Original Article

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Pathology Section

Diagnostic Accuracy of Fine Needle Aspiration Cytology of Thyroid Lesion by Bethesda System and its Histopathological Correlation: An Institutional Experience of Two Years

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ABSTRACT

Introduction: Fine Needle Aspiration (FNA) is a primary investigation for diagnosis and management of Thyroid lesions. But thyroid FNA suffers from reporting confusion due to multiplicity of category name and variable diagnostic terminology. To overcome this, National Cancer Institute (NCI) in 2007 introduced The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), which provides standardised nomenclature along with Risk Of Malignancy (ROM) for each category.

Aim: (1) To classify Fine Needle Aspiration Cytology (FNAC) of thyroid lesion according to Bethesda System and calculate ROM for each category. (2) To find out accuracy of FNAC of thyroid lesion.

Material and Methods: A prospective study was conducted in the Department of Pathology, MKCG Medical College and hospital over a period of 2 years (2012-2014) which included 285 cases. FNA for Thyroid swelling were obtained from OPD and IPD of various departments of MKCG Medical College and Hospital Berhampur. Smears prepared in glass slide from aspirated material were stained using May Grunwald Giemsa (MGG) stains, Diff-Quik stain and Haematoxylin and Eosine (H&E) stain. All FNAC were classified according to TBSRTC 2007 guidelines into 6 categories as Cat I (Catagory 1)-Non Diagnostic/Unsatisfactory, Cat II-Benign, Cat III-Atypia of Undetermined Significance (AUS)/Follicular lesion of Undetermined Significance, Cat IV-Follicular Neoplasm/ Suspicious for Follicular Neoplasm, Cat V- Suspicious for Malignancy and Cat VI- Malignant. The cytological findings were correlated with the histopathology in available cases. Statistical test used for the study was Z-Test. It is the likelihood that the test is correctly rejecting the null hypothesis. This study has 90% power means that the study has 90% chances of test having significant result.

Results: The distribution of FNA of 285 cases according to Bethesda System were CAT I to CAT VI as 05 (1.8%), 236 (82.8%), 11 (3.8%), 12 (4.2%), 07 (2.4%) and 14 (5%), respectively. Biopsy was available in 85 cases. The ROM reported on histopathological follow-up according to Bethesda System were CAT I 0 (0%), CAT II 2 (4.2%), CAT III 01 (14.2%), CAT IV 02 (20%),CAT V 04 (66.6%) and CAT VI 11 (100%). The Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV) and Diagnostic Accuracy were found to be 92%, 91.8%, 85.2%, 95.7% and 91.9%, respectively.

Conclusion: FNA is sensitive, specific and accurate initial investigation for evaluation of thyroid lesion but it needs a uniform reporting system for proper categorisation and management.

Bethesda System is an excellent reporting system for Thyroid FNAC consisting of clear categorical nomenclature including ROM and proposed clinical management for each category which helps surgeon in preventing unnecessary surgery.

Keywords: Diagnostic category, Risk of malignancy, Thyroid disease, Thyroid nodule

INTRODUCTION

Thyroid disease is common in India and 42 million people were suffering from it til 2013 [1]. In India the prevalence of palpable thyroid nodule is approximately 12.2% while the incidence of thyroid cancer is 8.7 per 100000 populations per year [2]. Thyroid FNA plays main role in triaging patient for either surgery or conservative management [3]. The percentages of resected nodules that are malignant surpass 50% with current thyroid FNA practice [4]. Different terminologies were used for reporting thyroid cytology due to lack of standardised reporting system. About 60% of the thyroid nodules are classified cytologically as Benign, <10% as Malignant and remaining 30% as Atypical, Indeterminate or Suspicious for Malignancy were used to describe those diagnostically challenging cases [5]. During past decade various professional organisations proposed many diagnostic guidelines for reporting thyroid cytology which included Papanicolaou Society of Cytopathology, American Thyroid association and American Association of Clinical Endocrinology but none have been universally accepted [6]. In the year 2007, the NCI, Bethesda, Maryland proposed Bethesda System which includes six diagnostic categories with unique ROM and recommended clinical management for each category [4].

Literature review show different authors published different studies on Bethesda System. Bhagat VM et al., only classified Bethesda System [7]. Jo VY et al., and Mondal SK et al., classified and calculated malignancy risk for each category [8,9]. Sinna EA et al., categorised Bethesda System and calculated accuracy of FNAC of thyroid lesion but did not calculate malignancy rate [10]. Evaluation of accuracy of FNAC by Bethesda system and calculation of ROM were done for the first time in our institution. The aim of the study was: 1) To classify FNAC of thyroid lesion according to Bethesda system and calculate ROM for each category. (2) To find out accuracy of FNAC of thyroid lesion.

MATERIALS AND METHODS

The present study was a prospective study, carried out in the Department of Pathology Maharaja Krushna Chandra Gajapati Medical College and Hospital Berhampur, Odisha over a period of two years from October 2012 to September 2014. Permission from Institutional Ethics Committee was obtained (clearance no. 107 / 07. 05.2014).

Inclusion criteria: All patients having clinically palpable thyroid swelling who underwent FNA during study period were included in this study.

Exclusion criteria: Patient having thyroid swelling but not willing for FNAC were excluded from study.

All the patients having thyroid swelling referred to Cytology section of Department of Pathology for FNAC from both OPD and IPD of various Departments of MKCG Medical College and Hospital, Berhampur. Before FNAC, relevant clinical history, physical examination, provisional diagnosis and thyroid function test were noted. Then the patient was made to lie down in supine position and a pillow was put shoulder for hyperextension of the neck. Under all aseptic precautions. FNA was done using 24-26 gauge needle. Smears were prepared in four glass slides for each case from aspirated material. Half of the Smears were air dried for MGG or Diff- Quik stain while the rest were wet fixed in 95% alcohol for Haematoxylin and Eosine (H&E) stain. Then stained slide was examined under light microscope. The FNA results were classified in to 6 categories according to the Bethesda system.

CAT I (Category 1)- Non Diagnostic/Unsatisfactory

CAT II- Benign

CAT III- AUS/ Follicular lesion of Undetermined Significance.

CAT IV- Follicular Neoplasm or Suspicious for Follicular Neoplasm

CAT V- Suspicious for Malignancy

CAT VI- Malignant

Smears were adequate for evaluation if it contained at least six groups of well preserved and well stained follicular cells, each containing at least ten cells on a single slide [11]. Then the patients were subjected to surgery and specimens were sent for histopathological study. Cytological diagnoses were correlated with the histopathology.

The Sensitivity, Specificity, diagnostic Accuracy, PPV, NPV, False Positive Rate (FPR) and False Negative Rate (FNR) lesions were calculated by using equation [10,12]. It is difficult to include CAT I (ND/UNS) and CAT III (FLUS/AUS) under any benign and malignant cytology category. So for calculating statistical parameters, CAT I and CAT III were excluded from the calculation [5,10].

STATISTICAL ANALYSIS

Statistical test used for the study was Z-Test. Statistical parameters like Sensitivity, Specificity, diagnostic Accuracy, PPV, NPV were calculated in percentage by using simple software MS excel.

RESULTS

Out of 285 cases majority of cases 242 (85%) were females and only 43 (15%) cases were males with female: male ratio was 5.6:1. Age of patients ranged between 8 to 68 years with mean age 35.1 years. The maximum number of cases 89 (31.2%) were within 31-40 year age group.

According to Bethesda system maximum number of cases 236 (82.8%) belonged to CAT II-Benign group followed by Malignant 14 cases (5%) and minimum number of cases 5 (1.8%) in Non diagnostic group shown in [Table/Fig-1]. Out of 236 cases in CAT II, the majority of cases were colloid goiters/multinodular goiter 174 (61%).

Among 285 cases, histopathology was available in 85 cases. Colloid goiter/Multinodular Goiter was the most common benign lesion and Papillary Carcinoma was commonest malignant lesion [Table/Fig-2].

Out of 85 cases 55 (64.6%) were non neoplastic and 30 (23.5%) were neoplastic lesions [Table/Fig-3]. Histopathological correlation show statistical significance association with FNAC with that of histopathology (p= 0.0336).

Diagnostic category	Number of cases	Percentages	Cytological diagnosis	Number of Cases
CAT I- ND/UNS	05	1.8%	ND/UNS	05 (1.8%)
CAT II-Benign	236	82.8%	Colloid goiter/ Multinodular goiter	174 (61%)
			Hashimoto's thyroiditis	52 (18.3%)
			Granulomatous thyroiditis	04 (1.4%)
			Thyroglossal duct cyst	06 (2.1%)
CAT III-AUS/FLUS	11	3.8%	AUS/FLUS	11 (3.8%)
CAT IV-FN/SFN	12	4.2%	FN/SFN	12 (4.2%)
CAT V-SFM	07	2.4%	Suspicious for Papillary CA	07 (2.4%)
CAT VI-Malignant	14	05%	Papillary CA	10 (3.6%)
			Medullary CA	02 (0.7%)
			Anaplastic CA	02 (0.7%)
Total	285	100%		285 (100%)

[Table/Fig-1]: Distribution of individual thyroid lesions on cytology according to the Bethesda system (n=285).
CAT: Category; ND: Nondiagnostic; UNS: Unsatisfactory; AUS, FLUS: Follicular lesion of undetermined significance; FN: Follicular neoplasm; SFN: Suspicious for follicular neoplasm; SFM: Suspicious for malignancy; CA: Carcinoma

Cytolological categorisation (n=285)	No. of histopathology specimen (n=85)	Cytological diagnosis	No. of cases	Histopathological diagnosis	No. of cases
ND/UNS n=05	04 (4.7%)	ND/UNS	04 (4.7%)	Colloid goiter/ Multinodular goiter	04 (4.7%)
Benign n=236	47 (55.3%)	Colloid goiter/ Multinodular goiter	43 (50.5%)	Colloid goiter/ Multinodular goiter	41 (48.2%)
		Thyroglossal duct cyst	04(4.7%)	Thyroglossal duct cyst	04 (4.7%)
				Papillary CA	02 (2.3%)
AUS/FLUS n=11	07 (8.2%)	AUS/FLUS	07 (8.2%)	Multinodular goiter	02 (2.3%)
				Follicular adenoma	04 (4.7%)
				Papillary CA	01 (1.2%)
FN/SFN n=12	10 (11.8%)	FN/SFN	10 (11.8%)	Multinodular goiter	02 (2.4%)
				Follicular adenoma	06 (07%)
				Follicular CA	02 (2.4%)
SFM n=07	06 (07%)	Suspicious for Papillary CA	06 (07%)	Hyperplastic colloid nodule	02 (2.3%)
				Papillary CA	04 (4.7%)
Malignant n=14	11 (13%)	Papillary CA	09 (10.6%)	Papillary CA	09 (10.6%)
		Anaplastic CA	02 (2.4%)	Anaplastic CA	02 (2.4%)

[Table/Fig-2]: Cytohistopathological correlation.

No of histopathology specimen n=(85)	Non neoplastic	Neoplastic	
		Benign	Malignant
ND/UNS n=04	04 (4.7%)	0 (0%)	0 (0%)
BN n=47	45 (53%)	0 (0%)	02 (2.3%)
AUS/FLUS n=07	02 (2.3%)	04 (4.7%)	01 (1.2%)
FN/SFN n=10	02 (4.7%)	06 (4.7%)	02 (4.7%)
SFM n=06	02 (2.3%)	0 (0%)	04 (4.7%)
Malignant n=11	0 (0%)	0 (0%)	11 (13%)
Total=85	55 (64.6%)	10 (11.9%)	20 (23.5%)

[Table/Fig-3]: Distribution of non-neoplastic and neoplastic lesion.

Based on cytohistological correlation Sensitivity, Specificity, PPV, NPV and Total Accuracy for overall neoplasm as follows 92%, 91.8%, 85.2%, 95.7% and 91.9%, respectively [Table/Fig-4].

Cytology	Histopathology		Total
	Non-neoplastic	Neoplastic	
Benign (CAT II)	45 (TN)	02 (FN)	47
SFN (CAT IV)	02 (FP)	08 (TP)	10
SM (CAT V)	02 (FP)	04 (TP)	06
MGT (CAT VI)	0 (FP)	11 (TP)	11
Total	49	25	74

[Table/Fig-4]: Cytological and histological correlation in discordant case.
But for calculation of statistical parameters ND/UNS, AUS/FLUS group excluded from the calculation; TN: True negative; FN: False negative; FP: False positive; TP: True positive

ROM rate in present study were ND/UNS 0 (0%), BN 02 (4.2%), AUS/FLUS 01 (14.2%), FN/SFN 02 (20%), SFM 04 (66.6%) and Malignant 11 (100%).

DISCUSSION

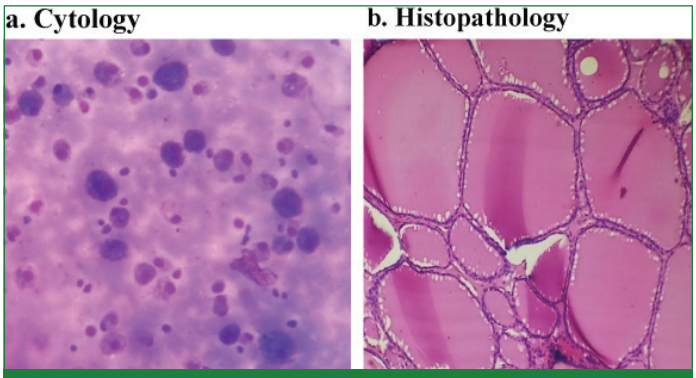
As all endocrine lesions including thyroid shows female predominance, the present study shows female predilection with female to male ratio 5.6:1.0 which correlates well with study conducted by Bhagat VM et al., who reported female to male ratio 5.6:1 [7]. The youngest patient was eight-year-old and the oldest patient was 68-year-old with a mean age of 35.1 years. The maximum number of cases 89 (31.2 %) were seen in 31-40 years. Kumari NS et al., also showed maximum number of cases 112 (38.7%) in 31-40 year age group [13].

The distribution of Bethesda system of this study were compared with other studies as shown in [Table/Fig-5] [3,7-9,12,14-17]. The present study was well corroborated with findings of Mondal SK et al., [9] with slightly higher percentages 3.8% in CAT III in present study. But when compared with Jo VY et al., and Nayar R et al., studies this study showed higher percentage in CAT II and CAT IV [8,14]. Most of the patients come directly and on referral basis in our Medical college. As benign cases are higher in the general population, benign cases constituted more percentages. On the other hand Jo VY et al., and Nayar R et al., studies were done in tertiary care centers, where patients come only on a referral basis which did not exactly represent benign category in the general population [8,14].

Study	Year	Sample size	Bethesda Category					
			I	II	III	IV	V	VI
Yang J et al., [3]	2007	4703	10.4	64.6	3.2	11.6	2.6	7.6
Nayar R et al., [14]	2009	5194	5	64	18	6	2	5
Jo VY et al., [8]	2010	3080	18.6	59	3.4	9.7	2.3	7
Mondal SK et al., [9]	2013	1020	1.2	87.5	1	4.2	1.4	4.7
Bhagat VM et al., [7]	2014	160	5.63	87.5	0	3.12	0.63	3.12
Mehrotra D et al., [12]	2016	175	4.57	68.58	5.72	17.14	1.14	2.85
Alshaikh S et al., [15]	2018	632	10.1	68.8	12.4	2.9	2.6	4.1
Upadhyaya P et al., [16]	2019	109	2.8	61.5	0	11.9	4.6	19.3
Rupareliya N et al., [17]	2020	250	5.2	87.6	2.8	2.4	1.6	0.4
Present study	2020	285	1.8	82.8	3.8	4.2	2.4	5

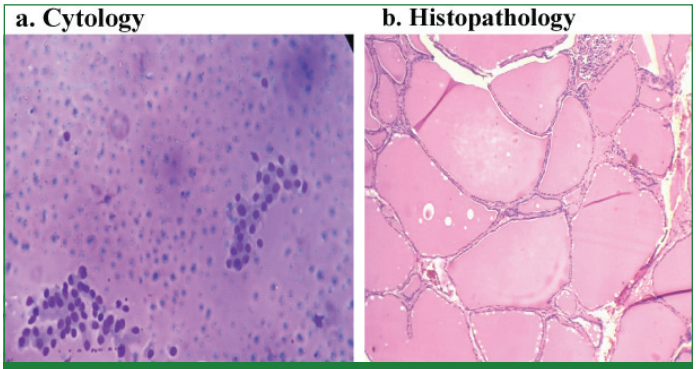
[Table/Fig-5]: Comparison of distribution of cases in TBSRTC with other study [3,7-9,12,14-17].

The present study had 5 cases (1.8%) in ND/UNS category. Bethesda system recommended that Non diagnostic interpretation should be <10% however various studies reported ND/UNS ranging between 1.2%-18% in literature [3,7-9,12,14-17]. On histopathology all cases of CAT I proved to be benign as Colloid Goiter/Multinodular Goiter as shown in [Table/Fig-6]. So ROM is 0%.

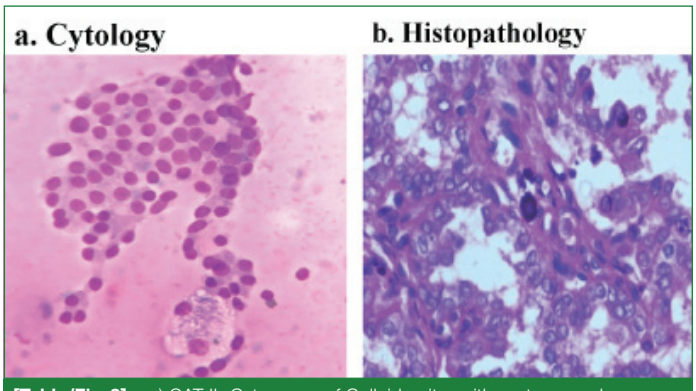


[Table/Fig-6]: a) CAT I- Cytosmear show haemosiderin-laden cyst macrophage only (Diff-Quik 40X); (b) Microsection of Colloid Goiter (H &E 10X)

In CAT II, 47 cases were available for surgery, out of which 45 cases confirmed to be benign as Colloid Goiter/Multinodular Goiter as shown in [Table/Fig-7] on histopathology. Remaining 2 cases turned out to be Papillary carcinoma of thyroid which were diagnosed as Colloid Goiter with cystic degeneration on cytology [Table/Fig-8 a,b]. So, ROM in CAT II was 4.2%. These discordant 2 cases considered as false negative cases with FNR of 8%. Some authors reported FNR ranging from 4%-11.1% [18,19]. FNR depends on variable factors like sampling error, co-existence and overlapping of benign and malignant lesions with associated cystic and degenerative changes. On grossing small nodular focus was present which was probably missed during FNAC.



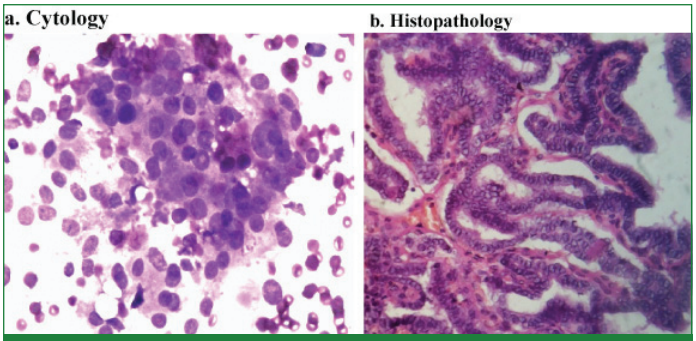
[Table/Fig-7]: a) CAT II- Cytosmear of a Colloid Goiter (Diff-Quik stain 10X); b) Microsection of Colloid Goiter (H &E 10X).



[Table/Fig-8]: a) CAT II- Cytosmear of Colloid goiter with cyst macrophage (Diff-Quik 40X); b) Microsection of Papillary carcinoma show papillae, nuclear atypia, intranuclear pseudo-inclusion and psammoma bodies (H &E 40X).

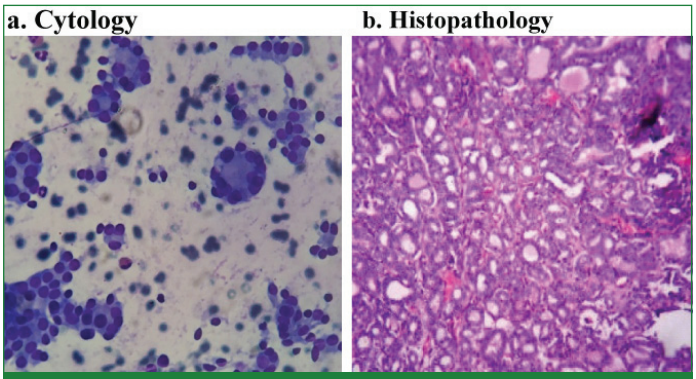
Bethesda system recommended that reporting of AUS/FLUS group should not be exceeding 7% in individual laboratory [20] but Nayar R et al., showed 18% [14].

In CAT III one case reported as Papillary carcinoma of thyroid on histopathology. Hence, ROM was 14.2%.That case was a known case of Hashimoto's thyroiditis show focal feature of nuclear atypia, nuclear pseudo inclusion and aggregate of lymphocytes on cytology [Table/Fig-9 a,b].

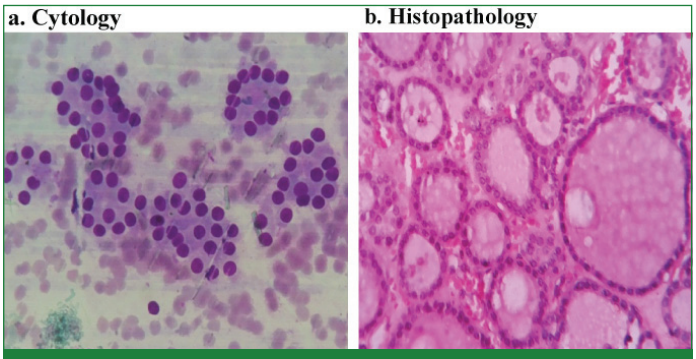


[Table/Fig-9]: a) CAT III-Cytosmear of AUS/FLUS show focal nuclear atypia and intranuclear pseudo- inclusion (Diff-Quik 40X); b) Micro section of Papillary carcinoma of thyroid (H &E 40X).

The diagnostic category FN/SFN (CAT IV) plays as screening test because FNA cannot distinguish Follicular and Hurthle cell Adenomas from their malignant counterparts. Histopathology follow-up was available in 10 cases. Out of 10 cases 6 were diagnosed as Follicular Adenoma as shown in [Table/Fig-10], 2 cases as Follicular Carcinoma and rest 2 cases as Nodular goiter. So, number of false positive cases in this group was 2 cases. Cytology features from these two nodular goiter show good number of microfollicle with repetitive pattern. Aspirate was probably from hypercellular area of nodular goiter, which lead to over diagnosis in cytology [Table/Fig-11 a,b]. The ROM in this group is 20%.

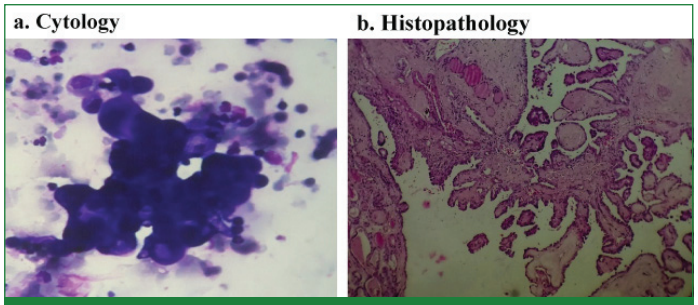


[Table/Fig-10]: a) CAT IV Cytosmear show microfollicle and macrofollicle. (MGG 40X); b) Microsection of Follicular Adenoma (H&E 40X).



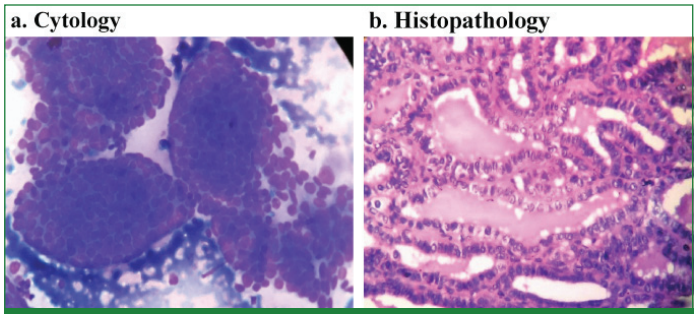
[Table/Fig-11]: a) CAT IV-Cytosmear show micro follicle with scant colloid, (MGG 40X); b) Micro section show features of Nodular Goiter (H &E 10X).

In Suspicious for Malignancy (CAT V), 6 cases available for histology correlation and all were diagnosed as suspicious for Papillary carcinoma in cytology. Out of 6 cases 4 cases diagnosed as Papillary carcinoma of thyroid but two cases proven to be papillary hyperplastic nodule. So ROM in this group was 66.6%. False positive cases in this group were 2 cases. Cytosmear from two cases show hypocellular smear but focally showing papillae, nuclear pleomorphism, pseudo inclusion with over staining of slide. So these two case interpreted wrongly as Suspicious for papillary carcinoma [Table/Fig-12 a,b]. Non branching papillary frond can be seen in both conditions. Multiple samples collected from different parts of the lesion could help in proper diagnosis.



[Table/Fig-12]: a) Cytosmear of SFM show nuclear atypia and intranuclear pseudo- inclusion (Diff- Quik 40X). (b) Micro section show features of Hyperplastic colloid Nodule (H & E).

In Malignant (CAT VI) group out of 14 cases 10 cases were reported as Papillary Carcinoma of Thyroid as shown in [Table/Fig-13], 2 cases were Medullary carcinoma of thyroid and 02 cases were Anaplastic carcinoma of thyroid on Cytology. Histopathological correlation could not be done for Medullary carcinoma of thyroid since patient referred to higher center for further investigation. There was 100% cyto-histo correlation in all 11 cases; hence the ROM rate in present study was 100%. Papillary carcinoma was the most common malignancy.



[Table/Fig-13]: a) CAT VI-Cytosmear of Papillary carcinoma of thyroid showing papillae, nuclear atypia, and thick colloid (MGG 10X); b) Microsection of Papillary Carcinoma of thyroid (H &E 40X).

In comparison to TBSRTC, malignancy risk of this study was well comparable with slightly higher in CAT II (4.2% compare to 0-3%). The malignancy risk for different categories in this study was compared with other study as shown in [Table/Fig-14]. Present study results well corroborated with Mondal SK et al., study with slightly higher percentage 20% in AUS/FLUS category [9]. When this study was compared with findings of Jo VY et al., and Nayar R et al., study, Non diagnostic category showed higher percentage [8,14].

Study	Year	Sample size	Bethesda category					
			I	II	III	IV	V	VI
Yang J et al., [3]	2005	1052	10.9	7.3	13.5	32.2	64.7	98.6
Nayar R et al., [14]	2009	1843	09	02	06	14	53	97
Jo VY et al., [8]	2010	892	8.9	11	17	25.4	70	98.1
Mondal SK et al., [9]	2013	323	0	4.5	20	30.6	75	97.8
Dawish MAA et al., [21]	2017	369	25	8.9	14.3	47.2	69.3	96.7
Upadhyaya P et al., [16]	2019	109	33.33	1.49	0	7.6	80	95.23
Present study	2020	85	0	4.2	14.2	20	66.6	100

[Table/Fig-14]: Comparision of Risk Of Malignancy (ROM) with other study.

The results of various statistical parameters like Sensitivity, Specificity, NPV, PPV and diagnostic accuracy were 92%, 91.8%, 95.7%, 85.2% and 91.9%, respectively. The present data were comparable with published data as shown in [Table/Fig-15] where the Sensitivity ranges from 57.14% to 93.4% [22,23], a Specificity of 64.6 to 100% [16,20,22], a PPV of 70.8% to100% [17,22, 23], a NPV of 79.5% to 98% [22,23] and Total Accuracy 77.3% to 97.7% [24,25]. The wide

range of values vary due to number of samples, categorisation of diagnostic category including and excluding of CAT I, CAT III and CAT IV [4,10,24,26].

Study	Year	Sample size	Sensitivity	Specificity	PPV	NPV	Accuracy
Nggada H et al., [18]	2005	69	88.9	96.1	-	-	94.2
Sangalli G et al., [22]	2006	5469	93.4	74.9	98.6	-	95.4
Bagga PK et al., [19]	2010	252	66	100	100	96	96.2
Sinna EA et al., [10]	2012	296	92.8	94.2	94.9	91.8	93.6
Pandey P et al., [23]	2012	447	57.14	90	70.8	83.33	80.28
Muratli A et al., [24]	2014	126	87.1	64.6	76.1	79.5	77.3
Nandedkar SS et al., [25]	2018	606	85.7	98.6	90	98	97.7
Rupareliya N et al., [17]	2020	21	85.7	100	100	92.8	95
Present study	2020	85	92	91.8	85.2	95.7	91.9

[Table/Fig-15]: Comparision of Statistical parameters with other study.

Limitation(s)

Unavailability of higher investigations like Ancillary Test, Immunohistochemistry and molecular markers, due to which patient was referred to higher centre. Another limitation of this study was the disagreement of the patient and the surgeon regarding the management protocol for CAT III lesions. The Bethesda System recommends repeat FNA within 3-6 months for definitive diagnosis. But the patient did not undergo repeat FNA and the surgeon also elected for surgical resection.

Future recommendations: By applying Bethesda system for reporting thyroid cytopathology along with higher diagnostic modality, excellent diagnostic approach and patient management will be achieved.

CONCLUSION(S)

FNAC is a sensitive and specific method of evaluating thyroid nodules for malignancy but histopathology is gold standard for diagnosing thyroid lesions. The Bethesda system is a standard scheme for reporting thyroid cytopathology and ROM rate will help in clinical management. This system shows excellent specificity in diagnosing malignant nodules and in screening neoplasm.

REFERENCES

[1] Amita K, Vijayshankar S. Efficacy of fine needle aspiration cytology in the diagnosis of thyroid lesion in children and adolescents. National Journal of Laboratory Medicine. 2013;2(3):1-5.
[2] Awasthi P, Goel G, Khurana U, Joshi D, Majumdar, Kapoor N. Reproducibility of "The Bethesda system for reporting thyroid cytopathology". A retrospective analysis of 107 patient. Journal of Cytology. 2018;35(1):40-47.
[3] Yang J, Schnadig V, Logrono R, Wasserman PG. Fine-needle aspiration of thyroid nodules: a study of 4703 patients with histologic and clinical correlations. Cancer. 2007;111(5):306-15.
[4] Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Am J Clin Pathol. 2009;132:658–65.
[5] Theoharis CG, Schofield KM, Hammers L, Udelsman R, Chhieng DC. The Bethesda thyroid fine-needle aspiration classification system: year 1 at an academic institution. Thyroid. 2009;19(11):1215-23.
[6] Baloch ZW, LiVolsi VA, Asa SL, Rosai J, Merino MJ, Randolph G, et al. Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: A Synopsis of the national cancer institute thyroid fine-needle aspiration state of the science conference. Diagn Cytopathol. 2008;36:425-37.
[7] Bhagat VM, Tailor HJ, Bhargav RK, Baladawa V. Diagnostic role of the Bethesda system for reporting thyroid lesions: effective tool for managing thyroid lesions. Global Journal of Medical Research: c Microbiology and Pathology. 2014;14(1):
[8] Jo VY, Stelow EB, Dustin SM, Hanley KZ. Malignancy risk for fine needle aspiration of thyroid lesions according to the Bethesda system for reporting thyroid cytopathology. Am J Clin Pathol. 2010;134:450-56.
[9] Mondal SK, Sinha S, Basak B, Roy DN, Sinha SK. The Bethesda system for reporting thyroid fine needle aspirates: A cytologic study with histologic follow-up. Journal of Cytology. 2013; 30(2):94-99.
[10] Sinna EA, Ezzat N. Diagnostic accuracy of fine needle aspiration cytology in thyroid lesions. Journal of Egyptian National Cancer Institute. 2012;24:63-70.
[11] Crothers BA, Henry MR, Firat P, Hamper UM. The Bethesda System for reporting thyroid cytopathology. Springer Science + Business Media, LLC 2010.Chapter 2, Non diagnostic/Unsatisfactory: 7
[12] Mehrotra D, Anita AM, Andola SK, Patil AG. Thyroid cytology evaluation based on the Based system wih clinic-morphological correlation. Annals of Pathology and Laboratory Medicine. 2016;3(4):348-55.
[13] Kumari NS, Parigi M, Afroze S. Accuracy of fine needle aspiration cytology with histopathology of thyroid lesions-1.5 years study at Government ENT hospital, Hyderabad, Telangana. IAIM. 2017; 4(8):49-63.
[14] Nayar R, Ivanovic M. The indeterminate thyroid fine needle aspiration: experience from an academic center using terminology similar to that proposed in the 2007 National Cancer Institute Thyroid Fine Needle Aspiration State of the Science Conference. Cancer Cytopathol. 2009;11(7):195-202.
[15] Alshaikh S, Harb Z, Aliufairi E, Ali Almahari S. Classification of thyroid fine-needle aspiration cytology into Bethesda categories: An institutional experience and review of the literature.Cytojournal. 2018;15:4.
[16] Upadhyaya 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. Journal of Cytol. 2019;36(1):48-52.
[17] Rupareliya N, Patel PR, Bhagat VM, Neb V. Cytomorphological study of thyroid nodule and categorisation according to Bethesda system and its histopathological correlation. Annals of Pathology and Laboratory Medicine. 2020;7(2):72-75.
[18] Nggada H , Musa A, Gali B, Khalil M. Fine Needle Aspiration Cytology Khalil Of Thyroid Nodule(S): A Nigerian Tertiary Hospital Experience. The Internet Journal of Pathology. 2005;1:1-4.
[19] Bagga PK, Mahajan NC. Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it? Indian J Cancer. 2010;47:437-42.
[20] Ali SZ. Thyroid cytopathology Bethesda and Beyond. Actacytologica. 2011;55:4-12.
[21] Dawish MAA, Robert AA, Muna A, Eyad A, Ghamdi AA, Hajeri KA, et al. Bethesda system for reporting Thyroid cytopathology: A three-year study at a tertiary care referral center in Saudi Arabia. World J Clin Oncol. 2017;8:151-57.
[22] Sangalli G, Serio G, Zampatti C, Bellotti M, Lomuscio G. Fine needle aspiration cytology of the thyroid: A comparison of 5469 cytological and final histological diagnoses. Cytopathology. 2006;17:245-50.
[23] Pandey P, Dixit A, Mahajan NC. Fine-needle aspiration of the thyroid: A cytohistologic correlation with critical evaluation of discordant cases. Thyroid Res Pract. 2012;9(2):32-39.
[24] Muratli A, Erdogan N, Sevim S, Unal I, Akyuz S. Diagnostic efficacy and importance of fine needle aspiration cytology of thyroid nodules. Journal of Cytology. 2014;31(2):73-77.
[25] 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(2):76-82.
[26] Mehra P, Verma AK. Thyroid cytopathology reporting by the Bethesda System: A two-year prospective study in an academic institution. Pathology Research International. 2015;2015:240505. 11 pages, 2015. doi:10.1155/2015/240505M.

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