European Journal of Molecular & Clinical Medicine (EJMCM)
ISSN: 2515-8260 Volume 09, Issue 01, 2022

Original research article

The Bethesda System for Reporting Thyroid Cytopathology and to Assess Risk of Malignancy in Bastar Region

Dr Nitya Thakur[1], Dr Deepika Dhruw[2], Dr B P Singh[3], Dr Kasturi Mangrulkar[4]

[1]Associate Professor, Department of Pathology, Chandulal Chandrakar Memorial Government Medical College, Durg (CG)

[2]Associate Professor, Department of Pathology, Lt BRKM Government Medical College, Jagdalpur, (CG)

[3]Director ,Professor and HOD Department of Pathology, CIMS, Bilaspur(CG)

[4]Associate Professor, Department of Pathology, Lt BRKM Government Medical College, Jagdalpur, (CG)

Corresponding Author: Dr Kasturi Mangrulkar

Abstract

Introduction: Thyroid lesions are of great importance because most are amenable to Medical or Surgical management. The Medical diagnosis of Thyroid lesions is crucial as Malignancy necessitates Surgery while follow-up is important just in case of Benign lesions. The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was introduced in 2007 to standardize terminology utilized in reporting thyroid cytology.

Material and Methods: A retrospective observational study of already diagnosed cases of Thyroid in FNAC was performed in the Department of Pathology at Late BRKM Medical College, Bastar over a three years period from January 2017 to December 2019. The FNAC smears were reclassified according to the 6 diagnostic categories of TBSRTC.We could pursue follow up Histology for 160 cases. The diagnosis offered in FNAC was compared with that observed on Histopathological examination.

Results: On cytology out of 386 cases, 21(5.44%) categorized as Non-Diagnostic/ Unsatisfactory Samples, 338 (87.56%) cases as Benign Follicular Nodule, And 10 (2.59%) as Atypia of Undetermined Significance/Atypical Follicular Lesion of Undetermined Significance (AUS/AFLUS), 3 (0.78%) as Follicular Neoplasm/Suspected Follicular Neoplasm (FN/SFN), 4 (1.04%) as Suspicious For Malignancy, and 10 Cases (2.59%) as Malignant. Histopathological follow-up of 160 cases. The malignancy rate for the Non-Diagnostic category was 0%, Benign category was 1.44%, AUS/FLUS category was 33.33%, FN/SFN category was 50%. Suspicious for Malignancy category was 66.66%, malignant category was 100%.

Conclusion: The Bethesda system is the most suitable reporting system for cytopathology of Thyroid lesions. It minimizes the surgical procedure for benign lesions.

Keyword: TBSRTC, Fine-needle aspiration cytology, Histopathology, Malignancy Rate.

Introduction

Thyroid diseases are frequently encountered in India with a prevalence of a palpable Thyroid swelling approximately 12.2%.[1],[2] Fine-needle aspiration (FNA) of the Thyroid gland has proven to be an important and widely accepted, cost-effective, simple, safe, and accurate method for categorizing patients with Thyroid lesions. [3] The main role of Thyroid FNA is to categorize patients for either surgery or conservative management. Patients with FNA diagnoses that suggest malignancy and/or neoplasia are managed surgically whereas patients with FNA diagnoses that favor a benign lesion are often followed clinically.[4]

The National Cancer Institute (NCI) sponsored the NCI Thyroid Fine-needle Aspiration (FNA) State of the Science Conference on October 22-23, 2007 in Bethesda, MD. The meeting concluded with the introduction of "Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)" was introduced.[5] It has been widely used for assessment and interpretation of Thyroid specimens with standardized nomenclature and definition.

Its use has decreased the number of Thyroid surgeries performed and increased the ratio of Malignant to Benign lesions resected.[6]It tells about the Risk of Malignancy, and gives the idea about TBSRTC. The Bethesda System (2007) for reporting of Thyroid lesion (TBSRTC) in Cytopathology has been divided in to six categories.[5]

Each category has an implied malignancy risk, which ranges from 0% to 3% for the "Benign" category to virtually 100% for the "Malignant" category. [6]

Aim & Objectives

1) To evaluate the Cytomorphology of the Thyroid lesions by Fine Needle Aspiration Cytology based on TBSRTC (2007)

2) To correlate the Cytomorphological features of the Thyroid lesions with Histopathological features for its Malignancy Risk.

Inclusion Criteria: All patients with palpable thyroid swelling who had undergone FNAC in Cytology section.

Exclusion Criteria: Patients already diagnosed to have thyroid lesions on Histopathological examination.

Material and Methods

A retrospective observational study of already diagnosed cases of Thyroid in FNAC was performed in the Department of Pathology at Late BRKM Medical College Dimrapal, Bastar over a three years period from 1st January 2017 to 31st December 2019.

The data was retrieved from the records, maintained in the department, includes age, sex, clinical findings. For cytomorphological analysis of smears with Papanicolaou stain, M G Giemsa stain, H&E stain were reviewed and cases were studied for their adequacy, cellularity and cytomorphological features and categorized into six Bethesda categories. The FNAC smears were reclassified according to the 6 diagnostic categories of TBSRTC as Nondiagnostic/Unsatisfactory (ND/US); Benign; Atypia of Undetermined Significance/Follicular Lesion of Undetermined Significance (AUS/FLUS); Follicular Neoplasm/Suspicious for a Follicular Neoplasm (FN/SFN), Suspicious for Malignancy (SM), and Malignant.

We could pursue follow up Histology for 160 cases. The diagnosis offered in FNAC was compared with that observed on Histopathological examination. All the tissues were adequately fixed in 10% formalin. The tissues were processed routinely, prepared paraffin blocks, sections cut into 3-5 micron thickness and subsequently sections stained with Haematoxylin and Eosin (H&E). The calculation of Malignancy rate, and Implied Risk of Malignancy by TBSRTC was done.[7]

Results

On cytology 386 cases were reviewed by Bethesda system, of which 21(5.44%) categorized as Non-Diagnostic/ Unsatisfactory samples, 338 (87.56%) cases as Benign Follicular Nodule, and 10 (2.59%) as Atypia of Undetermined Significance/Atypical Follicular Lesion of Undetermined Significance (AUS/AFLUS), 3 (.78%) as Follicular Neoplasm/Suspected Follicular Neoplasm (FN/SFN), 4 (1.04%) as Suspicious for Malignancy, and 10 cases (2.59%) as Malignant. [Table no. 1]

Histopathological follow-up of 160 cases, out of which 143 were reported as Benign, 10 cases were Papillary Carcinoma, 3 cases of Follicular Carcinoma, 2 cases of Follicular Adenoma and 1 case each of Follicular Variant of Papillary Thyroid Carcinoma and Medullary Thyroid Carcinoma diagnosis of surgically resected nodule.[Table no.2]

Out of the total 386 FNAC cases, 21 were Non-Diagnostic. Of these, 6 had subsequent surgical resection specimens. None of them showed malignancy in Histopathology; the Malignancy rate for the Non-Diagnostic category was 0%.

In the Benign category, among, 138 had follow-up Histopathology and two cases of Follicular Adenoma; one case each of Follicular Carcinoma and Papillary Thyroid Carcinoma. The overall Malignancy rate for the Benign category was 1.44%. Out of the 10 cases of AUS/FLUS, 3 had follow-up Histopathology two were classified as a Benign category and one case of Follicular Carcinoma noted thus Malignancy rate for AUS/FLUS category was 33.33%. We classified 3 cases as FN/SFN among 386 FNACs. Of these, 2 had follow-up Histopathology one case turned out to be Benign category and one case of Follicular Carcinoma; thus Malignancy rate for FN/SFN category was 50%.Out of 4 cases of Suspicious for Malignancy three cases were available for Histopathology. Of these, two cases were found to be Papillary Thyroid Carcinoma, and 1 case was diagnosed as Benign; thus Malignancy Rate for Suspicious for Malignancy category was 66.66%.Out of 10 cases as Malignant among 389 FNAC cases. Of these, 7 had follow-up Histopathology. All 7 cases were found to be Malignant with seven cases of Papillary Thyroid Carcinoma, and 1 case of Medullary Thyroid Carcinoma; thus the Malignancy rate for Malignant category was 100%.[Table no. 3][Table no. 4]

Table 1: Cytological Diagnosis on FNA Thyroid of using TBSRTC (N = 386).

Diagnostic category	**No. of cases(N)**
Non-diagnostic /UNS	21(5.44%)
Benign	338(87.56%)
BFN	318(82.38%)
Hashimoto's Thyroditis	18(4.66%)
Granulomatous Thyroditis	1(0.26%)
Other (Grave's Diseases)	1(0.26%)
AUS/FLUS	10(2.59%)
FN/SFN	3(0.78%)
SM	4(1.04%)
MAILGNANT	10(2.59%)
PTC	8(2.07%)
MTC	1(0.26%)
UC	1(0.26%)

Table 2: Diagnosis and Distribution of Malignancies on Surgical Resection (N = 160)

Histopathological diagnosis	No. of cases (N)	Percentage (%)
Benign	143	89.38%
Follicular Adenoma	2	1.25%
Follicular Carcinoma	3	1.88%
PTC	10	6.25%
FVPTC	1	0.63%
MTC	1	0.63%
Total	160	100

Table 3: **Cyto-Histopathological correlation and Rate of Malignancy for each category.**

Cytological Diagnosis		Histopathological Diagnosis							Malignancy rate (%)
Bethseda category	No. of cases	Histology received	Benign	Follicular Adenoma	Follicular Carcinoma	PTC	FVPTC	MTC	
ND/UN	21	6	6						-
Benign	338	138	134	2	1	1			1.44%
AUS/FLUS	10	3	2		1				33.33%
FN/SFN	3	2	1		1				50%
SM	4	3	1			2			66.66%
Malignant	10	8				7		1	100%
Total	386	160	143	2	3	10	1	1	

Table 4: **Implied risk of malignancy in each category after TBSRTC implementation**

Diagnostic Category	No. of cases	Malignancy risk in our study (%)	Risk of malignancy according to TBSRTC (%)
Non-diagnostic	-	-	1-4
Benign	2	1.44%	0-3
AUS	1	33.33%	5-15
Suspicious of FN	1	50%	15-30
Suspicious of malignancy	2	66.66%	60-75
Malignant	7	100%	97-99

Table 5: Distribution of Bethesda diagnostic categories of the present cases with published studies.

Study	Year	No. of cases	ND (%)	Benign (%)	AUS (%)	FN (%)	SM (%)	Malignant (%)
Williams et al	2010	1481	28.9	45.7	4.4	4.4	1.3	0.9
Mufti et al	2010	250	11.6	77.6	4	4	2.4	3.6
Mondal et al	2012	1020	1.2	87.5	4.2	4.2	1.4	4.7
Arul P et al	2014	603	2.7	65.3	10.6	10.6	5.3	6.3
Agarwal et al	2019	87	4.6	74.7	10.3	10.3	2.3	4.6
Present study	2020	386	5.44	87.56	2.59	0.78	1.04	2.59

Table 6: Distributions the Rate of malignancy of each Bethesda category of our study with the previous studies.

Study	Year	No. of cases	ND (%)	Benign (%)	AUS (%)	FN (%)	SM (%)	Malignant (%)
Mufti et al	2010	84	20	3.1	50	20	80	100
Williams et al	2010	388	18.2	16	24.7	32.6	94.1	100
Mondal et al	2012	323	-	4.5	20	30.6	75	97.8
Arul et al	2014	392	-	0.8	24.4	28.9	70.8	100
Al Dawish et al	2017	369	25	8.9	14.3	47.2	69.3	96.7
Upadhya et al	2019	27	33.33	1.49	0	7.60	80	95.23
Present study	2020	386	-	1.44	33.33	50	66.66	100

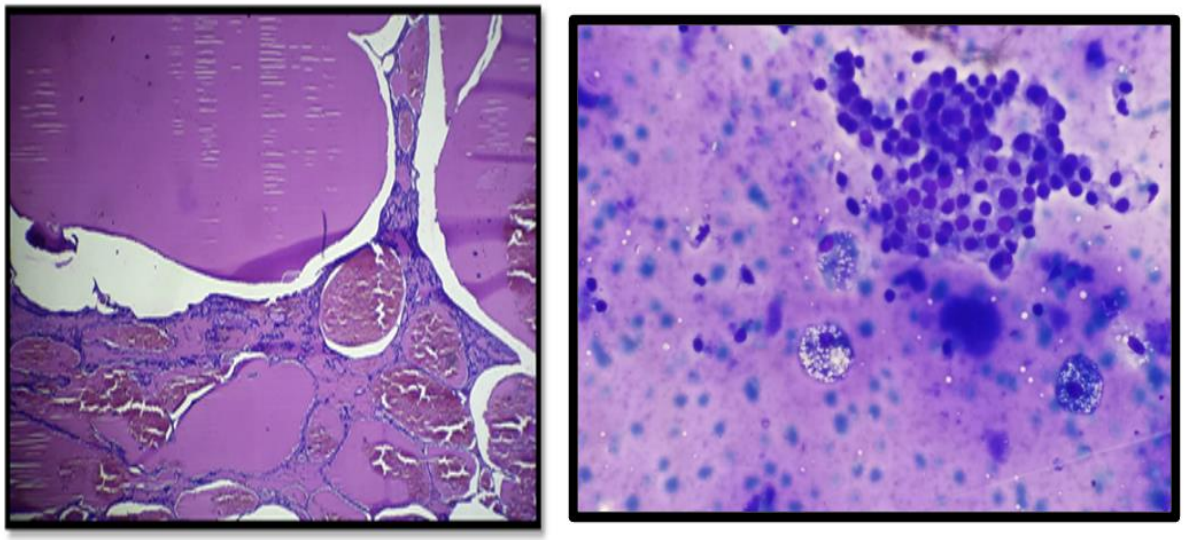

Fig: 2A: A) **Colloid Goitre** showing benign looking follicular cells in sheets, macrophage against thick and thin colloid in the background. Inset showing Histopathological section of Colloid Goitre.

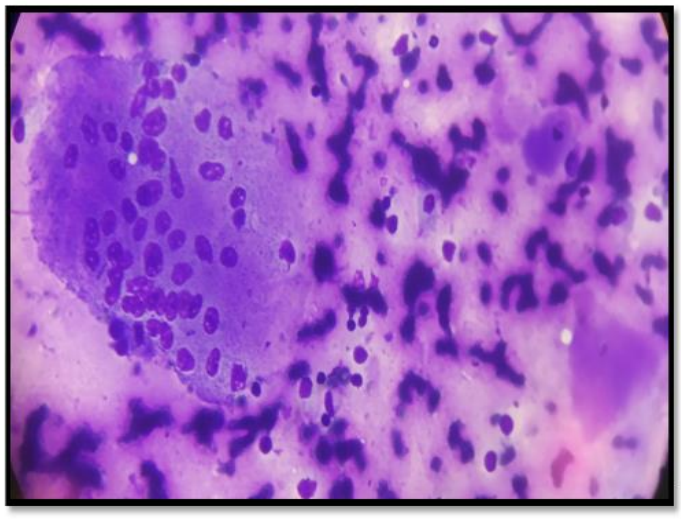

Fig: 3: **Granulomatous Thyroiditis** showing Granuloma comprised of Epitheloid cells along with thick and thin colloid in the background.

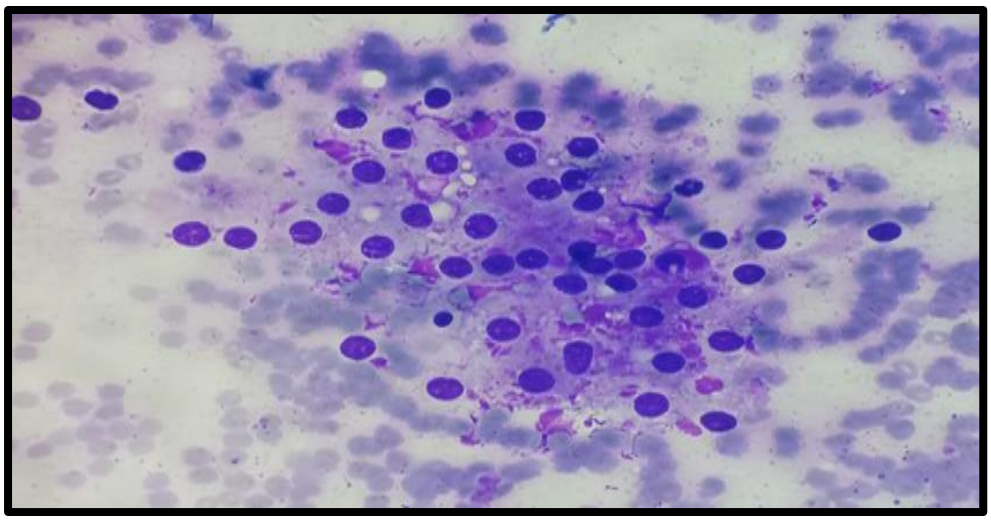

Fig: 4: **Graves's diseases** showing cells in monolayered sheets have abundant cytoplasm with red to pink frayed edges. (MGG 40x)

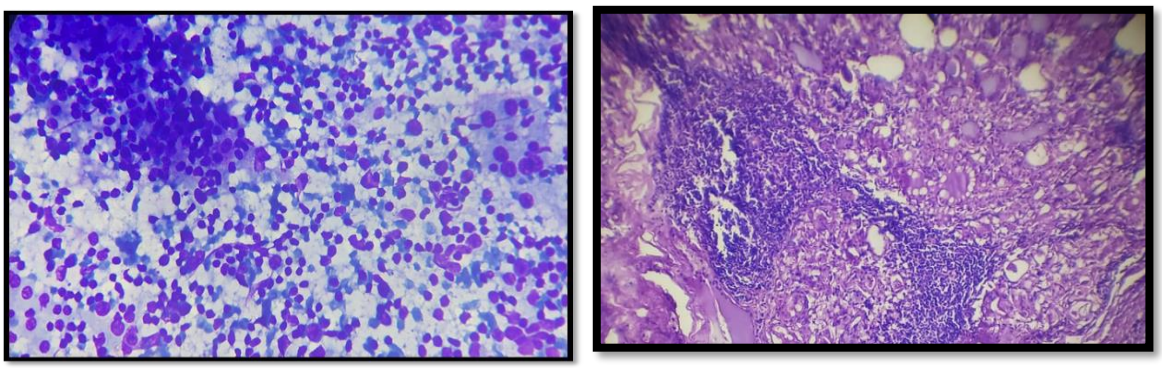

Fig: 5A&B: A) **Hashimoto's Thyroiditis** with Thyroid follicular cells showing Hurthle cell change and polymorphic lymphoid background. (MGG 40x);B)Histopathogical finding of Hashimoto's Thyroiditis.

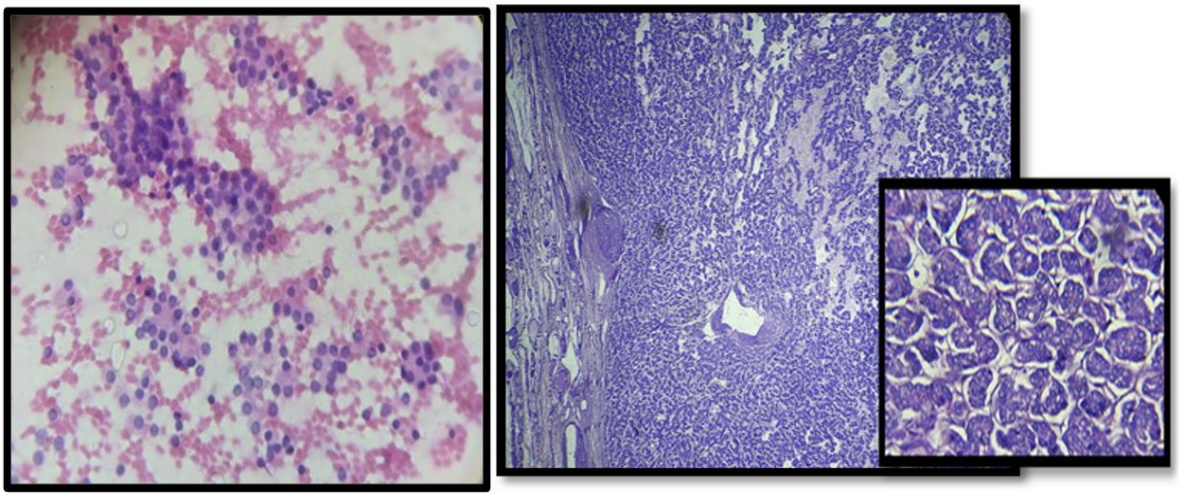

Fig: 6 A&B: A) **Follicular Neoplasm** showing Microfollicular pattern of follicular cells with nuclear pleomorphism. (H&E 40x); B) Histopathogical finding of Follicuar Adenoma (H&E 40x)

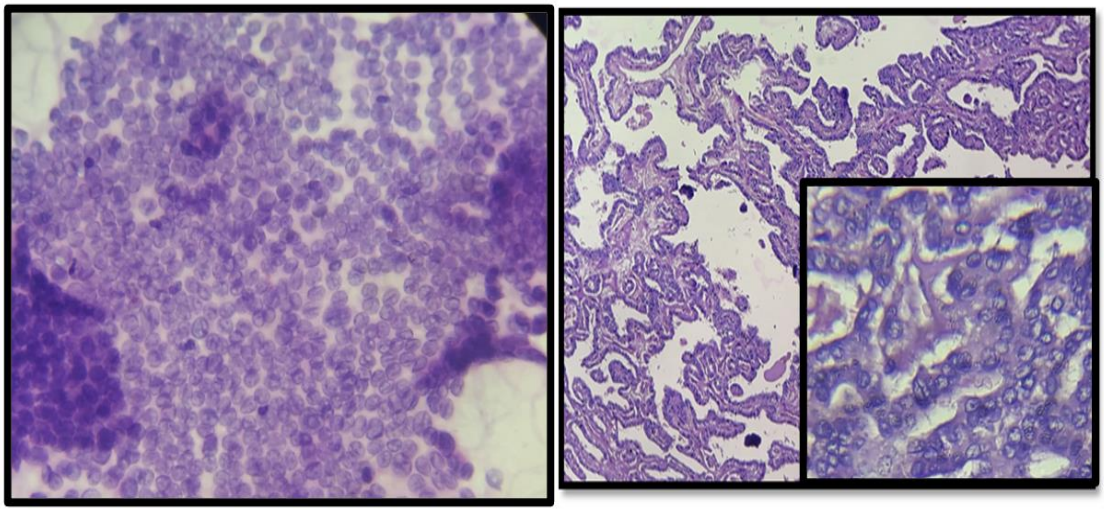

Fig: 7A & B :A) **Papillary Thyroid Carcinoma** showing large pale oval nuclei with prominent nuclear grooving. (H& E 40x); B) Histopathological section of PapillaryThyroid Carcinoma showing fibrovascular core and tumor cells inset showing nuclear grooving. (H&E 10x, inset 40x).

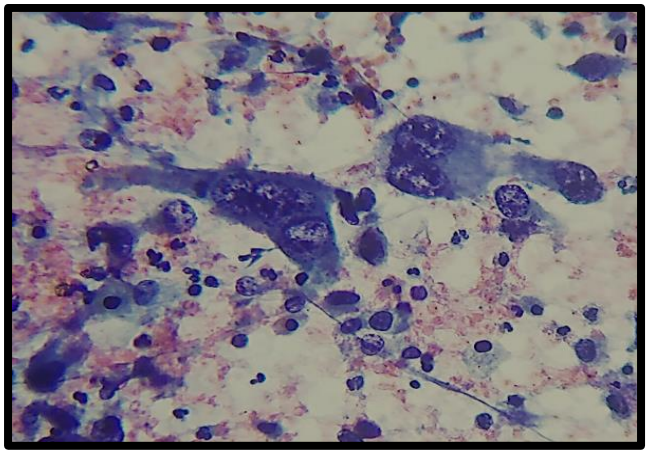

Fig: 8: **Anaplastic Thyroid Carcinoma** showing bizarre Malignant cells against an inflammatory background. (PAP 40X)

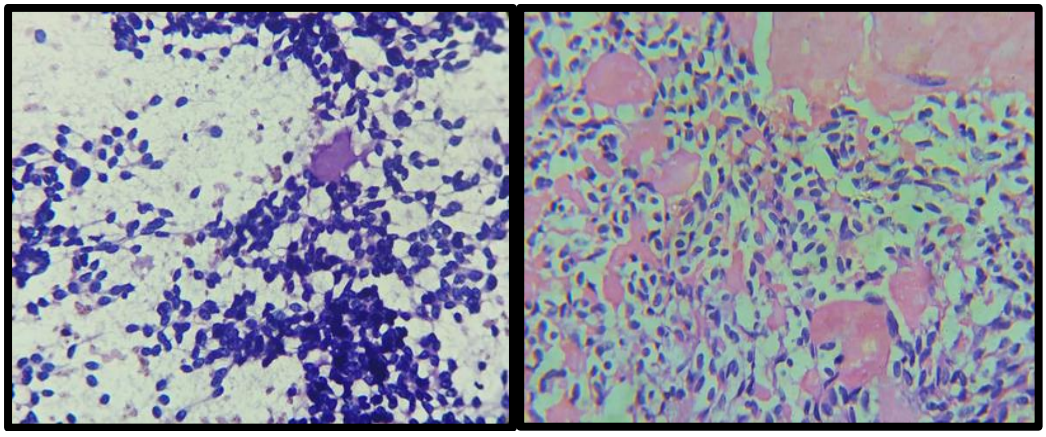

Fig: 9 A & B: A)**Medullary Carcinom of Thyroid** showing spindle cells with amyoid material.(H&E 40x); B) Histopathological finding of Medullary Carcinoma of Thyroid (H&E40x)

Discussion

Fine needle aspiration and cytology (FNAC) is a well-established out-patient procedure used in the primary diagnosis of Thyroid swellings and assumed the dominant role in the management mainly to rule out the need for surgery. [8]After having categorized the FNAC reports into the TBSRTC system, the subsequent step was to compare these diagnostic categories with histopathology reports.The next step was to calculate the strength of the 160 FNAC reports given using the TBSRTC category in predicting malignancy was also calculated. The distribution of the Cytological diagnosis of Thyroid lesions by using TBSRTC system in our study was compared with the studies done by Agarwal et al[1], Mufti et al[3], Arul P et al[10], William et al[11], Mondal et al[12], [Table no. 5]. The Benign, Suspicious for Malignancy, and Malignant categories of our study were equivalent to frequencies found by the most of the published studies. However there were low percent of cases observed of Follicular Neoplasm compared with the other study. The Rate of Malignancy in our study was comparable in most of the categories to that mentioned in TBSRTC [7] and other published studies [Table no. 6] except the ND/UNS, AUS, and FN. The Malignancy rate of Non-Diagnostic category could not be assessed because out of 21cases of FNAC, only six cases were available for histopathological Follow-up, which came off to be Benign, rather there were two cases which came up for follow up FNAC after six months of its initial procedure and one was diagnosed as Colloid Goitre and another was Non-Diagnostic subsequently. Cystic lesions with a Non-Diagnostic /Unsatisfactory aspirate should undergo repeat FNA and ultrasound guidance. [14]In category II (Benign) the Risk of Malignancy was 1.44% which was similar to the study done by Upadhya et al [15], higher range seen in a study done by Dawish et al. [16] The recommended management of this category is clinical follow-up.

In our study, category III (AUS/FLUS) has a much higher Risk of Malignancy (33.33%) than that outlined by TBSRTC (5%–15%) Similar study was done by Arul P et al [11], Williams et al[12], they also noted higher Risk of Malignancy. The cancer risk for this category according to TBSRTC is 5–15% and the recommended management protocol is repeated FNA after sufficient time gap.The Malignancy Rate of category IV (FN/SFN/FN HCT/ SFN HCT) category was 50% which was slightly higher in comparison to other studies and could be due to a low sample size in our study. The TBSRTC recommends lobectomy for this category.

The Rate of Malignancy of Suspicious for Malignant category was 66.66% which was similarly observed by Dawish et al [16]. The TBSRTC recommends near-total thyroidectomy or surgical lobectomy for cases in this category. The Malignancy rate of the Malignant category was observed to be 100% similar to the study done byMufti et al [3]. The TBSRTC recommends near-total thyroidectomy for these cases of malignancy.

One case each of Spindle Cell variants of Medullary Carcinoma of Thyroid and Anaplastic Carcinoma of Thyroid on cytology was reported in our study. On histopathology of the Spindle Cell variant of Medullary Carcinoma of Thyroid was confirmed and Anaplastic Carcinoma of Thyroid histopathology report wasn't available.

Anaplastic Carcinoma of Thyroid accounts for fewer than 2% of thyroid malignancies, although rates vary geographically, and characteristically it occurs in older adults. [5]

The two most common pitfalls were seen for the interpretation of Malignancy.

One was, limited cellularity presence of sheets of follicular cells with pale nuclei with the presence of intranuclear inclusion and absence of nuclear grooving were considered as part of Cystic Degeneration in Colloid Goiter and not as Papillary Thyroid Carcinoma, resulting in misinterpretation as Benign nodules in cytology. Similar to a study done by Upadhya et al. [15]

Another case was Multinodular Goiter diagnosed on cytology proved to be Follicular Carcinoma on Histopathology and this finding was similar to the study of Nandedkar et al.[17] The beauty of TBSRTC is that the diagnosis is well accompanied by an implied malignancy risk for that particular category and it comes along with recommendations for surgical management. [15],[7] In the end, our study continues to be limited by being a retrospective observational study with other published studies, which will account for a few of the differences when comparing diagnostic category frequencies and malignancy risks. There should be prospective studies using the Bethesda System it will give a better insight into the usefulness of the nomenclature together with radiological finding, biochemical finding, and surgical follow-up. Also, clinicians should always be aware of the malignancy rate within the Bethesda categories and providing guidelines in surgical management decisions taken regarding patients with thyroid nodules.[18]

Conclusion:

Due to some lack of uniformity with regards to the reporting system for thyroid cytology by pathologist it leads to miscommunications among health care persons. The Bethesda system is the most suitable reporting system for cytopathology of Thyroid lesions and therefore the rate of malignancy in each diagnostic category of Bethseda System is clarified.It minimizes the surgical procedure for Benign lesions. It accurately guides the surgeon for further management of Thyroid swellings as well as it is very helpful for maintaining effective communication between the Pathologist, Surgeon, and Endocrinologists.

References

1. Agarwal P,Dahiya S, Shams A. Cytomorphological spectrum of Thyroid lesions using Bethesda system of reporting with Histopathological correlation: A study of 87 cases. Indian Journal of Pathology and Oncology, July-September 2019; 6(3):454-459.
2. Unnikrishnan AG, Menon UV. Thyroid Disorders in India: An Epidemiological Perspective. Indian J Endocrinol Metab 2011; 15:78-81.
3. Mufti ST, Molah R. The Bethesda system for reporting Thyroid cytopathology: A five-year retrospective review of one center experience. Int J Health Sci (Qassim) 2012; 6:159-73.
4. Yang. Fine-needle Aspiration of Thyroid Nodules: A Study of 4703 Patients with Histologic and Clinical Correlations. Cancer (Cancer Cytopathology).2007; 111(5):306-315.
5. Bhat. The Bethesda System for reporting Thyroid cytopathology: a two year institutional audit. Int J Cur Res Rev.2016; 8(6):5-11
6. [6] Ramteke DJ. Cyto-histopathological correlation of Thyroid lesions. Int J Res Med Sci. 2017 ;5(4):1425-1429.
7. Cibas E, Ali S. The Bethesda system for reporting thyroid cytopathology. Am J Clin Pathol. 2009; 132: 658-665.
8. Mehar R. Comparative reporting of Thyroid cytology using Bethesda system with that of conventional system. JMSCR.2019; 7(3):1075-1081.
9. Agrawal D, Bhake AS, Rastogi N, Laishram S, Wankhade A, Agarwal A. Role of Bethesda system for reporting thyroid lesion and its correlation with histopathological diagnosis. J Datta Meghe Inst Med Sci.2019;14:74-81.
10. Patel MM. Fine Needle Aspiration Cytology As A First Line Investigation In Thyroid Lesions. National Journal Of Medical Research Volume 3 │ Issue 2 │ Apr – June 2013
11. Arul P, Akshatha C, Masilamani S. A Study of Malignancy Rates in Different Diagnostic Categories of the Bethesda System for Reporting Thyroid Cytopathology: Institutional Experience. Biomed J. 2015:517-22

12. Williams BA, Bullock MJ, Trites JR. Rates of Thyroid Malignancy by FNA Diagnostic Category.J Otolaryngol Head Neck Surg 2013;61:1-5.
13. Mondal SK, Sinha S, Basak B, Roy DN. The Bethesda System for Reporting Thyroid Fine Needle Aspirates: A Cytologic Study with Histologic Follow up. J Cytol 2013; 30:94-99.
14. Baloch ZW, Alexander E K, Gharib H, and Raab SS. Chapter 1; Overview of Diagnostic Terminology and Reporting In: Ali SZ and Cibas ES Edi, The Bethesda System for Reporting Thyroid Cytopathology. New York, NY: Springer; 2010:1-4.
15. Upadhya P, Dhakal S, Adhikari P, Adhikari B, Khadka D, Niraula SR. Histopathological review of diagnostic categories of the Bethesda system for reporting Thyroid cytopathology – An institutional experience of 5 years. J Cytol 2019; 36:48-52
16. Dawish MA, Robert AA, Muna A, Eyad A, Ghamdi AA, Hajeri KA. Bethesda system for reporting Thyroid cytopathology: A three-year study at a tertiary care referral center in Saudi Arabia. World J Clin Oncol . 2017; 8:151-157.
17. Nandedkar SS, Dixit M, Malukani K, Varma AV, Gambhir S. Evaluation of Thyroid lesions by fine-needle aspiration cytology according to bethesda system and its histopathological correlation. Int J App Basic Med Res. 2018; 8:76-82.
18. Alshaikh S, Harb Z. Classification of thyroid fine-needle aspiration cytology into Bethesda categories: An institutional experience and review of the literature. Cytojournal. 2018; 15:4.