

**CYTOPATHOLOGIC PATTERNS OF THYROID GLAND MASS AMONG
PATIENTS IN JIMMA UNIVERSITY SPECIALIZED UNIVERSITY
HOSPITAL, JIMMA, SOUTH WEST ETHIOPIA: A TWO YEARS
RETROSPECTIVE STUDY.**



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A RESEARCH THESIS TO BE SUBMITTED TO JIMMA UNIVERSITY
DEPARTMENT OF PATHOLOGY FOR PARTIAL FULFILLMENT OF
SPECIALITY IN HUMAN ANATOMIC PATHOLOGY.

AUGUST 2020

JIMMA, ETHIOPIA

**CYTOPATHOLOGIC PATTERNS OF THYROID GLAND MASS IN
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ETHIOPIA: A TWO YEARS RETROSPECTIVE CROSS-SECTIONAL
STUDY.**

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August, 2020

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ABSTRACT

Background: Thyroid gland is one of the largest endocrine organs, with a remarkable potential for growth and enlargement. Thyroid diseases are among the most common endocrine disorders in humans. Prevalence and incidence of thyroid diseases are not well studied in Ethiopia and other African countries; Characterizing type of the lesions in a given setup has paramount importance to design effective strategy. Hence, the purpose of this study is to determine the frequency of various cytological thyroid lesions among patients in Jimma University Specialized Hospital (JUSH). **Objective:** This study aimed to determine cytopathologic patterns of thyroid gland mass on Fine Needle Aspiration Cytology (FNAC) in JUSH. **Methods:** A retrospective descriptive study was applied on patients with thyroid gland mass diagnosed at JUSH pathology department with from 1st September, 2018 to 30th August, 2019. Data was collected using structured check lists from the patients FNAC report record manually by trained cytopathology technicians working in the department. Data was entered into Epi data v.3.1. cleared and exported to SPSS V.20 for analysis. Descriptive statistics such as frequency, percentage, mean and median were used for analysis the results in tables and figures. **Results:** A total of 1841 cases were undergone thyroid FNAC from 1st September 2018 to 30th August 2019 in the pathology department. Majority of these (83.2%) were females; and 310(16.8%) were males. The highest prevalence (30.3%) of thyroid swelling cases has been occurred in the age group of 21-30 years. The most common thyroid lesion found by FNAC is colloid goiter 1603 (87.1%). A total of 40(2.1%) cases are found to be malignant and the most common type is papillary carcinoma accounting 20 (50%) followed by anaplastic carcinoma 16(40%). Although thyroid swelling was common in and around Jimma, the prevalence of thyroid cancer was quite low. **Conclusion:** Benign lesions were the predominant thyroid lesion; of which the proportion of colloid goiter was higher compared to another subtype of benign thyroid lesions. Malignant thyroid lesions had also contributed. Future research with histological technique, detail socio-demographic information, and clinical feature is crucial to determine the patterns of thyroid lesions and associated factors.

Key words: FNAC, thyroid gland, mass, Pattern, Ethiopia

ACKNOWLEDGEMENTS

First of all, I would like to thank Jimma University for giving me an opportunity to conduct the research.

I extend my gratitude to pathology department in identifying area which needs investigation and helping me to develop an action proposal.

I am very grateful to my advisors Dr. Abdo Kedir and Dr. Lelisa Sena for giving me necessary and supportive comments devoting their precious time during the research work.

ABBREVIATION AND ACRONYMS

AITD	Autoimmune thyroid diseases
ATC	Anaplastic thyroid carcinoma
AUS	Atypia of undetermined significance
EPI	Epidemiological information
FNAC	Fine needle aspiration cytology
FTN	Follicular thyroid neoplasm
HCN	Hurthle cell neoplasm
IDD	Iodine deficiency disorders
IRB	Institutional review board
JUSH	Jimma University Specialized Hospital
MTC	Medullary thyroid carcinoma
NCI	National cancer institute
NCG	Nodular colloid goiter
PPE	Personnel protective equipment
PDTC	Poorly differentiated thyroid carcinoma
PTC	Papillary thyroid carcinoma
ROM	Risk of malignancy
SPSS	Statistical Package for the Social Science.
TBSRTC	The Bethesda System for Reporting Thyroid Cytopathology

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CHAPTER 1: INTRODUCTION

1.1. Background

The thyroid gland is a butterfly-shaped endocrine gland that is located on the antero-inferior aspect of the neck, below and anterior to the larynx, and consists of two bulky lateral lobes connected by a relatively thin isthmus. The normal adult thyroid gland weighs 16 to 25 g. (1). It secretes thyroid hormones which are essential for growth, neuronal development, reproduction and regulation of energy metabolism (2).

Thyroid disease is a global health problem that can substantially impact well-being, as it is one of the most common endocrine disorder next to diabetic mellitus accounting around 30% to 40% of the endocrine disorder (3). Thyroid gland diseases can be functional structural or combination of the two. The most common clinical presentation of thyroid diseases is thyroid mass (enlargement), which is can be caused by non-neoplastic as well as neoplastic lesions. Generally non-neoplastic conditions are the most common causes of thyroid enlargement (4).

Goiter, which is caused by impaired synthesis of thyroid hormone, is the commonest cause of thyroid enlargement. Depending on etiology, goiter can be classified into two endemic and sporadic. Endemic goiter is caused by mainly iodine deficiency and ingestion of goitrogens while sporadic goiters are due to hereditary enzymatic defects that interfere with thyroid hormone synthesis (dys hormonogenic goiter), ingestion of substances that interfere with thyroid hormone synthesis and due to unknown causes (4).

Inflammatory conditions are also other non-neoplastic causes of thyroid enlargement which accounts up to approximately 20% of all thyroid diseases. According to the clinical course, thyroiditis has been subdivided into acute, subacute, and chronic forms. Recent classifications are based on the fact that the majority of thyroiditis cases have an autoimmune background. The most common form of this disease is autoimmune hashimoto's thyroiditis, with or without clinical manifestation of hypothyroidism, less common forms of autoimmune thyroiditis comprise subacute granulomatous (de Quervain's) thyroiditis, postpartum thyroiditis, silent ("painless") thyroiditis, and invasive-sclerosing thyroiditis (Riedel's thyroiditis). Non-autoimmune thyroiditis is very rare (acute suppurative thyroiditis, radiation thyroiditis).

Thyroiditis is both clinically and morphologically an important differential diagnosis of thyroid tumors (5).

The other diseases entity that affect the thyroid gland which also results thyroid enlargement are thyroid neoplasms, which can be benign or malignant. Eventhough benign neoplasms are very few in type, follicular adenoma and its variant hürthle cell adenoma, they out number thyroid carcinomas by 10:1 (4,6).

The vast majority of thyroid malignancies derive from thyroid follicular epithelium. (7,8). Malignancies derived from thyroid follicular epithelium are classified based on their degree of differentiation as well-differentiated, poorly differentiated, or anaplastic carcinomas. Well-differentiated thyroid carcinoma includes papillary and follicular types. Other rare malignancies arise in the thyroid gland. These include neoplasms arising from the thyroid C cells that produce calcitonin, medullary carcinoma, lesions derived from other ultimobranchial tissues such as thymus and parathyroid, and malignancies derived from stromal elements and lymphomas can also affect thyroid gland. Metastases to thyroid occur in patients with disseminated malignancy (1).

There is a large number of imaging techniques used in the diagnosis of thyroid nodules, but guidelines indicate that fine-needle aspiration cytology (FNAC) is the first-line diagnostic test, being the most accurate and cost-efficient procedure. These attributes are greatly enhanced when ultrasound is used as a guide for better sampling (9). Published data suggest that fine-needle aspiration (FNA) has a sensitivity ranging from 65% to 98%, a specificity from 72% to 100%, and an overall accuracy of 75% to 90% (10).

Fine-needle aspiration (FNA) of the thyroid gland was first introduced by Söderström in 1952 (11). In Ethiopia, the practice of cytopathology and FNA began sometimes after the establishment of the department of pathology in Addis Ababa University, Faculty of Medicine, Black Lion Hospital, in 1965 (12). In fact, it has become the initial test in the management of most patients with a thyroid nodule because it is rapid, safe and inexpensive and provides better selection of patients for surgery than any other test. Given the high prevalence of thyroid nodules, thyroid FNAC could easily be the most common type of FNA specimens in a cytology laboratory. However, the reporting of thyroid FNA is the most confusing of reporting cytology

results. The technique has its own shortcomings mainly due to interobserver and intra-observer variability, especially in indeterminate cases. In addition, there is also a lack of uniformity in the reporting systems used, which vary not only from country to country but also from laboratory to laboratory and even among individuals working at the same laboratory. This hampers accurate interpretation by the clinician, thus affecting patient management. To address this common issue, the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) was introduced based upon the proceedings of “The National Cancer Institute” (NCI) Thyroid Fine Needle Aspiration State of the Science Conference” held in Bethesda, Maryland, in 2007. TBSRTC encompasses six thyroid cytology categories, with each category having an implied cancer risk and the best modality of management (13).

1.2. Statement of the problem

Thyroid diseases are among the commonest endocrine disorders worldwide (14). Generally, women are at the greatest risk, developing thyroid problems seven times more often than men, facing as high as a one-in-five chance of developing thyroid problems during her lifetime. Even this proportion increases with age and for those with a family history of thyroid problems (15,16). The worldwide prevalence of goiter in the general population is estimated at 4 to 15% and ten times more people are estimated to have clinically impalpable thyroid swellings diagnosed on ultrasound which is up to 30% and autopsy results show that about 50% of the general population may have thyroid enlargements but luckily, less than 10% of these thyroid swellings are malignant (17). Of the autoimmune diseases of the thyroid, Grave’s disease is the predominantly documented in Africa (18). The overall incidence of AITD in Tunisia is 9.9% and this was noted to have occurred in conjunction with 6.3% of other autoimmune disease (19). In Ethiopia, the prevalence of autoimmune thyroid disease is reported to be 1.2% (20).

Worldwide, the overall prevalence of thyroid malignancy is approximately 1–5% of all cancers in women and less than 2% in men. During the past several decades, an increasing incidence of thyroid cancer has been reported in European countries, USA and Canada. It is now the fastest growing cancer type and the sixth most common cancer. In Europe alone, thyroid malignancy affects approximately 24,826 individuals annually, with an estimated mortality rate of 5,993 patients each year (23,24,25). It is also one of the thyroid disease problems in sub Saharan

Africa due to high prevalence of iodine deficiency goiter. For instance, the iodine deficiency is suggested to play a role for follicular cancer increment in South Africa (24). It is the cause significant mortality and morbidity of patients, particularly from undifferentiated thyroid carcinoma. Death from differentiated thyroid carcinoma, however, may also occur unless early diagnosis and treatment is initiated (11).

Even though thyroid gland lesions are among the commonest endocrine disorders worldwide, there is no sufficient study done particularly in our country and specifically in south western Ethiopia. So, knowing the cytopathologic patterns of various thyroid lesions helps us to design specific strategy. Since thyroid malignancies are among the most rapidly increasing malignancies worldwide nowadays, having up to date information is important to know time variation in prevalence.

1.3. Significance of the study

Conducting research on thyroid gland mass in southwest Ethiopia, JUSH can provide baseline information on the cytopathologic patterns in this part of the country. The study will benefit policy makers and health institution to increase quality of service given for patient with thyroid gland mass. The study will help health care professional to gain knowledge on the cytopathologic patterns of thyroid gland mass in south west Ethiopia. The final result of this paper will serve as a basis of reference for further research on the area for interested individuals, it can also used as an indicator to conduct large scale community based study to determine causes of thyroid swelling so as to prevent before its health, social and economic impact on the community.

CHAPTER 2: LITERATURE REVIEW

2.1 Global burden of thyroid mass

Thyroid cancer is the most common endocrine malignancies which occurs two to four times more frequently in females than in males (21). It is the second leading cause of death among endocrine cancers next to carcinoma of the ovary (25). In most areas of the world, thyroid cancer incidence has been appreciably increasing over the last few decades, whereas mortality has steadily declined. International comparisons are complex due to differences in diagnosis and ascertainment of the disease. About 230,000 new cases of thyroid cancer were estimated in 2012 among women and 70,000 among men, with an age-standardized (world population) rate of 6.10/100,000 women and 1.90/100,000 men (26).

Thyroid carcinoma can arise from either follicular or non-follicular thyroid cells. Follicular cancers include papillary thyroid cancer (PTC, 80%), follicular thyroid cancer (FTC, up to 11%), Hürthle cell cancer (HCC, 3%) and anaplastic thyroid cancer (ATC, 2%). PTC and FTC, which together account for the vast majority of cancers, are commonly referred to together as differentiated thyroid cancer (DTC). HCC, a subtype of FTC, is often classified on its own because it has a distinct histological appearance and is often less responsive to standard therapy. Similar to HCC, several subtypes of DTC, including tall cell, columnar and insular thyroid cancers, are thought to be more aggressive. In contrast to DTC, ATC represents undifferentiated thyroid cancer. Medullary thyroid cancer (MTC) arises from non-follicular thyroid cells called calcitonin-producing cells and accounts for about 4% of thyroid cancers (27).

Thyroid cancer is the most common endocrine malignancy, with an estimated 44,670 new cases diagnosed in the United States in 2010. Its prevalence continues to rise; in 2008 it became the sixth most diagnosed cancer in women. For reasons that are unclear, thyroid cancer is 2-3 fold more common in females than males (27).

A 4 years retrospective institution-based study done in Iran shows about 64.3% of thyroid mass is due to benign conditions; 7.8% were malignant and 18.66% were suspicious for malignancy. The most common benign lesions were multinodular goiter accounting about 94.4%, the remaining found to be inflammatory thyroid diseases. Among the malignant lesions PTC was

common accounting about 66.4%, FTC 10.9%, MTC 10.1%, ATC 10.9%, non-Hodgkin's lymphoma 0.78% and metastatic carcinoma 0.78% (28). A similar study in Saudi Arabia shows as female to male ratio of 5.2:1, benign non-neoplastic lesions accounting 77.7%, 5% suspicious for malignancy and 5.2% malignant, 80% of which were papillary thyroid cancer (29).

2.2. Burden of thyroid mass at continental level.

In Africa, Iodine deficiency disorders (IDD) which top the list of thyroid disorders and remain the commonest cause of thyroid disorders in the continent is often affected not only by the iodine status in the region but sometimes also by selenium deficiency and thiocyanate toxicity. The reported prevalence rates of endemic goiter range from 1% to 90% depending on the area of study with myxedematous cretinism still a prominent feature of IDD in only a few regions of the continent. The extent of autoimmune thyroid disorders remains unknown because of underdiagnosis and underreporting but the few available studies note a prevalence rate of 1.2% to 9.9% of which Graves disease is the commonest of these groups of disorders.

The documented prevalence rates of thyroid CA in the African continent are as follows (papillary: 6.7–72.1%, follicular: 4.9–68%, anaplastic: 5–21.4%, and medullary: 2.6%–13.8%). For the differentiated thyroid CA, there is a changing trend toward the more frequent occurrence of papillary CA compared to follicular CA and this may be attributable to widespread iodization programs (30).

A descriptive retrospective, clinic-based study done in Sudan shows females are about 5-6 times more commonly affected than males by thyroid mass. Similar study shows about 94.9% were non neoplastic and 2.4% were malignant; 2.6% were indeterminate for malignancy. Among the malignant ones anaplastic carcinoma is found to be the commonest accounting about 28.2% followed by papillary (17.9%). Patients aged 61–70 years showed higher frequency of malignancy (31).

2.3. Burden of thyroid mass at the national level.

A meta-analysis of 19 articles were done to determine the pooled prevalence of goiter and its associated factors among children in Ethiopia and estimated to be 40.50%. The regional

distribution of goiter ranged from 44.22% in Southern Nations Nationalities and Peoples' Region, to 32.79% in Benishangul Gumez region. The prevalence of goiter among female children (44.34%) was higher than among male (32.88%) children. Goiter prevalence was also significantly higher among children who consumed vegetables three or more times per week; those who had family history of goiter; and those whose family stored salt near to fires (32).

A 15 years retrospective study done at Gondar university hospital shows, 76% were female patients. The median age of patients with thyroid lesions was 26 years; 24 year for males; and 28 year for woman. Benign lesions account 91% of the lesions followed by malignant 4.1%. Colloid goiter, follicular neoplasm, and PTC were the major subtypes of the benign, neoplastic and malignant lesions respectively. Medullary thyroid carcinoma was the least lesion of all malignant cases. Metastasized cancer to thyroid gland which includes squamous cell carcinoma were also noticed in 9.8% of malignant cases. Except under the age of 10 years, all types of thyroid lesions were predominant in female with the overall male to female ratio of 1:3.17. In addition, except the non-diagnostic cases, all type of lesions was predominant in female than male. About 55 of thyroid lesions were observed in patients who were under 30 years old. Thyroiditis was only observed in the age group of 20-39 years old individuals (33).

A similar study done in JUSH, shows, 18.9% were male 81.1% female patients, signifying as females are about 4 to 5 times more commonly affected by thyroid mass lesions. The mean age for the diagnosis was 33.8 years. Among these cases, 94.3% of the lesions were benign and only 4.4% were found to malignant and 0.9% were suspicious for malignancy. The leading type of thyroid malignancy was papillary carcinoma accounting 49.43% of the cases followed by follicular neoplasms with 31.4% and the least common type of malignancy that was found was anaplastic carcinoma with 19.1% cases observed. During the study, no case of medullary, hurtle cell or metastatic carcinoma was found (34).

CHAPTER 3: OBJECTIVE

3.1 General objective

To describe the cytopathology of thyroid gland mass on FNAC in Jimma University Medical Center from September 2018 to August 2019.

3.2 Specific objectives

- ❖ To describe cytomorphology of thyroid gland mass
- ❖ To describe the relationship of age and thyroid gland mass.
- ❖ To describe the relationship of sex, and thyroid gland mass.
- ❖ To describe the relationship of residency and thyroid gland mass.

CHAPTER 4: METHODS

4.1. Study Area and period

Study was conducted in Jimma University Specialized Hospital (JUSH), pathology department, located in Jimma Town, south western part of Ethiopia, 352km from the capital city of Ethiopia, Addis Ababa, from 1st September 2018 to 30th August 2019. JUSH is the only tertiary and referral hospital in southwest part of the country. About 6000 -7000 patients come to the hospital annually; and 20%-30% of of these patients come for thyroid FNAC. The pathology department of JUMC has four pathology seniors, 14 residents, and 2 histopathology technicians and 7 assistant technicians. Services given by the pathology department of JUMC include FNAC, fluid cytology, histopathology and hematopathology. The study was conducted from May to August 2020.

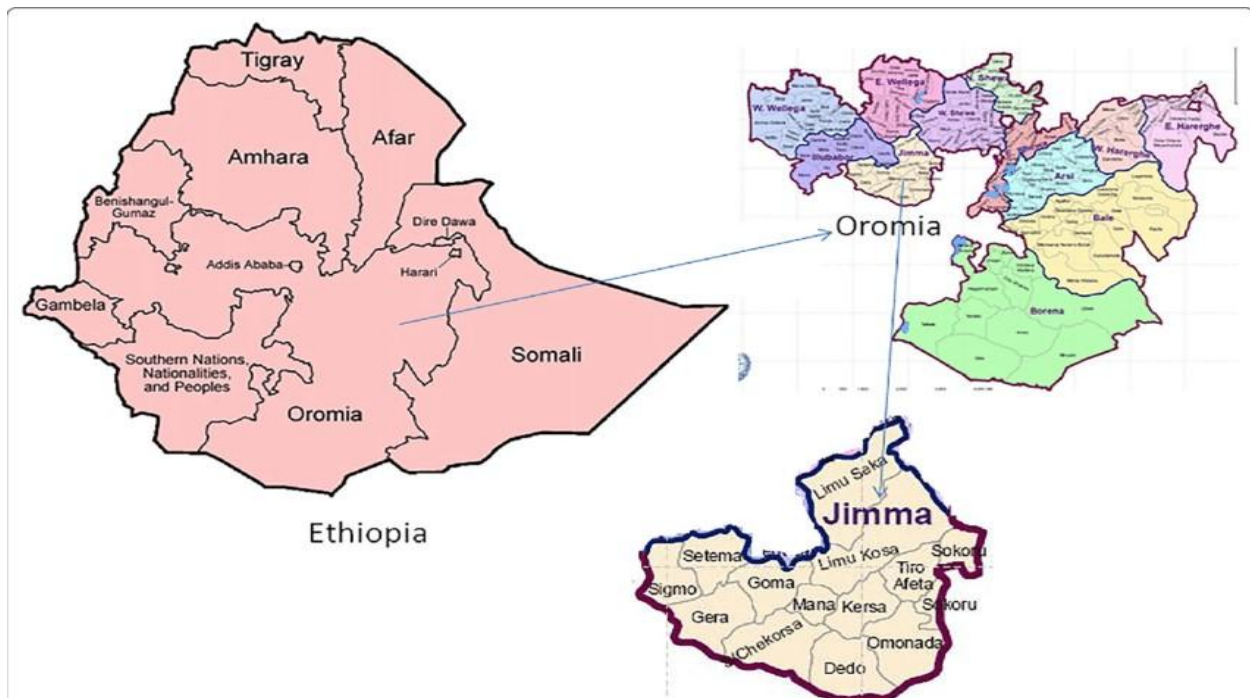


Figure 2 map of Jimma zone and neighboring zones

4.2. Study Design

Facility based retrospective descriptive study design was applied.

4.3. Population

4.3.1. Source population

Source population included all patients with thyroid gland mass for whom cytological diagnoses were made between September 2018 and August 2019.

4.3.2. Study population

All patients with thyroid gland mass who were subjected to FNAC from September 2018 to August 2019 fulfilling inclusion and exclusion criteria.

4.4. Inclusion and Exclusion criteria

4.4.1. Inclusion criteria

All FNAC reports records on thyroid gland mass having; Age, Sex, and diagnosis.

4.4.2. Exclusion criteria

All FNAC result records thyroid gland mass with missing either of sex, age or cytodiagnosis.

4.5. Sampling technique

All FNAC records with thyroid gland mass filled on FNAC request form September 2018 to August 2019 was identified. Case fulfilling the inclusion criteria and exclusion criteria was reviewed.

4.6. Data collection procedures

Data was collected using structured check lists from the patients FNAC report record in pathology department manually by principal investigator and cytopathology technicians working in the from patients FNAC report records. One supervisor from junior pathology residents and

three data collectors from cytopathology technician was enrolled. Training was given for data collectors and supervisor for two days on objective of the study, data collection tools and procedures. The principal investigator supervised data collection daily.

During training and data collecting activities, appropriate PPE was used. Social distancing and proper hand hygiene was implemented before and after data collection as the national protocol (35).

4.7. Study variables

Dependent variables

Cytopathologic Diagnosis

Independent Variables

Age

Sex

Address

4.8. Data processing and Analysis

Data was entered into Epi data v.3.1. cleared and exported to SPSS V.26 for analysis and descriptive statistics such as frequency, percentage, mean and median were computed. Tabulation was done to measure degree of association between dependent and independent variables. Results were presented using narration, tables and figures.

4.9. Data quality management

Data was collected by trained cytopathology technicians and completeness, accuracy and clarity of collected data were checked carefully by the principal investigator and supervisor on daily basis.

4.10. Ethical consideration

Before the study begins ethical clearance was obtained from the Institutional Review Board (IRB) of JUSH. Before conduct of the study permission was also obtained from pathology department to use the records of clients for research purpose. Name of patient was excluded from all records of patients and confidentiality was ensured.

4.11. Dissemination plan

The results of this study will be disseminated or communicated to the Jimma University, the Regional Health Bureau, and other concerned bodies. The findings of this study will be published on a reputable journal to reach the wide scientific community.

4.12. Operational definition

Nondiagnostic or Unsatisfactory: Cyst fluid only, virtually acellular specimen, other (obscuring blood, clotting artifact, drying artifact, etc.)

Benign: Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.), consistent with chronic lymphocytic (Hashimoto) thyroiditis in the proper clinical context, Consistent with granulomatous (subacute) thyroiditis, others.

Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance: Atypia of follicular epithelial cells which don't fall into any of the diagnostic categories.

Follicular Neoplasm or Suspicious for a Follicular Neoplasm / Specify if oncolytic (Hürthle cell) type

Suspicious for Malignancy: Suspicious for papillary thyroid carcinoma, suspicious for medullary thyroid carcinoma, suspicious for metastatic carcinoma, suspicious for lymphoma, other.

Malignant: Papillary thyroid carcinoma, poorly differentiated carcinoma, medullary thyroid carcinoma, undifferentiated (anaplastic) carcinoma, squamous cell carcinoma, Carcinoma with mixed features (specify), metastatic malignancy, Non-Hodgkin lymphoma, other

CHAPTER 5: RESULTS

A total of 1985 cases had undergone FNAC examination of enlarged thyroid gland with in the past two years, from 1st September 2018 to 30rd August 2019. Out of these, 144 of patients' FNAC records were incomplete, so they were excluded from the study. From 1841 patients included in the study 1531 (83.2%) were females and 310 (16.8%) were males with female to male ratio of 4.9:1. Age of patients ranges from 1 to 95 years. Mean age of patients was found to be 35.77 (\pm 14.0) years. Close to a third (30.3%) of the study participants were in the age group of 21-30 years followed by the age group 31-40 years that accounted 468 (25.4%) of the cases. In this particular study thyroid gland mass was not common in the age group of 1-10 and >70 years accounting 26 (1.4%) and 18 (1%) of the cases, respectively.

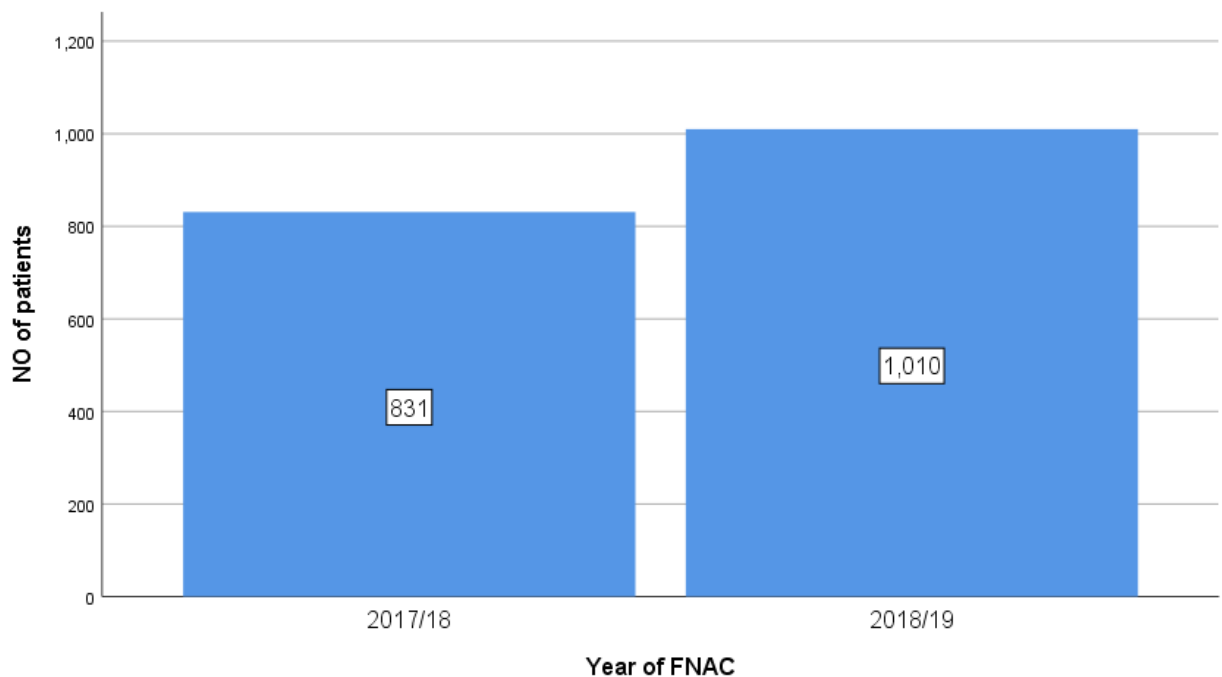


Figure 2. Number of patients with thyroid gland mass by year, in JUSH, Jimma, Ethiopia, from Sep. 2018 to Aug. 2019 N=1841

The majority of patients who come to JUSH for thyroid FNAC are in the year 2018/19; accounting about 1,010 (54.86%). The remaining 831 (45.86%) done in 2017/18 (Figure 2.).

The majority of patients' address with thyroid gland mass who came to Jimma University for thyroid FNAC is not recorded which accounts 1167 (63.4%) of the subjects of study population. 341 (18.4%) were from Jimma zone outside Jimma town. Cases from Jimma town and outside Jimma zone are the least accounting 218 (11.8%) and 115 (6.2%) of the cases respectively.

Cytomorphology of thyroid mass; TBSRTC.

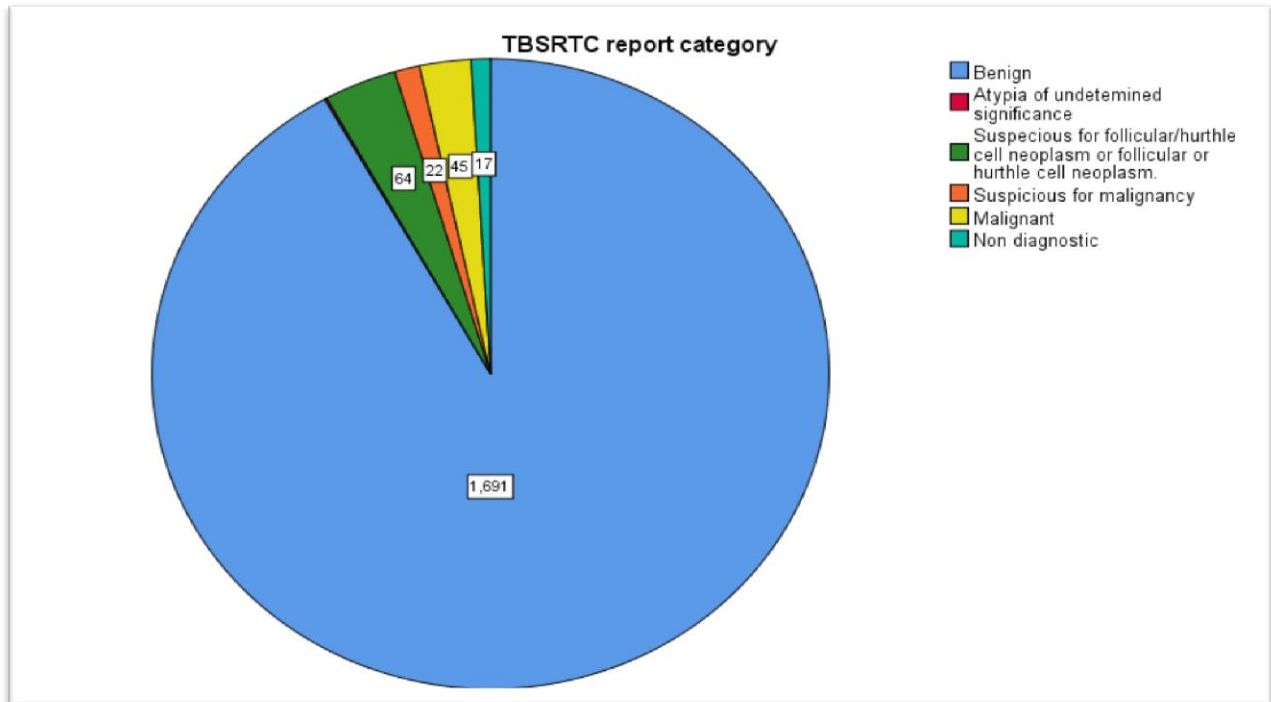


Figure 3. Cytomorphologic distribution of thyroid mass in JUSH, Jimma, Ethiopia, from 2017/18 to 2018/19; N=1841

The study shows 1691 (91.9%) of the thyroid mass lesions are benign non-neoplastic lesions, 64 (3.5%) follicular/hurthle cell neoplasm and suspicious for follicular/hurthle cell neoplasm, 22 (1.2%) suspicious for malignancy, 45 (2.4%) malignant, 2 (0.1%) atypia of undetermined significance, 17 (0.9%) are deemed to be non-diagnostic (Figure 3).

Table 1. Cytomorphologic distribution of thyroid mass by sex; in JUSH, Jimma, Ethiopia, from 2017/18 - 2018/19; N=1841

		TBSRTC Reporting Category						Total
		Benign	AUS	FN/HCN Suspicious for FN/HCN	Suspicious for malignancy	Malign- ant	Non diagnostic	
Patients' sex	Female	1422	2	50	16	28	13	1531
	Male	269	0	14	6	17	4	310
Total		1691	2	64	22	45	17	1841

From the benign non neoplastic lesions 1422 (84.1%) are found in females where as 269 (15.9%) are in males. The majority of FN/HCN or suspicious for FN/HCN cases are also found in females accounting 50 (78.1%). Females are found to be more commonly affected by thyroid mass in all diagnostic categories of TBSRTC (Table 1.)

Table 2. Distribution of thyroid lesions by age category, in JUSH, Jimma, Ethiopia, from 2017/18 - 2018/19; N=1841

		patients' age category in years								Total
		1-10	11-20	21-30	31-40	41-50	51-60	61-70	>70	
TBSRT report category	Benign	21	221	523	439	287	131	55	14	1691
	AUS	0	0	1	1	0	0	0	0	2
	FN/HCN or suspicious for FN/HCN	1	5	22	14	8	9	3	2	64
	Suspicious for malignancy	0	3	5	6	4	3	1	0	22
	Malignant	3	1	4	3	17	13	3	1	45
	Non diagnostic	1	1	2	5	6	1	0	1	17
Total		26	231	557	468	322	157	62	18	1841

Majority of benign non neoplastic thyroid lesions 523 (30.9%) are found in the age group of 21-30 years followed by 439 (25.9%) in the age group of 31-40 years. FN/HCN suspicious for

hurthle cell neoplastic lesions which are the second most common reported cases has also the same age distribution as benign non neoplastic thyroid lesions, majority 22 (34.7%) are found in 21-30 years followed by 31-40 years which accounts 14 (21.9%) (Table 2.).

Table 3. Frequency of thyroid lesions with age categories in JUSH, Jimma, Ethiopia from 2017/18-Aug. 2018/19 ; N=1841

		patients' age category in years								Total
		1-10	11-20	21-30	31-40	41-50	51-60	61-70	>70	
Cytological diagnosis	NCG	21	206	492	420	272	126	52	14	1602
	BFH	0	6	14	14	6	2	3	0	45
	Suppurative thyroiditis	0	4	5	2	2	1	0	0	14
	Subacute and chronic thyroiditis	0	5	12	4	7	2	0	0	30
	Suspicious for FTN	1	1	6	3	0	1	0	1	13
	Suspicious for hurthle neoplasm	0	1	1	3	1	1	0	0	7
	FTN	0	2	10	7	6	5	3	1	34
	Hurthle cell neoplasm	0	1	5	1	2	2	0	0	11
	suspicious for PTC	0	3	4	6	2	3	1	0	20
	Suspicious for MTC	0	0	1	0	1	0	0	0	2
	PTC	1	1	3	3	8	4	0	0	20
	PDTC	0	0	1	0	0	1	1	1	4
	ATC	1	0	0	0	5	8	2	0	16
	Others	1	0	1	0	4	0	0	0	6
	Non diagnostic	1	1	2	5	6	1	0	1	17
	Total		26	231	557	468	322	157	62	18

The most common thyroid lesion diagnosed in the two years study was nodular colloid goiter accounting 1602 (87%) of the total thyroid mass lesions that undergone cytologic examination. The next two most common thyroid diseases in descending order of frequency are BFH 45

(2.4%), FN 34 (1.8%). The other reported cases account less than 10% of the total thyroid diseases all together. The least common cases found in the study period are 2 cases reported as suspicious for medullary carcinoma (Table 3.)

Benign non neoplastic lesions

Table 4. Distribution of benign non neoplastic lesions by sex in JUSH, Jimma, Ethiopia, from 2017/18 – 2018/19; N=1691

		Benign non-neoplastic lesions				
		NCG	BFH	Acute suppurative thyroiditis	Chronic thyroiditis	Total
Sex	female	1347	39	12	25	1423
	male	255	6	2	5	268
Total		1602	45	14	30	1691

Among the benign thyroid lesions NCG accounts the major component, 1602 (94.7%), followed by benign follicular hyperplasia 45 (2.3%), inflammatory lesions are found to account the least. All these benign lesions are predominant in females (Table 4.).

Table 5. Distribution of benign non neoplastic lesions by age category in JUSH, Jimma, Ethiopia, from 2017/18 – 2018/19; N=1691

		Benign non neoplastic lesions				
		NCG	BFH	Acute suppurative thyroiditis	Chronic thyroiditis	Total
Age category	1-10	21	0	0	0	21
	11-20	206	6	4	5	221
	21-30	492	14	5	12	523
	31-40	419	14	2	4	439
	41-50	272	6	2	7	287
	51-60	126	2	1	2	131
	61-70	52	3	0	0	55
	>70	14	0	0	0	14
Total		1602	45	14	30	1691

NCG and BFH are common in the 3rd and 4th decades where as both acute suppurative and chronic inflammatory lesions are common in 2nd and 3rd decades. The study also shows relative reduction of benign lesions before 10 years and >70 years (Table 5).

Thyroid malignant neoplasms

Prevalence of thyroid malignancies among patients who come thyroid mass is found to be 2.1%. Five other malignant thyroid neoplasms are also reported in the study period; two of them reported as poorly differentiated malignancy; the other two as carcinomas and the remaining one reported as malignancy.

Table 6. Distribution of top three thyroid carcinomas by year , JUSH, Jimma, Ethiopia from 2017/18-2018/19 N=40

		Year of FNAC		Total
		2017/18	2018/19	
Carcinomas	PTC	14	6	20
	PDTC	3	1	4
	ATC	9	7	16
Total		26	14	40

Majority of thyroid carcinomas are detected in the year 2017/18 accounting 26 (65%) of the total cancer cases (Table 6).

Table 7. Distribution of top three thyroid carcinomas by sex , JUSH, Jimma, Ethiopia from 2017/18-2018/19 N=40

		Sex		Total
		Female	Male	
Carcinomas	PTC	14	6	20
	PDTC	1	3	4
	ATC	8	8	16
Total		23	17	40

Generally among malignant thyroid neoplasms found in this study papillary thyroid carcinoma is the leading type accounting 20 (50%) followed by anaplastic thyroid carcinoma 16 (40%). The least common type of thyroid malignancy detected was poorly differentiated thyroid carcinoma 4(0.2%). Papillary thyroid carcinoma is commonest in females but in males anaplastic thyroid carcinoma is found to be common in our study. We found thyroid carcinomas are more common in females accounting 23 (57.5%). Sex specific prevalence of thyroid cancer among female with thyroid swelling is 1.2% and among males 5.4% (Table 7.).

Table 8. Distribution of top three thyroid cancers based on patients' age category in JUSH, Jimma, Ethiopia from 2017/18 to Aug. 2018/19; N=40

		patient's age category								Total
		1-10	11-20	21-30	31-40	41-50	51-60	61-70	>70	
Thyroid	PTC	1	1	3	3	8	4	0	0	20
carcino	ATC	1	0	0	0	5	8	2	0	16
mas	PDTC	0	0	1	0	0	1	1	1	4
Total		2	1	4	3	13	13	3	1	40

Age specific prevalence of thyroid cancer is higher in the age group of 41-60 years accounting 26 (65%). Peak incidence of papillary thyroid cancer is in the age group 41-50 years while anaplastic and poorly differentiated thyroid carcinomas are common after 50 years of age (Table 8).

CHAPTER 6: DISCUSSIONS

Cytomorphological identification of thyroid mass lesions have a paramount importance for selection of proper management, since most patients need surgical or medical management. FNAC is a reliable and cost-effective diagnostic procedure to diagnose thyroid lesions so that we can select the appropriate treatment modality (18). Currently thyroid FNAC specimens are reported according to TBSRTC which has established a uniform, tiered reporting system. Apart from enabling the cytopathologists to have succinct, unambiguous and uniform report of thyroid FNAC it also provides clinically useful information to the referring clinician (6,13).

Our study, as compared to a previous five year retrospective study which has the same study design and area (34), shows increased number of patients who came to JUSH with thyroid gland mass for FNAC. This might be increased service of the health sector, increased prevalence of diseases or increased health seeking behaviour of the society, needs further study.

In this study age of patients ranges from 1 to 95 years which signifies thyroid lesions can occur in all age groups which agrees with studies done in Taiwan 1-93 years (36), Sudan 3-87 years (31), India 18-78 years (37). Peak age for the occurrence of thyroid mass is 20-40 years with mean age of 35.77 years which also agrees most of the studies; Bangladeshi (38), Nigeria (18).

In this study, except the age group of ≤ 10 and > 70 years, females are affected about 5 times more commonly than men which agrees with standard text books and most studies done in different parts of the world, Sudan 5.3:1 (31), India 4.9:1 to 6.6:1 (39-41). Under the 10 years the female to male ratio is comparable because of absence of sex hormone variation (33).

Generally thyroid lesions are more common in females and majority of them are nonneoplastic diseases which is also seen in this particular study and so many researches done in different areas of the world Brazil 96.7% (42), India 73.68% (39), USA 73.8% (40), Taiwan 89.4% (36). Previous studies done in JUSH and UOG, northwestern part of and southwestern Ethiopia also shows the same result (33,34). NCG accounts the majority of benign non neoplastic thyroid diseases which agrees with standard text books (4) and many other studies. Inflammatory diseases of thyroid gland are found to account 2.39% which is quite lower than most of the reported studies; Sudan 4.7% (31), Tunisia 9.9%, Libya 3.7% (30). Saudi Arabia 17.6% (43).

In this study the number of follicular/hurthle cell neoplasms reported is high as compared to other studies; this finding contrasts with other study findings (18,33,34,36,44). Possible reasons could be goiter may be endemic in this study area and population as follicular neoplasm is common in iodine deficiency goiter (40,45). Or maybe false diagnosis as follicular patterned lesions are the most commonly encountered type of thyroid FNAC specimen (40); hyperplastic nodule, follicular adenoma and follicular variant of papillary carcinoma may be diagnosed as follicular neoplasm as we don't use histologic examination which is more sensitive and specific. Many cytology/histologic correlation studies show that cytologic diagnosis of follicular neoplasm/suspicious for follicular neoplasm are frequently turned into follicular adenoma, benign follicular hyperplasia or follicular variant of papillary carcinoma when histologic examination is done (13,44).

Peak age for neoplastic lesions both hurthle and follicular is 21-30 years which is lower than stated in standard text books. Over diagnosis of follicular patterned lesions such as hyperplastic nodule as follicular neoplasm could be possible reason. Females are found to be more commonly affected than males with female to male ratio of 3.8:1 which is comparable to previous studies done in Jimma and Gondar (33,34) and other different countries; Sudan (31),India (39), Luxenberg (22).

Thyroid carcinoma is the leading type among endocrine carcinomas. Worldwide its incidence also increases rapidly in the past decades. But in this study a lower incidence is noted 40 (2.17%) which is lower than the previous study done in JUSH (34) and that of the stated in the NCCP of Ethiopia (4.8% as national level). A similar study conducted in northwestern part of Ethiopia Gondar observed 7.3% of thyroid cancer (33) , Saudi Arabia 5.2% (29), Iran 7.8% (28), India (37), England (46). Possible reasons for lower prevalence in our study is our choice of method and design of study, all of the previous studies use other ultrasound guided FNAC techniques which is very important to take a representative sample, radioisotope scan and histologic examination which is also important for confirmation of suspicious cases for carcinoma and the fact tha we didn't include follicular neoplasm with thyroid cancer analysis.

Well differentiated thyroid carcinomas are the commonest form of malignant thyroid tumors. They are more common in young adults, whereas, the least differentiated and anaplastic tumors

of the thyroid are prevalent in older age (6), likewise the study shows the peak incidence of papillary carcinoma is in the age group of 41-50 years while poorly differentiated thyroid carcinomas and anaplastic thyroid carcinomas are more common above 50 years of age. In this study thyroid cancer is predominant in the age group of 41-60 years with peak age group of 41-50 years which is comparable with the previous studies (34), (33). and this is in agreement with studies done in Sudan 31-60 years (31), Nigeria 40-50 years (47), India 41-50 years (39).

Among thyroid malignancies papillary carcinoma is the most common type accounting 50% which is comparable with studies done in JUSH (34), Gondar University hospital (33). Increased report of anaplastic carcinoma is also found to accounting 40% similar finding is also reported in South Africa (45), Sudan (31).

Limitations of the study

Residence of the patient is not appropriately and consistently mentioned.

Some clinically important variables, such as duration of illness, size of the mass, nature of the mass, some socio-demographic data are not included.

No follow up for suspicious for neoplasm and malignant cases.

Only cytomorphicologic diagnosis of the lesions was used and other molecular and immunohistochemical markers were not used.

Serological markers are also not used for chronic thyroid inflammatory cases.

CHAPTER 7: RECOMMENDATIONS

Finally, pathology department should update patients' FNAC reports storage so that all are easily accessible for future research.

All the necessary patients clinical and socio-demographic data including address should be included in the request form so that future researcher can gather more information and draw better conclusions.

Further large scale community based study is also recommend to determine goiter endemicity and take appropriate measure.

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ANNEX I

DATA COLLECTION CHECKLIST

Table 8: Data collection tool (Checklist) to study the cytopathologic patterns of thyroid gland mass.

No	Variables		Choice
1	FNAC No		
2	Year	1=2018 2=2019	
3	Sex	1=Male(M) 2=Female(F)	
4	Age		
5	Age categories	1=0-10 years 2=11-20 years 3=21-30 years 4=31-40 years 5=41-50 years 6=51-60 years >70 years	
6	Address	1=Jimma town 2=Jimma zone outside Jimma town 3=Outside Jimma zone 4=Address not specified	
7	Cytopathology by TBSRTC Category.	1. Nondiagnostic / unsatisfactory 2. Benign 3. Atypia of undetermined significance 4. Suspicious for follicular neoplasm/follicular neoplasm	

		<p>5. Suspicious for malignancy</p> <p>6. Malignancy</p>	
8	<p>Cytomorphologic diagnosis by patients FNAC result report</p>	<p>1, NCG with or with out secondary degeneration</p> <p>2, BFH</p> <p>3, Acute suppurative thyroiditis</p> <p>4, Chronic lymphocytic thyroiditis</p> <p>5, Suspicious for follicular neoplasm</p> <p>6, Suspicious for hurthle cell neoplasm</p> <p>7, Follicular neoplasm</p> <p>8, Hurthle cell neoplasm</p> <p>9, Suspecious for PTC</p> <p>10, Suspicious for MTC</p> <p>11, PTC</p> <p>12, MTC</p> <p>13, PDTC</p> <p>14, ATC</p> <p>15, Others</p> <p>16, Non diagnostic</p>	

ANNEX II

INSTITUTIONAL CONCENT

To:- Department of Pathology, JUSH

I am Dr. Melkamu Mitikie, a final year pathology resident; I am conducting a research on cytopathologic patterns thyroid mass in JUSH in the years 2018 to 2019. The general objective of the research is to determine cytologic patterns of thyroid mass and point out burden of the diseases. Secondary data from patient's record, both hard and soft copies, will be used; all the patients' confidentiality will be handled.

I sincerely ask JUSH to give me the opportunity to conduct a research on cytopathologic patterns of thyroid mass for partial fulfillment specialty on human anatomic pathology.

DECLARATION

ASSURANCE OF PRINCIPAL INVESTIGATOR

The undersigned agrees to accept responsibility for the scientific ethical and technical conduct of the research project and for provision of required progress reports as per terms and conditions of the college of public and medical science in effect at the time of grant is forwarded as the result of this application.

Name of the principal investigator	Signature	Date
Dr. Melkamu Mitikie (MD)	_____	_____

APPROVAL OF THE ADVISORS

This thesis proposal has been submitted with my approval as university advisor

Name of the advisors:	Signature	Date
Dr. Abdo Kedir	_____	_____
Dr. Lelisa Sena	_____	_____