rd to 4th decade. Least common age group affected was less than10 years. In this study, no cases were encountered above the age of 80 years. Cytohistopathological concordance was seen in 15 cases. [Table/Fig-3] and discordance in 4 cases [Table/Fig-4]. Based on analysed cytohistopathological data, the sensitivity and specificity of Follicular Neoplasm (FN) excluded, FN included as benign as well as malignant was calculated [Table/Fig-5].

| Bethesda diagnostic category | | Total |
|---|---|---|
| I | Nondiagnostic or Unsatisfactory (Nd) | 8 (5.16%) |
| II | Benign (BN) | 133 (85.80%) |
| | Colloid goitre | 24 |
| | Nodular goitre with cystic change | 3 |
| | Toxic goitre | 2 |
| | Nodular goitre | 37 |
| | Acute thyroiditis | 1 |
| | Hashimotos thyroiditis | 42 |
| | Adenamatoid goitre | 4 |
| | Lymphocytic thyroiditis | 2 |
| | Nodular hyperplasia | 5 |
| | Colloid cyst | 10 |
| | Benign follicular lesion | 3 |
| III | Atypia of undetermined significance (AUS) or Follicular lesion of undetermined significance (FLUS) | 0 |
| IV | Follicular neoplasm or suspicious for follicular neoplasm (FN/SFN) | 8 (5.16%) |
| V | Suspicious for malignancy (SM) | 3 (1.93%) |
| | Suspicious for Papillary carcinoma | 2 |
| | Suspicious for Anaplastic carcinoma | 1 |
| VI | Malignant (M) | 3 (1.93%) |
| | Papillary carcinoma | 2 |
| | Anaplastic carcinoma | 1 |
| | Total number of cases | 155 |

**[Table/Fig-1]:** Distribution of cases as per The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).

| Lesions | Age (Years) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | <10 yrs | 11-20 yrs | 21-30 yrs | 31-40 yrs | 41-50 yrs | 51-60 yrs | 61-70 yrs | 71-80 yrs | Total |
| • **Nondiagnostic or unsatisfactory (ND)** | 0 | 1 | 2 | 2 | 3 | - | - | - | 8 |
| • **Benign (133)** | | | | | | | | | |
| Goitre (88) | | | | | | | | | |
| Benign Follicular Lesion | - | - | 1 | 1 | 1 | -- | - | - | 3 |
| Colloid goitre | - | 2 | 11 | 4 | 6 | 1 | - | - | 24 |
| Colloid cyst | - | - | 4 | 1 | 3 | 1 | 1 | - | 10 |
| Nodular goitre | - | 4 | 11 | 10 | 8 | 2 | 2 | - | 37 |
| Nodular goitre with cystic change | - | - | 1 | | 1 | 1 | - | - | 3 |
| Nodular hyperplasia | | 2 | -1 | - | 2 | - | - | - | 5 |
| Adenamatoid goitre | -- | - | 1 | 2 | 1 | - | - | - | 4 |
| Toxic Goitre | - | - | - | 2 | - | -- | - | - | 2 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| • **Thyroiditis (45)** | | | | | | | | | |
| Hashimotos thyroiditis | 1 | 6 | 14 | 15 | 5 | 1 | - | - | 42 |
| Lymphocytic thyroiditis | | - | - | 1 | 1 | - | - | - | 2 |
| Acute thyroiditis | - | - | 1 | - | - | - | - | - | 1 |
| • **ATUS** | - | - | - | - | - | - | - | - | 0 |
| • **FN(8)** | - | - | 3 | 3 | 1 | - | 1 | - | 8 |
| • **Suspicious for malignancy (3)** | - | 1 | 1 | - | - | - | - | 1 | 3 |
| Malignant (3) | - | - | - | - | -- | 1 | 1 | 1 | 3 |
| Total | 1 | 16 | 51 | 41 | 32 | 7 | 5 | 2 | 155 |
| Percentage | 0.64 | 10.3 | 32.90 | 26.45 | 20.64 | 4.57 | 3.22 | 1.2 | 100 |

**[Table/Fig-2]:** Age distribution of thyroid lesions.

| S no. | Age/Sex | Cytology | Histopathology |
|---|---|---|---|
| 1 | 35/F | Nodular Goitre | Multinodular Goitre with Colloid cyst |
| 2 | 47/F | Nodular Goitre | Multinodular Goitre |
| 3 | 48/F | Nodular Goitre | Multinodular Goitre |
| 4 | 41/M | Nodular Goitre | Multinodular Goitre |
| 5 | 33/F | Nodular Goitre | Multinodular Goitre |
| 6 | F/39 | Follicular neoplasm | Follicular Adenoma |
| 7 | F/27 | Follicular neoplasm | Follicular Adenoma |
| 8 | F/35 | Follicular neoplasm | Follicular Adenoma |
| 9 | F/43 | Follicular neoplasm | Follicular Adenoma |
| 10 | F/68 | Follicular neoplasm | Follicular Carcinoma |
| 11 | F/27 | Hurthle cell neoplasm | Hurthle cell adenoma |
| 12 | F/16 | Suspicious of Papillary Carcinoma | Papillary Carcinoma |
| 13 | F/26 | Suspicious of Papillary carcinoma | Papillary Carcinoma |
| 14 | F/65 | Papillary Carcinoma | Papillary Carcinoma |
| 15 | F/56 | Papillary Carcinoma with Cystic change | Intra cystic papillary carcinoma |

**[Table/Fig-3]:** Case wise cytohistpathological concordance.

| S no | Cytology | Histopathology |
|---|---|---|
| 1 | Papillary Hyperplastic nodular Goitre (CAT II) | Papillary carcinoma |
| 2 | Follicular neoplasm (CAT IV) | Nodular hyperplasia |
| 3 | Follicular neoplasm (CAT IV) | Nodular hyperplasia |
| 4 | Suspicious of Anaplastic Carcinoma (CAT V) | Hashimotos thyroiditis |

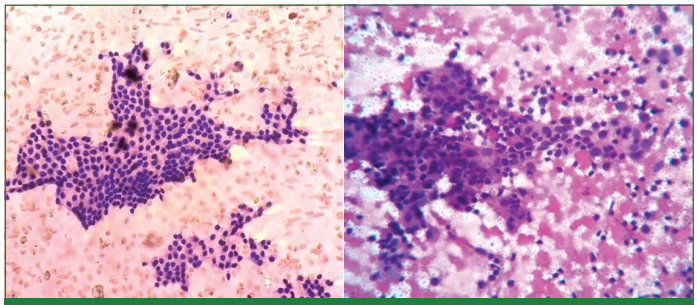
**[Table/Fig-4]:** Cytohisto pathological discordance.

| Criteria | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|
| FN excluded | 80 | 83.33 | 80 | 83.33 |
| FN included as benign | 66.67 | 92.31 | 80 | 85.71 |
| FN included as malignant | 83.33 | 38.46 | 38.46 | 83.33 |

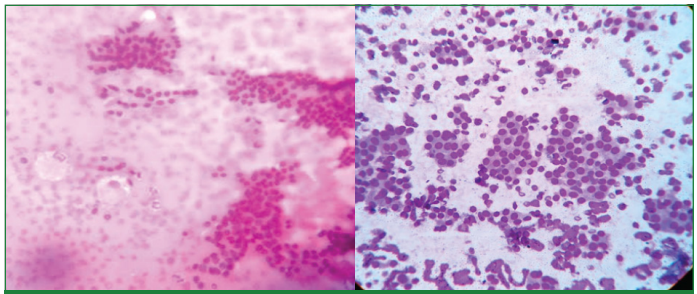
**[Table/Fig-5]:** Statistical parameters of present study.

A total of 8 cases (5.16%) were unsatisfactory for evaluation (Category I) which showed blood cellular elements and sparse cellularity on repeated aspirations. Simple colloid goiter [Table/Fig-6] with diffuse enlargement were under observation and treated medically. Diffuse Toxic Goitre with repeated T3,T4,TSH assays were managed medically by anti-thyroid drugs. Benign lesions (Category II) was the largest comprising of 133 cases (85.80%) followed by Follicular neoplasm/Suspicious of Follicular neoplasm (Category IV) accounting for 8 cases (5.16%), 3 cases (1.93%) each were noted as suspicious for malignancy (Category V) and malignant categories (Category VI). In the present study, Aypia of undermined significance (Category IV) was not reported. Most common Thyroid malignancy was Papillary carcinoma seen most commonly in 5$^{th}$ to 7$^{th}$ decade. Most common lesion less than 20 years was Hashimoto Thyroiditis. In the Non diagnostic category, all the cases on repeated aspirations yielded blood cellular elements only.

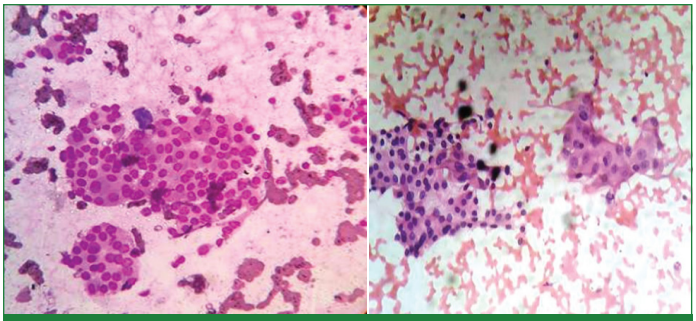
In The Benign Category, the majority of cases were of Hashimoto Thyroiditis (42 cases) in which follicular cells showed Askanazy cell change (Hurthle cell change) with lymphocytes impinging on the Thyroid epithelial cells [Table/Fig-7]. The next common category was of Nodular Goitre (37 cases) which showed sheets and clusters of Thyroid acinar epithelial cells admixed with cyst macrophages [Table/Fig-8]. 24 cases were diagnosed as Colloid goitre which showed predominantly colloid with Thyroid epithelial cells. A total of 7 cases of Follicular neoplasm were noted which had high cellularity comprising of Thyroid acinar epithelial cells arranged in repetitive micro follicular pattern with scant colloid [Table/Fig-9,10]. A single case comprising of cellular aspirate showed abundant Hurthle cells was reported as Hurthle cell neoplasm. Two cases were reported as suspicious for papillary carcinoma with high cellularity, Papillary patterns but paucity of nuclear enlargement, grooves, overlapping and/or pseudo-inclusions and one case with nuclear atypia was reported as suspicious for Anaplastic carcinoma. Two cases were diagnosed as Papillary carcinoma of Thyroid which showed true Papillary configuration, cellular crowding, nuclear grooving, powdery chromatin and intra-nuclear pseudo-inclusions [Table/Fig-11,12]. One case was reported as Anaplastic carcinoma with cells showing marked pleomorphism and tumour diathesis. The study is continued further prospectively for better understanding of Thyroid cytopathology.



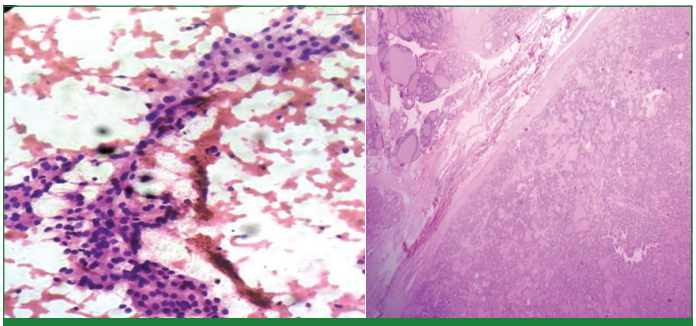
**[Table/Fig-6]:** Photomicrograph of FNAC smears show sheets Thyroid follicular epithelial cells with Benign morphology-Simple Goitre (Category II) (H&E stain 10x magnification). **[Table/Fig-7]:** Photomicrograph of FNAC smears show Thyroid Follicle cells with Askanazy cell change and Lymphocyte infiltration:Hashimotos Thyroiditis (Category II)(H&E stain 40x magnification). (Images from left to right)



**[Table/Fig-8]:** Photomicrograph of FNAC smears show sheets Thyroid follicular epithelial cells with Benign morphology and cyst macrophages-Nodular Goitre (Category II) (H&E stain 10x magnification). **[Table/Fig-9]:** Photomicrograph of FNAC smears show follicular cells in repetitive follicle pattern: Follicular Neoplasm (Category IV) (H&E stain 40x magnification). (Images from left to right)

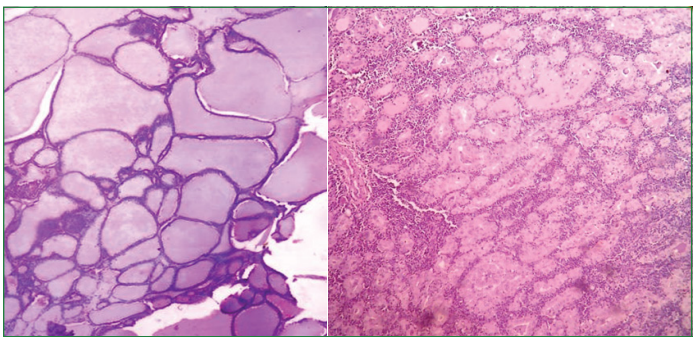


**[Table/Fig-10]:** Photomicrograph of FNAC smears show follicular cells in repetitive follicle pattern: Follicular Neoplasm (Category IV) (H&E stain 40x magnification). **[Table/Fig-11]:** Photomicrograph of FNAC smears show Thyroid follicular cells in papillary pattern with intra nuclear inclusions and nuclear grooving:Papillary Carcinoma (Category VI). (Images from left to right)



**[Table/Fig-12]:** Photomicrograph of FNAC smears show Thyroid follicular cells in papillary pattern with intra nuclear inclusions and nucleargrooving: Papillary Carcinoma Thyroid (Category VI) (H&E stain 40x magnification). **[Table/Fig-13]:** Photomicrograph showing Thyroid follicles lined by hyperplastic epithelium with epithelium: Nodular Goitre (H&E 10x Magnification). (Images from left to right)

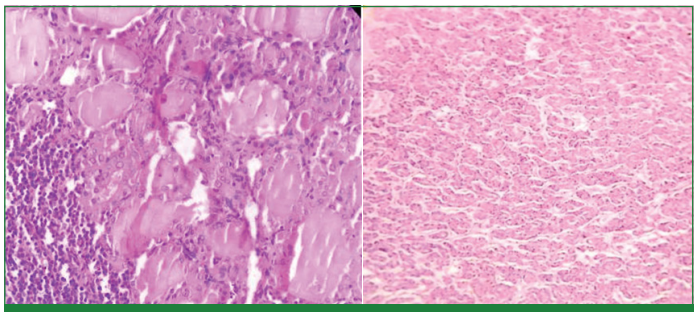
A total of 19 resected Thyroid specimens were received for histopathological examination. Out of these 19 cases, 15 cases showed cytohistopathological concordance and 4 cases showed cytohistopathological discordance.Cytohistopathological concordance could be done in 5 cases of category II diagnosed as Nodular goitre on Cytology which were diagnosed as Multi nodular goitre on Histopathology [Table/Fig-13]. Two cases diagnosed as follicular neoplasm on Cytology were reported as Nodular Hyperplasia on Histopathology [Table/Fig-14]. A diagnosis of Follicular neoplasm was given in one case showing large nucleus and mega nucleolus on FNAC and it turned to be Follicular carcinoma on histology. One case showed about 80%. Hurthle cell neoplasm on Cytology cells and was reported as Hurthle cell adenoma on histopathology.



**[Table/Fig-14]:** Photomicrograph showing thyroid follicles of varying sizes lined by flattened Overlying capsule: Hyperplastic nodule (H&E 10x Magnification). **[Table/Fig-15]:** Photomicrograph showing Thyroid follicles lined by Hurtle cells admixed with Lymphoid infiltrate: Hashimotos thyroiditis (H&E 10x Magnification). (Images from left to right)

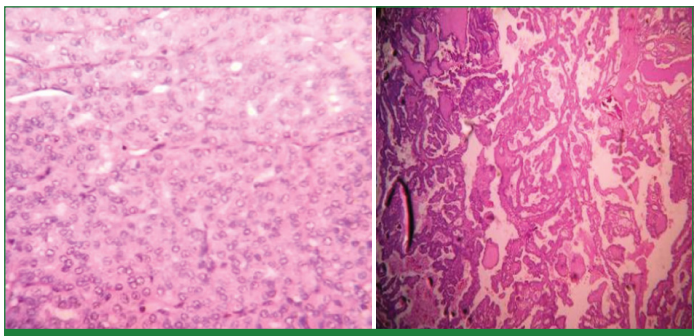
On Cytohistopathological Concordance the case reported as Suspicious of Anaplastic Carcinoma on cytology turned out to be Hashimotos Thyroiditis on Histopathology [Table/Fig-15,16]. The smears on Cytology showed thyroid epithelial cell atypia without lymphocytes in background. The degeneration atypia in Hashimotos Thyroiditis was mistaken. One case reported as Papillary Hyperplastic nodular goiter on cytology turned out to be Papillary carcinoma on Histopathology, these cases were resected.

In TBSRTC category IV 4 cases diagnosed as Follicular neoplasm on cytology were diagnosed as Follicular adenoma on Histopathology [Table/Fig-17,18].

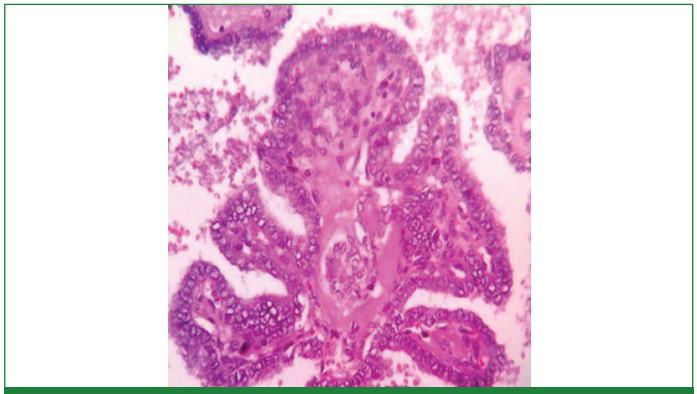


**[Table/Fig-16]:** Photomicrograph showing Thyroid follicles lined by Hurtle cells admixed with Lymphoid infiltrate:Hashimotos Thyroiditis (H&E- 40xMagnification). **[Table/Fig-17]:** Photomicrograph showing Thyroid follicles arranged in microfollicularPattern: Follicular Adenoma (H&E- 10x & 40xMagnification). (Images from left to right)

Two cases reported as suspicious of Papillary Carcinoma on Cytology correlated with Histopathology.In the Malignant Category two cases of Papillary Carcinoma on Cytology turned out to be Papillary Carcinoma on histopathology [Table/Fig-19,20]. One of the case presented as Cystic lesion, cyst fluid was aspirated,centrifuged smear showed papillary fragments. The cyst was evacuated, repeat aspiration was done in same sitting, smears studied show features of papillary Carcinoma and the report was issued as Cystic papillary carcinoma. Hence all cystic lesions should be evaluated for Papillary carcinoma. One more case which was reported as Anaplastic Carcinoma on Cytology was referred to Higher center. Cases reported as Papillary Carcinoma on FNAC were advised Total Thyroidectomy. We found recurrence of Papillary Carcinoma when Hemithyroidectomy was done on follow-up. All nodular lesions irrespective of cytological diagnosis were advised lobectomy for histopathological diagnosis. Cases diagnosed in Category IV (Follicular neoplasm/Suspicious for Follicular neoplasm) and were advised lobectomy All the cases suspicious for malignancy (category V) or malignancy (category VI) on cytology were advised single stage Total Thyroidectomy.



**[Table/Fig-18]:** Photomicrograph showing Thyroid follicles arranged in microfollicular Pattern: Follicular Adenoma (H&E- 10x & 40x Magnification). **[Table/Fig-19]:** Photomicrograph showing Thyroid tissue arranged in Papillary configuration with Fibrovascular core: Papillary Carcinoma (H&E-10x Magnification). (Images from left to right)



**[Table/Fig-20]:** Photomicrograph showing Thyroid tissue arranged in Papillary configuration lined by optically clear nuclei: Papillary carcinoma (H&E-40x Magnification).

## DISCUSSION

Cytology is the first line of investigation in the evaluation of Thyroid lesions. This Bethesda reporting system acts as a bridge between the cytopathologist, Physician, Surgeon, endocrinologist in understanding Thyroid and management protocol [13]. In the present study, the cytopathological spectrum of Thyroid lesions was studied and categorised according to the TBSRTC. Cytohistopathological concordance was done [14-16].

The mean age in the present study was 35.75. Females outnumbered males in this study with a ratio of 14.5:1 which is comparable with studies of Renuka IV et al., [17] Bamanikar S et al., [18] and Silvermann JF et al., [19] which had female to male ratio 9:1, 8.6:1 and 10.8:1 respectively. In this study a total of 8 cases (5.16%) were diagnosed as unsatisfactory for evaluation. According to TBSRTC for a Thyroid FNA specimen to be satisfactory for evaluation, at least six groups of benign follicular cells are required, each group composed of at least 10 cells with some exceptions like presence of abundant colloid in the smears or features of atypia [14]. In this study the category II or Benign category dominated the picture with 133 cases (85.80%) of the cases which was similar to Pattanashetti MA et al., [15], Jaiswal YP and Chawhan S, [16] Mehra P and Verma AK, [8] whose studies also showed female preponderance. According to Bethesda System the recommendations for Benign category include ultrasound and clinical follow-up, avoiding unnecessary surgery. Among the Benign category Hashimotos Thyroiditis (42/155) was the most common entity followed by Nodular goiter while Pattanashetti MA et al., [15] the commonest category was Simple Colloid Goitre (79/173) followed by Colloid goiter with Cystic Change. The other lesions in the benign category are Colloid goiter, Nodular Goitre with cystic change, Toxicgoiter, Acute Thyroiditis, Adenamatoid goiter, Lymphocytic Thyroiditis, colloidcyst, Nodular Hyperplasia, Benign follicular nodule. There were no cases of Atypia of undetermined significance in this study which was similar to Pattanashetti MA et al., [15], while Jaiswal Y and Chawhan S, [16] and Mehra P and Verma AK, [8] reported 15 and 5 cases in their studies respectively. This study showed 8 cases of follicular neoplasm or suspicious of follicular neoplasm/Hurthle cell neoplasm accounting for 5.16% which was similar to Pattanashetti MA et al., [15] who documented 9 cases accounting for 5.20%, Mehra P and Verma AK, [8] study showed 5 cases (2.2%) while Jaiswal YP and Chawhan S, [16] showed 15 (7.14%) cases. This study showed 3 cases (1.93%) suspicious for malignancy while Pattanashetti MA et al., [15], Jaiswal Y and Chawhan S, [16] and Mehra P and Verma AK, [8] studies revealed 1 cases (0.57%), 7 (3.33%) and 8 cases (3.6%) respectively. There were 3 cases (1.93%) of malignancy of Thyroid in this study which was less than in other studies like Pattanashetti MA et al., [15], Jaiswal YP and Chawhan S, [16] and Mehra P and Verma AK, [8] who reported 9 cases (5.20%), 11 cases (5.23%), 5 cases (2.2%) in the malignant category respectively [Table/Fig-21-23].

| Lesions | Mehra P and Verma AK, [8] (2015) N=225 | Pattanashetti MA et al., [15] (2017) N=173 | Jaiswal YP and Chawhan S, [16] (2020) N=210 | Present study N=155 |
|---|---|---|---|---|
| Non diagnostic/ Unsatisfactory | 16 (7.2%) | 9 (5.20%) | 13 (8.66%) | 8 (5.16%) |
| Benign | 180 (80%) | 145 (83.81) | 150 (71.42%) | 133 (85.80%) |
| ATUS | 11 (4.9%) | 0 | 14 (6.66%) | 0 |
| Follicular neoplasm | 5 (2.2%) | 9 (5.20%) | 15 (7.14%) | 8 (5.16%) |
| Suspicious for malignancy | 8 (3.6% | 1 (0.57%) | 7 (3.33%) | 3 (1.93%) |
| Malignant | 5 (2.2%) | 9 (5.20%) | 11 (5.23%) | 3 (1.93%) |

**[Table/Fig-21]:** Comparison to other studies; The procedure of data analysis might change the results of statistical variables.
*2015: Department of Pathology, ESI Postgraduate Institute of Medical Sciences and Research and ESI Model Hospital, Basai, Darapur, New Delhi; **2017: Department of Pathology, S. Nijalingappa Medical College, Bagalkot, Karnataka; ***2020: Department of Pathology, Government Medical College, Gondia, Maharashtra

| Study | Number | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|---|
| Al-Sayer HM et al., [20] 1985, Aberdeen Thyroid clinic, Scotland | 70 | 86 | 93 | 80 | 96 |
| Silverman JF et al., [19], 1986, East Carolina University School of Med- icine, Greenville, North Carolina. | 309 | 93 | 96.5 | 88.9 | 96.5 |
| Cusick EL et al., [21] 1990, Thyroid clinic in Grampian region. | 283 | 76 | 58 | 72 | 64 |
| Altavilla G et al.,[22] 1990, Institute of Pathology, University of Ferrara, Italy | 257 | 71.4 | 100 | 100 | 94.4 |
| Bouvet M et al., [23] 1992, Department of Surgery, University of California San Diego Medical Center | 78 | 93.5 | 75 | 85.3 | 88.2 |
| Kessler A et al., [24] 1992, Assaf Harofeh Medical Center, Zerifin, Israel | 170 | 79 | 98.5 | 98.7 | 76.6 |
| Ko HM et al., [25] 2003, Department of Pathology, Chonnam National University Hospital | 207 | 78.4 | 98.2 | 99 | 66.3 |
| Handa U et al., [26] 2008, Government Medical College and Hospital, Chandigarh, India | 66 | 97 | 100 | 96 | 100 |
| Gupta M et al., [27] 2010,Government Medical College Jammu, and Department of ENT, SMGS Hospital, Jammu (India) | 75 | 80 | 86.6 | 80 | 86.6 |
| Present study (FN/SFN excluded) | 19 | 80 | 83.33 | 80 | 83.33 |
| Present study (FN/SFN included as benign) | 19 | 66.67 | 92.31 | 80 | 85.71 |
| Present study(FN/SFN included as Malignant) | 19 | 83.33 | 38.46 | 38.46 | 83.33 |

**[Table/Fig-22]:** Comparison of results of the present study and random studies over the last 30 years [19-27, present study].

| Studies | Criteria | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---|---|---|---|---|---|
| Mehra P and Verma AK, [8], 2015, Department of Pathology, ESI postgraduate Institute of Medical Sciences and Research and ESI Model Hospital, Basai, Darapur, New, Delhi. | FN excluded | 76.92 | 88.46 | 76.92 | 88.46 |
| | FN includedas benign | 73.33 | 89.66 | 78.57 | 86.67 |
| | FN included as malignant | 78.57 | 81.25 | 64.71 | 89.66 |
| Kulkarni C et al., [28], 2016, Department of Pathology, M.G.M. Medical College, Indore (M.P.), India | FN excluded | 100 | 100 | 100 | 100 |
| | FN included as benign | 66.7 | 100 | 100 | 92.9 |
| | FN included as malignant | 75.0 | 75.0 | 50.0 | 90.0 |
| Gupta C et al., [29], 2019, Department of Pathology, Government Medical College, Jammu, Jammu and Kashmir, India | FN excluded | 100 | 100 | 100 | 100 |
| | FN included as benign | 80 | 100 | 100 | 96 |
| | FN included as malignant | 100 | 95.83 | 83.33 | 100 |
| Present study | FN excluded | 80 | 83.33 | 80 | 83.33 |
| | FN included as benign | 66.67 | 92.31 | 80 | 85.71 |
| | FN included as malignant | 83.33 | 38.46 | 38.46 | 83.33 |

**[Table/Fig-23]:** Comparison of results of the present study and other studies.
PPV: Positive predictive value; NPV: Negative predictive value

The sensitivity increases and the specificity decreases when suspicious lesions are considered positive. The sensitivity decreases and the false negative rates increases when suspicious lesions are excluded. “SFM” and “malignant” are taken as malignant for statistical analysis. Non diagnostic or unsatisfactory category are excluded from stastistical analysis. Hence cytohistopathological correlation could not be made in those cases. Repeat aspiration by two Pathologists improved the diagnosis.

## CONCLUSION(S)

The TBSRTC is a system which categorises the Thyroid lesions and provides management options. All nodular lesions irrespective of cytological diagnosis were advised lobectomy for histopathological diagnosis which is gold standard since there are false positives and false negatives. In this study, no cases were reported in Category III (Atypia of undetermined significance/Follicular lesion of undetermined significance). Such cases were diagnosed in Category IV (Follicular neoplasm/Suspicious for Follicular neoplasm) and were advised lobectomy and in Category V (Suspicious for malignancy) were advised Total Thyroidectomy. All the cases suspicious for malignancy or malignancy on cytology were advised single stage Total Thyroidectomy to avoid recurrence while the TBSRTC recommends lobectomy/near total thyroidectomy. We conclude that FNAC with TBSRTC system is an efficient tool in diagnosing,categorizing and deciding the line of management of Thyroid lesions.

### Limitations

The limitations of this study were inadequate aspirate,skill of the performing pathologist and cases being referred to higher center for surgical excision.

## REFERENCES


[1] Gupta A, Jaipal D, Kulhari S, Gupta N. Histopathological study of thyroid lesions and correlation with ultrasonography and thyroid profile in western zone of Rajasthan, India. Int J Res Med Sci. 2016;4(4):1204-08.

[2] Wong LQ, Baloch ZW. Analysis of the Bethesda System for reporting Thyroid Cytopathology and Similar Precursor Thyroid Cytopathology Reporting Schemes. Adv Anat Pathol. 2012;19(5):313-19.

[3] Guhamallick M, Sengupta S, Bhattacharya NK, Basu N, Roy S, Ghosh AK, M Chowdhury. Cytodiagnosis of Thyroid lesions-usefulness and pitfalls: A study of 288 cases. J Cytol. 2008;25(1):6-9.

[4] Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab. 2011;15(Suppl 2):S78-81.

[5] Kumar M, Potekar R, Yelikar BR, Patil V, Karigoudar M, Pande P, et al. Diagnostic accuracy of frozen section in comparison with fine needle aspiration cytology in Thyroid lesions: A prospective study. Iran J Pathol. 2013;8(4):219-26.

[6] Ucler R, Usluogulları CA, Tam AA, Ozdemir D, Balkan F, Yalcın S, et al. The diagnostic accuracy of ultrasound-guided fine-needle aspiration biopsy for Thyroid nodules three centimeters or larger in size. Diagn Cytopathol. 2015;43(8):622-28.

[7] Grace MK. Role of Fine needle aspiration cytology in the diagnosis of Thyroid lesions. JR SOC Med. 1998(33);91:28-32.

[8] Mehra P, Verma AK. Thyroid cytopathology reporting by the bethesda system: a two-year prospective study in an academic institution. Patholog Res Int. 2015;2015:240505. doi: 10.1155/2015/240505. Epub 2015 Jan 22. PMID: 25688327; PMCID: PMC4320899.

[9] Davies L, Welch HG. Increasing incidence of Thyroid cancer in the United States, 1973-2002. JAMA. 2006;295:2164-67.

[10] Anil G, Hegde A, Chong FH. Thyroid nodules: risk stratification for malignancy with ultrasound and guided biopsy. Cancer Imaging. 2011;11(1):209-23. Published 2011 Dec 28. doi:10.1102/1470-7330.2011.0030

[11] Cibas ES. Fine needle aspiration in the workup of Thyroid nodules. Otolaryngol Clin North Am. 2010;43(2):257-71.

[12] Park JH, Kim HK, Kang SW, Jeong JJ, Nam KH, Chung WY, et al. Second opinion in Thyroid fine needle aspiration biopsy by the Bethesda System. EndocrJ. 2012;59(3):205-12.

[13] Zarif HA, Ghandurah SE, Al-Garni MA, Binmahfooz SK, Alsaywid BS, Satti MB, et al. Thyroid nodules cytopathology applying the bethesda system with histopathological correlation. Saudi J Med Med Sci. 2018;6(3):143-48

[14] Cibas ES, Ali SZ. The 2017 Bethesda System for Reporting Thyroid Cytopathology. Thyroid. 2017;27(11):1341-46. doi: 10.1089/thy.2017.0500. PMID: 29091573.

[15] Pattanashetti MA, Kangle RP, Bannur HB, Spectrum of Thyroid lesions in a tertiary care hospital using Bethesda System for Reporting Thyroid Cytopathology, Annals of Pathology and Laboratory Medicine. 2017;A279-A283. 10.21276/APALM.1340.

[16] Jaiswal Y, Chawhan S. The spectrum of Thyroid lesions on fine needle aspiration cytology. International Journal of Research in Medical Sciences. 2020;8(2):630-35.

[17] Renuka IV, Bala GS, Aparna C, Kumari R, Sumalatha K. The Bethesda System for Reporting Thyroid Cytopathology: Interpretationand Guidelines in Surgical Treatment. Indian J Otolaryngol HeadNeck Surg. 2012;64(4):305-11.

[18] Bamanikar S, Bamanikar A, Jadhav S, Jadhav P, Kumar H, Soraisham P, et al. Cyto-histology and clinical correlation of Thyroid gland lesions:A 3 year study in a tertiary hospital. Clin Cancer Investig J.2014;3(3):208-12.

[19] Silverman JF,West RL, Larkin EW, Park HK, Finley JL, Swanson MS,et al. The role of fine-needle aspiration biopsy in the rapid diagnosisand management of Thyroid neoplasm. Cancer. 1986;57(6):1164-70.

[20] H.M.Al-Sayer,Z.H.Krukowski,V.M.M.Williams,andN.A. Matheson,“Fineneedleaspirationcytologyinisolated thyroid swellings: a prospective two year evaluation,” British Medical Journal, vol. 290, no. 6480, pp. 1490-1492, 1985

[21] Cusick EL, MacIntosh CA, Krukowski ZH, Williams VMM, Ewen SWB, Matheson NA, et al. Management of isolated thyroid swelling: a prospective six year study of fine needle aspiration cytology in diagnosis. British Medical Journal. 1990;301(6747):318-21.

[22] Altavilla G, Pascale M, Nenci I. Fine needle aspiration cytology of thyroid gland diseases. Acta Cytol. 1990;34(2):251-56.

[23] Bouvet M, Feldman JI, Gill GN, Dillmann WH, Nahum AM, Russack V, et al. Surgical management of the thyroid nodule: Patient selection based on the results of fine-needle aspiration cytology. Laryngoscope 1992;102:1353-56. Doi: 10.1288/00005537-199212000-00008.

[24] Kessler A, Gavriel H, Zahav S, Vaiman M, Shlamkovitch N, Segal S, et al. Accuracy and consistency of fine-needle aspiration biopsy in the diagnosis and management of solitary thyroid nodules. Isr Med Assoc J. 2005;7(6):371-73.

[25] Ko HM, Jhu IK, Yang SH, Lee JH, Nam JH, Juhng SW, et al. Clinicopathologic analysis of fine needle aspiration cytology of the thyroid. A review of 1,613 cases and correlation with histopathologic diagnoses. Acta Cytol. 2003;47(5):727-32.

[26] Handa U, Garg S, Mohan H, Nagarkar N. Role of the fine needle aspiration cytology in diagnosis and management of thyroid lesions: A study of 434 patients. J Cytol. 2008;25(1):13-17.

[27] Gupta M, Gupta, GuptaVB, Gupta VB. “Correlationoffineneedle aspiration cytology with histopathology in the diagnosis of solitarythyroidnodule. Journal of Thyroid Research. 2010;2010:379051.

[28] Kulkarni C,Mittal M, Nema M, Verma R. Diagnostic role of the Bethesda system for reporting Thyroid cytopathology in an academic institute of Central India: one year experience,Indian Journal of Basic and Applied Medical Research. 2016;5(2):157-66.

[29] Gupta C, Bhardwaj S, Sharma S. Diagnostic utility of thyroid fine needle aspiration cytology using The Bethesda System for Reporting Thyroid Cytopathology: A one year prospective study. J Diagn Pathol Oncol 2019;4(4):320-26.



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