

**Cytopathologic Patterns of Thyroid Lesions and correlation of FNAC reports with the corresponding histopathologic results at a tertiary hospital in Ethiopia, a five-year retrospective study between January 2015 and August 2019.**

For partial fulfillment of Post Graduate Program in Pathology.

Woldie Jember, (MD), Final Year Pathology Resident.

Advisor

Dr Tufa Gemechu, (MD), Associate professor of pathology.

# Contents

## Table of Contents

Contents .....	ii
List of tables.....	iii
List of figures .....	iv
Abstract.....	v
Background .....	v
Methods .....	v
Results.....	v
Conclusion .....	vi
Acronyms and Abbreviation .....	vii
Introduction.....	1
Literature review .....	3
Objective.....	10
General objective.....	10
Specific objective .....	10
Method.....	11
Results .....	13
Discussion.....	27
Conclusion .....	30
Limitation of the study .....	31
Recommendation.....	32
Acknowledgements .....	33
References.....	34

## List of tables

Table 1 The Bethesda System for Reporting Thyroid Cytopathology: implied risk of malignancy and recommended clinical management.....	9
Table-2, Distribution of thyroid lesion cases with Cytopathologic evaluation by year, Gender, age group, Clinical presentation and type of FNAC procedure.....	21
Table-3 Frequency of benign lesions and neoplasms.....	24
Table-4, Distribution of the categories of Cytopathologic diagnosis of thyroid lesions among Male & Females, different age groups and type of thyroid enlargement.....	25
Table-5 shows age sex distribution of different Cytopathologic Malignant Diagnosis.....	29
Table-6 shows comparison of Cytopathologic Diagnosis of benign (non-neoplastic lesions) with their corresponding histopathological diagnosis.....	31
Table-7 shows comparison of Cytopathologic malignant diagnosis of thyroid lesions with their corresponding histopathological diagnosis.....	32
Table-8 shows comparison of Cytopathologic Diagnosis by Category with histopathologic diagnosis.....	33

## List of figures

Fig-1A graph showing distribution of all thyroid lesions with cytopathologic diagnosis in the five years period among different age groups .....	22
Fig-2, A graph showing the proportion of the cytopathologic categories during the five years period.....	163
Fig-3, A graph showing distribution of categories of Cytopathologic diagnosis of thyroid lesions among Males and Females.....	26
Figure-4 shows distribution of Cytopathologic malignant diagnosis among different age groups and gender.....	26
Fig-5, graph showing distribution of cytopathologic diagnostic categories of thyroid lesions in relation to different types of thyroid enlargement among females(A)and males(B).....	27
Figure-6 shows frequencies of cytopathologic malignant diagnosis of thyroid lesions.....	30

# **Abstract**

## **Background**

Thyroid diseases are among the most common endocrine disorders worldwide including in Ethiopia and Patients with thyroid diseases can present with diffuse or nodular thyroid enlargement. Determining the type of the lesions in a given setup has paramount importance to design effective therapeutic strategy. As a result, the aim of this study was to find out the cytological patterns of thyroid lesions and compare these cytopathologic reports with their corresponding histopathologic diagnosis at Black Lion Hospital.

## **Methods**

This was a retrospective cross sectional descriptive study conducted on 687 patients having cytopathologic evaluation for thyroid lesions at Black Lion Hospital between January 2015 and August 2019.

## **Results**

Most of the patients were in the age range of 20-60 years, accounting for 521/663(77.3%) cases with Mean age of 41.98 and F:M ratio of 4.69:1. Non-diagnostic(Inconclusive), Benign (Non-neoplastic lesions), Follicular neoplasm, Hurthle Cell neoplasm, Suspicious for malignancy and malignant cytopathologic diagnosis accounted for 33(4.8%),504(73.4%),51(7.4%),11(1.6%),3(0.4%) and 85(12.4%) of the cases respectively. Among the Benign (Non-neoplastic lesions), Colloid Goitre was the most common diagnosis occurring in 458(90.9%) of the cases. The minimum and maximum age for the occurrence of malignancy in the study was 21 and 80 years old respectively and Papillary Carcinoma was the leading type of malignancy accounting 43(48.9%) of all malignant cases followed by Anaplastic(Undifferentiated) Carcinoma constituted 20(23.6%) of the malignant

cases.

From all 687 patients with cytopathologic evaluation, only for 19 of them were histopathologic reports available for comparison. Eleven of the 19 cases were diagnosed benign(non-neoplastic) lesions by FNAC and 2 ended up with malignant diagnosis histologically. Six of the 19 cases had malignant diagnosis by FNAC and 2 became adenoma up on histologic examination.

### **Conclusion**

FNAC is an important tool for the management of thyroid lesions. It is simple, cost-effective technique without any major complications and with minimal discomfort to the patient.

**Keywords:** FNAC, Thyroid lesions, Non-Neoplastic lesions, Neoplasms

## **Acronyms and Abbreviation**

BLH -Black Lion Hospital

FMAAU-Faculty of Medicine, Addis Ababa University

FNAC – Fine needle aspiration cytology

FTC- Follicular thyroid carcinoma

GCMS -Gondar College of Medical Sciences

MNG-Multi nodular goitre

NY -New York

PTC -papillary thyroid carcinoma

TB-Tuberculosis

US-Ultrasound

## Introduction

Thyroid gland is an endocrine organ which is located in the anterior neck and consists of two lateral lobes connected by isthmus[1]. Thyroid diseases are among the most common endocrine disorders worldwide next to diabetes accounting around 30% to 40% of the endocrine disorders. Patients with thyroid diseases present with diffuse or nodular thyroid enlargement[2, 3]. Thyroid disorders are common endocrine disorders encountered in the African continent. The reported prevalence rates of endemic goiter range from 1% to 90% depending on the area of study which is 39.9% in Ethiopia[4]. Palpable thyroid nodules are common clinical finding with a prevalence rate of 4–7% in adult population and from 0.2% to 1.2% in children at areas where iodine is not deficient. Small nodules less than 1cm can be detected by Ultrasonography which makes the prevalence up to 30% among adult population and autopsy findings show that 50% of the general populations have goitre. Most nodules are non-neoplastic lesions or benign neoplasms, and malignancy rate is less than 5% of adult thyroid nodules. Thyroid nodules are more common in female than male, and the incidence increases with age. The main goal of evaluating these nodules is to identify nodules with malignant potential. A multitude of diagnostic tests like ultrasound, thyroid nuclear scan, and fine needle aspiration cytology (FNAC) are available to the clinician for evaluation of thyroid nodule. FNAC is considered the first line diagnostic preoperative test in the evaluation of patients with thyroid nodule, and other tests like ultrasound and nuclear scan should be used in conjunction with FNAC. It is a simple, cost effective, readily repeated, and quick to perform procedure in the outpatient department with excellent patient compliance. Important factor for the satisfactory

test includes representative specimen from the nodule and an experienced cytopathologist to interpret findings[3, 5, 6].

A retrospective done at the department of Pathology, Faculty of Medicine, Addis Ababa University (FMAAU) from January 1994 to December 2000 to determine discordance rate between thyroid fine needle aspiration cytology and histopathologic diagnosis involved a total of 344 cases and revealed the overall sensitivity and specificity for cytological diagnosis were 67% and 84.7% respectively. The accuracy of FNA in the series was 82%[6]. Occasionally FNAC results can be inconsistent since in approximately 10%-30% of cases, cytology is indeterminate and non-diagnostic. Various diagnostic terminologies, including “indeterminate”, “atypical”, and “suspicious for malignancy,” were used to describe these challenging cases and until recently there were no uniform criteria for the various diagnostic categories in thyroid cytopathology. This resulted in diagnostic inconsistencies among different laboratories and difficulty in communicating the implications of thyroid FNA results both to clinicians and pathologists and radiologists. In order to establish a standardized diagnostic terminology/classification system for reporting thyroid FNAC results, the Bethesda System for Reporting Thyroid Cytopathology (BSRTC I 2010), a 6-tiered diagnostic classification system is established in the United States[7]. The atlas is organized by the general categories (Table 1) and these six original categories with implied risk of malignancy have been retained in the second edition (BSRTC II 2018)[8].

**Table 1** The Bethesda System for Reporting Thyroid Cytopathology: implied risk of malignancy and recommended clinical management.

Diagnostic category	Risk of malignancy (%)	Usual management
Non diagnostic or Unsatisfactory	5–10 <sup>b</sup>	Repeat FNA with ultrasound guidance
Benign	0–3 <sup>c</sup>	Clinical and sonographic follow-up
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	~10–30 <sup>d</sup>	Repeat FNA, molecular testing, or lobectomy
Follicular Neoplasm or Suspicious for a Follicular	25–40 <sup>f</sup>	Molecular testing, lobectomy

Neoplasm		
Suspicious for Malignancy	50-75	Near-total thyroidectomy or lobectomy
Malignant	97-99	Near-total thyroidectomy or lobectomy

## Literature review

Fine needle aspiration cytology(FNAC) of the thyroid has been accepted as a first-line screening test for patients with thyroid nodules. It is a safe, accurate and cost-effective way for evaluating thyroid nodules and its utility has increased significantly in recent years. The main role of thyroid FNAC is to triage patients for either surgery or conservative management. Patients with FNAC diagnoses that suggest malignancy and/or neoplasia are managed surgically, whereas patients with FNAC diagnoses that favour a benign lesion can be followed clinically.FNA can be done using palpation or with ultrasound guidance with US guided FNA is preferred for difficult to palpate nodules, predominantly cystic or posteriorly located nodules[9].

Occasionally FNAC results can be inconsistent and can be a source of dispute among clinicians since in approximately 10%-30% of cases, cytology is indeterminate and non-diagnostic. Various diagnostic terminologies, including “indeterminate”, “atypical”, and “suspicious for malignancy,” were used to describe these challenging cases. Until recently there were no uniform criteria for the various diagnostic categories in thyroid cytopathology. This resulted in diagnostic inconsistencies among different laboratories and difficulty in communicating the implications of thyroid FNA results both to clinicians and pathologists and radiologists. In order to establish a standardized diagnostic terminology/classification system for reporting thyroid FNAC results, the National Cancer Institute (NCI) in the United States sponsored the NCI Thyroid FNA State of the Science Conference with a group of experts at Bethesda, MD, in October 2007.This conference established the Bethesda System for Reporting

Thyroid Cytopathology (BSRTC), a 6-tiered diagnostic classification system based on a probabilistic approach.

Almost simultaneously, in Europe, the British Thyroid Association-Royal College of Physicians and the Italian Society for Anatomic Pathology and Cytopathology-International Academy of Pathology (SIAPEC-IAP) thyroid reporting systems, each comprised of 5 diagnostic classes, have been introduced. In several countries the Cytological Communities have adopted the first system or the other, as there is still an ongoing dispute on whether the 5-tiered system or the 6-tiered system is more efficient. In US, the Bethesda System for Reporting Thyroid Cytopathology is the most commonly used. The use of molecular markers in thyroid nodules has been suggested for diagnostic purpose in case of indeterminate cytological diagnosis, to assist with decision making about management option which include Afirm Gene-expression Classifier, seven-gene panel of genetic mutations and rearrangements and galectin-3 immunohistochemistry[7, 9]. Published data regarding thyroid cancer detection for thyroid FNA indicate a sensitivity for malignancy of typically between 65% and 98%, specificity of 76–100%, with a false-negative rate of 0–5%, a false-positive rate of 0–5.7%, and an overall accuracy of 69–97% [10]. From studies done in Long Island Jewish Medical Center (New York, NY) between January 1992 and December 2003 and, the University of Texas Medical Branch (Galveston, Tex) between January 1993 and May 2005 to correlate Fine-needle aspiration cytology diagnoses of thyroid Nodules with histologic diagnoses, a total of 4703 thyroid FNA specimens from 3337 women and girls and 612 specimens from men and boys were reviewed. The age of patients ranged from 2 months to 99 years. Data from the 2 study institutions were similar; therefore, they were analysed jointly and the sensitivity and specificity of thyroid FNAC were 94% and 98.5%, respectively, for

the diagnosis of malignancy and 89.3% and 74%, respectively, for the diagnosis of neoplasm [11].

In Republic of Korea a study published in 2007, retrospectively correlated the results of US-guided FNAs performed by a single experienced radiologist in 315 thyroid nodules in 292 patients (246 women, 46 men aged 12–79 years) with their surgical pathologic results. The FNAC results were non diagnostic (inadequate sampling) in 31 cases (9.8%), indeterminate (aspirates showing follicular or Hurthle cell neoplasm) in 97 cases (30.8%), and determinate (negative, or positive for malignancy) in 187 cases (59.4%). Of the 187 conclusive cases, 169 (90.4%) were concordant with the final histopathologic results, whereas 18 (9.6%) were discordant with 14 false-positive and 4 false-negative results [12].

In India a prospective analysis of seventy-five consecutive patients of clinically diagnosed solitary thyroid nodule was done between January 2003 and December 2005 to correlate Fine Needle Aspiration Cytology with Histopathology and there were 6 (8%) males and 69 (92%) females. The age of the patients ranged from 22 to 58 years. After FNAC, all the patients were subjected to surgery and correlation of histopathological findings was performed with FNAC. Statistical analysis of neoplastic lesions showed sensitivity, specificity, accuracy, false positive rate, false negative rate, positive predictive value, and negative predictive value of FNAC to be 80%, 86.6%, 84%, 13.3%, 20%, 80%, and 86.6%, respectively, whereas statistical analysis of carcinomatous lesions showed sensitivity, specificity, accuracy, false positive rate, false negative rate, positive predictive value, and negative predictive value of FNAC to be 80%, 95%, 92%, 5%, 20%, 80%, and 95%. A total of 15 cases of solitary thyroid nodules were diagnosed as having malignancy and the most common malignant lesion detected was papillary carcinoma, 12 out of 15 (80%) [5].

From a study done in Turkey between October 2008 and March 2013 to determine diagnostic efficacy and importance of fine needle aspiration cytology of thyroid nodules compared with histopathologic diagnoses, the results of 1607 cytological aspirates (obtained by FNAC) of 1333 patients were evaluated retrospectively. Cytological and histopathologic diagnoses of 126 nodules of 123 patients (who had undergone surgical excision after FNAC) were compared. In this study, the false positive rate of 15.5% and false-negative rate of 7.3% were found when non diagnostic cases were excluded. Statistical analysis of FNAC showed sensitivity, specificity, positive and negative predictive value and accuracy to be 87.1%, 64.6%, 76.1%, 79.5%, and 77.3%, respectively [13]. In another study done retrospectively in Turin (Italy) to compare cytological reports with their corresponding histological diagnoses during the 10-year period between January 2005 and December 2015 to establish when thyroidectomy is the right choice in the management of thyroid diseases, 260 patients underwent both FNAC and a thyroid surgical procedure. The population was composed of 182 females (70%) and 78 males (30%), and the mean age was 51.71 years (range 15–85). Of the 260 cases, 111 (42.69%) had a malignant histological report; Among the 260 cases, the final cytological diagnosis was non diagnostic in 19 cases (7.31%), benign in 83 cases (31.92%), indeterminate in 96 cases (36.92%), suspicious for malignancy in 22 cases (8.46%), and diagnostic for malignancy in 40 cases (15.38%) with Prevalence of malignancy (n (%)) 5/19 (26.32), 14/83 (16.87), 9/44 (20.45), 28/52 (53.85), 16/22 (72.73) and 39/40 (97.5) respectively in the five categories [14].

In Uganda: tertiary hospital experience, Patients who underwent clinical and laboratory evaluation and thyroidectomy were consecutively recruited over a four months period to estimate the sensitivity and specificity of FNAC in detecting malignancy for thyroid disease using histopathology as the gold standard. A total of 99 patients were enrolled (45 prospective and 54 retrospective). The F:M ratio was 15.5:1 with the median age of 42 years. Majority of the goitres were benign (86.9%), the proportion of patients with malignancy was 13.3%. Of the malignant histopathology, majority (84.6%) were papillary thyroid carcinoma (PTC) and the rest were follicular thyroid carcinoma (FTC). The sensitivity and specificity of FNAC was 61.5% and 89.5% respectively and the accuracy was 85.9% [15].

In Ethiopia, a retrospective review of the reports of a total of 344 cases that fulfilled the study criteria was performed at the Department of Pathology, Faculty of Medicine, Addis Ababa University (FMAAU) from January 1994 to December 2000 to determine discordance rate between thyroid fine needle aspiration cytology and histopathologic diagnosis. FNAs with diagnostic results were categorized as either 'correlating' with histologic diagnoses or discrepant. All histopathologic specimens were adequate to make the final histopathologic diagnoses. There were 273 female and 71 male patients. The mean age of males was 39 years and females was 34 years. When compared with the histopathologic (the gold standard) diagnosis, 60 (18%) of the diagnostic cases were discrepant (15 false negative and 45 false positive but 274 cases (82%) were correlated (30 true positive and 244 true negative). The false negative rate was 4.5% and a false positive rate of 13.5%. The overall sensitivity and

specificity for cytological diagnosis were 67% and 84.7% respectively. The accuracy of FNA in the series was 82% [6].

A One-Year Prospective Study in a Tertiary Centre, Government Medical College, Jammu, India was conducted on 140 patients of palpable thyroid lesions to identify the various cytological patterns of thyroid lesions and revealed that Most of the patients were in their 3rd decade of life with Mean age of 38.17 years and F:M ratio of 5.36:1. A total of 89.29% thyroid lesions were non neoplastic with Colloid goitre the most frequent (observed in 51.43% patients), followed by lymphocytic thyroiditis in 28.57% patients. 10.71% were neoplastic and included follicular neoplasm and papillary carcinoma observed in 4.29% patients each, followed by anaplastic carcinoma in 1.42% patients and medullary carcinoma in 0.71% patient [16].

A retrospective study done in Gondar, Ethiopia, to determine Cytological patterns of thyroid lesions during 2009 to 2013 with a total of 1010 cases revealed 768 (76%) were females. Benign thyroid lesions were the commonest diagnoses (916 [90.7%]) followed by malignant and neoplastic lesions that account 41 (4.1%) and 38 (3.76%) respectively with Colloid goitre (862/919 [93.8%]), follicular neoplasm (30/38 [78.9%]) and papillary carcinoma (25/41 [61%]) were the major subtype of benign, neoplasm and malignant lesions respectively. Thyroid tuberculosis (TB) was also found in 3 (0.29%) cases of benign lesions. A recent study done in the same region to determine Cytological Patterns of thyroid lesions included 144 study participants of the total, 3 (2.1%) had thyroid carcinoma, 46 (32%) had cystic degenerated follicular cells, and 82 (57%) had nodular thyroid goitre. In addition, a clinical presentation of a study participants, showed lymphadenitis in 7 participants (4.8%) [17, 18].

Another retrospective study done in Jimma, Ethiopia to determine the Prevalence of thyroid cancer among thyroid swelling in five years period from September 2012 to July 2017 showed that Out of the 2008 patients included in the study, there were 378 (18.9%) male subjects and 1626(81.1%) female subjects. The age of the participants ranged from age of 2 to 98. Among these cases, 1893 (94.3%) of the lesions were benign and only 89 (4.4%) were found to be malignant and 18 (0.9%) were suspicious for malignancy and the remaining 8 (0.4%) samples taken were deemed inconclusive. The leading type of thyroid malignancy was papillary carcinoma with 44 (49.43%) number of the cases followed by follicular neoplasms with 28 (31.4%) and the least common type of malignancy was anaplastic carcinoma with 17 (19.1%) cases observed. During the study, no case of medullary, hurthle cell or metastatic carcinoma was found [19].

## **Objective**

### **General objective**

To determine Cytopathologic Patterns of Thyroid Lesions and to correlate with their corresponding histopathologic results.

### **Specific objective**

To determine Cytopathologic Patterns of Thyroid Lesions.

To see the relationship of different Thyroid Lesions with age and sex of individuals.

To compare the FNAC reports with various standard reporting(classification) systems.

To correlate FNAC reports with the corresponding histopathologic results.

To compare the result with different studies.

## **Method**

This is a retrospective cross-sectional descriptive review of requests and reports of all the consecutive Fine needle aspiration cytology and histopathology evaluation of thyroidectomies/lobectomies performed at Black Lion specialized teaching Hospital in Addis Ababa, Ethiopia in a five years period from January 01, 2015 to August 30, 2019.

Ethiopia is a country located in the Eastern Horn of Africa, has a population of more than 100 million. The Black Lion Hospital in Addis Ababa is a teaching hospital of the Addis Ababa University and the largest referral hospital in the country. The practice of cytopathology and fine-needle aspiration began sometime after the establishment of the department of pathology in Addis Ababa University, Faculty of Medicine, Black Lion Hospital, in 1965. The department gives haematology, cytopathology, surgical pathology and neonatal autopsy services. All of the pathologist staff and residents rotate to work through the FNAC service. FNA is the only non-surgical method of determining whether a thyroid nodule is benign or malignant. All patients who had Fine needle aspiration cytology performed for thyroid lesions at Black Lion specializes teaching Hospital during the study period were included in the study.

All the hard copy of requests and reports of thyroid Fine needle aspiration cytology of patients with thyroid lesions seen during the study period and their corresponding histopathology were reviewed from the archive of pathology department.

Demographic data, clinical presentation of the patients and Fine needle aspiration

cytology and their corresponding histopathology diagnoses were extracted using data extraction sheet.

The cytopathologic (FNAC) reports of thyroid lesions were classified in to six diagnostic groups: **Non Diagnostic/Unsatisfactory**: involving See description, Inconclusive and Cyst fluid only; **Benign Lesions** involving: Colloid Goitre, Adenomatous Goitre, Acute thyroiditis, Sub acute granulomatous (de Quervain) thyroiditis, Chronic Lymphocytic(Hashimoto) thyroiditis, Tuberculosis, Riedel thyroiditis/Disease, Colloid Goitre with cystic degeneration and Hurthle cell change Thyroglossal duct cyst, Graves' disease and Lymphocytic thyroiditis; **Follicular Neoplasm** involving: Follicular neoplasm, Suggestive of Follicular neoplasm, Suspicious for Follicular neoplasm and Colloid Goitre with focal features of follicular neoplasm; **Hurthle Cell Neoplasm** involving: Hurthle cell neoplasm and Suggestive of Hurthle cell neoplasm; **Suspicious for Malignancy** involving: Suspicious for Papillary carcinoma, Suspicious for Malignancy and Lymphocytic thyroiditis with suspicious clusters for malignancy and **Malignant** involving: Papillary carcinoma, Suggestive of Papillary carcinoma, Papillary carcinoma with Lymph node secondary, Recurrent Papillary carcinoma, Recurrent Papillary Carcinoma with Lymph node secondary, Papillary carcinoma with features of anaplastic carcinoma, Anaplastic (undifferentiated carcinoma), Suggestive of anaplastic carcinoma, Anaplastic Carcinoma with Lymph node secondary, poorly differentiated carcinoma, poorly differentiated carcinoma with LN secondary, Medullary carcinoma, Suggestive of Medullary carcinoma, Recurrent Follicular Carcinoma, Follicular Carcinoma with metastases to the Scalp, Suggestive of Squamous Cell Carcinoma, DDX: Medullary Carcinoma Anaplastic Carcinoma and Carcinoma. The data were entered and analysed using statistical software, SPSS version 23.

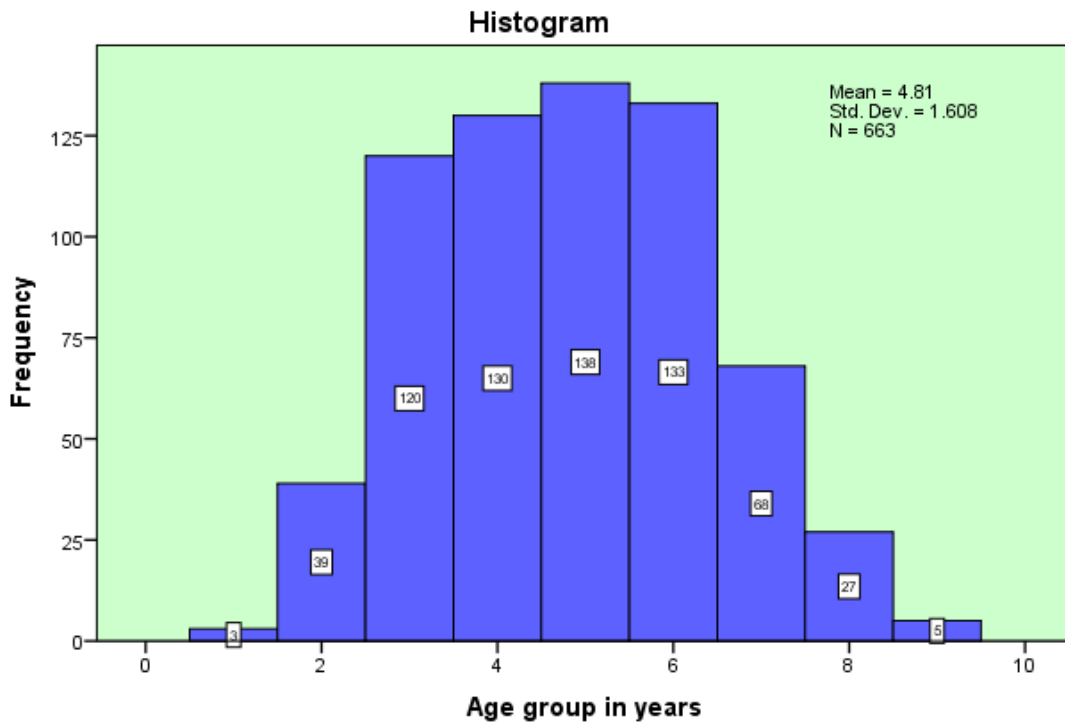
## Results

A total of 687 cases that fulfilled the study criteria were identified with 115,68,149,169 and 189 cases seen in the years 2015,2016,2017,2018 and 2019 respectively. Of the total cases, 563(82.0%) were Females and 120(17.5%) were males making F:M ratio of 4.69:1 with 4(0.6%) gender non-specified cases. Most of the patients were in the age range of 20-60 years, accounting for 521(77.3%) cases with Mean, std. Deviation, lowest and highest age limits of 41.98,15.285,4 and 84 years respectively. The mean age for males and females separately was 43.09(std. Deviation16.825) and 41.74(std. Deviation 14.944) respectively. The ages of 24(3.5%) cases were not mentioned. With regard to the type of thyroid enlargement: Multinodular Goitre, Solitary nodule and Diffuse enlargement were seen in 200(29.1%),174(25.3%),108(15.7%) of the cases respectively and the type of thyroid enlargement was not mentioned for 205(29.8%) cases by the clinicians or the pathologists .665(96.8%) of FNA procedures were palpation guided while the rest 22(3.2%) were Ultrasound guided cases.

**Table-2,** Distribution of thyroid lesion cases with Cytopathologic evaluation by year, Gender, age group, Clinical presentation and type of FNAC procedure.

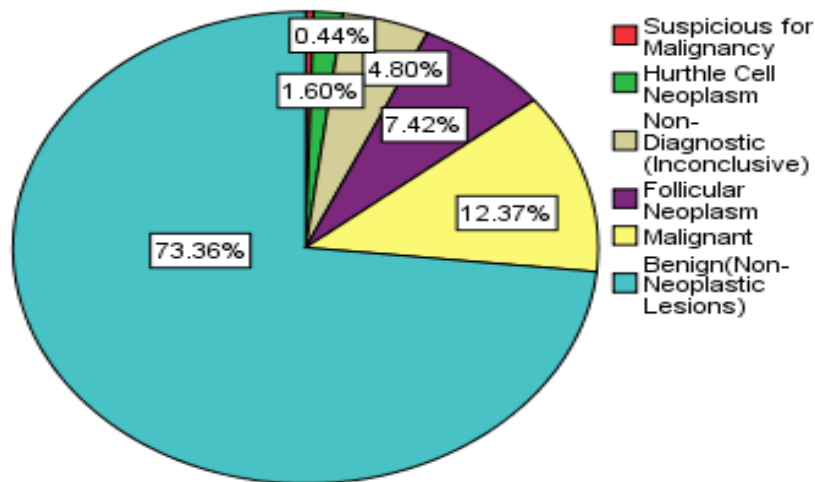
	<b>Year</b>	Frequency(no)	Percent (%)	Cumulative Percent (%)
Valid	2015	115	16.7	16.7
	2016	68	9.9	26.6
	2017	149	21.7	48.3
	2018	169	24.6	72.9
	2019	186	27.1	100.0
	Total	687	100.0	
<b>Gender</b>				
		Frequency(no)	Percent (%)	Valid Percent (%)
Valid	Male	120	17.5	17.6
	Female	563	82.0	82.4
	Total	683	99.4	100.0
Missing System		4	.6	
Total		687	100.0	
<b>Age group(in years)</b>				
		Frequency(no)	Percent(%)	Valid Percent(%)
Valid	< 10	3	.4	.5
	10 – 19	39	5.7	5.9
	20 – 29	120	17.5	18.1
	30 – 39	130	18.9	19.6
	40 - 49	138	20.1	20.8
	50 – 59	133	19.4	20.1
	60 – 69	68	9.9	10.3
	70 – 79	27	3.9	4.1
	80+	5	.7	.8
	Total	663	96.5	100.0
Missing System		24	3.5	
Total		687	100.0	
<b>The type of thyroid enlargement</b>				
		Frequency(no)	Percent(%)	Cumulative Percent(%)
Valid	Multinodular	200	29.1	29.1
	Solitary nodule	174	25.3	54.4
	Diffuse enlargement	108	15.7	70.2
	Not specified	205	29.8	100.0
	Total	687	100.0	
<b>Type of FNAC Procedure</b>				
		Frequency(no)	Percent(%)	Cumulative Percent(%)
Valid	Papation guided	665	96.8	96.8
	Ultrasound guided	22	3.2	100.0
	Total	687	100.0	

**Fig-1,** A graph showing distribution of all thyroid lesions with cytopathologic diagnosis in the five years period among different age groups.



From all 687 studied cases, 33 (4.8%) were Non-diagnostic (Inconclusive), while Benign (Non-neoplastic lesions), Follicular neoplasm, Hurthle Cell neoplasm, Suspicious for malignancy and malignant diagnosis accounted for 504 (73.4%), 51 (7.4%), 11 (1.6%), 3 (0.4%), 85 (12.4%) of the cases respectively.

The 33 non-diagnostic (Inconclusive) cases were reported as: see description 17 (51.5%), Inconclusive 9 (27.3%) and cyst 7 (21.2%) and five of them were among the 22 Ultrasound guided cases making the proportion 22.7%. Though the non-diagnostic percentage was lower 28/665 (4.2%) for palpation guided cases, the difference between the two procedures in the non-diagnostic (Inconclusive) rate was not analyzed since the total number of ultrasound guided cases was very low.



**Fig-2,** A graph showing the proportion of the cytopathologic categories during the five years period.

Among the Benign (Non-neoplastic lesions), Colloid Goitre was the most common diagnosis occurring in 458(90.9%) of the cases followed by Adenomatoid Goitre 28(5.6%). There were also diagnoses of Tuberculosis and Riedel thyroiditis with 01(0.1%) case for each. From the 51 cases of Follicular neoplasm diagnoses, one was diagnosed as Colloid Goitre with focal features of Follicular neoplasm, 03 as Suspicious for Follicular neoplasm, 08 as Suggestive of Follicular neoplasm and the rest 39 cases as Follicular neoplasm whereas the 11 Hurthle Cell neoplasm cases were diagnosed as suggestive of Hurthle Cell neoplasm in the two and the rest 09 as Hurthle cell neoplasm.

**Table-3** Frequency of benign lesions and neoplasms.

	Frequency	Percent	Valid(%)	Cumulative(%)
Colloid Goitre	458	66.7	90.9	90.9
Adenomatoid Goitre	28	4.1	5.6	96.4
Acute thyroiditis	2	.3	.4	96.8
Sub-acute granulomatous (de Quervain) thyroiditis	5	.7	1.0	97.8
Chronic Lymphocytic (Hashimoto) thyroiditis	3	.4	.6	98.4
Tuberculosis	1	.1	.2	98.6
Riedel thyroiditis/Disease	1	.1	.2	98.8
Colloid Goitre with cystic degeneration and Hurthle cell change	1	.1	.2	99.0
Thyroglossal duct cyst	1	.1	.2	99.2
Graves' disease	3	.4	.6	99.8
Lymphocytic thyroiditis	1	.1	.2	100.0
Total	504	73.4	100.0	
System missing	183	26.6		
Total	687	100.0		
Follicular Neoplasm	51	7.4	82.3	82.3
Hurthle Cell Neoplasm	11	1.6	17.7	100.0
Total	62	9.0	100.0	
Missing System	625	91.0		
Total	687	100.0		

The gender specific Cytopathologic malignant diagnosis (including malignant and suspicious for malignancy) proportion was 30/120(25%) for males and 58/563(10.3%) for females which was a statistically significant difference(p=0.001). The age group specific distribution of malignant cytopathologic diagnosis looks like the following: zero for <19 years and 8/120(6.6%),9/130(6.9%),22/138(15.9%),25/133(18.8%),14/68(20.6%),6/27(22.2%) and 3/5(60%) for the age groups of 20-29,30-39,40-49,50-59,60-69,70-79 and >80 years old individuals respectively. Regarding to the malignant diagnosis rate among the different types of thyroid enlargement, it is highest among non-specified cases 44/205(21.5%) followed by 24/200(12%),14/174(8%) and 6/108(5.5%) among multinodular, solitary nodule and diffuse enlargement types respectively.

Variables		Cytopathologic diagnosis by category count(%)						Total
		Inconclusive(Non-diagnostic)	Benign (Non-Neoplastic)	Follicular Neoplasm	Hurthle Cell Neoplasm	Suspicious for malignancy	Malignant	
Gender	Male	7(5.8%)	73(60.8%)	8(6.7%)	2(1.7%)	1(0.8%)	29(24.2%)	120(100.00%)
	Female	26(4.6%)	428(76.0%)	42(7.5%)	9(1.6%)	2(0.4%)	56(9.9%)	563(100.0%)
Total		33(4.8%)	501(73.4%)	50(7.3%)	11(1.6%)	3(0.4%)	85(12.4%)	683(100.0%)
Age Group In Years	<10	0(0.0%)	3(100.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	3(100.0%)
	10-19	2(5.1%)	34(87.2%)	2(5.1%)	1(2.6%)	0(0.0%)	0(0.0)	39(100.0%)
	20-29	4(3.3%)	98(81.7%)	8(6.7%)	2(1.7%)	1(0.8%)	7(5.8%)	120(100.0%)
	30-39	6(4.6%)	106(81.5%)	7(5.4%)	2(1.5%)	0(0.0%)	9(6.9%)	130(100.0%)
	40-49	9(6.5%)	93(67.4%)	12(8.7%)	2(1.4%)	1(0.7%)	21(15.2%)	138(100.0%)
	50-59	5(3.8%)	89(66.9%)	13(9.8%)	1(0.8%)	0(0.0%)	25(18.8%)	138(100.0%)
	60-69	4(5.9%)	45(66.2%)	4(5.9%)	1(1.5%)	1(1.5%)	13(19.1%)	68(100.0%)
	70-79	2(7.4%)	15(55.6%)	2(7.4%)	2(7.4%)	0(0.0%)	6(22.2%)	27(100.0%)
	>80	0(0.0%)	2(40.0%)	0(0.0%)	0(0.0%)	0(0.0%)	3(60.0%)	5(100.0%)
Total		32(4.8%)	485(73.2%)	48(7.1%)	11(1.7%)	3(0.5%)	84(12.7%)	663(100.0%)
Type Of Enlargement	Multi-nodular	5(2.5)	148(74.0)	19(9.5)	4(2.0)	1(0.5)	23(11.5)	200(100.0)
	Solitary nodule	6(3.4)	136(78.3)	16(9.2)	2(1.1)	0(0.0)	14(8.0)	174(100.0)
	Diffusely enlarged	3(2.8)	95(88.0)	4(3.7)	0(0.0)	1(0.9)	5(4.6)	108(100.0)
	Not specified	19(9.3)	125(62.0)	12(5.9)	5(2.4)	1(0.5)	43(21.0)	205(100.0)
Total		33(4.8)	504(73.4)	51(7.4)	11(1.6)	3(0.4)	85(12.4)	687(100.0)

**Table-4, Distribution of the categories of Cytopathologic diagnosis of thyroid lesions among Male & Females, different age groups and type of thyroid enlargement.**

Fig-3, A graph showing distribution of categories of Cytopathologic diagnosis of thyroid lesions among males and females.

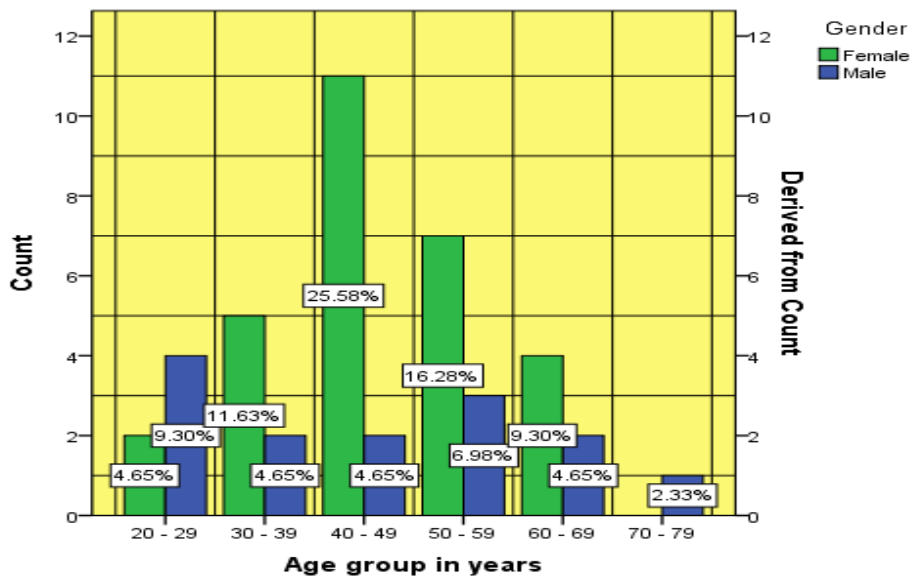
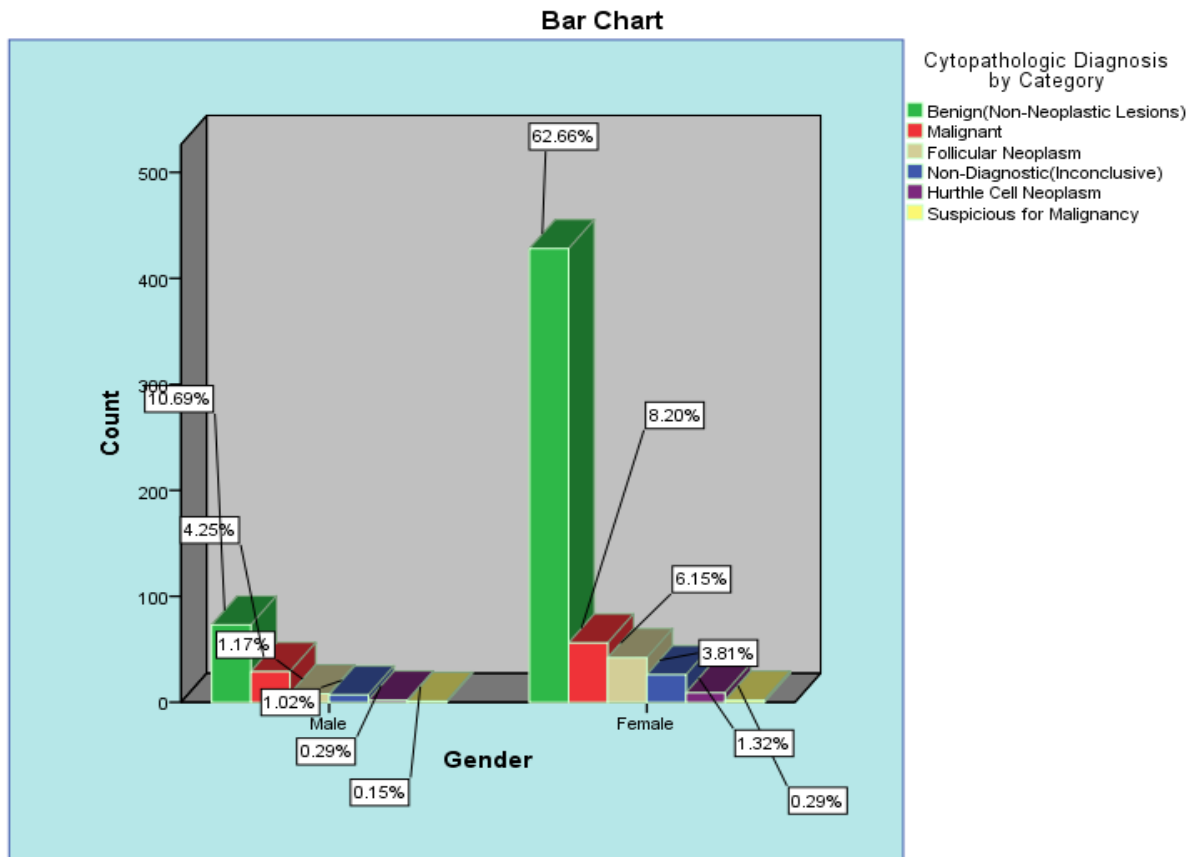
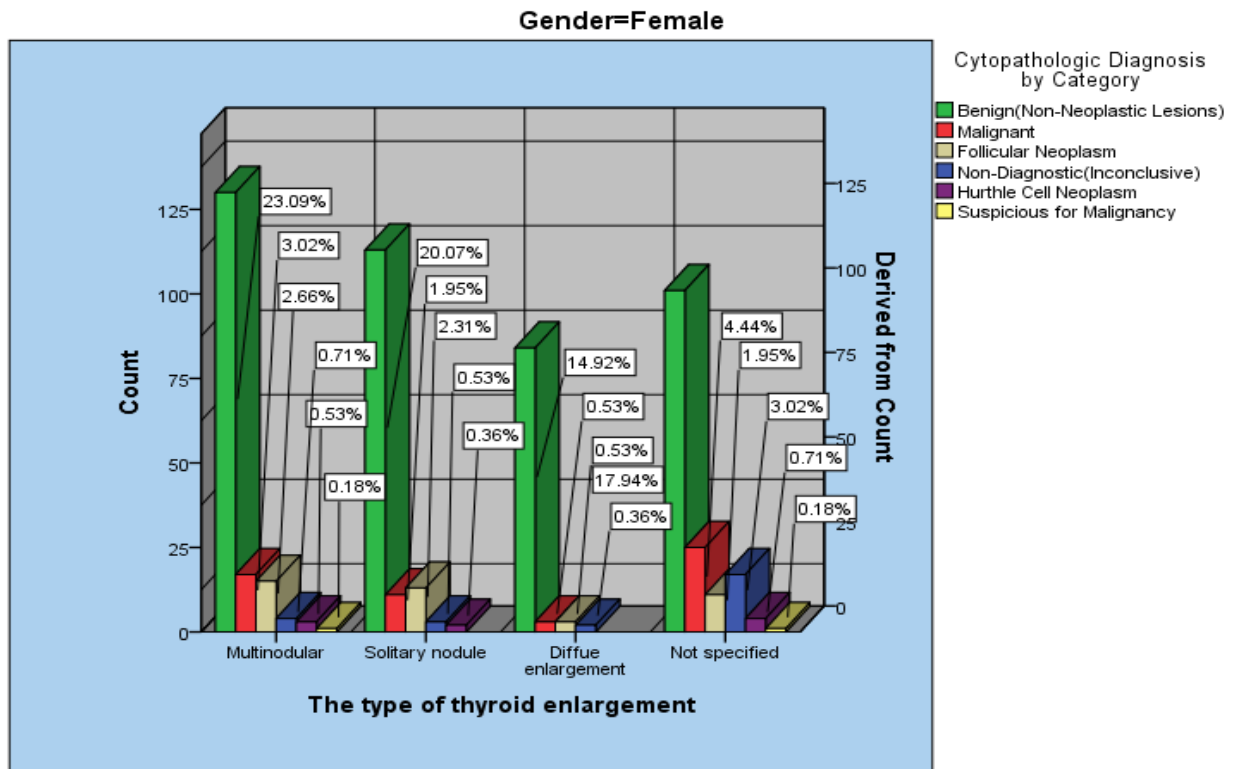
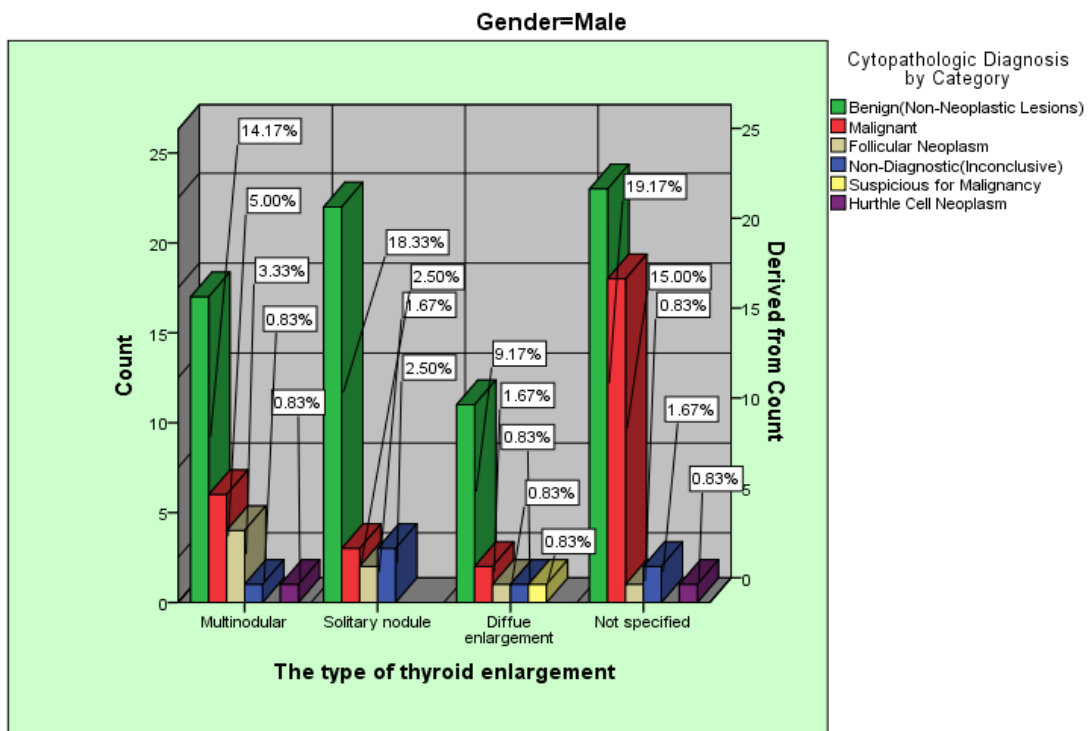


Figure-4 shows distribution of Cytopathologic malignant diagnosis among different age groups and gender.

Fig-5, A graph showing distribution of cytopathologic diagnostic categories of thyroid lesions in relation to different types of thyroid enlargement among females(A)and males(B).



A)



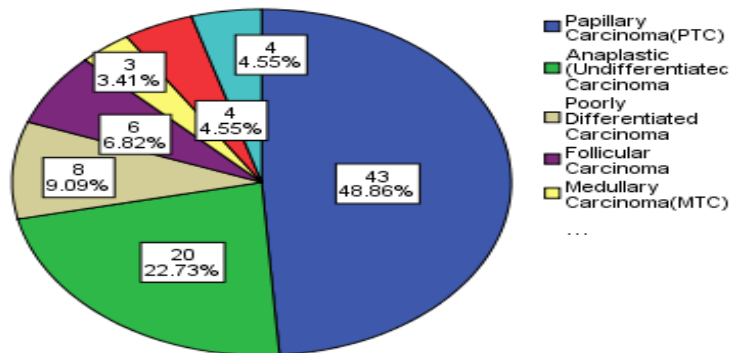
B)

The minimum and maximum age for the occurrence of malignancy in the study was 21 and 80 years old respectively with F:M ratio of 1.9:1. Among the 03(0.4%) suspicious for malignancy and 85(12.4%) malignant diagnosis cases, Papillary Carcinoma was the leading type of malignancy accounting 43(48.9%) of all malignant cases and diagnosed as Suspicious for Papillary Carcinoma, Suggestive of Papillary Carcinoma and Papillary Carcinoma in 01, 08,34 of the cases respectively. Eight of the Papillary Carcinoma cases were recurrent whereas ten of them presented with lymph node secondary. The remaining two Suspicious for malignancy cases were diagnosed as Suspicious for malignancy and Lymphocytic thyroiditis with suspicious clusters for malignancy. Anaplastic(Undifferentiated) Carcinoma was the second most common malignant diagnosis, which constituted 20(23.6%) of malignant cases with two cases presented with lymph node secondary. There were 08(9.4%) cases of Poorly differentiated Carcinoma diagnoses with one of them had lymph node secondary. The remaining malignant diagnoses were: Follicular Carcinoma 6(7.1%) with two cases have scalp metastasis and the rest four were recurrent cases, four cases of carcinoma with mixed features with two reported as Papillary Carcinoma with features of anaplastic carcinoma and the other two as DDx of Medullary and Anaplastic carcinomas, suggestive of Squamous Cell Carcinoma 01 and Carcinoma 01.

Table-5 shows age sex distribution of different Cytopathologic Malignant diagnosis.

Cytopathologic Malignant Diagnosis	N	% of Total N	% of Total Sum	Minimum	Maximum	Range	Mean	Std. Deviation	Gender[N(%)]		Total
									Female	Male	
Papillary Carcinoma(PTC)	43	49.4%	44.7%	21	70	49	45.37	12.775	29 67.4%	14 32.6%	43 100.0%
Anaplastic(Undifferentiated Carcinoma)	19	21.8%	25.1%	30	80	50	57.79	11.287	15 75.0%	5 25.0%	20 100.0%
Poorly Differentiated Carcinoma	8	9.2%	8.3%	23	75	52	45.13	15.075	4 50.0%	4 50.0%	8 100.0%
Follicular Carcinoma	6	6.9%	6.9%	40	65	25	50.17	8.841	6 100.0%	0 0.0%	6 100.0%
Medullary Carcinoma(MTC)	3	3.4%	4.6%	50	80	30	66.67	15.275	1 33.3%	2 66.7%	3 100.0%
Carcinoma with mixed features	4	4.6%	5.2%	45	70	25	57.00	10.424	2 50.0%	2 50.0%	4 100.0%
Carcinoma/Malignant Diagnosis	4	4.6%	5.3%	28	80	52	57.50	21.626	1 25.0%	3 75.0%	4 100.0%
Total	87	100.0%	100.0%	21	80	59	50.22	13.993	58 65.9%	30 34.1%	88 100.0%

Figure-6 shows frequencies of cytopathologic malignant diagnosis of thyroid lesions



Though about 800 Histopathologic reports of thyroid lesions during the study period were reviewed, only 19 of 687 Cytopathologic diagnoses had corresponding histopathologic report and the findings were as follows: nine (47.4%) of the 19 cases were diagnosed by FNAC as colloid goiter and histopathologically, 05 of them diagnosed as colloid goitre, 01 colloid goiter with adenomatous and hashimoto thyroiditis focus, 02 as Follicular adenomas and 01 as papillary carcinomas. Two cases of FNAC diagnosis of suggestive for papillary carcinoma were reported as Hurthle Cell adenoma and Follicular adenoma hayalinizing trabecular variant up on histopathologic evaluation. Another two cytopathologic reports of poorly differentiated carcinoma were found to be papillary carcinoma histologically. The other difference was in two cases that were reported as see description and colloid goiter with cystic degeneration and Hurthle cell change and histologically diagnosed as colloid goitre and colloid goiter with papillary carcinoma of columnar type.

Table-6 shows comparison of Cytopathologic Diagnosis of benign (non-neoplastic lesions) with their corresponding histopathological diagnosis.

		Corresponding Histopathologic diagnoses						Total
		Colloid Goitre	Colloid Goitre with Adenomatous and hashimoto thyroiditis focus	Colloid Goitre with Papillary thyroid carcinoma of columnar type	Adenomatous Goitre	Follicular Adenoma	Papillary Carcinoma	
Benign (non-neoplastic) Cytopathologic Diagnosis	Colloid Goitre No(%)	5(55.6%)	1(11.1%)	0(0.0%)	0(0.0%)	2(22.2%)	1(11.1%)	9(100.0%)
	Adenomatoid Goitre No(%)	0(0.0%)	0(0.0%)	0(0.0%)	1(100.0%)	0(0.0%)	0(0.0%)	1(100.0%)
	Colloid Goitre with cystic degeneration and Hurthle cell change No(%)	0(0.0%)	0(0.0%)	1(100.0%)	0(0.0%)	0(0.0%)	0(0.0%)	1(100.0%)
Total No(%)		5(45.5%)	1(9.1%)	1(9.1%)	1(9.1%)	2(18.2%)	1(9.1%)	11(100.0%)

		Corresponding Histopathologic diagnoses					Total
		Follicular Adenoma hayalinizing trabecular variant	Hurthle cell Adenoma	Papillary Carcinoma	Papillary Carcinoma with Cervical Lymph node positive for both PTC&SCC(Known SCC of the parotid	Papillary Carcinoma with Jugular & central neck Lymph nodes secondary	
Cytopathologic Malignant Diagnoses	Papillary carcinoma No(%)	0(0.0%)	0(0.0%)	1(100.0%)	0(0.0%)	0(0.0%)	1(100.0%)
	Suggestive of Papillary carcinoma No(%)	1(50.0%)	1(50.0%)	0(0.0%)	0(0.0%)	0(0.0%)	2(100.0%)
	Poorly differentiated carcinoma No(%)	0(0.0%)	0(0.0%)	1(50.0%)	0(0.0%)	1(50.0%)	2(100.0%)
	Papillary carcinoma with Lymph node secondaries(%)	0(0.0%)	0(0.0%)	0(0.0%)	1(100.0%)	0(0.0%)	1(100.0%)
Total No(%)		1(16.7%)	1(16.7%)	2(33.3%)	1(16.7%)	1(16.7%)	6(100.0%)

Table-7 shows comparison of Cytopathologic malignant diagnosis of thyroid lesions with their corresponding histopathological diagnosis.

If the results are seen by category, 11/19 of the cases were diagnosed as benign (non-neoplastic lesions) by FNAC and histologically 9/11 were benign and 2/11 cases found to be carcinoma. Out of the 6/19 cytopathologic malignant diagnoses, 4/6 were malignant histologically as well whereas the remaining 2/6 cases were actually adenomas. The discrepancy between the two diagnostic procedures was not analyzed further since the sample is very small.

Table-8 shows comparison of Cytopathologic Diagnosis by Category with histopathologic diagnosis.

		Histopathologic Diagnostic Category			Total
		Benign (Non-Neoplastic Lesion)	Adenoma	Carcinoma	
Cytopathologic Diagnosis by Category	Non-Diagnostic(Inconclusive) No(%)	1(100.0%)	0(0.0%)	0(0.0%)	1(100.0%)
	Benign(Non-Neoplastic Lesions) No(%)	7(63.6%)	2(18.2%)	2(18.2%)	11(100.0%)
	Follicular Neoplasm No(%)	0(0.0%)	1(100.0%)	0(0.0%)	1(100.0%)
	Malignant No(%)	0(0.0%)	2(33.3%)	4(66.7%)	6(100.0%)
Total No(%)		8(42.1%)	5(26.3%)	6(31.6%)	19(100.0%)

## Discussion

In this retrospective cross-sectional descriptive study of 687 thyroid lesions with cytopathologic evaluation during a 5-year period from January 01, 2015 to August 30, 2019, most of the patients with cytopathologic evaluation were in the age range of 20-60 years accounting 521(77.3%) cases with Mean and std.Deviation of 41.98,15.28 respectively. Females constituted 563/683(82.0%) of patients and males accounted for 120/683(17.3%) cases with F:M ratio of 4.69:1. Benign lesion (non neoplastic) was the predominant cytopathologic diagnosis of thyroid lesion in the study seen in 504/687(73.4%) of patients with colloid goitre being the predominant lesion that accounted for 458/504(90.9%) of the cases followed by Adenomatous Goiter 28/504(5.6%). This result is in agreement with studies done in India, a one-year prospective study conducted on 140 patients of palpable thyroid lesions with F:M ratio of 5.36:1, with 89.29% non- neoplastic lesions and Colloid goitre accounting 51.43% of the non-neoplastic cases[16] and with another study done in Gondar, Ethiopia, which was a retrospective study of 1010 thyroid lesions with 768 (76%) being females that showed Benign thyroid lesions constituted (916 [90.7%]) and Colloid gaiter (862/919 [93.8%])[17]. The study showed 13 cases of thyroiditis accounting 2.6%(13/504) of benign cases with Tuberculosis and Riedel thyroiditis/Disease constitute 01(0.2%) each and Sub-acute Granulomatous (de Quervain) thyroiditis and Chronic Lymphocytic(Hashimoto) thyroiditis constituted 5/504(1%) and 3/504(0.6%) of cases respectively. This finding is lower for Chronic Lymphocytic(Hashimoto) thyroiditis and higher for Sub-acute granulomatous (de Quervain) thyroiditis when compared with other studies, such as a study in Iran, A 5-year prospective study of 1639 cases from October 2007 to September 2011 to determine the accuracy and reliability of FNAC revealed 55 (5.2%) cases of Hashimoto's thyroiditis and 2 (0.2%) cases of Dequervain's subacute thyroiditis, and one (0.1%) case of Riedel's thyroiditis[20] and a One-Year Prospective Study done in India showed Lymphocytic thyroiditis

40 (28.57 %) and Subacute thyroiditis 2 (1.43%)[16].

A retrospective study of 1010 thyroid lesions during 2009 to 2013 done in Gondar, Ethiopia to determine Cytological patterns of thyroid lesions showed thyroid TB in 0.3% (3/919)[17]. In this study, Neoplasm diagnoses accounted 61/687(8.9%) of cases with Follicular Neoplasm constituting 50/61(82.3%) of them with 42/50(84%) occurred in females and the rest 8/50(16%) in males with the minimum and maximum age, Range, Mean and Std. Deviation: 15 and 71 years, 56, 43.46 and 13.778 respectively and Hurthle Cell Neoplasm accounted 11/61(17.7%) of the cases most [9/11(81.8%)] occurring in females with no significant difference in minimum and maximum age, Range, Mean and Std. Deviation with that of follicular neoplasm. This finding is slightly lower than the result of a retrospective study done in New York, NY) between January 1992 and December 2003 and Texas between January 1993 and May 2005 involving a total of 4703 cases that showed 544/4703(11.6%) FN[11] and higher than the results of a study done in India on 945 thyroid FNAs between January 2010 and December 2014 which revealed 48 (6.6%) were follicular lesions[21]. The result is also higher than observed from study done in Gondar, Ethiopia in which Neoplasm lesions constituted (n=39 [3.9%]) with 30/39(76.9%) Follicular thyroid neoplasm and 9/39(23.1%) Hurthle cell neoplasm[17]. The prevalence of cytopathologic malignant diagnosis in this study was 88/687(12.8%) with Papillary Carcinoma being the leading type accounting 43/88(49.3%) of the cases with 29/43(67.4%) cases occurred in females and 14/88(32.4%) in males and minimum and maximum ages of 21&80 years respectively. There were also 19/88(21.8%) cases of Anaplastic (Undifferentiated Carcinoma, 8/88(9.2%) Poorly Differentiated Carcinoma, 6/88(6.9%) Follicular Carcinoma and 3/88(3.4%) Medullary Carcinoma(MTC) diagnoses. This finding is a bit higher than that seen in other study done in India which showed 8/140(6.8%) malignant diagnosis with 6/140(4.29%) PTC and 2/140(1.42%) Anaplastic carcinoma[16] and three domestic studies two done in

Gondar revealed malignant diagnosis of 4.1% (41/1010) and 62/846(7.3%)[17, 22] and another study in Jimma showed 107/2024(5.3%) malignant

diagnosis[23].The proportion of malignant diagnosis and non-diagnostic reports were comparable with what is expected according to the Bethesda reporting system[8].

Histopathologic reports were available Only for 19 of the 687 patients with cytopathologic evaluation for thyroid lesion during the study period and 11 of them diagnosed as benign (non-neoplastic lesion) and 6 as malignant by FNAC. Two of the 11 benign and 2/6 malignant cytopathologic diagnosis were found to be malignant and adenoma respectively up on histopathologic evaluation.

## **Conclusion**

Although benign thyroid lesions were the predominant cytopathologic diagnosis, malignant lesions also account a significant proportion with anaplastic(undifferentiated) and poorly differentiated carcinomas taking unusually high share. A significant number of cases especially with indeterminate cytopathologic features were reported differently which otherwise would have belonged to the same category in the Bethesda reporting system for thyroid cytopathology. It was difficult to determine the accuracy rate of FNAC due to the very small number of available histopathologic reports for patients with cytopathologic diagnosis of thyroid lesions, which may be due to the fact that many thyroid specimens are submitted to Black Lion Hospital from other Hospitals where the preoperative cytopathologic evaluation might have been done.

## **Limitation of the study**

We were unable to achieve the estimated number of histopathologic reports to compare with the corresponding cytopathologic reports during the study period.

It was difficult to ascertain the association of different thyroid lesions with the type of thyroid enlargement since the type of enlargement was not mentioned for a large number of cases.

## **Recommendation**

It is crucial to improve the data keeping methods

It is good to document the type of thyroid enlargement by the clinician and the pathologist so that future studies will determine the relation with different thyroid lesions.

There is inconsistency in reporting terminologies which can be improved by having local or adopting standard international reporting systems like the Bethesda System for reporting thyroid cytopathology and avoid confusion for the treating clinician.

## **Acknowledgements**

I would like to express my deepest gratitude to my instructor and advisor, Dr Tufa Gemechu (MD), Associate professor of pathology for his expertise, guidance and constructive advice in the course of this study.

Next, I would like to extend my sincere gratitude to college of health sciences, Addis Ababa University.

## References

1. Ackerman DLV Ra: **ROSAI AND ACKERMAN'S SURGICAL PATHOLOGY**, Eleventh Edition edn. Philadelphia: Elsevier; 2018.
2. Toyib S, Kabeta T, Dendir G, Bariso M, Ret W: **Prevalence, Clinical Presentation and Patterns of Thyroid Disorders Among Anterior Neck Mass Patients Visiting Jimma Medical Center, Southwest Ethiopia**. *Biomed J Sci & Tech Res* 2019.
3. Bekele A, Osman M: **Goitre in a Teaching Hospital in North Western Ethiopia**. *East And Central African Journal of Surgery* 2006.
4. Okeoghene Ogbera A, Flunrusho kuku S: **Epidemiology of thyroid diseases in Africa**. *Indian Journal of Endocrinology and Metabolism* 2015.
5. Gupta M, Gupta S, Gupta VB: **Correlation of Fine Needle Aspiration Cytology with Histopathology in the Diagnosis of Solitary Thyroid Nodule**. *Journal of Thyroid Research* 28 February 2010.
6. Ergete W, Abebe D: **Discordance Rate between Thyroid Fine Needle Aspiration Cytology and Histopathologic Diagnosis**. *EthiopJHealth Dev* 2002.
7. P Misiakos E, Margari N, Meristoudis C, Machairas N, Schizas D, Petropoulos K, Spathis A, Karakitsos P, Machairas A: **Cytopathologic diagnosis of fine needle aspiration biopsies of thyroid nodules**. *World Journal of Clinical Cases* February 16, 2016, 4(2): 38-48.
8. al Be: **The Bethesda System for Reporting Thyroid Cytopathology**. 2018.
9. Tamhane S, Gharib H: **Thyroid nodule update on diagnosis and management**: *Clinical Diabetes and Endocrinology* 2016.
10. Cross DP, Chandra DA, Giles DT, Johnson DS, Kocjan DG, Poller DD, Stephenson PT: **Guidance on the reporting of thyroid cytology specimens**: publishing@rcpath.org; January 2016.
11. Yang M, Jack , Logrono M, Schnadig, , Roberto MD1 V, Wasserman M, Patricia G. : **Fine-needle Aspiration of Thyroid Nodules: A Study of 4703 Patients With Histologic and Clinical Correlations**. *Wiley InterScience* 6 August 2007.
12. Hen Lee YM, Lee NJM, Kim JH, MD,1, Suh M, 1,Sang-il , Kim M, 1 ,Taik-Kun, Song M, Jae Jun **Sonographically Guided Fine Needle Aspiration of Thyroid Nodule:Discrepancies between Cytologic and Histopathologic Findings**. *Wiley InterScience* 2008.
13. muRatli a, eRDoGan1 n, Sevim S, unal i, akyuz S: **Diagnostic efficacy and importance of fne-needle aspiration cytology of thyroid nodules**. *Journal of Cytology* April 2014 **Volume 31**( Issue 2).
14. Quaglinoa F, Marchesea V, Mazzab E, Cristina G, Leminia R, Taraglio S: **When Is Thyroidectomy the Right Choice? Comparison between Fine-Needle Aspiration and Final Histology in a Single Institution Experience**. *Eur Thyroid J* December 8, 2016.
15. Masereka1 R, Okeny2 PK, Fualal3, Jane .O, Wamala4 D: **Diagnostic accuracy of fne needle aspiration cytology in patients undergoing thyroidectomy in Uganda: tertiary hospital experience**. *African Health Sciences* December, 2016, **Vol 16**.
16. Kour B, Singh P, Kour A: **Cytological Patterns of Thyroid Lesions: A One-Year Prospective Study in a Tertiary Centre**. *Journal of medical science and clinical research* 2017, **05**(07).

17. Melak<sup>1</sup> T, Abebe<sup>1</sup> M, Tesfaye<sup>2</sup> W, Melku<sup>3</sup> M: **Cytological patterns of thyroid lesions at Gondar University Hospital, Northwest Ethiopia: A retrospective study.** *Journal of Molecular Pathophysiology* 23 September 2015.
18. Asmelash D, Tesfa K, Biadgo B: **Thyroid Dysfunction and Cytological Patterns among Patients Requested for Thyroid Function Test in an Endemic Goiter Area of Gondar, North West Ethiopia.** 14 August 2019.
19. Dandena<sup>1\*</sup> A, MeleseSinaga T, Bezabeh<sup>3</sup> M: **Prevalence of thyroid cancer among thyroid swelling in Jimma University Medical Center, South West Ethiopia: A five-year retrospective study.** *International Journal of Medicine and Medical Sciences* May 2018, **Vol. 10(5),**.
20. Ali Esmaili H, Taghipour H: **Fine-Needle Aspiration in the Diagnosis of Thyroid Diseases: An Appraisal in Our Institution.** *International Scholarly Research Network* August 2012.
21. \* CS: **Diagnostic accuracy of fine needle aspiration cytology of thyroid and evaluation of discordant cases.** *Journal of the Egyptian National Cancer Institute* 14 July 2015.
22. Melak<sup>1\*</sup> T, Mathewos<sup>2</sup> B, Enawgaw<sup>3</sup> B, Damtie<sup>2</sup> D: **Prevalence and types of thyroid malignancies among thyroid enlarged patients in Gondar, Northwest Ethiopia: a three years institution based retrospective study.** *BioMed Central Ltd* 2014 14:899.
23. Dandena<sup>1\*</sup> A, Teshome<sup>2</sup> MS, Bezabeh<sup>3</sup> M: **Prevalence of thyroid cancer among thyroid swelling in Jimma University Medical Center, South West Ethiopia: A five-year retrospective study.** *International Journal of Medicine and Medical Sciences* May 2018.