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A study of thyroid lesions using fine needle aspiration cytology technique

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ABSTRACT

Background

Thyroid swellings are very common and can occur in various clinical settings and in various age groups. The modalities of treatment differ in different conditions. Some require therapeutic management and some others surgery. FNAC was proved to be the single most sensitive investigation in differentiating neoplastic from non- neoplastic conditions, and benign from malignant conditions. At present this procedure is utilized extensively in diagnosing the condition and planning for surgery in necessary cases thus decreasing the unnecessary surgeries

Objective(s)

To prove the importance of FNAC as the first line diagnostic procedure for the evaluation of goiter. To study the scope of FNAC in differentiating neoplastic from non neoplastic lesion and its role as a diagnostic tool in picking up unsuspected malignancies and metastatic malignancies.

Methods

This study was conducted in the department of Pathology, on patients with thyroid swellings who attended the Medical, Surgical & ENT OPs. FNAC full clinical examination of the patient was done and data like present, past and personal history of the patient along with laboratory investigations including thyroid profile and ultrasound reports were collected. FNAC was done as an outpatient procedure.

Results

Out of the 330 cases diagnosed, majority were non neoplastic lesions (276) neoplastic were (54). Nodular goiter was found to be the commonest among all the lesions with 106 cases [32%] showing high prevalence between 21-30yrs and a male to female ratio of 1:8.7

Conclusion

FNAC has been found to be a most valuable, economized, safe and simple diagnostic procedure in the evaluation of thyroid swellings.

Keywords: Thyroid lesions, fine needle aspiration cytology, malignancy, non malignancy.

INTRODUCTION

Fine needle aspiration cytology method for studying the thyroid was first developed in Sweden in the Radium Helmet hospital of Stockholm during 1950.Martin & Ellis of the memorial hospital for cancer reported its use even earlier in 1930. [1, 2, 3] At present FNAC of the thyroid is considered by many as first line procedure and it is fully accepted in the diagnostic work up of patients in conjunction with traditional methods.[4,5] FNAC is widely accepted as the most accurate, non-invasive, sensitive, specific and cost effective diagnostic procedure in the assessment of thyroid nodules and helps to select people pre operatively for surgery.[6,7] The main purpose of FNAC thyroid is to distinguish patients with malignant nodules and those with benign nodules. It is the procedure of choice in the initial screening of thyroid nodules and it can be repeated as many times as necessary due to the minimal invasiveness and low morbidity. [8, 9] With FNAC, the number of thyroidectomise has been halved whereas the incidence of malignant lesions has doubled which indicates that it is possible to diagnose even the latent and occult malignancies. The consequences of this conservative methodology are yet to be evaluated. Definitely there is a chance of missing a co-existing lesion.[10,11] FNA is also indicated in the evaluation of goiter and in follow up of individuals who were exposed to irradiation of head and neck.[12] FNA is also useful as a therapeutic procedure for drainage of cystic lesions. Principal function of the thyroid gland is to act as a catalyst-of the nature of the spark for the maintenance of oxidative metabolism in most tissues.[13,14,15] It is also necessary for normal growth and maturation and tissue differentiation. The active circulating hormones of the thyroid gland are Tri-iodothyronin [T3] and Thyroxine [T4]. [16] The FNA smears show Follicular epithelial cells, Colloid, ` C' Cells, Cartilage, Tracheal epithelium and sometimes fragments of skeletal muscle. The cytological appearance of normal thyroid gland varies with age and functional state.[17] Aspirations of normal thyroid yield little blood stained material Smears contain few Follicular cells and scant colloid with Follicular cells dispersed or in small clusters. Categorizing the diseases of the thyroid is of great importance because some lesions require medical management, such as thyrotoxicosis, hypothyroidism and diffuse or focal enlargement of thyroid due to thyroiditis and other lesions need surgical intervention such as neoplasms and Nodular goiters causing compression. Follicular epithelial cells are fragile and the epithelial cells may vary in size from low cubical or flat to high columnar, the height and the configuration of the thyroid Follicular cells reflect to some extent the functional activity.[18] Bare nuclei of the Follicular cells that are similar in size & shape as lymphocytes are common. Small nucleoli may be evident. Cytoplasm stains pale blue. Rarely follicles may be recovered. Colloid stains blue to purple and forms a thin membrane like coat, often with folds and cracks. 'C' cells resemble Medullary Carcinoma cells that are difficult to find in thyroid smears without resorting to immuno staining for calcitonin. The finding of 'C'cell may indicate significant c cell hyperplasia. [19, 20]

Table 1. Major types of thyroid hyperplastic disorders. [21]

Major types of thyroid hyperplastic disorders.			
Name	**Mechanism**	**Pathology**	**Functional status**
Dyshormonogenetic Goiter	Genetically determined error in thyroid hormone metabolism	Nodular or less frequently diffuse hyperplasia.	Hypothyroid
Graves disease	Auto immune	Diffuse hyperplasia.	Hyperthyroid
Nodular hyperplasia-endemic goiter	Iodine deficiency	Nodular hyperplasia proceeded by a transient phase of diffuse hyperplasia.	Usually euthyroid sometimes hypothyroid
Sporadic goiter	Unknown	Nodular hyperplasia	Usually euthyroid sometimes hyperthyroid or hypothyroid.

Neoplastic lesions

The neoplastic lesions were divided on the basis of direction of dedifferentiatoin

Tumours of thyroid Follicular or metaplastic epithelium

1. Follicular Adenoma and variants.
2. Follicular Carcinoma – Minimally invasive, widely invasive.
3. Papillary Carcinoma and variants.
4. Poorly differentiated thyroid Carcinoma including Insular Carcinoma
5. Undifferentiated [anaplastic] and Squamous cell Carcinoma including Carcinosarcoma.
6. Columnar cell Carcinoma.
7. Mucoepidermoid Carcinoma.
8. Sclerosing Mucoeidermoid Carcinoma with eosinophils.
9. Mucinous Carcinoma.

Tumors showing 'C' cell differentiation

1. Medullary Carcinoma and variants.
2. 'C' cell Adenoma.

Tumors showing both Follicular and 'C' cell differentiation

1. Collision tumor Follicular/Papillary and Medullary Carcinoma.
2. Mixed Follicular – paraFollicular Carcinoma.

Tumors showing thymic or related branchial pouch differentiation

1. Ectopic thymoma.
2. Spindle epithelial tumour with thymic like differentiation [SETTLE] [Intra thyroid spindle cell tumor with mucus cysts].
3. Carcinoma showing thymic like differentiation [CASTLE so called intrathyroid epithelial thymoma.]

Tumors of lymphoid cells

1. Malignant Lymphoma
2. Plasmacytoma.

Mesenchymal and other lesions

1. Benign and malignant mesenchymal tumors including angiosarcoma.
2. Paraganglioma.
3. Teratoma.[22]

WHO Histological Classification of Thyroid Tumors

Thyroid Carcinomas

- Papillary Carcinoma
- Follicular Carcinoma
- Poorly differentiated Carcinoma
- Undifferentiated (anaplastic) Carcinoma
- Squamous cell Carcinoma
- Mucoepidermoid Carcinoma
- Sclerosing Mucoepidermoid Carcinoma with eosinophilia
- Mucinous Carcinoma
- Medullary Carcinoma
- Medullary Carcinoma
- Mixed Medullary and Follicular cell Carcinoma
- Spindle cell tumour with thymus-like differentiation
- Carcinoma showing Thymus-like differentiation [23]

Thyroid Adenoma and related tumors

- Follicular Adenoma
- Hyalinizing trabecular tumour

Other Thyroid tumours

- Teratoma
- Primary Lymphoma and Plasmacytoma
- Ectopic Thymoma
- Angiosarcoma
- Smooth muscle tumors
- Peripheral nerve sheath tumors
- Paraganglioma
- Solitary fibrous tumour
- Follicular dendritic cell tumour
- Langerhans cell histiocytosis
- Secondary tumours[24]

AIM

A prospective work aimed to study the spectrum of cytological features of thyroid lesions in patients with thyroid swellings and to correlate the histological appearances where ever tissues were available in patients, who attended the Govt General Hospital, Vijayawada

OBJECTIVES

1. To demonstrate the utility and limitations of aspiration cytology in thyroid lesions.
2. To prove the importance of FNAC as the first line diagnostic procedure for the evaluation of goiter.
3. To confirm its utility as a screening procedure for selecting cases to surgery
4. To study the scope of FNAC in differentiating neoplastic from non neoplastic lesions
5. To study its role as a diagnostic tool in picking up unsuspected malignancies and metastatic malignancies

MATERIAL AND METHODS

This study was conducted in the department of Pathology ,on patients with thyroid swellings who attended the Medical, Surgical & ENT OPs Rajiv Gandhi Institute of Medical sciences, a south Indian tertiary care teaching Government hospital Kadapa during the period of July 2015 to November 2017. A total number of 375 aspirations were performed on patients with thyroid swellings, both male and female, who attended Medical, Surgical & ENT OPs during the above period. Smears prepared were stained with H&E. Among the 375 cases aspirated material obtained was sufficient for diagnosis in 330 cases. Remaining 45 cases showed only blood cellular elements and occasional thyroid acinar cells. Before proceeding to FNAC full clinical examination of the patient was done and data like present, past and personal history of the patient along with laboratory investigations including thyroid profile and ultrasound reports were collected. FNAC was done as an outpatient procedure. A 23-24 gauge needle was used for aspiration. No local anesthetic was used. Spirit swab, 10ml disposable syringe with 23-24 gauge needles, sclean glass slides, Fixative [methanol] used for aspiration procedure. The contents were expelled on to the labelled slides and smears were prepared. The slides were placed in the fixative for 20 minutes and stained. The numbers of aspirations made were 2-4 in each case. In a diffusely enlarged thyroid both the lobes were aspirated. In a Nodular goiter multiple aspirations were made. The stain used in the present study was H&E. According to Hamberger et al in the assessment of a dominant nodule 6 clusters of benign cells in at least 2 slides prepared from separate aspirates constitute a reasonable minimum material for diagnosing benign lesions. For the present study criteria of Hamberger and Orell were taken into consideration in case of dominant nodule and colloid goiter .For the diagnosis of inflammatory and malignant lesions , type of inflammatory cells along with the back ground and cellular features were taken into consideration ,irrespective of the amount of cellularity. Basing on the above criteria the lesions aspirated were categorized as Benign, Malignant and Inadequate.

RESULTS

Out of the 330 cases diagnosed, majority were non neoplastic lesions (276) neoplastic were (54) [315]. Nodular goiter was found to be the commonest among all the lesions with 106 cases [32%] showing high prevalence between 21-30yrs and a male to female ratio of 1:8.7. Clinical presentation in most of the cases was Multi Nodular goiter involving both the lobes. In a small fraction of cases [15%] it presented as solitary nodule. Association of Nodular goiter with Hashimoto's thyroiditis was found in two cases and in one case Papillary Carcinoma.

27 cases of Adenomatous hyperplasia were diagnosed of which 26 were females. Solitary nodular presentation was found in 22 %{ 6} cases. Common age group affected were 41- 50yrs. Cases of simple goiter diagnosed were 25, all in women, with a peak incidence in 21-30yrs.

15 cases of cystic lesions were diagnosed, mostly in the 31-40yrs age group with a female preponderance [12 females and 3 males].

Thyroiditis cases which were 94 presented as diffuse swellings involving the entire gland in the 2^{nd} to 5^{th} decade. Lymphocytic thyroiditis was diagnosed in 30 cases of which 2 were males. All the cases of Hashimotos thyroiditis [59] and granulomatous thyroiditis [5] were diagnosed in middle aged women.

39 cases were diagnosed as Follicular neoplasms, of these 34 were females and 5 were males. Clinical presentations of all these Follicular neoplasms were solitary nodules. They were commonly diagnosed in the 3rd to 4^{th} decades. Malignant neoplasms comprised 15 cases, Papillary Carcinoma accounting for 13 cases [86.67%] and

the remaining two were Medullary Carcinoma and Anaplastic Carcinoma [13.33%]

Most of the Papillary Carcinomas were diagnosed in the 2nd -3rd decade and the female to male ratio was 3:1. Both the Medullary and Anaplastic Carcinomas were diagnosed in the 40-50yrs age group and in males. Surgical excision was done in 58 cases. Out of these, 26 patients with cytological diagnosis of Nodular goiter showed consistent picture in 17 cases. The remaining 11 cases were inconsistent. 6 cases were Follicular Adenomas, 2 cases were Papillary Carcinomas and 1 case of Thyrotoxicosis.

5 Cases diagnosed as cystic lesions were biopsied, 4 cases showed consistent picture (2 cases of thyroglossal cyst & 2 cases of infected cyst) and one case showed Nodular goiter. 18 cases diagnosed as Follicular neoplasms were subjected to histopathological examination. 12 cases showed Follicular Adenoma and two cases showed Follicular Carcinoma. The remaining 4 cases were hyperplastic lesions of MNG. 4 Cases of Papillary Carcinoma, 1 case of Anaplastic Carcinoma and 1 case of Medullary Carcinoma were excised and the histopathology was consistent in all the cases. 3 Cases were reported as inadequate on FNAC but after excision showed Follicular Adenomas.

As follicular carcinomas cannot be differentiated from follicular adenomas on cytology we considered 12 cases of follicular adenoma and two cases of follicular carcinoma as true positive. These 14 cases of follicular neoplasms, 4 cases of papillary carcinomas, one case of medullary carcinoma and one case of anaplastic carcinoma were considered as true positive (total20). 4 cases of MNG which were diagnosed as follicular neoplasms on cytology were considered as false positive. 2 cases of papillary carcinoma and 6 cases of follicular adenoma which were diagnosed as nodular goiter on cytology were considered as false negative.

The 18 cases of nodular goiter on FNAC (excluding 2 cases of papillary carcinoma and 6 cases of follicular adenoma) and five cases of cystic lesions were found to be non neoplastic on histopathology and were considered as true negative.

Table 2. Showing distribution of neoplastic & non neoplastic cases

Sl.No	Item	Number	Percentage
1	Non neoplastic lesions	276	83.64 %
2	Neoplastic	54	16.36 %
Ratio of non neoplastic to neoplastic lesions is 5:1			

Table 3. Showing details of FNAC

Sl.No	Item	Number	Percentage
1	Adequate for reporting	330	88 %
2	Inadequate for reporting	45	12 %
3	Total aspirations done	375	100 %
Percentage of adequacy 88%			

Table 4. showing the lesions diagnosed on FNAC

Sl.No	Type of Lesion	No of cases	Percentage
1	Nodular goiter	106	32.11%
2	Nodular goitre with hyperplasia	27	8.18%
3	Simple goiter	25	7.58%
4	Cystic lesions	15	4.55%
5	Thyrotoxicosis	9	2.73%
6	Lymphocytic thyroiditis	30	9.09%
7	Hashimoto's thyroiditis	59	17.88%
8	Granulomatous thyroiditis	5	1.52%
9	Follicular neoplasm	39	11.82%
10	Papillary Carcinoma	13	3.94%

11	Medullary Carcinoma	1	0.30%
12	Anaplastic Carcinoma	1	0.30%
Total		330	100%

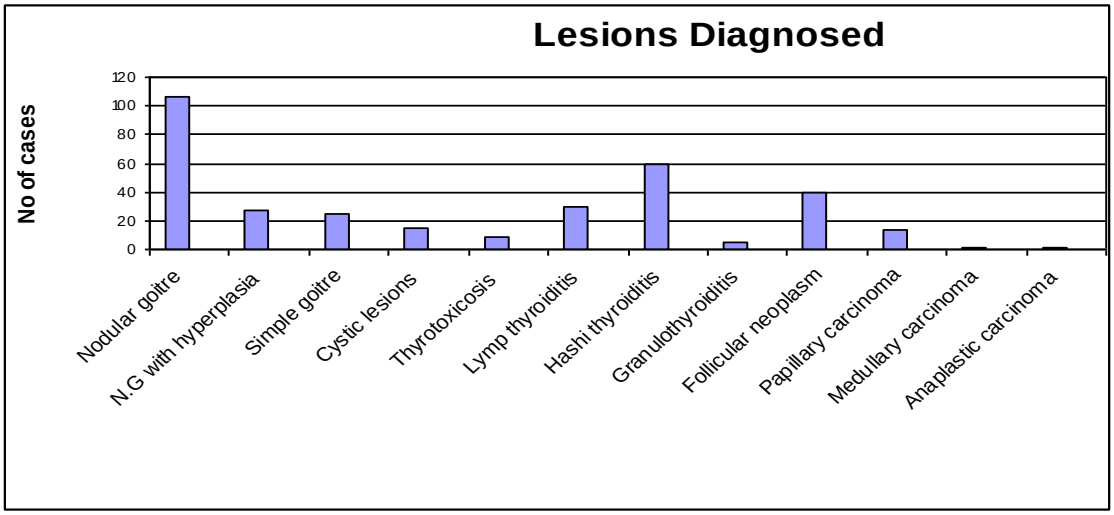

Figure 1. Chart showing distribution of lesions

Table 5. Showing age wise distribution of cases

Sl.No	**Type of Lesion**	Age in years							**Total**
		1-10	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**	
1	Nodular goiter	1	8	37	34	14	8	4	106
2	NG with hyperplasia		2	8	6	9	1	1	27
3	Simple goiter		4	11	6	3		1	25
4	Cystic lesions		2	1	6	3	2	1	15
5	Thyrotoxicosis		1	2	3	2		1	9
6	Lymph thyroiditis		8	7	10	5			30
7	Hashi thyroiditis		12	18	22	4	3		59
8	Granulo thyroiditis			2	3				5
9	Follicular neoplasm		4	15	10	5	5		39
10	Papillary Carcinoma			7	3	1	2		13
11	Medullary Carcinoma					1			1
12	Anaplastic Carcinoma					1			1
13	Inadequate	2	4	13	12	11	1	2	45
Total		**3**	**45**	**121**	**115**	**59**	**23**	**10**	**375**
Commonest age group affected is between 21-30 yrs									

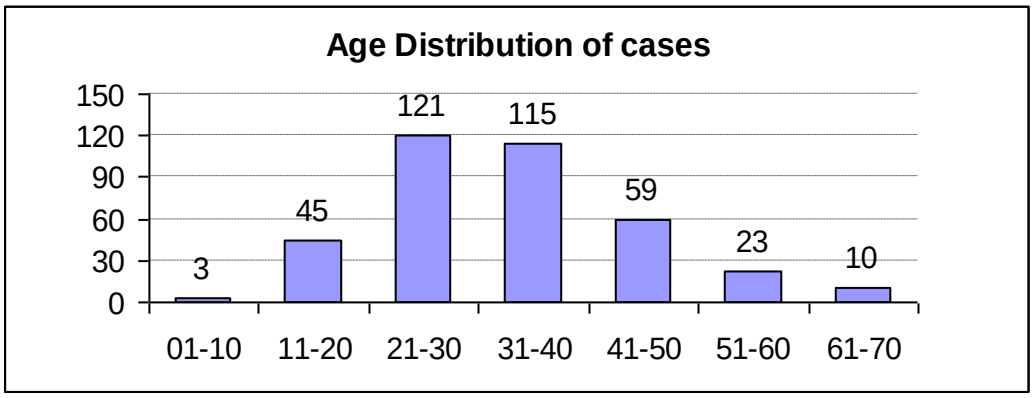

Figure 2. Chart showing age wise distribution of cases in the study

Table 6. showing common affected age group

Sl.No	Type of Lesion	Age group
1	Nodular goiter	21-30
2	Nodular goitre with hyperplasia	41-50
3	Simple goiter	21-30
4	Cystic lesions	31-40
5	Thyrotoxicosis	31-40
6	Lymphocytic thyroiditis	31-40
7	Hashimoto's thyroiditis	31-40
8	Granulomatous thyroiditis	31-40
9	Follicular neoplasm	21-30
10	Papillary Carcinoma	21-40
11	Medullary Carcinoma	41-50
12	Anaplastic Carcinoma	51-60

Table 7. Showing sex wise distribution of cases

Sl.No.	Type of Lesion	Females	Males	Total No. Cases
1	Nodular goiter	95	11	106
2	Nodular goitre with hyperplasia	26	1	27
3	Simple goiter	25	0	25
4	Cystic lesions	12	3	15
5	Thyrotoxicosis	6	3	9
6	Lymphocytic thyroiditis	28	2	30
7	Hashimoto's thyroiditis	59	0	59
8	Granulomatous thyroiditis	5	0	5
9	Follicular neoplasm	34	5	39
10	Papillary Carcinoma	10	3	13
11	Medullary Carcinoma	0	1	1
12	Anaplastic Carcinoma	0	1	1
13	Inadequate	41	4	45
Total		341	34	375
Female to male ratio of thyroid lesions is 10 : 1				
Female to male ratio of among neoplastic lesions is 4.4 : 1				

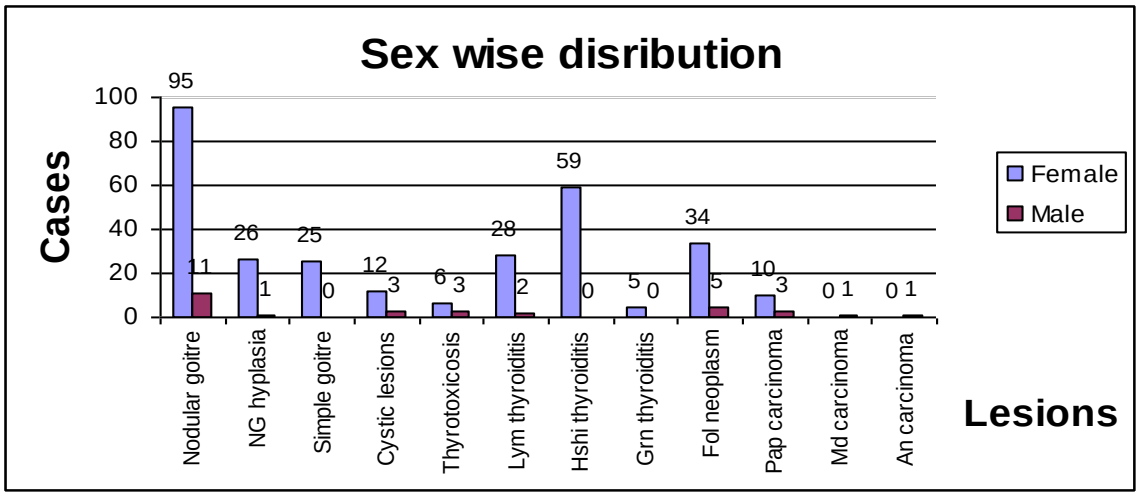

Figure 3. Chart showing sex wise distribution of cases in the study

Table 8. Showing lesions with solitary nodular presentation

Sl.No.	Lesion	No of cases	%
1	Nodular goiter	11	18.33
2	Nodular goitre with hyperplasia	6	10
3	Cystic lesion	2	3.33
4	Follicular neoplasm	39	65
5	Papillary Carcinoma	2	3.33
Total		60	100%

Table 9. Showing percentage of non neoplastic lesions

Sl.No.	Lesion	No of cases	%
1	Nodular goiter	106	38.41
2	Nodular goitre with hyperplasia	27	9.78
3	Simple goiter	25	9.06
4	Cystic lesions	15	5.43
5	Thyrotoxicosis	9	3.26
6	Lymphocytic thyroiditis	30	10.87
7	Hashimoto's thyroiditis	59	21.38
8	Granulomatous thyroiditis	5	1.81
Total		276	100%
Nodular goitre is the commonest lesion			

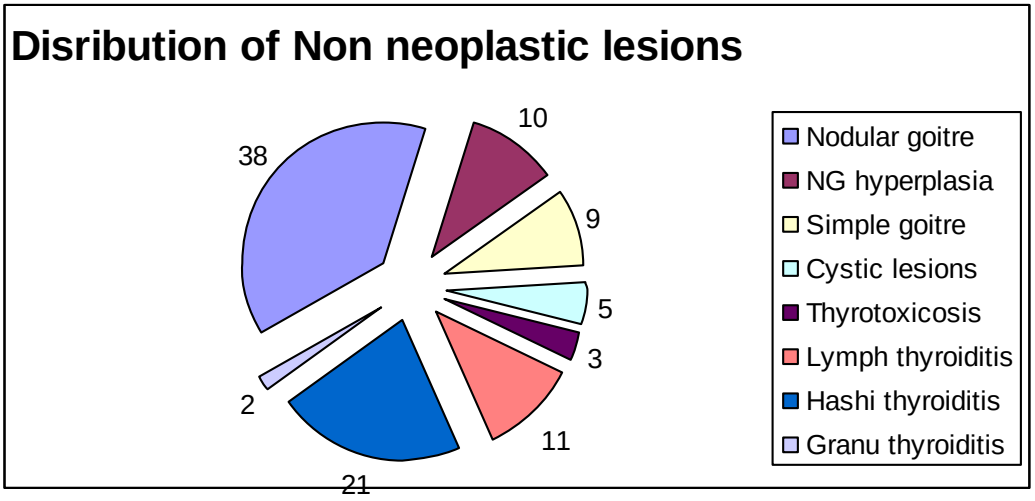

Figure 4. Chart showing distribution of non neoplastic lesions

Table 10. Showing percentage of neoplastic lesions

Sl.No.	Name of tumor	No of cases	%
1	Follicular neoplasm	39	72.22
2	Papillary Carcinoma	13	24.08
3	Medullary Carcinoma	1	1.85
4	Anaplastic Carcinoma	1	1.85
Total		54	100%

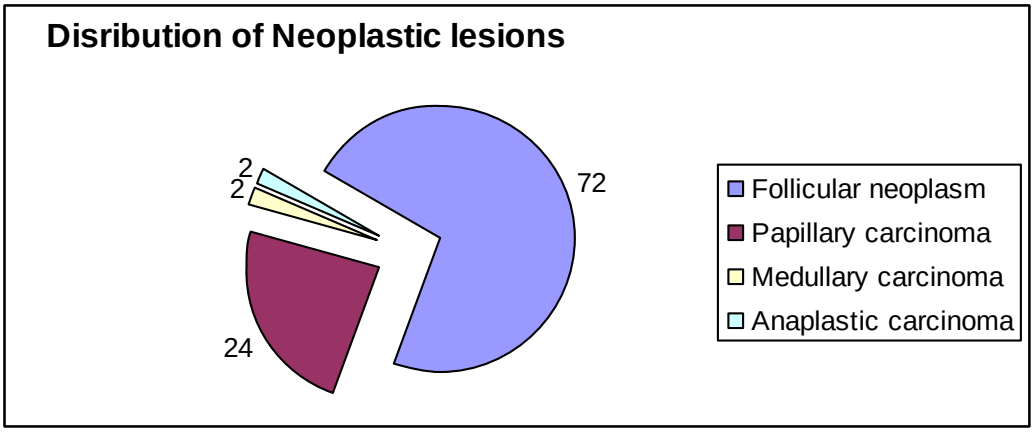

Figure 5. Chart showing distribution of neoplastic lesions

Table 11. Showing number of cases subjected to HPE

Sl.No.	Lesion	No of cases
1	Nodular goiter	26
2	Cystic lesion	5
3	Follicular neoplasm	18
4	Papillary Carcinoma	4
5	Anaplastic Carcinoma	1
6	Medullary Carcinoma	1
	TOTAL	55

Table 12. Showing Cytological Vs histopathological correlations

Cytological diagnosis	Histopathological diagnosis								
	Nodular goitre	Cystic lesion	Follicular Adenoma	Follicular Carcinoma	Papillary Carcinoma	Anaplas Carcinoma	Medullary Carcinoma	Toxicosis	Total
Nodular goiter	17	0	6	0	2	0	0	1	26
Cystic lesion	1	4	0	0	0	0	0	0	5
Follicular neoplasm	4	0	12	2	0	0	0	0	18
Papillary Carcinoma	0	0	0	0	4	0	0	0	4
Anaplastic Carcinoma	0	0	0	0	0	1	0	0	1
Medullary Carcinoma	0	0	0	0	0	0	1	0	1
Total	22	4	18	2	6	1	1	1	55

Table 13. Showing Histopathological correlation

Sl.No.	Type of lesion	Diagnosed on FNAC	Biopsy correlation	% of correlation
1	Nodular goitre	26	17	65.83
2	Cystic lesion	5	4	80
3	Follicular neoplasm	18	14	77.78
4	Papillary Carcinoma	4	4	100
5	Anaplastic Carcinoma	1	1	100
6	Medullary Carcinoma	1	1	100

Statistical analysis of correlation

True positive =20, True negative =23, False positive=4, False negative=8

Table 14. Showing Statistical Analysis

Cytology	Histology	
	Non neoplastic	Neoplastic
Non neoplastic	TN 23	FN 8
Neoplastic	FP 4	TP 20

- Sensitivity=TP X100/TP+FN =71.42%
- Specificity=TNX100/TN+FP=85.19%
- Positive predictive value=TPX100/TP+FP=83.33%
- Negative predictive value=TN X100/TN+FN=74.20%
- False positive ratio= FPX100/ FP+TN=14.81%
- False negative ratio=FNX100/FN+TP=28.57%
- Accuracy=TP+TNX100/TP+TN+FP+FN=78.18%

Table15. Showing statistical comparision

Study	FNAC	Histopath	Sensitivity	Specificity	PPV	NPV	Insufficient	Accuracy
Kendrel	113	34	-	-	-	-	6%	-
Piromali et al	795	216	95%	98%	95%	97%	-	-
Godinho matos et al	144	28	73%	100%	100%	69%	13%	83%
Mandrekar et al	1992	238	53%	93%	82%	78%	12%	79%
Holemm et al	112	53	84%	52%	53%	83%	11%	65%
Burch et al	504	-	80%	73%	-	-	-	75%
Leonard & Melcher	335	187	88%	78%	46%	97%	18%	80%
Present	375	55	71.4%	85.2%	83.3%	74.2	12%	78.2%

DISCUSSION

Thyroid swellings are very common and can occur in various clinical settings and in various age groups [25].The modalities of treatment differ in different conditions. Some require therapeutic management and some others surgery. FNAC was proved to be the single most sensitive investigation in differentiating neoplastic from non- neoplastic conditions, and benign from malignant conditions [26,27]. At present this procedure is utilized extensively in diagnosing the condition and planning for surgery in necessary cases thus decreasing the unnecessary surgeries [28].

In the present study FNAC of Thyroid was done in 375 cases. Material sufficient for reporting was obtained in 330 cases [88%] and 45 cases [12 %] were inadequate showing only blood cellular elements and occasional thyroid acinar cells. The rate of inadequacy ranged from 9-31% according to various publications. Various factors are responsible for getting inadequate material [29]. It depends on the experience of the aspirator, the size of the nodule, type of the nodule, number of aspirations and the duration of the aspiration [30]. Rate of inadequacy in our study was 12%.

In our experience 23 and 24G needles yielded sufficient material. Material obtained was scanty with 25 G needle and was very hemorrhagic with 22G needle. Increased number of aspirations yielded more material when compared to a single aspiration for extended time. Aspirations from cases of thyrotoxicosis and certain Adenomas were very hemorrhagic. Non- aspiration technique described by Jayaram et al was used in these cases

FNAC is safe, less expensive and of great patient compliance [31]. Piramol reported skin bruises in 3.3% of cases and Safinullah [32] recorded skin bruises and haematomas in 6% of cases ; So the complication rate in our study was not high. We didn't experience any major complications except in one case where the patient went into a shock like state, but recovered in a few minutes without any treatment. Minor complications like haematoma and skin bruises were observed in 3% of cases.

In the large series of Mayo clinic [6300cases] benign diseases represented 65% of the total lesions which included benign goiters and thyroiditis. In the series of Schenek benign diseases represented 83%.

In the present study benign non -neoplastic cases were 276 representing 80% of the total cases, so our results were almost the same with the other studies.

CONCLUSIONS

FNAC has been found to be a most valuable, economized, safe and simple diagnostic procedure in the evaluation of thyroid swellings. The present study was found to be very useful in differentiating Neoplastic from Non neoplatic thyroid lesions. The present study aided in the diagnosis of Malignant Thyroid lesions with great accuracy. The utility of FNAC as a screening procedure, in selecting patients for Surgery was satisfactory (No surgery was performed in cases of thyroiditis).

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