

Comparison of Cytological and Histopathological Findings in Thyroid Lesions at a Tertiary Care Institute

Modh Yash Girishkumar¹, Shah Khyati Bhupendra², Kunal Purohit³, Matariswa Samanta⁴

¹Post Graduate Department of Pathology, Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India

^{2,3}Assistant Professor Department of Pathology, Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India

⁴Associate Professor Department of Pathology, Pacific Institute of Medical Sciences, Udaipur, Rajasthan, India

Received: 18-02-2023 / Revised: 11-03-2023 / Accepted: 05-04-2023

Corresponding author: Dr. Matariswa Samanta

Conflict of interest: Nil

Abstract

Fine-needle aspiration cytology (FNAC) is an invaluable tool in the management of thyroid lesions with a high degree of accuracy. With the main goal of verifying benign lesions and preventing unnecessary surgery, FNAC of the thyroid gland is currently a well-established, first-line diagnostic technique for the examination of diffuse thyroid lesions as well as of thyroid nodules. The objective of the study was to compare the findings of cytological and histopathological features of thyroid lesions.

Materials and methods: The present study was carried out in the Department of Pathology, Pacific Institute of Medical Sciences over a period of 18 months from April 2021 to September 2022. A total of 100 patients with thyroid lesions were studied by FNAC and results were compared with histopathology wherever possible.

Results: Majority of cases (29%) in the present study were in middle age group (31- 40 years) followed by 23% cases seen in (51-60 years) age group. Male female ratio was 1:8.09. We found that the most common benign diagnosis seen by cytology was colloid goitre (53%) and malignant was papillary carcinoma (10%). Histopathology showed same diagnosis in 85 out of 100 as diagnosis by cytology. For malignant lesions, both sensitivity and specificity were 100.00%. For benign lesions sensitivity ranged from 78.57% to 93.48% for various lesions, while specificity ranged from 81.48% to 100%. For malignant lesions both PPV and NPV were 100%. For benign lesions PPV ranged from 81.13% to 100% while NPV ranged from 92.21% to 93.62%.

Conclusion: The Bethesda system review of thyroid FNAs for reporting provided accurate cytological diagnosis. In reporting thyroid cytology, it represents uniformity and consistency with increased clinical importance and higher predictive value. The utility of the diagnostic test depends on the nature of the disease, experience and knowledge of cytopathologist.

Keywords: Cytohistologic correlation, fine-needle aspiration, thyroid lesions.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Thyroid gland is a unique organ due to its anatomical position which gives easy access for physical examination, cytological assessment and histopathological findings. In places like India where iodine shortage is endemic, thyroid gland swellings are common. In surgical surgery, thyroid lesions afflict women more frequently than men and are seen in 4-7% of the population.[1] Males, young patients, and solitary nodules have higher neoplastic risk factors.[2] Therefore, thyroid gland removal is only performed on patients in whom cancer is suspected and it is avoided in a benign lesion just to prevent recurrent laryngeal nerve injury,

The most frequent reason for thyroid surgery worldwide is a solitary nodule with the possibility of malignancy. The prevalence of thyroid nodules has increased during the past few decades. As a result, it is not unusual to discover a thyroid nodule by accident in a patient who is asymptomatic. The differential diagnosis of a thyroid nodule is essential since surgery is required for malignancy while thorough patient follow-up is required in the case of benign nodules.[3]

Fine needle aspiration cytology (FNAC), which is quick, dependable, safe, minimally invasive, economical, and capable of high sensitivity and specificity,[4] has taken the lead in the examination of thyroid nodules. Surgery for thyroid nodule illnesses in patients has been drastically reduced. Thanks to FNAC, increasing the proportion of malignant operated nodules to over 50%.[5]

A definitive diagnosis of malignancy, together with the type of tumour, can be made via thyroid cytology, allowing for one-stage therapeutic surgery. Thyroid cytology serves both therapeutic and diagnostic purposes. [6,7] After aspirating fluid from their thyroid swellings, patients

experienced relief from compressive sensations, fulfilling a therapeutic purpose.

There are some downsides to FNAC, such as insufficient specimens, improper sample preparation methods, expert aspiration, and expert cytological interpretation. Since capsular and vascular invasion are not visible in cytology, follicular adenoma and follicular carcinoma cannot be separated from one another. Therefore, a histological study is required.[8]

Papillary carcinoma is a slow-growing tumour that typically manifests in a site of metastasis. It can be challenging to determine in FNAC whether a patient with multinodular goitre has a tiny papillary carcinoma focus. Therefore, the histological analysis of this tumour is a crucial prognostic tool for the patient. This study links the histological findings to the cytological distribution of various thyroid lesions in order to establish a definitive diagnosis.

However, limitations in FNAC caused by a small sample size, thyroid swelling's vascularity, variations in sampling technique, the performing expert's skill, and the pathologist's experience reading the aspirate do present a challenge for making a conclusive diagnosis. The Bethesda System for Reporting Thyroid Cytopathology was first presented in 2007 at the "Thyroid Fine Needle Aspiration State of the Science Conference" held in Bethesda, Maryland, to address this issue by standardizing terminology and morphologic criteria as well as the associated risk of malignancy.[10]

The present study was conducted to compare the cytological and histopathological findings in the thyroid lesion at a tertiary care center.

Materials and Methods

The present study was a cross-sectional study, conducted in the Department of

Pathology of Pacific Institute of Medical Science, Udaipur Rajasthan from April 2021 to September 2022. The sample size of 90 was calculated using the formula $4pq/12$. [10] The study was conducted after obtaining the ethical clearance from the Institutional Ethical Committee of PIMS, Udaipur dated 23.10.2021 with reference no. STU/IEC/2021/21. The patient who have palpable lesions of thyroid gland irrespective of their age and sex, clinically non palpable lesion through USG guided FNAC and all suspected lobectomy or thyroidectomy specimens accepted for histopathological examination were included in the study. Those patient from whom the swellings arises from skin and surrounding structures of thyroid gland were excluded from the study.

The current study was conducted on patients presenting with various thyroid lesion in ENT department. Detailed history, clinical examination and radiological finding was done in every case. The patient was explained in detail about the procedure of FNAC. If the aspirate sample is large enough, several slides prepared both air dried and wet fixed so that special staining can be carried out if required. Smears was stained by rapid pap's stain, fields stain, Giemsa stain or by standard hematoxylin and eosin methods. The basic constituent of both stains is Harris hematoxylin. The results were classified into six categories according to Bethesda System of reporting thyroid cytology.

CAT-I: Non diagnostic/Unsatisfactory (ND/UNS)

CAT-II: Benign (BN)

CAT-III: Atypia of undetermined significance (AUS)/Follicular lesion of undetermined significance (FLUS)

CAT-IV: Follicular neoplasm (FN)/Suspicious of follicular neoplasm (SFN)

CAT-V: Suspicious for malignancy (SM)

CAT-VI: Malignant (M)

The biopsy samples from the thyroid swelling received in the histopathology section of the Pathology department will be evaluated. After the surgery histopathology department will receive the specimen in formalin filled container. The specimen was fixed in 10% formalin for 24 hrs. After that tissue will be taken for grossing and it will be done according to standard procedure being followed in the department. Paraffin blocks will be made and with the help of the microtome, sections will be cut off 4-5 mm thickness and stained by Hematoxylin and Eosin and was studied by light microscopic examination 3-4 μ m thickness paraffin blocks sections made with the help of microtome and sections kept on hot plate at 65°C temperature. Sections were stained by Haematoxylin and Eosin.

Statistical analysis:

The data were collected and entered into Microsoft Excel sheet. The data was expressed in the form of absolute numbers and percentage. Diagnostic accuracy was determined by calculating sensitivity, specificity, positive and negative predictive values by using SPSS version 22.0.

Result

Majority of cases taken in the present study were seen in middle age group (31-40 years) with total no. of cases being 29 which was followed by 23 cases seen in (51-60 years) age group. The mean age of study participants was 43.23 ± 12.98 years. Age ranged from 15 to 70 years. In our study, 89 (89.0%) cases were females and 11(11.0%) were males with peak age range of third and fourth decade of life. In our study, majority of case were seen in age group 31-40 years in both gender.(Table 1)

Table 1: Age and Gender Distribution of study participants

Age	Gender					
	Female		Male		Total	
	N	%	N	%	N	%
<20 years	5	5.6%	0	0.0%	5	5.0%
21-30 years	12	13.5%	1	9.1%	13	13.0%
31-40 years	25	28.1%	4	36.4%	29	29.0%
41-50 years	19	21.3%	2	18.2%	21	21.0%
51-60 years	20	22.5%	3	27.3%	23	23.0%
61-70 years	8	9.0%	1	9.1%	9	9.0%
Total	89	100.0%	11	100.0%	100	100.0%

The Bethesda System Reporting Thyroid Cytology (TBSRTC) categorization was done in all the cytological diagnosed cases. The maximum cases were in benign group 76 (76.0 %) followed by 10 (10.0%)

follicular neoplasm /suspicious of follicular neoplasm -IV, 10 (10.0%) suspicious of malignancy -V and 4(4.0%) cases of follicular lesion of undetermined significance – III

Table 2 : Distribution of cases based on cytology

		N	%
Benign (n=88)	Colloid goitre	53	53.0
	Granulomatous thyroiditis	5	5.0
	follicular lesion of undetermined significance	4	4.0
	Hashimoto's thyroiditis	11	11.0
	Lymphocytic thyroiditis	7	7.0
	Follicular neoplasm	8	8.0
Malignant (n=12)	Papillary carcinoma	10	10.0
	Non-invasive Follicular neoplasm with papillary like nuclear features	2	2.0
Total		100	100.0

In our study, the most common benign goitre (53%) and malignant was papillary carcinoma (10%).(Table 2)

Table 3: Distribution of cases based on histopathology

		N	%
Benign (n=88)	Colloid goitre	46	46.0
	Granulomatous thyroiditis	5	5.0
	Hashimoto's thyroiditis	15	15.0
	Follicular Adenoma	14	14.0
	Lymphocytic thyroiditis	8	7.0
Malignant (n=12)	Papillary carcinoma	10	10.0
	Non-invasive Follicular neoplasm with papillary like nuclear features	2	2.0
Total		100	100.0

In our study, the most common benign colloid goitre (46%) and malignant was papillary carcinoma (10%).(Table 3)

Table 4: Cytology and histopathology correlation

Diagnosis by Cytology		N	Diagnosis by histopathology	Accuracy
Benign (n=88)	Colloid goitre	53	Colloid goitre-43 Follicular Adenoma-4 Hashimoto's thyroiditis-5 Lymphocytic thyroiditis-1	81.13%
	FLUS	4	Colloid goitre-2 Follicular Adenoma-2	-
	Granulomatous thyroiditis	5	Granulomatous thyroiditis-5	100%
	Hashimoto's thyroiditis	11	Hashimoto's thyroiditis-10 Colloid goitre-1	90.90%
	Follicular neoplasm	8	Follicular Adenoma-8	100%
	Lymphocytic thyroiditis	7	Lymphocytic thyroiditis-7	100%
Malignant (n=12)	Papillary carcinoma	10	Papillary carcinoma-10	100%
	Non-invasive Follicular neoplasm	2	Non-invasive Follicular neoplasm-2	100%
Total		100	Same diagnosis-85	85%

In our study, histopathology showed same diagnosis in 85 out of 100 as diagnosis by cytology. The most common cases of mismatched diagnosis were colloid goitre.(Table 4)

Table 5: Diagnosis by cytology

Diagnosis*	Diagnosis by Cytology			
	True positive	False negative	True negative	False positive
Colloid goitre (46)	43	3	44	10
Thyroiditis (28)	22	6	71	1
Follicular Adenoma (14)	8	6	86	0
Malignant (12)	12	0	88	0

*Diagnosis by histopathology (gold standard)

Out of 46 cases of colloid goiter, true positive was[43],false negative was[3],true negative was[44],false positive was[10]. In case of total 28 cases of thyroiditis 22 was true positive,6 was false negative,71 was true negative and 1 was false positive. In total 14 cases of follicular adenoma 8 was

true negative,6 was false negative, 86 was true negative and no false positive cases identified. Out of 12 malignant cases of thyroid cancer 12 was showing true positive and 88 was true negative, where as no false negative and false positive cases seen. (Table 5)

Table 6 : Diagnostic accuracy of cytology

Diagnosis	Diagnostic accuracy of cytology				
	Sensitivity	Specificity	PPV	NPV	Accuracy
Colloid goitre	93.48%	81.48%	81.13%	93.62%	87.00%
Thyroiditis	78.57%	98.61%	95.65%	92.21%	93.00%
Follicular Adenoma	57.14%	100.00%	100.00%	93.48%	94.00%
Malignant	100.00%	100.00%	100.00%	100.00%	100.00%

In cases of colloid goiter 93.48% sensitivity and 81.48% specificity was found, diagnostic accuracy was 87.00%.and cases of thyroiditis sensitivity was 78.57%, specificity was 98.61%and diagnostic accuracy was 93.00%. in cases

of follicular adenoma sensitivity was [57.14%], specificity was [100%] and diagnostic accuracy was 94.00%, where as 100% diagnostic accuracy of cytology was found for malignant lesion. (Table 6)

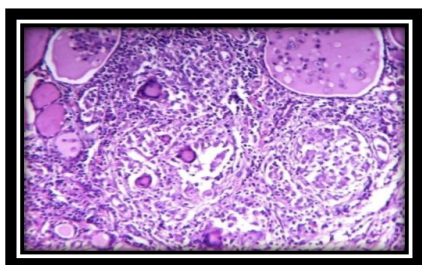


Fig-1 Granulomatous thyroiditis: Photomicrograph shows macrophages, plasma cells, damaged thyroid follicles and Multinucleate giant cells (H&E-400x)

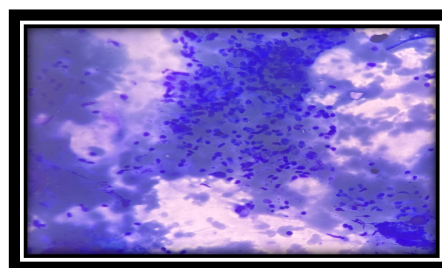


Fig-2 Hashimoto thyroiditis : smear shows hurthle cells (Giemsa-400x)

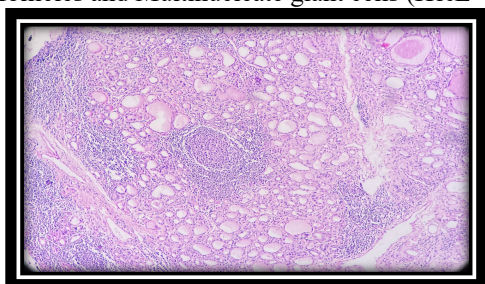


Fig-3. Hashimoto thyroiditis : Shows clusters of colloid filled thyroid follicles and lymphoid cells forming germinal center (H&E-100x)

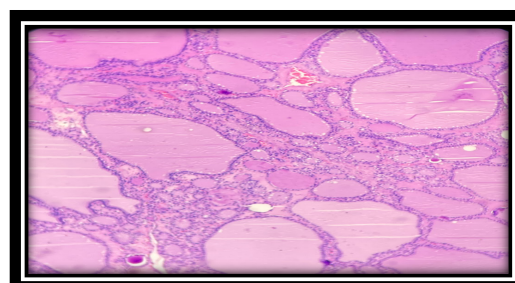


Fig-4. Colloid goitre : Photomicrograph shows colloid-rich follicles and areas of follicular hyperplasia (H&E-100x)

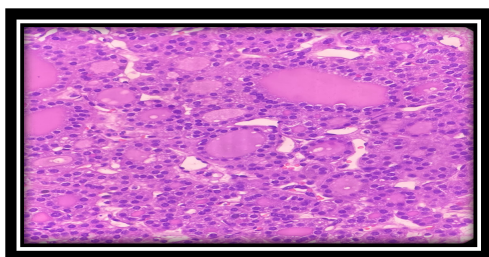


Fig-5 .Follicular adenoma: Follicle cells arranged in normo, macro and microfollicular pattern (H&E-400x)

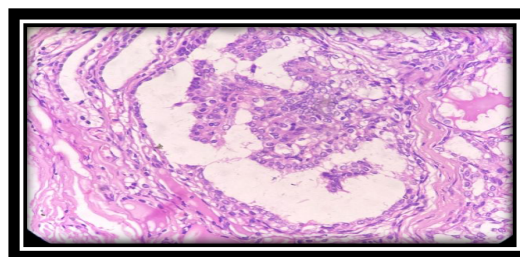


Fig-6. Papillary carcinoma : Photomicrograph shows branching papillae having a fibrovascular stalk covered by a single to multiple layers of cuboidal epithelial cells (H&E-400x)

Discussion

The main indication for fine-needle aspiration (FNA) of the thyroid is a thyroid nodule. Thyroid nodule can be seen in a variety of pathologic entity, ranging from benign nodular colloid goitres to malignant lesions such as papillary thyroid carcinoma or poorly differentiated carcinomas. FNAC has been shown to be the safest and most accurate of diagnostic tools in thyroid lesions [11] with a sensitivity as high as 93.4% and a specificity of 74.9%. FNAC is considered the gold standard diagnostic test in the evaluation of a thyroid nodule. However, FNACs cannot rule out the possibility of metastasized tumour masses until subsequent tissue biopsy is performed. FNAC is an invaluable tool in the management of thyroid lesions with a high degree of accuracy. It is safe, simple, cost effective procedure with absence of major complications and can be performed on out-patients with wide patient compliance. FNAC provides a more rapid and accurate diagnosis of thyroid lesions than any other combination of clinical laboratory tests. But, histopathology is always required to confirm the diagnosis and for further management.

Majority of cases (29%) in the present study were in middle age group (31- 40 years) followed by 23% cases seen in (51-60 years) age group. Similarly in the study by Roy PK et al, [12] a majority of the patients belonged to 31-40 years. In the present study, age ranged from 15 to 70 years. Wide range of age groups from 5 years to 90 years 65 have been observed in the previous studies. The mean age of study participants was 43.23 ± 12.98 years. This was similar to the studies by Handa U et al [13] and Singh P et al [14]. In our study, 89% were females and majority of cases were seen in age group 31-40 years in both genders. Study by Roy PK et al [12] showed sex differentiation of female 89% and male 11% preponderance of thyroid nodule disorders, same as our study.

The Bethesda System Reporting Thyroid Cytology (TBSRTC) categorization was done in all the cytological diagnosed cases. The maximum cases were in benign group (76%). This observation was similar to other studies Yassa L et al [5] (66%) and Mondal SK et al (84%) [16], all of which found that benign lesions were more common. In our study, the most common benign diagnosis seen by cytology was colloid goitre (53%) followed by Hashimoto's thyroiditis and among malignant lesions; papillary carcinoma (10%) was most common followed by Non-invasive Follicular neoplasm.

Results obtained in a study by Rizvi SA et al [17] showed that the non-neoplastic group consisted of 82% of patients with colloid goitre. In study by Roy PK et al [12] majority was Colloid/Nodular Goitre (88.75 Hashimoto's Thyroiditis 5%, Adenomatoid goiter 3.75% and benign cystic lesion 2.5%. Similar to our observation, in the study by Islam MS et al [18] on evaluation FNAC of the neoplastic thyroid swellings, papillary carcinoma was the most common. In the study by Roy PK et al [12] majority of neoplastic disease was papillary carcinoma (53.84) followed by follicular neoplasm (30.76%) and (7.69%) anaplastic carcinoma. In our study, the most common benign diagnosis seen by histopathology was colloid goitre (46%) and malignant was papillary carcinoma (10%) similar to the incidence with cytology. Solitary colloid goitre was the most common benign condition and the papillary carcinoma was the most common malignant lesion identified by FNAC in the study by Babu SBK et al [19]. The results was almost similar to the study done by Handa U et al [13]. In this study the FNAC showing inadequacy in getting the sample was only 6% and a similar type of study done by Mahar SA et al [20] had shown that 9% of the FNAC sample was found to be inadequate and so our study was almost in pair with it.

In our study, histopathology showed same diagnosis in 85 out of 100 as diagnosis by cytology. The most common cases of mismatched diagnosis were colloid goitre (81.3%), while in case of Hashimoto's thyroiditis the correlation was 90.90%. 100% diagnostic accuracy of cytology was found for malignant lesions while the accuracy was 94%, 93% and 87% respectively for Follicular Adenoma, Thyroiditis and Colloid goitre. Mundasad B et al [21] conducted a study on Accuracy of FNAC in diagnosis of thyroid swellings. In their study among 144 patients FNAC revealed 94% benign, 6% malignant 4% suspicions. 13% inadequate, 4% indeterminate. But histopathology showed 82% benign, 18% malignancy. In their study the inadequate sample rate was 13%. The authors concluded that the most important factors for inadequate sample include experience of the aspirator and criteria used to define a satisfactory sample.

Out of 100 cases, 11 had false positive results, of which 10 were Colloid goitre and 1 was Thyroiditis. This observation was similar to the study by Mandal S et al [22] in which out of 120 patients 12 had a False positive result. This observation was in contrast to the study by Singh P et al [14] in which out of 108 cases only 3 were false negatives.

In the study by Rout K et al [23] among 76 cases of thyroid swellings that underwent surgery and subsequent histopathological study, 73 cases showed positive correlation between FNAC and histopathology result. However, it differed in three cases when diagnosis by FNAC proved otherwise. The diagnostic accuracy of FNAC for thyroid swellings in this series was 96.05%.

Fine Needle Aspiration Cytology from hyperplastic nodule will show marked cellularity of the smear which may mimic follicular neoplasm. Since this is a focal phenomenon, samples from other different

areas should be taken to avoid misdiagnosis.

Cystic Papillary Carcinomas often contain abundant colloid. This can cause diagnostic problem especially if smears are poor in cells. In Nodular goitre groups of large cells with irregular nuclei of uncertain origin are frequently seen. They may be regenerating epithelial cells consistent with repair or may be histiocytes. These aggregates of histiocytes can mimic cells of papillary carcinomas in some cases due to similar nuclear features. [24] so we can reduce false negative results by a close look at the nuclear features to make a correct diagnosis. According to Handa U et al [13] marked cellularity or increased cellularity of the smear is another difficulty in thyroid fine needle aspiration cytology giving false negative diagnosis of carcinoma.

In young patients and children, florid lymphocytic type of thyroiditis with scant epithelial cells are commonly seen. The smears are dominated by a mixed population of lymphoid cells showing centroblasts, immunoblasts and dendritic reticulum cells. Follicular to Lymphoid cell ratios are often as high as 1:10. The epithelial cells are so inconspicuous and smears resemble reactive lymphoid hyperplasia mimicking lymphocytic thyroiditis. The presence of hyperplastic follicular cells on FNAC samples from Hashimoto thyroiditis may mimic follicular neoplasm and result in a false interpretation. This can be avoided by adequate sampling of the thyroid.

The differentiation between Follicular neoplasm and Nodular goitre is the most common diagnostic problem in solitary nodules as cytological appearances may overlap. A microfollicular focus in colloid nodule cytologically may mimic a microfollicular neoplasm, while smears from macro follicular (colloid) adenoma resemble a dominant nodule in multinodular goitre. Jaffar indicated that after excluding Papillary Carcinomas and

Hurthle cell neoplasms presence of hemosiderin laden macrophages strongly favors the diagnosis of benign colloid nodule. [25]

In the study by Priya S et al [26] 60 cases reported to be having Nodular colloid goitre with / without cystic degeneration in HPE report were diagnosed as not having any neoplasm in FNAC, thus presenting as true negative. 2 cases (n = 2) reported to be Papillary thyroid carcinoma (PTC) in HPE were actually reported as negative for malignancy or neoplasm in FNAC, thus presenting false negative cases. Likewise, 2 cases (n = 2) which was reported as follicular adenoma in HPE was misdiagnosed as negative for follicular neoplasm in FNAC, thus being counted as false negative. 6 cases (n = 6) were reported as Hashimoto's thyroiditis in HPE, which was reported as negative for neoplasm in FNAC, thus presenting as true negative. [26]

In the present study, sensitivity and specificity for colloid goitre was 93.48 and 81.48% respectively. For Thyroiditis it was 78.57% and 98.61% and for Follicular Adenoma sensitivity was 57.14% and specificity was 100.00%. Significantly, for malignant lesions, both sensitivity and specificity were 100.00%. For malignant lesions both PPV and NPV were 100%. For benign lesions, the PPV was 81.13%, 95.65% and 100.00% respectively for Colloid goitre, Thyroiditis and Follicular Adenoma. NPV was 93.62%, 92.21% and 93.48% Colloid goitre, Thyroiditis and Follicular Adenoma respectively.

In a study by Islam MS et al [18] sensitivity and specificity of FNA diagnosis of thyroid swelling was evaluated to be 73.68% and 97.26%. In the study by Roy PK et al [12], the Sensitivity was found to be 81.48% and Specificity is 95.29%. Cytologic and histologic diagnoses were compared in 4069 patients and the sensitivity and specificity of FNAC were found to be 91.8% and 75.5%, respectively.11 In the study by Gupta A et

al [27] the overall sensitivity of FNAC to detect malignancy in the present study was 88.8%, specificity 100%, PPV 100%, NPV 94.87%, and diagnostic accuracy 96.3%. Several international studies have documented the sensitivity of FNAC in thyroid nodules to range from 52 to 98%. Similarly, the international normal range is for specificity is 72-100% and for PPV is 50-90%.91 In the study by Babu SBK et al [19] the sensitivity of FNAC in detecting all the benign and malignant type of thyroid lesions was found to be in the range of 80-100%, whereas the specificity and the positive predictive value was almost 100% for all the lesions detected by FNAC.

Similarly, Priya S et al [26] compared the FNAC results with HPE report. Statistical analysis of neoplastic lesions studied showed sensitivity, specificity, positive predictive value, and negative predictive value of FNAC to be 67%, 94%, 84%, 100%, and 94%, respectively. In the present study, accuracy of FNAC was 100% for malignancy, similar to the observations in the study by Jain K et al. [28] The accuracy was 87%, 93.00% and 94.00% for colloid goitre, Thyroiditis and Follicular Adenoma respectively compared to 95%, 73.3% and 73% for the same lesions in the Jain K et al study. [28]

Conclusion:

We would like to extend our sincere thanks to all the participants who participated in the study. We also like to thank the Central Research Department for approving the study and the Institute to carry over the study.

References

1. Jain K, Ahmad F, Dutta S, Awasthi S, Kumar A, Mittal A. Fine Needle Aspiration Cytology: A Reliable Tool for Diagnosis & Management of Various Thyroid Lesions. *Annals of International Medical and Dental Research*. 2017;3(2):4.

2. Vinay K, Abdul K. Abbas, Jon C. Aster. Pathology of The Endocrine System, Robbins & Cotran Pathologic Basis of Disease, 10th Edition (2). Elsevier; 2020; (24):1085.
3. Polyzos SA, Kita M, Avramidis A. Thyroid nodules-stepwise diagnosis and management. Hormones-Athens. 2007 Apr 1;6(2):101
4. Ashcraft MW, Van Herle AJ. Management of thyroid nodules. II: Scanning techniques, thyroid suppressive therapy, and fine needle aspiration. Head & neck surgery. 1981 Mar;3(4):297-322.
5. Yassa L, Cibas ES, Benson CB, Frates MC, Doubilet PM, Gawande AA, Moore Jr FD, Kim BW, Nosé V, Marqusee E, Larsen PR. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer Cytopathology: Interdisciplinary International Journal of the American Cancer Society. 2007 Dec 25;111(6):508-16.
6. Ogilvie JB, Piatigorsky EJ, Clark OH. Current status of fine needle aspiration for thyroid nodules. Advances in surgery. 2006 Sep 1; 40: 223-38.
7. Mckee G. The role of fine needle aspiration cytology in the diagnosis of thyroid lesions. Journal of the Royal Society of Medicine. 1998 Dec; 91(33_suppl):28-32.
8. Sharma C. Diagnostic accuracy of fine needle aspiration cytology of thyroid and evaluation of discordant cases. Journal of the Egyptian National Cancer Institute. 2015 Sep 1;27(3):147-53.
9. Pandey P, Dixit A, Mahajan NC. Fine-needle aspiration of the thyroid: A cytohistologic correlation with critical evaluation of discordant cases. Thyroid Research and practice. 2012 May 1;9(2):32.
10. Cibas ES, Ali SZ. NCI Thyroid FNA State of the Science Conference. The Bethesda system for reporting thyroid cytopathology. Amer. J. Clin. Pathol.; 2009; 132(5): 658.
11. Ravetto C, Colombo L, Dottorini ME. Usefulness of fine-needle aspiration in the diagnosis of thyroid carcinoma. A retrospective study in 37,895 patients. Cancer (Cancer Cytopathology). 2000; 90:357-63.
12. Roy PK, Bandyopadhyay S, Dubey AB, Sengupta A. A Comparative Study on Aspiration Cytology and Histopathology in Diagnosis of Thyroid Nodule and Its Correlation. Indian J Otolaryngol Head Neck Surg. 2019 Oct;71(Suppl 1):997-1001.
13. Handa U, Sukant G, Mohan H, Nagarkar N. Role of fine needle aspiration cytology in diagnosis and management of thyroid lesions: A study on 434 patients. J Cytol. 2008; 25(1):13-7.
14. Singh P, Chopra R, Calton N, Kapoor R. Diagnostic Accuracy of Fine Needle Aspiration Cytology of Thyroid lesions. Journal of Cytology. 2000;17(3):135-9.
15. 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.
16. 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. J Cytol. 2013; 30(2):94-9.
17. Rizvi SA, Husain M, Khan S, Mohsin M. A comparative study of fine needle aspiration cytology versus non-aspiration technique in thyroid lesions. Surgeon. 2005; 3(4):273-276.
18. Islam MS, Siddiquee BH, Akhtar N, Salam KS, Aktaruzzaman M. Comparative study of FNAC and histopathology in the diagnosis of thyroid swelling. Bangladesh J Otorhinolaryngol. 2010;16(1):35-43.

19. Babu SBK, Raju R, Radhakrishnan S. Correlation of fine needle aspiration cytology with histopathology in the diagnosis of thyroid swellings. *Int Surg J.* 2016; 3:1437-41.
20. Mahar SA, Husain A, Islam N. Fine needle aspiration cytology of thyroid nodule: diagnostic accuracy and pitfalls. *J Ayub Med Coll Abbottabad.* 2006;18(4):26-9
21. B. Mundasd. I McAllister, J. Carson and P. Pyper Accuracy of fine needle aspiration cytology in diagnosis of thyroid swellings. *Internet journal of Endocrinology.* 2006; 2(2)>
22. Mandal S, Barman D, Mukherjee A, Mukherjee D, Saha J, Sinha R. Fine needle aspiration cytology of thyroid nodules-evaluation of its role in diagnosis and management. *J Indian Med Assoc.* 2011;109(4):258-61.
23. Rout K, Ray CS, Behera SK, Biswal R. A comparative study of FNAC and histopathology of thyroid swellings. *Indian Journal of Otolaryngology and Head & Neck Surgery.* 2011 Oct; 63:370-2.
24. Nassar A, Gupta P, LiVolsi VA, Baloch Z. Histiocytic aggregates in benign nodular goiters mimicking cytologic features of papillary thyroid carcinoma (PTC). *Diagn Cytopathol.* 2003 Nov;29(5):243-5.
25. Jaffar R, Mohanty SK, Khan A, Fisher AH. Hemosiderin laden macrophages and hemosiderin within follicular cells distinguish benign follicular lesions from follicular neoplasms. *Cytojournal.* 2009; 6:3:1-9.
26. Priya S, Akhtar Z. FNAC and HPE correlation of thyroid lesions in the district of Kanchipuram. *International Journal of Scientific Research.* 2017; 6(9):692-693.
27. Gupta A, Tyagi S, Yadav ML. Association of Fine Needle Aspiration Cytology with Histopathology and Thyroid stimulating Hormone in the Diagnosis of Thyroid Lesions. *J Mahatma Gandhi Univ Med Sci Tech.* 2020;5(1):9–15.
28. Jain K, Ahmad F, Dutta S, Awasthi S, Kumar A, Mittal A. Fine Needle Aspiration Cytology: A Reliable Tool for Diagnosis & Management of Various Thyroid Lesions. *Ann. Int. Med. Den. Res.* 2017; 3(2):4- 9.