International Journal of Medical and Health Sciences

Journal Home Page: http://www.ijmhs.net

Original article

Panorama of solitary thyroid nodule

Prakash H Muddegowda*[1], Jyothi B Lingegowda[2], Hiremath S S[3], Kishanprasad H L[4], Nagesh T S[5], Joshua DJM[6].

[1,2]Assistant Professor, Department of Pathology, VMKV Medical College, Salem. Tamilnadu

[3]Professor and HOD, Department of Pathology, JJM Medical College, Davangere, Karnataka.

[4]Assistant Professor, Department of Pathology, K S Hegde Medical College, Mangalore. Karnataka

[5]Assistant Professor, Department of Dermatology, Sapthagiri institute of Medical Sciences, Bangalore, Karnataka.

[6]Assistant Professor, Department of Immunohematology and Transfusion Medicine, VMKV Medical College, Salem. Tamilnadu.

ABSTRACT:

BACKGROUND: Fine needle aspiration cytology is a diagnostic tool used in the clinical workup of solitary thyroid nodules, to triage them into operative and non-operative lesions, as they have higher incidence of malignancy.

METHODS: Prospective study to find the utility of fine needle aspiration cytology (FNAC) in solitary thyroid nodules, conducted at JJM Medical College, Davangere from June 2005 to May 2007. Fine needle aspiration specimens from 162 patients with solitary thyroid nodule were analyzed. In 70 patients histopathological study was made and cytohistopathological correlation was done.

RESULTS: Out of 162 cases, female sex was found predominant (87.65%) and mean age of the patients was 35.67 yrs. Sensitivity, specificity and efficacy of the study for malignancy were 40%, 100% and 95.71% respectively.

CONCLUSION: Although FNAC is a good diagnostic tool for solitary thyroid nodules, ultrasound guided FNAC would have been better option for increasing accuracy of the diagnosis.

Keywords: Cyto histopathological correlation, FNAC, Solitary thyroid nodule

*Corresponding Author: Dr. Prakash H Muddegowda

E-mail: medicoprakash@gmail.com

INTRODUCTION:

A localized thyroid enlargement with rest of the thyroid apparently normal is clinically defined as solitary nodule of thyroid. The major issues in the management of solitary thyroid nodule (STN) being the diagnostic workup and extent of thyroidectomy.[1,2] Thyroid nodularity being so common, it would be impossible to operate on every patient with a thyroid mass, as incidence of malignancy is quite low compared with the overall incidence of thyroid nodularity. So, the goal of diagnostic workup now is to select those patients for surgery who have high likelihood of harbouring malignancy in the nodule. [2]

Medical historians have traced needle biopsy to a report in 1847 by Kun. The technique of FNA had its pioneering start at Sloan-Kittering Memorial hospital in New York, where its creators foresaw the advantages of establishing morphologic diagnosis in a small sample. Frable WJ and Frable MAS employed thin needle aspiration biopsy for diagnosis of head and neck lesions and found it valuable in their management. Aspiration biopsy cytology of the thyroid is found to be a valuable adjunct to pre-operative screening in the diagnosis of thyroid nodules. [3,4,5,6]

There is an ongoing debate as to appropriate evaluation and management of individuals with thyroid nodules. Need to address these issues and to provide a clinically applicable and cost-effective approach to the evaluation and management of single thyroid nodule has prompted to take up this study.[4]

There is now a large body of world literature attesting to the accuracy and advantages of FNAC, although the need for caution in interpretation, meticulous attention to technique and the limitations of diagnosis are also well documented.[5,6,7]

STN is seen in 4-6% of the adult individuals. Fortunately the likelihood that a single thyroid nodule is malignant is approximately 5%. Nodules decreasing in size have negligible risk of cancer and no treatment is required. However, enlarging solid nodules have a definite risk for thyroid cancer.[8.9] Hence the role of a cost effective diagnostic modality like FNAC becomes important in such cases.

Thyroid aspiration is useful:

1. To detect patients with thyroid malignancy (sensitivity)
2. To exclude patients without malignancy (specificity)
3. To predict the presence or absence of cancer (positive and negative predictive value) and
4. To correctly classify patients as those who should have their nodules excised and those for whom excision is unnecessary (efficiency).

MATERIALS AND METHODS:

In this prospective study undertaken during a period of two years, consenting patients who were referred with a clinical diagnosis of STN were included in this study. Non co-operative patients and patients having diffuse and multi-nodular thyroid enlargement were excluded.

All the referred patients, who had undergone routine investigations, were clinically examined in detail and a careful palpation of the thyroid nodule was done to judge precisely the location for aspiration. Under aseptic precautions, FNAC was done on the nodule using a 23 gauge needle attached to a 5 ml syringe. Then several smears were prepared and promptly fixed in a fixative containing equal amounts of ether and 95% ethyl alcohol. These were stained by Papanicolaou's stain and Hematoxylin and Eosin (H&E) stain. Air dried smears were also prepared and stained with Giemsa stain.

Whenever fluid was obtained, an attempt was made to empty all the contents by gentle pressure in the thyroid gland. Macroscopic examination of the fluid was done and the centrifuged smears were made from the sediment and stained by the above stains. Re-aspiration of residual mass if felt, was done.

Hamburger et al suggested that, in the assessment of a dominant nodule six clusters of benign cells in at least two slides prepared from separate aspirates constitute reasonable minimum material for diagnosing benign lesions. Other authors rely on similar criteria (5–6 groups of cells with more than 10 cells per group). It is believed that abundant clean colloid without altered blood or debris also indicates a benign diagnosis in a STN, but nevertheless the presence of a certain number of intact and well-fixed follicular epithelial cells is obligatory for a smear to be satisfactory. In any instance the presence of epithelial cells is not required for diagnosis. Clearly, the issue is dependent on the type of lesion (cystic or solid) and the skill combined with experience of the performer and it is said that the latter is paramount.[10,11,12,13,14] The specimen adequacy was decided based on the above criteria.

Surgical removal of the lesion was done at the discretion of the surgeons. Whenever the excised specimen was received in the department, it was routinely processed to obtain paraffin sections which were stained by H&E. Histopathological study was done independently. Results of cytological and histopathological studies were later correlated to evaluate the efficacy of FNAC.

RESULTS:

There were 162 patients who presented with STN on whom FNAC was performed. Patients in the fourth decade of life constituted the major group (29.62%) with females out numbering the males in a ratio of 1.7:1. The duration of the lesions varied from 6 months to ten years and all the cases were in euthyroid state.

Out of 162 cases, 138 (85.18%) were diagnosed as non-neoplastic lesions, while the rest 24 (24.82%) were diagnosed as a neoplastic entity.

Table: 1. Incidence of non-neoplastic lesions in STN

Non-neoplastic lesions	No. of cases	Total no.	Percentage
A) Nodular Goitre		128	
a) Nodular colloid goitre	56		35.46%
b) Nodular colloid goitre with hemorrhage	14		8.64%
c) Nodular colloid goitre with adenomatous hyperplasia	14		8.64%
d) Nodular colloid goitre with lymphocytic thyroiditis	12		7.41%
e) Nodular colloid goitre with adenomatous hyperplasia and lymphocytic thyroiditis	2		1.23%
f) Nodular colloid goitre with cystic change	11		6.79%
g) Nodular colloid goitre with cystic change and hemorrhage	11		6.79%
h) Nodular hyperplastic goitre	4		2.47%
i) Nodular hyperplastic goitre with lymphocytic thyroiditis	4		2.47%
B) Thyroiditis		10	
a) Hashimoto thyroiditis	7		4.32%
b) Lymphocytic thyroiditis	3		1.86%
TOTAL	138		85.18%

Table: 2. Incidence of various neoplastic lesions

Cytological diagnosis	Number of cases	Percentage
a) Follicular neoplasm	16	9.87%
b) Follicular neoplasm with cystic change	2	1.23%
c) Hurthle cell adenoma	1	0.62%
d) Hyalinizing trabecular adenoma	1	0.62%
e) Papillary carcinoma	3	1.86%
f) Medullary carcinoma	1	0.62%
Total	24	14.82%

Table: 3. Showing the statistical values for malignant lesions calculated by Galen and Gambino's method [15, 16]

S. No.	Statistical Index	For neoplasm	For malignancy
1.	True Positive	10	2
2.	True Negative	29	65
3.	False Positive	3	0
4.	False Negative	28	3
5	Sensitivity	26.31%	40%
6	Specificity	90.62%	100%
7	Positive Predictive value	76.92%	100%
8	Negative Predictive value	50.87%	95.58%
9	False Positive error rate	4.28%	0%
10	False Negative error rate	40%	4.28%
11	Efficacy	55.71%	95.71%

Among the 138 non-neoplastic lesions, the commonest lesion was nodular colloid goitre (Fig.1), seen in 56 cases. Hashimoto's thyroiditis (Fig.2) was the commonest type of thyroiditis seen. Incidence of the non-neoplastic lesions in this study is as shown in Table 1. The various neoplasms diagnosed are depicted in Table 2. Follicular neoplasm (Fig.3) was the commonest neoplasm encountered followed by papillary carcinoma (Fig.4).

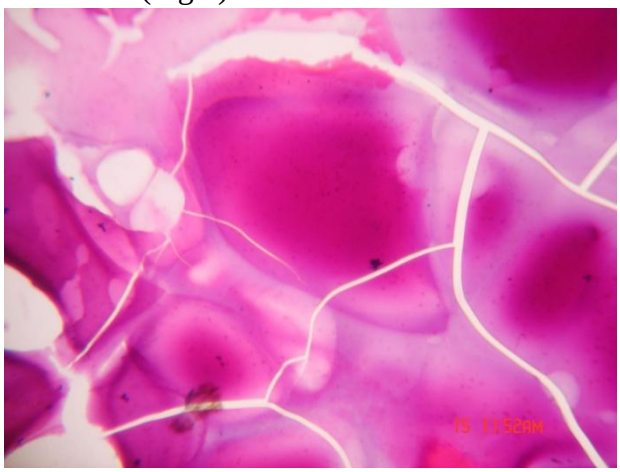

Fig: 1. Crackling colloid on FNAC H&E 10x

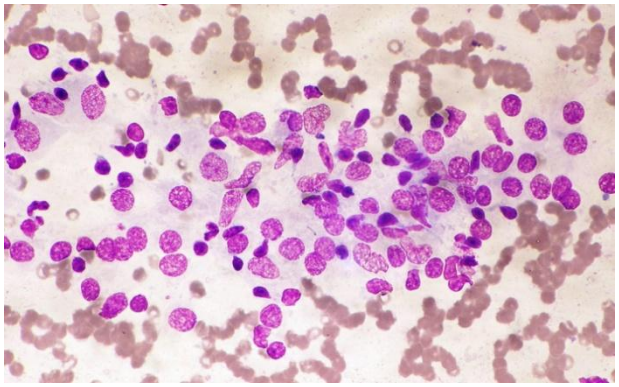

Fig: 2. FNAC showing clinging of lymphocytes to follicular cells in Hashimoto thyroiditis. H&E. 10x

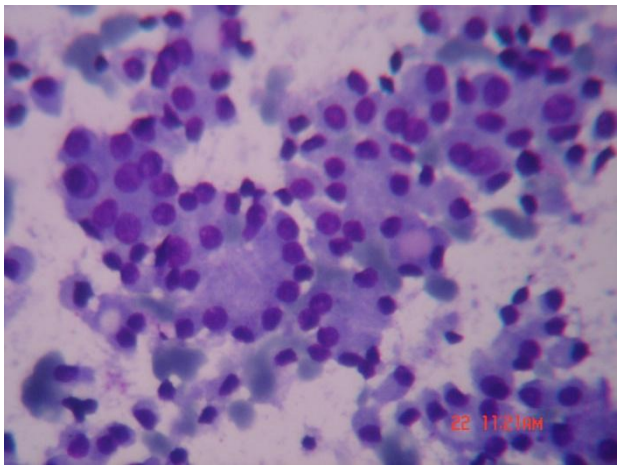

Fig: 3. FNAC of Follicular neoplasm showing microfollicles. Giemsa. 10x

In the present study histopathology study was possible in 70 cases. Specimens received were lobectomy done in 35 cases (50%) followed by hemithyroidectomy in 25 cases (35.71%), subtotal thyroidectomy in nine cases (12.86%) and total thyroidectomy was done in one case (2.43%).

Cytohistopathological correlation in the present study showed 36 cases (51.42%) having similar histopathological diagnoses as cytological diagnoses. Among non-neoplastic lesions diagnosed by cytology, histopathological study was possible in 57 cases. The cytological diagnosis remained same in 27 (47.36%) patients. Among neoplastic lesions diagnosed by cytology, histopathological correlation was possible in 13 cases. The histopathological diagnosis remained the same in nine cases (69.23%).

Fig: 4. Histopathology of Papillary carcinoma - Thyroid showing orphan anne eyed nuclei, nuclear grooves and nuclear overlapping. H&E. 40x

For neoplastic lesions statistical analysis showed 3 false positive reports and 28 false negative reports, while for malignant lesions there were no false positive reports but 3 false negative reports. (Table 3)

DISCUSSION:

FNAC plays an important role in the diagnosis of STN. Nature of disease, experienced and understanding of certain limitations determine its diagnostic utility.

FNAC of STN has many advantages:

1. FNAC is safe, simple, and cost effective procedure that can be performed on out patients with wide patient acceptance.
2. It provides a more rapid and accurate diagnosis of the thyroid nodule than any other combination of clinical or laboratory tests. [2,3]

Although the greatest application of thyroid FNAC is the non-surgical alternative provided in the investigation of solitary nodular goitre, it is also useful in detecting neoplastic lesion especially, in the diagnosis of malignancies. All types of false negative and false positive results cause concern because the reliability of cytology is in question. Apparently false negative cases are encountered when there are no recognizable diagnostic cells in the smear because of sampling or processing error. True false negative cases are those where the diagnostic cells presents in the smears are not correctly interpreted by cytopathologist. The incidence of false negative in diagnosis of thyroid aspirates may be high and it is usually attributable to overlooking of malignancy in favour of (1) Follicular adenoma, (2) Cystic lesions, and (3) Hashimoto thyroiditis. A false positive result is usually the result of misinterpretation of the nature of benign cell than of a sampling failure. False positive diagnosis are usually encountered in (1) Hashimoto thyroiditis, (2) Follicular, parathyroid and atypical adenoma and (3) Colloid nodule. [1,7,14]

The cytodiagnosis of thyroid nodules (TN) by FNA is complex for the following reasons:

a. Overlap of cytological patterns between neoplastic and non-neoplastic lesions.
b. Overlap of cytological features between various neoplasms.
c. Coexistence of non-neoplastic and neoplastic processes and multiple malignancies in the same gland.
d. Poor cellularity of the aspirated sample and suboptimal cytopreparation
e. Degenerative changes masking or mimicking malignancy
f. Inexperience [12,13]

In this study STN aspirates were examined for their diagnostic utility.

Mean age of the patients under study was 35.67 yrs which correlated with the study of other authors and the majority of them were females. These observations were similar to observations of other authors.[1,17,18,19,20] Overall incidence of malignancy in STN of thyroid in various studies showed variation, and in our study it was 14.81% as shown in Table 4.[2,21,22,] The efficiency of FNA is responsible for a marked increase in the rate by which malignancies is found at surgery. The incidence of false positive error rate for malignancy was zero in the present study.

The different statistical values indicating the diagnostic efficacies observed in the present study can be well compared with the studies of other authors. Efficacy of various studies has varied from 64.6-97.3%.[2,18,23,24,25,26,28] In the present study, the efficacy was 95.71%.(Table 5)

TABLE: 4. Comparative study of incidence of malignancies in various studies

Incidence of malignancy in STN	Percentage
Sarda AK et al [21]	10.8%
Kaur k et al [2]	18%
Mundsad B et al [22]	4.16%
PRESENT STUDY	14.81%

TABLE: 5. Comparison of sensitivity and specificity of FNAC of STN

Series	Cases			Sensitivity	Specificity
	Total	Operated	Malignant		
Aggarwal SK [23]	36	36	16	68.1%	100%
Bapat RD [24]	105	105	6	75%	100%
Gupta C [17]	507	145	30	89.47%	99.2%
Duek SD [25]	206	206	61	78.1%	76.5%
Kaur K [2]	50	50	5	83.3%	100%
Hurtado-Lopez LM [27]	130	130	50	81.3%	97.8%
Nggada HA [28]	69	69	18	88.9%	96.1%
Chao CT [26]	619	619	35	86.1%	59.7%
PRESENT STUDY	162	70	2	40%	100%

Akerman et al quoted four reasons for low sensitivity. These include:

1. Tumors missed at aspiration
2. Microscopic misinterpretation
3. Diagnosis of cellular atypia

4. Indeterminate diagnosis. [29]

Similar problems were also encountered during our present study. While no indeterminate diagnosis was offered in the present study, three cases of papillary carcinoma were missed. This was because all the three cases were very small and focal in nature in the histopathology sections and were likely to have been missed at aspiration.

Interpretation of adenomatous hyperplasia and follicular neoplasm continued to be a diagnostic dilemma with many cases of follicular adenoma being diagnosed as nodular goitre with adenomatous hyperplasia and vice versa. This diagnostic dilemma is well discussed in many expert comments on this subject. [2,10,11]

CONCLUSION:

In the present study, the specificity of FNAC of thyroid tumors was found to be high enough to permit surgical intervention after a cyto-diagnosis of malignancy. FNAC can also be used for monitoring therapy. Ultrasound guided biopsy is advised in case of small lesions to avoid giving false negatives. Also application of various techniques like advanced imaging techniques, immunocytochemistry, immunologic analysis, analysis of hormone receptors and electron microscopic study can result in further reduction in misdiagnosis and can considerably broaden the diagnostic spectrum and increase the diagnostic accuracy.

REFERENCES:

1. Dorairajan N, Jayashree N. Solitary nodule of the thyroid and the role of fine needle aspiration cytology in diagnosis. J Indian Med Assoc 1996; 94(2):50-2.
2. Kaur K, Sonkhya N, Bapna AS, Mital P. A. comparative study of fine needle aspiration cytology, ultrasonography and radionuclide scan in the management of solitary thyroid nodule: A prospective analysis of fifty cases. Ind J Otolaryngol head neck surg 2002 June; 54(2):96-101.
3. Jayaram G. Fine needle aspiration cytologic study of the solitary thyroid nodule: Profile of 308 cases with histologic correlation. Acta Cytol 1985; 29:967-73.
4. Singer PA. Evaluation and management of the solitary thyroid nodule. Otolaryngol clin of North Am 1996; 29:577-91.
5. Frable WJ. Fine needle aspiration biopsy. Human Pathology 1983 Jan; 14(1):9-28.
6. Bottles K, Miller TR, Cohen MB, Ljung BM. Fine needle aspiration biopsy: has its time come? Am J Med 1986; 81:525-31.
7. Singh A, Kahlon SK, Chahal KS, Kaur B, Kaur J. Hashimoto's thyroiditis – an unusual presentation as cystic solitary nodule – a diagnostic dilemma. Journal of Cytology 2003; 20(4):193-5.
8. Kuma K, Matsuzuka F, Kobayashi A, Hirai K, Morita S, Miyauchi A et al. Outcome of long standing solitary thyroid nodules. World J Surg1992; 16:583-8.
9. Nguyen GK, Lee MW, Ginsgerg J, Wragg T, Bilodeau D et al. Fine needle aspiration of the thyroid: an overview. Cytojournal 2005; 2:12-16.
10. Sanchez MA, Stahl RE. The thyroid, parathyroid, and neck masses other than lymph nodes. In: Koss LG, Melamed MR, editors. Koss' diagnostic cytology and its histopathologic basis. 5th ed. Philadelphia: Lippincott Williams and Wilkins; 2005. P.1148-85.
11. Cibas ES. Thyroid gland. In: Cibas ES, Ducatman BS, eds. Cytology-diagnostic principles and clinical correlates. Edinburgh: Saunders; 1996. P.217-42.
12. Nguyen GK, Lee MW, Ginsgerg J, Wragg T, Bilodeau D et al. Fine needle aspiration of the thyroid: an overview. Cytojournal 2005; 2:12-16.
13. Hay ID. Thyroiditis: a clinical update. Mayo Clin Proc 1985; 60:836-43.
14. Giacomini G. Accuracy of diagnostic cytology. Acta Cytol 1981; 25:4-5.
15. Afroze N, Kayani N, Hasan SH. Role of fine needle aspiration cytology in the diagnosis of palpable thyroid lesions. Indian J Pathol Microbiol 2002 July;45(3):241-6
16. Das DK, Khanna CM, Tripathi RP, Pant CS, Mandal AK, Chandra S et al. Solitary nodular goitre-Review of cytomorphologic features in 441 cases. Acta Cytol 1999; 43:563-74.

17. Gupta C, Sharma VK, Agarwal AK, Bisht D. Fine needle aspiration cytology of Solitary Nodule of Thyroid and its histopathological correlation. Journal of Cytology 2001; 18(3):151-6.
18. Waseer MH, Malik MA, Hussain R. Solitary thyroid nodule: Role of FNAC. Professional Med J 2001 Jun; 8(2):251-6.
19. Talepoor M, Karbankhsh M, Mirzaii FA, Zargar M. Management of solitary thyroid nodules: the dilemma of multinodular goitre as false-positive cases. In: www. Priory.com1/1/2005http://Priory.com/med/ thyroid nodule.html (2/6/2005).
20. Quari F. Unnecessary tests and delay in the diagnosis of solitary thyroid nodules at the university hospital. www.bhj.org April2005. http://www.bhj.org/journal/april2005/htm/ original unnecessary 138.htm (2/6/2006).
21. Sarda AK, Gupta A, Jain PK, Prasad S. Management options for solitary thyroid nodules in an endemic goitrous area. Postgrad Med J 1997; 73:560-4.
22. Mundasad B, Mcallister I, Carson J, Pyper PC. Accuracy of fine needle aspiration cytology in diagnosis of thyroid swellings. In: The internet journal of endocrinology 2006. 30th July 2006 http://www.ispub.com/ostia/index.php?xml FilePath=journals/ijen/vol2n2/fna.xml (2nd Aug 2007).
23. Aggarwal SK, Jayaram G, Kakar A, Guel GD, Prakash R, Pant CS. Fine needle aspiration cytologic diagnosis of the solitary cold thyroid nodule - comparison with ultrasonography, radionuclide perfusion and xeroradiography. Acta Cytol 1989; 33(1):41-7.
24. Bapat RD, Shah SH, Relekar RG, Pandit A, Bhandarkar SD. Analyis of 105 uninodular goitres. J Postgrad Med 1992; 38:60-1.
25. Duek SD, Goldenberg D, Linn S, Krausz MM, Hershko DD. The role of fine-needle aspiration and intraoperative frozen section in the surgical management of solitary thyroid nodules. Surg Today 2002; 32(10):857-61.
26. Chao CT, Lin JD, Chao HH, Hsueh C, Chen MF. Surgical treatment of solitary thyroid nodules via fine needle aspiration biopsy and frozen section analysis. Ann Surg Oncol 2007; 14:712-8.
27. Hurtado-Lopez LM, Arellano-Montano S, Torres-Acosta EM, Zaldivar-Ramirez FR, Duarte-Torres RM, Alonso-de-Ruiz P et al. Combined use of fine-needle aspiration biopsy, MIBI scans and frozen section biopsy offers the best diagnostic accuracy in the assessment of the hypofunctioning solitary thyroid nodule. Eur J Nucl Med Mol Imag 2004 Sept; 31(9):1273-9.
28. Nggada HA, Musa AB, Gali BM, Khalil MIA. Fine needle aspiration cytology of thyroid nodules: A Nigerian tertiary hospital experience. The internet journal of Cardiovascular Research 2006. http://www.ispub.com/ostia/index.php?xml FilePath=journals/ijpa/vol5n1/thyroid.xml (2/4/2007).
29. Akerman M, Tennvall J, Biorklund A, Martennson H, Moller T. Sensitivity and specificity of fine needle aspiration cytology in the diagnosis of tumors of the thyroid gland. Acta Cytol 1985; 29:850-5.