

## Cytological spectrum of Thyroid Lesions Using Recent Bethesda System of Reporting and its Correlation with Histomorphology: A Retrospective Study of 208 Cases in a Tertiary Care Rural Centre

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**Cite this paper as:** Dr. Sanjay Kumar Kannaujia, Dr. Roopak Aggarwal, Dr. Manzeela Swale, Dr. Shabana A Ansari, Dr. Azmat Ansari, Dr. Hira Qamar, (2025) Cytological spectrum of Thyroid Lesions Using Recent Bethesda System of Reporting and its Correlation with Histomorphology: A Retrospective Study of 208 Cases in a Tertiary Care Rural Centre. *Journal of Neonatal Surgery*, 14 (13s), 477-487.

### ABSTRACT

**Introduction :** Enlargement of the thyroid gland or goiter is one of the important manifestation of thyroid lesions. It can be unilateral, bilateral or solitary nodule. It is very important to differentiate these lesions by clinical examination, thyroid function test and fine needle aspiration cytology (FNAC). It has been proved that fine needle aspiration cytology of the thyroid lesion is not only widely accepted but also simple, safe, cost effective, less painful and accurate method

**Material and Methods :** The present study was a retrospective study conducted at Uttar Pradesh University of Medical Sciences (UPUMS), Saifai, Etawah. UPUMS is a 1500 bedded tertiary care rural hospital in north India. We collected data of 208 cases from January 2022 to June 2024 of all patients who underwent fine needle aspiration of thyroid lesions. The skin overlying the swelling was cleaned with alcohol and FNAC was done using 22-23 gauge disposable needle attached to a 10 ml plastic disposable syringe. Smears were prepared, air dried and fixe

**Results :** The total 208 cases were archived from the Hospital Information System from January 2022 to June 2024. Out of which 24 were (11.5%) male and 184 (88.5%) were females with male to female ratio of (1:7.6). We reported 11 cases as malignant in TBSRTC Category VI on FNAC, of which only eight cases were received for histopathological examination. We have found 100% correlation with cytological diagnosis in all the eight cases. Of these seven cases were reported as papillary carcinoma of thyroid and single case was reported as medullary carcinoma which was also confirmed by immunohistochemistry showed diffuse and strong positivity of calcitonin [Fig 13], focal weak positivity of TTF1 and negative thyroglobulin, giving the rate of malignancy 100% for this category

**Discussion :** The malignancy rate of malignant category was observed to be 100% which is compatible with the studies conducted by Agarwal P et al [5], Arun et al [16], Williams et al [18], Mufti et al [19] and Theoharis et al [21]. While few of the studies conducted by Yang et al [22], Jo et al [20], Mondal et al [17] Nayar et al [23] and Yassa et al [6] had malignant rate between 97-99% in category VI.

**Conclusion :** FNAC is very useful first line investigation of thyroid nodule and has been proved that it is not only widely accepted but also simple, safe, cost effective, minimally invasive, less painful and accurate method. Although it is used with success in diagnosing clear cut malignant cases but difficulty arises in follicular as well as Grey zone lesions. Hence by using TBSRTC system for reporting thyroid lesions, not only standardize the reporting but also help the clinician in planning further management of the patients.

**Keywords:** Thyroid nodule, Fine needle Aspiration Cytology, Bethesda system, Risk of Malignancy

## 1. INTRODUCTION

Enlargement of the thyroid gland or goitre is one of the important manifestation of thyroid lesions. It can be unilateral, bilateral or solitary nodule[1]. It is very important to differentiate these lesions by clinical examination, thyroid function test and fine needle aspiration cytology (FNAC). It has been proved that fine needle aspiration cytology of the thyroid lesion is not only widely accepted but also simple, safe, cost effective, less painful and accurate method[2,3]. One of the important advantage is that it is minimally invasive OPD procedure and patients can get their reports on the same day. Some of the thyroid lesions are small and we could not get enough material for reporting while some lesions are cystic and we could only get cyst fluid, also few of the cases are suspicious in radiology, in such cases FNA should be performed under ultrasound guidance. Thyroid gland is very vascular organ hence chance of getting haemorrhagic aspirate is more but with the help of ultrasound, reaching to area of interest and taking out cellular material is more[4]. The primary objective of the initial evaluation is to distinguish between benign and malignant lesions sothat treatment should be planned accordingly[5,6].

Like every procedure, FNA has it's own prone and cones like improper sampling technique, inadequate material for interpretation, subjective error, morphological overlap and mimickers between certain benign, malignant and certain Grey zone lesions especially lesions having papillary architecture [7,8] . In an attempt to standardize the reporting system for thyroid FNA, The National Cancer Institute (NCI) hosted a multidisciplinary Thyroid State of the Science Conference in Bethesda, Maryland, in October 2007[5,9]. The first edition of the TBSRTC book was published in 2010 and second edition in 2018 while third edition is published recently in 2023. The categories are Non-diagnostic (Cat. 1), Benign (Cat. 2), Atypia of undetermined significance (Cat. 3), Follicular neoplasm (Cat. 4), Suspicious for malignancy (Cat. 5) and Malignant (Cat. 6). The TBSRTC nomenclature has been updated-to align with the 2022 WHO Classification of Thyroid Neoplasms[10].

The current study was planned to evaluate the diagnostic accuracy of fine needle aspiration cytology by using Bethesda System of Reporting Thyroid lesions and the results are correlated with corresponding histopathological examination of the specimen.

## 2. MATERIAL AND METHODS

The present study was a retrospective study conducted at Uttar Pradesh University of Medical Sciences (UPUMS), Saifai, Etawah. UPUMS is a 1500 bedded tertiary care rural hospital in north India. We collected data of 208 cases from January 2022 to June 2024 of all patients who underwent fine needle aspiration of thyroid lesions. Patients who were not ready to give consent and patients having bleeding diathesis were excluded from the study. After receiving approval from the institutional ethics review board, , data were retrieved from the hospital's archives.

FNA procedure was done after taking consent, the patient was asked to lie down in supine position with neck hyper-extended and was asked not to swallow and cough during the procedure. The skin overlying the swelling was cleaned with alcohol and FNAC was done using 22-23 gauge disposable needle attached to a 10 ml plastic disposable syringe. Smears were prepared, air dried and fixed.MGG, Haematoxyline & Eosin (HE) and Pap staining were done and FNA smears were studied for their adequacy, cellularity and cytomorphological features. Patients demographic details such as age,, sex, residential address, relevant clinical and radio-logical details were also archived from the hospital information system. We reported the cases according to the 6 diagnostic categories of recent TBSRTC 2023.

**Table 1: Six categories of “The 2023 Bethesda System for Reporting Thyroid Cytopathology” are :[11]**

Categories
<p><b>I. Nondiagnostic</b></p> <p>Cyst fluid only</p> <p>Virtually acellular specimen</p> <p>Other (obscuring blood, clotting artifact, drying artifact, etc.)</p>
<p><b>II. Benign</b></p> <p>Consistent with follicular nodular disease (includes adenomatoid nodule, colloid nodule, etc.)</p> <p>Consistent with chronic lymphocytic (Hashimoto) thyroiditis in the proper clinical context</p> <p>Consistent with granulomatous (subacute) thyroiditis</p> <p>Other</p>
<p><b>III. Atypia of undetermined significance Specify if AUS-nuclear atypia or AUS-other</b></p>
<p><b>IV.Follicular Neoplasm Specify if oncocytic (formerly Hu`rthle cell) type</b></p>
<p><b>V.Suspicious for malignancy</b></p>

Suspicious for papillary thyroid carcinoma
Suspicious for medullary thyroid carcinoma
Suspicious for metastatic carcinoma Suspicious for lymphoma
Other
<b>VI. Malignant</b>
Papillary thyroid carcinoma
High-grade follicular-derived carcinoma
Medullary thyroid carcinoma Undifferentiated (anaplastic) carcinoma
Squamous cell carcinoma Carcinoma with mixed features (specify)
Metastatic malignancy
Non-Hodgkin lymphoma
Other

On follow up we could get histology of only 63 cases, the diagnosis given in FNAC was compared with that of histopathology.

### 3. RESULT

The total 208 cases were archived from the Hospital Information System from January 2022 to June 2024. Out of which 24 were (11.5%) male and 184 (88.5%) were females with male to female ratio of (1:7.6). The age of the patients ranges from 10 years to 64 years with peak incidence was found in the age group between 10-30 years.

Table 1 shows the distribution of cases according to The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) 2023. Out of 208 cases, we have two cases (0.96%) in non diagnostic (Category I) Both the cases had haemorrhagic aspirate, no thyroid follicular cells were seen hence interpreted as non diagnostic and repeat FNA was advised. But both the patients were lost to follow up. Bethesda category II included maximum number of cases (181/208, 87.0%), These cases were categorized as colloid goiter (105/208, 58.1%), Lymphocytic thyroiditis (65/208, 35.9%) and follicular nodular disease (11/208, 6.1%). The smears of colloid goitre were scanty cellular and showed monolayered sheets of benign follicular epithelial cells with negligible nuclear crowding and overlapping in a colloid filled background. [fig. 1]. The cases of lymphocytic thyroiditis were consisting of cellular smears along with mixed population of thyroid follicular cells, hurthle cells in a background of lymphocyte and occasional plasma cells. Some of the cluster of thyroid follicular cells also showed lymphocytic impinging. [fig. 2]. Smears of 11 cases were cellular and revealed mono-layered sheets of benign follicular epithelial cells with few macro and microfollicular arrangement, mild pleomorphism along with fire flare in most of the cases. These cases were put under the category of follicular nodular disease.

We had 4 (1.9%) cases in Category III, out of which 2 were sparsely cellular and showed few micro and macrofollicular pattern without significant atypia. 2 were cellular with significant micro and macrofollicular pattern with absence of colloid in all cases [Fig. 3]. Category IV included 8 (3.8%) cases out of which 7 showed highly cellular smears arranged in clusters with several repetitive micro-follicular pattern with significant atypia, crowding and overlapping and absence of colloid. [Fig 4] while single case showed predominantly hurthle cells arranged in clusters as well as scattered singly and no colloid in the background., this case was reported as Follicular neoplasm hurthle cell type.

Category V included 2 (0.96 %) cases both showed cellular smears, enlarged nuclei, nuclear overlapping, crowding, nuclear moulding with powdery chromatin and nuclear grooves, however nuclear pseudo-inclusion, papillary architecture and colloid were absent. Both were reported as suspicious for papillary carcinoma thyroid.

In this study total 11 (5.3%) cases belonged to Category VI. Out of which 9 (81%) were reported as papillary thyroid carcinoma all showed papillary architecture having nuclear enlargement, nuclear overlapping, crowding, nuclear moulding and powdery chromatin with nuclear grooves and pseudo-inclusion in a colloid free background. [Fig. 5] while two cases each were diagnosed as follicular variant of papillary carcinoma and medullary carcinoma respectively. The cytology of medullary carcinoma showed marked cellularity with spindle cells as well as plasmacytoid tumour cells having mild to moderate pleomorphism, salt and pepper chromatin and moderate cytoplasm with scanty eosinophilic homogeneous material (amyloid) in the background. [Fig. 6]. Another case which was reported as follicular variant of papillary carcinoma in the malignant category showed highly cellular smears with microfollicular arrangement of tumour cells with papillary thyroid carcinoma like nuclear features. [Fig. 7] [Table 2]

The confirmatory histopathological diagnoses were available in only 63 of 208 cases. The reason of receiving less number of histopathological specimen may be due to benign cases usually not undergone surgical intervention unless and until they

were suspicious on imaging.

Table 2 shows the detailed correlation of cytological diagnosis and histopathological diagnosis of 63 cases. Out of the 2 cases reported as ND/UN, the repeat FNA as well as histology was not available in both the cases. There were total 181 benign cases, the follow up histology was available in 46 cases, out of which 45 cases were reported as colloid goitre and 3 cases were turned out to be follicular adenoma, the rate of malignancy for this category came out to be 6.5%.

The histopathology was available in all the four cases reported as AUS/FLUS (TBSRTC category III), out of which two cases were downgraded as colloid goitre while two cases were upgraded and reported as non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) hence the rate of malignancy came out to be 50% for this category.

For the TBSRTC Category IV (FN/SFN/FN HCT/SEN HCT), there were 8 cases, on follow up histology was received only for three cases. These cases were reported as colloid goitre, follicular adenoma and Hurthle cell adenoma respectively [Fig. 8,9]. Follicular adenoma and Hurthle cell adenoma giving the rate of malignancy of 66.6% for this category. Unfortunately we could not get the other cases in this category for histopathological correlation.

Of two cases reported as suspicious for malignancy, on follow up, histology of both the cases were received, out of which single case was turned out to be papillary carcinoma of thyroid while another case was diagnosed as follicular variant of papillary carcinoma of thyroid giving the rate of malignancy 100% for this category [Fig. 10].

We reported 11 cases as malignant in TBSRTC Category VI on FNAC, of which only eight cases were received for histopathological examination. We have found 100% correlation with cytological diagnosis in all the eight cases. Of these seven cases were reported as papillary carcinoma of thyroid and single case was reported as medullary carcinoma which was also confirmed by immunohistochemistry showed diffuse and strong positivity of calcitonin [Fig 13], focal weak positivity of TTF1 and negative thyroglobulin, giving the rate of malignancy 100% for this category [Fig. 11, 12] [Table 3]

#### 4. DISCUSSION

Enlargement of the thyroid gland or goitre is one of the important manifestations of thyroid lesions and it most commonly occurs in the sub-Himalayan region comprising of the world's biggest goitre belt. [5,12]. It has been proved that fine needle aspiration cytology of the thyroid lesion is not only widely accepted but also simple, safe, cost-effective, less painful and accurate method [2,3]. However for standardization and uniformity of reporting of thyroid lesions and also to reduce the interobserver differences there is introduction of TBSRTC in October 2007. [5, 13].

We reported the cases according to the 6 diagnostic categories of recent TBSRTC 2023 which was very beneficial for the surgeons and clinicians to decide further management of the patients. Out of 208 cases, 24 were (11.5%) male and 184 (88.5%) were females with male to female ratio (1:7.6) with peak incidence was found in the age group between 10-30 years. Mandekar et al [14]. reported a male female ratio of 1:6.1 in their study of 238 cases of various thyroid lesions. Male female ratio in the study conducted by Agarwal et al [5] on 87 cases was 1:8.6, Al Rikabi et al [15] observed a male female ratio of 1:5.2 in their study on 125 cases of various thyroid lesions.

Out of 208 cases, we have two cases (0.96%) in Category I, 181 (87.0%) cases in Category II, 4 (1.9%) cases in Category III, 8 (3.8%) cases in Category IV, two cases (0.96%) in Category V and total 11 (5.3%) cases belonged to Category VI. We compared our results with previous studies conducted by Syed et al [4], Kadam et al [3], Agarwal et al [5], Jeelani et al [2], Reddy et al [13], Arun et al [16], Mondal et al [17], Williams et al [18], Mufti et al [19] and Jo et al [20]. [Table 3] We have found that there are some similarities as well as marked variations in the results, this is because of huge differences in the sample size.

We have also calculated the malignancy rate for each Bethesda category and it was compared with the other studies [Table 5]. We noticed that malignancy rate for each category was different and was comparable with other previous studies. Malignancy rate of ND category could not be assessed because out of 2 cases of FNAC, none were available for histopathological follow up. The rate of malignancy for benign category was observed to be 6.5% which is almost similar to the study conducted by Agarwal P et al [5] and Mondal et al [17]. The malignancy rate of AUS/FLUS category was 50%, our results were compatible with the studies of Agarwal P et al [5], Mufti et al [19], Theoharis et al [21]. Who found malignancy rate of 50%, 50% and 48% respectively. The malignancy rate of FN/SFN/FN HCT/ SFN HCT category was 66.6% which was exactly similar to Agarwal P et al [5] but rest of the studies had lower malignancy rate in Category III. The discrepancy may be due to low sample size and less number of histopathological samples for comparison on follow up. The rate of malignancy of suspicious for malignant category was 100%. None of the studies had 100% malignant rate as compared to ours, this may be due to we had very less number of cases in this category while rest of the studies had much higher percentage of the cases in category V. The malignancy rate of malignant category was observed to be 100% which is compatible with the studies conducted by Agarwal P et al [5], Arun et al [16], Williams et al [18], Mufti et al [19] and Theoharis et al [21]. While few of the studies conducted by Yang et al [22], Jo et al [20], Mondal et al [17], Nayar et al [23] and Yassa et al [6] had malignant rate between 97-99% in category VI.

The present study has certain limitations like small sample size and histopathological diagnosis for comparison was not

available for all the cases.

## 5. CONCLUSION

FNAC is very useful first line investigation of thyroid nodule and has been proved that it is not only widely accepted but also simple, safe, cost effective, minimally invasive, less painful and accurate method. Although it is used with success in diagnosing clear cut malignant cases like papillary, medullary and anaplastic carcinoma but difficulty arises in follicular as well as Grey zone lesions. Hence by using TBSRTC system for reporting thyroid lesions, not only standardize the reporting but also help the clinician in planning further management of the patients. Each category has its own risk of malignancy which reflects the importance of categorization which guide the surgeons on the extent of the surgery. Hence we strongly recommend to use TBSRTC reporting system in day to day practice to minimize the errors for the benefit of the patients.

**Table 2: Distribution of cases according to the Bethesda category of reporting thyroid cytopathology.**

Category	Distribution of cases
I. Unsatisfactory/ Non Diagnostic	02 (0.96%)
II. Benign	181 (87.0%)
Colloid goiter	
Lymphocytic thyroiditis	105 (58.1%)
Follicular nodular disease	65(35.9%)
	11(6.1%)
III. Atypia of Undetermined Significance/ Follicular Lesion of Undetermined Significance	04 (1.9%)
IV. Follicular Neoplasm/ Suspicious For Follicular Neoplasm/ Follicular Neoplasm Hurthle Cell Type/ Susupicious For Follicular Neoplasm Hurthle Cell Type	08(3.8%)
V. Suspicious for Malignancy	02 (0.96%)
VI. Malignant	11(5.3%)
Papillary thyroid carcinoma	09(81.8%)
Medullary thyroid carcinoma	
Follicular variant of Paillary thyroid carcinoma	01(9.0%)
	01 (9.0%)

**Table3: Cytohistologic correlation and malignancy rate for each Bethesda category**

Cytology		Histopathology										Malignancy rate (%)
Bethesda category	No. of case	Histology received	Benign	Follicular adenoma	Hurthle cell adenoma	NIFTP	Follicular carcinoma	Hurthle cell carcinoma	Papillary carcinoma	Follicular variant of papillary carcinoma	Medullary carcinoma	
ND/UN	02	00	-	-	-		-	-	-	-	-	00
BENIGN	181	46	45	03								6.5
AUS/FLUS	04	04	02	00		02						50
FN/SFN/FN HCT/SFN HCT	08	03	01	01	01							66.6
SM	02	02							01	01		100
Malignant	11	08							07		01	100
Total	208	63										

**Table 4 Comparison of cases diagnosed on cytology according to 2023 TBSRTC with other studies**

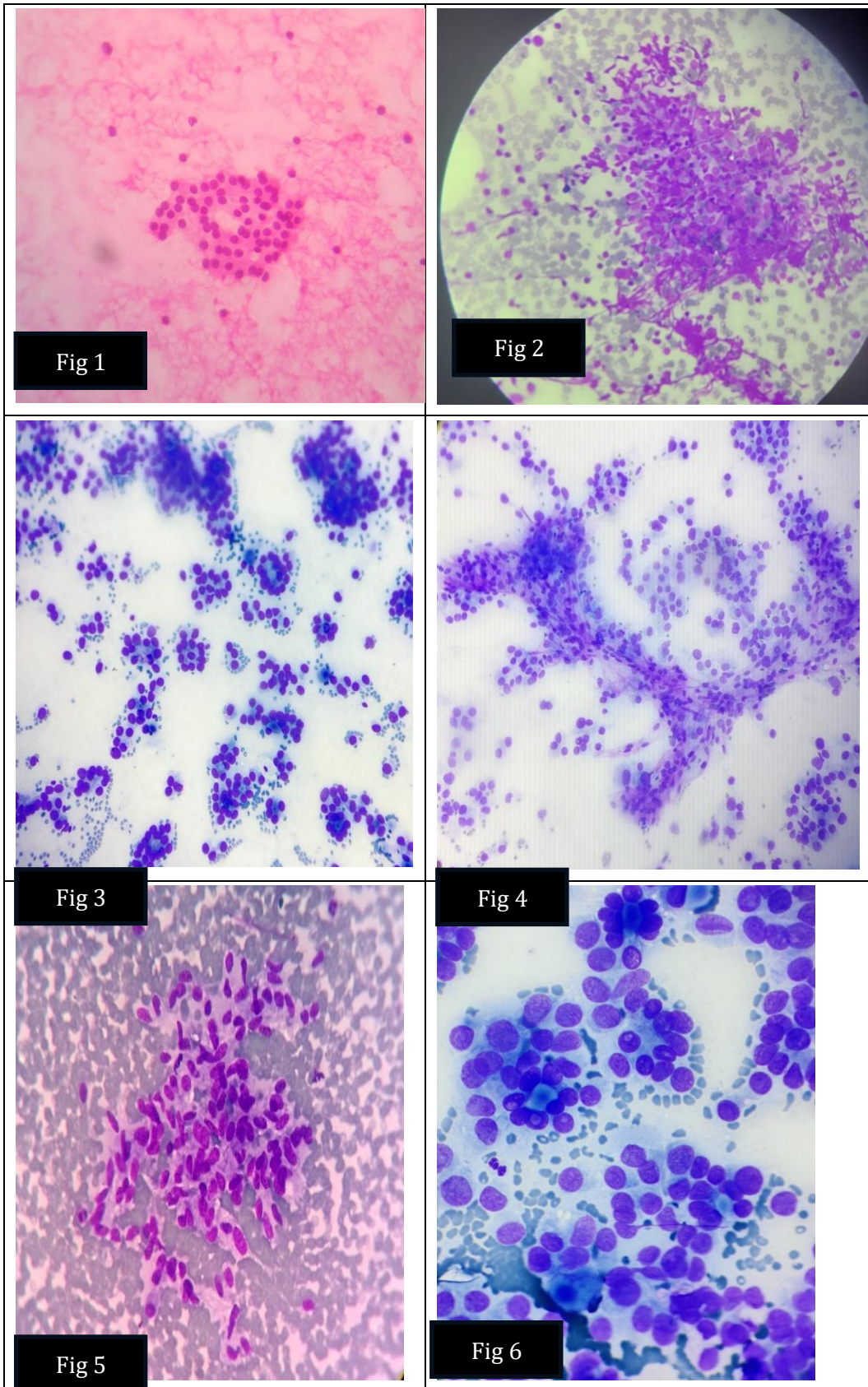
Study	Year	Total No. of cases	UNS/ND (Cat I) (%)	BENIGN (Cat II) (%)	AUS/FLUS (Cat III) (%)	FN/SFN/FN HCT/SN HCT (Cat IV) (%)	Susp. for malignancy (Cat V) (%)	MALIGNANT (Cat VI) (%)
Present study	2024	208	0.96	87	1.9	3.8	0.96	5.3
Syed M et al	2022	36	13.9	33.3	25	5.6	5.6	16.7

Kadam PN et al	2020	423	0	92.43	0	5.91	0.7	0.94
Agarwal P et al	2019	87	4.6	74.4	10.3	10.3	2.3	4.6
Jeelani T et al	2018	400	4	51.8	3	8.5	12.8	20
Reddy et al[11]	2017	484	3.7	89.2	0.002	2	0.6	4.1
Arul et al[10]	2014	603	2.7	65.3	10.6	10.6	5.3	6.3
Mondal et al[18]	2012	1020	1.2	87.5	4.2	4.2	1.4	4.7
Williams et al[17]	2010	1481	28.9	45.7	4.4	4.4	1.3	0.9
Mufti et al[16]	2010	250	11.6	77.6	4	4	2.4	3.6
Jo et al[15]	2009	3080	18.6	59	9.7	9.7	2.3	7

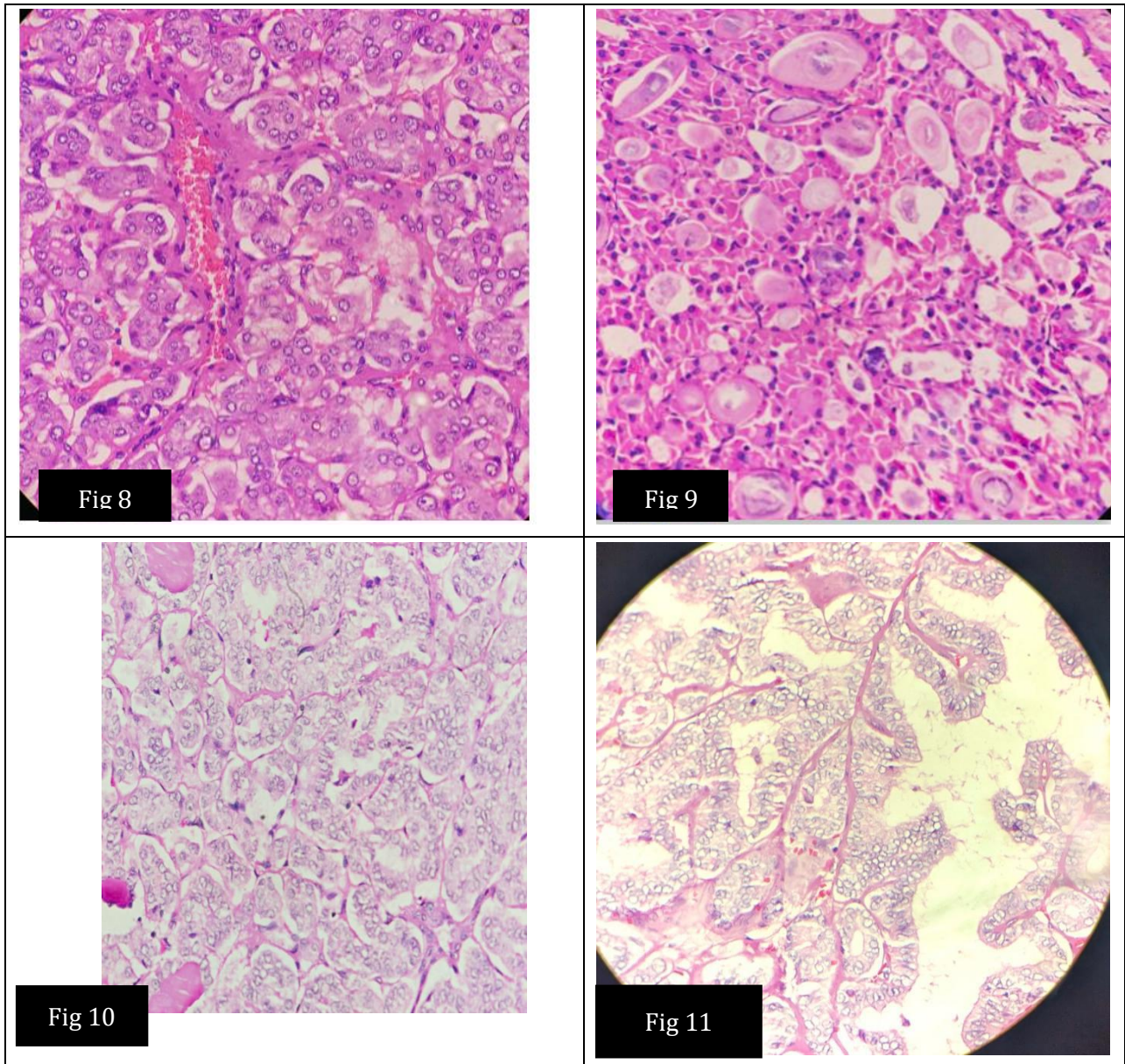
**Table 5: Comparison of the Rate of malignancy with the previous studies for each Bethesda category**

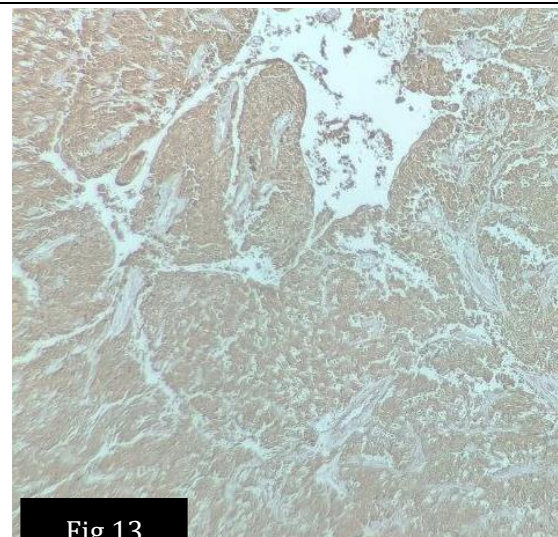
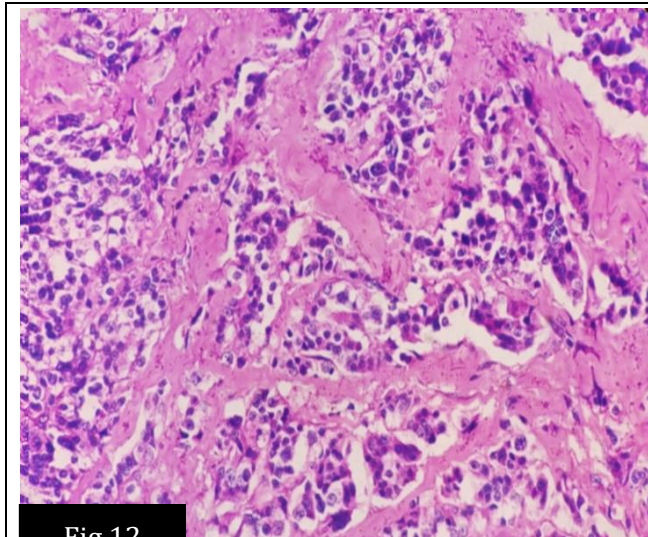
Study conducted by	Year	No. of cases	UNS/ND (%)	BENIGN (%)	AUS/F LUS (%)	FN/SFN/FN HCT/SF HCT (%)	SM (%)	MALIGNANT (%)
<b>Present study</b>	<b>2024</b>	<b>63</b>	0	6.5	50	66.6	100	100
Agarwal P et al	2019	24	-	6.6	50	66.5	100	100
Arul et al[10]	2014	392	0	0.8	24.4	28.9	70.8	100
Mondal et al[18]	2012	323	0	4.5	20	30.6	75	97.8
Williams et al[17]	2010	388	18.2	16	24.7	32.6	94.1	100
Mufti et al[16]	2010	84	20	3.1	50	20	80	100
Jo et al[15]	2009	892	8.9	1.1	17	25.4	70	98.1
Theoharis et al[14]	2008	378	-	9.8	48	34	87	100
Nayar et al[7]	2006	1413	9	2	6	14	53	97
Yang et al[13]	2005	1052	10.7	0.7	19.2	32.2	64.8	98.4
Yassa et al[3]	2004	1242	10	0.3	24	28	60	97

6. PHOTOGRAPHS



**Fig 1. Colloid goitre. Fig 2. Lymphocytic thyroiditis. Fig 3. Microfollicular pattern with nuclear overlapping and crowding. Fig 4. Papillary Thyroid Carcinoma. Fig 5. Medullary thyroid carcinoma. Fig 6. Follicular variant of papillary carcinoma.**





**Fig 8 : Follicular adenoma. Fig 9 :Hurthle cell adenoma .Fig 10: follicular variant of papillary carcinoma. Fig 11 :papillary carcinoma. Fig 12 :Medullary carcinoma Fig 13: Calcitonin positivity in Medullary carcinoma**

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