Original Research Article

Accuracy of fine needle aspiration cytology with histopathology of thyroid lesions - 1.5 years study at Government ENT hospital, Hyderabad, Telangana

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Abstract

Background: Swellings of thyroid gland are common in most parts of the world, including countries like India where iodine deficiency is endemic. Its prevalence ranges from 4% to 10% in the general adult population and from 0.2% to 1.2% in children, affecting females more commonly than males.

Aim and objective: To evaluate diagnostic accuracy of Fine needle aspiration cytology of thyroid lesions, to categorize thyroid lesions as per the Bethesda system, to correlate cytomorphology with histopathology, to determine the accuracy of FNAC in terms of sensitivity, specificity, positive predictive value and negative predictive value in comparison with histopathology in the diagnosis of a thyroid lesions.

Materials and methods: It was a retrospective study undertaken over a period of one and half years from October 2016 to March 2017 in the Department of Pathology, Government ENT Hospital, Hyderabad. FNAC was performed with 26 gauge needle; smears were fixed in ether-95% alcohol solution and stained with Haematoxylin and Eosin stain. Different types of excised thyroid specimens received were subjected to routine processing, cutting, staining and histopathological features were analysed.

Results: The sensitivity, specificity, positive predictive value, and negative predictive value of aspiration cytology in detecting all the benign and malignant lesions of thyroid were 67.4%, 99.2%,

93.9%, and 94.2% respectively. The diagnostic accuracy of detecting thyroid lesions by FNAC was 94.1%.

Conclusion: Fine needle aspiration cytology is a minimally invasive, simple, reliable, safe and cost effective gold standard cytology technique with minimal discomfort and complications to the patient. FNAC avoids unnecessary thyroidectomies for benign thyroid pathologies.

Key words

Fine-Needle Aspiration Cytology (FNAC), Biopsy, Histopathology, Thyroid lesions.

Introduction

Swellings of thyroid gland are common in most parts of the world, including countries like India where iodine deficiency is endemic. Its prevalence ranges from 4% to 10% in the general adult population and from 0.2% to 1.2% in children [1], affecting females more commonly than males. Majority of thyroid lesions are non-neoplastic and 5%-10% are malignant. Clinical features alone cannot distinguish between benign and malignant nodules [2]. Thyroid cytology provides a definite diagnosis of malignancy and also categorises the subtypes in some instances, thus enabling clinician to take appropriate measures of surgery. Benign lesions can be managed conventionally. The incidence of thyroid malignancy is quite low, 1 in 20 clinically identified nodules turn out to be malignant, thus thyroid FNAC helps in reducing the rate of surgery for benign thyroid diseases [3, 4]. However, FNAC has its own limitations, such as accuracy is low in suspicious cytology, presence of dual lesions and follicular neoplasms seen in the background of non-neoplastic lesions. The main aim of FNAC is to identify lesions that require surgery and those benign nodules that can be observed clinically and decrease the overall thyroidectomy rate in patients with benign diseases [3]. The present study was undertaken to correlate the FNAC findings with histopathology so that rate of unnecessary thyoidectomies in benign pathologies could be avoided.

Materials and methods

A retrospective study was undertaken over a period of one and half year from October 2016 to march 2017 in the Department of Pathology at Government ENT Hospital, Hyderabad. A total of 1200 thyroid FNACs were performed during this time period, out of which 290 cases had undergone surgery providing histopathological specimens available for correlation, so as to determine the accuracy of FNAC in terms of sensitivity, specificity, positive predictive value and negative predictive value in comparison with histopathology in the diagnosis of thyroid lesions. FNAC was performed with 26 gauge needle; smears were fixed in ether-95% alcohol solution and stained with Haematoxylin and Eosin stain. Different types of excised thyroid specimens received such as hemithyroidectomy (right/ left), subtotal thyroidectomy and total thyroidectomy along with or without lymph-node dissection. Specimens were subjected to routine processing, cutting, staining and histopathological features were studied. Patients of all age groups, both males and females were included in the study.

Inclusion criteria

Those patients presented with thyroid swelling, who underwent FNAC, thyroid surgery within the study period were included in the present study.

Exclusion criteria

Those patients having FNAC done but did not have thyroid surgery for histopathological evaluation were excluded.

Results

Tables 1 to 8 are projecting Age and gender distribution (**Table - 1**), spectrum of presenting clinical symptoms (**Table - 2**), distribution of lesions based on the Bethesda system (**Table - 3**), categorization of non-neoplastic lesions on

FNAC (**Table - 4**), categorization of neoplastic lesions on FNAC (**Table - 5**), Distribution of lesions based on histopathology (**Table - 6**), categorization of thyroid lesions on histopathology (**Table - 7**) and correlation of cytology with histopathology (**Table - 8**) respectively and **Figures from A to L**.

Table - 1: Age and gender distribution of patients.

Age range (in years)	Female		Male		Total (n=290)	
11-20	14	4.8%	01	0.34%	15	5.1%
21-30	90	31.0%	07	2.42%	97	33.5%
31-40	102	35.2%	10	3.45%	112	38.7%
41-50	44	15.2%	05	1.72%	49	16.9%
51-60	09	3.1%	03	1.03%	12	4.1%
61-70	04	1.4%	01	0.34%	05	1.7%
Total	263	90.7	27	9.30	290	100.0%

Table - 2: Spectrum of clinical presentation.

Clinical symptoms	No. of cases	% of cases
Swelling in front of neck	290	100.00%
Pain	12	4.13%
Lymphadenopathy	10	3.44%
Dysphagia	09	3.10%
Dyspnoea	07	2.41%
Hoarseness of vioce	02	0 .68%

Table - 3: Distribution of thyroid lesions based on the Bethesda system.

Bethesda	Type of lesion	No. of cases	(%)
Type I	Non diagnostic(Cystic degeneration in thyroid nodule)	12	4.13%
Type II	Non - neoplastic	245	84.48%
Type III	Atypia of undetermined significance	Nil	Nil
Type IV	Follicular neoplasm / Suspicious for Follicular neoplasm	16	5.52%
Type V	Suspicious for malignancy	12	4.14%
Type VI	Neoplastic	05	1.73%
Total		290	100.0%

Of the 290 patients, 27 (9.3%) were males and 263 (90.7%) were female patients with M: F ratio of 1: 9.75. The age of the patients ranged from11-70 years (median of 31 years). The most common presentation was swelling in front of neck. Of the 290 cases 12 (4.12%) were considered inadequate/ non-diagnostic on FNAC as they showed cystic degenerative changes in thyroid nodules. Of the remaining 278, 245 (84.48%) were diagnosed as non-neoplastic lesions and 33 (11.38%) were diagnosed as neoplastic lesions. Nodular goiter was the most common non-neoplastic lesion diagnosed on FNAC, followed by Hashimotos thyroiditis. Amongst the neoplastic lesions follicular neoplasm was the most common lesion, followed by Papillary carcinoma of thyroid (PTC) on FNAC. One of the diagnostic pitfall of FNAC is follicular adenoma cannot be distinguished from follicular carcinoma as criteria for carcinoma like vascular/ capsular invasion cannot be detected on FNAC. Of the 290 patients who underwent both FNA as well as thyroidectomy, thyroid lesions were categorized into non-neoplatic, neoplastic on histomorphology.

Figure – A (Nodular Goiter) - (1 &2: 10x & 40x Views) : Cytosmears showing abundant colloid in the background along with sparse histiocytes & thyroid follicular cell clusters. (3 & 4) : H&E (10x & 40x Views) Sections showing areas of haemorrhages, cystic changes, collections of haemosiderin laden macrophages and variably sized follicles filled with colloid.

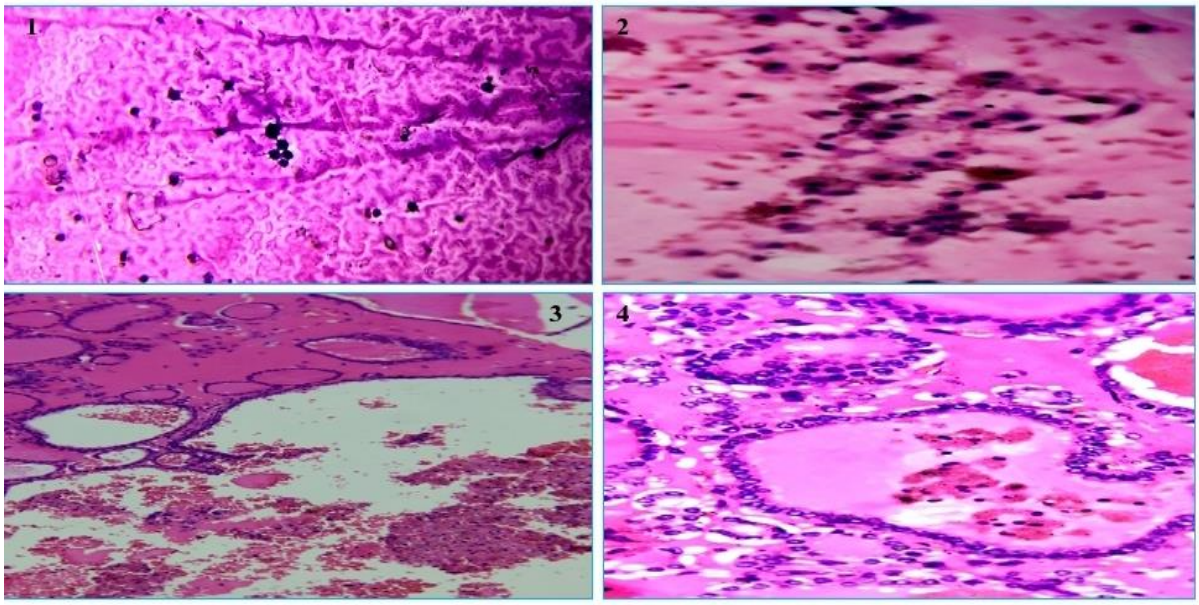


Figure B (Gross images of Goitre & Hashimoto's thyroiditis) : 5 : Solitary cystic nodule filled with colloid – Nodular Goiter. 6- & 7: Multinodular areas filled with colloid. 7- Separated by grey white areas suggestive of associated thyroiditic changes. 8: Showing tan grey white areas suggestive of dense lymphocytic infiltrates in Hashimoto's thyroiditis

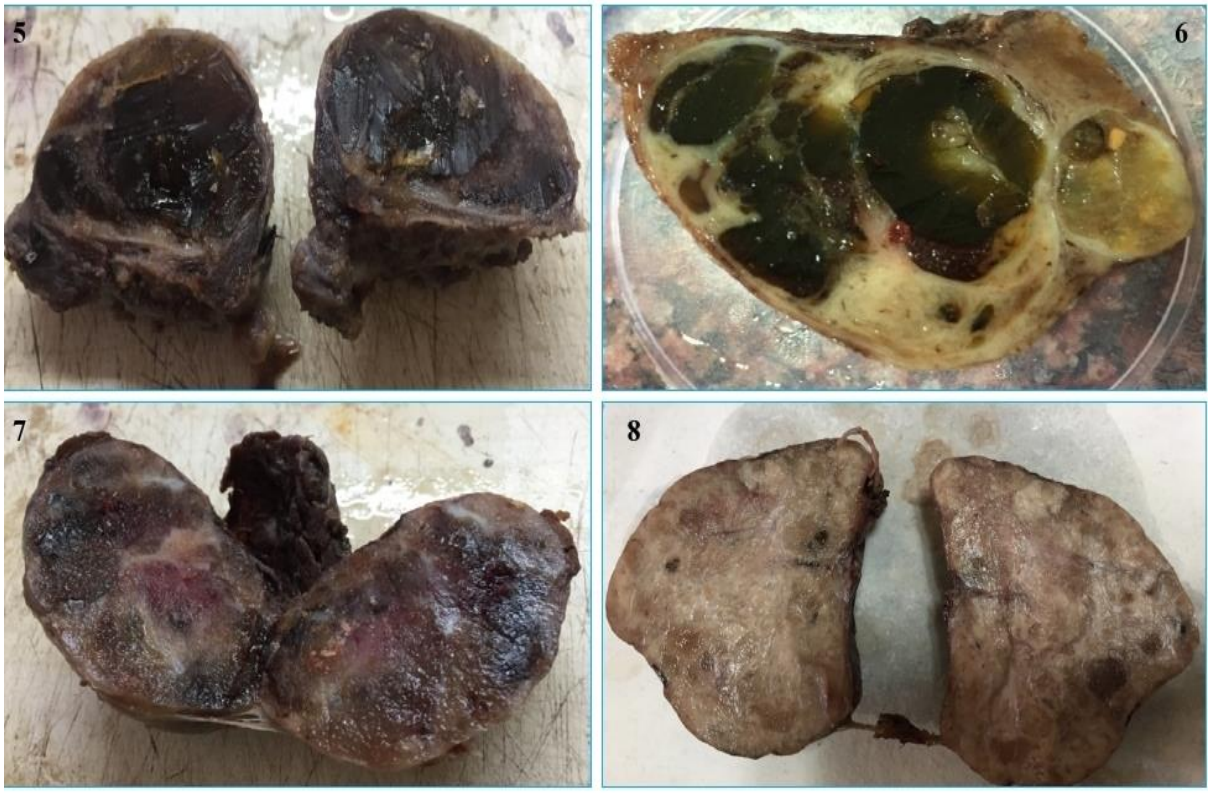
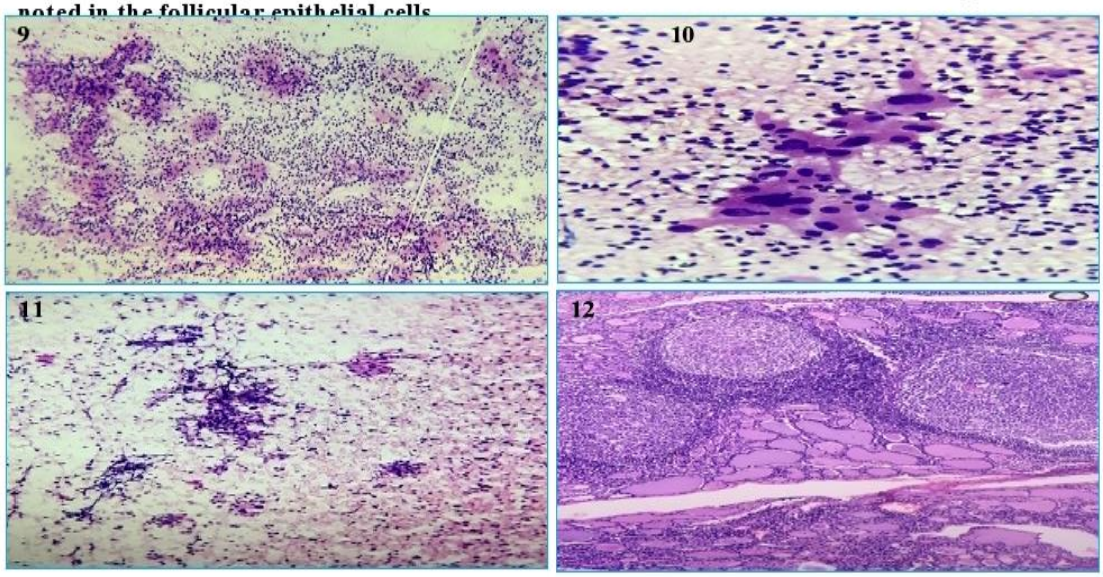


Figure C : (Immune thyroiditis) 9 & 10: Cytosmears 10x & 40x Views showing thyroid follicular cells in clusters with marked askanization admixed & impinged by lymphocytes suggestive of Hashimoto's thyroiditis with focal anisonucleosis. 11 – Cytosmear 10x view showing features as in 10 excepting askanization, compatible with lymphocytic thyroiditis. 12 . H&E(10 x view) section showing marked lymphoid follicular hyperplasia with secondary reactive germinal centres in the interfollicular stroma. Hurthle cell changes are noted in the follicular epithelial cells



F igure D : (Follicular Neoplasm) 13 & 14 : 10x & 40x Views of cytosmears showing follicular epithelial cells in clusters, sheets, repetative follicles, composed of isomorphic cells with no atypia, mitosis, necrosis. 15 & 16 : 10 x & 40x views of H &E sections showing well encapsulated nodule surrounded by compressed native thyroid parenchyma, composed of follicles lined by cuboidal cells. No evidence of necrosis/ mitosis/ atypia/ capsular or vascular invasion, consistent with Follicular Adenoma . 16. Microfollicular type & 17 . Macrofollicular type.

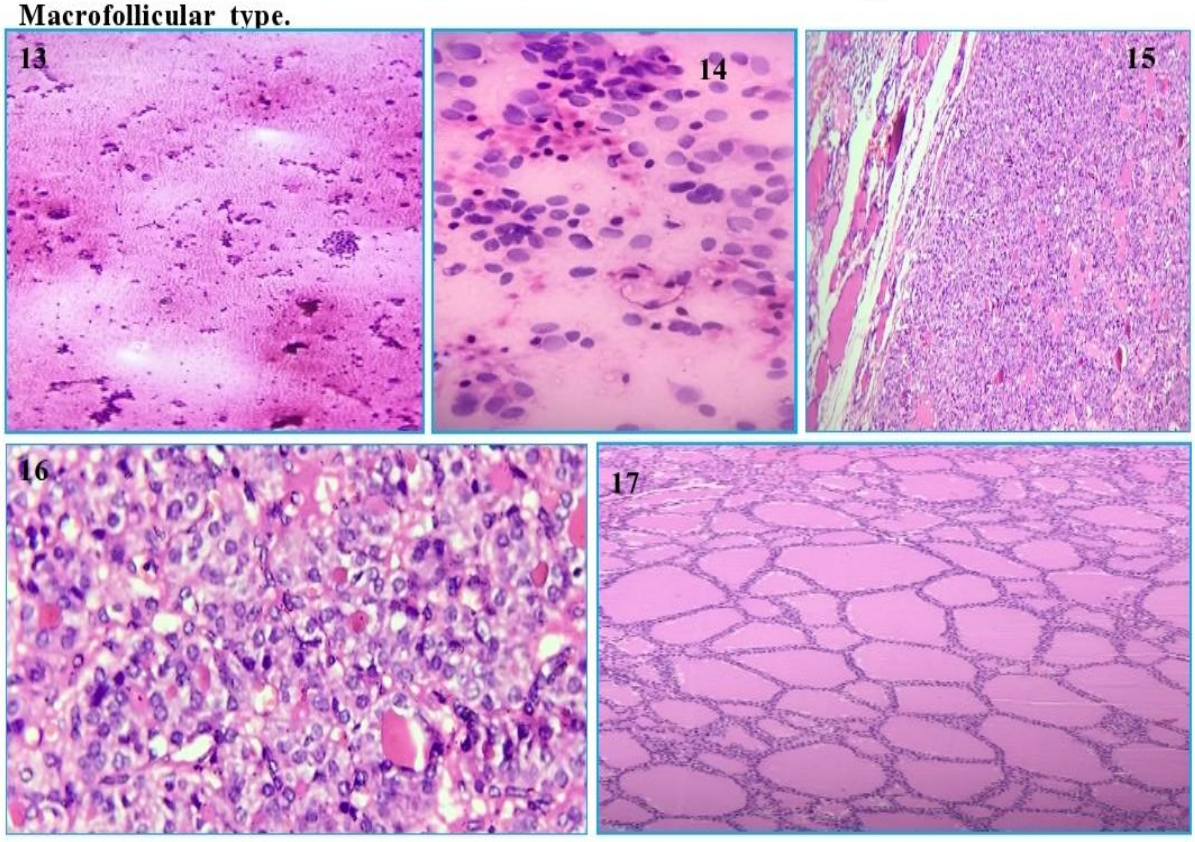


Figure E (Gross images of Follicular Neoplasm) : 18 – 20 Showing well delineated & encapsulated oval to round solitary grey white nodule surrounded by normal thyroid tissue with small nodular goiterous change in 18 thyroiditic changes in 20. 21 : colour is yellowish, suggestive of hurthle cell nature with adjacent small nodule showing goiterous changes.

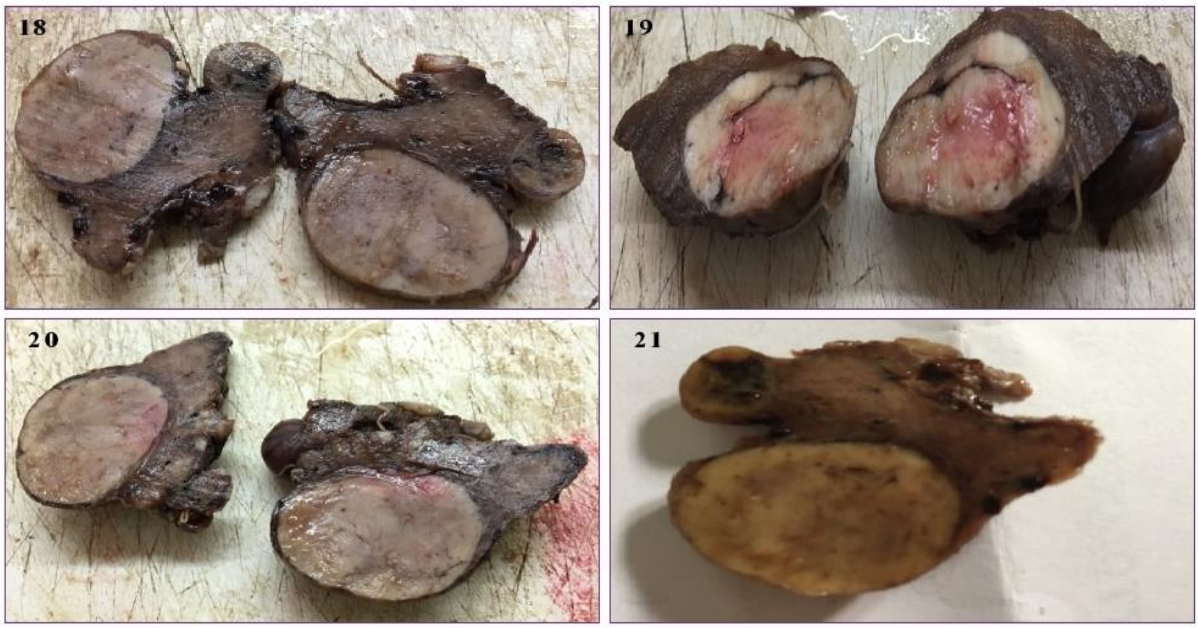


Figure F (Huthle cell neoplasm) 22 & 23 (Cytosmears), 24 & 25 (H & E sections) Showing polygonal cells with abundant eosinophilic cytoplasm with mild anisonucleosis and follicular arrangement on section with no capsular or vascular invasion (Hurthle cell adenoma).

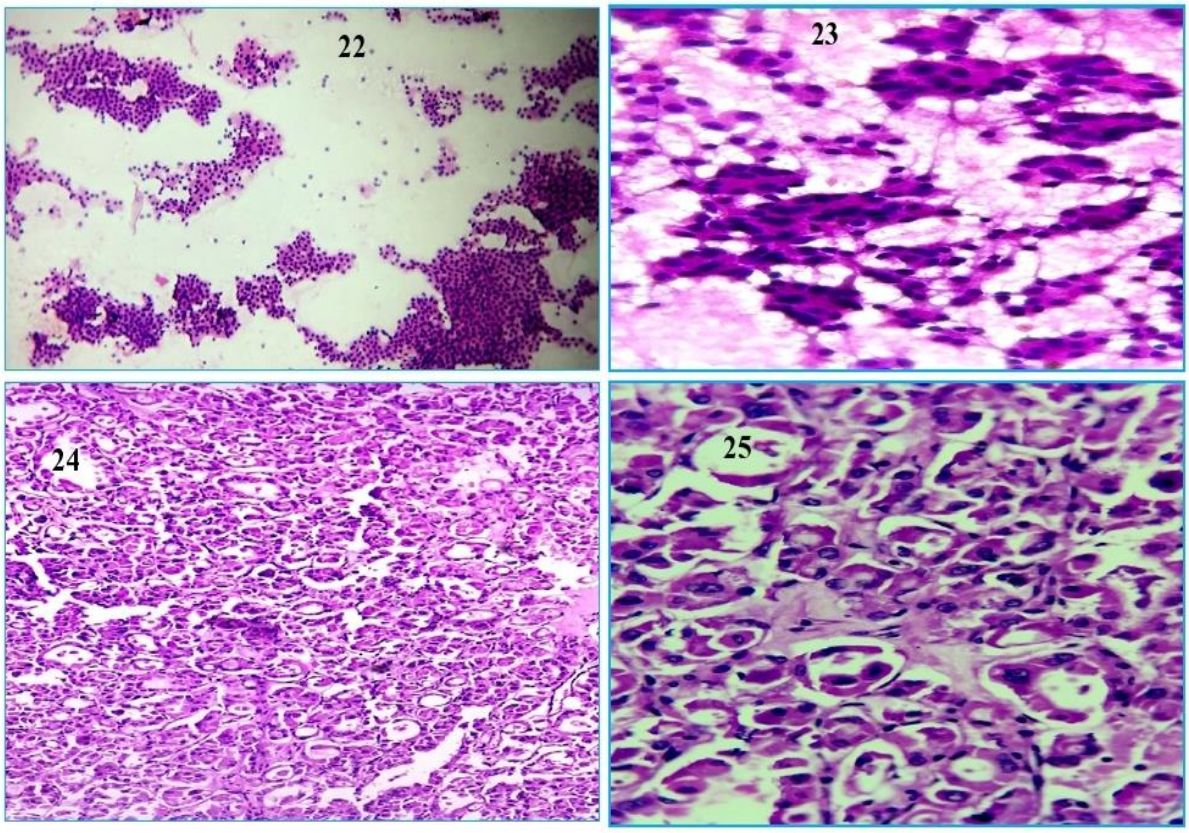


Figure G (Gross images of Various types of thyroid carcinomas). 26 : diffuse tumour almost involving the whole parenchyma with papillary architecture & friability. 27 : Showing multifocal growth with intricate papillary pattern (Papillary carcinoma) 28 : Solid grey white mass with areas of necrosis & haemorrhage with lymphnode dissection (Follicular carcinoma). 29 : Grey tan to reddish solid growth with necrotic areas (Medullary carcinoma).

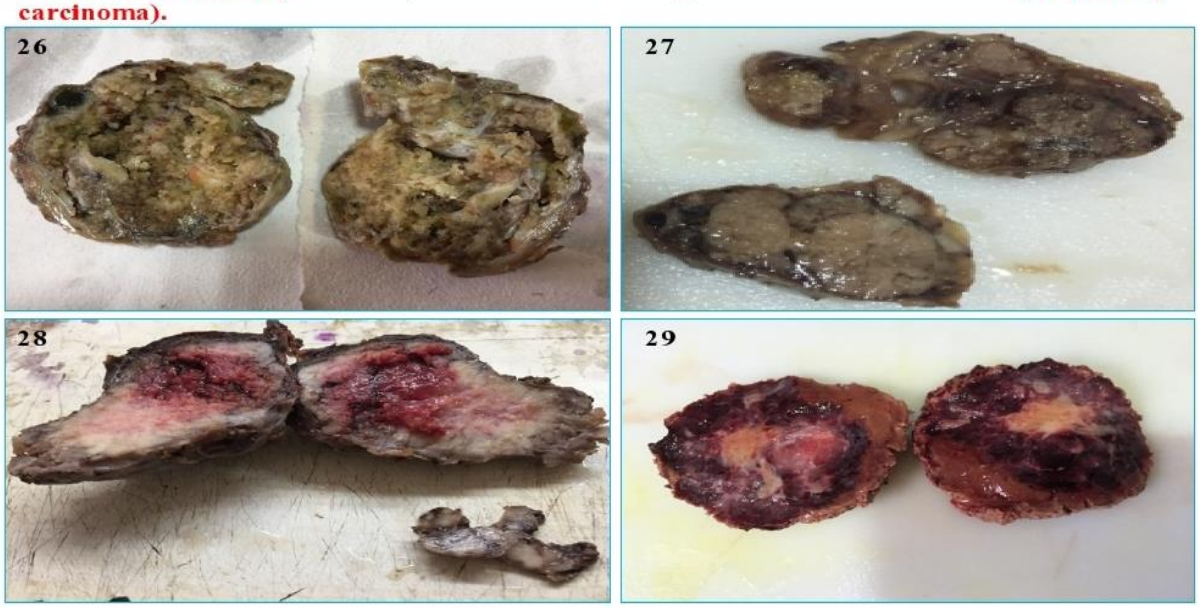


Figure H : (Follicular carcinoma) 30 : H & E, 10x View showing 2 foci of capsular invasion. 31 : 40 x view showing a focus of complete transcapsular invasion with rupture of capsule. 32 : Showing tumour seen outside the capsule. 33 : Showing Vascular invasion. 34 : Showing Extrathyroidal extension , infiltrating into the skeletal muscle bundles.

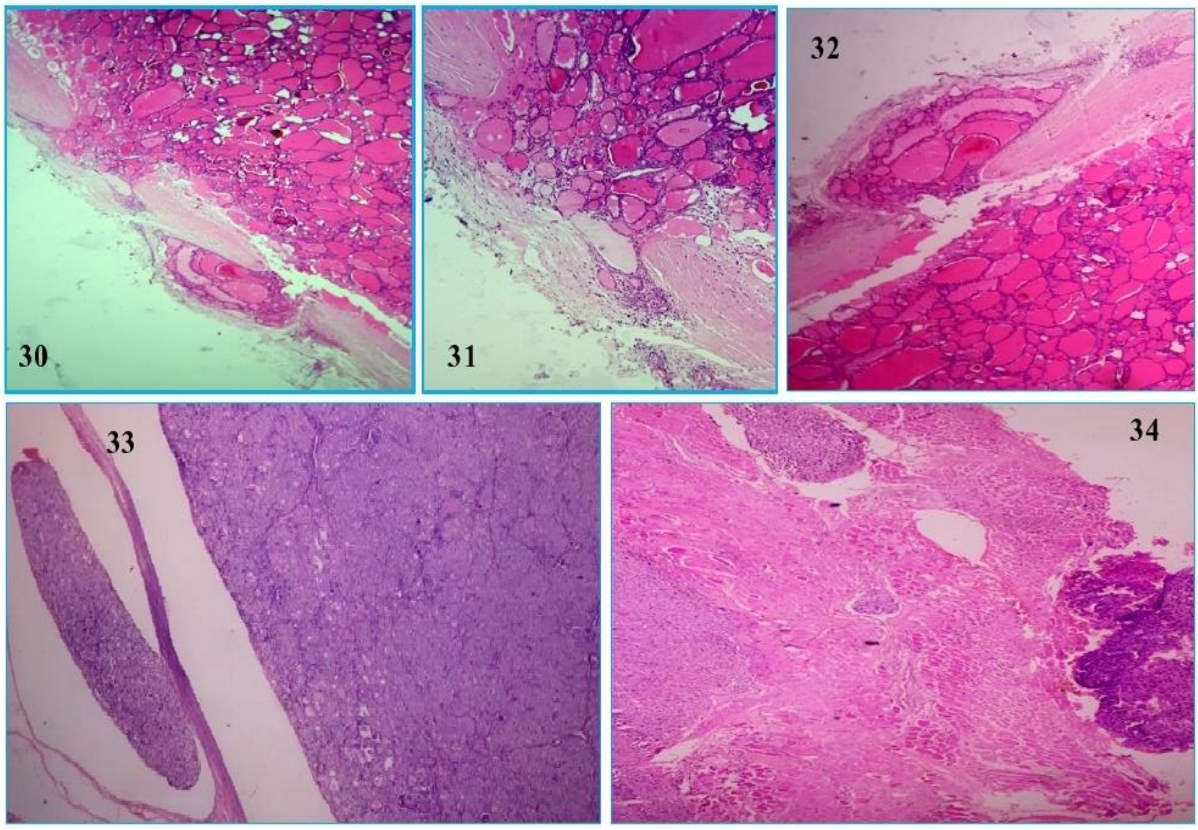


Figure I : (Papillary Carcinoma) 35 & 36 : 10x & 40x Views of cytosmears showing 3D clusters, papillary fragments of oval cells with crowding, occasional intranuclear inclusions with definite border peripherally admixed with sparse lymphoctes. 37 & 38 : 10x & 40x Views on H&E sections showing papillary arrangement with classical nuclear features of papillary carcinoma.

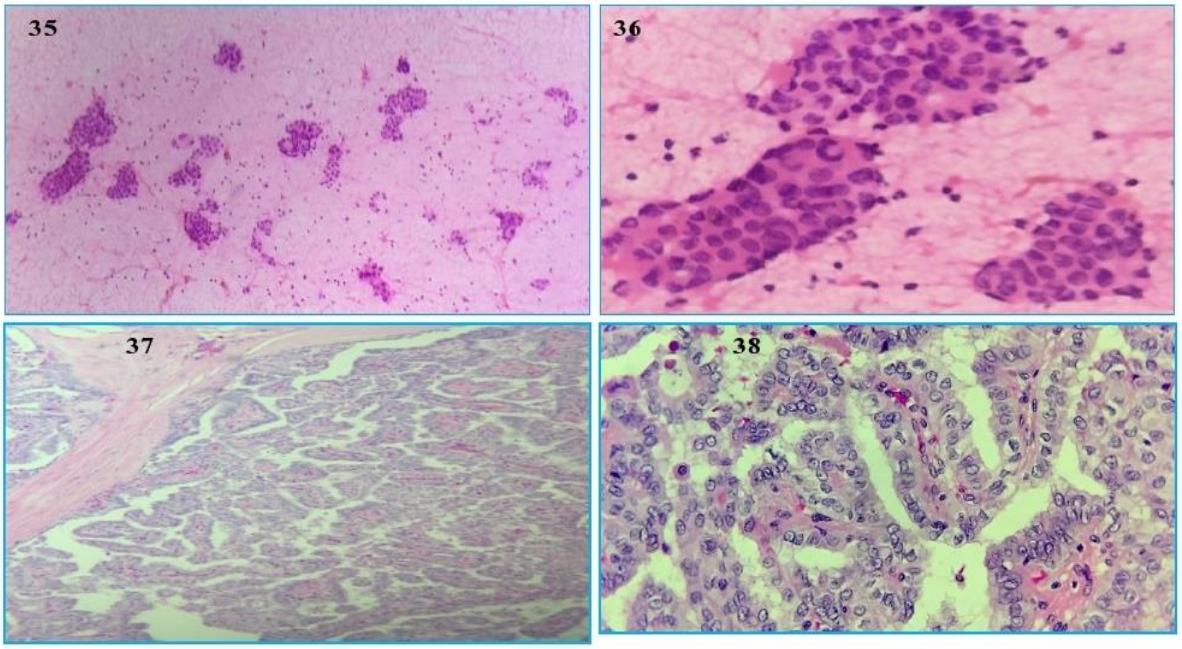


Figure J : FNAC smears on 4x, 10x & 40x Views showing high cellular yield composed of round, polygonal & spindle cells with moderate cytoplasm, hyperchromatic eccentric nucleus admixed with bi & multinucleated giant cells & mitoses, suggesting the possibility of Medullary carcinoma.

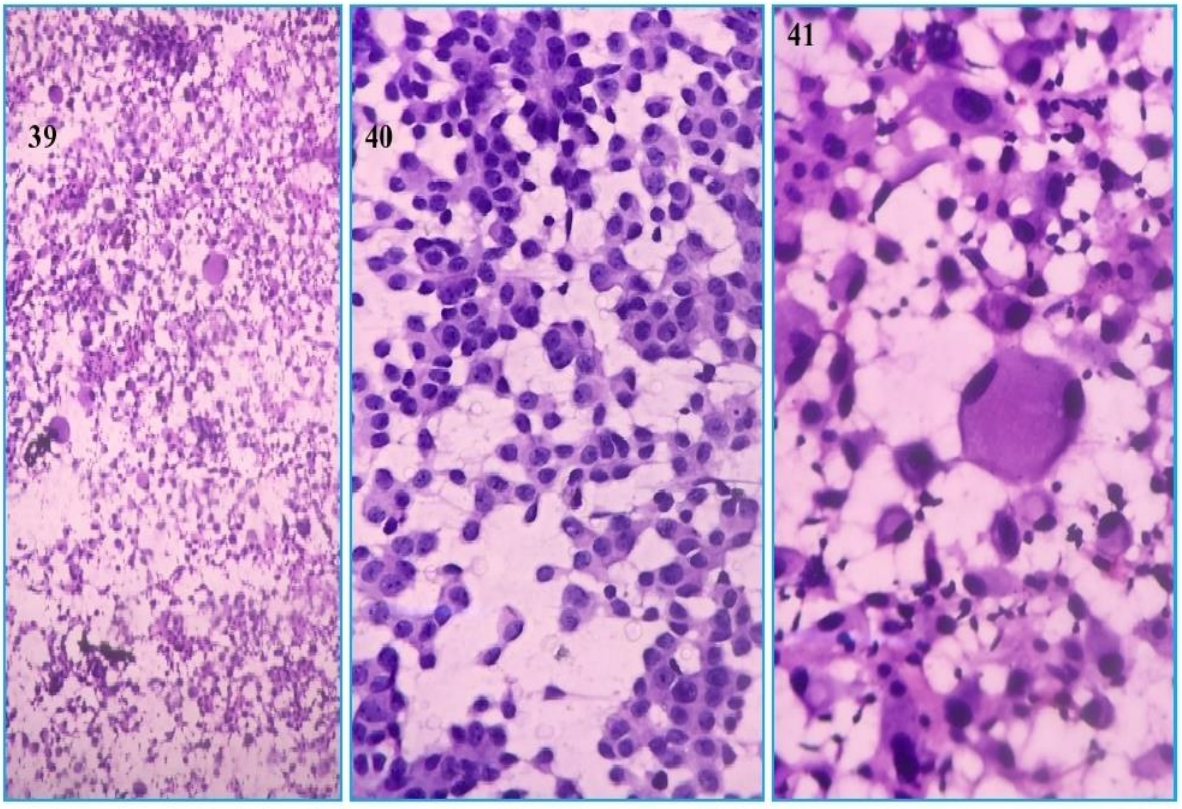


Figure K : Medullary Carcinoma. 42 : H&E section showing vascular invasion on 4 x view. 43 & 44 : Cellular tumour arranged in nesting and diffuse patterns composed of polygonal and focal spindle cells interspersed by extracellular amorphous eosinophilic deposits of amyloid.

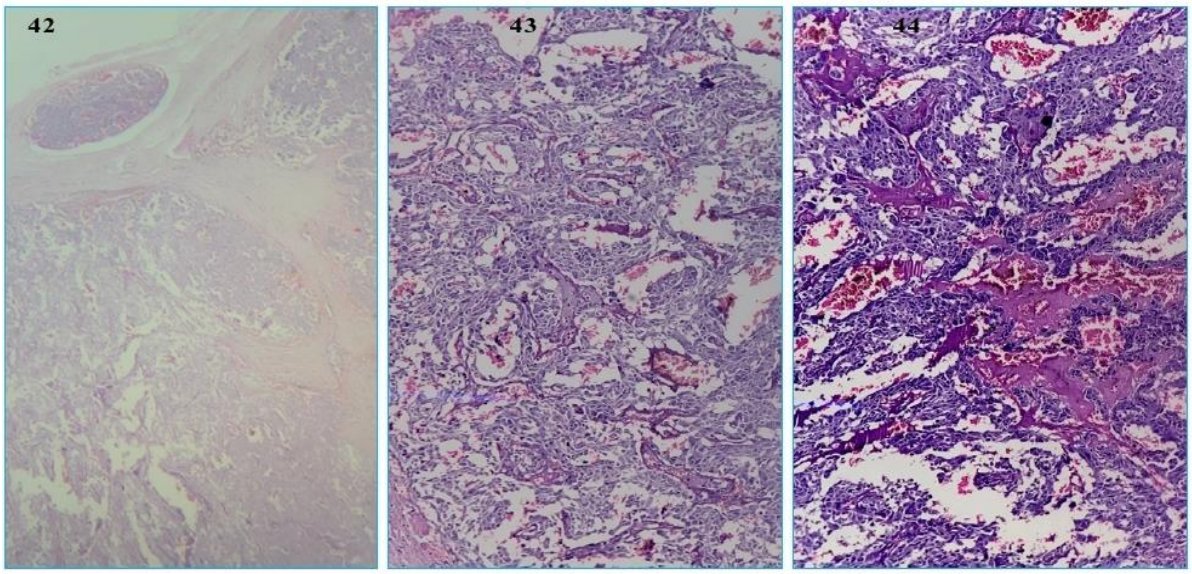
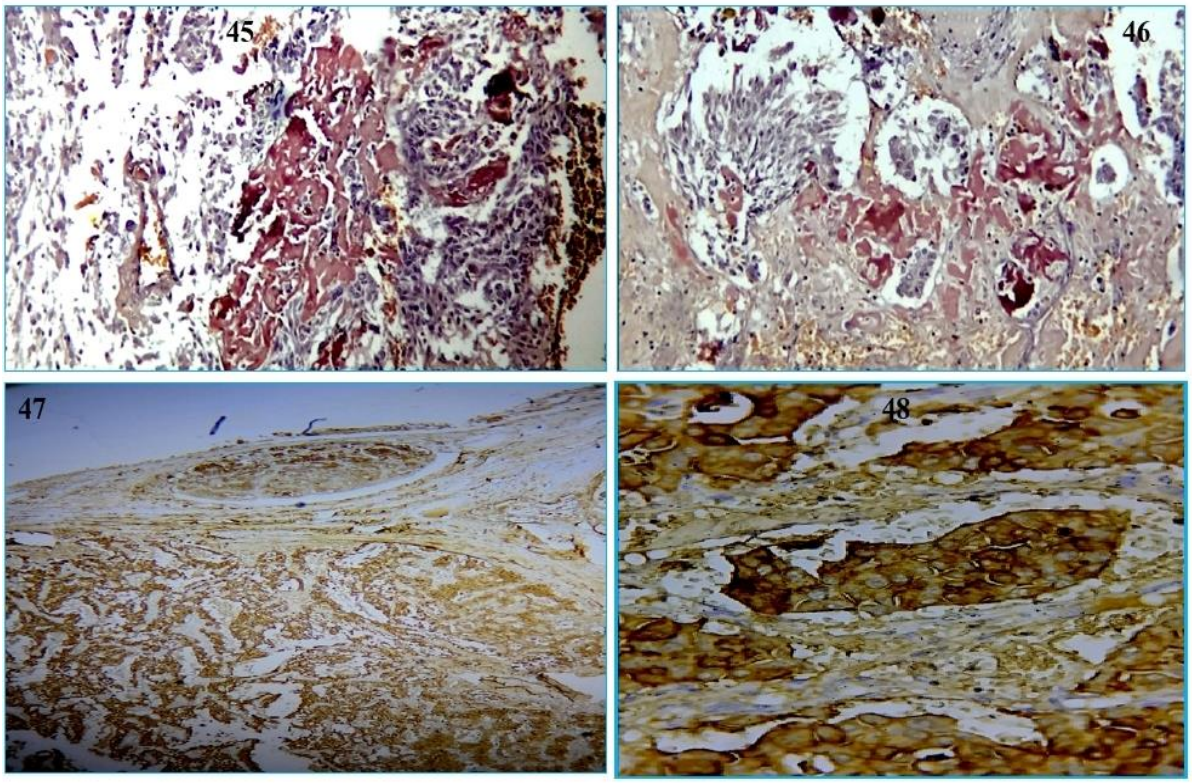


Figure L : Special histochemical & immunohistochemical stains for Medullary Carcinoma. 45 & 46 : Red colouration of the amorphous extracellular deposits of amyloid on Congo red stain. 47 & 48 : IHC with Calcitonin showing diffuse & intense positivity.



In our study, on histopathology we have encountered dual lesions such as nodular goiter associated with hashimoto's thyroiditis/ lymphocytic thyroiditis/follicular adenoma and papillary carcinoma of thyroid in the background of hashimoto's thyroiditis. Of the non-neoplastic

lesions nodular goiter (180 cases) was the most commonest lesion followed by nodular goiter with immune thyroiditis including hashimoto's and Lymphocytic thyroiditis (42 cases) and then immune thyroiditis (7 cases) and 6 cases of nodule goiter with follicular adenoma. Follicular adenoma was the most common benign neoplasm, whereas papillary carcinoma was most common amongst the malignant lesions followed by follicular carcinoma. Lymph node dissection was done for 8 out of 20 cases of papillary thyroid carcinoma. Excepting 2 cases remaining 6 cases revealed metastatic deposits in lymph nodes. Among PTCs 17 cases were reported in females of which 16 were detected in the 20-40 years age group, one case was of 50 years old and remaining 3 cases were detected in males seen in ages of 29, 30 and 60 years respectively. One case diagnosed as medullary carcinoma of thyroid along with metastatic deposits in lymph nodes was noted in a 39 year old male patient.

Table - 4: Cytomorphological diagnosis of non-neoplastic thyroid lesions.

Bethesda system	**Non – Neoplastic**	**No. of cases**	**percentage**
Type -I	Cystic degeneration in thyroid nodule	12	4.10%
Type-II	Colloid cyst/colloid nodule	04	1.37%
	Nodular goiter	215	74.13%
	Nodular goiter with Hashimotos thyroiditis	04	1.37%
	Nodular goiter with hurthle cells	02	0 .68%
	Hyperplastic nodule	01	0.34%
	Benign nodule with cystic degeneration	01	0.34%
	Lymphocytic thyroiditis	01	0.34%
	Hashimotos thyroiditis	17	5.86%
Type III	Nil	Nil	Nil
Total		257	88.62%

Table - 5: Cytomorphological diagnosis of neoplastic thyroid lesions.

Bethesda system	**Neoplastic**	**No. of cases**	**%**
Type-IV	Follicular neoplasm	16	5.51%
Type-V	Nodular goiter with suspicious areas of papillary carcinoma of thyroid	01	0.34%
Type-V	Suspicious of papillary carcinoma thyroid	11	3.79%
Type-VI	PTC in the background of hashimotos thyroiditis	01	0.34%
	Papillary carcinoma of thyroid	03	1.03%
	Medullary carcinoma of thyroid	01	0.34%
Total		33	11.36%

Table - 6: Histomorphological diagnosis of thyroid lesions.

Type of lesion	**No. of cases**	**%**
Non - neoplastic	238	82.1%
Neoplastic	52	17.9%
• Benign	29	10.0%
• Malignant	23	7.9%
Total	290	100%

Table - 7: Distribution of various types of thyroid lesions based on histomorphological features.

Type of lesion	Histopathological diagnosis	Cases	%
Non-neoplastic			
	Colloid cyst	03	1.03%
	Nodular goiter	180	62.06%
	Nodular goiter with Hashimotos thyroiditis	38	13.1%
	Nodular goiter with lymphocytic thyroiditis	04	1.3%
	Nodular goiter with follicular adenoma	05	1.72%
	Lymphocytic thyroiditis	01	0.3%
	Hashimotos thyroiditis	06	2.0%
	Hashimotos thyroiditis with Follicular adenoma and changes of Nodular goiter.	01	0.3%
Neoplastic			
Benign	Hurthle cell adenoma	03	1.03%
	Follicular adenoma	20	6.89%
	Follicular adenoma with nodular goiter changes	03	0.3%
	Follicular Adenoma with Lymphocytic thyroiditis	01	0.3%
	Follicular adenoma with hashimotos thyroiditis	02	0.6%
Malignant	Minimally invasive follicular carcinoma	01	0.3%
	Follicular carcinoma in the background of Hashimotos thyroiditis	01	0.3%
	Papillary carcinoma of thyroid	19	6.59%
	PTC in the background of Hashimotos thyroiditis	01	0.3%
	Medullary carcinoma of thyroid	01	0.3%
	Total	290	100.0%

Cytohisto-correlation was done in 290 cases that underwent FNA as well as surgery. 12 cases which were non-diagnostic on FNAC, proved to be nodular goiter in 11 cases and colloid cyst in 1 case on histopathology. One case which was diagnosed as nodular goiter with suspicious areas of papillary carcinoma of thyroid (PTC) has been diagnosed as PTC on histopathology; this case was taken as true positive. Two cases diagnosed as suspicious of PTC on FNAC turned out as nodular goiter on histopathology; this was considered as false positive.

The sensitivity, specificity, positive predictive value, and negative predictive value of FNAC, determined by correlating with histomorphology in diagnosing the thyroid lesions were 67.4%, 99.2%, 93.9%, 94.2%, & 98.03%, respectively. The diagnostic accuracy of FNAC in determining thyroid lesions was 94.1%.

Discussion

FNAC has been considered as one of the important preoperative investigative procedures in evaluating the thyroid swellings. It is safe, simple, reliable and a quick procedure with a low complication rate. Other tests like ultrasonography, radioisotope scanning and anti-thyroid anibody titer assays were also done wherever needed for evaluation of thyroid swellings before proceeding to thyroid surgery. It has been demonstrated that among all these diagnostic modalities, FNAC is the most accurate, cost effective screening test for rapid diagnosis of thyroid swellings. Factors that influence the efficacy of FNAC of thyroid include adequate sampling, cooperation of the patient, expertise of the reporting cytopathologist. On FNAC distinction between follicular adenoma and follicular carcinoma cannot be made [5-8].

Table - 8: Cytomorphological-histomorphological correlation (n=290).

Cytomorphological diagnosis	Cases	Histomorphological diagnosis	Cases
Cystic degeneration in thyroid nodule	12	Nodular goiter Nodular goiter with Hashimotos thyroiditis Nodular goiter with lymphocytic thyroiditis Colloid cyst	08 02 01 01
Colloid cyst	04	Colloid cyst Nodular goiter	01 03
Nodular goiter	215	Nodular goiter Nodular goiter with Hashimotos thyroiditis Nodular goiter with lymphocytic thyroiditis Nodular goiter with follicular adenoma Follicular adenoma Colloid cyst Papillary carcinoma of thyroid Follicular Adenoma with Lymphocytic thyroiditis Follicular Adenoma with nodular goiter Hurthle cell neoplasm	162 30 03 05 04 01 04 01 02 03
Nodular goiter with Hashimotos thyroiditis	04	Nodular goiter with Hashimotos thyroiditis	04
Nodular goiter with hurthle cells	02	Hashimotos thyroiditis	02
Hyperplastic nodule	01	Follicular carcinoma (Minimally invasive)	01
Benign nodule with cystic degeneration	01	Follicular adenoma	01
Lymphocytic thyroiditis	01	Lymphocytic thyroiditis	01
Hashimotos thyroiditis	17	Hashimotos thyroiditis Nodular goiter Nodular goiter with Hashimotos thyroiditis Follicular adenoma Follicular adenoma with hashimotos thyroiditis Follicular adenoma with nodular goiter changes Hashimotos thyroiditis with FA & NG changes Follicular carcinoma (widely invasive) in the background of Hashimotos thyroiditis	04 05 02 01 02 01 01 01
Nodular goiter with suspicious areas of papillary carcinoma of thyroid	01	Papillary carcinoma of thyroid	01
Suspicious of papillary carcinoma thyroid	11	Papillary carcinoma of thyroid Nodular goiter	09 02
PTC in the background of hashimotos thyroiditis	01	PTC in the background of Hashimotos thyroiditis	01
Papillary carcinoma of thyroid	03	Papillary carcinoma of thyroid	03
Medullary carcinoma of thyroid	01	Medullary carcinoma of thyroid	01
Follicular neoplasm	16	Follicular adenoma Papillary carcinoma of thyroid	14 02
Total	290	Total	290

Table - 9: Comparison of statistical data of different studies (in %).

Study	Sensitivity	Specificity	PPV	NPV	Accuracy
Cusick, et al. [19]	76.0	58.0	72.0	64.0	69
Afroze, et al. [20]	61.9	99.3	92.8	94.7	94.5
KO HM, et al. [21]	78.4	98.2	99.0	66.3	84.7
Kantasueb, et al. [22]	74.7	93.2	79.49	91.29	88.40
Bagga, et al. [23]	66.0	100.0	100.0	96.0	96.2
Present study	67.4	99.2	93.9	94.2	94.1

To distinguish between these lesions it requires detailed histological examination to look for vascular or capsular invasion, which cannot be made out on FNAC [9-12]. Inadequate sampling may result from sclerotic, calcified nodule, or nodules with large areas of cystic degeneration [13]. In our study of 290 patients, majority of patients were seen in the age group of 21-40 years, constituting upto72.2%, similar to that of rupam, et al. [14]. Female preponderance was noted constituting 91% while male incidence was 9%. Male to female ratio was 1:9.75 similar to the study done by Sarath Babu Kumara Rama, et al i.e. 1: 9 [15]. The youngest patient of our study was girl of 16 years with colloid goitre and the oldest patient was a man of 70 years with follicular carcinoma. In our study, 238 cases were non-neoplastic and 52 cases were neoplastic and their ratio was 4.6 :1 almost similar to the study done by Disha J. Ramteke, et al.; Leung CS, et al. and Godinho L, et al. with ratios of 4.92:1, 4.93:1 and 4.95:1 respectively [16-18].

The efficacy of a particular test depends on the ability to detect the presence of the disease (sensitivity) and to verify the absence of disease when it is not present (specificity). In our study, sensitivity was 67.4%, and specificity was 99.2%, which correlates with other studies [11, 13-18]. This shows that FNAC is more specific than sensitive. The reason for the wide range of sensitivity and specificity is contributed by subjective categorization of lesions by different cytopathologists. Comparison of statistical data of different studies was as per **Table – 9** [19-23].

Conclusion

FNAC is simple, reliable, cost-effective, quick and minimally invasive procedure that can be undertaken as one of the pre-operative investigative cytological procedure in diagnosing thyroid lesions. Unnecessary thyroid surgeries for benign lesions can be avoided, however clinical suspicion of malignancy with benign morphology on FNAC needs close clinical follow up and if necessary surgery. Bethesda categorization appraises the surgeon and aids him in taking the right decision for surgical intervention.

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