



PATTERN OF THYROID NEOPLASMS IN NELLORE AREA - A CLINICOPATHOLOGICAL CORRELATION

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ABSTRACT

Thyroid tumours in a population can be compared to an iceberg – partly visible (clinically evident tumours) but mostly hidden (occult tumours). This study was done to evaluate histological features of various thyroid neoplasms with cytological and clinical correlation. The material for the present study included resected biopsy specimens of the thyroid lesions, submitted to the Department of Pathology, Narayana Medical College Hospital, Nellore, between August 2006 to July 2008. The details of each case were obtained from the clinical records. A total of (293) Two hundred & ninety three cases of Fine needle aspiration cytology and diagnosis were performed in all the cases. Two cases were reported as Thyroglossal cyst. Excluding these 2 cases, 242 cases (83.16%) were diagnosed as Non-neoplastic and 49 cases (17%) as Neoplastic. Out of these 293 cases, only 102 patients underwent surgical excision and so a histopathological correlation was obtained in all 102 cases. Out of 102 cases, Non-neoplastic lesions of thyroid were seen in 52 cases (51%) and Neoplastic lesions in 50 cases (49%), which are nearly equally distributed. Out of 49 cases of cytologically proven neoplasms, 48 correlated with histopathology cases showed similar neoplasms. The histological correlation was 98% and the overall accuracy was 98.63% and sensitivity was 95%. Non-neoplastic lesions and neoplastic lesions were equally distributed. Correlation between Fine needle aspiration cytology and histopathology can improve sensitivity & specificity of diagnostic accuracy of thyroid lesions. Performing Fine needle aspiration prior to biopsy is effective.

KEYWORDS Papillary Carcinoma, Follicular Carcinoma, Fine Needle Aspiration Cytology, Follicular Variant of Papillary Thyroid Carcinoma



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INTRODUCTION

The thyroid gland is a butterfly shaped endocrine gland situated in the anterior aspect of the root of the neck. It is unique because of its superficial location allowing access for direct physical examination and biopsy. The thyroid gland secretes active hormones influencing the diversity of metabolic process. Nodular enlargement of thyroid raises a diagnostic problem to all physicians, surgeons and to pathologists. The benign and malignant nature of the nodule is the major diagnostic concern of the pathologists. The incidence of various thyroid disorders shows a striking variation both on a regional and national basis, the incidence shows marked variation when endemic and non endemic areas are compared. Epidemiological factors have been studied and apart from the known factors, such as age, sex, diet, drugs, radiation and geographic region, some unknown factors or even genetic factors also may be significant for the thyroid disorders. Many abnormalities also reflect on the environmental factors. In recent years many advances in medical field have taken place. Use of radio isotope and immunopathological technique have increased our understanding of pathophysiology of thyroid disorders and have contributed to precise diagnosis. Still many of these techniques are beyond the reach of most of the institution due to higher cost, people with the required expertise and prudent knowledge are scarce and so the diagnosis is arrived by histopathological, clinicopathological and traditional laboratory investigations. The thyroid enlargement can occur from a variety of causes like thyroiditis, nodular goiter, benign and malignant tumors of thyroid.

OBJECTIVES

1. To study the incidence of various neoplastic lesions of the thyroid gland. (2) To study the age & the gender incidence of each thyroid lesions. (3)To determine its ability in confirmation of clinically obvious malignancy.

Out of 102 specimens 52 were non-neoplastic lesions and 50 were neoplastic lesions.

(4)To find out the pathological spectrum of different thyroid lesions. (5)To compare the results with published data.

MATERIALS & METHODS

The material for the present study included resected biopsy specimens of the thyroid lesions, submitted to the Department of Pathology, Narayana Medical College Hospital, Nellore, between August 2006 to July 2008. The details of each case were obtained from the clinical records. The Specimens were fixed in 10% formalin for 24 hours after recording the gross morphological features. Depending on the size and appearance of the tumour, appropriate number of 5mm thick bits were cut from the lesion and submitted for processing, 4 – 5 micron thick sections were cut with a microtome and stained with Haematoxylin and Eosin stain. Special stains like Per-iodic acid schiff, van-Gieson, and mucicarmine were employed whenever indicated. The stained section were studied by light microscopy. For retrospective cases, the respective paraffin blocks were selected and treated similarly. The procedures for processing and staining of tissue given in cellular pathology technique, 4th edition, C.F.A. culling¹ and "Laboratory technique in surgical pathology" by Shameem sherriff² were followed. The diagnosis of thyroid lesions was made on the basis of Clinical Presentation, Gross morphology and Light microscopic features of H & E and special stained sections.

RESULTS

The present study conducted from August 2006 to July 2008 included a total number of 102 Surgically excised specimen received in the department of Pathology, Narayana Medical College Hospital, Nellore, and Andhra Pradesh.

Presenting Symptoms of various Thyroid Lesions in the present (102 cases)

Table 1

S.no	Symptoms	Non-neoplastic lesion(N=52)		Neoplastic lesions (N=50)	
		No of Cases	Percentage	No of Cases	Percentage
1.	Diffuse enlargement	47	46.07%	-	-
2.	Solitary nodule	24	23.52%	50	49.01%
3.	Dysphagia	22	21.56%	34	33.33%
4.	Cough	6	5.88%	10	9.80%
5.	Dyspnoea	3	2.94%	6	5.88%

Presenting Signs of various Thyroid lesions in the present (102 cases)

Table 2

S.no	Signs	Non-neoplastic lesion(N=52)		Neoplastic lesions (N=50)	
		No of Cases	Percentage	No of Cases	Percentage
1.	Hoarseness of voice	5	4.90%	35	34.31%
2.	Loss of weight	2	1.96%	26	25.49%
3.	Sleepless nights	-	-	34	33.33%
4.	Palpitation	5	4.90%	18	17.64%
5.	Excessive sweating	-	-	12	11.76%
6.	Irritability	-	-	10	9.80%
7.	Enlargement of cervical lymph nodes	-	-	8	7.84%

Solitary nodules was the commonest symptoms of any thyroid lesions, least being dyspnoea. Dysphagia was seen in both groups to the same extent. All these symptoms occurred to a greater extent in neoplastic lesions rather than in non-neoplastic lesions. (Table-1). Though same signs occur in both groups, the signs occur to a larger extent in neo-plastic lesions. Sleepless nights, excessive sweating, enlargement of cervical lymphnodes are exclusively seen in neoplastic lesions. (Table-2).

Frequency of Thyroid lesions as diagnosed by FNAC (293 cases)

Table 3

S No	Thyroid lesions	No of cases	percentage
1	Colloid goiter	107	36.86%
2	Multinodular goiter	83	28.67%
3	Adenomatous goiter	21	7.16%
4	Autoimmune thyroiditis	32	10.92%
5	Thyroglossal cyst	2	0.68%
6	Follicular neoplasm	29	9.89%
7	Hyalinizing trabecular adenoma	-	-
8	Papillary carcinoma	19	6.14%
9	Medullary carcinoma	-	-
10	Anaplastic carcinoma	1	0.34%
	Total	293	

Out of 293 cases, colloid goiter was the commonest lesion in non-neoplastic category followed by MNG, Adenomatous goiter and Autoimmune thyroiditis. In neoplastic lesions 29 cases were reported as follicular neoplasms, 19 as papillary carcinoma and one case as Anaplastic carcinoma. (Table-3)

Frequency of Histologically confirmed thyroid lesions – (102cases)**Table 4**

S.no	Thyroid lesions	No of cases	Percentage
1.	Colloid goiter	2	1.96%
2.	Multinodular goiter	24	23.52%
3.	Adenomatous goiter	10	9.8%
4.	Auto immune thyroiditis	14	13.72%
5.	Thyroglossal cyst	2	1.96%
6.	Follicular adenoma	27	26.47%
7.	Papillary carcinoma	19	18.62%
8.	Follicular carcinoma	4	3.92%
9.	Medullary carcinoma	-	-
10.	Anaplastic carcinoma	-	-
Total		102	-

Out of 102 cases, multinodular goitre was the commonest lesion in non neoplastic category followed by auto immune thyroiditis, adenomatous goitre and colloid goiter. In neoplastic lesions 27 cases were as follicular adenoma followed by 19 as papillary carcinoma and 4 as follicular carcinoma. (Table-4)

Histologic Follow - up of patients in whom the retrospective diagnosis was discordant with the official diagnosis.**Table 5**

Previous FNA Diagnosis (no)	Revised FNA Diagnosis (no)
Colloid goitre (1)	Papillary carcinoma (1)
Multinodular goitre (1)	Follicular neoplasm (1)
Adenomatous goitre (2)	Follicular neoplasm (2)

Table:5 Shows retrospective FNAC diagnosis with the official histologic diagnosis. One case of colloid goitre was reported as papillary carcinoma in the reviewed FNA diagnosis. One case of multinodular goitre and two cases of adenomatous goitre were reported as follicular neoplasms.

Gender distribution of thyroid Lesions (102 cases)**Table 6**

S.no	Thyroid neoplasms	Female	Female Percentage	Male	Male Percentage
1.	Colloid goiter	2	1.96%	-	-
2.	Multinodular goiter	23	22.54%	1	0.98%
3.	Adenomatous goiter	9	8.82%	1	0.98%
4.	Auto immune thyroiditis	14	14.7%	-	-
5.	Thyroglossal cyst	2	1.96%	-	-
6.	Follicular adenoma	22	21.56%	5	4.90%
7.	Hyalinizing trabecular adenoma	-	-	-	-
8.	Papillary carcinoma	16	15.68%	3	2.94%
9.	Follicular carcinoma	3	3.92%	1	0.98%
10.	Medullary carcinoma	-	-	-	-
11.	Anaplastic carcinoma	-	-	-	-
Total		91		11	

Table:6 Explains the gender distribution in the present study, 91 are females, 11 are males, the ratio being 8:1 approximately. It is obvious from the table that female preponderance is seen all types of lesions whether it is non-neoplastic or neoplastic.

MICROSCOPICALLY

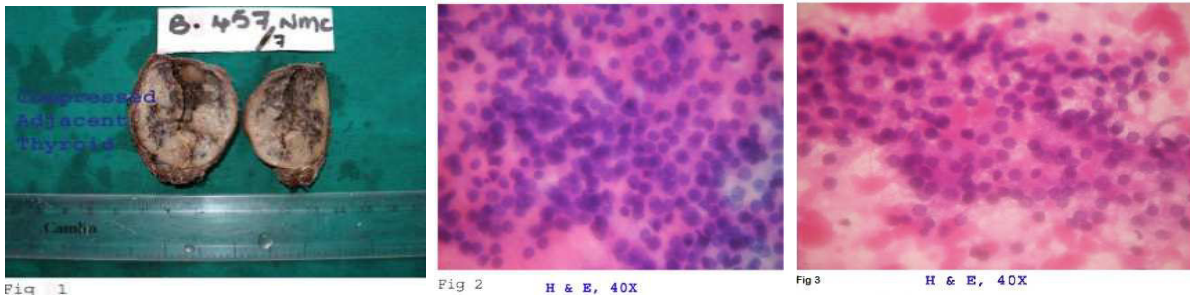


Figure 1: shows cut-section of thyroid comprising of greywhite and hemorrhagic areas with adjacent compressed thyroid tissue. **Figure 2&3:** Shows repetitive follicular pattern and microfollicular pattern.

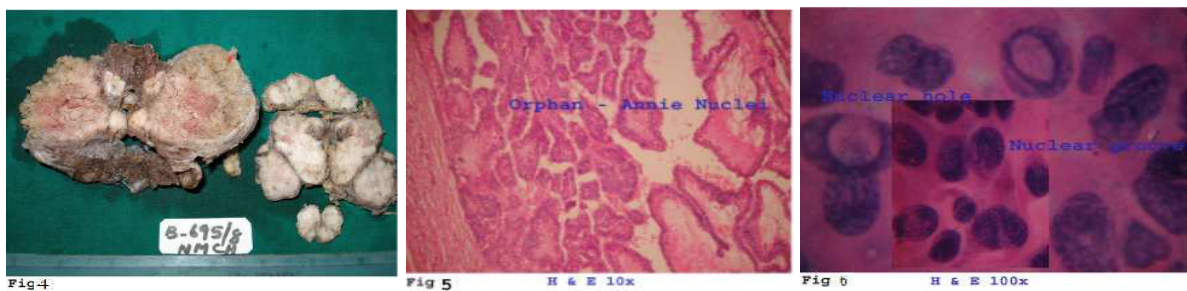


Figure 4: shows cut-section of thyroid comprising of papillary excrescence along with enlarged lymph nodes also showing papillary excrescence. **Figure 5&6:** shows finger like papillae with Orphan Annie nuclei, nuclear grooves and Intranuclear cytoplasmic inclusion.

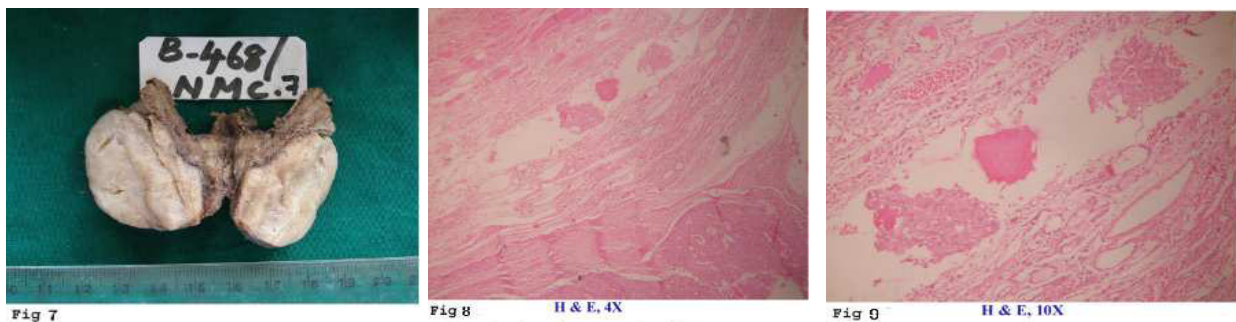


Figure 7: Shows cut-section of thyroid comprising of greywhite solid areas with adjacent thyroid tissue. **Figure 8&9 :** Shows vascular invasion, capsule with tumour and low power view showing vascular invasion.

DISCUSSION

The biology of thyroid cancer represents a spectrum of characteristics ranging from well-differentiated lesions which has an excellent prognosis to anaplastic carcinoma which is almost uniformly fatal. In the present study, out of 102 cases of thyroid lesions, 27(26.47%) cases were as follicular adenoma followed by

19(18.62%) as papillary carcinoma and 4(3.92%) as follicular carcinoma. The average age of the patient reported as follicular adenoma ranged between 20 to 40 years, followed by age group of 40 -50 which correlated with study of Chan J et al.³ The average age group for papillary carcinoma to ranged from 30-50 years Maximum

cases were observed in the same age group, herewith our findings are comparable to Gillespie M et al⁴. 4 cases (3.92%) of follicular carcinoma was reported, average age for follicular carcinoma was ranged from 50-60 years, correlated with study of Carcangiu M et al⁵ and Maitra A et al⁶. Female preponderance was observed in all lesions of thyroid with F: M ratio = 8:1, this might be due to geographical variations and the different etiological factors correlates with the study of De groot et al⁷.

Cytology

Follicular Neoplasm

The distinction between follicular neoplasm and nodular goiter is the most common differential diagnostic problem in solitary nodules. The cytological appearances overlap in solitary nodules. A microfollicular focus in a colloid nodule looks identical in smears to microfollicular neoplasms. A follicular adenoma with a predominantly macrofollicular structure and with a high colloid content looks the same in smears as a dominant nodule in multinodular goiter. 70% to 90% of follicular neoplasms are detected by cytology and the proportion of carcinoma in lesions designated as follicular neoplasms ranges from 14% to 44% in large series by Kini SR et al⁸ (1996). The present study depicts 29 cases of follicular neoplasms out of a total 102 cases (9.89%). Suen KC et al⁹ Nunez C et al¹⁰ described that the cytological findings of follicular adenoma compared with follicular carcinoma are similar. In both, smears are cellular, composed of syncytial clusters of crowded cells. There is a tendency for uniform nuclear enlargement in malignant nodules, whereas anisokaryosis is more a feature of benign lesions. These differences may be subtle with much overlapping. Aron M et al¹¹ studied cytomorphologic features of 59 cases of papillary carcinoma. In the present study (19 cases of papillary carcinoma (6.48%) correlated with Aron M et al.¹¹

Histopathological diagnosis

In the present study, the frequency of histologically confirmed thyroid neoplasms were 50 out of 102 cases. 27 were follicular adenoma,

19 were papillary carcinoma and 4 follicular carcinoma. In our evaluation of 19 cases of papillary carcinoma, we found that the majority fell into the classical group thus ensuring good prognosis. Classical Papillary carcinoma is characterized by 5 well-known histopathological features: ie, papillae; empty-looking nuclei; calcospherites; nuclear grooves; and nuclear pseudo inclusions. Compared to Khan A et al¹² in his study of 35 cases, 20 were classical papillary carcinoma (5.71%). (Fig 4, 5&6). 4 out of 19 cases of papillary carcinoma showed secondary deposits in the lymph nodes by the same tumor. Females show more predilection for thyroid lesions but have less nodal deposits. The current study shows carcinoma thyroid when it occurs in males shows more aggressive behaviour than females. Heffers CS et al., Thompson LD et al¹³ in their study encountered a common problem in handling of well-differentiated follicular neoplasm in which capsular interruption is incomplete. In the sense of involving only the inner half or being represented by tumor islands embedded within, a situation in which there is considerable interobserver variability¹⁴. Greaves TS et al¹⁵ in his study of retrospective analysis of 92 patients found that there is a gray area in the cytologic diagnosis of patients with thyroid lesions between follicular adenoma and follicular carcinoma. However, increased specificity may be achieved by careful attention to cytologic features and morphologic details. Histopathologically 4 cases of follicular carcinoma were reported, One case as Follicular carcinoma others as, Follicular neoplasm without capsular invasion, Follicular neoplasm with uncertain malignant potential and Non-invasive follicular carcinoma with cytoarchitectural changes. (Fig 7, 8&9).

Correlation of FNAC & Histopathology

The use of thyroid gland fine-needle aspiration cytology led to major improvements in the care of patients with thyroid gland nodules, although with the widespread adoption of FNA, new challenges arose. These challenges included the optimization and standardization of diagnostic criteria and the development of patient

management protocols based on diagnostic schema. Much of the thyroid gland FNA literature has established diagnostic criteria, documented performance metrics and highlighted the diagnostic pitfalls¹⁶. The sensitivity and specificity of thyroid gland FNA reportedly range from 57% to 99% and 90% to 99%, respectively^{17,18,19}. These performance metrics depend on a number of factors, including the diagnostic categorical schema, availability of

immediate interpretation, and operator experience²⁰. FNAC is superior for in distinguishing between benign and malignant thyroid nodules, regardless of presentation²¹. Because of its accuracy, simplicity, and low cost, FNAC is recommended as the primary diagnostic procedure to select those patients who will benefit therapeutically from thyroid surgery²².

Overall comparison of FNAC and histopathological diagnosis of different benign and malignant thyroid lesions.

FNAC Diagnosis	Histopathological Diagnosis		Total
	Malignant	Benign	
Positive	19 (TP)	0 (FP)	19
Negative	1 (FN)	53 (TN)	54
Total	20	53	73

Sensitivity = $TP/TP+FN \times 100 = 19/19+1 \times 100 = 95.0\%$.

Specificity = $TN/TN+FP \times 100 = 53/53+0 \times 100 = 100\%$.

Predictive value of Negative test = $TN/TN + FN \times 100 = 53/53+1 \times 100 = 98.14\%$.

Accuracy rate = $TP+TN/TP+TN+FP+FN \times 100 = 19+53/19+53+0+1 = 98.63\%$.

Percentage of False Positive = $FP/FP+TN \times 100 = 0/0+53 \times 100 = 1.8\%$.

Percentage of False Negative = $FN/FN+TP \times 100 = 1/1+19 \times 100 = 5\%$.

Table
Statistical Analysis of Predictive Value Results

No of Cases	Sensitivity	Specificity	Predictive value of negative test	Accuracy rate	Percentage of false positive	Percentage of false negative.
73	95.0%	100%	98.14%	98.63%	1.8%	5%

The above statistical analysis correlates with Manna A K et al and Stephen S et al.²³

CONCLUSION

Non-neoplastic lesions and neoplastic lesions were equally distributed. The best diagnostic test results for thyroid neoplasms are obtained by using Fine Needle Aspiration cytology. FNAC and Histopathology can improve sensitivity & specificity of diagnostic accuracy of thyroid lesions. This study has undertaken to assess the efficacy and diagnostic accuracy of Fine needle aspiration cytology in the diagnosis of thyroid lesions and to compare the results of cytological diagnosis with the histopathological examination.

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REFERENCES

1. Culling C . F. A, Allison R. T, Barr W. T. Cellular pathology technique 4th ed. Butter worth ; 1985 : 642.
2. Shariff Shameem. Routine and special stains. Laboratory techniques in surgical pathology : Prism books Pvt. Ltd. ; 1999. 161-183.
3. Chan JK, Rosai J (1991). Tumors of neck showing thymic or releted branchial pouch differentiation: a unifying concept. Hum Pathol 22: 349-367
4. Gillespie MB, Thyroid Papillary carcinoma, journal of Head and Neck surgery, September 6, 2006, page1-3.
5. Carcangiu M and De Iellis R.A et al IN Anderson's Pathology tenth edition volume II: page 1955-1956.
6. Maitra A et al and Abbas A K etal IN Robbins and Cotran Pathologic basis of disease 7th edition 2004, pages 1182-1184.
7. DeGroot Leslie J : thyroid and its disease 1984 ; 5th edition : p756-331.
8. Kini SR, Miller JM, Hamburger JI, Smith – Purslowe MJ, In Fine Needle Aspiration cytology, Orell S R, Sterret GF, fourth edition, page 142.
9. Suen KC. In Fine Needle Aspiration cytology, Orell S R, Sterret GF, fourth edition, page 141.
10. Nunez C, Mendelsohn G. In Fine Needle Aspiration cytology, Orell S R, Sterret GF, fourth edition, page 142-141.
11. Aron M, Mallik A and Verma K. Fine Needle Aspiration Cytology of Follicular variant of papillary carcinoma of the thyroid. Morphologic pointers to its diagnosis, the international academy of cytology, Acta cytological November 18, 2005. Pages 6632-6637.
12. Khan A.R and Abu-eshy S.A: Variants of Papillary carcinoma of the thyroid: Experience at Asir Central Hospital, Am J clin Pathol 12 November 1996, pages 1-9.
13. Heffers CS, Wenig BM, Thompson LD, (2002), Metastatic renal cell carcinoma to the thyroid gland: a clinico pathological study of 36 cases, cancer 95:1869-1878.
14. Juan Rosai 1996, Ackerman's Surgical Pathology, 8th edition (two volume), Chapter 9, p : 493-554.
15. Greaves TS et al, Olvera M et al and Florentine B.D et al Follicular lesions of thyroid. A 5 year Fine Needle Aspirtion Experience, American Cancer of Society 2000, December 25, volume 90, Number 6, pages 335-339.
16. Gharib H, Goellner JR. fine-needle aspiration biopsy of the thyroid: an appraisal. Ann Intern Med. 1993;118:282-289.
17. Belfiore A, LaRosa GL, La Porta GA, et al. cancer risk in patients with cold thyroid nodules: relevance of iodine intake, sex, age and multinodularity. Am J Med. 1992;93:363-369.
18. Clark K, Moffat F, Ketcham A. Nonoperative techniques for tissue diagnosis in the management of thyroid nodules and goiters. Semin Surg Oncol. 1991;7:76-80.
19. Giard RWM, Hermans J. In Fine Needle Aspiration cytology, Orell S R, Sterret GF, fourth edition, page 140-141.
20. Hamburger JI. Diagnosis of thyroid nodules by fine needle biopsy: use and abuse.J Clin Endocrinol Metab. 1994;79:335-339.
21. Woeber KA. Cost-effective evaluation of the patient with a thyroid nodule. Surg Clin North Am 1995;75:357-63.
22. Greenspan FS. The role of fine-needle aspiration biopsy in the management of palpable thyroid nodules. Am J Clin Pathol 1997;108(Suppl 1):s26-30.
23. Manna AK et al, Ray S et al Sen S et al Pathak S et al Chakraborty D et al Bhattacharya P et al Journal of Cytology 2006; 23(3): 113-118.