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A Prospective Study: Cytological Evaluation Of Non Neoplastic Lesions Of Thyroid With Histomorphology Correlation.

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ABSTRACT

The thyroid gland is very unique and it is considered largest among the endocrine glands. The thyroid gland is superficial and hence easily approachable. Enlargement of the thyroid gland is a common issue. For accurate precision of the diagnosis and early intervention of these lesions, a combination of investigations are necessary. Thyroid lesions may be developmental, inflammatory, non - neoplastic, neoplastic. Thyroid gland lesions comprise a spectrum of entities causing a systemic effect or localized such as a nodular goitre or a tumour mass. There are different modalities used to evaluate and diagnose efficiently thyroid lesions. These include fine needle aspiration cytology (FNAC), histomorphology examination, thyroid hormone assay. FNAC has proven to be a first line tool to evaluate the thyroid lesions because of its cost effectiveness and high patient acceptance. To evaluate the morphology of the non-neoplastic thyroid lesions by Fine Needle Aspiration Cytology in an adult with swelling of the thyroid gland. A total of 100 patients with thyroid swelling were included in this study who had FNAC during these three years – study period from 2017-2019 in the department of pathology Thanjavur medical college. All patients with thyroid swelling will be assessed by medical history, clinical examination, biochemical tests. The FNAC diagnoses will correlate with clinical features, hormonal findings and subsequent histological examination of the thyroid specimens. Among the autoimmune disease of thyroid, we received only Hashimoto's thyroiditis which was common in females. Concordance between FNAC and Histopathology is only 75 % .This study shows 76.3 % sensitivity for diagnosing colloid goitres and accuracy of diagnosing colloid goitre is 71 %.

Keywords: FNAC of thyroid, Cytology and Histopathology correlation, Nodular goitre

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INTRODUCTION

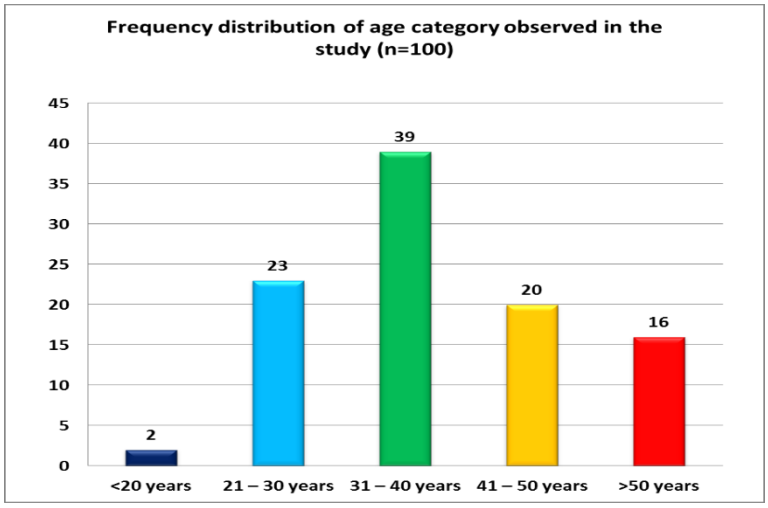
Thyroid is a butterfly shaped largest endocrine gland which is the first endocrine organ to appear in foetus [1]. The thyroid gland is very superficial in location and hence easily approachable. Enlargement of thyroid gland is now emerging as a common issue accounting for 4-7 % in adults. Hence accurate precision of the diagnosis and early intervention of the lesions are necessary and hence a multitude of diagnostic tests have become mandatory [2]. The lifetime risk of developing thyroid dysfunction is common [3]. Although thyroid nodules are commonly seen in females, thyroid nodules in males are more likely to be malignant than in the females [4]. Nodules are most likely to be malignant in patients who are younger than 20 years of age and older than 60 years of age 8. To make an effective surgical intervention in these lesions, it is very vital to make an assessment of the morphological nature of lesions pre operatively [5]. Fine needle aspiration is the simplest, safest, cost effective and most accurate with a sensitivity as high as 93.4% and specificity as high as 74.9% and is considered the first line screening and diagnostic test for patients with thyroid nodules [6]. The main role of thyroid fine needle aspiration cytology is to triage or categorise patients for either surgery or conservative management.

MATERIALS AND METHODS

A prospective study of non-neoplastic lesions of thyroid, irrespective of age and sex with patients referred from Thanjavur Medical College and Hospital During June 2017 – September 2019 was carried out. The protocol for the purpose of inclusion in this study were history, clinical examination thyroid nodule which was defined as single clinically palpable discrete lesions either involving lobe or isthmus of the thyroid gland with thyroid function tests. Initial cytological evaluation with Fine Needle Aspiration cytology was done in 100 cases and in which further HPE correlation was done. Fine needle aspiration cytology was done as per standard guidelines recommended by Svante Rowell. A minimum of 3 aspirates from different areas were undertaken and the smears were fixed in isopropyl alcohol. Smears were then stained with routine Haematoxylin and Eosin. The smears were interpreted as per guidelines following BETHSEDA system. Thyroidectomy specimens were fixed in 10 % buffered neutral formalin. In all the specimen type, the extent of surgery, overall size, dimensions, capsule, presence of nodules, cystic lesions and lymph nodes were evaluated. The specimens were then cut longitudinally and two sections from each lobe along with capsule was taken. If suspicious of any neoplasm, minimum 5 sections from the lesion area were taken and routinely processed Minimum thickness of 3-5 microns were cut and stained with routine Haematoxylin and Eosin.

OBSERVATIONS AND RESULTS

Graph 1: Frequency distribution of type of age category in years observed in the study.



This study covered 100 fine needle aspiration sample and corresponding histopathological specimens of patient clinically suspected to have nodular thyroid lesions at Thanjavur Medical College and Hospital and undergone further surgical procedures who were correlated with thyroid function tests. Statistical analysis: Data were entered in the excel spread sheet and variables were coded accordingly. The

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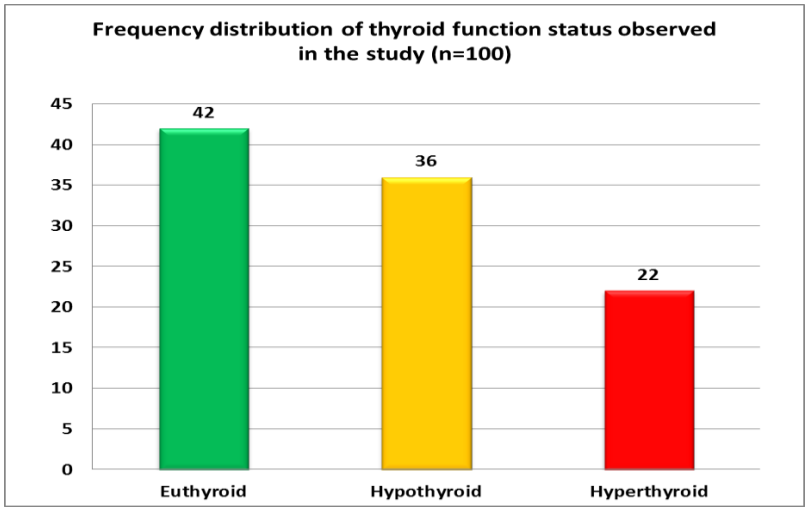
statistical analyses were performed using Graph Pad Prism version 5 software. Data were presented as mean with Standard deviation for normal distribution/scale data (age and various time durations). Data were presented as frequency with proportion n (%) for categorical data. Fisher's exact test was used to compare the frequencies between the groups. $p < 0.05$ were considered statistically significant

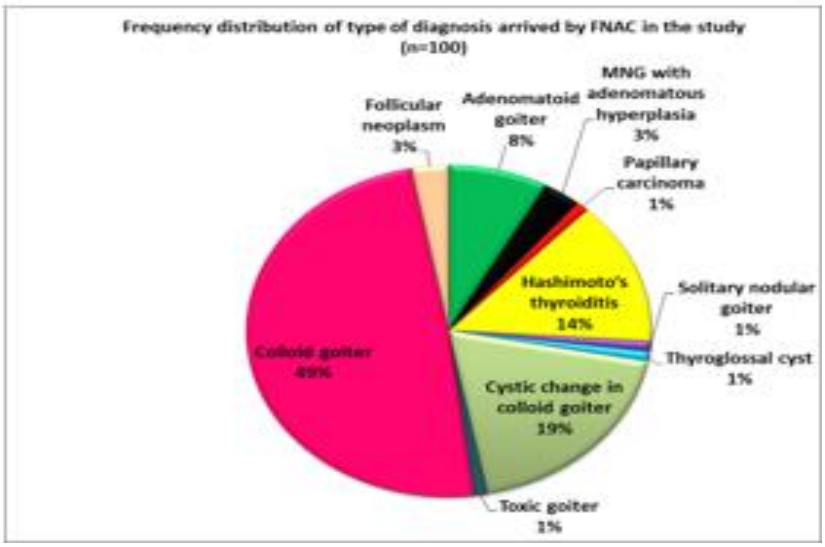
Data are expressed as n with %. Total number of patients were N= 100. The age group was divided into groups of five. The minimum age group was classified as less than 20 years ,21-30 years ,31-40 years , fourth group were belonging to 41-50 years and the last group was classified as more than 50 years. In the study done the mean age was 39.8 years with SD of 11.5. The age ranged between 15 – 80 years. The highest incidence of non-neoplastic lesions of thyroid was observed in the age group of 31-40 years (39%) followed by 21-30 years (23%) and 41-50 years (20 %).

Graph 2: Showing the frequency of thyroid function status among the patients



Data are expressed as n with %. The total N=100.Among the 100 cases Multinodular goiter was the most common diagnosis among the Histopathological examination .42 % patients presented in euthyroid status, followed by 36 % with features of hypothyroidism, 22 % presented with hyperthyroidism. Hypothyroid features included in generalized fatigue, mental sluggishness, constipation, and shortness of breath, increase in weight. Among the 100 patients who were hypothyroidism mostly presented with fatigue, weight gain, constipation. Hyperthyroid features included weight loss, increased sweating, diarrhea, palpitations and tremor. Among the 100 who were clinically diagnosed as hyperthyroidism had complaints of palpitations and weight loss.

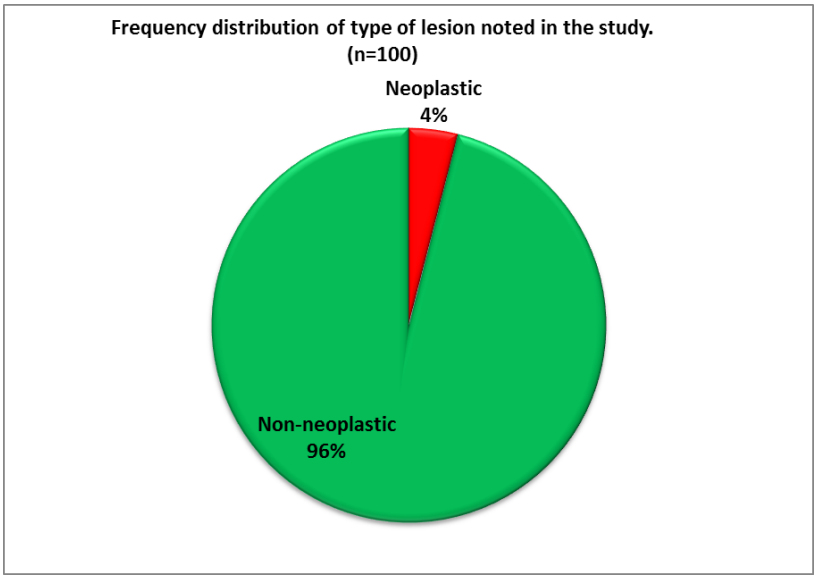
Graph 3: Shows the type of diagnosis – 49% contributed by colloid goitre.



ISSN: 0975-8585

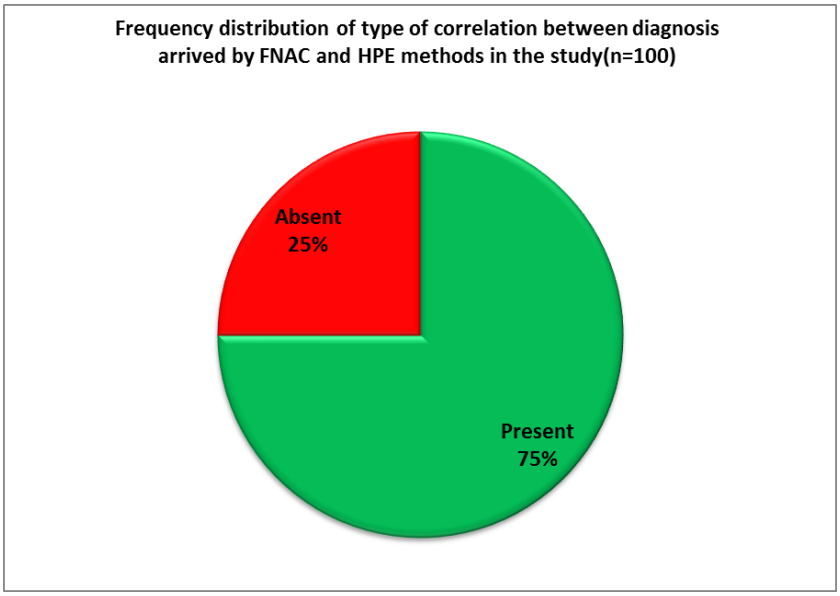
The above Graph indicates the maximum diagnosis is the colloid goiter which accounts for about 49 cases out of 100 cases followed by Hashimoto's thyroiditis contributing for 14 %. In FNAC, colloid goiter is diagnosed clinically as a butterfly shaped swelling diffusely enlarged with smears showing either eosinophilic material with occasional thyroid follicular epithelial cells or epithelial cells arranged in clusters with no nuclear pleomorphism in a background of thick and thin colloid. Occasionally the smear may have cystic macrophages. One case was reported as thyroglossal cyst. The aspirate yielded clear fluid and the smear contained squamous epithelial cells in a background of colloid

Graph 4: Incidence of non-neoplastic and neoplastic lesions in the study:



In the given 100 cases around 96 cases were reported to be non-neoplastic lesions and 2 cases in FNAC were reported to be follicular neoplasm came as non-neoplastic lesion in HPE. 2 cases reported as non-neoplastic lesion in FNAC came as neoplastic lesion in HPE with one being reported as microinvasive follicular carcinoma given as nodular goiter in FNAC.

Graph 5: Frequency distribution of type of correlation between diagnosis arrived by FNAC and HPE methods in the study.



Among the 100 cases 75 % of the cases correlated with FNAC and HPE. One case given in FNAC was reported to be follicular adenoma in HPE. Six cases reported in FNAC as colloid goitre proved to be

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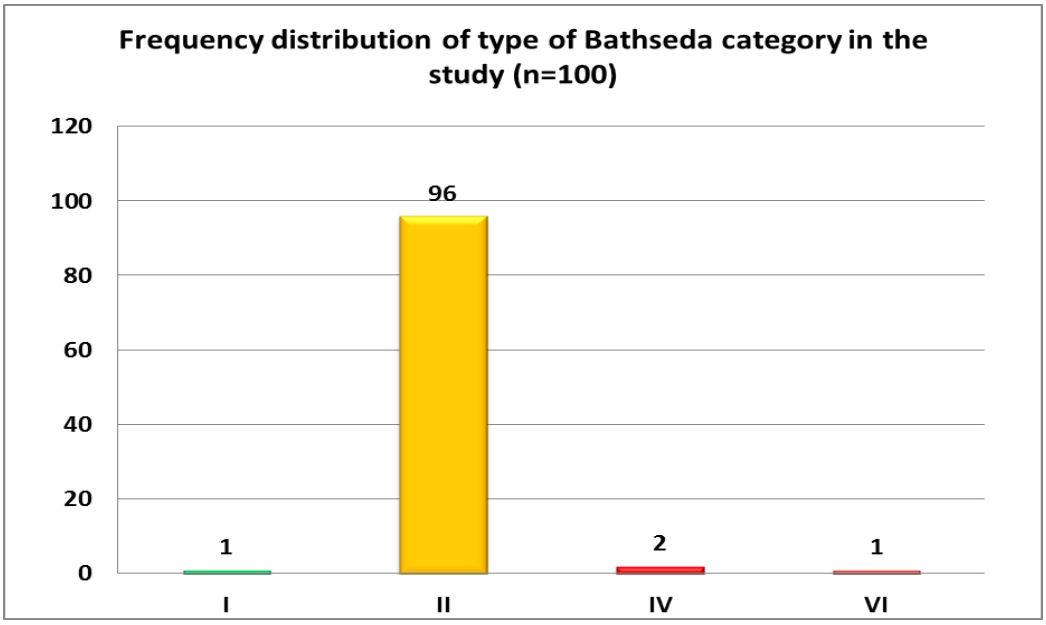
Hashimoto's thyroiditis in HPE. One case given as solitary nodular goitre was reported to be MNG in HPE. One case given as colloid goitre was reported as Micro invasive follicular carcinoma in HPE. One case of adenomatoid goitre in FNAC had features to be given as Follicular carcinoma in HPE. One case of papillary carcinoma reported in FNAC had features of only nodular colloid goitre with cystic degeneration. One case reported to have cystic change in a nodular goitre showed features of toxicity with papillary hyperplasia in HPE. One case reported in FNAC as cystic change in colloid goitre reported as adenomatoid goitre with papillary hyperplasia in HPE. One case of toxic goitre reported as adenomatoid goitre in HPE.

Graph 6: Frequency distribution of type of Bethesda category in the study.



Among the 100 cases taken 96% had to be grouped under Bethesda category II. Since this study is based on non-neoplastic lesions of thyroid majority of cases came under category II

Table 1: Comparison of age category in years with respect to thyroid function status in the study.

S. No	Age category	Euthyroid (n=42)		Hypothyroid (n=36)		Hyperthyroid (n=22)		P value
		n	%	n	%	n	%	
1	<20 years	2	4.8	0	0	0	0	0.301 (NS)
2	21 – 30 years	6	14.3	11	30.6	6	27.3	
3	31 – 40 years	20	47.6	14	38.9	5	22.7	
4	41 – 50 years	7	16.7	7	19.4	6	27.3	
5	>50 years	7	16.7	4	11.1	5	22.7	
	Chi-square value =9.503; degree of freedom = 8							

Data are expressed as n (%). Fisher's exact test was used to compare the proportions frequency between the groups. NS = not significant. Twenty patients presented with euthyroid status among the common age group 31 -40 years followed by fourteen patients who presented with hypothyroidism features. Among the 21-30 years group 11 belonged to hypothyroid group whereas equal proportions were euthyroid and hyperthyroid.

ISSN: 0975-8585

Table 2: Comparison of HPE diagnosis arrived with respect to age category in the study

S.No	HPE diagnosis	<20y (n=2)		21-30y (n=23)		31-40y (n=39)		41-50y (n=20)		>50y (n=16)	
		n	%	n	%	n	%	n	%	n	%
1	Adenoma with toxicity	0	0	0	0	0	0	0	0	1	6.2
2	Adenomatoid goitre	0	0	2	8.7	3	7.7	1	5	3	18.8
3	Adenomatoid goitre with papillary hyperplasia	0	0	1	4.3	0	0	0	0	0	0
4	Colloid goitre	0	0	1	4.3	2	5.1	2	10	0	0
5	Cystic degeneration in a nodular colloid goitre	0	0	0	0	5	12.8	3	15	1	6.2
6	Follicular adenoma	0	0	0	0	1	2.8	0	0	0	0
7	Follicular carcinoma	0	0	0	0	0	0	0	0	1	6.2
8	Granulomatous thyroiditis	0	0	1	4.3	0	0	0	0	0	0
9	Hashimoto's thyroiditis	0	0	1	4.3	8	20.5	6	30	2	12.5
10	Hashimoto's thyroiditis with focal adenomatous hyperplasia	0	0	0	0	1	2.6	0	0	0	0
11	Micro-invasive follicular carcinoma	0	0	0	0	0	0	0	0	1	6.2
12	MNG	1	50	10	43.5	13	33.3	5	25	3	18.8
13	MNG with adenomatous hyperplasia	0	0	5	21.7	5	12.8	3	15	2	12.5
14	Nodular colloid goitre with Hashimoto's thyroiditis	0	0	0	0	1	2.6	0	0	0	0
15	Nodular hyperplasia of thyroid	0	0	1	4.3	0	0	0	0	0	0
16	Thyroglossal cyst	1	50	0	0	0	0	0	0	0	0
17	Toxic nodular goitre	0	0	1	4.3	0	0	0	0	1	6.2
18	Toxic nodular goitre with papillary hyperplasia	0	0	0	0	0	0	0	0	1	6.2

Data are expressed as n with %. The total N=100

Table 3: Correlation thyroid lesion diagnosed by FNAC and HPE method in the study

S.No	FNAC diagnosis	HPE diagnosis	n	%
1	Adenomatoid goiter (n=8)	Adenoma with toxicity	1	12.5
		Adenomatoid goiter	5	62.5
		Follicular carcinoma	1	12.5
		MNG	1	12.5
2	Colloid goiter (n=49)	Adenomatoid goiter	3	6.1
		Colloid goiter	3	6.1
		Follicular adenoma	1	2.04
		Hashimoto’s thyroiditis	5	10.2
		Micro-invasive follicular carcinoma	1	2.04
		MNG	24	48.9
		MNG with adenomatous hyperplasia	8	16.2
		Nodular colloid goiter with cystic degeneration	1	2.04
		Nodular colloid goiter with Hashimoto’s thyroiditis	1	2.04

ISSN: 0975-8585

		Nodular hyperplasia of thyroid	1	2.04
		Toxic nodular goiter	1	2.04
3	Cystic change in colloid goiter (n=19)	Adenomatoid goiter with papillary hyperplasia	1	5.26
		Colloid goiter	2	10.5
		Cystic degeneration in a nodular colloid goiter	4	21
		MNG	7	14.3
		Nodular goiter with adenomatous hyperplasia	1	5.26
		Nodular goiter with cystic degeneration	3	6.12
		Toxic nodular goiter with papillary hyperplasia	1	5.26
4	Follicular neoplasm (n=3)	Adenomatous goiter with toxic change	1	33.3
		MNG with adenomatous hyperplasia	2	66.4
5	Hashimoto's thyroiditis (n=14)	Granulomatous thyroiditis	1	7.15
		Hashimoto's thyroiditis	12	85.7
		Hashimoto's thyroiditis with focal adenomatous hyperplasia	1	7.15
6	MNG with adenomatous hyperplasia (n=3)	MNG with adenomatous hyperplasia	3	100
7	Papillary carcinoma (n=1)	Nodular Colloid goiter with cystic degeneration	1	100
8	Solitary nodular goiter (n=1)	MNG with adenomatous hyperplasia	1	100
9	Thyroglossal cyst (n=1)	Thyroglossal cyst	1	100
10	Toxic goiter (n=1)	Adenomatous goiter	1	100

From the above tabular column out of the 8 adenomatoid goitre reported in FNAC 5 cases were reported and correlated as adenomatoid goitre in HPE. 1 case was reported as follicular carcinoma in HPE and 1 case as adenoma with toxic goitre.1 case reported in papillary carcinoma in FNAC was further reported in HPE as nodular colloid goitre with cystic degeneration. The current study was done to evaluate the diagnostic accuracy of FNAC and to correlate FNAC with histopathology in thyroid lesions. One of the organs in our body where FNAC has wide application is the thyroid. A team work among pathologist, clinicians, and radiologists is essential to yield the best results in FNAC. Hence FNAC can be used as a safe diagnostic method for categorizing the thyroid lesions [7]. In our study there was a female preponderance with male-female ratio of 18.5: 81.5 similar to Kumar S et al study [7]. Benign cases were most common. Most of the cases among benign lesions were nodular goitre. Papillary carcinoma thyroid was most common among malignancy. In our study the data analysed showed sensitivity of FNAC in detecting thyroid lesions is 91.6%, specificity is 97.01%. FNAC has a positive predictive value of 95.6% and negative predictive value of 94.2%. Our data is comparable with other published datas in which the range of sensitivity 65% to 98%, specificity 72% to100%, PPV 34%to 100% NPV 83% to 100% [8].The diagnostic accuracy in our study is 94.78% which is concordant with other published data which reveals 95% in the differentiation of benign from malignant nodules in thyroid glands [4]. The false negative rate in our study was 8.3%. False positive rate was 2.98%. In our study 2 cases of follicular adenoma were reported as colloid goitre and 2 cases of nodular goitre were reported as follicular adenoma. Clary et al have referred this inter observer variability in their study [9]. However, overlapping epithelial hyperplasia and neoplasia is unavoidable. This sampling error could have been overcome by repeat aspiration [10]. One case of follicular adenoma in our study revealed features of papillary carcinoma in histopathology. Confusion between follicular adenoma and papillary carcinoma is unavoidable especially in follicular variant of papillary carcinoma [11] as the smear revealed tumor cells arranged in follicles without colloid. Mundasad et al have referred that indefinite to diagnose nodules should be subjected to surgery for conformation [12]. Aspiration cytology is not very effective in predicting neoplasia in cystic thyroid swellings. The cystic change could be seen in congenital, nodular hyperplasia, and neoplastic entities like cystic papillary thyroid carcinoma and rarely in follicular neoplasm. Only 10-15% of the cysts are neoplastic. In our study, out of 10 cases of papillary carcinoma of thyroid, 2 cases presented with a cystic swelling. In both the cases, the centrifuged material from the aspirate revealed papillary architecture with nuclear features of

malignancy. Borget et al. have told that guided FNAC would be an aid in proper diagnosis in such cases [13]. The cytologic accuracy with largely degenerated nodules is lower, in that the ability to differentiate benign and malignant follicular neoplasm is limited. It is important not only to enhance the specificity of preoperative diagnosis but also to increase simultaneously the sensitivity of detection. So those patients with carcinoma are discovered early for effective therapy. Bukhari et al. in their study of the FNAC procedure of the solitary thyroid nodule strongly suggest that FNAC should be used as an initial investigation of thyroid diseases, in all tertiary hospitals [14]. The transition of differentiated thyroid carcinoma to anaplastic thyroid cancers seems to be well established [9]. The incidence of anaplastic carcinoma in our present study is two cases in middle-aged persons. About 20% to 30% of all giant cell anaplastic carcinomas have a long history of thyroid swelling more than 15 years. Thus one type of very serious thyroid neoplasm can be prevented by early detection highlighting the role of FNAC as a screening procedure in the high-risk group [15]. The incidence of dual pathology was seen in 2 cases. One was Hashimoto's thyroiditis with papillary carcinoma. The other was medullary carcinoma with papillary carcinoma. In both these cases, we arrived at only one diagnosis. In both these cases, papillary carcinoma foci were not struck during aspiration. Chronic thyroiditis can coexist with many types of thyroid cancers and we overlooked the neoplastic lesion in the above cases. This sampling error could have been avoided if repeat aspiration was performed. False negative diagnosis arises from inadequate samples, geographic misses of lesions, dual pathology, and errors of interpretations and also in relation to the cystic neoplasm. This is of great concern because it indicates the potential to miss the malignant lesions [16].

CONCLUSION

The results of the accuracy of FNAC in thyroid vary but, in most series, overall accuracy rate exceeds 90% with 5 - 10% frequency of false positive and false negative. Diagnostic accuracy found in this study was 95.65% and false positive rate 2.98% false negative rate 6.25%. The present study confirms the view that FNAC has potential ability to detect both benign and malignant lesions of thyroid with accuracy. Thus, FNAC can be used as non-invasive, cost effective and a safe diagnostic method for defining thyroid disorders. It can be used as a screening test and helps in selection of patients for the appropriate treatment modality.

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