IJPRP

Indian Journal of Pathology: Research and Practice

Volume 7 Number 5, May 2018
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.7518.7

Original Research Article

A Prospective Study of Thyroid Diseases- Cytological Evaluation and It's Histopathological Correlation with Review of Literature

Dharani V.C.[1], Manjunatha H.K.[2], Geethamani V.[3], Bhargavi Mohan[4], Sushma T.A.[5], Thejaswini M.U.[6]

[1,4]Assistant Professor, [2]Professor [3]Professor & Head [5,6]Associate Professor, Dept. of Pathology; BGS GLobal Institute of Medical Sciences, Uttarahalli main Road, Kengeri , Bengaluru, Karnataka 560060, India.

Corresponding Author:

Manjunatha H.K.,
Professor, Dept. of Pathology;
BGS Global Institute of Medical Sciences, Uttarahalli Main Road, Kengeri, Bangalore–560060, Karnataka, India.
E-mail:
hk_manjunath70@yahoo.in

(Received on 24.03.2018,
Accepted on 10.04.2018)

Abstract

Introduction: Thyroid lesions are common in surgical practice and are observed in 4-7% of the population. Fine needle aspiration cytology [FNAC] is a highly accurate, economical, safe, minimally invasive and rapid , pre-operative diagnostic modality in detecting thyroid lesions. The use of FNAC as the first line of investigation in thyroid lesions has reduced the number of unnecessary thyroidectomy procedures.

Objectives: The present study was undertaken to correlate the fine needle aspiration cytology [FNAC] findings with histopathology wherever possible.

Methods: In the present study, 95 cases of thyroid FNACwhich were subsequently followed by excision biopsy has been statistically analyzed and cyto-histopathological correlation has been interpreted.

Results: Out of 95 cases studied, with cyto-histopathological correlation, the majority of lesions were non- neoplastic. The accuracy was found to be 93%, sensitivity 71.45%, and specificity 100%.

Conclusion: FNAC can be used as a baseline investigation in patients with thyroid lesions and has high accuracy in detecting and differentiating malignant lesions from the benign.

Keywords: FNAC; Accuracy; Sensitivity; Specificity; Cyto-histopathological Correlation.

Introduction

The thyroid gland is a superficially located , easily accessible and thus is an ideal organ for fine needle aspiration cytology[FNAC] [1]. FNAC evaluation of thyroid cancer was originally used by Martin and Eliis in 1930 [2]. The routine use of FNAC in the assessment of thyroid nodules has reduced the number of patients subjected to thyroidectomy for benign diseases of the thyroid [3]. The incidence of thyroid malignancy has increased from 5-10% to 30-50% recently [4]. The present study was done to correlate the FNAC diagnosis with the histopathology and to find the diagnostic accuracy of FNAC in detecting various benign and malignant lesions of the thyroid.

Materials and Method

The present study was a prospective study of 300 cases referred to the cytopathology section for FNAC during the period from January 2015-June 2017. FNAC was performed in 300 patients with thyroid enlargement referred to the department of cytopathology, BGS Global Institute of medical sciences. The procedure was performed under aseptic precautions using 24 gauge needle. The aspirated material was spread onto the slides and fixed with 95% ethyl alcohol, which was stained with May-Grunwald Giemsa,Hematoxylin and Eosin and Papanicolaou stains. Out of these 300 cases, excision biopsies were available for 95 cases.

© Red Flower Publication Pvt. Ltd.

The excision biopsy material were received in 10% formalin. They were made to undergo routine histological processing, and slides were stained using Hematoxylin and Eosin.

Inclusion Criteria

All palpable and non-palpable thyroid lesions, referred for FNAC and which were subsequently followed by surgical excision and subjected for histopathological examination were included in the study.

Exclusion Criteria

1. Thyroid FNAC cases which were not followed by surgical excision and histoapthological examination.
2. Thyroidectomies which were not preceded by FNAC

Results

During the period of this study from January 2015- June 2017,300 FNACs were performed out of which 95 cases underwent surgery and were subsequently subjected to histopathological study. Only those cases with histopathological diagnosis were selected for this study.

The present study deals with the FNAC of the thyroid lesions and determination of the diagnostic accuracy of the aspiration cytology with histopathology correlation. Out of 95 patients, 90 presented with a solitary swelling in front of the neck and five patients presented with diffuse thyroid swellings. Biochemical investigations were available in 90 cases and revealed hyperthyroidism in thirty cases, hypothyroidism in 20 cases and rest in euthyroid state. There were no complications following fine-needle aspiration.

The majority of the aspirates were blood mixed to frankly hemorrhagic and in 40 patients aspiration yielded either brown or dark brown colloid-like fluid, amount ranging from 0.5 ml to 5ml.

The satisfactory cell sample was obtained in 91 patients, while in the remaining four cases aspiration was unsatisfactory, with satisfactory to unsatisfactory ratio of 22.7:1%. For the four unsatisfactory aspirations, ultrasound [USG] guided FNAC was done, which yielded adequate sample.

Females were more commonly affected in our study with male to female ratio of 1:18 (Figure 1). The majority of the age of the patients ranged from 11-70 years with a mean age of 40.1yrs. (Table 1).

In the present study, the non-neoplastic lesions were most common than neoplastic lesions (Table 2).

Table 1: Age distribution of all thyroid lesions

	11-20	21-30	31-40	41-50	51-60	61-70	Total
Non neoplastic	03	10	33	23	12	04	85
Neoplastic		1	2	2	4	1	10

Table 2: Distribution of Neoplastic and Non neoplastic Lesions Based On Cytological Study

Lesions	n[%]
Non neoplastic	80[84.2%]
Neoplastic	15[15.8%]
Total	95[100%]

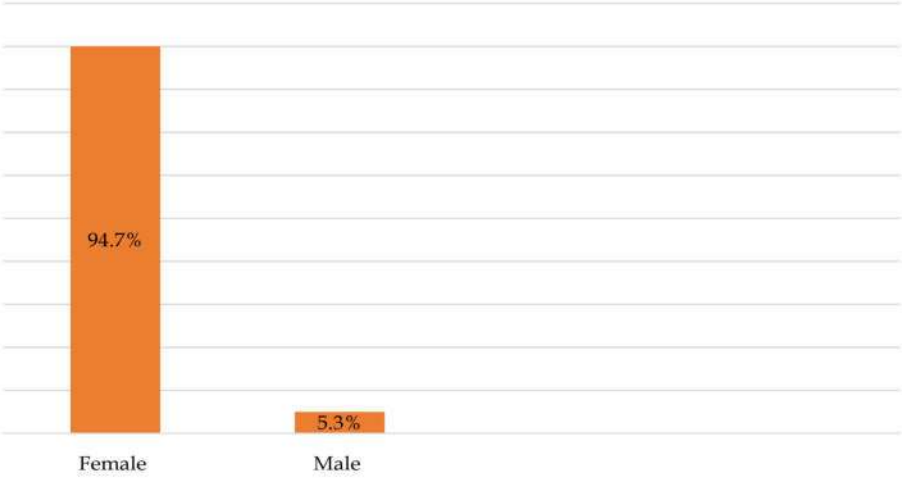

Fig. 1: Sex distribution of all thyroid lesions

Cytohistological Correlation of Non-Neoplastic Lesions

This study showed , among 80 non-neoplastic lesions, nodular goiter was the most common lesion encountered in 50 cases. The histopathological study confirmed the diagnosis in 45 cases, and three were diagnosed as follicular adenoma and two as papillary carcinoma. Out of 20 FNAC cases of lymphocytic thyroiditis, 19 cases were confirmed on histopathology, while one case turned out to be papillary carcinoma on histopathology. Thus out of 80 cases, 74 cases were true negative and six were false negative. In the present study, 100% correlation was observed with benign thyroid cyst, lymphocytic thyroiditis and colloid goiter with lymphocytic thyroiditis.

Cytohistological Correlation of Neoplastic Lesions

In our study cytohistological correlation of neoplastic lesions revealed that out of 15 cases which were reported as neoplastic, seven cases were follicular adenoma on cytology while on histopathology, 10 cases were diagnosed as follicular adenoma. One case of hurtle cell neoplasm on cytology turned out to be Hurthle cell adenoma on histopathology.

Table 3: Thyroid gland lesions on FNA

Histopathology diagnosis	Number of patients (%)
Non-neoplastic	**74**
Multinodular goiter	45 (47.39)
Lymphocytic thyroiditis	19 (20)
Colloid goiter with lymphocytic thyroiditis	06 (6.31)
Benign thyroid cyst	04 (4.25)
Neoplastic	**21**
Papillary carcinoma	10 (10.5)
Follicular adenoma	10 (10.5)
Hurtle cell adenoma	01 (1.05)
Total	95 (100)

Table 4: Thyroid gland lesions on histopathology

Histopathology diagnosis	Number of patients (%)
Non-neoplastic	**74**
Multinodular goiter	45 (47.39)
Lymphocytic thyroiditis	19 (20)
Colloid goiter with lymphocytic thyroiditis	06 (6.31)
Benign thyroid cyst	04 (4.25)
Neoplastic	**21**
Papillary carcinoma	10 (10.5)
Follicular adenoma	10 (10.5)
Hurtle cell adenoma	01 (1.05)
Total	95 (100)

Table 5: Statistical analysis

Sensitivity	71.4%
Specificity	100%
Accuracy	93.6%
Positive predictive value	100%
Negative predictive value	92.5%

Table 6: Non-neoplastic lesions diagnosed by FNAC and their correlation with histopathological diagnosis

FNAC REPORT	Number of patients	HP report	Number of patients	Remarks
Nodular colloid goiter	50	Multinodular goiter	45	True negative
		Papillary carcinoma	02	False negative
		Follicular adenoma	03	False negative
Lymphocytic Thyroiditis	20	Lymphocytic Thyroiditis	19	True negative
		Papillary carcinoma	01	False negative
Colloid goiter with lymphocytic thyroiditis	06	Colloid goiter with lymphocytic thyroiditis	06	True negative
Benign thyroid cyst	04	Benign thyroid cysts	04	True negative
Total	80		80	

Table 7: Neoplastic lesions diagnosed by FNAC and their comparison with histopathological diagnosis

FNAC REPORT	Number of patients	HP report	Number of patients	Remarks
Follicular neoplasm	7	Follicular adenoma	10	True positive [7] False negative [3]
Hurtlecell neoplasm	1	Hurthlecell adenoma	1	True positive
Papillary carcinoma	6	Papillary carcinoma	09	True positive[6] False negative[3]
Suspected malignancy	1	Papillary carcinoma	1	True positive
Total	15		21	

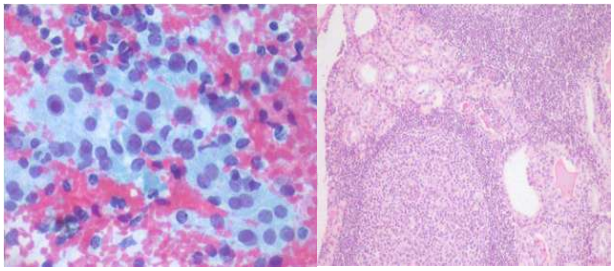

Image 1: FNAC And Histoapathology of Mutlinodular Goitre (H&E Stain, X40)

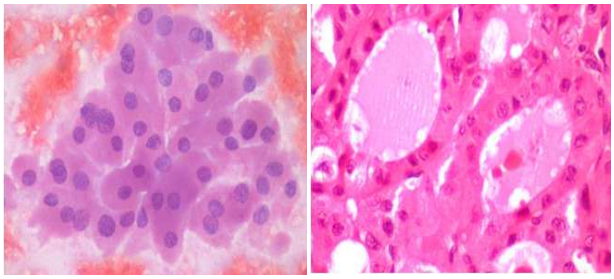

Image 2: FNAC And Histopathology of lymphocytic thyroiditis (H&E Stain, X40)

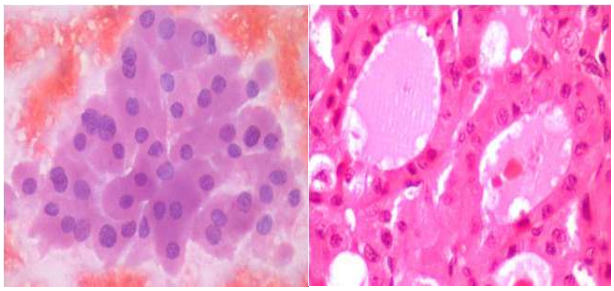

Image 3: FNAC And Histopathology of Hurthle Cell Adenoma (H&E Stain, X40)

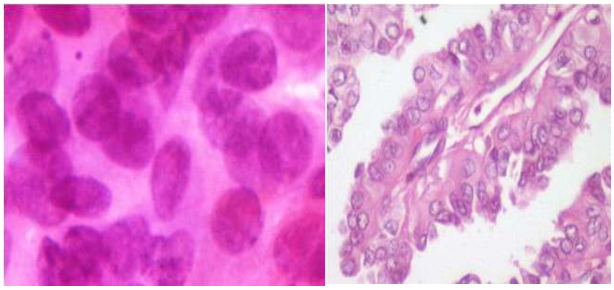

Image 4: FNAC And Histopathology of Papillary Carcinoma (H&E Stain, X40)

Among malignant tumors, six cases were diagnosed as papillary carcinoma on cytology and one as suspicious for papillary carcinoma, while ten cases were diagnosed as papillary carcinoma on histopathology.

Discussion

FNAC is considered as safe, simple, minimally invasive and quick technique with low complication rate and is regarded as the gold standard initial investigation in the diagnosis of thyroid lesions along with other tests like high-resolution ultrasonography, radioisotope scanning, and thyroid profile.

Advantages and limitations of FNAC biopsy should be recognized and the procedure should be knowledgeably applied to evaluate thyroid diseases. In the present study, cytological features of thyroid lesions were studied and correlated with histopathology wherever available to determine its diagnostic accuracy in detecting neoplastic lesions.

In the present study, females were more commonly affected with the male to female ratio of 1:18 and similar female preponderance was found in the studies done by Silverman et al . [6] with a ratio of 1:10.8. The age of the patient ranged from 11-70 years with a mean age of 40.1yrs. Majority of the patients [35.9%] were in their third decade of life which is comparable with the study by Manoj Gupta et al. [1].

The majority of the aspirates [91] done by routine FNAC were satisfactory for evaluation with unsatisfactory to the satisfactory ratio of 22.7:1. Among the remaining four inconclusive aspirates, USG guided FNAC was done which yielded sufficient material for the cytological evaluation. FNAC aspirate adequate for interpretation requires five to six groups of well-preserved cells with each group consisting of 10 or more cells. Many studies have applied the same criteria for the satisfactory aspirates.

FNAC was done in 300 cases, and histopathology was available for 95 cases. Out of these 95 cases, 80 cases were non neoplastic, and 15 cases were neoplastic with non-neoplastic to the neoplastic ratio of 8.5:1. Altavilla et al. [7] and Mandrekar et al. [8] observed the benign to malignant

ratio of 59.1:1 and 51.9:1 respectively. In the present study ratio was lower than observed in other studies due to inclusion of thyroid lesions on which FNAC was performed and followed by surgical resection.

Microscopic FNAC Key Findings in Various Non-Neoplastic Lesions [5,9]

Normal thyroid gland aspirate shows few follicular cells isolated or in clusters with a background of bare benign nuclei and scant colloid and blood.

Acute inflammatory infiltration in the thyroid gland ischaracterized by the presence of neutrophilic infiltrate and seen in diseases like acute thyroiditis, infected thyroglossal cyst, and reaction caused by trauma, radiation or necrosis. Giant cells are observed in conditions like De-Quervain thyroiditis, granulomatous thyroiditis, Hashimoto thyroiditis, Graves's disease, palpation thyroiditis and malignant tumors like papillary carcinoma, medullary carcinoma, and undifferentiated carcinoma.

Lymphoid infiltrates can be seen in Hashimoto thyroiditis, Infection, Graves's disease and malignant tumors like papillary carcinoma and malignant lymphoma.

Nodular hyperplasia can present as hypocellular nodules, hypercellular or cystic nodules. Hypocellular nodules are composed of follicular cells in sheets or macro follicles and dark nuclei with even chromatin pattern with a background of abundant colloid while hypercellular nodules consist of follicular cells in monolayered sheets, rosettes, microfollicles or 3-dimensional clusters with a background of scant colloid, stromal fragments, and macrophages. This causes confusion with follicular neoplasm. Cystic nodules show many foamy macrophages, siderophages, cholesterol crystals with few follicular degenerated cells and background made of the variable amount of colloid.

Microscopic FNACKey Findings in Various Neoplastic Lesions [5,9]

Follicular neoplasm is most commonly highly cellular smears with follicular cells arranged in three- dimensional clusters, microfollicles, rosettes and trabeculae with scant colloid in the background.

Hurthle cell neoplasm shows cellular aspirates consisting of follicular cells which are large and polygonal with abundant cytoplasm with granules and nuclei with nucleomegaly and prominent nucleoli. The background shows scant colloid and absence of lymphocytic infiltrate.

Papillary carcinoma thyroid aspirate consists of cellular smears with follicular cells in papillary fragments, follicular structures,and monolayered sheets or in singles. Cells have distinct nuclear features like powdery chromatin, grooves, intranuclear cytoplasmic inclusions, irregular contour, crowding, moulding and overlapping. Background shows chewing gum colloid, psammoma bodies, macrophages and multinucleate giant cells.

However, the presence of multiple above mentioned features is the criteria todiagnose lesion as papillary carcinoma, asthe presence of the single nuclear feature is not significant. Nuclear folds are also seen in follicular neoplasm, medullary carcinoma, nodular goiter, Hashimoto thyroiditis, and metastatic tumors like malignant melanoma and carcinoma. Likewise intranuclear cytoplasmic inclusions are also seen in, Hashimoto thyroiditis, anaplastic thyroid carcinoma, medullary carcinoma, Hurthle cell neoplasm and metastatic tumors like renal cell carcinoma. psammoma bodies can also be seenin medullary thyroid carcinoma, toxic diffuse goiter, Hashimoto thyroiditis and Hurthle cell neoplasm.

Role of Ultrasonography in Thyroid Diagnosis [5]

The presence of ultrasonography findings like microcalcification, hypoechoic solid nodule, irregular/lobulated margins, intranodular vascularity and signs of extracapsular spread rises the suspicious of malignancy which has to be confirmed by FNAC followed by histopathology.

Diagnostic histological features in various non-neoplastic thyroid lesions [9,10]

Adenomatoid nodule

Presentsas asymmetric, multinodular thyroid gland enlargement due to follicular epithelial hyperplasia as a result of impaired thyroid hormone production or increased thyroid stimulating hormone [TSH] secretion. The differential diagnosis that has to be considered is follicular adenoma which is characterized by a thick fibrous connective capsule with smooth muscle walled vessels, usually having a single histological pattern, compressing adjacent parenchyma, and limited colloid. Tends to lack degeneration and lacks colloid lakes. Both lesions may be present. But philosophically, multiple follicular nodules without invasion are within adenomatoid nodule category.

Lymphocytic thyroiditis

It is characterized by goiter and elevated circulating thyroid antibodies often associated with hypothyroidism due to thyroid destruction by autoimmune process or presence of thyroid stimulating hormone blocking antibodies.

The differential diagnosis for this includes

a. *Nonspecific chronic lymphocytic thyroiditis*: non-mass forming scattered but limited foci of lymphocytic infiltrates, typically the absence of oncocytic cytoplasmic changes of follicular cells, the absence of laboratory evidence of abnormal thyroid function.

b. *Non–Hodgkin lymphoma:* effacement of thyroid parenchyma monomorphic malignant cellular infiltrate, the presence of lymphoepithelial lesions characterized by colonization of thyroid follicles by neoplastic cells. Cellular infiltrates often spills out into peri thyroidal soft tissue.

c. *Invasive fibrous thyroiditis [Riedel's disease]:* fibrous variant of lymphocytic thyroiditis, fibrosis outside thyroid gland often adhere to surrounding structures and lacks high titers of anti-thyroglobulin antibodies.

Diagnostic Histological Featuresin Various Non - Neoplastic Thyroid Lesions **[9,10]**

Follicular adenoma

Is a benign encapsulated tumor surrounded by variable thick fibrous connective tissue capsule. Presence of smooth muscle walled vessels helps to confirm the presence of the capsule. Differential diagnoses to be considered are a follicular adenoma, follicular variant of papillary carcinoma, medullary carcinoma, and adenomatoid nodule.

Non-invasive follicular thyroid neoplasm with papillary like nuclei

It is partially to completely encapsulated thyroid follicular neoplasm arranged in almost exclusively follicular architecture, showing papillary carcinoma like nuclear features in an adenomatous sampled tumor.

This has to be differentiated by a follicular adenoma, papillary carcinoma follicular variant and follicular carcinoma.

Papillary carcinoma

Is characterized by the presence of tumor cells arranged in papillarypattern and cells have a moderate amount of cytoplasm and oval nuclei with open chromatin and clearing with presence of nuclear grooves, and intra nuclear inclusions. This has to be differentiated by non-invasive follicular thyroid neoplasm with papillary likenuclei, follicular carcinoma, and medullary carcinoma.

Post FNAC Changes in Thyroid **[5]**

Most commonly reactive and regenerative morphological alterations in the thyroid are observed post-FNAC. These include: Acute changes like hemorrhage, granulation tissue are most commonly observed within 3 weeks after FNAC, Chronic changes include infarction, metaplasia like squamous, and capsular alterations with pseudo invasive growth. Vascular alterations like dilated vascular spaces with organized thrombosis, papillary endothelial hyperplasiaand endothelial cell atypia. Post procedure spindle cell nodule /proliferation.

The above discussed post FNAC changes pose diagnostic difficulty on histopathology in the following diseases:

a. Vascular neoplasm which is characterized by widely dilated and blood filled spaces and papillary endothelial hyperplasia.

b. Papillary carcinoma differentiated by the presence of constellation and diagnostic nuclear features that are absent in post FNAC changes favors papillary carcinoma.

c. Undifferentiated thyroid carcinoma on histopathology is characterized by high cellularity and marked nuclear pleomorphism.

In the present study among non-neoplastic lesions colloid goiter, 50 cases [61.1%] was the most common and lymphocytic thyroiditis was the second most common with 20 cases [23.5%]. Similar observations were made by Ramteke DJ et al. [11], Fernandes H et al. [12] and Nagadda H.A et al. [13]

In the neoplastic category, follicular adenoma was the most common benign tumor and among malignant lesions, papillary carcinoma is the most common lesion. Similar observations were made by Fernandes H et al. [12]

The methods used for calculation of sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were similar to previous studies. Sensitivity, specificity, and accuracy in the present study were 76.1%, 100%, and 93% respectively and is comparable with the below study.

Table 8: Comparison of statistical values

Study	Sensitivity[%]	Specificity[%]	Accuracy[%]
Parik et al[14]	71.43	100	90.24
Pinky pandey et al[15]	57.14	90	80.28
Harsoulis et al[16]	89.4	95.4	94.2
Present study	71.4	100	93.6%

Cytohistological correlation of thyroid lesions.

Of 95 cases in the present study, the discrepancy was found only in 6 cases. 80 cases were diagnosed as non-neoplastic and 74 correlated with the histopathological diagnosis, while 3 cases of nodular colloid goiter were diagnosed as follicular adenoma, two cases of nodular colloid goiter as papillary carcinoma and one case of lymphocytic thyroiditis as papillary carcinoma. True negatives were 74 cases and false negative were 6 cases. The causes of detection failure of papillary carcinoma of

3 cases were like the presence of a microscopic focus of papillary carcinoma and failure of a needle to hit the focus of papillary carcinoma. The cause of detection failure of 3 cases of follicular adenoma was to pauci cellularity of follicular adenoma and overlapping features between adenomatoid nodule and follicular adenoma.

In the present study 15 cases were diagnosed as neoplastic of which 8 were benign consisting of 7 cases of follicular adenoma, 1 case of Hurthle cell neoplasm. 7 cases were malignant lesions all being papillary carcinoma.

The positive predictive value was 100% in our study which was higher when compared to other studies as we did not report even a single case as false positive. The negative predictive value was 93.75% which was lower than other studies because there were 6 false negative cases in our study. FNAC is the powerful diagnostic tool for thyroid lesions and can be carried out in outdoor patients with excellent compliance and considered to have high sensitivity and specificity.

However, it has some limitations in specimen adequacy, sampling technique, skill, and experience of pathologist and inability to distinguish follicular lesions reliably, like follicular neoplasm and papillary carcinoma.

Conclusion

FNAC is recommended as the procedure of choice in the diagnosisof thyroid lesions since it enables benign lesions to be distinguished from the malignant lesions, helps in aiding the design of treatment plan and thus decreases the overall thyroidectomy rate in patients with benign diseases. The present study was undertaken to correlate the FNAC findings with histopathology and our study showed an accuracy of 93% in detecting thyroid malignancy and results are consistent with those available in the literature. If the cytology report is malignant, surgery is the recommended procedure. For benign lesions, no further immediate diagnostic studies are required. Our study suggests that FNAC gives good positive correlation with cytopathology with high sensitivity and specificity. False negativity was observed in our study and can be reduced by correct sampling and multiple sites aspiration. Thus FNAC combined with clinical examination, ultrasonography and thyroid function tests is simple, reliable test and remains the mainstay in selecting the patients for thyroidectomies. Although immuno-histochemistry and cytometry do not help in distinguishing benign from the malignant, in thyroid nodules with indeterminate lesions, molecular biology techniques appear promising.

Acknowledgement

I would like to thank teaching staff of the department of surgery, BGS GIMS for support in completing the work

References

1. Gupta M, Gupta S, Gupta VB. Correlation of Fine Needle Aspiration Cytology with Histopathology in the Diagnosis of Solitary Thyroid Nodule. Journal of Thyroid Research. 2010:379051.
2. Martin HE, Ellis EB. Biopsy by puncture and aspiration. Annals of surgery 1930;92:169-81.
3. Handa U, Garg S, Mohan H, Nagarkar N. Role of fine needle aspiration cytology in diagnosis and management of thyroid lesions: A study on 434 patients. Journal of cytology, 2008;25:13-7.
4. Ridgway EC. Clinician evaluation of a solitary thyroid nodule. Endocrinol Med 1982;96:221-32.
5. Biboo M, Wilbur DC, eds. Thyroid In;Comprehensive Cytopathology. 4th ed.Elsevier; 2015.pp.511-544.
6. Silverman JF, West RL, Larkin EW, Park HK, Finley JL, Swanson MS, et al. The role of fine-needle aspiration biopsy in the rapid diagnosis and management of thyroid neoplasm. Cancer 1986;57:1164-70.
7. Attavilla G, Pascale M, Nenci I. Fine needle aspiration cytology of thyroid gland diseases. Acta Cytology 1990;34: 251-6.
8. Mandreker, SR., Nadkarni, NS, Pinto, RG and Menezes, S. Role of fine needle aspiration cytology as the initial modality in the investigation of thyroid lesions. Acta Cytologica. 1995;39:898-904.
9. Wick Mark R, LiVolsi, Virginia A, Pfeifer John D, Stelow, Edward B, Wakely Paul eds. Thyroid gland In; Silverberg's Principles and practice of surgical pathology and cytopathology. Vol 4, 5th ed. Cambridge university press; 2015.pp.2897-2928.
10. Thompson Lester D R, Weing Bruce M, eds. Thyroid gland In;Diagnostic Pathology , Head and Neck. 2nd edition, Elsevier; 2016.pp.882-1088.
11. Ramteke DJ, Mulay PS. Cytohistopathological correlation of thyroid lesions. International Journal of Research and Medical Sciences 2017;5:1425.
12. Fernandes H, D'souza C R S, et al. FNAC Head and Neck Masses. Journal of Clinical and Diagnostic Research. 2009;3:1719-1725.
13. Naggada HA, Musa AB, Gali BM et al. Fine needle aspiration cytology of thyroid nodules: a Nigerian tertiary hospital experience. The Internet Journal of Pathology. 2006;5:7.
14. Parikh UR., Goswami HM., Shah AM., Mehta NP., Gonsai RN. Fine Needle Aspiration Cytology (FNAC) Study of Thyroid Lesions(Study of 240 Cases). Gujarat Medical Journal. 2012;76 .2: 25-30.
15. Pandey P, Dixit A, Mahajan NC. Fine-needle aspiration of the thyroid: A cytohistological correlation with critical evaluation of discordant cases. Thyroid Research and Practice 2012;9:32-9.
16. Harsoulis P, Leontsini M, Economou A, Gersimidis T, Sambarounis C. Fine needle aspiration biopsy cytology in the diagnosis of thyroid Cancer: comparative study of 213 operated patients. Br J Surg. 1986;73:461-4.