

Original Research Article

Comparative study of FNAC and histopathology of thyroid swellings, diagnostic accuracy and role in its management

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ABSTRACT

Background: Even if non-surgical and non-invasive techniques can provide a diagnosis, the ultimate answer rests in the histopathological examination of the excised thyroid tissue. This study was carried out with the objective of comparing the findings of the two tests namely FNAC and HPE and suggestions for the future.

Methods: This two year prospective study involved 295 outdoor cases with thyroid lesions at UPRIMS & R, Saifai, Etawah, U.P. The preoperative FNAC and postoperative histopathology reports were correlated and conclusions drawn after statistical analysis.

Results: More than half (65.4% cases) the number of thyroid FNACs were diagnosed as colloid goitre. Diagnostic categorization of 295 thyroid FNACs based on Bethesda classification showed that 239 (81.01%) cases were cytologically benign, 2 cases (0.68 %) were under atypia of undetermined significance (AUS) while six cases (2.03%) under the neoplasm category- follicular. Suspicious for malignancy category included two cases (0.68%)- hyalinizing trabecular adenoma/columnar variant of papillary carcinoma and medullary carcinoma/oncocytic neoplasm. Under the malignant category, there were fourteen cases (4.05%) cytologically diagnosed and in the inadequate/non-diagnostic category there were 32 cases (10.85%) of cases.

Conclusions: FNAC is a simple, safe and cost effective modality in investigation of thyroid disease with high accuracy and specificity.

Keywords: FNAC, Histopathology, Thyroid swellings

INTRODUCTION

Thyroid gland is unique among endocrine organs. It is the largest endocrine gland in the body and the first to develop in fetal life.¹ Thyroid swelling are very frequent. It is estimated 4-7% adults have palpable enlargement of thyroid and 10 times more have impalpable nodules. Most of them are benign and fewer than 5% are actually malignant.²

A multitude of diagnostic tests like ultrasound, thyroid nuclear scan, fine needle aspiration cytology (FNAC) and

many more are available to evaluate goitre. Final diagnosis requires morphological examination of lesions for which FNAC and histopathological examination (HPE) becomes mandatory tests.³

FNAC as a method was first published by Leyden in 1883.⁴ The diagnosis of thyroid lesions using aspiration cytology was first reported by Martin and Ellis in 1930.⁵ Practice guidelines set forth by American Thyroid Association and National Comprehensive Cancer Network states that FNAC should be used as initial

diagnostic test because of its superior diagnostic reliability and cost effectiveness.⁴

FNAC is diagnostic test for thyroid swelling. It is a simple, cost effective, and quick to perform procedure in the outpatient department, with excellent patient compliance. Important factor for satisfactory test includes representative specimen from the goiter and an experienced cytologist to interpret the findings.³

FNAC, however, is not without limitations related to specimen adequacy, sampling techniques, skill of performing the aspiration, interpretation of the aspirate and overlapping cytological features between benign and malignant follicular neoplasm and also in the detection of some papillary carcinomas because of associated thyroid pathology including multinodular goiter, thyrotoxicosis and marked cystic changes. Here arises the need for histopathological examination, as it is considered the final diagnostic test. Thus even if non-surgical and non-invasive techniques can provide a diagnosis, the ultimate answer rests in the histopathological examination of the excised thyroid tissue. This also raises the question of how much corroborative is FNAC and HPE.⁴

This study was carried out with the objective of comparing the findings of the two tests namely FNAC and HPE and suggestions for the future.

METHODS

This cross sectional study was carried out among patients undergoing thyroidectomy in Department of ENT, Head and Neck Surgery and General surgery at UPRIMS & R, Saifai, Etawah, U. P. Period of study is from February 2016 – June 2017.

Fine needle aspiration cytology of thyroid swellings was done on OPD basis. Thyroidectomy specimens preserved in 10% formalin was sent for histopathology examination to the pathology department in our hospital.

The patients were selected consecutively as and when they presented during the study period considering inclusion and exclusion criterias. The selected patients were subjected to clinical examination, thyroid function tests, FNAC, routine hematologic investigations, ultrasound scans and CT scans (where indicated) and histopathologic examination of the thyroidectomy specimen. The preoperative FNAC and postoperative histopathology reports were correlated and conclusions drawn after statistical analysis.

Statistical analysis

The data collected was analysed using SPSS Version 20 and depicted using descriptive statistics. Diagnostic tests were carried out to calculate specificity, sensitivity, positive predictive value and accuracy of the diagnostic test.

Inclusion criteria

Patients with thyroid swellings with normal thyroid hormone profile undergoing thyroidectomy.

Exclusion criteria

Cases of thyroiditis, patients with co-morbidities and unfit for surgery, patients who refused surgery, patients with inoperable thyroid malignancy and patients who do not give consent for the study were excluded.

The Investigations or interventions conducted on patients were complete blood count , coagulation profile, blood urea, serum creatinine, serum electrolytes, HBs Ag, HCV, HIV, chest X-ray, ECG, thyroid function tests, FNAC, histopathologic examination and computed tomography scan (where indicated). Specimens were obtained for cytological study by one of the techniques such as Fine needle aspiration cytology (FNAC), non-aspiration technique (FNC/FNCB) and cyst fluid.^{4,5}

The final provisional diagnosis on cytopathology was given out in the following manner:

- Benign
- Atypia of undetermined significance (AUS)
- Neoplasm
- Suspicious of malignancy
- Malignancy

The cytopathologists were asked to identify the predominant pattern (primary) first, and then give out a diagnosis and then to identify the next dominant pattern (secondary) and give the combined pattern diagnosis. The variation between primary, secondary pattern and final cytological diagnosis was matched with the final histopathological diagnosis for correlation and statistical data were prepared.

RESULTS

The age of presentation ranged from 3 to 75 years in our study of two years, with a mean age of 38.41±14.49 years (Table 1).

Table 1: Age wise distribution of the 295 thyroid cases.

Age group in years	No. of cases	Percentage (%)
0-10	6	2.03
11-20	21	7.11
21-30	66	22.37
31-40	94	31.86
41-50	51	17.29
51-60	34	11.55
61-70	20	6.77
71-80	3	1.02
Total	295	100

The thyroid lesions were more common in females than males-in the ratio of 6.02:1. The most common clinical symptom in patients with thyroid lesions was swelling in the neck which was present in total 293 cases i.e., 98.98% incidence which moved with deglutition followed by dysphagia in 53 cases (17.97%). No thyroid swelling palpated in two cases. The maximum number of patients (32.88%) presented with duration of symptoms being more than one year. Thyroid swelling was not palpable in two cases on local examination out of 295 cases.

The size of smallest thyroid swelling was 0.9x0.8 cms and the size of the largest swelling was 8x6 cms. Out of total 293 palpable thyroid swellings cases, 98.98% were mobile on palpation. Only three thyroid cases were fixed on palpation which turned out to be malignant. 293 thyroid swellings moved up with deglutition. Nine thyroid swellings moved up with both deglutition and protrusion of tongue.

Out of total 293 palpable thyroid swellings, majority of the thyroid cases-88.74% were not associated with tenderness on clinical Palpation of the thyroid swelling. It was observed that the maximum number of thyroid lesions were firm in consistency-55.56%, followed by thyroid lesions of mixed consistency. Hard thyroid lesions were few on palpation.

Out of total 295 cases, TFT was done in 221 (74.92%) patients and not done in 74 cases. Out of 221 cases, 85.07% were euthyroid. Among the thyroid derangements, 21 cases (9.5%) were hyperthyroid and 12 cases (5.43%) were hypothyroid.

In two cases referred for cytology, thyroid swelling was not palpable and could only be detected on USG examination. Out of 293 palpable thyroid swellings the most common type of presentation was solitary thyroid nodule observed in 84.64% patients while 15.26% patients had multinodular goiter.

Out of 295 cases, the maximum number of thyroid cases that were investigated on USG was diagnosed as MNG accounting for 56.27% of cases. Colloid goitre in a solitary nodule was diagnosed in 26.78% cases on USG thyroid (Table 2).

Table 2: USG diagnosis of 295 cases.

USG diagnosis	No. of cases	Percentage (%)
Thyroglossal cyst	9	3.05
Thyroiditis	23	9.83
Solitary-colloid goiter	52	26.78
MNG	166	56.27
Neoplasm	11	3.73
Hyperplastic thyroid nodule	1	0.34
Total	295	100

In our study in 293 out of 295 thyroid cases the swellings were palpable while in remaining two cases, only USG examination detected the thyroid swelling. 84.64% of thyroid cases were solitary on palpation but only 43.73% proved to be solitary on USG examination. On comparison of nodularity on clinical examination with USG thyroid examination, the Chi square value and p value was highly significant showing that USG thyroid was better in diagnosing STN cases than clinical examination (Table 3).

Table 3: Comparison of nodularity on clinical examination with USG thyroid.

Cases	On clinical examination		On USG neck examination	
	No. of cases	%	No. of cases	%
Single swelling	248	84.64	129	43.73
Multiple swellings	45	15.36	166	56.27
Total	293	100	295	100
Chi square-value	36.71			
P-value	P<0.0001, significant			

Table 4: Nature of aspirate in 295 cases.

Nature of aspirate	No. of cases	Percentage (%)
Haemorrhagic aspirate	144	48.81
Blood mixed colloid	117	39.66
Frank colloid	34	11.53
Total	295	100

Table 4 shows that the aspirate obtained most of the times from thyroid lesions was haemorrhagic (48.81%), followed by blood mixed colloid (39.66%). Least number of cases i.e., 11.53% cases were frank colloid in nature.

Table 5 shows that more than half the number of thyroid FNACs in our study was diagnosed as colloid goitre (65.4% cases).

Table 6 shows that 81.01% of 295 thyroid FNACs were cytologically benign and colloid goitre comprised 65.4%. The two cases under atypia of undetermined significance (AUS) were follicular neoplasm/multi-nodular goitre and follicular neoplasm/adenomatoid goitre. There were six cases under the neoplasm category-all six cases cytologically diagnosed as follicular neoplasm. Suspicious for malignancy category included two cases-hyalinizing trabecular adenoma/ columnar variant of papillary carcinoma and medullary carcinoma/oncocytic neoplasm.

Under the malignant category, there were fourteen cytologically diagnosed cases-nine cases as Papillary carcinoma, two cases each of Anaplastic carcinoma and Medullary carcinoma and a single case of insular carcinoma respectively. Also, in the inadequate/non-diagnostic category there were 32 cases comprising 10.85% of cases. Out of 295 cases, there were 106 solitary thyroid nodules (STN) detected on USG neck. The 106 STN cases showed following interpretation of cell pattern analysis.

Table 5: Routine cytological diagnosis of 263 cases.

Routine cytological reporting	No. of cases	Percentage (%)
Colloid cyst /cystic colloid nodule	38	14.46
Colloid goiter	172	65.40
Hyperplastic nodule/adenomatoid goiter	6	2.28
Thyroglossal cyst	8	3.04
Infected cystic lesion	1	0.38
Granulomatous thyroiditis	4	1.52
Hashimoto's thyroiditis	4	1.52
Lymphocytic thyroiditis	9	3.42
Intra-thyroid reactive lymph node	1	0.38
Follicular neoplasm	6	2.28
Papillary carcinoma	9	3.42
Anaplastic carcinoma	2	0.76
Medullary carcinoma	2	0.76
Insular carcinoma	1	0.38

Table 6: Diagnostic categorization of 295 thyroid FNACs based on Bethesda classification.

Groups	Categories	No. of cases	Percentage (%)
Group 1	Benign	239	81.01
Group 2	Atypia with undetermined significance	2	0.68
Group 3	Suspicious for neoplasm	6	2.03
Group 4	Suspicious for malignancy	2	0.68
Group 5	Malignant	14	4.75
Group 6	Inadequate/non-diagnostic	32	10.85
Total		295	100

Inter observer variation

Out of 47 STN cases in which cyto-histopathologic correlation was possible, unanimous agreement between the two reviewers was observed in 43 (91.49%) cases, including 27 benign, six AUS, five neoplasms and four malignancies and one suspicious for malignancy category. One case diagnosed as benign by one reviewer and neoplasm by the other turned out to be benign lesion histologically.

Six cases diagnosed as AUS by reviewer 1 and 2, were histologically proven to be benign lesions. This proves the fact that AUS category mainly includes benign lesions that need not be resected but rather followed-up with subsequent FNAC.

Table 7: Comparison of routine cytological diagnosis, pattern diagnoses of 47 STN cases with histopathologic correlation.

S. No.	Regular cytological diagnosis	No. of cases	Pattern diagnosis	Histopathological diagnosis	
				Diagnosis	Nos
1.	Thyroglossal cyst	5	Benign	Thyroglossal cyst	5
				NCG	3
2.	Colloid goiter	7	Benign	CCN	1
				CG	1
				FA	1
				PC	1
				MNG	2
3.	Colloid cyst	4	Benign	CG	1
				CGS	1
				CGS	1
4.	Goitre with colloid	1	Benign	CGS	1
				FA	1
5.	Hyperplastic nodule	1	Neoplasm	CG	1
			Benign (3)	HT	1
				FA	1
6.	Nodular colloid goitre	7	AUS (2)	CG	1
			Neoplasm (2)	FA	1
				FA	1

7.	Colloid goitre /neoplasm	1	AUS	PC	1
8.	Thyroiditis	1	Benign	HT	1
9.	Granulomatous thyroiditis	2	Benign	GT	1
			AUS	GT	1
10.	Lymphocytic thyroiditis	4	Benign	LT	2
				HT	1
				FA	1
11.	Hashimoto's thyroiditis	1	Benign	HT	1
12.	Thyroiditis/nodular colloid goitre	1	Benign	HT	1
13.	Follicular neoplasm	6	Neoplasm	FA	1
			Malignant	FC	5
14.	Follicular neoplasm/adenomatoid goiter	1	Neoplasm	MNG	1
15.	Medullary carcinoma/oncocytic neoplasm	1	Suspicious	MC	1
16.	Medullary carcinoma	1	Malignant	AC	1
17.	Anaplastic carcinoma	1	Malignant	AC	
18.	Papillary carcinoma	2	Benign	NCG	1
			Malignant	PC	1

A single case diagnosed as neoplasm by reviewer 1 and benign by the other turned out to be malignant on histopathology. There was another discrepant case diagnosed as neoplasm by reviewer 1 and malignancy by reviewer 2 that was confirmed as malignancy on histopathology. A single case diagnosed as malignant by reviewer 1 and neoplasm by the other, turned out to be benign (nodular colloid goitre) on histopathology.

Benign, AUS and neoplasm were categorized together under 'benign lesions', while suspicious for malignancy and malignant categories were included under 'malignant lesions'. Considering this, the kappa measure of agreement for benign and malignant lesions on cell pattern diagnosis between the two reviewers was found to be 0.95 in our study, which was a reliable value.

DISCUSSION

Thyroid cytology comprised 5.16 % of total FNACs conducted at our institution over the two years period. In present study the youngest patient was three years- two patients with cytological diagnosis of thyroglossal cyst and colloid cyst respectively. The oldest patient was of 75 years with cytological diagnosis of nodular colloid goiter.

Table 8 shows that wide age distribution was noted for various thyroid lesions in most of the study series. The mean age of patients with thyroid lesions in our study was 38.41±14.49 years. Our findings are comparable to the other mentioned studies.⁷⁻¹¹

Table 9 shows that female:male ratio in our study was 6.02:1. It was comparable to the previous studies.^{7,9,10}

Our findings are comparable to those reported by Bhargav et al.¹²

Clinical presentation

In 1993, Ananthakrishnan et al reported a clinic-pathological profile of 503 patients with a single thyroid nodule where the commonest symptom apart from swelling of thyroid gland was pain.⁴ Handa et al stated in their study that the major presenting symptom was diffuse swelling and/or nodular swelling of the thyroid. Other less frequent symptoms included pain in the swelling, dysphagia, hoarseness of voice and cough.⁹

Three most common complaint of swelling in front of the neck in present study is in accordance to above mentioned studies.

Duration of thyroid swelling(s)

Duration of thyroid lesions depends on severity of symptom, awareness of the patients at the time of consultation and socio-economic status of the patients. The duration thus varies from study to study. In the present study the maximum number of patients- 32.88% were having thyroid lesions with symptoms more than one year. Our study correlates with study by Handa et al.⁹

Size of thyroid swelling

The lower size of the thyroid swelling mostly favours benign pathology. In our study, the majority of the patients-216 cases (73.72%) had the size of the thyroid swelling between 1 to 3 cms. These belong to stage 2

according to WHO classification that is, swelling visible with neck in normal position.

Maximum size of the swelling was ≤ 8 cms diameter in three of our cases. Two separate thyroid swellings were palpated in five of our cases.

Table 8: Age groups encountered in different studies.

Author(s)	Year	No. of cases	Age range (in years)	Mean age (in years)
Sangalli G et al ⁷	2006	5469	6-91	47.2
Aravinthan et al ⁸	2007	110	26-59	46
Handa U et al ⁹	2008	434	5-80	37.69
Mandal S et al ¹⁰	2011	120	15-71	-
Rangaswamy M et al ¹¹	2011	585	11-70	40.57
Present study	2013	295	3-75	38.41

Table 9: Female to male ratio of thyroid lesions in various studies.

Authors	Year	Female:male ratio
Sangalli G et al ⁷	2006	4.21:1
Handa U et al ⁹	2008	6.35:1
Mandal S et al ¹⁰	2011	5:1
Present study	2013	6.02:1

Table 10: Site of thyroid swelling in previous studies.

Authors	Year	Site (%)			
		Right lobe	Left lobe	Isthmus	Diffuse
Bhargav PRK & Shekhar S ¹²	2011	-	-	-	41
Present study	2013	32.54	21.02	10.17	36.27

Table 11: Comparison of duration of thyroid swelling(s).

Authors	Year	Duration of swelling(s) (%)			
		<1 month	1-6 months	6-12 months	>1 year
Handa U et al ⁹	2008	-	7.6	6.68	62.2
Present study	2013	23.39	29.83	13.9	32.88

Table 12: Comparison of TFTs by different studies.

Authors	Year	Total cases in which TFTs done	Functional thyroid status (%)		
			Euthyroid	Hyperthyroid	Hypothyroid
Godinho-Matos L et al ¹⁴	1992	144	88	9	3
Present study	2013	221	85.07	9.5	5.43

Aravinthan et al suggested that non-palpable thyroid nodules less than 1 cm diameter are usually non-malignant. Jayaram et al stated that nodules less than 1 cm in diameter are not detected by palpation, but rather detected during USG thyroid examination.^{8,13} The risk of malignancy being low, such small nodules as an incidental USG finding should not be made to undergo guided FNAC unless they have some strong clinical suspicion or family history.

In our study, the majority of the swellings 260 (88.74%) out of total 293 cases were not associated with tenderness on clinical palpation of the thyroid lesions This finding is

in accordance to study by Ananthkrishnan et al, which had 10% of their cases with associated pain and tenderness and non-tender thyroid lesions comprised 90% of the cases.⁴

TFT levels

Number of needle passes and nature of aspirate

The maximum number of patients yielded good cellularity on FNAC/FNC done once (65.08% cases). Least number of cases-11.12% cases were frank colloid in nature mainly seen in cystic thyroid lesions. Out of 295

thyroid aspirates, repeat aspiration due to sample inadequacy, poor preparation, cystic lesions, suspected neoplastic lesions or bigger lumps was done in 34.92% cases (n=103). This discrepancy in our study can be attributed to inexperienced cytopathologists with rotational posting performing the sampling procedure. In our study, the number of needle passes was restricted to less than four. In cases of inadequate smears by first sampling, repeat sampling was advised each time following a different needle track which reduced chances of blood aspirated from previous trauma. The FNAC technique was used early for cystic thyroid lesions in our study and later residual lesion was sampled.

Jayaram and Orell et al suggested that the average number of needle passes recommended for adequate sampling of thyroid lumps is two to five.¹³ As thyroid gland is a highly vascular organ, with each impending trauma the chances of aspirating haemorrhagic fluid rises each time, so they advised to keep the number of aspirates to minimum. Mandal et al performed repeat aspiration in 5.5% (n=6) wherever the first thyroid aspirate was inadequate in their study of 120 cases.¹⁰

Adequacy of aspirated thyroid material

A FNA sample must be sufficient for an interpretation with a low likelihood of a false-negative diagnosis. Depending on the clinical and ultrasonographic findings, persistently inadequate FNA results from a nodule necessitate surgery. Adequacy defines the quality and quantity of a sample, a definition that varies not only with respect to the site sampled but also with respect to the type of lesion sampled. Hence, adequacy criteria are organ-specific.

Some authors believe cellularity criteria for adequacy also vary depending on whether the aspirated lesion is solid or cystic and whether the aspirate was performed under palpation or ultrasound guidance. All thyroid FNAs must be technically adequate, with well-preserved and well-prepared thyroid follicular epithelial cells for interpretation. Aspirates that contain only cyst fluid, histiocytes, and erythrocytes are inadequate.

Usually, 1-4 thyroid aspirates are suffice in single nodular lesion of diameter less than 3 cms whereas 4-8 aspirates are required for thyroid lesions more than 3 cms, which help reduce false negative rate.

Jayaram and Orell suggested that abundant clean colloid without altered blood or debris also indicates a benign diagnosis in a solitary nodule, but nevertheless the presence of a certain number of intact and well-fixed follicular epithelial cells is obligatory for a smear to be satisfactory. They opined that more than four needle passes were not readily accepted by patients causing local tissue trauma.¹³

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