

## **A Prospective Comparative Study Of Fine Needle Aspiration Cytology And Histopathology In Thyroid Disorders**

**Dr. Shampa Mishra<sup>1</sup>, Dr. Nilam U. Sathe<sup>2</sup>, Dr. Kamini Chavan<sup>1</sup>, Dr. Pravin Misal<sup>1</sup>**

<sup>1</sup>Senior Resident, Dept of ENT and Head – Neck Surgery, Seth G. S. Medical College and KEM Hospital. Parel. Mumbai - 400 012.

<sup>2</sup>Associate Professor, Dept of ENT and Head – Neck Surgery, Seth G. S. Medical College and KEM Hospital. Parel. Mumbai - 400 012.

### ARTICLE INFO

#### Article History:

Received on 18<sup>th</sup> Sept 2019  
Peer Reviewed on 29<sup>th</sup> Sept 2019  
Revised on 14<sup>th</sup> October 2019  
Published on 28<sup>th</sup> October 2019

#### Keywords:

fine needle aspiration cytology;  
histopathology; thyroid disorders

### ABSTRACT

**Introduction-** Fine needle aspiration cytology is generally recognized as an effective first-line investigation in the evaluation of a thyroid swelling. It is technically easy to perform procedure that provides specific diagnosis rapidly with minimal complications. The correlation of FNAC with histopathology is necessary before starting treatment.

**Material and Methods-** This study was conducted as a prospective study in 30 cases. It consisted of patients presenting with anterior neck swelling. A thorough history and physical examination of the patient was conducted. Once FNAC category for the patients established according to Bethesda, treatment was carried out in the form of surgery, considering other risk factors. An adequately and correctly grossed specimen provides information which helps to stage the tumor and also helps with prognosis.

**Conclusion-** FNAC is sensitive, specific, cheap, easy to perform, cost effective procedure with minimal side effects. Correct reporting of FNAC is important as false positive & false negative rates are high. Benign disorders are over treated. Quality assurance of FNAC is crucial as it helps in the final diagnosis and planning further management of the patient.

Br J Bio Med Res Copyright©2019, **Shampa Mishra** et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material for any purpose, even commercially, provided the original work is properly cited and states its license.

**Corresponding Author:** *Dr. Nilam U. Sathe Associate Professor, Dept of ENT and Head – Neck Surgery, Seth G. S. Medical College and KEM Hospital. Parel. Mumbai - 400 012*

## INTRODUCTION

The thyroid gland derives its name from the Greek *thyreos* or Shield whereas thyroid enlargement or Goitre is derived from the Latin term gutter which means throat. A normal thyroid gland weighs 15-25 g<sup>1</sup>. The thyroid gland itself is not necessary for life but low levels of thyroid hormone (hypothyroidism) can cause severe mental and physical impairment and disability.<sup>2</sup>

Of all the endocrine glands, thyroid gland is unique because it is the largest, superficial and only one amenable to physical examination. It is affected by a vast array of developmental, inflammatory, hyperplastic and neoplastic disorders. The patients presenting with thyroid swellings are investigated with thyroid function tests, USG (ultrasonography) and FNAC (Fine needle aspiration cytology).

The most widely used form of imaging for thyroid swellings is ultrasonography which has many favorable features including detection of non palpable nodules, estimation of nodule size and guidance of FNAC. Some ultrasonographic characteristics such as hypoechogenicity, solid nodules, microcalcifications, irregular margins, vascularity, local lymph node invasion or regional lymphadenopathy are associated with increased risk.<sup>3</sup> The drawback of ultrasound is that it may reveal thyroid swellings that are not clinically relevant and risks a cascade of unnecessary investigations, intervention and anxiety when used indiscriminately.<sup>1</sup>

Fine needle aspiration cytology (FNAC) is generally recognized as an effective first-line investigation in the evaluation of a thyroid swelling. It is a cost effective, sensitive, less demanding, technically easy to perform procedure that provides specific diagnosis rapidly with minimal complications.<sup>1</sup> Several national and international studies have documented the sensitivity of FNAC in thyroid nodules to range from 65-98% and specificity from 72-100%.<sup>4</sup>

The main aim of thyroid surgery is to provide complete surgical management in a single step and improve quality of life of the patient. If a benign diagnosis on FNAC for a patient

operated with hemithyroidectomy comes as malignant on histopathology post surgery, patient has to undergo completion thyroidectomy. There is an increased risk of bilateral recurrent laryngeal nerve palsy, permanent hypoparathyroidism, hypocalcemia etc. associated with the surgery. Whereas when a malignant diagnosis on FNAC comes as benign on histopathology, patient has been unnecessarily exposed to the risks and complications associated with total thyroidectomy.

Hence, the purpose of the present study is to correlate the fine needle aspiration cytology findings with histopathology of excised specimens and to evaluate the accuracy, sensitivity and specificity of both in patient management.

Fine-needle aspiration (FNA) cytology is the study of cells obtained by puncturing organs of human body with the use of small-gauge needle.<sup>6</sup> The process of aspiration cytology involves the puncture of the lesion with the use of a fine needle (22-gauge needle) of various lengths (from 5 cm to 20 cm) with external diameters between 0.6 mm and 1.0 mm. The history of the technique needle cytology spans a period of over 10 centuries, whereas FNAC has undergone a great deal of improvements during the last century.<sup>7</sup>

But, the first report on the use of fine, 22-gauge needle should be attributed to Manheim. The elaboration of FNA by the Swedish school in the forthcoming years was crucial for the establishment of the technique and its world-wide acceptance.

The expansion of FNAC in primary diagnosis of tumors in the last 30 years or so has been impressive. It has also been used for the diagnosis of inflammatory, infectious and other pathologies. The interpretation of FNAC by an experienced cytopathologist has had a major impact in the management of nodular thyroid disease. It is a safe, cheap and reliable investigation and, along with FT4 (Free Thyroxine), thyroid stimulating hormone (TSH), serum calcium and thyroid antibody

levels together with an ultrasound scan should encompass the primary investigations in the management of thyroid nodules.

FNAC plays 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 triages patients with thyroid cancer to appropriate surgery.

It is critical that cytopathologists 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. To address terminology and other issues related to thyroid FNA, the National Cancer Institute (NCI) hosted the "NCI Thyroid Fine Needle Aspiration State of the Science Conference." The meeting was organized by Doctor Andrea Abati, and took place on October 22 and 23, 2007, in Bethesda<sup>8</sup>. The conclusions formed the framework for The Bethesda System for

Reporting Thyroid Cytopathology. A uniform reporting system for thyroid FNA facilitates effective communication among cytopathologists, endocrinologists, surgeons, radiologists, and other health care providers; facilitate cytologic-histologic correlation for thyroid diseases; facilitate research into the epidemiology, molecular biology, pathology, and diagnosis of thyroid diseases, particularly neoplasia; and allow easy and reliable sharing of data from different laboratories for national and international collaborative studies.

For clarity of communication, TBSRTC (The Bethesda System for Reporting Thyroid Cytopathology) recommends that each report begin with 1 of 6 general diagnostic categories. 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 (or explicit) risk of malignancy on which recommendations for patient management (e.g. annual follow-up, repeated FNA, surgical lobectomy, near total thyroidectomy) can be based.<sup>9, 10</sup>

*Table 1: The Bethesda System for Reporting Thyroid Cytopathology<sup>11</sup>:*

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) /lymphocytic (Hashimoto) thyroiditis/granulomatous (subacute) thyroiditis
III.	Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	
IV.	Follicular Neoplasm or Suspicious for a Follicular Neoplasm	Specify if Hürthle cell (oncocytic) type)
V.	Suspicious for Malignancy	Suspicious for papillary carcinoma/medullary carcinoma /metastatic carcinoma/ lymphoma

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
-----	-----------	---

The Bethesda system is very useful for a standardized system of reporting thyroid cytopathology, improving communication between cytopathologists and clinicians, and inter-laboratory agreement, leading to more consistent management approaches. An additional point which is in favor of the implementation of this system is that the classification is directly related to the risk of malignancy in each category, which in turn, prompts the recommended clinical management of that category, thus truly embodying the clinico-pathological correlation in its true spirit. The correlation of FNAC with histopathology is necessary before starting treatment.<sup>8, 11</sup>

The aspiration can be guided either by palpation or Ultrasound. The benefits of palpation guidance include its reduced cost and logistical efficiency. Ultrasound guidance permits the operator to be certain that the nodule of interest is aspirated. It reduces the number of unsatisfactory FNAs, and improves accuracy. For these reasons, ultrasound guidance is preferred for nonpalpable nodules, nodules that have a significant cystic component (>25%), and nodules that were previously aspirated and yielded an unsatisfactory sample.

## MATERIALS AND METHODS

This study was conducted as a prospective study. The subjects for this study consisted of patients presenting to our Otorhinolaryngology Out Patient Department with anterior neck swelling. A thorough history and physical examination of the patient was conducted. Physical examination was done by palpation. A laryngeal examination was done to exclude vocal cord paralysis as it suggests a malignant process with involvement of the recurrent

laryngeal nerve. Proximal trachea inspected for possible compression or intraluminal extension of a neoplasm. Careful and systematic history and examination may reveal features that are suggestive of malignancy. This is of paramount importance when other diagnostic tests are equivocal or inconclusive, because the decision to proceed with surgery may be based solely on risk factors.

**Sample size: 30**

**Duration of study: 18 months**

### Inclusion criteria:

- Age 20 to 60 Years
- Patients presenting with thyroid swelling confirmed by palpation
- Patients with recurrent thyroid swelling after previous surgery
- Patients with clinically detected thyroid swelling with normal thyroid function tests

### Exclusion criteria:

- Pregnancy
- Lactation
- Patients < 20 years of age >65 years of age
- Hyperthyroidism, hypothyroidism, thyroiditis requiring medical management
- Patients with abnormal thyroid function tests (deranged TSH, T3, and T4)

After this, patients are subjected to FNAC and imaging modalities like ultrasound. Ultrasound is performed with high frequency transducers (**7-13 MHz**) and can detect solid nodules of 3 mm to 4 mm and cystic nodules of 2 mm in diameter.

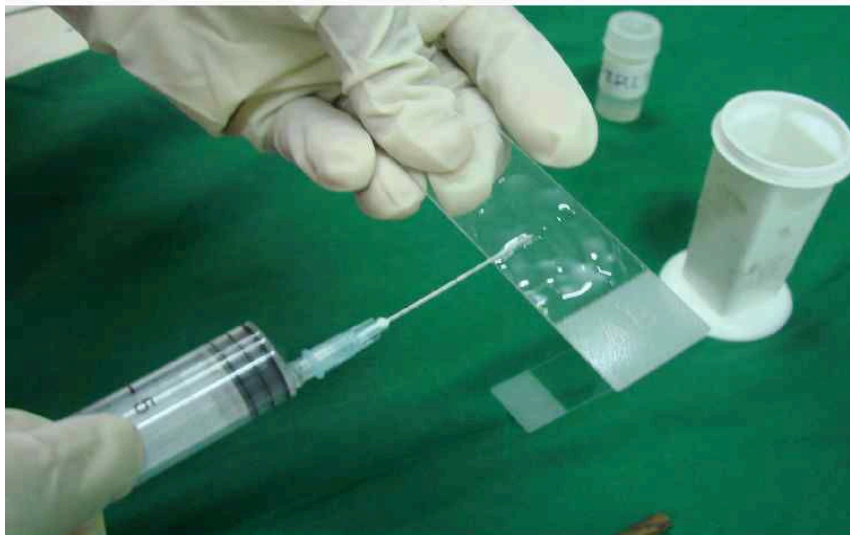
The FNAC technique involves use of a fine (25-27 gauge needle) as thyroid gland is vascular.

Aspiration can be performed with or without suction applied by a syringe. Local anesthesia by subcutaneous lignocaine is optional. The skin is wiped clean with an alcohol swab. The dwell time of each pass should be short, 2 to 5 seconds in most cases, with rapid back and forth oscillations of the needle (3 per second) within the nodule. If suction is used, it should be released before the needle is withdrawn from the nodule. The number of passes needed to

ensure adequacy varies. Mostly between 2 to 5 passes for each nodule. Aspiration is done. The agreed criterion for adequate sampling is that samples from solid lesions should contain at least 6 groups of thyroid follicular epithelial cells across all the submitted slides, each composed of at least 10 well visualized epithelial cells. Slides are prepared by expelling and smearing cells on a slide. Smears are alcohol fixed and papanicolaou stained.



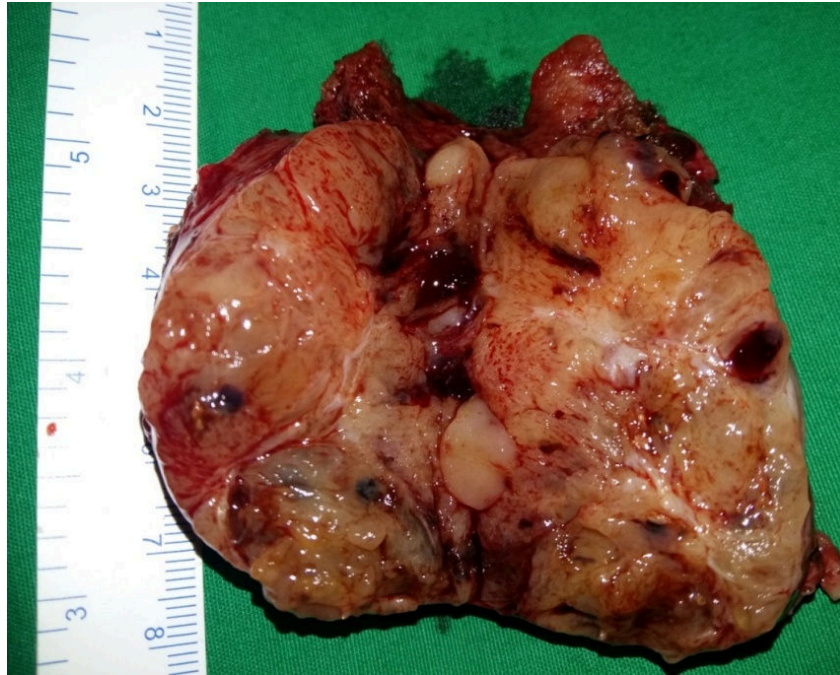
*Fig 1: FNAC being performed in a patient with thyroid nodule*



*Fig 2: Preparation of a cytology slide after FNAC*

**Evaluation of the specimen:** This begins with a review of the slides under microscope. Most benign follicular nodules are sparsely cellular, consisting of predominantly colloid. Once FNAC category for the patients established

according to Bethesda, treatment was carried out for them in the form of hemi or total thyroidectomy, considering other risk factors as well.



*Fig 3: Cut open specimen: Left Hemithyroidectomy, showing focal areas of hemorrhage*

If enlarged lymph nodes are present intraoperatively or on ultrasound examination, the lymph node is sent for frozen section, if reported as malignant, modified radical neck

dissection is done on the same side or bilaterally depending on the disease/risk factors.



*Fig 4: Right supraclavicular lymph node with cystic changes in case of papillary carcinoma thyroid*

**Total thyroidectomy** involves similar procedure as hemithyroidectomy being carried out on the other side. It requires life-long thyroxin therapy and has a potential for bilateral vocal cord paralysis and permanent

hypocalcaemia. However, if performed in a meticulous fashion with the knowledge of the altered surgical anatomy, the risks to the recurrent laryngeal nerves and parathyroid glands can be kept to a minimum.

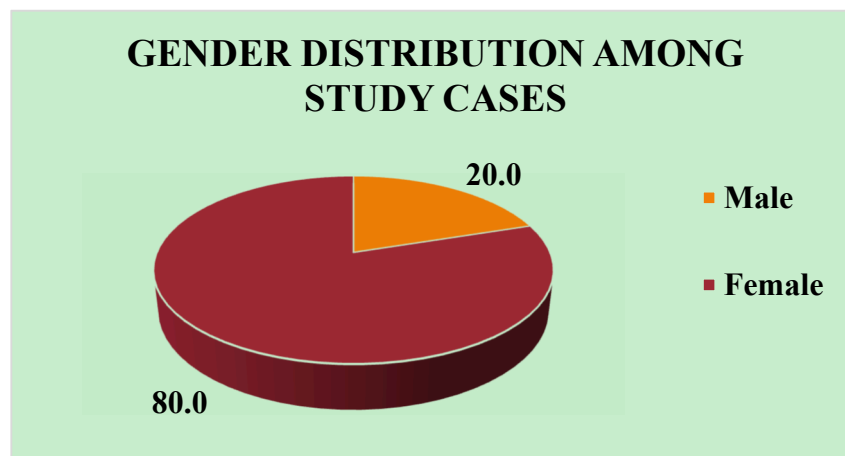
**HISTOPATHOLOGY:**

Grossing is the first basic step in surgical pathology. An adequately and correctly grossed specimen provides information which helps to stage the tumor and also helps with prognosis. Good fixation of tissues is a prerequisite for anatomic pathology studies. Formalin is the fixative used. The thyroidectomy specimens are oriented using sutures, ink or clips. Small specimens are fixed after noting all gross features namely size, shape, color, consistency, hemorrhage, necrosis etc. Big thyroid resections are preliminarily examined for the salient features, then inked and blotted dry. (Inking is essential to document extent of lesion and status of inked margin) The gland is then cut open for fixation. Large specimens have to be sliced in a regular manner taking care to avoid distortion. To facilitate penetration by formalin and prevent autolysis of contiguous tumor slices it is essential that wads of formalin soaked gauze or cotton wool are neatly packed between the slices of tissue. Small specimens are fixed for 4 to 6 hours, whereas big specimens are fixed for 8-12 hours. Margins are appropriately named and inked according to

anatomy e.g. Anterior, posterior, anterolateral, medial etc. Then the specimen is thoroughly examined, describing the findings and subsequently taking appropriate sections. The gross findings should be concise and precise and should include weight, measurements of the specimen, surface, capsule-breached or not, color, consistency, shape or borders, any secondary pathology. On slicing- consistency, appearance of the gland- cystic, papillary, presence of calcifications, necrosis, hemorrhage, circumscription (encapsulated/invasive), presence of extrathyroidal extension. The sections are then submitted for microscopic evaluation. Representative sections should be taken from suspicious nodules; should include capsule of the nodule and adjacent thyroid. Representative sections from isthmus and opposite lobe should also be taken. Lymph nodes should be separately sampled.

**RESULTS**DEMOGRAPHICAL DATA

- Age of the cases were ranging from **17.00 - 65.00** years with **average being 37.40** years.



*Fig 5: Pie chart showing gender distribution among study cases 20.0% of the cases were male and 80.0% of the cases were female.*

**Profile Of Anterior Neck Swelling Among Study Cases** In this analysis, 46.7% of the

cases had Anterior neck swelling at Right lobe followed by 20.0% of the cases had at Left side.

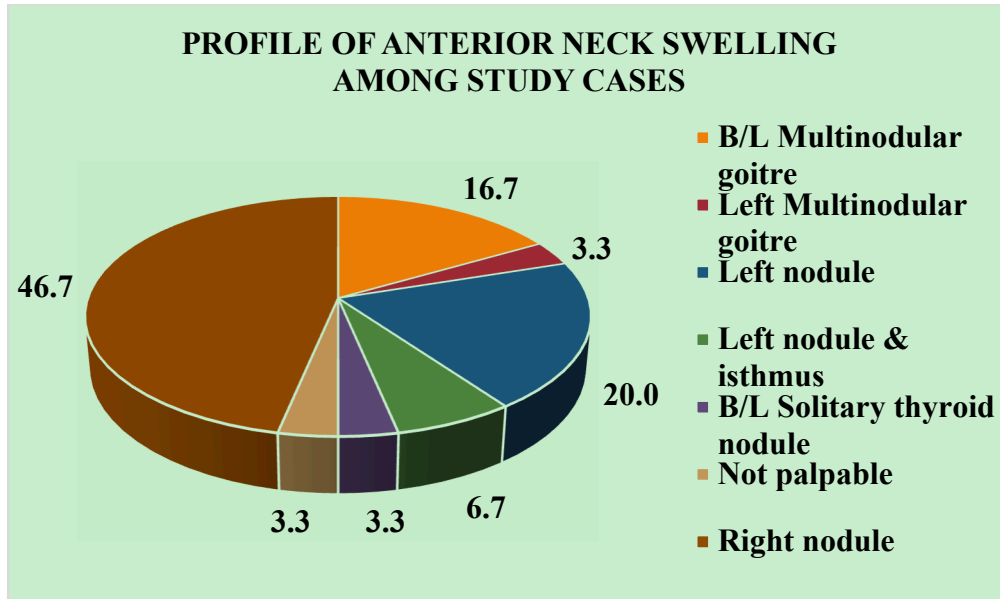


Fig 6: Pie chart showing profile of anterior neck swelling

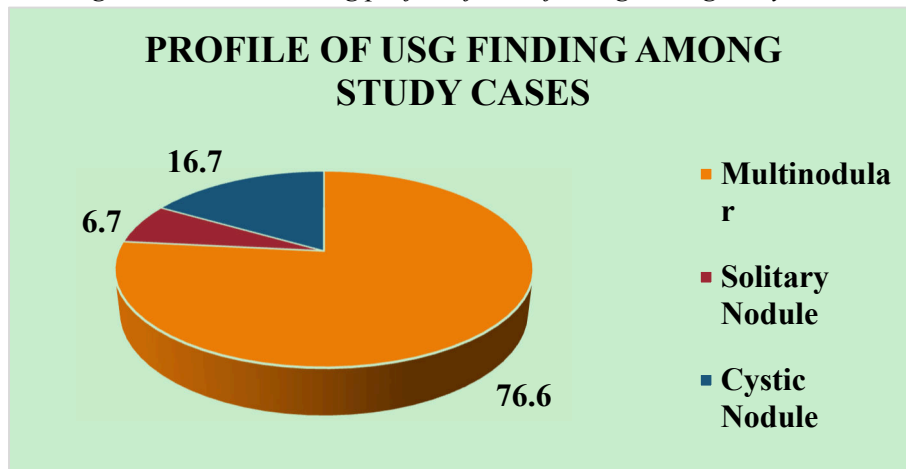
**Profile Of USG Finding Among Study Cases**

This data states that 76.6% of the cases had

Multinodular finding where as 16.7% of the

cases had Cystic nodule

Fig 7: Pie chart showing profile of USG finding among study cases



**Profile Of FNAC Among Study Cases As**

per above data, 36.7% of the cases were

Bethesda category II and 30.0% of the

cases were Bethesda category V on FNAC.

Fig 8: Pie chart showing profile of FNAC (Bethesda Category)

This data states that 60.0% of the cases had FNAC as Malignant and 40.0% of the cases had Benign FNAC.

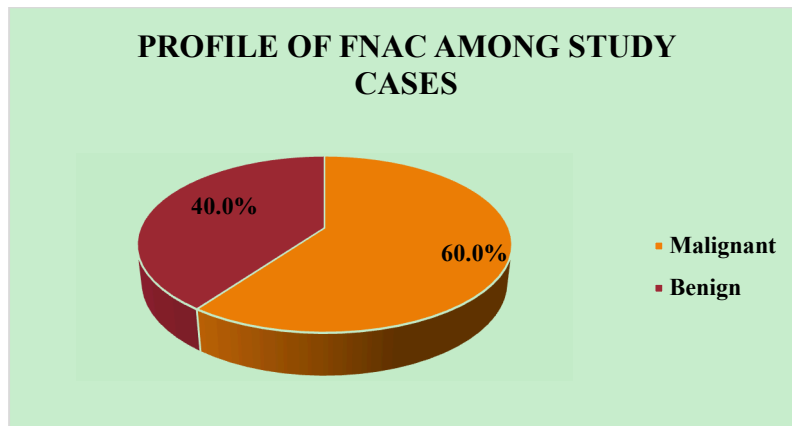


Fig 9: Pie chart showing profile of FNAC among study cases

**Association between FNAC and surgery:**

According to this data, 33.3% of the cases who had Benign FNAC had TT (total

thyroidectomy) surgery which was significantly less as compared to 94.4% of the cases which had Malignant FNAC

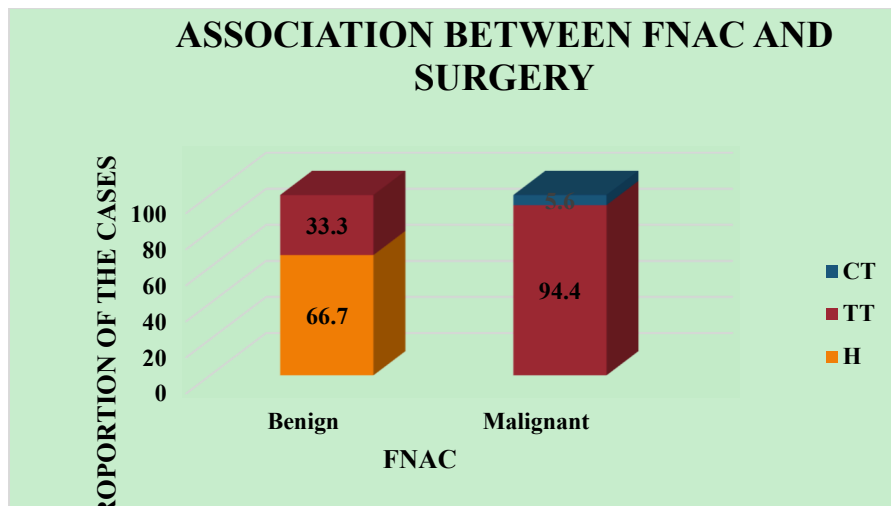


Fig 10: Chart showing association between FNAC (Benign and malignant) and Surgery

94.4% cases with a malignant FNAC diagnosis underwent Total Thyroidectomy. 5.6 % cases underwent a completion thyroidectomy, after being diagnosed as malignant after hemithyroidectomy which was done previously. 66.7% patients with a benign FNAC diagnosis underwent hemithyroidectomy and 33.3% patients with a benign FNAC diagnosis underwent Total Thyroidectomy.

**Association Between FNAC (Bethesda Category) And Surgery:**

\*Significant 100.0% of the cases each of were of category V and VI FNAC had TT (Total Thyroidectomy) surgery which was significantly more as compared to 36.4% and 80.0% of the cases which were of category II and IV FNAC respectively.

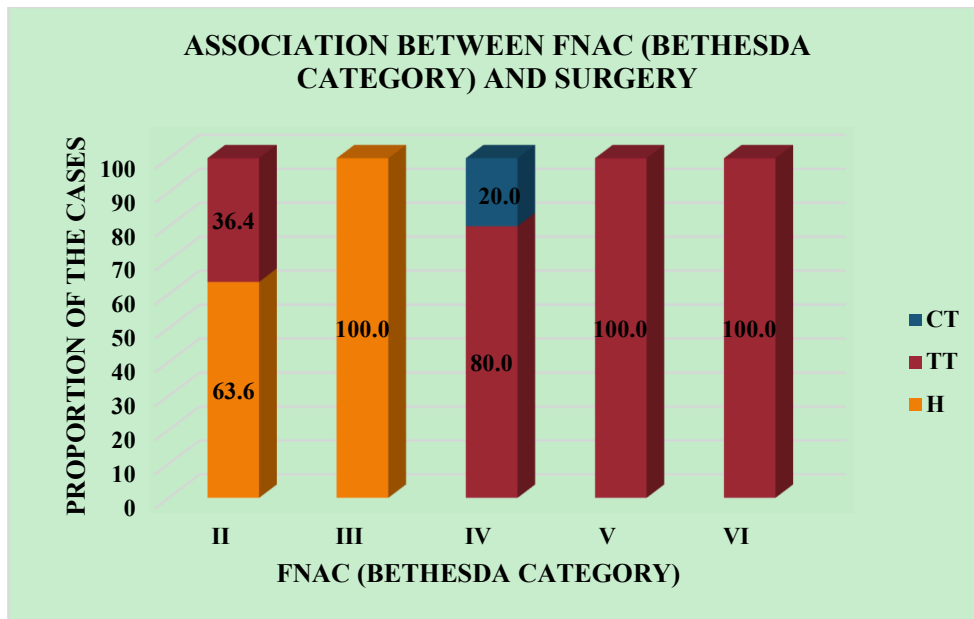


Fig 11: Chart showing association between FNAC (Bethesda Category) and surgery

36.4% of patients of category II (benign) underwent total thyroidectomy. 63.6% of patients of Bethesda category II underwent hemithyroidectomy. All patients of Bethesda category IV, V and VI underwent total thyroidectomy. A patient who underwent

hemithyroidectomy before was diagnosed as malignant on histopathology, so underwent a completion thyroidectomy.

**profile of HPR among study cases** This data states that 50.0% of the cases each had Malignant and Benign HPR.

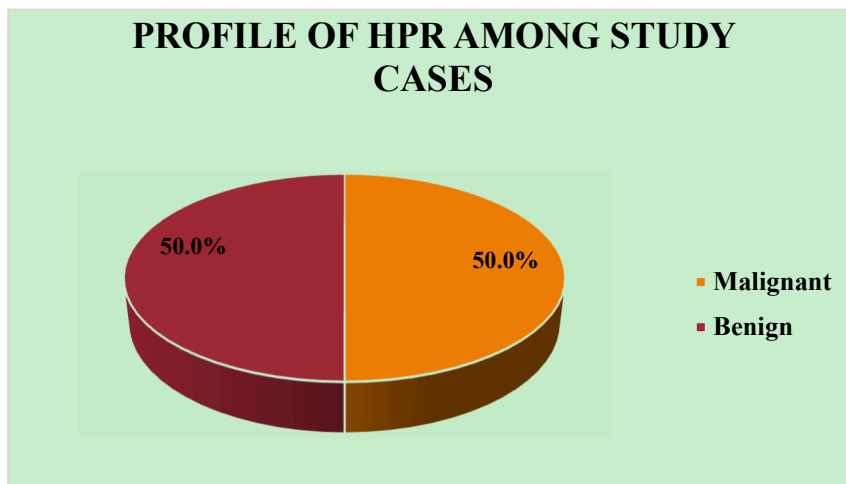


Fig 12: Figure showing Profile of HPR among study cases (benign, malignant)

Table 1: Profile Of HPR According To Bethesda Category

HPR	NO. OF CASES (N = 30)	PERCENTAGE
Follicular Variant of Papillary Carcinoma	09	30%
Nodular Hyperplasia (NH)	06	20%
Papillary Thyroid Carcinoma (PTC)	04	13.33%
Autoimmune (AI) Thyroiditis	03	10%
Goitre with degeneration	02	6.66%

Colloid Cyst	02	6.66%
Follicular Variant of Papillary Microcarcinoma	01	3.33%
Papillary Microcarcinoma	01	3.33%
Multinodular Goitre (MNG)	01	3.33%
Hurthle Cell	01	3.33%

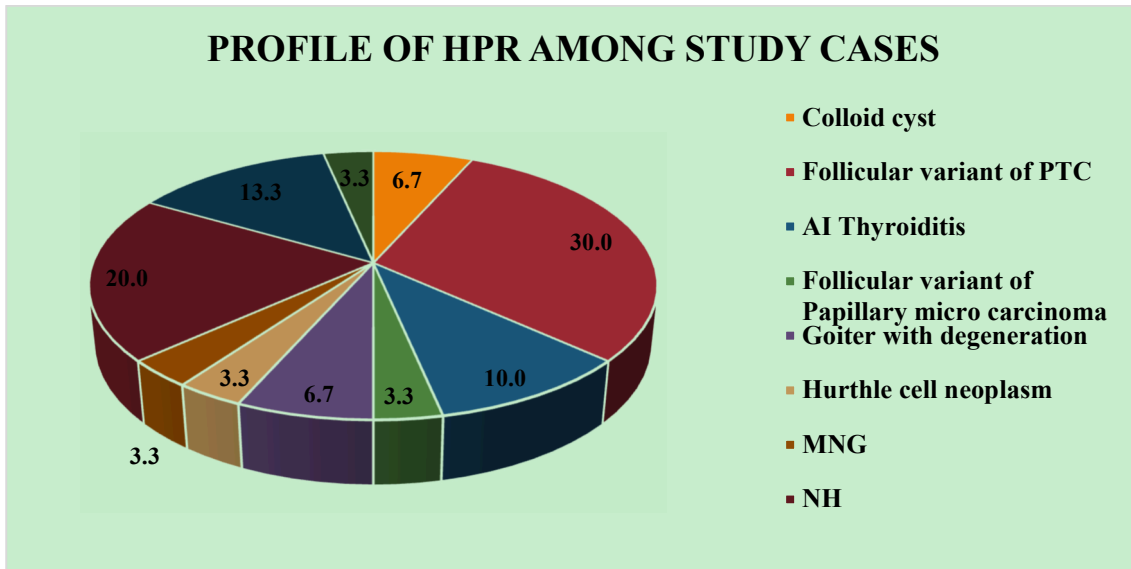


Fig 13: Pie chart showing profile of HPR among study cases

**Association Between HPR And Surgery**

51.2% of the cases which belonged to Benign HPR had TT (total thyroidectomy)

surgery which was significantly less as compared to 81.2% of the cases which belonged to Malignant HPR (histopathology)

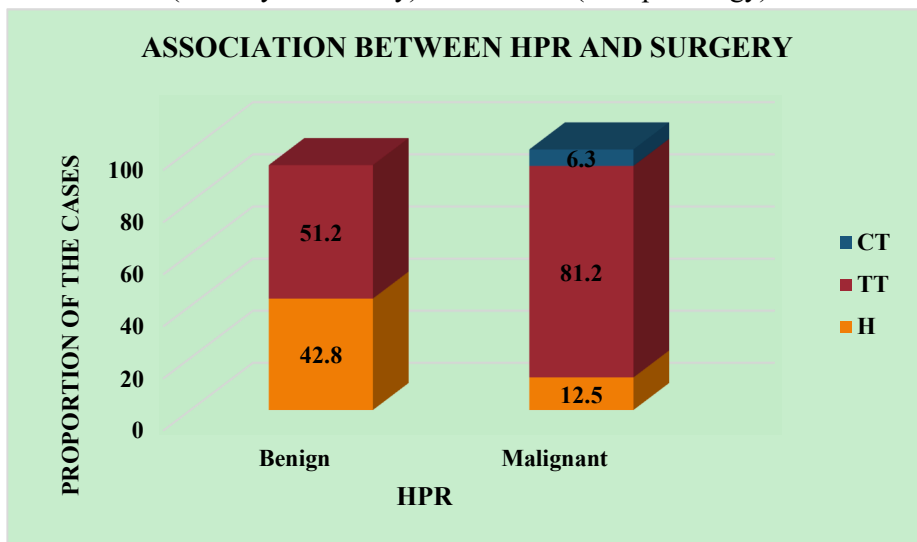


Fig 14: Chart showing association between HPR and surgery

**Association Between FNAC (Bethesda Category) and HPR**

100.0% of the cases which belonged to category IV, V and VI FNAC had HPR Malignant which was significantly more as

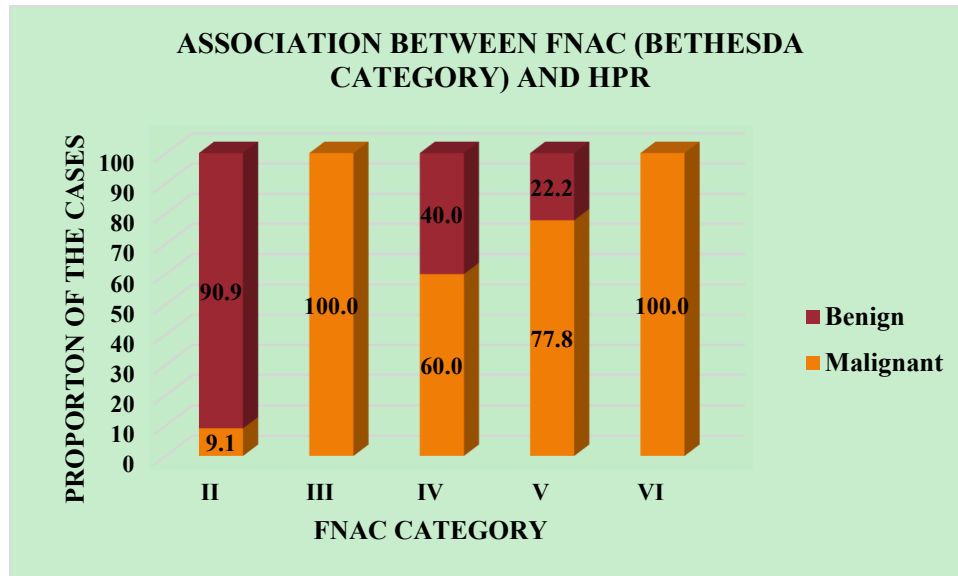
compared to none of the cases which belonged to category II and III FNAC respectively but the difference was not significant.

**Association Between FNAC (Bethesda Category) and HPR**

100.0% of the cases each who belongs to category III and VI FNAC had HPR Malignant which was more as compared

to 60.0% and 77.8% of the cases which belonged to category IV and V FNAC respectively.

*Fig 15: Chart showing association between FNAC (Bethesda category) and benign or malignant on HPR*



90.9% patients of FNAC category II were benign on HPR and 9.1% was malignant.  
 All of patients of FNAC category III and VI were malignant on HPR.  
 40% of patients of FNAC category IV were benign on HPR and 60% were malignant.  
 22.2% of patients of FNAC category V were benign on HPR and 77.8 % were malignant.

*Table 2: validity test of FNAC*

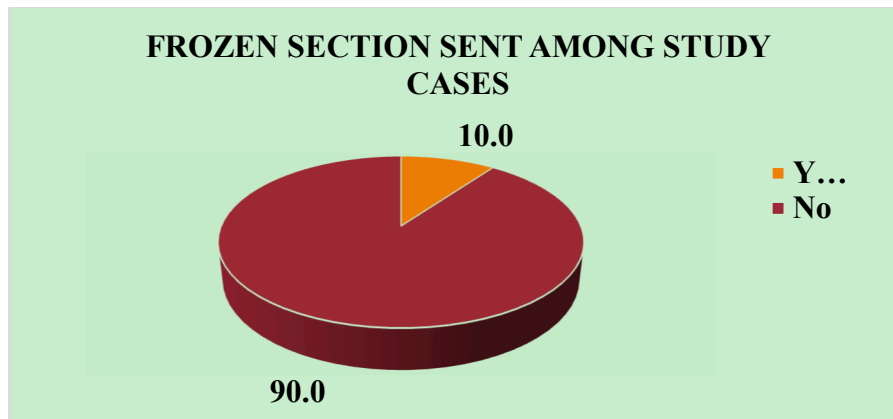
FNAC	HPR		Total
	Malignant	Benign	
Malignant	12	04	16
Benign	01	13	14
Total	13	17	30

*Table 3: Results Of Validity Test:*

Sensitivity:	92.3%
Specificity:	76.5%
Positive Predictive Value	75%
Negative Predictive Value	92.8%
Accuracy:	83.3%

**Frozen section sent among study cases:**

This data states that 10.0% of the cases had Frozen section sent from lymph node.

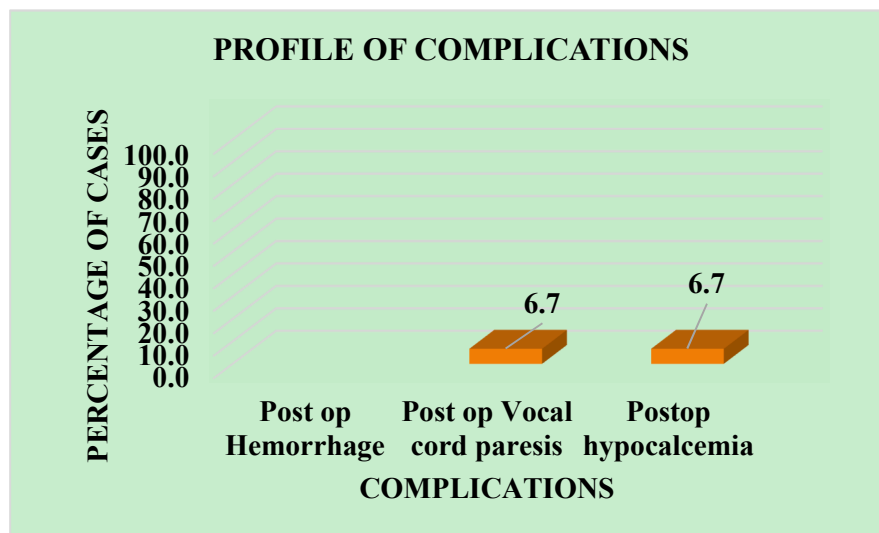


*Fig 16: Pie chart showing comparison between frozen section sent intraoperatively among study cases*

Out of the 2 cases for which frozen section from positive lymph nodes was sent, for one of the case the result came positive for malignancy,

for which type 3 unilateral modified neck dissection was performed.

*Profile of complications:*



*Fig 17: Chart showing profile of complications among study cases*

*Discussion*

Palpable thyroid swelling is a common reason for seeking medical advice all over the world. The majority of thyroid nodules are asymptomatic being four times more common in women than men. Factors that increase risk of malignancy include<sup>1</sup>:

- Previous head and neck irradiation, Rapid growth, Symptoms of compression or invasion such as dysphagia, dysphonia, and hemoptysis, Male sex, Pain, Age younger than 20 or older than 60, Family history of thyroid cancer or multiple endocrine neoplasia

Physical examination is done by palpation, nodules of at least 0.5 to 1 cm can usually be

detected. It can be difficult to palpate any nodule in a patient with a thick, short neck.

Worrisome findings on physical examination include<sup>1</sup>:

Nodules larger than 4 cm, Fixation to adjacent skin and soft tissue which may indicate extra glandular invasion, Firm nodules, as they may more frequently harbor cancer than softer nodules, Palpable cervical lymphadenopathy in the presence of thyroid nodules which raises the possibility of regional metastasis.

FNAC is an invaluable first line investigation for diagnosis of thyroid swellings. Several national and international studies have documented the sensitivity of FNAC in thyroid nodules to range from 52-98%.<sup>12</sup> Similarly, the international normal range for specificity is 72

to 100% and for PPV is 50 to 90%.<sup>12</sup> In our study the Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value,

Accuracy of FNAC were found to be 92.3%, 76.5%, 75%, 92.8%, 83.3% respectively which is comparable to other studies.

*Table 4: Comparison between Validity tests in current study with other studies*

Parameter	Current Study	Qureishi <sup>52</sup>	Sinna <sup>53</sup>	Bagga <sup>54</sup>
Sensitivity	92.3%	70%	92.8%	66%
Specificity	76.5%	98.68%	94.2%	100%
Positive Predictive value	75%	87.5%	94.9%	-
Negative Predictive Value	92.8%	96.15%	91.8%	-
Accuracy	83.3%	95.34%	93.6%	96.2%

In our study also it was found that thyroid swellings were found in 80% women and 20% men. Ratio being 4:1. According to Bagga et al<sup>13</sup> in a similar study thyroid swelling were detected in 88% women and 12% men. According to Rout et al<sup>55</sup>, 70% women and 30% men presented to their OPD with thyroid swellings. Thyroid diseases are seen to be more common in women than in men. This data states that 76.6% of the cases had Multinodular finding where as 16.7% of the cases had Cystic nodule.

According to Caren et al<sup>15</sup>, nodular thyroid disease was most common in their study as well. Utilization of FNAC in euthyroid patients with suspicious nodules has been studied to be an effective technique for distinguishing benign

from malignant thyroid nodules. Due to its simplicity, low cost and absence of major complications this procedure is being performed on an increasing number of patients, which has led to the detection of thyroid cancer at earlier stages and its adequate management. The thyroid swellings in FNAC are classified according to the Bethesda system for uniformity in diagnosis and clarity of communication between various cytopathologists and surgeons.

In this study, overall, 60% of the cases were malignant on FNAC and 40% were benign. 36.7% of the cases were Bethesda category II and 30.0% of the cases were Bethesda category V.

*Table 5: Profile Of FNAC (Bethesda Category)*

Category (Bethesda)	No. of cases (N = 30)	Percentage
II (Benign)	11	36.7
III (Atypia of Undetermined Significance)	01	03.3
IV (Follicular Neoplasm/ Suspicious for follicular neoplasm)	05	16.7
V (Suspicious for Malignancy)	09	30.0
VI (Malignant)	04	13.3

*Table 6: Comparison between cases of Bethesda category in current study and other studies*

Bethesda category (FNAC)	Current study (N = 30)	Sukumaran et al <sup>57</sup> (N = 248)	Sinna et al <sup>53</sup> (N = 252)
I	None	6.04%	7.1%
II	36.7%	12.5%	33.1%

III	3.3%	4.43%	13.5%
IV	16.7%	13.3%	16.5%
V	30%	4.03%	10.1%
VI	13.3%	59.68%	19.5%

According to Sukumaran et al<sup>17</sup>, maximum cases were malignant of Bethesda category VI, According to Sinna et al<sup>53</sup>, maximum cases were Benign, Bethesda category II, Similar to the current study in which maximum cases were also of Bethesda category II- 36.7%. In the final Histopathological diagnosis, maximum number of cases were of follicular variant of Papillary

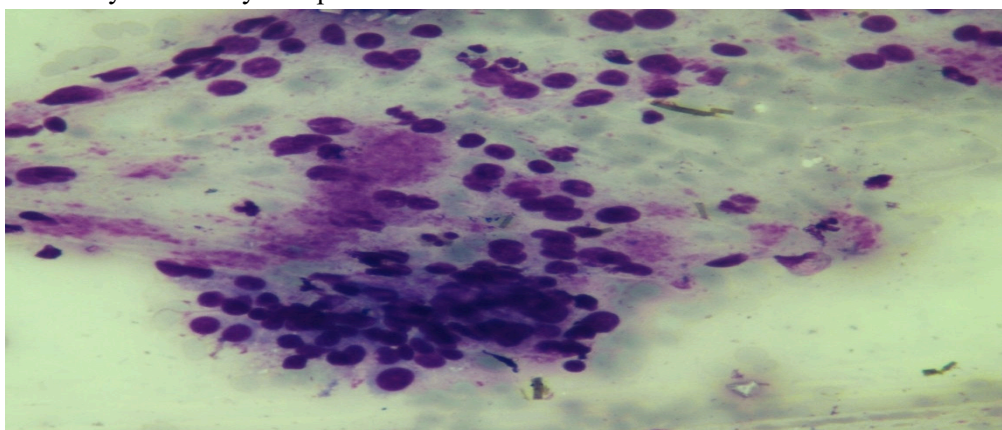
Carcinoma. In the studies done by Sinna et al<sup>12</sup> and Bagga et al<sup>13</sup>, maximum cases were of Nodular Goitre with maximum malignant cases of papillary carcinoma. In the study done by Sukumaran et al<sup>16</sup>, maximum cases were malignant and were of papillary carcinoma. Nodular Hyperplasia was 2<sup>nd</sup> most commonly found in 20% cases.

*Table 7: Table showing over or under diagnosis by FNAC as compared to HPR*

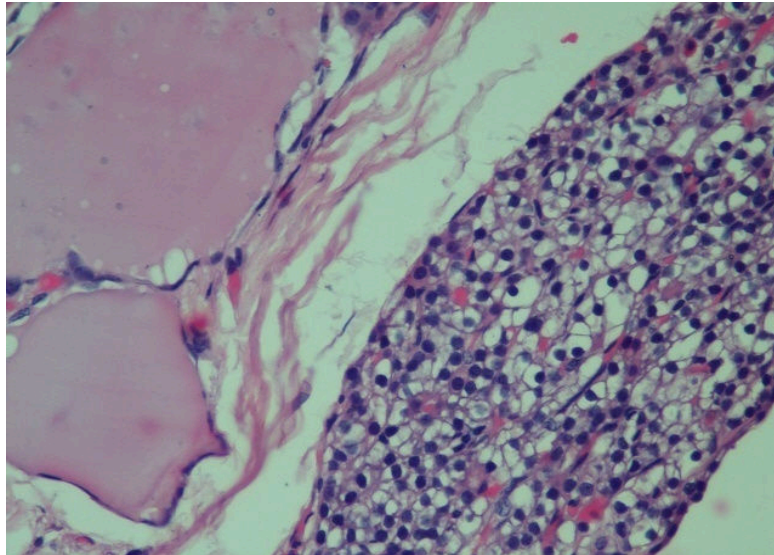
Bethesda category	HPR	FNAC over diagnosis	FNAC under diagnosis
V	Nodular hyperplasia	Present	Absent
V	Nodular hyperplasia	Present	Absent
IV	Autoimmune thyroiditis	Present	Absent
IV	Multinodular Goitre	Present	Absent
II	Follicular variant of papillary carcinoma	Absent	Present

There were 2 cases of category V on FNAC which were diagnosed as Nodular Hyperplasia on histopathological diagnosis. There was one case of category IV of FNAC which came as Autoimmune Thyroiditis on histopathology. One case of category IV which came as multinodular Goitre on histopathology. A case of category II on FNAC which came as follicular variant of papillary carcinoma. A case of category III on FNAC which came as papillary microcarcinoma on Histopathology for which hemithyroidectomy was performed.

4 benign cases were wrongly diagnosed as malignant on FNAC in this study and 1 malignant case was misdiagnosed as benign. False Positive Rate in this study- 13% (percentage of healthy individuals incorrectly receiving a positive test result). 13% with malignant FNAC were found to be benign on histopathology. In other National and International studies<sup>53</sup>, false positive rate has been found to be 0-8%. According to Sinna et al<sup>53</sup> it was 7.8%.



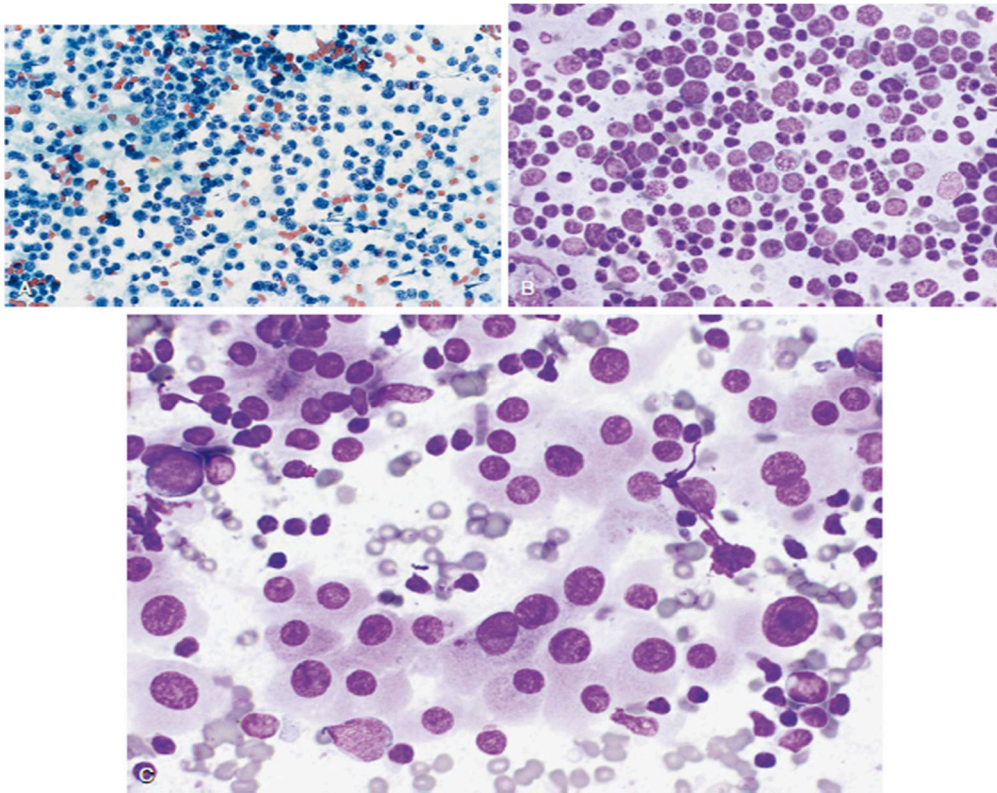
*Fig 18: Cytology slide of a patient diagnosed as Bethesda Category V on FNAC. (Papanicolou stain)*



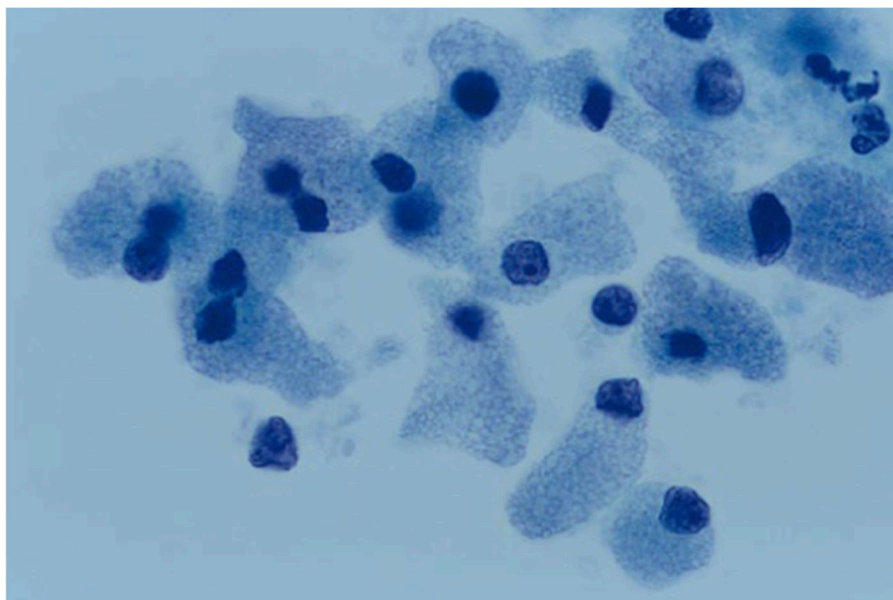
*Fig 19: Histopathology slide of the same patient diagnosed as Nodular Hyperplasia (Benign)*

*Table 8: Cytomorphological comparison between benign and malignant follicular thyroid lesions*

<b>Cytomorphology Benign follicular nodules</b>	<b>Cytomorphology of follicular neoplasm</b>
<ul style="list-style-type: none"> <li>• Predominantly macrofollicles-fragmented (flat sheets), intact spheres</li> </ul>	<ul style="list-style-type: none"> <li>• Predominantly microfollicles or trabeculae</li> </ul>
<ul style="list-style-type: none"> <li>• Low to moderate cellularity</li> </ul>	<ul style="list-style-type: none"> <li>• Marked cellularity</li> </ul>
<ul style="list-style-type: none"> <li>• Cohesive cell</li> </ul>	<ul style="list-style-type: none"> <li>• Enlarged, crowded follicular cells</li> </ul>
<ul style="list-style-type: none"> <li>• Colloid (abundant and often watery but not always visible)</li> </ul>	<ul style="list-style-type: none"> <li>• Scant colloid</li> </ul>
<ul style="list-style-type: none"> <li>• Hurthle cells (usually a minor component)</li> </ul>	Vascular invasion for follicular carcinoma
<ul style="list-style-type: none"> <li>• Macrophages and cyst lining cells (in cases of cystic degeneration)</li> </ul>	
<ul style="list-style-type: none"> <li>• Coarse chromatin</li> </ul>	



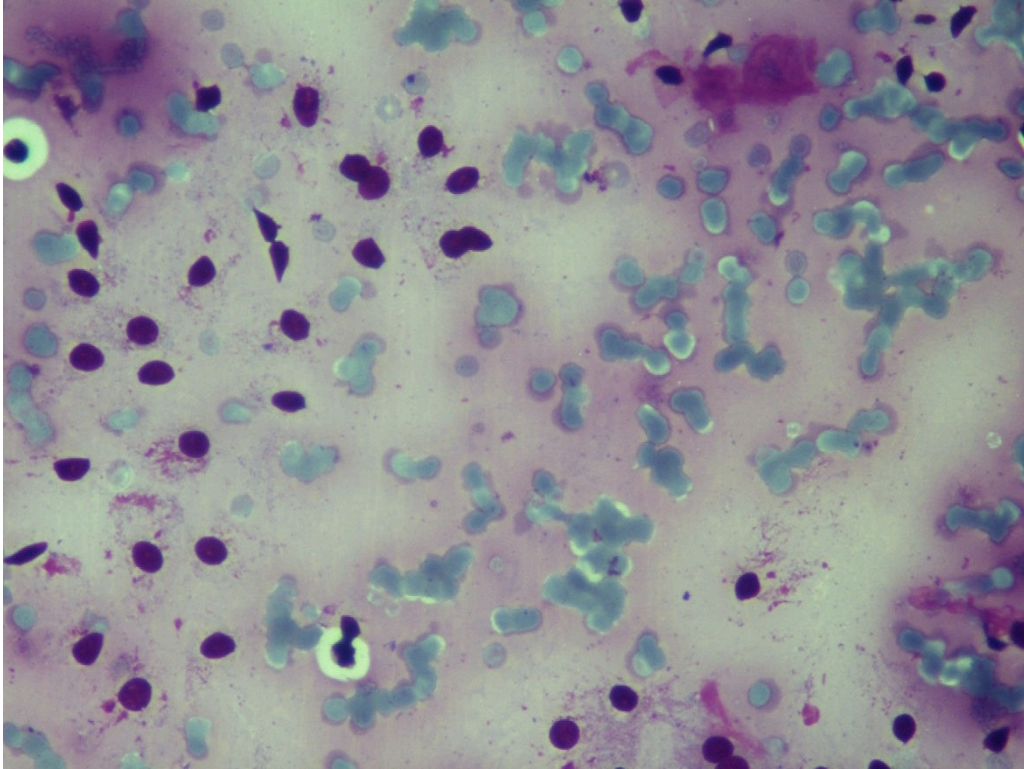
*Fig 20: Hashimoto thyroiditis (HT). Slide 1: Lymphoid cells seen predominantly (Papanicolaou stain). Slide 2: Heterogeneity of the lymphoid cells better appreciated with air-dried preparations (Wright-Giemsa stain). Slide 3: Hurthle cells with abundant cytoplasm are usually identified in clusters in Hashimoto's thyroiditis*



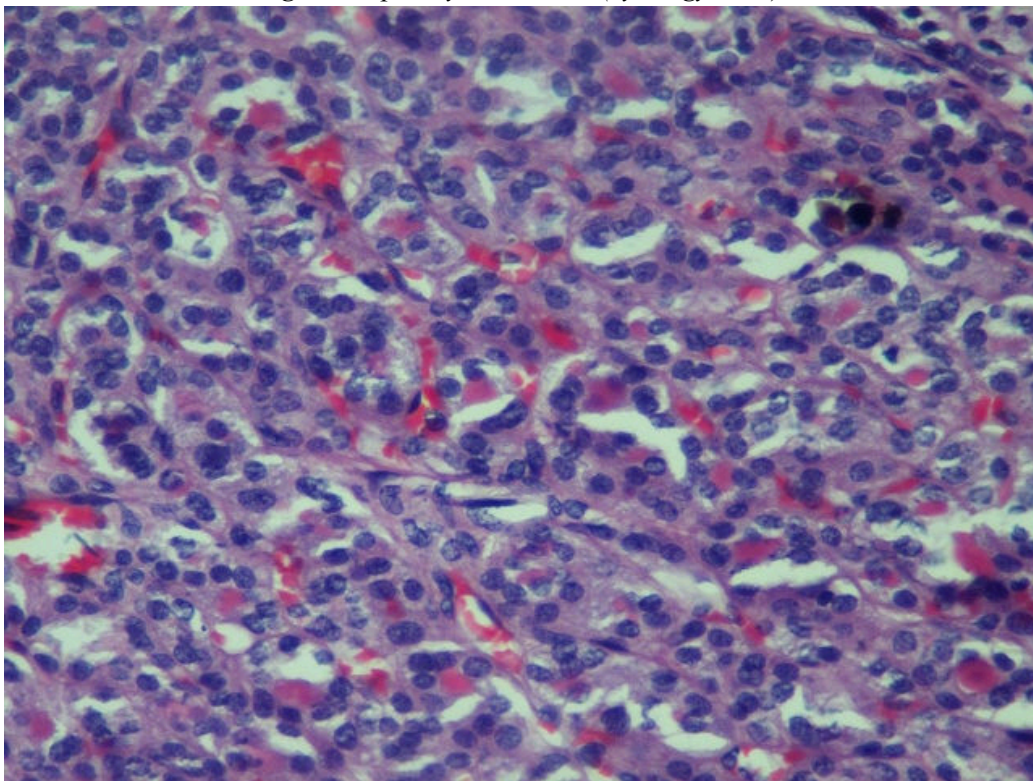
*Fig 21: Numerous Hurthle cells seen (Papanicolaou stain) (Bethesda category IV)*

Hurthle cells also called as oncocytes or oxyphil cells are metaplastic follicular cells characterized by abundant mitochondria. Transformation of follicular cells into Hurthle cells is poorly understood, but they have

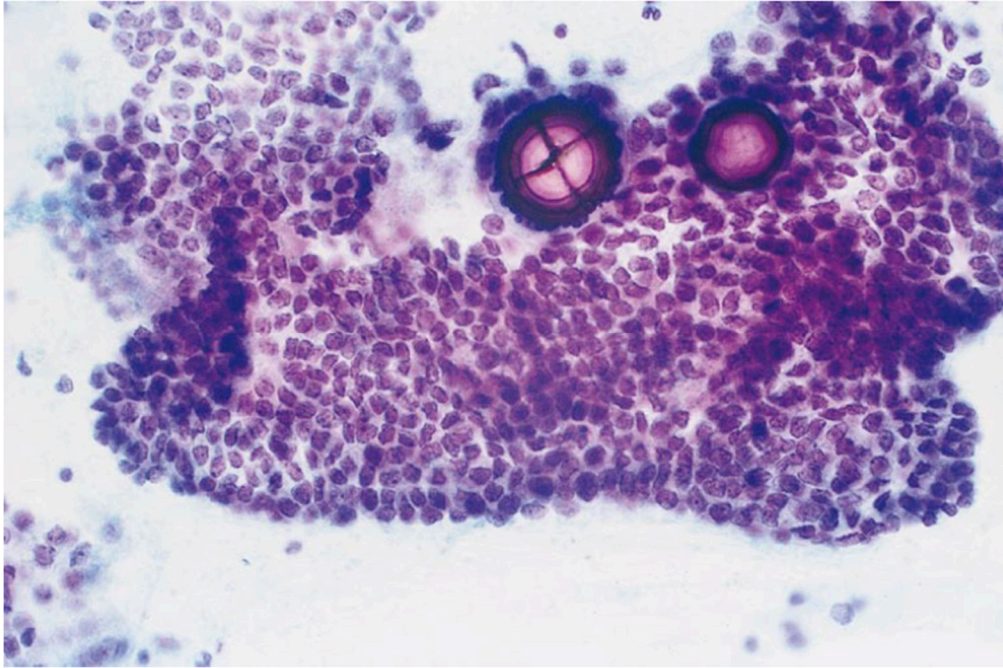
striking appearance on cytologic preparations: polygonal, with abundant cytoplasm. Nuclei are enlarged and sometimes pale, and nucleoli can be inconspicuous or absent.



*Fig 22: Papillary carcinoma (cytology slide)*



*Fig 23: Follicular variant of papillary carcinoma (histopathology slide)*



*Fig 24: Papillary carcinoma- In some cases, papillae are absent, and the neoplastic cells are arranged in crowded sheets. Psammoma bodies are present (Papanicolaou stain).*

Papillary carcinoma has a propensity to invade lymphatic spaces and, therefore, leads to microscopic multimodal lesions in the gland as well as a high incidence of regional lymph node metastases. Once FNAC category has been established, surgical management decided according to the Bethesda<sup>6,9</sup> category, lobectomy +/- isthmectomy depending on the

involvement of the isthmus, for benign lesions and total thyroidectomy for malignant ones.

#### **Correlation Between FNAC And Surgery**

According to this study, 33.3% of the cases which belonged to Benign FNAC had Total thyroidectomy surgery which was significantly less as compared to 94.4% of the cases which belonged to Malignant FNAC.

*Table 9: Implied Risk of Malignancy and Recommended Clinical Management for each category<sup>11</sup>:*

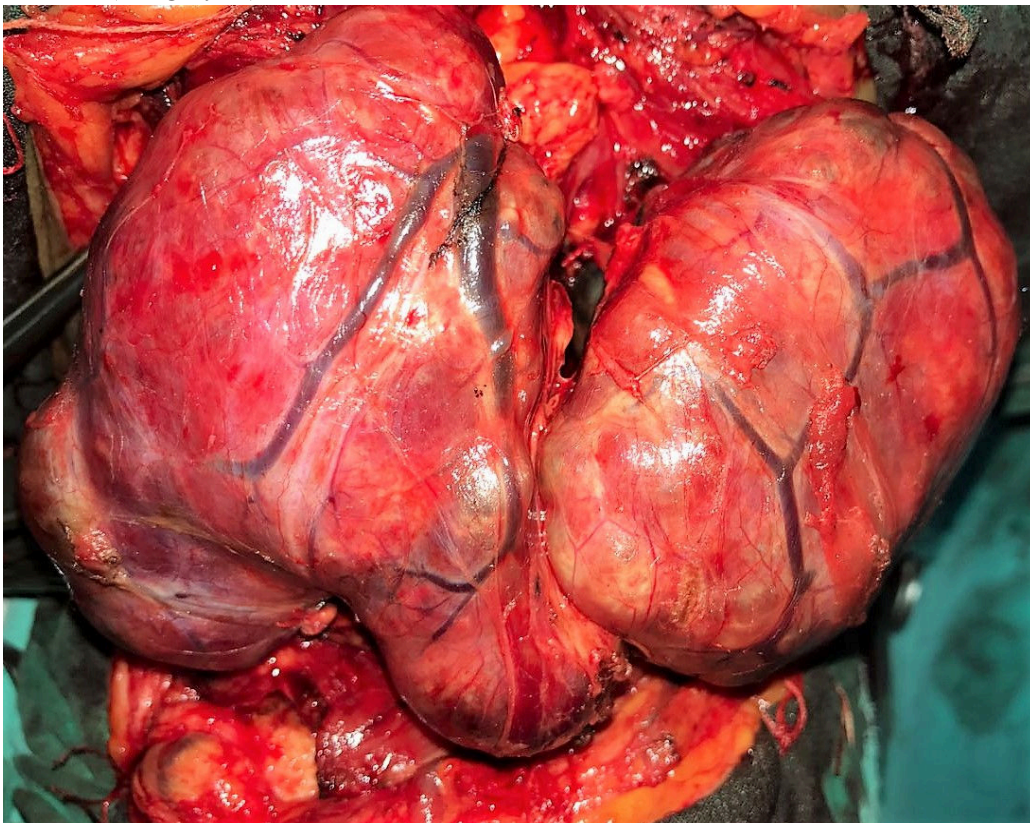
Bethesda Category	% Malignant	Management
I (Non diagnostic/ Unsatisfactory)	1-4 %	Repeat FNA with ultrasound guidance
II (Benign)	0-3 %	Clinical follow-up
III (Atypia of Undetermined Significance or Follicular Lesion)	Approximately 5-15%	Repeat FNA
IV (Suspicious for a Follicular Neoplasm)	15-30%	Lobectomy
(Suspicious for a Hurthle cell Neoplasm)	15-45%	Lobectomy
V (Suspicious for Malignancy)	60-75%	Lobectomy/ Thyroidectomy
VI (Malignant)	97-99%	Total Thyroidectomy

This table shows according to Bethesda, the risk of malignancy and planned clinical management for each category of FNAC.

In this study, 100.0% of the cases of Bethesda V and VI category on FNAC had Total Thyroidectomy surgery which was significantly more as compared to 36.4% and 80.0% of the cases which were of category II and IV FNAC respectively.

Surgery (Hemi or Total Thyroidectomy) for Benign lesions (category II) was undertaken

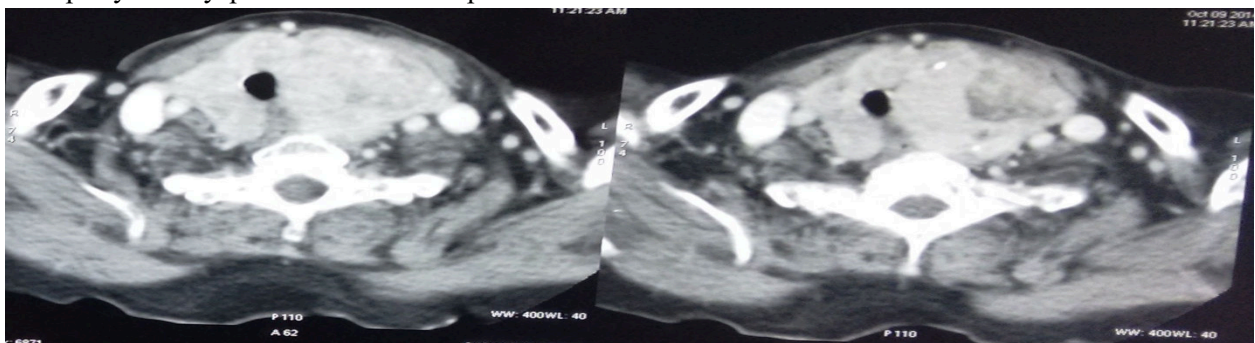
when there was a large multinodular Goitre in case of mechanical obstruction by a large retrosternal Goitre causing airway obstruction, tracheal deviation and if patient wishes so for cosmetic reasons. The management cannot be decided according to Bethesda guidelines<sup>8-11</sup> alone, holistic consideration of risk factors, clinical judgment and patient choice is essential in determining adequate treatment.



*Fig 25: Large multinodular Goitre Bethesda (category II) causing airway compression and mechanical symptoms for which Total Thyroidectomy was undertaken*

An elderly patient presented with a large retrosternal Goitre and preoperative right vocal cord palsy. No dyspnea or stridor was present.

The tumor was removed, but cord palsy persisted post surgery.



*Fig 26: Retrosternal Goitre showing tracheal compression*

**Computed Tomography/Magnetic Resonance Imaging** is useful in evaluating the extent of large, fixed, or substernal Goitres

(which cannot be evaluated by ultrasound) and their relationship to the airway and vascular structures.<sup>1,2</sup>



*Fig 27: Retrosternal, Multinodular Goitre specimen, showing focal areas of hemorrhage and cystic degeneration*

A young female with Bethesda category III was operated with hemithyroidectomy for cosmetic reasons. The histopathology came as papillary thyroid microcarcinoma. These are defined as papillary thyroid carcinoma with a maximum diameter of  $\leq 10$  mm. They generally have an excellent prognosis, with majority of patients with small primary tumors alive at 20 years. If no other risk factors present and if patient has undergone a hemithyroidectomy, then the patient is kept on a regular follow up and need for completion thyroidectomy usually doesn't arise.<sup>17</sup>

80% of the patients of Category IV underwent Total Thyroidectomy because of presence of

large, hard nodules, patient wish and other risk factors.

A patient in this study initially diagnosed as Bethesda category IV on FNAC, underwent hemithyroidectomy, the histopathology report was suggestive of follicular variant papillary thyroid carcinoma, so a completion thyroidectomy was carried out for the patient.

Completion Thyroidectomy: Is performed when thyroid cancer is diagnosed histologically after hemithyroidectomy for a putative or suspected benign nodule. It is conducted to remove any residual disease.<sup>17</sup>

*Table10: Prognostic factors in Differentiated Thyroid Cancer<sup>1</sup>*

Patient factors	Tumor Factors	Management factors
Age	Tumor size	Delay in therapy
Sex	Tumor Histology	Extent of surgery
	Nodal metastases (in elderly patient)	Experience of the surgeon
	Local invasion	Thyroid Hormone Therapy
	Distant metastases	Treatment with postoperative radioiodine

In this study all patients of category V and VI were operated with Total Thyroidectomy, as

per the Bethesda and ATA (American Thyroid Association)<sup>18</sup> Guidelines.

**Association between HPR and Surgery:**

This data states that 50.0% of the cases each had Malignant and Benign HPR. 51.2% of patients which had Benign HPR underwent

Total Thyroidectomy which was significantly less as compared to 81.2% of patients with malignant HPR who underwent total thyroidectomy.

*Table 11: Comparison of patients who underwent Total Thyroidectomy:*

	Benign	Malignant
<b>FNAC</b>	33.3%	94.4%
<b>HPR</b>	51.2%	81.2%

94.2% patients who underwent Total thyroidectomy were Malignant on FNAC. But on final HPR 51.2% of the patients who underwent Total thyroidectomy were benign and 81.2% were malignant. This table shows that more patients were diagnosed as malignant on FNAC and underwent Total Thyroidectomy, which were later diagnosed as benign lesions on HPR which implies overtreatment of patients and exposing them to the risks of total thyroidectomy.

In the study by Sukumaran et al<sup>14</sup>, all cases which were diagnosed as malignant on FNAC came as malignant on final histopathology as well.

In this study, 2 cases had clinically positive lymph nodes (Right upper jugular level III), so intraoperatively frozen section was sent. The lymph node came positive for malignancy for one of the case, then for clearance of the disease, type 3 unilateral modified neck dissection was performed.

According to Chen et al<sup>19</sup>, Frozen section on benign aspirates is unhelpful in the management of thyroid nodules. It need not be performed for cytologically proven malignant thyroid nodules. Selective use of frozen section complements fine needle aspiration cytology findings of suspicious or follicular lesions, especially in the subset with papillary cancer, allowing one-stage total thyroidectomy.

After Histopathological examination, if extrathyroidal spread is present, or patient has been adjudged to have high risk factors pre operatively, post surgery whole body iodine scanning is typically performed 1 week after Iodine-131 treatment (low dose of 1 to 3 milliCurie) to identify metastases. In those

elected to receive RAI (Radioactive iodine), quantitation of uptake is assessed by whole-body Iodine-131 scan and customization of dose is decided based on this. Postoperative Radioablation is typically performed after approximately 6 weeks of total thyroidectomy. The most common side effects from radioiodine therapy include sialadenitis, nausea, and temporary bone marrow suppression. Women undergoing Iodine-131 treatment should be advised to avoid pregnancy during and 6 to 12 months after treatment due to risk of miscarriage and fetal malformation.<sup>17</sup> Adjuvant therapy includes postoperative TSH(thyroid stimulating hormone) suppression with thyroxin therapy, usually to a level around 0.1 mIU/L(milli International Units/Litre). If the patient is considered low risk, TSH(thyroid stimulating hormone) levels are acceptable into the low range of normal. High-risk patients are often maintained at  $\leq 0.1$  mIU/L (milli International Units/Litre)

Thyroglobulin levels are also monitored regularly on follow up as it's a protein binding thyroid hormones, raised levels indicate recurrence of carcinoma. Thyroid ultrasound is done after 1 and 6 months and then yearly for 5 years. Regular speech therapy is undertaken for patients having pre or post operative hoarseness of voice.<sup>17</sup>

**Complications that can be seen post total thyroidectomy surgery<sup>1</sup>:**

1. Laryngeal nerve damage:
  - a. Recurrent laryngeal nerve
  - b. Superior laryngeal nerve
2. Hypocalcaemia
3. Haematoma
4. Wound infection
5. Tracheomalacia

6.7% of the cases in this study had Post operative vocal cord paresis and 6.7% of the

cases had Postoperative hypocalcemia. No intraoperative or post operative hemorrhage was noted. According to **Filho et al**<sup>20</sup> transient hypocalcemia was present in **13.1%** patients and transient vocal cord palsy in **1.4 %** of patients.

The vocal cord palsy improved with speech therapy and hypocalcemia improved with calcium supplements. Transient hypocalcaemia is commonly due to the initial vascular shock on the preserved parathyroid tissue and requires calcium supplementation. Factors playing a role in hypocalcaemia postoperatively include the extent of surgery, experience of the operator and the number of functioning glands left in situ. The majority of patients will have had a significant amount of thyroid tissue removed which results in a hypothyroid state, and thyroxin replacement therapy is usually started upon discharge from hospital. If carcinoma is present, thyroxin may be withheld in preparation for a whole body iodine scan to search for residual or metastatic disease.<sup>1, 17</sup>

#### **Complications in thyroid surgery can be prevented by**<sup>1</sup>-

- Adequate Preoperative evaluation
- Understanding anatomy
- Routine identification of the recurrent laryngeal nerve and parathyroid glands
- Meticulous haemostasis

**LIMITATIONS OF FNAC-** Even though FNAC is a very useful investigation for the diagnosis of thyroid nodules, it does have limitations. The interpretation of cytology slides is highly user dependent. Misdiagnosis and over/under treatment can occur due to improper reporting.

Distinction between an adenomatoid nodule in MNG and a follicular neoplasm may not always be achievable.

**FNAC induced iatrogenic change**<sup>1</sup>: Although FNAC is considered atraumatic, the technique is known to induce histologic changes. Factors affecting such changes include the nature and size of target lesion, caliber of needle used, the number of passes attempted, and the interval between FNAC and excision surgery. Such changes called as WHAFFT<sup>21</sup> (Worrisome

Histologic Alterations following fine needle aspiration of the thyroid gland), and are divided into acute and chronic. Tissue damage and repair artifacts include hemorrhage, fibrovascular granulation tissue organization and regenerative/ degenerative atypia. Infiltration of fibroblasts/myofibroblasts along needle tract may on occasion undergo atypia and become exuberant and kaposiform to closely mimic sarcoma, so called post FNAC spindle nodule.<sup>1</sup>

**Post FNAC vascular effects**<sup>1</sup> include venous thrombosis, recanalisation and papillar endothelial hyperplasia, sometimes resembling angiosarcoma ('pseudo-angiosarcomatoid)

Mitochondrion-rich oncocytic (oxyphil) cell lesions are exquisitely sensitive to ischemia, therefore characteristically susceptible to partial or global infarction, either spontaneously or post FNAC. Epithelial displacement and/or tumor implantation along the FNAC needle tracks into soft tissues or skin does occur, but any viable tumor seeding is rarely of serious clinical importance.<sup>1, 2</sup>

#### **SUMMARY**

The sex ratio in this study was 4:1, females: males, which is comparable to other studies showing thyroid disorders to be more common in females than in males. Maximum number of cases (46.7%) presented as a right nodule clinically. In ultrasonography, multinodularity was found to be 76.6%

60% cases had malignant FNAC diagnosis and 40% were benign. Maximum number of cases belonged to Bethesda category II on FNAC (36.7%) and 30% of the cases belonged to Bethesda category V. 94.4% cases with a malignant FNAC diagnosis underwent total thyroidectomy. 5.6 % cases underwent a completion thyroidectomy, after being diagnosed as malignant after hemithyroidectomy which was done previously. 66.7% patients with a benign FNAC diagnosis underwent hemithyroidectomy and 33.3% patients with a benign FNAC diagnosis underwent Total Thyroidectomy. 36.4% of patients of category II (benign) underwent total thyroidectomy. 63.6%

of patients of Bethesda category II underwent hemithyroidectomy. All patients of Bethesda category IV, V and VI underwent total thyroidectomy. A patient who underwent hemithyroidectomy in another centre was diagnosed as malignant on histopathology, underwent completion thyroidectomy at our centre.

In histopathology, 50% cases came as malignant and 50% benign. 30% of the cases in HPR were Follicular Variant of Papillary Carcinoma. 81.2% of the patients with malignant HPR underwent Total thyroidectomy and 51.2% with benign HPR underwent total thyroidectomy. 90.9% patients of FNAC category II were benign on HPR and 9.1% was malignant. All of patients of FNAC category III and VI were malignant on HPR. 40% of patients of FNAC category IV were benign on HPR and 60% were malignant. 22.2% of patients of FNAC category V were benign on HPR and 77.8 % were malignant. 2 cases had clinically positive lymph nodes (Right upper jugular level III), so intraoperatively frozen section was sent. The lymph node came positive for malignancy for one of the case, then for clearance of the disease, type 3 unilateral modified neck dissection was performed. 6.7% of the cases in this study had post operative vocal cord paresis and 6.7% of the cases had postoperative hypocalcemia.

## CONCLUSION

- FNAC is an important tool for diagnosis of thyroid disorders.
- FNAC has a high degree of patient acceptance as it is sensitive, specific, cheap, easy to perform, cost effective procedure with minimal side effects.
- Correct reporting of FNAC by cytopathologist is important- when false positive rates are high, benign disorders are over treated, and patient exposed to risks of total thyroidectomy and life long thyroxin and calcium supplementation. When false negative rates are high, patients are under treated.

- Quality assurance of FNAC by conducting histopathological examination is crucial as it helps in the final diagnosis and planning further management of the patient.

## REFERENCES

- 1) Stell & Maran's, Textbook of head and neck surgery and oncology. 5th ed. London: Hodder Arnold; 2012. p. 328-494
- 2) Scott-Brown W, Gleeson M. Scott-Brown's otolaryngology, head and neck surgery. 7<sup>th</sup> ed. London: Hodder Arnold; 2008. p. 314-338
- 3) Bailey & Love's Short Practice of Surgery 26th ed. Boca Raton: Taylor & Francis; 2013. p. 742-72
- 4) Hamburger JI. Diagnosis of thyroid nodules by fine needle biopsy: Use and abuse. *J Clin Endocrinol Metab* 1994;79:335-9.
- 5) Drake R, Vogl W, Mitchell A, Gray H. *Gray's Anatomy for students*. 3rd ed. p. 1020-34
- 6) Kline TS. General Considerations. In: Kline TS, ed. *Handbook of Fine Needle Aspiration. Biopsy Cytology*. New York, Edinburgh, London and Melbourne: Churchill Livingstone; 1988:1.
- 7) Diamantis A, Magiorkinis E, Koutselini H. Fine-needle aspiration (FNA) biopsy: historical aspects. *Folia Histochemica et Cytobiologica*. 2009;47(2).
- 8) Cibas ES, Ali SZ. The Bethesda System for Reporting Thyroid Cytopathology. *Thyroid*. 2009;19(11):1159-1165.
- 9) Baloch ZW, LiVolsi VA, Asa SL, et al. 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. *Diagn Cytopathol*. 2008;36:425-437.
- 10) Baloch ZW, Cibas ES, Clark DP, et al. The National Cancer Institute Thyroid Fine Needle Aspiration State of the Science Conference: a summation. *Cytojournal*. 2008;5:6. doi:10.1186/1742-6413-5-6.

- 11) Ali SZ, Cibas ES. The Bethesda System for Reporting Thyroid Cytopathology. New York, NY: Springer. 2010.
- 12) Sinna EA, Ezzat E. Diagnostic accuracy of fine needle aspiration cytology in thyroid lesions. Journal of the Egyptian National Cancer Institute. 2012;24(2):63-70.
- 13) Bagga PK, Mahajan N. Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it? Indian Journal of Cancer. 2010;47(4):437.
- 14) Rout K, Ray C, Behera S, Biswal R. A Comparative Study of FNAC and Histopathology of Thyroid Swellings. Indian Journal of Otolaryngology and Head & Neck Surgery. 2011;63(4):370-372.
- 15) Dsouza C, Rao V.V. Role of Ultrasonography in thyroid swellings. IJBRFA. 2014;05(07):474-476
- 16) Sukumaran R, Kattoor J, Pillai K, Ramadas P, Nayak N, Somanathan T et al. Fine Needle Aspiration Cytology of Thyroid Lesions and its Correlation with Histopathology in a Series of 248 Patients. Indian Journal of Surgical Oncology. 2014;5(3):237-241.
- 17) Devita V, Lawrence T, Rosenberg S. DeVita, Hellman, and Rosenberg's cancer. 1st ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins; 2008. p. 1175-88
- 18) [Internet]. 2016 [cited 15 December 2016]. Available from: <http://americanthyroid.org/guidelines> Rout
- 19) Chen H. Follicular Lesions of the Thyroid. Annals of Surgery. 1995;222(1):101.
- 20) Filho J, Kowalski L. Surgical complications after thyroid surgery performed in a cancer hospital. Otolaryngology - Head and Neck Surgery. 2005;132(3):490-494.
- 21) LiVolsi VA, Merino MJ. Worrisome histologic alterations following fine-needle aspiration of the thyroid (WHAFFT). Pathology Annual 1994; 29: 99-120.

**How to cite this article:**

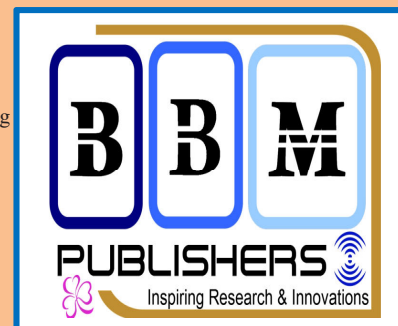
**Shampa Mishra, Nilam U. Sathe, Kamini Chavan, Pravin Misal. A Prospective Comparative Study Of Fine Needle Aspiration Cytology And Histopathology In Thyroid Disorders. Br J Bio Med Res , Vol.03, Issue 05, Pg.1121-1145, September - October 2019. ISSN:2456-9739 Cross Ref DOI : <https://doi.org/10.24942/bjbmr.2019.581>**

**Source of Support:** Nil

**Conflict of Interest:** None declared.

Your next submission with **British BioMedicine Publishers** will reach you the below assets

- Quality Editorial service
- Swift Peer Review
- E-prints Service
- Manuscript Podcast for convenient understanding
- Global attainment for your research
- Manuscript accessibility in different formats (Pdf, E-pub, Full Text)
- Unceasing customer service
- Immediate, unrestricted online access
- Global archiving of articles



Track the below URL for one-step submission

<http://www.britishbiomedicine.com/manuscript-submission.aspx>