

## Diagnostic Utility Of Fine Needle Aspiration Cytology In Thyroid Lesions

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**Abstract:** Background: Fine-needle aspiration cytology (FNAC) cited as an inexpensive and highly accurate means in diagnosing neoplastic and non-neoplastic lesions of the thyroid. It is safe, quick, and cost effective outpatient department (OPD) procedure. Aim: The current study was done to evaluate the diagnostic utility of FNAC in thyroid lesions and to calculate sensitivity, specificity and diagnostic accuracy of FNAC in the diagnosis of thyroid lesions. Materials And Methods: The present study was conducted in the Department of Pathology, BPSGMC(W),Khanpur Kalan,Sonipat over a period of 1 year. A total of 278 cases of thyroid swelling were studied in whom FNAC of thyroid was done and diagnosis was given on conventional cytology.It was further categorized according to the Bethesda System. Cytological diagnosis was compared with the histopathology wherever available. Result: Statistical analysis of the data showed the diagnostic accuracy of fine needle aspiration cytology to be 92.2%. Fine needle aspiration cytology showed a sensitivity of 76% and a specificity of 100%.On conventional cytology, the commonest lesion in the thyroid gland was colloid goiter 124(44.6%). Fine needle aspiration cytology results revealed Category II 172 (61.86%), Category IV 30 (10.8%), Category VI 20 (7.19%) , Category V 9 (3.27%) , Category III 4 (1.43%) Category I 43 (15.45%) in thyroid lesions according to the Bethesda System. Conclusion: FNAC may be considered as a significant tool in the diagnosis of patients with thyroid lesions. [Goel S Natl J Integr Res Med, 2020; 11(1):3-10]

**Key Words:** Bethesda, colloid goiter, FNAC, Papillary carcinoma thyroid

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**Introduction:** Diseases associated to thyroid gland are frequently observed in current era though its spectrum ranges from systemic disease (Grave's disease) to a localized abnormality, such as nodular enlargement (goitre) or a tumour mass. Benign thyroid diseases are commonly encountered in enormous magnitude all over the world however in India it is seen in about 4-7% of Indian adult population as well as 0.2 to 1.5% in children.<sup>1</sup>Although prevalence may be as high as 40% in iodine deficiency goiter belt areas.<sup>2</sup>

Thyroid nodules are highly prevalent in women and in older persons.<sup>3</sup>Though rare in children and adolescents, affecting 1% to 2% of the pediatric population.<sup>4</sup>The incidence of cancer in pediatric solitary nodules ranges from 14% to 40% as compared to 5% in clinically dominant nodule in adults".<sup>4</sup> Thyroid gland is unique among endocrine organs, because of its superficial location, amenable to direct physical examination, cytological evaluation and histo pathological study.<sup>5</sup>

Thyroid scintigraphy, ultrasonography and biochemical tests provide little help in excluding malignancy as thyroid function test are within normal limits and ultrasonographic appearance is not diagnostic. Therefore an effective test is needed to exclude malignancy thereby avoiding

unwanted surgery.The routine use of Fine needle aspiration cytology in the assessment of thyroid lesions has reduced the number of patients subjected to thyroidectomy for benign lesions. This technique is almost non-invasive, cost effective and free of complications in expert hands and an efficient method of differentiating benign and malignant lesions thereby reducing unnecessary surgeries except in follicular adenoma and carcinoma.This study is undertaken to find the diagnostic utility of fine needle aspiration cytology in thyroid lesions.

**Material And Methods:** This cross sectional study was conducted in the Department of Pathology, Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Sonapat, during year 2018. 278 cases were included in the study those who were having thyroid lesion referred from various department of the institute . FNAC was done in department of Pathology after obtaining informed written consent. Patient confidentiality was ensured by de identifying data and patient was given a unique code in numbers. Other relevant history, clinical and biochemical findings was collected from requisition form. Under complete aseptic precautions, FNAC was done by 21-23G needle.USG guided FNAC was done where ever required (in cases of colloid aspiration, insufficient material). Smears were air dried and then stained with Leishman stain, May

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Grunwald Giemsa stain and alcohol fixed smears with Papanicolaou (PAP) stain. All histopathology and cytology slides of these cases was studied. Cytology was reported according to the Bethesda System.<sup>6</sup>The histopathological diagnosis was grouped into following categories as per WHO classification 2017.<sup>7</sup> Data collected compiled and analysed by using standard statistical software SPSS ver.23, Mean , Standard deviation, sensitivity ,specificity ,positive predictive value , negative predictive value and diagnostic accuracy measured.

**Results:** The study was conducted on 278 cases with thyroid lesions referred to the Department of Pathology, BPSGMC(W),Khanpur Kalan for FNAC. Cytohistopathological correlation was done in 77 cases. The maximum patients were in the age group 31-40 years (27.34%) followed by 21-30 years(25.18%). The age of presentation ranged from 7 to 73 years in our study with a mean age of  $39.76 \pm 13.95$  years. In the present study, the thyroid lesions were more common in females than males in the ratio of 11.6:1.

Local examination of thyroid swelling showed that diffuse enlargement of thyroid lesions was most common finding seen in 84% cases followed by solitary nodule which accounted for 11 % cases .Multinodular swelling was present in 5% cases. On cytological diagnosis, 176 cases (63.3%) were non neoplastic and 59 cases (21.22%) were neoplastic.43 cases were considered unsatisfactory for cytological evaluation. On correlation with clinical findings, 148 cases of diffuse swelling were non-neoplastic and 49 were neoplastic while solitary swellings included 17 non-neoplastic and 9 neoplastic cases.

The maximum number of thyroid FNACs (conventional cytology) in our study were diagnosed as colloid goitre (44.6%) followed by lymphocytic thyroiditis (16.19%). 15.47% cases were considered to be unsatisfactory. Most common malignancy diagnosed was papillary carcinoma of thyroid in 6.83% cases.(Table 1),Figure 1a&b.

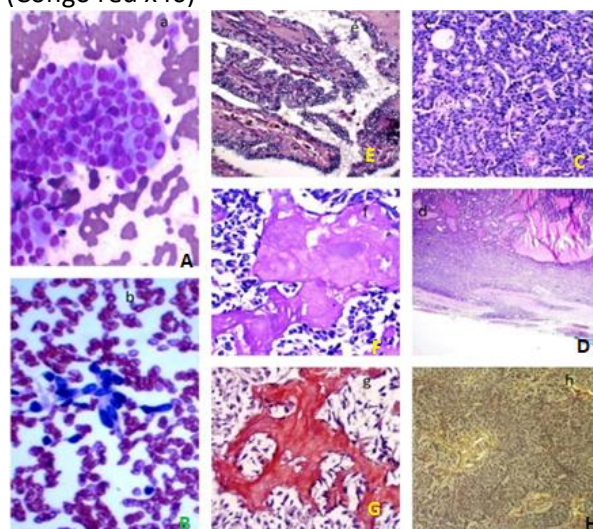
**Table 1: Cytological Diagnosis Of 278 Thyroid Cases**

Cytological diagnosis	No. of cases	Percentage%
Colloid Goitre	124	44.6
Lymphocytic	45	16.19

thyroiditis		
Colloid Goitre with lymphocytic thyroiditis	3	1.08
Atypia of undetermined significance	4	1.44
Follicular neoplasm	28	10.07
Hurthle cell neoplasm	2	0.72
Suspicious of malignancy	9	3.24
Papillary carcinoma	19	6.83
Medullary carcinoma	1	0.36
Unsatisfactory	43	15.47

Conventional cytology was further characterized according to the Bethesda system. Most of the cases belonged to category II (61.86%) which included benign lesions followed by category I (15.45%) including unsatisfactory smears.(Table 2)

Figure 1a: Photomicrograph of FNA smears from Papillary carcinoma showing intranuclear cytoplasmic inclusion. (Leishman x400); Figure 1b: Photomicrograph of FNA smears of Medullary carcinoma. (Pap x200); Figure 1c: Photomicrograph of tissue sections showing features of follicular adenoma.(H&E x100); Figure 1d: Photomicrograph of tissue sections from follicular carcinoma with capsular invasion. (H&E x40); Figure 1e: Photomicrograph of tissue section from papillary carcinoma showing true papillae with fibrovascular core. (H&E x200); Figure 1f: Photomicrograph of tissue section of medullary carcinoma showing amyloid. (H&E x400); Figure 1g: Photomicrograph of tissue section from medullary carcinoma showing amyloid. (Congo red x100); Figure 1h: Photomicrograph of tissue section showing apple-green birefringence of amyloid in medullary carcinoma under polarizing light. (Congo red x40)



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**Table2: Diagnostic Categorization Of 278 Thyroid Fncs Based On Bethesda Classification**

Categories	No. of cases	Percentage %
I :Non diagnostic or unsatisfactory	43	15.45
II: Benign	172	61.86
III: Atypia of undetermined significance	4	1.43
IV: Follicular neoplasm	30	10.8
V : Suspicious of malignancy	9	3.27
VI : Malignant	20	7.19

Cytohistopathological correlation was done in 77 cases. Histological correlation was possible in 40 cases diagnosed as colloid goitre on cytology. 25 cases corroborated with cytological diagnosis while in 9 cases diagnosis of thyroiditis along with goiter was made. Out of remaining 6 cases, 5 were diagnosed as follicular adenoma and one as papillary carcinoma. Histological correlation was done in 3 cases of lymphocytic thyroiditis.1 case was concordant with cytological diagnosis and out of rest 2 cases, 1case was diagnosed as granulomatous thyroiditis and the other one hashimoto thyroiditis. Histological correlation was done in 13 cases of follicular neoplasm , 9 cases were diagnosed as follicular adenoma and rest as follicular carcinoma.

**Table3: Correlation Of Cytological And Histopathological Diagnosis**

Cytological diagnosis	Total	Histopathological diagnosis								
		Colloid goitre	Lymphocytic Thyroiditis	Granulomatous Thyroiditis	Follicular adenoma	Hurthle cell adenoma	Hurthle cell carcinoma	Follicular CA*	Papillary CA*	Medullary CA*
Colloid goiter (II)	40	25	09(goiter with thyroiditis)	-	05	-	-	-	01	-
Lymphocytic Thyroiditis (II)	03	-	02	01	-	-	-	-	-	-
Follicular Neoplasm (IV)	13	-	-	-	09	-	-	04	-	-
Hurthle cell Neoplasm(IV)	02	-	-	-	-	01	01	-	-	-
Papillary CA*(VI)	18	-	-	-	-	-	-	-	18	-
Medullary CA*(VI)	01	-	-	-	-	-	-	-	-	01
Total	77	25	11	01	14	01	01	04	19	01

CA\*: Carcinoma

Histological correlation was possible in 2 cases of hurthle cell neoplasm,one was diagnosed as hurthle cell carcinoma and the other as adenoma. Cytological diagnosis of malignancy was consistent with histopathological diagnosis in 19 cases. 18 cases of papillary carcinoma were diagnosed and 1 case of medullary carcinoma.Figure1 c-h. Number of true positive cases were 19 and true negative were 52.No false positive case was identified and false negative

were 6. For the diagnosis of malignant lesions, a sensitivity of 76%, specificity of 100%, positive predictive value of 100%, negative predictive value of 89.6% and diagnostic accuracy of 92.2% was calculated.

**Discussion:** Thyroid enlargement, whether diffuse or in the form of a nodule, leads to a series of investigations to be done. Fine needle aspiration cytology (FNAC) is usually the first line of investigation but the limitations of cytology

are well recognized in the diagnosis of follicular neoplasm, as it is not able to differentiate between follicular adenoma and carcinoma. FNAC helps in the establishment of early diagnosis of lesion and is a well known procedure for preoperative assessment of thyroid nodules. The age distribution pattern showed thyroid disease as a condition of the middle aged in the study population. These findings were concordant with studies done by Babu SKB et al<sup>8</sup> and Thapa et al.<sup>9</sup> Garg et al<sup>10</sup> also reported the maximum number of cases in the age group of 31-40 years.

Thyroid swellings were more common in females accounting for 256 cases as compared to 22 males with Female: Male ratio of 11.6:1. The observation regarding the gender distribution in our study matches to the majority of studies which have been conducted earlier for thyroid swellings. Damle et al<sup>11</sup>, Raniwala et al<sup>12</sup> and KC et al<sup>13</sup> had a ratio of 3.5:1, 5.7:1 and 6:1 respectively as the number of cases included were less than were in the range of 54-60 cases. Laishram RS et al also had the same observation with F:M ratio of 7.6:1.<sup>14</sup>

In the present study, local examination showed that diffuse/multinodular thyroid swelling was seen in 89% cases. Solitary nodule was present in 11 % cases. Local examination of thyroid swelling in the present study is in concordance with the study of Chavan et al<sup>15</sup> showing higher percentage of diffuse/multinodular thyroid swelling where as Sharma et al<sup>16</sup> had comparatively a higher percentage of solitary nodule. This could be due to the fact that the study by Sharma et al was conducted in hilly region where soil was devoid of iodine constantly leading to enlargement of thyroid. In the present study, there was higher percentage of diffuse/multinodular swelling which may be due to the effect of goitrogens or the role of thyroid autoimmunity due to increased salt intake in the post iodination era.<sup>17</sup>

In the present study, on FNAC, 176 cases (63.3%) were non neoplastic and 59 cases (21.22%) were neoplastic. 43 cases (15.47%) were considered unsatisfactory for cytological evaluation. The incidence of unsatisfactory cases in the present study and the study done by Alwahaibi et al<sup>18</sup> was high due to inadequate yield of follicular cells, thick smears, obscuring blood or inflammatory cells, and air-dry crush or artifacts. The higher

percentage is of non-neoplastic lesions on cytological diagnosis as compared to neoplastic lesions comparable with Sharma et al.<sup>16</sup> Patel et al<sup>19</sup> conducted study on 130 cases out of which only 3 cases were considered as unsatisfactory. USG guided FNAC was done in these 3 cases and cytological diagnosis was rendered.

Conventional cytology diagnosis was later characterized according to the Bethesda system in the present study. Most of the cases belonged to category II (61.86%) which included benign lesions, 1.43% cases were of category III (Atypia of undetermined significance), Follicular neoplasm in 10.8% cases belonging to Category IV, suspicious of malignancy (Category V) in 3.27% cases and malignant cases belonging to Category VI were seen in 7.19% cases. 15.45% cases belonged to Category I including unsatisfactory smears which may be due to insufficient yield of follicular epithelial cells, obscuring blood and thick smears. The percentage of cases in Category II was well compared to the study of Jo et al but Nandedkar et al had increased percentage of benign cases as more number of patients visit the tertiary care centre after having thyroid swelling which turn out to be benign on cytological evaluation.

**Table 4: Comparison Of Cytological Diagnosis (Bethesda System) With Various Studies**

Study	I	II	III	IV	V	VI
Nandedkar et al <sup>20</sup>	4.29 %	82.6 %	0.8 %	9.0 %	1.1 %	1.9 %
Jo et al <sup>21</sup>	18.6 %	59%	3.4 %	9.7 %	2.3 %	7.0 %
Present study	15.4 %	61.8 %	1.4 %	10.8 %	3.2 %	7.1 %

Cytohistopathological correlation was done in 77 cases. Histological correlation was possible in 40 cases diagnosed as colloid goiter on cytology. 25 cases were in concordance with cytological diagnosis while in 9 cases diagnosis of thyroiditis along with goiter was made. Out of remaining 6 cases, 5 were diagnosed as follicular adenoma and one as papillary carcinoma. Histological correlation was done in 3 cases of lymphocytic thyroiditis. One case corroborated with cytological diagnosis, 1 case was diagnosed as granulomatous thyroiditis and the other one as Hashimoto thyroiditis. Histological correlation was done in 13 cases of follicular neoplasm, 4

cases were diagnosed as follicular carcinoma and rest as follicular adenoma. Out of 2 cases of Hurthle cell neoplasm on FNAC, one was diagnosed as hurthle cell adenoma and other as hurthle cell carcinoma on histopathological examination.

Eighteen cases of papillary carcinoma in cytology turned out to be the same in histopathological examination and same was with the case of medullary carcinoma. FNAC of malignant cases were 100% correlated with histopathological diagnosis.

Out of total 20 malignant cases diagnosed on cytology, 19 cases were confirmed on biopsy thus leading to 100% true positive and no false positive cases while percentage of true negative cases was 89.65% and false negative was 10.35%.

The false positive and false negative results is a matter of concern as the reliability of cytology is in question. False positive results on cytology were uncommon and was not found in any case in our study. This finding was in consistent with the study of Gulia et al.<sup>22</sup> False negative rate in our study was 10.35 % while false negative rate in Gulia et al was 3.85% .The rate was less because only a small percentage of cases with benign cytological findings underwent surgery.

**Table5: Comparison Of Sensitivity And Specificity With Other Studies**

Study	Sensitivity	Specificity
Godinho –Matos et al <sup>23</sup>	73%	100%
Muratli et al <sup>24</sup>	87.1%	64.6%
Obaid S et al <sup>25</sup>	77.78%	100%
Tayde A et al <sup>26</sup>	75%	96.6%
Duek et al <sup>27</sup>	79.1%	96.5%
Sreeramulu et al <sup>28</sup>	74%	100%
Parikh et al <sup>29</sup>	71.43%	100%
Present study	76%	100%

Sensitivity of 76% and specificity of 100% was obtained in the present study. There was a wide range of sensitivity and specificity reported in different studies. It varies from 73%-87.1% for sensitivity and 64.6%-100% for specificity. The present study compares well with other studies in literature. The percentage of sensitivity and specificity in the present study is in concordant with other studies including Obaid S et al, Tayde A et al and others as shown in the above table. Muratli et al had a higher percentage of

sensitivity and lower percentage of specificity. The major reason for the wide range of sensitivity and specificity was the differences in the categorization of Follicular neoplasm, suspicious of follicular neoplasm, suspicious of malignancy, and atypia of undetermined significance that were considered in positive category for malignancy.

Positive predictive value of 100%, negative predictive value of 89.6% and diagnostic accuracy of 92.2% was obtained in the present study. There was a wide range of positive and negative predictive value along with diagnostic accuracy reported in different studies. It varies from 76.1%-100% for positive predictive value, 79.5%-96.9% for negative predictive value and 77.3%-97.56% for diagnostic accuracy. The present study compares well with other studies in literature.

**Table 6: Comparison Of Positive And Negative Predictive Value And Diagnostic Accuracy With Other Studies**

Study	Positive predictive Value	Negative predictive value	Diagnostic accuracy
Tseng C E et al <sup>30</sup>	94.4%	95%	94.9%
Gulia S et al <sup>22</sup>	100%	90.5%	92.3%
Muratli et al <sup>24</sup>	76.1%	79.5%	77.3%
Mahar S et al <sup>31</sup>	91%	93%	91%
Nautiyal S et al <sup>32</sup>	93.75	95.23%	95%
Mangshetty et al <sup>33</sup>	100%	96.9 %	97.56%
Present Study	100%	89.6%	92.2%

Positive predictive value of the present study is corresponding well with studies of Gulia S et al, Mangshetty et al and other studies shown in the above table. Muratli et al had a lower percentage of positive predictive value with a false positive rate as high as 15.5% .The most common lesion that was contributing to high false positivity rate was nodular hyperplasia with dense macropapillary structures which may be misdiagnosed for follicular malignancy.

In the present study, no false positive case was diagnosed thus resulting in 100% positive

predictive value. The percentage of negative predictive value of the present study was in concordance with the studies shown in the above table while Mangshetty et al had a higher percentage of negative predictive value as only one false negative case was reported which was misdiagnosed as hyperplastic nodule on cytology but histopathological diagnosis was of encapsulated variant of papillary carcinoma whereas in the present study there were 10.35% i.e. 6 false negative cases.

Muratli et al had negative predictive value of 79.5% due to false negative rate of 7.3%. The diagnostic accuracy of the present study was in concordance with many studies shown in the above table except that of Muratli et al which had a sensitivity and specificity of 64.6% and 87.1% respectively. FNAC of the thyroid can classify 70-80% as benign or malignant with 92% negative predictive value and 100% positive predictive value.<sup>34,35</sup>

**Conclusion:** In thyroid lesions, prior awareness of nature of disease, alters the treatment of choice significantly because benign nodules may require no treatment, hemithyroidectomy or lobectomy whereas malignant nodules require radical surgery, that is, total thyroidectomy alone or with neck dissection can be followed by radioiodine ablation, and thyroxine supplement throughout life.

It is concluded from the present study that FNA can be recommended as first line of investigation for thyroid lesions as it allows the distinction between benign and malignant lesions except in cases of follicular neoplasm. Technical procedure for the aspiration and smear preparation are important steps to obtain the satisfactory smears.

Thyroid FNAC has high sensitivity and specificity, and can act as a good screening test to avoid unnecessary thyroidectomies. Hence, FNAC is a valuable tool in the management of thyroid lesions with a high degree of accuracy. Thyroid FNAC is simple, safe, reliable, and well-known recognized procedure for preoperative assessment of thyroid nodules.

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