

DIAGNOSTIC UTILITY OF BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY

By

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In partial fulfilment of the requirements for the award of the degree of

DOCTOR OF MEDICINE

IN

PATHOLOGY

Under the Guidance of

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LIST OF ABBREVIATIONS USED

(In alphabetical order)

AFLUS	Atypia of follicular lesion of undetermined significance
FA	Follicular Adenoma
FNAC	Fine needle aspiration cytology.
FNA	Fine needle aspiration.
FC	Follicular carcinoma.
FN	Follicular neoplasm.
MNG	Multinodular Goitre.
ND	Non-Diagnostic.
PTC	Papillary thyroid carcinoma
SF	Suspicious of follicular neoplasm.
SM	Suspicious of malignancy.
TSH	Thyroid stimulating hormone.
TFT	Thyroid function test.
US	Unsatisfactory.
WHO	World health organisation

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ABSTRACT

Introduction

Fine needle aspiration cytology (FNAC) plays a vital role in the management of thyroid lesions. Historically terminologies used for reporting thyroid FNAC has varied significantly from one laboratory to another, creating confusion in some cases. A uniform reporting system for thyroid FNAC will facilitate effective communication among cytopathologists, endocrinologists, surgeons, radiologists and other health care providers. Present study is done to evaluate the efficacy of The Bethesda system for reporting thyroid cytopathology.

Material & methods-

Patients with thyroid lesions referred to the Pathology Department, of, B.L.D.E.U. Shri B.M.Patil Medical College, Hospital & Research Centre, and Bijapur from November 2010 to June 2012 for FNAC are taken. Interpretation of these cases were done as Per the Bethesda System.

Results-

Total number of cases studied on FNAC were 104. Out of 104 cases 82(78.8%) were benign lesions, 10(9.6%) were unsatisfactory/ nondiagnostic, 6(6.20%) were Follicular Neoplasm/suspicious for neoplasm, 4(4.16%) were suspicious of malignancy, 3(3.12%) were Malignant and 1 case was reported as Atypia of undetermined significance.

Surgical follow up was available for 46(44.2%) cases and in 8 cases (14.4%) cyto-histological discrepancy was noted.

Conclusion-

Bethesda system of reporting thyroid cytopathology is beneficial for clinical follow up and surgical management. It helps to reduce the rate of unnecessary thyroid surgery for benign thyroid lesion and helps to plan the surgical management in malignant thyroid lesion.

Key words-Thyroid, Fine needle aspiration cytology, The Bethesda system.

INTRODUCTION

Thyroid lesions are common among the general population and often represent a large proportion of endocrine referral. The diagnosis of thyroid lesions is of great importance because most are amenable to medical or surgical management. Clinical assessment of thyroid lesions by means of physical examination, thyroid scans and ultrasonography is not completely reliable.¹

Fine needle aspiration cytology (FNAC) is the cost-effective, safe and play an essential role in the in the pre-operative evaluation of thyroid lesions. An adequate thyroid aspirate is necessary for the interpretation of FNAC. The estimation of sensitivity and specificity of FNAC depends on how follicular proliferation is examined.² The diagnostic dilemma of the cytopathologist will be in the lesions of thyroid which are diagnosed as atypical or suspicious of malignancy in 15-30% cases. Though histopathological diagnosis is the gold standard, the fine needle aspiration diagnosis plays a vital role in the proper management of the patient.³

Historically, terminology for thyroid FNAC has varied significantly from one laboratory to another, creating confusion in some cases. A uniform reporting system for thyroid FNAC will facilitate effective communication among cytopathologists, endocrinologists, surgeons, radiologists and other health care providers.

The interpretation should provide relevant information that will assist referring physicians, in the management of patients. It should also facilitate cyto-histologic correlation of thyroid diseases and allow easy and reliable sharing of data from different laboratories for national and international collaborative studies. The terms

for reporting results should also have an implied risk of malignancy on which recommendations for patient's management is decided.⁴

The present study was done to interpret the Thyroid FNAC as per the Bethesda system and to evaluate the efficacy of the Bethesda system for reporting thyroid cytopathology by taking histologic findings as standard.

OBJECTIVES OF THE STUDY

1. Interpretation of thyroid FNAC as per The Bethesda system and to evaluate the efficacy of The Bethesda system for reporting thyroid cytopathology.

REVIEW OF LITERATURE

Anatomy:

The thyroid gland is one of the largest butterfly-shaped endocrine glands found in the neck, below the thyroid cartilage. The isthmus, bridge between the two lobes of the thyroid is located inferior to the cricoid cartilage.⁵

The thyroid gland is composed of two cone-like lobes connected via isthmus. It is situated on the anterior side of the neck, lying against and around the larynx and trachea, reaching posteriorly the oesophagus and carotid sheath. It starts cranially at the oblique line on the thyroid cartilage and extends inferiorly to the fifth or sixth tracheal ring.¹ It is difficult to demarcate the gland's upper and lower border with vertebral levels because it moves during swallowing. The thyroid gland is covered by a thin fibrous sheath composed of an internal and external layer. The external layer is anteriorly continuous with the lamina pretrachealis, fasciae cervicalis and posterioro - laterally continuous with the carotid sheath.⁶

The gland is covered anteriorly with infrahyoid muscles and laterally with the sternocleidomastoid muscle. On the posterior side, the gland is fixed to the cricoid and tracheal cartilage and cricopharyngeus muscle by a thickening of the fascia to form the posterior suspensory ligament of Berry. The thyroid gland's firm attachment to the underlying trachea is the reason behind its movement with swallowing. In variable extent a pyramidal extension of the thyroid lobe is present at the most anterior side of the lobe. In this region, the recurrent laryngeal nerve and the inferior thyroid artery pass next to or in the ligament and tubercle.⁷

Embryological development

In the fetus at 3–4 weeks of gestation, the thyroid gland appears as an epithelial proliferation in the floor of the pharynx at the base of the tongue between the tuberculum impar and the copula linguae at a point later indicated by the foramen cecum. The thyroid then descends in front of the pharyngeal gut as a bilobed diverticulum through the thyroglossal duct. Over the next few weeks, it migrates to the base of the neck, passing anterior to the hyoid bone. During migration, the thyroid remains connected to the tongue by a narrow canal, the thyroglossal duct. Thyrotropin-releasing hormone (TRH) and **thyroid-stimulating hormone**(TSH) secreted from the fetal hypothalamus and pituitary at 18-20weeks of gestation, and fetal production of thyroxine (T₄) reach a clinically significant level at 18–20 weeks.⁸ Fetal triiodothyronine (T₃) remains low (less than 15 ng/dl) until 30 weeks of gestation, and increases to 50 ng/dl at term.^[5] Fetal self-sufficiency of thyroid hormones protects the fetus against brain development abnormalities caused by maternal hypothyroidism. However, preterm births can suffer neuromuscular disorders due to lack of maternal thyroid hormones due their own thyroid being insufficiently developed to meet their postnatal needs. The portion of the thyroid containing the parafollicular C cells, those responsible for the production of calcitonin, are derived from the neural crest. This is first seen as the ultimobranchial body, which joins the primordial thyroid gland during its descent to its final location in the anterior neck. Aberrations in embryological development can cause various forms of thyroid dysgenesis.^{7,8}

Physiology and Histology.

The thyroid is composed of spherical follicles that selectively absorb iodine from the blood for production of thyroid hormone & also store iodine in thyroglobulin. Twenty-five percent of all the body's iodide ions are in the thyroid gland. Inside the follicles, colloid serves as a reservoir of materials for thyroid hormone production and also acts as a reservoir for the hormones themselves. Colloid is rich in a protein called thyroglobulin. The follicles are surrounded by a single layer of thyroid epithelial cells, which secrete T_3 and T_4 . When the gland is not secreting T_3/T_4 (inactive), the epithelial cells range from low columnar to cuboidal cells. When active, the epithelial cells become tall columnar. Parafollicular cells are scattered among these follicular cells and in spaces between the spherical follicles which secrete calcitonin. The primary function of the thyroid is production of triiodothyronine (T_3), thyroxine (T_4), and calcitonin. Up to 80% of the T_4 is converted to T_3 by peripheral organs such. T_3 is four to ten times more active than T_4 .⁹⁻¹¹

Historical aspects of thyroid FNAC

Virchow the father of cellular cytology published cellular pathology in 1855, later in 1869 Klebs described the technique of replacing intracellular water by molten paraffin wax. This technique has gained popularity over cytology because of its superior results.¹²

Cytology took its momentum in the nineteenth century due to work done by Thiersch and Waldeyer. Their contributions for development of human cytology was very important. In 1885 and 1867 they proposed the epithelial origin of carcinoma of skin and breast on cytology. Their critical observations were important for the development of diagnostic cytology as they formed the basis for recognition of precancerous epithelial abnormalities. This made cytological technique, an acceptable diagnostic tool.¹³

The introduction of aspiration cytology in twentieth century is attributed to surgeon Hayer Martin, Edward Ellis and Ewing's for cancer and Allied diseases. They in 1927 studied 1400 cases at memorial hospital Newyok,USA and advocated aspiration by using needle of thicker calibre (18-gauge).Professor Duggeon and Patrick from Great Britain in 1927 proposed the needling of tumor as a means of rapid microscopic diagnosis.¹²⁻¹⁴

FNAC has been practiced in scandivian Countries for more than four decades. Initial Scepticism of pathologists and clinicians with regard to FNA gradually diminished and by the seventies this technique gained acceptance in the United States and the United Kingdom. Today it is practised worldwide.¹⁵

In comparison with older, methods of preoperative morphological evaluation such as core biopsy, cytology has the advantage of being more rapid, less traumatic, less expensive and sampling is also more representative due to ease of several needle passes. complications are practically non-existent and diagnostic accuracy is better than the core biopsy.¹⁵

Cytology is an excellent method for the study of inflammatory and autoimmune thyroid lesions especially their natural history, that may be better understood by sequential cytological monitoring. The association of primary lymphoma of thyroid with Hashimotos thyroiditis is well known and cytological monitoring has been shown to be of value in early detection of the lymphoma and prompt treatment. Autoimmune thyroid lesions usually are diffuse goitre that may not present clinical or biochemical features of altered thyroid function. They occasionally present as cold thyroid nodules leading to a clinical suspicion of malignancy. In both situations, FNA cytology is of great value.¹⁶⁻¹⁹

Fine-needle aspiration (FNA) has an essential role in the evaluation of euthyroid patients with a thyroid nodule. It reduces the rate of unnecessary thyroid surgery for patients with benign nodules and appropriately triages patients with thyroid cancer to appropriate surgery. Before the routine use of thyroid FNA, the percentage of surgically resected thyroid nodules that were malignant was 14%. With current thyroid FNA practice, the percentage of resected nodules that are malignant surpasses 50%.⁴

It is critical that cytopathologists should communicate thyroid FNA interpretations to referring physicians in terms that are succinct, unambiguous, and clinically helpful. Historically, terminology for thyroid FNA has varied significantly

from one laboratory to another, creating confusion in some cases and hindering the sharing of clinically meaningful data among multiple institutions.⁴

To address terminology and other issues related to thyroid FNA, the National Cancer Institute (NCI) hosted the “NCI Thyroid FNA State of the Science Conference” which was organized by Andrea Abati. It took place on October 22 and 23, 2007, in Bethesda. Edmund , Cibas and Susan J M, served as moderators. Zubair W B, served as chair of the Terminology and Morphologic Criteria committee.⁴

An inspiration for the proposal of the Bethesda System for reporting of thyroid cytopathology was successful and effective adoption of the Bethesda system for reporting cervical cytology interpretations. It was first developed at an NCI workshop in 1988 and widely adopted in the United States for reporting Papanicolaou test results. It is expected that the many benefits, clinical of the Bethesda cervical terminology will also apply to the Bethesda thyroid terminology. A uniform reporting system for thyroid FNA will facilitate effective communication among cytopathologists, endocrinologists, surgeons, radiologists, and other health care providers. It also facilitates cytologic-histologic correlation for thyroid diseases and facilitate research into the epidemiology, molecular biology, pathology, and diagnosis of thyroid diseases, particularly neoplasia.⁴

It was discussed at the conference that the primary purpose of terminology used for interpretation is clarity of communication. The interpretation should provide clinically relevant information that will assist referring physicians in the management of patients. The terms for reporting results should have an implied risk of malignancy on which recommendations for patient management such as annual follow-up, repeated FNA, surgical lobectomy, near total thyroidectomy can be used .⁴

For clarity of communication, the Bethesda System for Reporting Thyroid Cytopathology recommends 6 general diagnostic categories are which were adapted with permission of Ali and Cibas.⁴

Table 1: The Bethesda System for Reporting Thyroid Cytopathology.⁴

I. Nondiagnostic or Unsatisfactory

Cyst fluid only

Virtually acellular specimen

Other (obscuring blood, clotting artifact, etc.)

II. Benign

Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)

Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context

Consistent with granulomatous (subacute) thyroiditis

Other

III. Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance

IV. Follicular Neoplasm or Suspicious for a Follicular Neoplasm

Specify if Hurthle cell (oncocytic) type

V. Suspicious for Malignancy

Suspicious for papillary carcinoma

Suspicious for medullary carcinoma

Suspicious for metastatic carcinoma

Suspicious for lymphoma

Other

VI. Malignant

Papillary thyroid carcinoma

Poorly differentiated carcinoma

Medullary thyroid carcinoma

Undifferentiated (anaplastic) carcinoma

Squamous cell carcinoma

Carcinoma with mixed features (specify)

Metastatic carcinoma

Non-Hodgkin lymphoma

DIAGNOSTIC CRITERIA FOR SUBCATEGORIES FOR THYROID LESIONS AS PER THE BETHESDA SYSTEM.

1. Nondiagnostic or Unsatisfactory

Inadequate samples are reported as “nondiagnostic” (ND) or “unsatisfactory” (UNS). This category applies to specimens that are unsatisfactory owing to obscuring blood, overly thick smears, air drying of alcohol-fixed smears, or an inadequate number of follicular cells. For a thyroid FNA specimen to be satisfactory for evaluation and benign, at least 6 groups of benign follicular cells are required, each group composed of at least 10 cells.^{20,21}

There are several exceptions to the numeric requirement of benign follicular cells. Any specimen that contains abundant colloid is considered adequate and benign, even if 6 groups of follicular cells are not identified. A sparsely cellular specimen with abundant colloid is, by implication, a predominantly macrofollicular nodule and, therefore, almost certainly benign. ND/UNS results occur in 2% to 20% of cases but ideally should be limited to no more than 10% of thyroid FNAs, excluding samples composed exclusively of macrophages.²¹⁻²⁴

Specimens that consist only of cyst contents are problematic. Many laboratories have traditionally considered macrophages-only sample unsatisfactory and included them in the ND/UNS category, with the understanding that the parenchyma of the nodule has not been sampled, one cannot exclude a cystic papillary carcinoma. In such laboratories, “macrophages only” often constituted the great majority of ND/UNS cases, with rates that ranged from 15% to 30%.²⁴⁻²⁷ Other

laboratories considered the risk of false-negative result negligible and reported macrophages only as benign.²²⁻²⁴

At the 2007 NCI Conference, it was decided that cyst-fluid-only (CFO) cases should be considered a clearly identified subset of ND/UNS. The significance and clinical value of a CFO result depend in large part on sonographic correlation. If the nodule is almost entirely cystic, with no worrisome sonographic features, an endocrinologist might proceed as if the CFO were a benign result. On the other hand, it might be clinically equivalent to an ND result if the sonographic features are worrisome and the endocrinologist is not convinced that the sample is representative. In a study that segregated CFO cases and analyzed them separately, the risk of malignancy for a CFO sample was 4%.⁶ The risk of malignancy for ND/UNS (not including CFO) is 1% to 4%.^{1,4}

2. Benign Follicular lesions

The benefit of thyroid FNA derives in large part from the ability to make a reliably benign interpretation that avoids unnecessary surgery. A benign result is obtained in 60% to 70% of thyroid FNAs. Descriptive comments that follow are used to sub classify the benign interpretation. The term benign follicular nodule applies to the most common benign pattern, an adequately cellular specimen composed of varying proportions of colloid and benign follicular cells arranged as micro-follicles and macro-follicle fragments. If resected, virtually all benign follicular nodules turn out to be nodules of a Multinodular goiter or follicular adenomas. This distinction cannot be made by FNA and is of no significant clinical consequence to the patient. The false-negative rate of a benign interpretation is low (0%–3%).^{28,29}

Other benign subcategories include consistent with lymphocytic /Hashimoto thyroiditis in the proper clinical context and consistent with granulomatous (subacute) thyroiditis. This is a partial list and does not include a variety of other benign conditions like infections and amyloid goiter that are occasionally sampled by FNA. Additional benign findings such as black thyroid, reactive changes, radiation changes, cyst lining cells can be mentioned as descriptive diagnoses at the discretion of the cytopathologists.^{31, 32}

3. Atypia of Undetermined Significance (AUS) or Follicular Lesion of Undetermined Significance (FLUS).

Some thyroid FNAs are not easily classified into the benign, suspicious, or malignant categories. Such cases represent a minority of thyroid FNAs and in the Bethesda System are reported as AUS or FLUS. The most common scenarios can be described as follows: There is a prominent population of microfollicles in an aspirate that does not otherwise fulfil the criteria for FN/SF. This situation may arise when a predominance of microfollicles seen in a sparsely cellular aspirate with scant colloid. More prominent population of microfollicles than usual may occur and may be disproportionately apparent on a minority of smear in a moderately or markedly cellular sample, but the overall proportion of microfollicles is not sufficient for a diagnosis of FN/SFN.

It is important to note that only nodules with atypia of undetermined significance should be placed in the AUS category. Recognizably benign cellular changes such as typical cyst lining cells, focal Hurthle cell change, changes ascribed to radioiodine therapy, black thyroid should not be interpreted as AUS. A moderately or even highly

cellular specimen by itself without significant nuclear or architectural Atypia does not qualify a nodule for an AUS interpretation.

An AUS result is obtained in 3% to 6% of thyroid FNAs. Higher rates likely represent overuse of this category when other interpretations are more appropriate. The recommended management is clinical correlation and a repeated FNA at an appropriate interval.

The risk of malignancy for an AUS nodule is difficult to ascertain because only a minority of cases in this category have surgical follow-up. Those that are resected represent a selected population of patients with repeated AUS results or patients with worrisome clinical or sonographic findings. In this selected population, 20% to 25% of patients with AUS prove to have cancer after surgery, but this is undoubtedly an overestimate of the risk for all AUS interpretations. The risk of malignancy is certainly lower and probably closer to 5% to 15%. An effort should be made to use this category as a last resort and limit its use to approximately 7% or fewer of all thyroid FNAs.³³

4. Follicular Neoplasm or Suspicious for a Follicular Neoplasm-

The purpose of this diagnostic category is to identify a nodule that might be a FC and triage it for surgical lobectomy. FNA is diagnostic for many thyroid conditions such as papillary carcinoma, lymphocytic/Hashimoto's thyroiditis but, with regard to follicular carcinoma, it is better considered a screening test. Cytomorphologic features of FC do not permit distinction from a follicular adenoma (FA), they are reportable as FN/SFN leading to a definitive diagnostic procedure, usually lobectomy.^{35,36}

The term suspicious for a follicular neoplasm is preferred by some laboratories over follicular neoplasm for this category because a significant proportion of cases up to 35% prove to be non-neoplastic lesions such as rather hyperplastic proliferations of follicular cells, most commonly those of MNG.³⁶ About 15% to 30% of cases called FN/SFN prove to be malignant.^{2,10,19,22} The majority of FN/SFN cases turn out to be FAs or adenomatoid nodules of MNG, both of which are more common than FC. Of those that prove to be malignant, many are FCs, but a significant proportion is follicular variants of papillary carcinoma.³⁷

Cytologic preparations typically have high cellularity, and colloid is scant or absent. The hallmark of this diagnostic category is a disturbed cytoarchitecture. Follicular cells are arranged predominantly in microfollicular or trabecular arrangements. Cases that demonstrate the nuclear features of papillary carcinoma are excluded from this category. Cellular crowding and overlapping are conspicuous, and the follicular cells are usually larger than normal. Nuclear atypia or pleomorphism and mitoses are uncommon. A minor population of microfollicles with intact spheres and fragments can be present. Conspicuous cellularity alone does not qualify the nodule for a suspicious interpretation.³⁸ If the sample is cellular but mostly macrofollicular, a benign interpretation is appropriate. Benign follicular nodules often have a small population of microfollicles and crowded groups. If these constitute the minority of the follicular cells, they have little significance and the FNA can be interpreted as benign. A suspicious interpretation is rendered only when the majority of the follicular cells are arranged in abnormal architectural groupings such as microfollicles, and crowded trabecular pattern.^{1,4,36}

The general category FN/SFN is a self-sufficient interpretation. In the WHO classification, Hurthle cell adenoma and Hurthle cell carcinoma are considered oncocytic variants of Follicular adenoma and FC, respectively.^{6,34} Studies suggest that follicular and Hurthle cell tumors have different underlying genetics. For this reason and because they have such distinctive morphologic features, hence it should be specified that a sample raises the possibility of a Hurthle cell rather than a FN. This interpretation applies to cellular samples that are composed exclusively or almost exclusively of Hurthle cells. Oncocytic cells with nuclear features of papillary carcinoma are excluded from this interpretation. A significant proportion of these cases (16%–25%) prove not to be neoplasm but rather hyperplastic proliferations of Hurthle cells in nodular goitre or lymphocytic thyroiditis. About 15% to 45% of nodules are malignant, and the remainder of the neoplasms prove to be Hurthle cell adenomas.^{1,32-38}

5. Suspicious for Malignancy

Many thyroid cancers especially PTC can be diagnosed with certainty by FNA. But the nuclear and architectural changes of some PTCs are subtle and focal. This is particularly true of the follicular variant of PTC, which can be difficult to distinguish from a benign follicular nodule.³⁵ Other PTCs may be incompletely sampled and yield only a small number of abnormal cells.³⁷ If only 1 or 2 characteristic features of PTC are present and if they are only focal and not widespread throughout the follicular cell population, or if the sample is sparsely cellular, a malignant diagnosis cannot be made with certainty. Such cases occur with are best classified as suspicious for malignancy and reported as suspicious for papillary carcinoma. Nodules called suspicious for papillary carcinoma are resected

by lobectomy or thyroidectomy. Most (60%–75%) prove to be papillary carcinomas, and the rest are usually follicular adenomas.^{6,39,40}

The same general principle applies to other thyroid malignancies like medullary carcinoma and lymphoma, but these are encountered less frequently than PTC. Ancillary testing such as immunohistochemical analysis and flow cytometry are more helpful in borderline cases of medullary carcinoma and lymphoma than with PTC.

6. Malignant

The general category malignant is used whenever the cytomorphic features are conclusive for malignancy. Descriptive comments are used to subclassify the malignancy and summarize the results of special studies, if any. Approximately 3% to 7% of thyroid FNAs have conclusive features of malignancy, and most are papillary carcinomas.^{6,41} Malignant nodules are usually removed by thyroidectomy, with some exceptions such as metastatic tumours, Non-hodgkins lymphomas, and undifferentiated carcinomas. The positive predictive value of a malignant FNA interpretation is 97% to 99%.

As with the Bethesda System for cervical cytology, it is expected that this terminology proposal of Bethesda system for thyroid cytopathology reporting will be a valuable first step toward uniformity in the thyroid cytopathology reporting.^{1,4}

MATERIALS AND METHODS

Source of data:

Patients with thyroid lesions referred to the Department of Pathology, B.L.D.E.U. Shri B.M.Patil Medical College, Hospital & Research Centre, Bijapur from November 2010 to July 2012 for FNAC and histopathological evaluation were taken.

Methods of collection of data:

Detailed clinical history and examination findings of the patients were noted. Standard FNAC procedure was performed by using Cameco syringe pistol, disposable syringe {10ml} and 24-20G needle. Multiple smears were prepared simultaneously. Wet-fixed smears in absolute alcohol were stained with Hematoxylin and Eosin {H&E} and Papanicolaou stains while air dried smears were stained with May-Grunewald Giemsa {MGG} stain.

Procedure of thyroid FNA:

The FNA was done with a 22-23 gauge needle disposable needle attached to a 20ml plastic disposable syringe mounted on a handle (syringe holder) for single – hand grip. The patient was made to lie down in supine position with neck hyper-extended. Extension of the neck was facilitated by avoiding a pillow under the head, and keeping under the neck to further extend the cervical spine and expose the gland more prominently. The patient was asked to refrain from swallowing during the procedure which takes about 5-20 sec.¹⁶

The skin overlying the swelling was cleaned thoroughly with alcohol. The needle is inserted into the nodule and plunger is retracted to create a vacuum in the syringe. The needle is then removed back and forth and from side to side gently within the lesion, all the time maintaining the negative pressure in the syringe. The plunger was then released. The needle with syringe was then withdrawn from the thyroid. The needle was quickly detached from the syringe and the plunger was retracted to allow air to fill the syringe barrel. The needle was then re-attached to the syringe and the contents ejected on to a glass slide by pushing down the plunger.^{3,16}

Thyroid specimens received were fixed in 10% formalin for 12 to 24 hrs after recording the gross morphological features. The specimens were routinely processed, embedded in paraffin wax and sections were cut at 3 to 6µm thickness. Sections were stained routinely with H&E stain. Special stains like Congo red were employed wherever indicated.

Inclusion criteria:

All cases of thyroid lesions for which FNAC and histopathological examination are performed were included.

Exclusion criteria:

Swellings in front of the neck other than thyroid lesions were excluded

Statistical Analysis:

- Diagrammatic presentation
- Chi square test

Interpretation of cytology smears:

Morphological criteria such as cellularity (mild, moderate, marked and scanty) Arrangement such as (clusters, follicles, trabecular, papillary and singly scattered) cytoplasmic, nuclear details and background colloid material were utilized for categorization of thyroid lesion.^{4,6}

RESULTS

Total number of cases studied on FNAC were 106. Out of 106 cases 82(77.3%) were benign lesions, 10(9.4%) were Unsatisfactory/Nondignostic, 6(5.7%) were Follicular neoplasm/Suspicious for neoplasm, 4(3.8%) were suspicious of malignancy, 3(2.8%) were Malignant and 1(0.9%) case was reported as Atypia of undetermined significance.

Table: 2 Cytological Diagnosis as per the Bethesda system

Cytological diagnosis	No of cases	Percentage
Unsatisfactory	10	9.4%
Benign follicular lesion	82	77.35%
Atypia of follicular lesion of undermined significance	1	0.9%
Follicular neoplasm /Suspicious for follicular neoplasm	6	5.6%
Suspicious for malignancy	4	3.77%
Malignant tumour	3	2.83%
Total	106	100

Maximum number of cases reported on cytology were benign thyroid lesion amounting to 77.35%

Bar diagram showing Categories of cytological diagnosis as per the Bethesda system

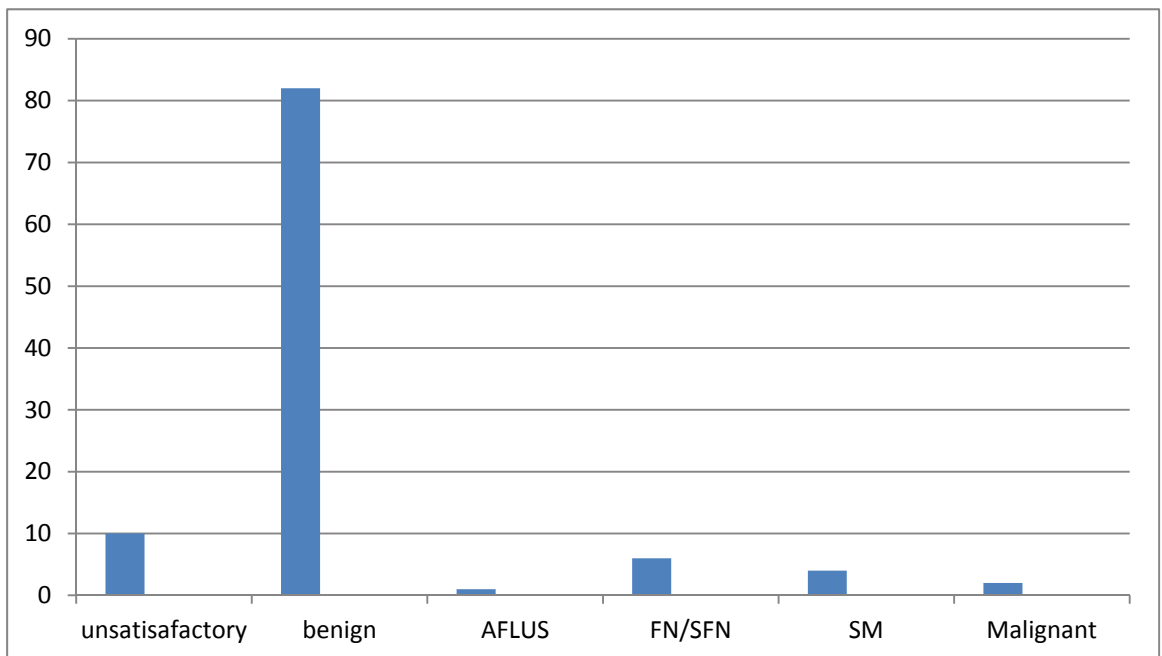


Table 3. Age and sex distribution

Sl. no	Age in years	No of males	No of females	Total no	Percentage%
1	11-20	00	07	7	6.6
2	21-30	00	14	14	13.2
3	31-40	00	12	12	11.3
4	41-50	4	28	32	30.1
5	51-60	3	26	29	27.3
6	61-70	2	07	9	8.4
7	71-80	1	02	3	2.8

The maximum number of cases were in the age group 41-60 years .In females the maximum numbers of cases were in the age group o 41-50 years. In males, the maximum number of cases were in the age group of 41-50 years .In males no cases were noted in the age group of 11-40 years.

Bar diagram showing Age and sex Distribution

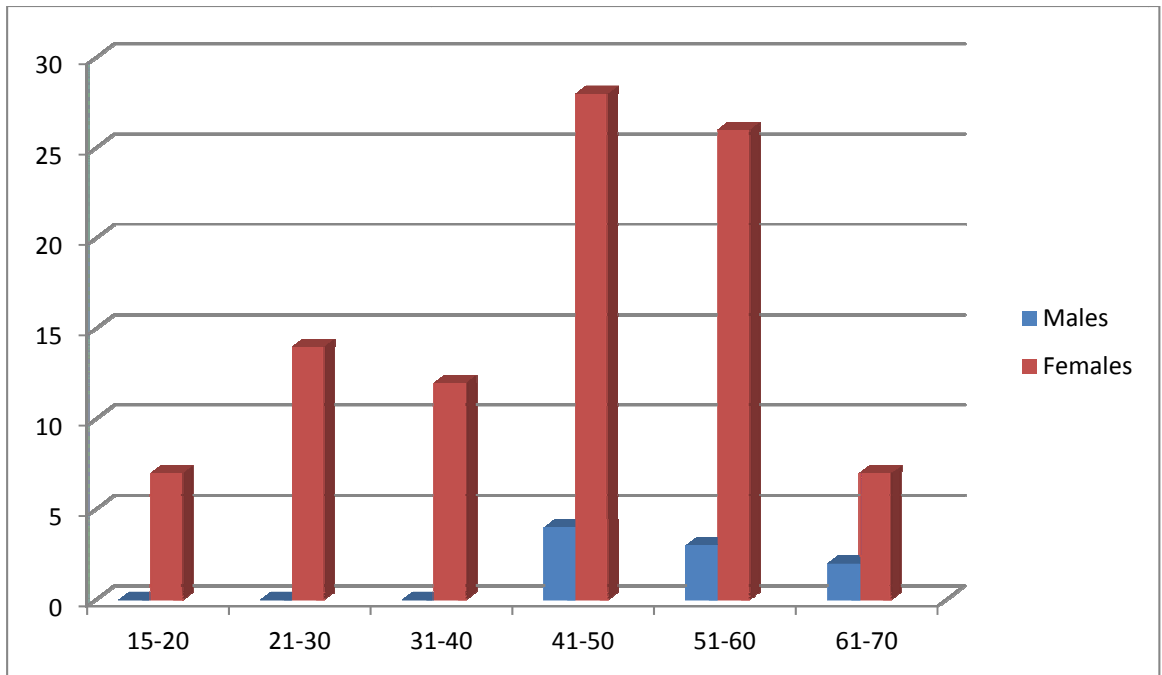


Table 4 Cytological diagnosis of Benign Follicular lesions

Benign follicular lesion	No of cases(n-82)	Percentage
Adenomatoid goitre	11	13.4
Multinodular goiter(colloid nodule)	56	68.3
Lymphocytic(Hashimotos thyroiditis)	14	17.07
Granulomatous (subacute thyroiditis)	1	1.21

Total no of benign follicular lesion were 82. Out of which 11 were Adenomatoid goiter, 56 were MNG (colloid nodule), Lymphocytic (Hashimotos thyroiditis) were 14 and 1 case was Granulomatous thyroiditis.

Table 5 Histopathological Diagnosis

Categories	No of cases(n=56)	Percentage
Benign thyroid lesion	50	89.3%
Follicular Neoplasm/Follicular carcinoma	2	3.57%
Follicular carcinoma	2	3.57%
Malignant	2	3.57%
Total	56	100

Histopathological follow up was available in 56 cases, out of which 50 cases were reported as benign thyroid lesion. Follicular carcinoma and malignant tumors were reported in 2 cases each.

Table 6: -Histopathological diagnosis of benign thyroid lesion.

Benign Thyroid lesion	No of cases (n=50)	Percentage %
MNG	37	74%
Adenomatoid goiter	3	6%
Colloid goiter	4	8%
Hashimotos thyroiditis	6	12%

Table 7 . Thyroid lesion for which surgical resection done.

Diagnosis on Cytology as per Bethesda system	Total no cases	Total no Histopathological follow up available	Percentage of follow up cases available	Diagnosis on Histopathology
Unsatisfactory	10	5	50	Nodular goitre with cystic change
Benign	82	44	48	MNG
Atypia of follicular lesion of undetermined significance	1	1	100	MNG with adenomatoid hyperplasia
Follicular neoplasm/suspicious of neoplasm	6	2	33.3	Follicular carcinoma
Suspicious of malignancy	4	2	50	Follicular carcinoma
Malignant	3	2	75	Malignant

Out of 10 cases reported as unsatisfactory on FNAC, 5(50%) cases had histopathological Follow up which were diagnosed as nodular goitre with cystic change on histopathology.

Out of 82 cases reported as Benign Follicular lesion on cytology, 44 (48%) cases had histopathological follow up and all were diagnosed as Multinodular Goitre.

One case was reported as Atypia of follicular lesion of undetermined significance on cytology which on histopathology was reported as MNG with adenomatoid hyperplasia.

Out of 6 cases reported as Follicular Neoplasm/Suspicious of follicular neoplasm on Cytology, 2 (33.3%) had histopathological follow up and reported as

Follicular carcinom, because both the cases showed Features of Follicular carcinoma having capsular invasion .

Four Cases reported as Suspicious of malignancy on FNAC because of the repetitive pattern of microfolicles and had cyto architectural dislodgment. Follicular cells were larger in size. Out of 4 cases 2 cases had histopathological follow up and proved to be follicular carcinoma.

Out of three Cases which were reported as Malignant on cytology 2(75%) had histopathological follow up and reported as malignant and one case reported as poorly differentiated malignancy and sent for radiotherapy.

One case had metastasis over gluteal region. Histopathology of both thyroid and gluteal region showed features of carcinoma.

Table 8. Comparison of cytological and histopathological diagnosis of 56 cases

Bethesda system categories	Total no of cases on cytology	Histopathology	Analysis of discrepancy
Unsatisfactory	5	0	Present
Benign-MNG	44	50	Absent
Atypia of undetermined significance	1	0	Present
Follicular Neoplasm/Suspicious of Neoplasm	2	2	Absent
Suspicious of malignancy	2	0	Present
Malignant	2	4	Absent

Out of 56 cases where cytological and histopathology correlation was available, 8 cases showed cyto-histologic discrepancies amounting to 14.4%

Table 10. Comparison of percentage of distribution of fine needle Aspiration Diagnoses among published studies

Diagnostic category	Present study	Yassa et al²⁷	Yang et al¹⁷	Nayar and Ivanovic²³
Nondiagnostic/Unsatisfactory	10	7	10.4	5
Benign	82	66	64.6	64
Atypia of follicular lesion of Undetermined significance	1	4	3.2	18
‘Suspicious for Follicular Neoplasm’	6	9	11.6	6
Suspicious for malignancy	4	5	2.6	2
Malignant	3	5	7.6	5

In the present study percentage of benign thyroid lesion was more as compared to the study done by other authors.

Table 9 Analysis of discrepancy

Diagnosis by FNA cytology by (Bethesda system)	Diagnosis by Histopathology (standard system)
Unsatisfactory(cyst fluid only)	MNG with cystic change
Unsatisfactory(cyst fluid only)	MNG
Unsatisfactory(cyst fluid only)	MNG with cystic change
Unsatisfactory(cyst fluid only)	MNG
Unsatisfactory(cyst fluid only)	MNG
Atypia of follicular neoplasm of undetermined significance	MNG with adenomatoid hyperplasia
Suspicious of malignancy	Follicular carcinoma

In 8 cases discrepancy was noted .Out of 8 cases 5 cases were reported as unsatisfactory on cytology which were reported on histopathology as MNG in 3 cases and MNG with cystic change in 2 cases. One case of AFLUS was reported as MNG with adenomatoid hyperplasia and 2 cases which were reported as suspicious for malignancy on cytology were diagnosed as follicular carcinoma on histopathology.

Statistical Significance (n-56)

		Testing method	
		D	ND
Gold standard	D	3	1
	ND	2	50

Fisher's exact test $p = 0.0014$

Statistically highly significant at $p = 0.0014$

Specificity =60%

Sensitivity =98%

Positive predictive value =75%

Negative predictive Value =96%

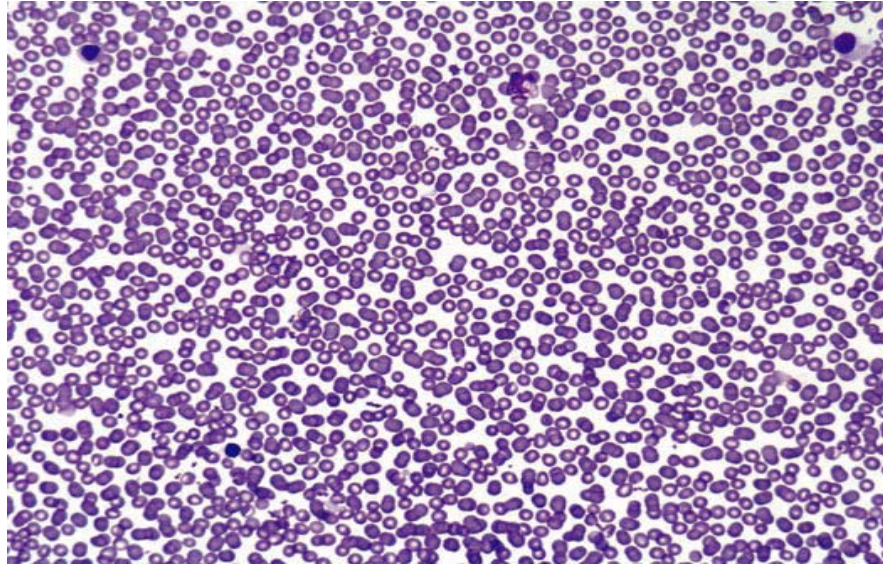


Fig 1 Photomicrograph showing Nondiagnostic/Unsatisfactory smear obscuring blood (MGG, 10x)

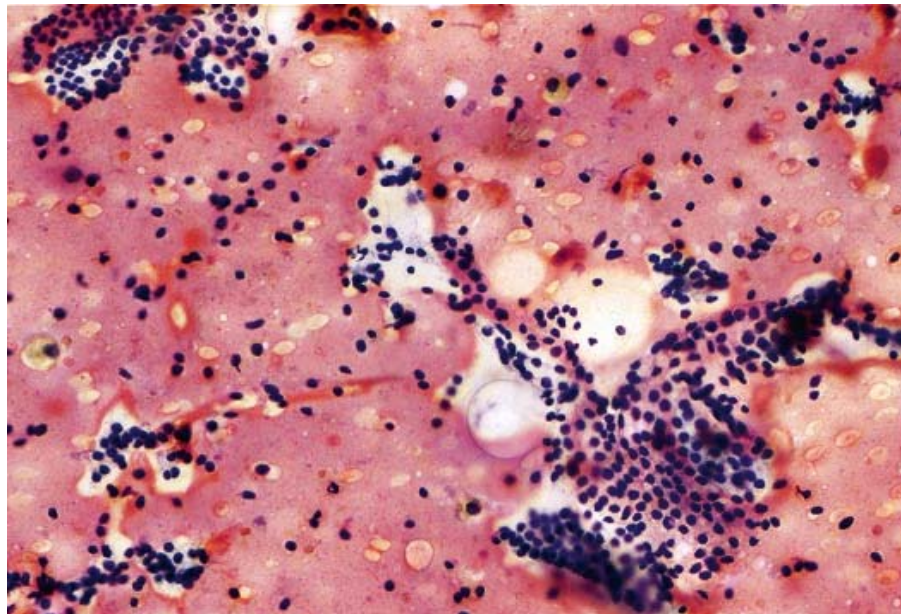
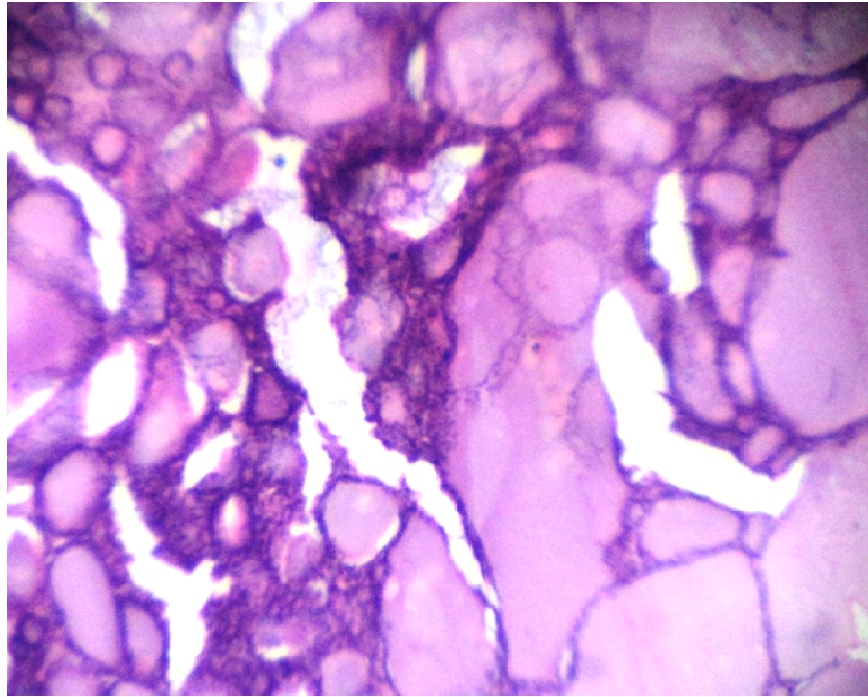
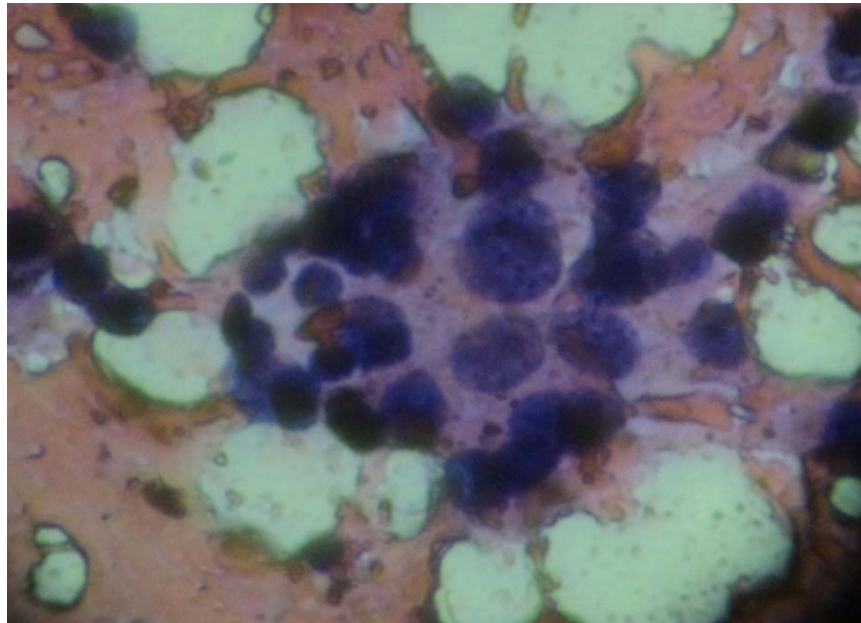


Fig 2 Photomicrograph of FNAC showing benign thyroid lesion suggestive of colloid goitre (H & E, 10x)



**Fig 3 Photomicrograph of HPR showing Multinodular goitre
(H &E, 10x)**



**Fig 4 Photomicrograph of FNAC showing Atypia of Undetermined
significance (H&E, 40x)**

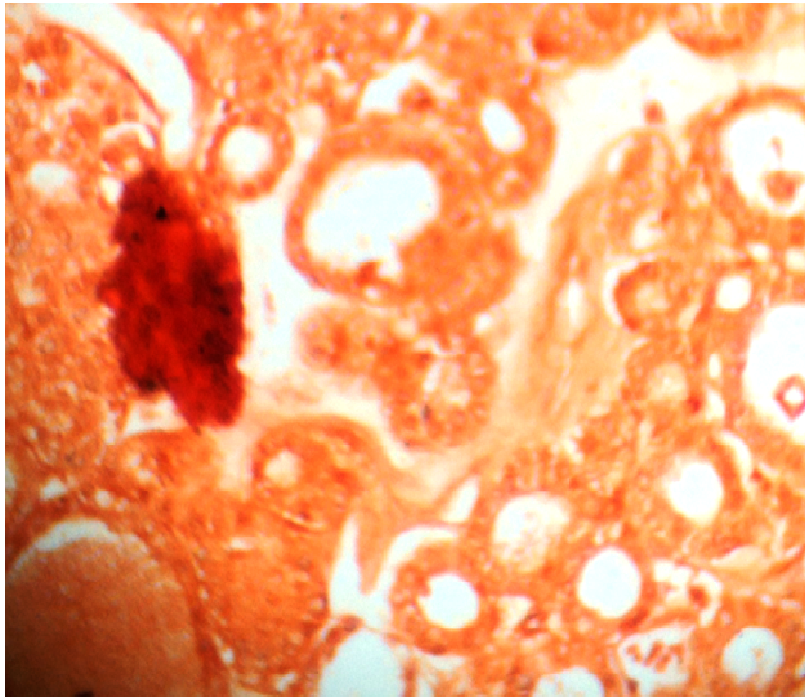


Fig 5 Photomicrograph of HPR showing MNG with adenomatoid hyperplasia (H&E, 10x)

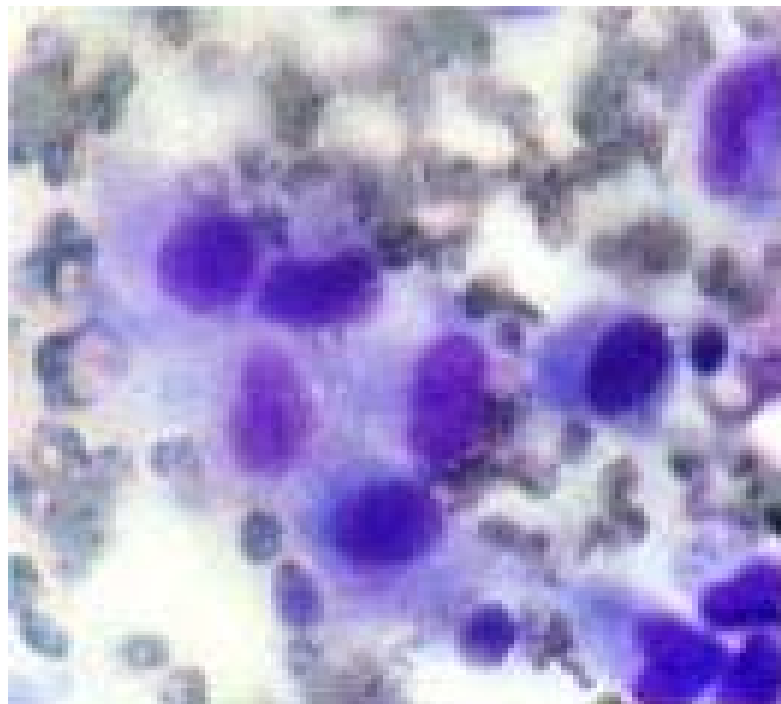
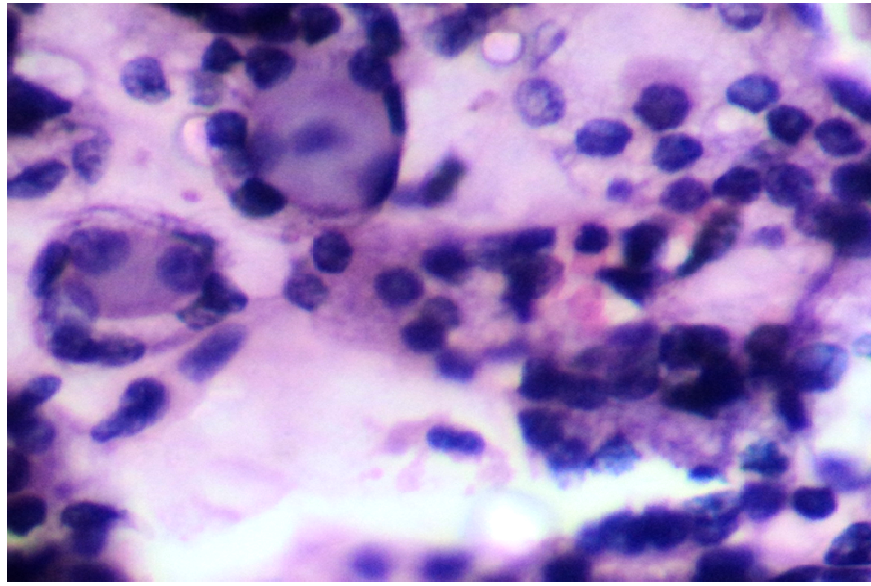
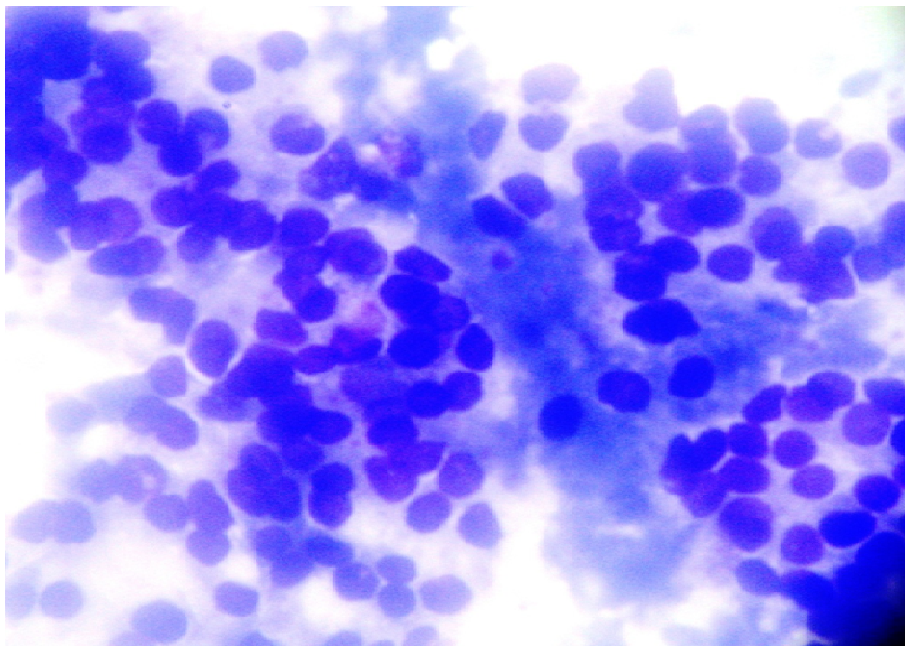


Fig 6 Photomicrograph of FNAC showing Follicular Neoplasm/Suspicious of neoplasm (H&E, 40x)



**Fig7 Photomicrograph of HPR showing Follicular carcinoma
(H & E, 10x)**



**Fig 8 Photomicrograph of FNAC showing Follicular carcinoma
(MGG, 40x)**

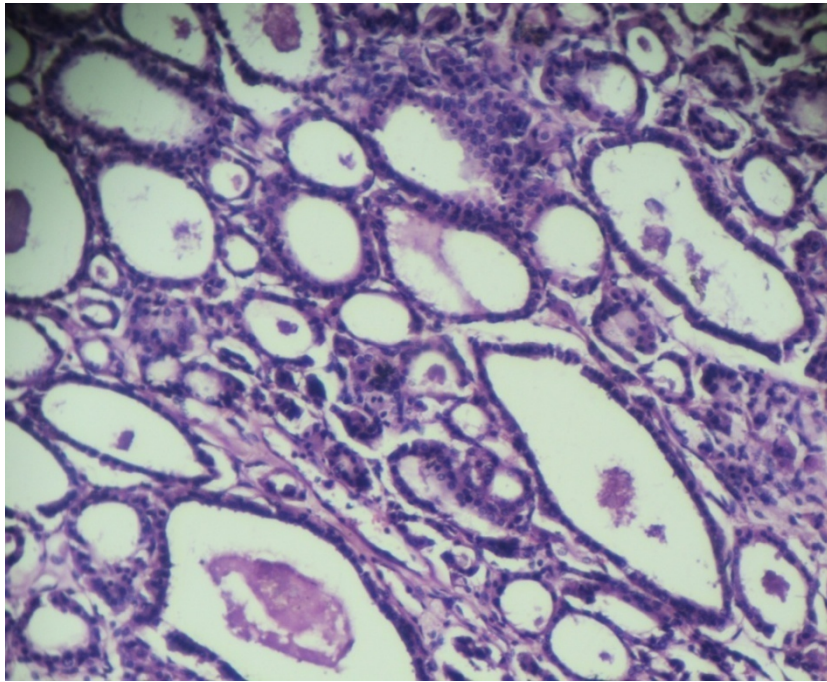
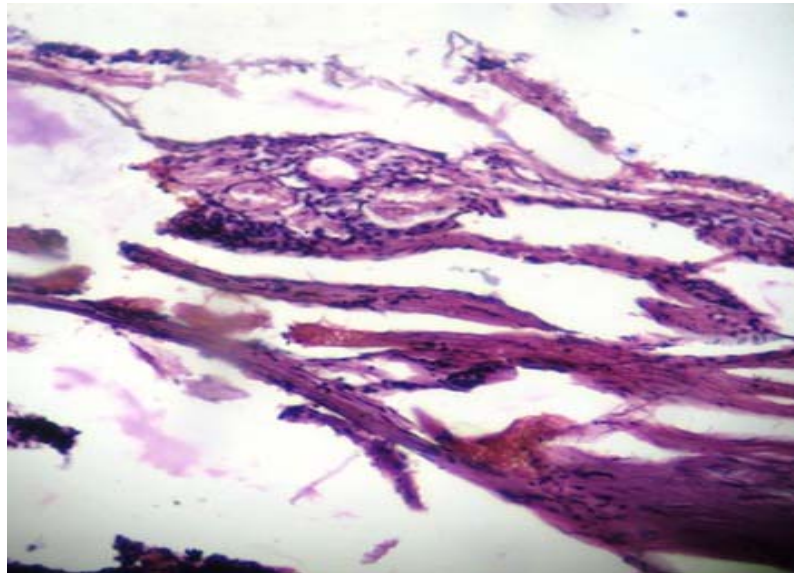


Fig9 HPR Follicular carcinoma (H&E, 10x)



**Fig 10 Photomicrograph of HPR showing capsular invasion
(H &E, 40x)**

DISCUSSION

FNA thyroid has been accepted as screening test for patients with palpable thyroid lesion. The main role of FNA thyroid is to plan the patients of thyroid lesion. Patients that are diagnosed as neoplasm /malignancy are managed surgically and non-neoplastic lesions can be managed clinically.²¹

Diagnostic categories of thyroid lesions are defined differently in different institution. To bring uniformity new 6 categories are recommended by Bethesda system.

In this study an attempt was made to report the thyroid FNA as per the Bethesda system and also to assess the efficacy by comparing with the histopathological diagnosis wherever possible.

Out of 106 samples in this study 9.4% were Unsatisfactory, 77.35% were benign follicular lesion, 0.9% were AFLUS, 5.6% were FN/SFN, 3.7% were suspicious for malignancy and 2.8% were Malignant. Similar findings were noted in study done by Yassa et al²⁷ in which unsatisfactory were 7%, Benign follicular lesion were 66%, AFLUS were 4%, FN/SN were 9% and 5% cases of suspicious of malignancy and Malignant each.

Maximum number of cases in the present study were in the age group of 21-50years. Our findings are similar to the study done by Siddique M et al.⁴²

Percentage of females in present study was 90%, which was similar to study done by Siddique M et al.⁴²

In the present study surgical follow up was available in 53% cases in which cyto-histological discrepancy was noted in 14.4%

In the study done by Yang et al¹⁷ out of 4713 FNA cases, 1052 patients had surgical follow up. The cytohistological discrepancy in their study was 15.3%. Cytohistological discrepancy in our study was similar to the study done by Yang et al.¹⁷

Rate of malignancy in benign thyroid lesion in study done by Jo V Y et al²³ was 1.1%. However in the present study out of 82 cases of benign thyroid lesion, 44 cases had histopathological follow up and all cases were reported as benign thyroid lesion. Thus the rate of malignancy in the present study was 0%.

If FNA yields low cellularity with small number of abnormal cells then the lesion will be interpreted as suspicious of malignancy. In a study done by Jo VY et al²³ 2.3% cases were reported as SM. In the present study 7.14% of cases were reported as SM. Rate of malignancy in the study done by Jo VY et al²³ was 70%. In the present study 4 cases were reported as suspicious of malignancy. Out of which 2 cases had surgical follow up and reported as malignant amounting to 100% risk of malignancy in categories reported as SM.

Rate of FN/SFN was 23.4% in the study done by Jo VY et al.²³ In the present study 6 cases were reported as FN/SFN, out of which 2 cases had surgical follow up and were reported as Follicular carcinoma amounting to 33.3% risk of malignancy in categories reported as FN/SFN.¹

Diagnostic category of AFLUS is heterogenous in various studies. Diagnostic frequency of AFLUS in study done by Jo VY et al²³ was 3.4% and was 18% in study done by Nayar and Ivanovic.²⁴ In the present study only

one case amounting to 0.9% was reported as AFLUS which was reported as benign lesion on histopathology.

In a study done by Nayar and Ivanovic²⁴ 6% cases of AFLUS turned out to be malignant. Malignant rate in AFLUS in study done by JO VY et al²³ was 17% and they concluded that AFLUS has an important role in triaging patients with AFLUS. In the present study sample size was small and was the limitation and underscores the interpretation of AFLUS.

FNAC is a sensitive and highly specific method of evaluating thyroid nodules for malignancy. FNAC of the thyroid nodule is reported to have sensitivity ranges from 65% -98% and a specificity of 72%-100%⁴³

In the study done by Nggada⁴¹ the sensitivity was 88.9% and specificity was 96%. In the present study sensitivity was 60% and specificity was 98% which is similar to the study done by Nggada.⁴¹

In the study done by Saddique M et al⁴³ the Positive predictive value was 81.8% and Negative predictive value was 93.81%. In the present study the Positive predictive value was 75% and Negative predictive value was 96% which is similar to that of Saddique M et al.⁴³

SUMMARY

The present study Diagnostic accuracy of Bethesda system of reporting thyroid cytopathology included 104 cases of thyroid lesions. The study was carried out from Nov2010 to July 2012 in B.L.D.E.U Shri B.M.Patil Medical College, Bijapur.

Considering age and sex incidence, thyroid lesions were common in 3rd and 4th decade and showed female predominance.

Total number of cases studied on FNAC were 104. Out of which 104 cases 82(78.8%) were benign lesions, 10(9.6%) were unsatisfactory/ nondiagnostic, 6(6.20%) were Follicular neoplasm/suspicious for neoplasm, 4(4.16%) were suspicious of malignancy, 3(3.12%) were Malignant and one case was reported as Atypia of undetermined significance. The available histopathological follow up was in 56 cases (53.8%). In 8 cases (14.4%) there was cyto histologic discrepancy.

In the present study the cyto-histopathological discrepancy was noted in 14.4% which is in correlation with the study done by Yang et al.¹⁷

The sensitivity and specificity in the present study is 60% and 98% respectively .P value is 0.0014 and statistically highly significant.

CONCLUSION

- Universal application of new standardized nomenclature of Bethesda system improves interlaboratory agreement and helps in consistent management of thyroid lesions.
- Guides the management of nodules by identifying patients who require surgical resection and patients who require no further interventions.
- Due to its high specificity and sensitivity FNAC play a significant role in the diagnosis and management planning of solitary thyroid nodules .It is cost effective.

Bibliography

1. Jo VY, Stele EB, Dustin SM, Hanley KZ. Malignancy risk for Fine needle aspiration of thyroid lesions according to Bethesda System for reporting thyroid cytopathology. *Am J Clin Pathol* 2010; 134: 450-456.
2. McHenry CR, Raeburn C, Strickland T, Marty JJ. The utility of routine frozen section examination for intraoperative diagnosis of thyroid cancer. *Am J Surg* 1996; 172: 658-661.
3. Rosen Y, Rosenblatt P, Saltzman E. Intraoperative pathologic diagnosis of thyroid neoplasm's. *Cancer* 1990; 66: 2001-2006.
4. Cibas ES and Ali SZ. The Bethesda System for reporting thyroid cytopathology. *Am J Clin Pathol* 2009; 132: 658-665.
5. Chaurasia BD. Thyroid gland. In: Human anatomy. Head and neck and brain. 1st ed. Delhi: CBS, 1980:88-91.
6. Snell RS. Thyroid gland. In: Clinical anatomy. 7th ed. Philadelphia: Lippincott Williams & Wilkins, 2004:745-8.
7. Dyson M. Thyroid gland. In: Williams PL, eds. Gray's anatomy. 38th ed. London: Churchill Livingstone, 2000:1891-7.
8. Singh I, Pal GP. Development of the thyroid gland. In; Human embryology. 7th ed. New Delhi: Macmillan, 2001:119-23.
9. Sadler TW. Thyroid gland. In: Langman's medical embryology. 9th ed. Maryland: Lippincott Williams & Wilkins, 2004:384-6.
10. Guyton Ac and Hall JE. The thyroid metabolic hormones. In: Textbook of medical physiology. 10th ed. Philadelphia: Saunders, 2000:858-68.
11. Ganong WF. The thyroid gland. In: Medical physiology. 21st ed. New York: McGraw-Hill, 2003:320-35.

12. Meleher D, John VG. In Practical Aspiration Cytology. Hampshire; Churchill Livingstone, 1984: p-1-27.
13. Koss L. Diagnostic cytopathology and its histopathologic basis. Philadelphia: JB Lippincott Co, 1992 10th ed: P-1293-1315.
14. Niab ZM. Cytopathology. 4th ed. Boston: Little brown and Co, 199: P 486-516.
15. Jayraam G .Introduction and general and technical considerations.InThyroid cytology:Arya publications,2006 Ist ed:P 6-26
16. Fine-needle aspiration biopsy of thyroid nodules: impact on thyroid practice and cost of care. Am J Med 1982; 73:381–384.
17. Yang J, Schnadig V, Logrono R, Wassermman PG. Fine needle aspiration of thyroid nodules: A study of 4073 patients with histologic and clinical correlations. Cancer 2007; 5:306-315.
18. Gharib H, Goellner JR, Johnson DA. Fine-needle aspiration cytology of the thyroid: a 12-year experience with 11, 000 biopsies. Clin Lab Med. 1993; 13:699-709.
19. Yassa L, Cibas ES, Benson CB. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. Cancer. 2007; 111(6):508-516.
20. Rosai J. Thyroid gland. In: Rosai and Ackerman's surgical pathology. Vol 1. 9th ed. New Delhi: Elsevier, 2004:515-94.
21. Stephen SR, Collen M, Dana MG, Daniel S, Ronald B, Richard J Z et al.In errors in thyroid gland fine needle aspiration. American journal for clinical Pathology 2006;125:873-882
22. Stanley MW. Thyroid cytology comes to Bethesda. Am J Clin Pathol 2009; 132: 665-657.

23. Jo VY, Stelow EB, Dustin SM, Simone M, Hanley KZ. Malignancy risk for Fine needle aspiration of thyroid lesions according to Bethesda System for reporting thyroid cytopathology. *Am J Clin Pathol* 2010; 134
24. Nayar R and Ivanovic M. The indeterminate thyroid fine needle aspiration: experience from an academic center using terminology similar to that proposed in the 2007 National Cancer Institute thyroid fine needle aspiration state of the science conference. *Cancer* 2009;3:195-202.
25. Grant CS, Hay ID, Gough IR, McCarthy PM, Goellner JR. Long-term follow-up of patients with benign thyroid fine-needle aspiration cytologic diagnoses. *Surgery*.1989;106:980-985.
26. Meissner WA, Warren S. Tumors of the thyroid gland. In: Harlan IF, eds. *Atlas of tumor pathology. Fascicle 4, 2nd series AFIP*, Washington: DC, 1969:43-50.
27. Yassa L, Cibas ES, Benson CB. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. *Cancer*. 2007;111(6):508-516.
28. Gharib H, Goellner JR, Johnson DA. Fine-needle aspiration cytology of the thyroid: a 12-year experience with 11, 000 biopsies. *Clin Lab Med*. 1993;13:699-709.
29. Baloch ZW, Cibas ES, Clark DP. The National Cancer Institute Thyroid fine needle aspiration state of the science conference: a summation. *Cytojournal*. 2008;5-6.
30. Baloch ZW, LiVolsi VA, Asa SL. Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: A synopsis of the National Cancer Institute Thyroid fine needle aspiration state of the science conference: a summation. *Cytojournal*,2008:9-20
31. Clark DP, Faquin WC. *Thyroid Cytopathology*. New York:4th ed Springer; 2005:p-234-254.
32. Berezowski K, Jovanovic I, Sidawy MK. Thyroid. In: Sidawy MK, Ali SZ, eds. *Fine needle Aspiration Cytology*. Churchill:Livingstone;2007:123-134

33. Atypia of Undetermined Significance and Nondiagnostic Rates in The Bethesda System for Reporting Thyroid Cytopathology Are Inversely Related
Am J Clin Pathol ,2012 137:462-465.
34. Deveci MS, Deveci G, LiVolsi VA, Baloch ZW. Fine-needle aspiration of follicular lesions of the thyroid Diagnosis and follow-Up Cytojournal. 2006;3:9.
35. Baloch ZW, Fleisher S, LiVolsi VA, Gupta PK. Diagnosis of follicular neoplasm: a gray zone in thyroid fine-needle aspiration cytology. Diagn Cytopathology. 2002;26(1):41-4.
36. Yang GC, Liebeskind D, Messina AV. Should cytopathologists stop reporting follicular neoplasms on fine-needle aspiration of the thyroid? Cancer. 2003;99(2):69-74.
37. Greaves TS, Olvera M, Florentine BD. Follicular lesions of thyroid: a 5-year fine needle aspiration experience. Cancer. 2000;90(6):335-41.
38. Agarwal S, Rao RS, Parikh DM. Histologic trends in thyroid cancer 1969–1993: a clinico-pathologic analysis of the relative proportion of anaplastic carcinoma of the thyroid. J Surg Oncol. 1996;63(4):251-255.
39. Hundahl SA, Fleming ID, Fremgen AM . A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S, 1985–1995. Cancer 1998;83(12):2638-2648.
40. Lam KY, Lo CY, Chan KW. Insular and anaplastic carcinoma of the thyroid: a 45-year comparative study at a single institution and a review of the significance of p53 and p21. Ann Surg. 2000;231(3):329-338.
41. Nggaada HA, Khalil MIA. Fine needle Aspiration Cytology(FNAC) technique as a diagnostic tool of tumours in the UMTH,Nigeria.Highland Medical Research Journal 2003:1(3);28-30
42. Saddique M, Islam U, Irbil P,Baloch Q.FNAC:A reliable diagnostic tool in solitary thyroid nodule and multinodular goiter.Karachi,Pakistan journal of surgery 2008:24(3) 188-192.
43. Tabaqchali MA, Hanson JM, Johnson SJ, Wadehra V, Lennard T W,Proud G.Thyroid aspirational cytology in Newcastle; a six year cytology/histology correlation study. Ann R coll Surg England 200;82(3);149-55.

**ANNEXURE
PERFORMA**

SCHEME OF CASE TAKING:

- | | | | |
|---------------------------------|----------|----------------|----------|
| 1) Name | : | CASE NO | : |
| 2) Age | : | IP NO | : |
| 3) Sex | : | DOA | : |
| 4) Religion | : | DOD | : |
| 5) Occupation | : | | |
| 6) Residence | : | | |
| 7) Presenting Complaints | : | | |
| 9) Past History | : | | |
| 10) Personal History | : | | |
| 11) Family History | : | | |
| 12) Treatment History | : | | |

13) General Physical Examination

Pallor	present/absent
Icterus	present/absent
Clubbing	present/absent
Generalized Lymphadenopathy	present/absent
Anasarca	present/absent
Built	Poor/Average /Well
Nourishment	Poor / Average /Well

Ophthalmic examination: Vitals:-

PR	:	BP	:
RR	:	Temp	:
Weight	:		

Local examination of Thyroid swelling:

Inspection:

Number	:	Diffuse/Nodular	:
Site	:	Shape	:
Size	:	Border	:
Others	:		

Palpation:

Consistency :

Local rise of temperature:

Tenderness :

Adjacent structures :

Lymph node examination:

Systemic Examination:

- i. Respiratory System**
- ii. Cardiovascular System**
- iii. Central Nervous System**
- iv. Per abdomen examination**

Provisional Diagnosis:

Investigations:

Heamatological examination:

Thyroid function tests:

Ultrasonography:

Cytology:

Aspirate:

Adequacy:

Cellular features:

Cytological Diagnosis:

(Diagnostic category as per Bethesda System)

Histopathological examination:

Macroscopy:

Microscopy:

Final Diagnosis:

**BLDEA'S SHRI B.M.PATIL MEDICAL COLLEGE HOSPITAL AND
RESEARCH CENTRE, BIJAPUR. RESEARCH INFORMED CONSENT
FORM**

**TITLE OF THE PROJECT: DIAGNOSTIC ACCURACY OF BETHESDA
SYSTEM FOR REPORTING THYROID
CYTOPATHOLOGY.**

GUIDE : Dr Surekha U Arakeri MD

P G STUDENT : Dr. Mahesh c Patil M.B.B.S

PURPOSE OF RESEARCH:

I have been informed that the present study will identify the diagnostic accuracy of frozen section in comparison with FNAC and histopathology in thyroid lesions.

PROCEDURE:

I understand that after having obtained a detailed clinical history and thorough clinical examination will be done. Fine needle aspiration cytology, frozen section and histopathological examination will be performed in all the patients with thyroid lesions.

RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomforts during the specimen examination or during FNAC. This is mainly the result of my condition and the procedures of this study are not expected to exaggerate these feelings which are associated with the usual course of treatment.

BENEFITS:

I understand that my participation in the study will have no direct benefit to me other than the potential benefit of the treatment.

CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of hospital records and will be subject to the confidentiality. Information of sensitive personal nature will not be part of the medical record, but will be stored in the investigations research file.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving the permission.

REQUEST FOR MORE INFORMATION :

I understand that I may ask more questions about the study at anytime Dr. Mahesh C Patil at the Department of Pathology is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr. Mahesh C Patil may terminate my participation in the study after he has explained the reasons for doing so.

INJURY STATEMENT :

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me. But, no further compensation would be provided by the hospital. I understand that by my agreements to participate in this study and not waiving any of my legal rights.

I have explained to _____ the
Purpose of the research, the procedures required and the possible risks to the best of
my ability.

Dr. Mahesh C Patil
(Investigator)

Date

STUDY SUBJECT CONSENT STATEMENT:

I confirm that Dr. Mahesh C Patil has explained to me the purpose of research, the study procedure, that I will undergo and the possible discomforts as well as benefits that I may experience in my own language. I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give consent to participate as a subject in this research project.

(Participant)

Date

(Witness to signature)

Date

MASTER CHART

Sl.No	Name	Age /Sex	Cyto No	FNAC Diagnosis	Histopathological Diagnosis	Histtopathologi cal No	Clinical presentation
1	Savitri	32/F	1351/11	Colliod goitre	MNG	1972/11	Painless thyroid enlargment sine 4 month
2	Rahul	20/F	491/11	Multinodular goitre	MNG	1811/11	Swelling in front of neck since 2 years
3	Padmavati	30/F	1441/11	Suspicious for malignancy	Follicular carcinoma	2723/11	Diffuse swelling in front of neck since 1 yrs
4	Bagawwa	26/F	1363/11	Cystic nodule	MNG	1511/11	Nodular swelling in front of neck one since 1 year
5	Raja	20/M	1201/11	MNG	MNG	3984/11	Swelling in front of neck since 2 years
6	Sureshgoud	53/M	1173/11	Benign thyroid nodule		-	Swelling in front of neck since 30 days
7	Arachana	11/F	1054/11	BTL (Lymphocytic thyroiditis)		-	Diffuse thyromegaly
8	Bhimawwa	55/F	927/11	Suspicious for malignancy	Follicular ca of thyroid	1632/11	Large thyroid swelling / small mobile spherical
9	Renuka	25/F	97/11	MNG		-	Swelling in front of neck since 30 days
10	Sujatha	29/F	1485/11	Nodular goitre	Multinodular goitre	2649/11	Swelling in front of neck since 30 days

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11	Savitri	32/F	1397/11	Colloid goiter	Mullti nodular Goiter	2066/12	Swelling in front of neck since 2 months
12	Putalabai	60/F	1596/11	Colloid goitrer	Colloid goitrer	3005/11	Cystic swelling in front of neck
13	Iranna	72/M	1886/11	D/D 1) Anaplastic ca 2) Poorly differentiated	Chemotherapy	-	Large swelling measuring 12X10 cm and it extends
14	Mahadevi	35/F	620/12	Follicular Neeplasm/SFN	-	-	Swelling in front of neck june 2 months
15	Nagappa	55/M	1318/11	Benign thyroid nodule S/o Adenomatoid goiter	-	-	Diffuse Enlargement of thyroid since 2 months
16	Sangappa	45/M	1295/11	Colliod cystic nodule	-	-	Cystic swelling in front of neck
17	Dundubai	40/F	1249/12	MNG	-	-	Nodular swelling in front of neck one since 2 months
18	Girijabai	35/F	1278/12	MNG	-	-	Diffuse Enlargement of thyroid since 2 months
19	Layamma	42/F	1283/12	MNG	-	-	Swelling in front of neck since 2 months
20	Sabawwa	35/F	797/12	Suspicious for malignancy	-	1732/12	Swelling in front of neck measuring 5X4cm
21	Irappa	55/M	903/12	Nodular goiter	-	-	Nodular swelling in front of neck one since 2 months
22	Gwappa	45/M	705/12	Nodular goiter	MNG	-	Nodular swelling in front of neck one since 2 months

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23	Sandeep	38/M	703/12	Collid cystic nodule		-	Cystic swelling in front of neck
24	Shridevi	23/F	1250/11	Benign thyroid nodule S/o Adenomatoid goiter		-	Swelling in front of neck since 20 days
25	S.K. Biradar	53/M	1173/11	Colloid cyst		-	Cystic swelling in front of neck
26	Gowry	65/F	1326/12	Unsatisfactory smear	MNG with cystic change	-	Cystic swelling in front of neck since 1 months
27	Ramu	50/M	1826/11	Suspicious for malignancy		-	Painless thyroid enlargement since 2 yrs
28	Shxarnamma	35/F	1642/11	Lymphocytic thyroiditis	-	-	Difuse painless enlargement of thyroid since
29	Laxmibai	60/F	2540/11	Colloid goiter		-	Swelling in front of neck since 2 months
30	Nirmaladevi	40/F	1243/12	Hashimotos thyroiditis	Hashiomotos thyroiditis	2364/12	Nodular swelling in front of neck one since 1 year
31	Mahendra	46/F	2004/12	Benign thyroid nodule S/o Adenomatoid goiter	-	-	Swelling in front of neck since 2 months
32	Ramabai	51/F	2319/11	Benign thyroid nodule S/o Adenomatoid goiter	-	-	Swelling in front of neck since 2 months
33	Ningappa	50/M	1239/12	BTC suggestive of Nodular goiter	Cystic Nodular Goiter	2289/11	Cystic swelling in front of neck since 1 months
34	Rachbai	40/F	1536/12	MNG	MNG	350/12	Painless thyroid enlargement since 4 months

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35	Mallamma	26/F	1823/12	BTL S/O Hashimoto thyroiditis	Hashimotos thyroiditis	426/12	Diffuse painless enlargement of thyroid since
36	Maharaj	43/M	1276/12	BTL (Lymphocytic thyroiditis)			Nodular swelling in front of neck one since 1 year
37	Durgabai	34/	432/12	Benign thyroid nodule S/o Adenomatoid goiter	MNG	3426/12	Swelling in front of neck since 2 months
38	Sunita	35/F	1934/12	Follicular neoplasm/ Suspicious for F.N	Follucular variant of papillary ca	2096/12	Swelling in front of neck since 2 yrs
39	Laxmi	30/F	1467/11	Benign thyroid lesion			Swelling in front of neck since 2 months
40	Malati Patil	32/F	1289/12	Benign Follicular lesion S/O Nodular Goiter	MNG with Secondary change	492/12	Thyroid enlargement since 4 months
41	Vijay Patil	40/F	1349/12	Benign follicular lesion suggestive of colloid			Difuse painless enlargement of thyroid since
42	Chanamma	44/F	835/12	Atypia oF undetermined signiicance (AUS)	MNG with Adenomatoid hyperplasia	2582/12	Swelling in front of Neck since 8 months
43	Sujatha	29/F	1145/11	Follicular Neoplasm/adenoma	Follucular adenomous hyperplasia with extensive	2640/11	Difuse painless enlargement of thyroid since
44	Sangayya	25/M	1982/12	Hashimotos thyroiditis	Hashimotos thyroiditis	1069/11	Painlers thyroid enlargement since 4 months
45	Rupa	38/F	1892/11	Follicular neoplasm/ Suspicious for F.N	Follucular Ca	718/12	Swelling in front of Neck since 1 year
46	Chandani	56/F	1098/12	Nodular goiter			Diffuse painless enlargement of thyroid since

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47	Kallappa	45/M	1361/11	Malignant follicular carcinoma	Malignant follicular carcinoma with metastatic deposits over	2582/11	Swelling in front of Neck since 1 year and swelling In
48	Laxmibai	42/F	460/11	Unsatisfactory smear	-	-	Cystic swelling measuring 2X2 cm in front of neck
49	Jakamma	45/F	1896/11	Unsatisfactory	MNG	-	Cystic swelling in front of neck since 1 months
50	Neeldwar	60/F	1562/11	Benign thyroid nodule S/o Adenomatoid goiter	Nodular Goiter	7157/11	Swelling in front of Neck since 11 months
51	Gemappa	45/M	1672/11	Nodular goiter	MNG	1077/12	Swelling in front of Neck since 1 year
52	Basamma	60/F	1209/12	Unsatisfactory smear	MNG with cystic change	1000/12	Diffuse thyroid enlargement
53	Shunikala	35/F	1562/11	Unsatisfactory smear	MNG with cystic change	2962/12	Nodular thyroid enlargement which moves
54	Ambabai	64/F	172/12	Hashimotos thyroiditis	-	-	Swelling in front of Neck since 2 months with fever
55	Rana	25/F	147/11	Malignant follicular carcinoma	Encapsulated variant of medullary of thyroid	717/12	Diffuse painless enlargement of thyroid since
56	Shivakumar	31/M	618/12	Unsatisfactory	MNG	1000/12	Cystic swelling in front of neck since 1 months
57	Mahadevamma	45/F	1220/12	Follicular Neoplasm/ Suspicious for F.N	-	-	Thyroid Swelling since 1 yr
58	S.M. Maddu	22/F	659/12	Hashimotos thyroiditis	-	-	Swelling in front of Neck since 2 months with fever

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59	Murluja	52/F	1150/12	Follicular neoplasm/ Suspicious for F.N	-	-	Hard Swelling in front of neck since 1 yr
60	Jarabai	48/F	1416/12	Colloid goiter		-	Cystic swelling in front of neck since 1 months
61	Hulagamma	30/F	1134/12	Benign thyroid lesion		2531/12	Nodular swelling in front of neck one since 1 year
62	Amulabai	48/F	1965/12	Benign follicular lesion S/O colloid goiter		-	Nodular swelling in front of neck one since 1 year
63	Lagamavva	40/F	1231/12	Benign thyroid nodule S/O Adenomatoid goiter			Swelling in front of neck since 2 months
64	Shivakumar	31/M	618/12	Benign follicular lesion S/O colloid goiter		-	Nodular swelling in front of neck one since 1 year
65	S.B. Patil	48/M	1256/12	Benign follicular lesion S/O colloid goiter		-	Thyroid enlargement since 2 months with associated
66	Reinabai	48/F	1410/12	Benign thyroid nodule S/O Adenomatoid goiter	MNG	3039/11	Swelling in front of neck since 2 months
67	Sobawwa	28/F	1802/12	Benign thyroid Lesion		-	Nodular thyroid enlargement which moves
68	Raja	20/M	564/12	Benign Follicular lesion S/O Nodular Goiter	MNG	3934/12	Painless thyroid enlargement since 4 month
69	Revabai	45/F	1876/12	MNG	MNG with cystic change	4287/12	Swelling in front of Neck since 1 year
70	Induabai	40/F	896/12	MNG			Swelling in front of Neck since 6 months

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71	Awamma	43/F	1493/12	Benign Follicular lesion S/O Nodular Goiter	MNG	1118/12	Diffuse painless enlargement of thyroid since
72	Chandvati kubar	20/F	1796/12	Colloid goiter	-	-	Thyroid enlargement since 2 months with associated
73	Maharaj	42/M	1732/12	Benign Follicular lesion S/O Nodular Goiter	-	-	Diffuse painless enlargement of thyroid since
74	Rukumabai	26/F	1981/12	MNG	MNG with secondary change	-	Nodular thyroid enlargement which moves
75	Sunanda	22/F	2091/12	Benign Follicular lesion S/O Nodular Goiter	Nodular goiter	1337/12	Painless thyroid enlargement since 4 months
76	Suresh Pralal	53/M	1323/11	Benign Follicular lesion S/O Nodular Goiter	Nodular goitre	-	Swelling in front of neck since 2 months
77	Geeta	32/F	134/12	Benign thyroid Lesion	MNG	1108/12	Painless thyroid enlargement since 4 months
78	Gurabai	50/F	296/12	Benign Follicular lesion S/oMNG	MNG	396/11	Swelling in front of neck since 2 years
79	Savarwalhi	33/F	928/11	Benign Follicular lesion S/oMNG	MNG	1303/11	Diffuse painless enlargement of thyroid since
80	Radhika	35/F	2311/11	Benign thyroid nodule S/o Adenomatoid goiter	MNG	1932/11	Thyroid enlargement since 2 months with associated
81	Paramamma	45/M	762/11	Cyst lesion	Thyro glossal cyst	697/11	Swelling in front of neck since 2 months
82	Chandabai	56/M	3491/11	MNG	MNG	4845/11	Swelling in front of Neck since 2 months with fever

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83	Sangayya	25/M	2431/12	Hashimotos thyroiditis	Hashimotos thyroiditis	1069/11	Diffuse thyroid enlargement since 4 months
84	Anuhalkar Nulla	48/F	172/11	Hashimotos thyroiditis	MNG	4399/11	Swelling in front of Neck since 2 months with fever
85	Shushail	17/M	1774/11	Unsatisfactory smear		-	C/o Enlargement of neck since 1 year
86	Gwappa	19/M	704/12	Benign Follicular lesion S/oMNG	-	-	Nodular thyroid enlargement which moves
87	Chayagan Kan	48/F	584/12	Subacute thyroiditis	-	-	Swelling in the front of neck measuring 3x3cm 2 months
88	Venu Joshi	30/F	1154/12	Benign follicular lesion S/O colloid goiter	MNG	1932/12	C/o diffuse Enlargement of neck 8 months
89	Heranhashi	50/F	1052/12	Benign follicular lesion S/O colloid goiter	-	-	Diffuse thyroid enlargement since 4 months
90	Anuya	47/F	473/12	Benign Follicular lesion S/oHashimotos	Hashimotos thyroiditis	1482/12	C/o Enlargement of neck since 1 year
91	Basanagoud	60/F	474/12	Hashimotos thyroiditis	Hashimotos thyroiditis	1672/12	C/o diffuse Enlargement of neck 8 months
92	Devamma	60/F	446/12	Benign follicular lesion S/O colloid goiter	MNG	1982/12	Diffuse thyroid enlargement since 4 months
93	Neelamma	55/F	264/12	Benign follicular lesion S/O colloid goiter	MNG	1922/12	Nodular swelling in front of neck one since 1 year
94	Sugamma	60/F	474/12	Hashimotos thyroiditis		-	C/o diffuse Enlargement of neck 8 months

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95	Geushabhi	30/F	1225/12	Unsatisfactory smear		-	C/o Swelling in the neck since 2 months
96	Suravu	22/F	928/12	Unsatisfactory smear		-	Diffuse thyroid enlargement
98	Hema	25/F	964/12	Benign follicular lesion S/O colloid goiter	MNG	1822/12	Diffuse thyroid enlargement since 4 months
99	Laxmi	30/F	1015/12	Benign follicular lesion S/O colloid goiter	MNG	1822/12	Nodular swelling in front of neck one since 1 year
100	Ramabai	51/F	1278/12	Benign follicular lesion S/O Nodular goiter	MNG	1589/12	Diffuse thyroid enlargement
101	Kaveri	30/F	2689/11	MNG	MNG with cystic change	711/12	Nodular swelling in front of neck one since 8 months
102	Sunanda	32/F	467/11	Unsatisfactory smear		2910/12	Cystic swelling in front of neck since 1 months
103	Iramma	29/F	2635/10	Adenomatoid Hyperplasia of thyroid	Adenomatoid Hyperplasia of thyroid	1420/10	Diffuse painless enlargement of thyroid since
104	S.Shobha	21/F	2666/10	Benign follicular lesion suggestive of colloid	MNG	1589/12	Diffuse thyroid enlargement since 6 months
105	Razeya	37/F	2754/10	Hashimotos thyroiditis	Hashimotos thyroiditis	711/12	Diffuse thyroid enlargement
106	Amenabai Sangan	40/F	758/11	Adenomatoid goiter	Adenomatoid goitre	1321/11	Nodular swelling in front of neck one since 1 year