HISTOPATHOLOGIC PATTERNS, CYTOHISTOLOGIC CORRELATION AND ASSOCIATED FACTORS OF THYROID LESIONS AMONG PATIENTS WITH THYROID BIOPSIES IN JIMMA MEDICAL CENTER, JIMMA, SOUTH WEST ETHIOPIA: RETROSPECTIVE STUDY

RESEARCH PAPER SUBMITTED TO DEPARTMENT OF PATHOLOGY, JIMMA UNIVERSITY FOR PARTIAL FULLFILMENT OF SPECIALITY DIPLOMA IN HUMAN ANATOMIC PATHOLOGY

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HISTOPATHOLOGIC PATTERNS, CYTOHISTOLOGIC CORRELATION AND ASSOCIATED FACTORS OF THYROID LESIONS AMONG PATIENTS WITH THYROID BIOPSIES IN JIMMA MEDICAL CENTER, JIMMA, SOUTH WEST ETHIOPIA: RETROSPECTIVE STUDY

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Abstract

Introduction: Thyroid diseases are major health problems, that are manifested by alteration in hormone secretion, enlargement of the thyroid gland (goiter), or both. Identifying and characterizing lesions of the thyroid gland have pivotal role since most of the lesions require medical or surgical management. Fine needle aspiration cytology (FNAC) is an important initial screening tool and histopathologic examination is important in the definitive diagnosis of thyroid disease.

Objective: To assess histopathologic patterns, cytohistologic correlation of thyroid lesions and associated factors among patients with thyroid biopsy.

Methods: A Five-year retrospective cross-sectional study was conducted from August 1 to September 30 2021. A review of 581 eligible biopsies, including 286 cases in which Fine needle aspiration was done prior to surgery, submitted from thyroidectomy specimens at Jimma medical center, pathology department from 14th September 2015 to 10th of September 2020. Data was cleaned, coded and entered into Epidata v3.1 and exported to SPSS version 26 for analysis. Descriptive and analytic studies were done. Cross tabulation, chi square test and logistic regression with multivariate analysis were done to look for associations between the study variables. A *p*-value<0.05 was used as a cut-off point for identifying predictors for histopathologic patterns. The findings were presented using text, tables, diagrams and charts.

Result: Majority of thyroid lesions,432 (74.4%), were found to be non-neoplastic and 149 (25.6%) were neoplastic. Colloid goiter was found in 417 (71.8%) cases. Adenoma, carcinoma and thyroiditis accounted for 54 (9.3%), 95 (16.3%) and 12 (2.1%) cases respectively. Among 286 FNAC results cyto-histologic correlation was achieved in 233 (86.6%) cases. Sensitivity and specificity of FNAC were 71% and 92.7% respectively with diagnostic accuracy of 86.6%.

Conclusion: Nodular colloid goiter is by far the most common thyroid lesion and Papillary thyroid carcinoma is the most frequent histologic type of malignancy. There is overall female predominance and peak age of occurrence of thyroid lesion is between 20 and 59. FNAC remains a good screening test and is an important tool for the management of thyroid lesions.

Keywords: Histopathology, FNAC, Cyto-histologic correlation, goiter, Iodine deficiency, Thyroid cancer, JMC, Jimma, Ethiopia

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Abbreviations/Acronyms

Thyroid CA	Thyroid Cancer
IHC	Immunohistochemistry
JMC	Jimma Medical Center
WHO	World Health Organization
IDD	Iodine deficiency disorders
FIG	Figure
ICCIDD	International Council for Control of Iodine Deficiency Disorders
NCG	Nodular Colloid goiter
NIFTP	Non-invasive follicular thyroid neoplasm with Papillary nuclear features
WDTUMP	Well differentiated tumor of uncertain malignant potential
PTC	Papillary thyroid carcinoma
PDTC	Poorly differentiated thyroid carcinoma
FN	Follicular neoplasm
SFN	Suspicious for follicular neoplasm
HN/SFHN	Hurthle cell neoplasm/Suspicious for Hurthle cell neoplasm
H & E	Hematoxylin and Eosin
TFT	Thyroid function test
EMOH	Ethiopian Ministry of Health
TASH	Tikur Anbessa Specialized Hospital
SPSS	Statistical Package for the Social Science
SD	Standard deviation
FNAC	Fine needle aspiration cytology

1. Introduction

The normal adult thyroid gland is composed of two lobes joined by the isthmus, which lies across the trachea anteriorly, below the level of the cricoid cartilage (1). The gland is affected in many physiologic and pathologic conditions. Diseases of the thyroid include conditions associated with excessive release of thyroid hormones (hyperthyroidism), thyroid hormone deficiency (hypothyroidism), and mass lesions of the thyroid (2). Thyroid pathologies, whether benign or malignant, give patients a variety of morbidities and can also cause deaths (3).

The most prevalent thyroid diseases are goiter, hypo or hyperthyroidism, thyroiditis, and neoplasms. Others include congenital anomalies such as thyroglossal cyst, thyroglossal fistula and aberrant thyroid tissue.(4) The incidence and prevalence of thyroid diseases in a community are variable which depends on various factors. (5) To diagnose different kinds of thyroid disease, complete clinical examination in addition to hormonal assays and morphology study should be done. In the end, Histopathologic examination provides a definitive diagnosis. (6)

Thyroid malignancies are divided into papillary carcinomas, follicular carcinomas, and medullary thyroid carcinomas, anaplastic carcinomas, primary thyroid lymphomas, and primary thyroid sarcomas. The incidence of thyroid diseases varies from one geographical region to another, mainly depending upon iodine deficiency status and range from non-neoplastic to neoplastic (7). The incidence varies in different regions depending upon different factors including age, sex, diet, environmental and radiation exposure (8). Thyroid disorders are four times more in females than in males. They are endemic in mountainous regions, where the soil, water and food contain little iodine (9).

Neoplastic diseases are also seen in the thyroid. Adenoma is the commonest benign tumor of the thyroid. Thyroid cancer is the most frequent endocrine malignancy (10). Papillary carcinoma is the most common thyroid cancer followed by follicular, medullary, anaplastic carcinoma and lymphoma (11). Marked variation in the prevalence of thyroid tumors has been observed in different regions of the world (12).

1.1. Problem statement

Thyroid lesions remain a problem of enormous magnitude all over the world (2). The vast majority of thyroid lesions are non-neoplastic (benign), however fewer than 5% are neoplastic (malignant) and require surgical intervention (3). Worldwide, the overall prevalence of thyroid malignancy is approximately 1–5% of all cancers in women and less than 2% in men (4). During the past several decades, an increasing incidence of thyroid cancer has been reported in European countries, USA and Canada (8). In Europe alone, thyroid malignancy affects approximately 24,826 individuals annually, with an estimated mortality rate of 5,993 patients each year (5).

Iodine deficiency disorders (IDD) which top the list of thyroid disorders and remain the commonest cause of thyroid disorders in Africa. The reported prevalence rates of endemic goiter range from 1% to 90% depending on the area of study (9). The documented prevalence rates of thyroid cancer 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%) (10). Studies show that diagnosis and evaluation of thyroid disorders are reliant in most regions of the continent on clinical acumen and suboptimal diagnostic facilities and expertise are limited in many practices (4).

As can be inferred from different literatures thyroid diseases are major health problems and are of major importance because most are amenable to medical and surgical treatment (4,9,11). Moreover, although few literatures can be obtained about the prevalence and incidence of different thyroid disease not much well documented information is available about histopathologic reports of thyroid diseases and the corresponding cytohistologic correlations in developing countries like Ethiopia. Little is known about histomorphologic patterns in this area because of the scarcity of published data. In addition to this, socio-demographic distribution of both benign and malignant thyroid diseases in these low-income countries is not well studied (10,12).

This study assesses the histopathologic patterns of thyroid lesions, cytohistologic correlation and associated factors from thyroidectomy specimens submitted to Jimma medical center pathology department from September 2015 to September 2020.

1.2 Significance of the study

This study helps in illuminating thyroid pathology as it reviews the frequency and distributions of histopathologic patterns of thyroid lesions and associated factors. It will also shed light on cyto-histologic correlation of thyroid lesions which will assess the overall specificity, sensitivity and diagnostic accuracy of the FNAC using histopathologic examination of the excised specimen as a gold standard. Even though FNAC is a powerful screening and diagnostic tool of thyroid lesions the diagnostic performance of FNAC in the hospital is not known.

The result of this study will benefit JMC, regional health bureau and other health institutions to create awareness, to set targets of intervention, to monitor and improve treatment quality and outcomes of patients with thyroid diseases by helping provide data about thyroid diseases coming to the institution which indirectly reflects what happens in the community. It will also help to influence preventive measures. More importantly, results of this study will be used as a baseline for further studies on related topics elsewhere in the country.

2. Literature Review

2.1 Global burden of thyroid diseases

Worldwide, the prevalence of goiter in the general population is estimated to be 15.8% varying between 4.7% in America and 28.3% in Africa (1) with the African continent representing over 25% of the global burden of the disease (2). Thyroid malignancies represent approximately 1% of diagnosed new cancer cases each year. Approximately 23,500 thyroid cancer cases are diagnosed each year in the United States of America (USA) (3). The incidence of thyroid malignancies is three times higher in women than men, and the incidence of thyroid cancer peaks in the third and fourth decades of life (4). The increased incidence of thyroid cancer is associated with an increase in the diagnosis of subclinical thyroid cancers thanks to the development of imaging methods, increased number of patients underwent fine-needles aspiration cytology (FNAC), more widespread application of total thyroidectomy over subtotal thyroidectomy, and increased precision in the examination of pathological specimens (5).

The worldwide prevalence of goiter in the general population is estimated at 4 to 15% and ten times more people are estimated to have 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 less than 10% of these thyroid swellings are malignant (6). The incidence of thyroid cancer has increased in different populations worldwide in the past 30 years (7). Papillary thyroid cancer was the main contributor to overall thyroid cancer in most of the studied countries (8).

2.2 Burden of Thyroid diseases in Ethiopia

Studies show that the prevalence of goiter in different geographic area of Ethiopia is high. A cross-sectional survey in Sekotta district showed the overall prevalence of goiter to be 22.8% (14). Similarly, a study carried out to detect the prevalance of goiter in school children and household members has shown the prevalence of goiter to be 30.6% and 18.7 % respectively. In Ethiopia, as of 2015, the national prevalence of goiter among children aged 6 to 12 was 39.9% (more than 4 million children) (6). According to the World Health Organization/International Council for Control of Iodine Deficiency Disorders/ United Nations Children's Fund (WHO/

ICCIDD/UNICEF) classification, both goiter prevalence and urinary iodine levels in Ethiopia indicate that the entire country is affected by iodine deficiency (9).

In a systematic review and meta-analysis study done in 2019 to assess prevalence of goiter and associated factors the pooled estimate of goiter among children in Ethiopia was 40.50% (15). The regional distribution of goiter ranged from 44.2 in Southern Nations Nationalities and Peoples' Region, to in Benishangul Gumuz region. The prevalence of goiter among female children (44.34%) was higher than among male (32.88%) children (19).

A study done in Gondar to determine the type and prevalence of thyroid malignancies found that among 846 thyroid enlarged patients, 62(7.3%) were confirmed to have malignancy. Among malignancies papillary thyroid carcinoma was the leading, 28 (45.2%), followed by follicular thyroid carcinoma, 18 (29%), and the least type of thyroid malignancies were medullary thyroid carcinoma and hurtle cell carcinoma, each accounts 1 (1.6%) (6).

A Two year retrospective study conducted in Addis Ababa (At St Paul millennium medical college) among a total of 222 patients who undergo thyroid surgery females accounted for 91.4% with Female to male ratio of 10:1. The common mode of presentations were anterior neck swelling (91.4%) and toxic (29.7%) and pressure symptoms (19.4%). Nodular colloid goiter was the commonest diagnosis (68.5%). Neoplasms accounted for 15.9% of the diagnosis of this follicular neoplasm make (54%) and papillary cancer (20%) (16).

Study done to assess the prevalence and patterns of thyroid disorders in Jimma majority of the patients were females; 64.8% of the study subjects were living in rural part while the rest 35.2% were from urban. Majority of the patients presented with visible and palpable goiter (15).

In another study done in Jimma the most common thyroid lesion that was found was goiter accounting for 85.4% of all thyroid swellings in patients that underwent FNAC and the most common malignancy that was found was papillary carcinoma (PTC) accounting for 49.3% of malignant lesions (9).

2.3 Histopathologic patterns of Thyroid lesions

A study done in Saudi Arabia shows a female to male ratio of 3.7:1. Age of the patients ranged from 14 to 95 years with a mean age 39.7 years. 72.3% of the cases were found to be non-neoplastic and 27.7% cases were neoplastic. The non-neoplastic group included: colloid goiter, including both diffuse and nodular goiter, nodular hyperplasia, Hashimoto/chronic lymphocytic thyroiditis, and Grave's disease. In neoplastic lesions, there were 7 benign tumors and 74 malignant tumors. Among the benign tumors, 5 were follicular adenomas and 2 were Hurthle cell adenomas. Papillary carcinoma was the commonest malignant tumor accounting for 87.8% of all thyroid malignancies, followed by lymphoma, follicular carcinoma and medullary carcinoma (17).

A retrospective study done in Barcelona, Spain, of nine years data showed average age was 56.5 years. Women presented thyroid pathology more often 88.7% against 11.3% (ratio 8:1). Among morphological disorders, 19 cases of thyroid nodule 3 carcinomas (15.7%): 2 papillary(10.5%) and 1 follicular (5.2%) and 16 cases of non-toxic diffuse goiter(84.2%) were recorded (18).

An extensive retrospective study of five decades done in Sao Polo, Brazil indicated non neoplastic lesions comprised 86.68% of the cases, and most of them were nodular goiter (91.4%). Of 1072 primary neoplasms, 49.4% were benign and 50.5% were malignant. Of the malignant neoplasms, papillary and follicular were the most frequent types (37% and 34.5%, respectively), followed by undifferentiated (15.8%), Hürthle (8.4%) and medullary (2.9%) (11).

A Fifteen-year retrospective study done in South eastern Nigeria on Histomorphologic patterns of Thyroid cancer shows among the thyroid biopsies received at the center 10.8% turnout to be Thyroid cancer during the period under review. Females to male ratio was 5.1:1, and a mean age of 45.9 years. The commonest histologic type was Papillary Thyroid Carcinoma (PTC) (42.6%), followed by; follicular thyroid carcinoma (37.7%), medullary thyroid carcinoma (4.9%), anaplastic carcinomas (3.3%), Non-Hodgkin lymphoma (1.6%) and metastatic squamous cell carcinoma (3.3%). Mixed papillary/ follicular carcinoma (4.9%) and mixed papillary/ anaplastic carcinoma (1.6%) were also identified (19).

A five-year retrospective study of thyroid disease in Uganda hospital showed that about 67% of cases are due to goitrous hyperplasia, with colloid diffuse goiter twice as common as nodular goiter. The rising incidence of thyrotoxicosis (11.4%) is in keeping with its increasing frequency elsewhere in Africa. The incidence of neoplastic diseases of the thyroid is low (20).

In a Five-year retrospective study done in Tikur Anbessa teaching and referral hospital 79% of cases were found to be non-neoplastic and 21% were neoplastic. Nodular colloid goiter (NCG) were found in 76.9% of cases. Adenoma, carcinoma and thyroiditis accounted for 12.8%, 8.2%and 2.1% cases respectively. Papillary carcinoma was the most frequent cancer seen in this series. Female to male ratio was 4.5:1. Eighty five point seven per cent of the thyroid diseases were found in the age group 20-59 years (21)**.**

A three-year retrospective study conducted in Gondar Among the 846 thyroid enlarged patients, 7.3% were confirmed to have malignancy. Among malignancies papillary thyroid carcinoma was the leading, 45.2%, followed by follicular thyroid carcinoma, 29%, and the least type of thyroid malignancies were medullary thyroid carcinoma and hurtle cell carcinoma, each accounts for 1.6%. Severe form of thyroid malignancy, undifferentiated thyroid carcinoma, was also accounted significant proportion, 12.9%. Older patients having an age of greater than 60 years and patients with solitary thyroid enlargement were more affected by malignancy compared to the reference age group, 11–20 years and diffused type of enlargement respectively (6).

2.4. Cytohistologic correlation of thyroid lesions

In a study conducted in USA to assess cyto-histologic correlation of thyroid lesions the FNA results were 76 (32%) positive for malignancy, 53 (22%) negative for malignancy, 100 (42%) indeterminate for malignancy, and 11 (5%) were nondiagnostic. There were 3 (4%) false-positive and 2 (4%) false-negative FNA results. There were 100 indeterminate FNA results among which carcinoma was found in 11 (15%) of 73 follicular neoplasms, 2 (20%) of 10 Hurthle cell neoplasms, and 14 (82%) of 17 suspicious for papillary carcinoma (8).

Similar study conducted in Italy reveals overall sensitivity of 93.4%, a positive predictive value of malignancy of 98.6%, and a specificity of 74.9%. At histological control, the cytological diagnosis of Hurthle cell neoplasm corresponded to a significantly higher incidence of malignant

neoplasms than the diagnosis of non-Hurthle cell follicular neoplasm (32.1% versus 15.5%). There were 66 false-negative findings, the main cause of diagnostic error (24 cases) being failure to recognize the follicular variant of papillary carcinoma. The number of inadequate FNACs was low (4.2%) (18).

Cytohistologic correlation study of thyroid nodules conducted in Jerusalem, Israel, shows among 89 patients with a carcinoma on FNA, 89% of cases were verified on final histopathology. Of 78 patients with "follicular lesion" on FNA, only 36% of cases were verified to be malignant at surgery. Only 13% of the 75 cases diagnosed as benign, mostly colloid nodules, on FNA were found to have a carcinoma on histopathology. A cytologic diagnosis of papillary carcinoma is highly predictive of thyroid cancer in this study. When dealing with follicular lesions the predictive value of FNA drops considerably. However a 13% false positive result was found to occur in FNA which were declared as benign lesions (22).

An Egyptian study which included 296 cases presenting with thyroid nodules who underwent diagnostic thyroid FNAC, Female to male ratio was 5.2:1, and the median age was 44 years. Ninety-eight cases (33.1%) were diagnosed as benign, 40 cases (13.5%) as follicular lesion of undetermined significance, 49 cases (16.5%) as follicular neoplasm, 30 cases (10.1%) as suspicious for malignancy, 58 cases (19.5%) as malignant, and 21 cases (7.1%) as unsatisfactory. Nodular hyperplasia represented the majority of benign cases (89.8%), while papillary carcinoma was the most frequent malignant lesion (72.4%). Cytologic diagnoses were compared with their corresponding final histologic ones and FNAC achieved a sensitivity of 92.8, a specificity of 94.2%, a positive predictive value of 94.9%, negative predictive value of 91.8%, a false positive rate of 7.2%, a false negative rate of 5.8%, and a total accuracy of 93.6% (23).

Study done in Uganda in which total of 99 patients were recruited, the female to male ratio was 15.5:1 and median age was 42 years. The median duration of symptoms was 364 weeks. The proportion of patients with malignancy was 13.3% with papillary thyroid carcinoma being the most predominant type and colloid goiter was the most predominant benign thyroid disease. The sensitivity was 61.5% and specificity 89.5% (24).

In a review of radiologic and cytopathologic studies in the evaluation of thyroid lesions in Tanzania reveals male to female ratio of 1:6; mean and median ages of 42.7 and 42.5 years respectively. The duration of the disease ranged from 1 to 20 years with a mean of 4 years. The overall incidence of malignancy was 18.6%. The sensitivity for detecting malignancy by FNAC was 66.7% while the specificity was 92.5% (25).

In a study done to assess the discordance rate of FNAC in black lion hospital revealed sensitivity and specificity of FNAC to be 67% and 84.7% respectively. The FNAC was non-diagnostic in 0.87 % of cases, suspicious in 2% and diagnostic in 97% of cases. The false negative and false positive rates in the study were 4.5% and 13.5% respectively (26).

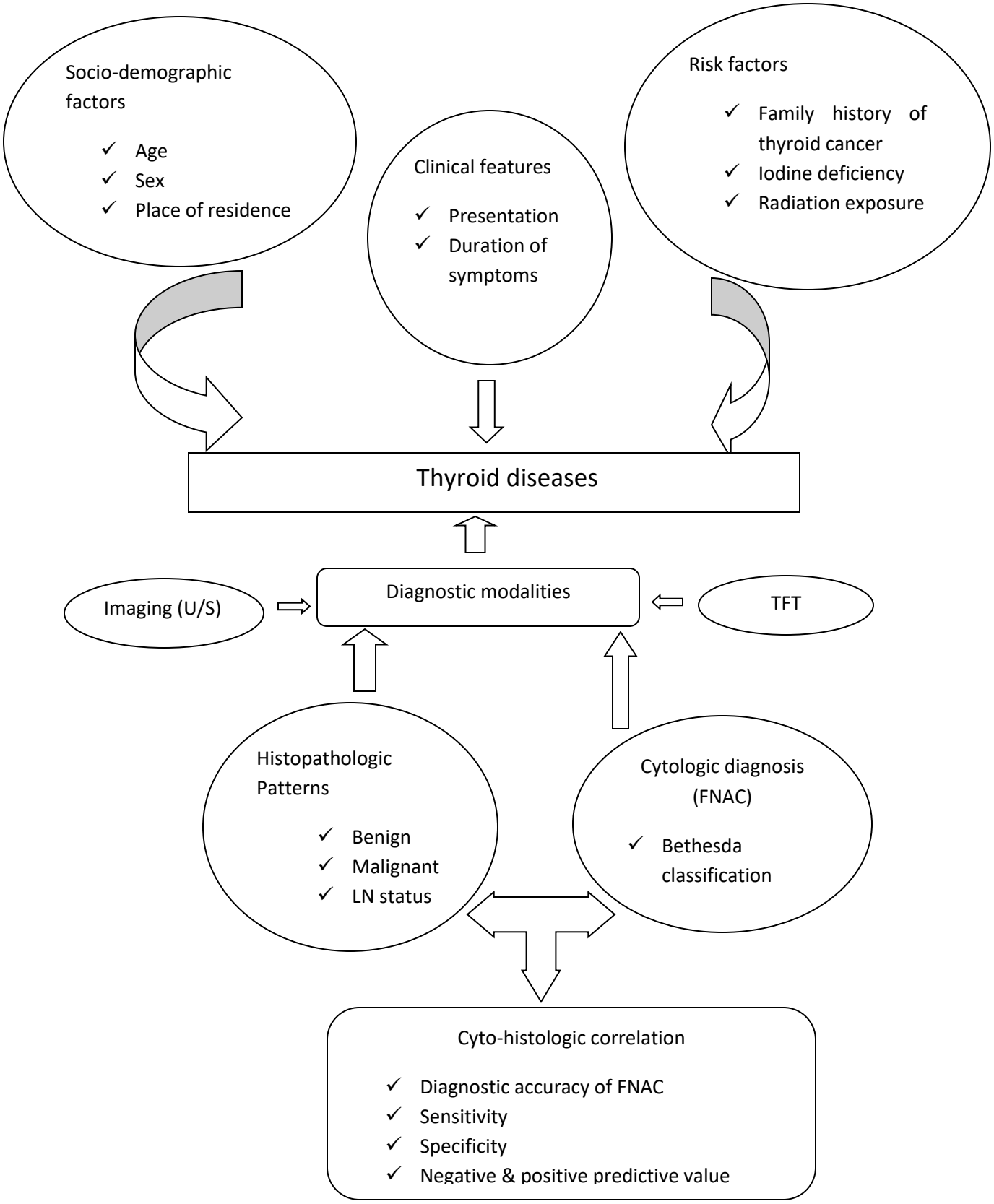

Figure 1: Conceptual framework of Thyroid lesions and associated factors in Jimma medical center, 2015-2020 (3) (6) (7-9)

3. Objectives

3.1. General objectives

To assess Histopathologic patterns, cyto-histologic correlation and associated factors of thyroid lesions among patients with thyroid biopsies in Jimma medical center, Jimma, south west Ethiopia, from September 2015 to September 2020.

3.2. Specific objectives

To determine the histopathologic patterns of thyroid lesions.

To analyze cyto-histologic correlation of thyroid lesions.

To evaluate cyto-histologic discordance rate.

To determine diagnostic accuracy of FNAC.

4. Methods

4.1 Study setting and period

The study was conducted in Jimma medical center which is located in Jimma city 352 km southwest of the capital Addis Ababa. Pathology department is one the main department in the center giving services like histopathologic diagnostic service, fine needle aspiration cytology, fluid cytology and other services including hematopathology with annual average patient flow of 1,636 for histopathology and 5,127 for fine needle aspiration cytology. The department has four pathologists, 12 practicing pathology resident, one general practitioner, and two technician and 7 assistant technicians. Currently, it is the only hospital that renders FNAC, surgical biopsy and other pathology services to this part of the country. The Histopathologic services is the area where this research is focusing uses the routine Hematoxylin and Eosin stain without any additional ancillary techniques having average annual patient flow of 1500 to 1700. The study was conducted from August 1 to October 30 2021.

4.2 Study design

Cross sectional study design was conducted

4.3 Population

4.3.1 Source population:

All patients who submitted biopsy specimen to pathology department for histopathologic diagnosis from September 2015 to September 2020

4.3.3 Study population

All patients who submitted thyroid biopsy specimen to pathology department for histopathologic diagnosis from September 2015 to September 2020

4.4 Inclusion and exclusion criteria

4.4.1 Inclusion criteria:

All biopsy reports of patients with the diagnosis of thyroid diseases which are done from September 2015 to September 2020

4.4.2 Exclusion criteria:

Biopsy reports which do not have at least one of those variables: patient Age, Sex, and histologic diagnosis

4.5 Sampling technique

Among a total of 8,412 biopsies received from 14th September 2015 to 10th of September, conveniently 582 histopathology reports of thyroidectomy specimens were retrieved from pathology department data archive and those reports that fulfilled the inclusion criteria were manually selected and then grouped by year. One biopsy report was excluded using exclusion criteria. A total of 286 FNAC results were also obtained from those reports in which FNAC was done prior to surgery.

4.6 Data collection procedures

Histopathology reports of Biopsies submitted from thyroid lesions to JMC, pathology department from 14th September 2015 to 10th of September 2020 were retrieved from pathology department data archive. Structured checklist was adopted through reviewing of literatures and books to include information that fulfill the objective of the study. Eligible 581 Reports fulfilling inclusion and exclusion criteria were extracted and recorded into a prepared checklist containing study variables. A total of 286 FNAC results were obtained using the hard copies (biopsy request papers) and soft copy archive.

4.7. Definition of terms

Histopathologic pattern: specific type of diagnosis made on biopsy specimen

Thyroid lesion: an abnormality in thyroid gland that can be developmental abnormality or manifest with hormonal imbalance or enlargement (goiter)

4.8 Variables

4.8.1 Independent variables

- Age
- Sex
- Residence
- Duration of symptoms
- Year of biopsy

4.8.2 Dependent variables

- Histopathologic patterns of thyroid lesions
- Cytologic patterns of thyroid lesions
- Diagnostic Accuracy of FNAC

4.9 Data processing and analysis

Data collected by checklist was coded, edited and entered into Epidata and then exported to SPSS for analysis. Descriptive analysis was done for frequency and distribution of the disease. Cross tabulation, chi square test and logistic regression was done to determine the association between the variables. Those variables with a *P*-value <0.25 in binary logistic regression was recruited for multiple logistic regressions. Then, a *p*-value<0.05 was used as a cut-off point for identifying predictors for histopathologic patterns. The findings were presented using text, tables and charts.

4.10 Data quality control

Checklist was adopted after reviewing different literatures and checklist was pretested on 58 cases (10% of total sample size) of biopsy hard copy reports done in the year 2021 which were not included in the current study.

Then the checklist was revised with some modification of the variable and the final revised checklist was used for data collection. Two days of training was given to the data collectors on how to locate, retrieve, categorize and record the data and initial data collection was accompanied by the principal investigator. The principal investigator subsequently followed and supervised while the data collectors were retrieving and recording the biopsy results from pathology department data archive using check lists. Consultation by senior pathologist was sought at time of technical difficulties. After checklist was checked for completeness, data was entered into Epi data on password protected computer and exported to SPSS version 26 for analysis.

4.11 Ethical consideration

Ethical clearance was obtained from Institutional Review Board of Jimma University and was submitted to the responsible authorities of JMC department of Pathology before proceeding to data collection. All the information collected from the study was handled confidentially by omitting their personal identification.

4.12 Limitation of the study

Biopsy results are not computerized and compiled with patients' clinical data, making it difficult to obtain clinical information regarding patients in the study. Only morphologic diagnosis of the cases is practiced and other molecular and immunohistochemical (IHC) markers are not available for confirmatory diagnosis.

4.13 Dissemination plan

The result of this study will be disseminated and communicated to Jimma University, regional health bureau, Ethiopian Ministry of Health (EMOH) and other institutions. The result can be used by policy makers and other concerned bodies and publication on an appropriate journal will be considered.

5. Result

5.1 Demographic characteristics

A total of 8,412 biopsies were received by the department and processed for histopathologic diagnosis in the five years period between 2015 and 2020. Out of these, 581 (6.9 %) were thyroid tissue specimens. Female patients constituted 468 (80.6%) of the total thyroid cases. The age distributions have minimum value of 3 years and maximum value of 70 years with mean age of 34.8 and the standard deviation of 11.4. The most commonly affected age group with thyroid lesions was between ages 30 and 59 (88.9%). Most of the patients, 353 (60.8%), were from surrounding areas with variable distance from Jimma town, while 208 (35.8%) patients were from Jimma town. Sociodemographic variables are shown in table 1 below.

Table 1: Sociodemographic characteristics of thyroid lesions, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

		Sex		
		Male	Female	Total
Age groups	<18	5	14	19
	18-30	36	135	171
	30-60	65	307	372
	≥ 60	7	12	19
Place of residence	Surrounding area	51	302	353
	Jimma town	55	153	208

The age distribution across different age groups is shown in the histogram below (Fig 2).

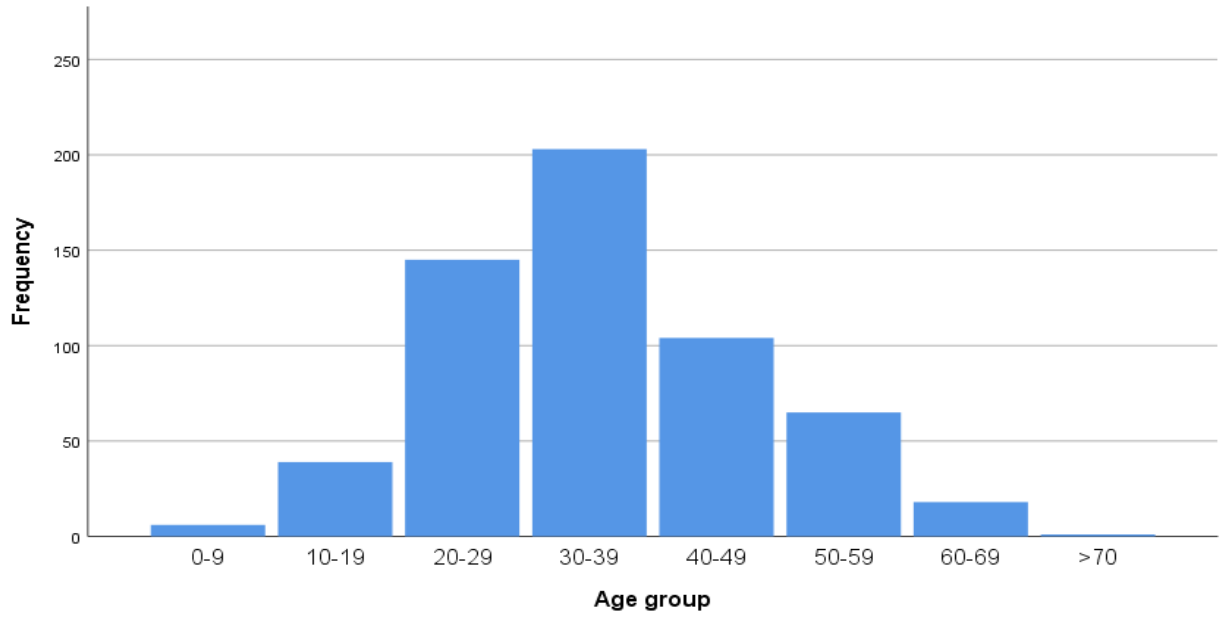

Figure 2: Histogram showing distribution of thyroid lesions across different age groups,2015–20, JMC, Jimma, Oromia, Ethiopia, N=581

5.2 Clinical presentation

Most patients, accounting for 239 cases (41.2%), presented with history of 1-5 years duration. Majority of malignant tumors, constituting about 42 (44.2%) cases present with relatively short duration of symptoms (<1year).

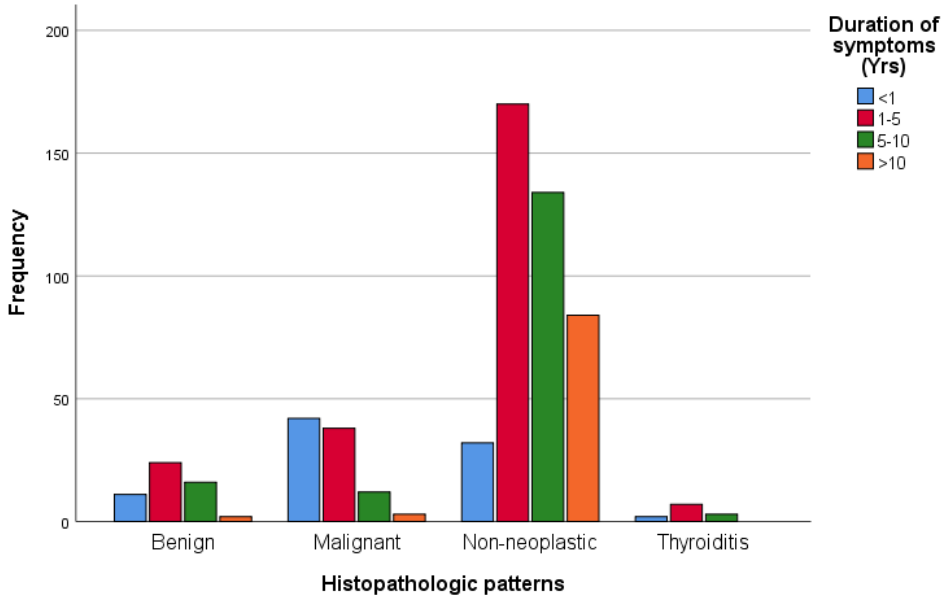

Figure 3: Bar graph showing duration of symptoms and histopathologic patterns of thyroid lesions, 2015–20, JMC, Jimma, Oromia, Ethiopia, N=581

5.3. Histopathologic patterns of thyroid lesions

Non-neoplastic lesions were encountered in 432 (74.3%) cases in which nodular colloid goiter (NCG) predominates. Among the non-neoplastic cases 417 (71.8%) were NCG and the remaining 3 cases were thyroglossal duct cysts. Thyroiditis constituted 12 (2.1%) of the cases. Thyroid neoplasms were encountered in 149 (25.6%) cases. Benign neoplasms i.e., adenomas were seen in 54 (9.3%) cases and include follicular adenoma, hurthle cell adenoma and Non-invasive follicular thyroid neoplasm with papillary like nuclear features (NIFTP).

Table 2: Categories of Histopathologic patterns of thyroid lesions and their frequencies, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

Histopathologic diagnosis	Frequency	%
Non-neoplastic	420	72.3
Thyroiditis	12	2.1
Benign neoplasms	54	9.3
Malignant neoplasms	95	16.3
Total	581	100

Details of the frequencies of histopathologic patterns can be seen in table 3 below

Table 3: Histopathological patterns of thyroid lesions encountered in thyroid biopsy specimens, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

Histopathologic pattern	Frequency	Percent	Valid Percent
NCG	417	71.8	71.8
Papillary thyroid carcinoma	69	11.9	11.9
Follicular adenoma	42	7.2	7.2
Follicular carcinoma	14	2.4	2.4
Lymphocytic thyroiditis	8	1.4	1.4
Hurthle cell adenoma	7	1.2	1.2
Hurthle cell carcinoma	6	1.0	1.0
NIFTP	4	.7	.7
Subacute thyroiditis	4	.7	.7
Medullary carcinoma	3	.5	.5
Thyroglossal duct cyst	3	.5	.5
Poorly differentiated carcinoma	2	.3	.3
Anaplastic carcinoma	1	.2	.2
WDTUMP	1	.2	.2
Total	581	100.0	100.0

Most of the non-neoplastic thyroid lesion are seen between the ages of 30-39 which is the commonest age group seen at presentation.

Table 4: Distribution of Histopathological patterns of thyroid lesions with age 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

		Histopathologic patterns				
		Benign	Malignant	Non-neoplastic	Thyroiditis	Total
Age group	0-9	-	2	4	-	6
	10-19	6	5	28	-	39
	20-29	20	26	94	5	145
	30-39	19	21	161	2	203
	40-49	6	21	75	2	104
	50-59	2	11	49	3	65
	60-69	1	8	9	-	18
	>70	-	1	-	-	1
Total		54	95	420	12	581

Among different histopathologic patterns 468 cases are seen in females with female to male ratio of 4.1:1.

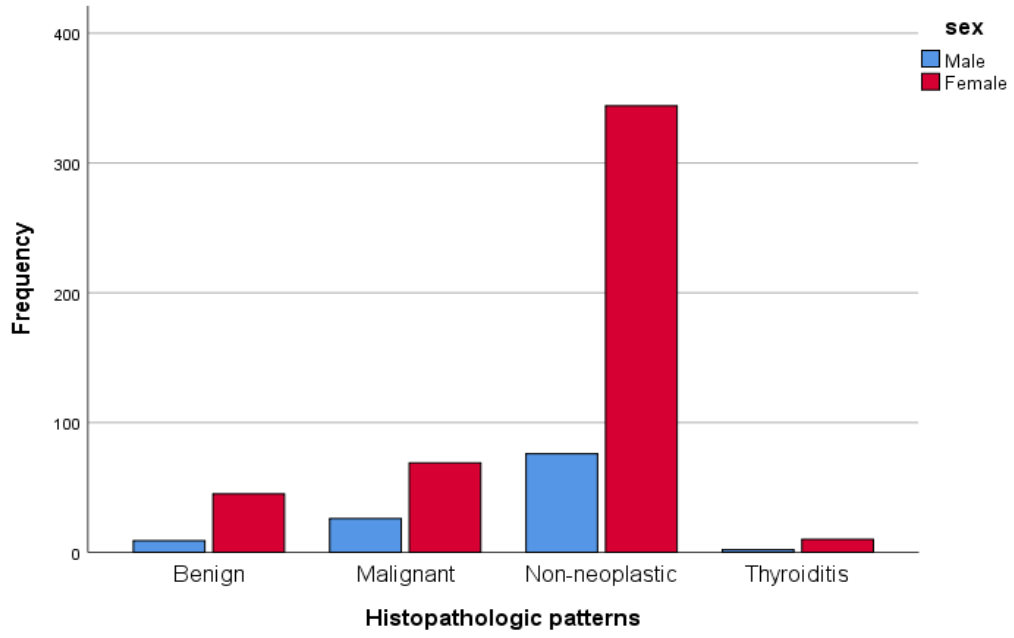

Figure 4: Bar graph showing the distribution of histopathologic patterns of thyroid lesions with sex, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

Inflammatory lesions (thyroiditis) represent twelve (2.1%) of the cases with female to male ratio of 5:1 and a mean age at presentation of 34.8 ± 11.4. Eight (66.6%) of the cases were chronic lymphocytic thyroiditis/Hashimoto's thyroiditis whereas the rest four cases were subacute thyroiditis.

Table 5: Distribution of thyroiditis by sex, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

		Sex		
		Male	Female	Total
Thyroiditis	Subacute thyroiditis	-	4	4
	Lymphocytic thyroiditis	2	6	8
Total		2	10	12

54 benign neoplasms were diagnosed in the time period which accounts for 9.3% of all cases. The most common benign neoplasm was follicular adenoma 42 (77.7%) with a female to male ratio of 5:1 followed by hurthle cell adenoma 7 (12.9%) and only 5 cases of NIFTP were diagnosed (9%). They were mostly diagnosed in the age group 20-39 in 72.2% of the time with average age of 34.8 and SD of 11.5.

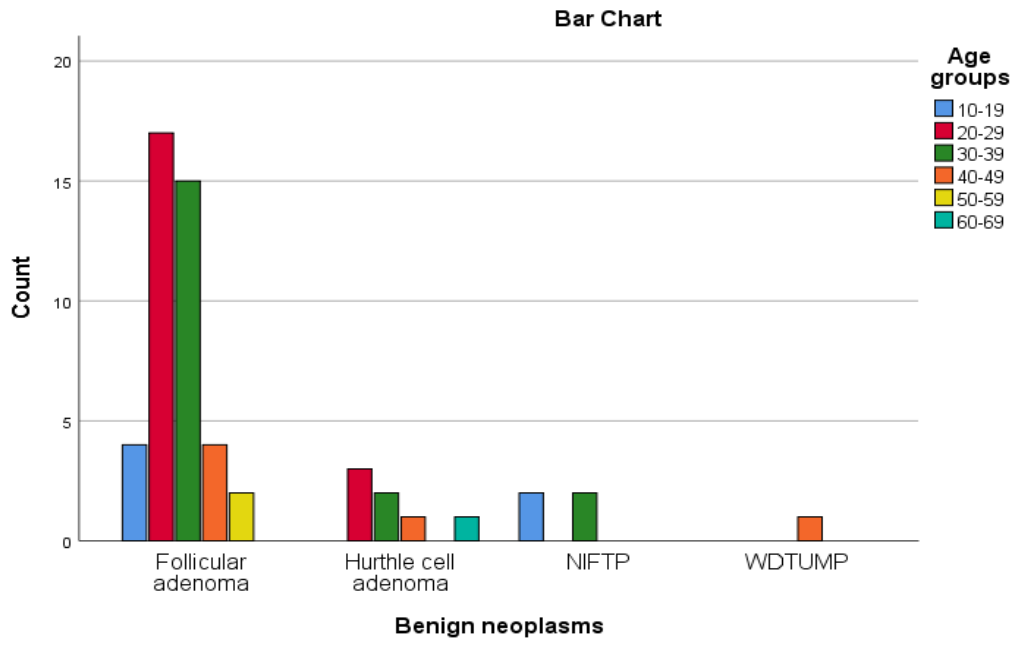

Figure 5: Bar graph showing distribution of benign thyroid tumors by age, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

The most common morphologic subtype of carcinoma was papillary thyroid carcinoma which accounts for 69 (72.6%) of the total 95 cases with a female to male ratio of 2.8:1 followed by follicular carcinoma 14(14.7%) and hurthle cell carcinoma 6 (6.3%).

Regarding the age distribution of malignant thyroid tumors most of the diagnosis are made in the 20-49 age group in 71.6% of cases with average age of 34.8 and SD of 11.5.

Table 6: Histopathological subtypes of thyroid carcinoma, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

Thyroid carcinoma	No.	%
Papillary thyroid carcinoma	69	72.6
Follicular carcinoma	14	14.7
Hurthle cell carcinoma	6	6.3
Medullary carcinoma	3	3.2
PDTC	2	2.2
Anaplastic carcinoma	1	1
Total	95	100

The highest case of thyroid cancer was seen during 2010 E.C with 30 (31.6%) cases turning out to be thyroid carcinoma followed by the year 2009 E.C with 21 (22.1%) cases. (Figure 9)

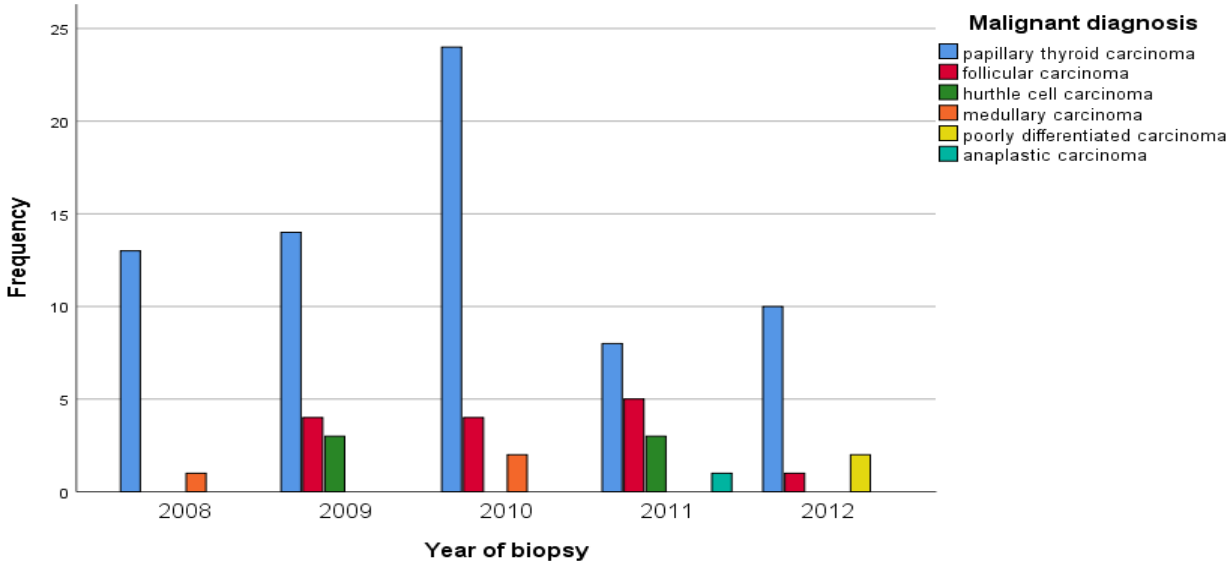

Fig 6: Bar graph showing frequency of histopathological subtypes of thyroid cancer over 5 years, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

5.4. Association of thyroid lesions with other variables

There is significant association between age (>40) and histopathologic patterns of thyroid lesion as depicted in table 7 X^2=6.05, DF=1, p= 0.014).

Table 7: Thyroid lesions and age groups cross tabulation, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

			Thyroid lesions		
			Benign	Malignant	Total
Age group	0-39	Count	339	54	393
		Expected Count	328.7	64.3	393.0
	≥40	Count	147	41	188
		Expected Count	157.3	30.7	188.0
Total		Count	486	95	581
		Expected Count	486.0	95.0	581.0

There is significant association between duration of symptoms (<1 year) and histopathologic patterns of malignancy as seen in table 8 below (X2 =8.538, df= 1, p=0.003)

Table 8: Thyroid lesions and duration of symptoms cross tabulation, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

			Duration of symptoms		
			<1 Year	≥1 Year	Total
Neoplasms	Benign	Count	11	43	54
		Expected Count	19.2	34.8	54.0
	Malignant	Count	42	53	95
		Expected Count	33.8	61.2	95.0
Total		Count	53	96	149
		Expected Count	53.0	96.0	149.0

Age (p=0.010), sex (p= 0. 016), place of residence (p=0.177) and duration of symptoms (p=0.00) were tested at P-value less than 0.05 for their association and selected as candidate variables for binary logistic regression. Binary logistic regression analysis was performed in backward method with likelihood ratio through two steps and two blocks on these variables and finally age (p=0.004) and duration of symptoms (p= 0.000) showed to be the independent predictors of benign and malignant thyroid lesions which was statistically significant as shown on the table. However, there was no statistically significant association between place of residence and thyroid lesions (p=0.144).

Table 9: Binary logistic regression of thyroid lesions and associated factors, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=581

Variables in the Equation

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	age regroup	.708	.254	7.768	1	.005	2.029
	residence	-.390	.267	2.137	1	.144	.677
	duration of symptoms	-2.049	.269	58.109	1	.000	.129
	sex	-.603	.293	4.236	1	.040	.547
	Constant	2.647	.879	9.062	1	.003	14.117
Step 2[a]	age regroup	.723	.253	8.154	1	.004	2.060
	duration of symptoms	-2.038	.268	57.946	1	.000	.130
	sex	-.525	.288	3.320	1	.068	.592
	Constant	1.943	.728	7.124	1	.008	6.983

a. Variable(s) entered on step 1: age regroup, residence, duration of symptoms, sex.

Thyroid cancer was found to be common in females than males with Female to male ratio of 2.6: 1. However, there was statistically significant association between male sex and incidence of thyroid malignancy (p=0.040). Based on histopathology result, of the 113 male patients operated for thyroid lesions at JMC during the study period, twenty-six (23%) were diagnosed with thyroid malignancy (18 with PTC, 5 with Follicular carcinoma, 2 with hurthle cell carcinoma and 1 with PDTC). In contrast, only 14.7% (69/95) of the women were diagnosed with thyroid cancer. Hence, the odds of being diagnosed with thyroid cancer is 1.7 times higher in males than females (P-value of 0.033, AOR (Adjusted Odds Ratio) of 1.73, and 95% CI (1.05 – 2.3).

5.5 Cyto-histologic correlation

A total of 286 FNAC results which were done prior to undergoing thyroidectomy were retrieved and correlated with the corresponding final histopathologic diagnosis. They were grouped according to the Bethesda system of reporting for thyroid cytology in to five groups. Only two (0.7%) were nondiagnostic/unsatisfactory for evaluation. In these two cases one turned out to be Thyroglossal duct cyst and the other NCG with the final histopathologic diagnosis. There were 225 female and 61 male patients with female to male ratio of 3.7:1 with mean age of 34.8.

Fifteen cases were categorized as Suspicious (i.e., indeterminate). Seven (46.7%) of the fifteen cases corresponded histologically as carcinoma (Papillary thyroid carcinoma). Seven (46.7%) cases turned out to be Non-neoplastic (NCG) and one case was follicular adenoma.

Table 10: Cross tabulation showing correlation of FNAC and histopathologic diagnosis, 2015-20, JMC, Jimma, Oromia, Ethiopia, N=286

		Histopathologic patterns				
		Benign	Malignant	Non-neoplastic	Thyroiditis	Total
FNAC diagnosis	Non-diagnostic	0	0	2	0	2
	Benign/NCG	22	22	157	2	203
	SFN/FN/HN/SFHN	23	18	9	1	51
	Suspicious for malignancy	1	7	7	0	15
	Malignant	1	10	4	0	15
Total		47	57	179	3	286

269 Aspirations (94.1%) were diagnostic (determinate). When compared with their corresponding histopathologic diagnosis 36 (13.4%) of the cases were discrepant (22 false negative and 14 false positive). However, 233 (86.6%) cases were correlated with histopathologic diagnosis (179 true negative and 54 true positive). The false negative rate was 8.2% and the false positive rate was 5.2%. The overall sensitivity and specificity for cytologic diagnosis was 71% and 92.7% respectively. The accuracy of FNAC in this series is 86.6%. Negative predictive value was 89.1%.

All of the 22 false negative cases were diagnosed as NCG and the corresponding histopathologic examination turned out to be papillary thyroid carcinoma in 16 cases, 5 cases were follicular carcinoma and 1 was hurthle cell carcinoma.

Among 14 false positive cases 10 cases were diagnosed as follicular patterned lesions (follicular neoplasm/suspicious for follicular neoplasm/hurthle cell neoplasm/suspicious for hurthle cell neoplasm) that upon confirmation with histopathology 9 cases were NCG and 1 case was lymphocytic thyroiditis. The remaining 4 cases were diagnosed as Papillary thyroid carcinoma on cytology but were colloid goiter histologically. The overall cytohistologic correlation results are summarized in table 11 and figure 7 below.

Table 11: Summary of FNAC results, 2015-20, JMC, Jimma, Oromia, Ethiopia

Summary of 286 FNAC results	
Non-diagnostic	0.7%
False negative	8.2%
False positive	5.2%
Sensitivity	71%
Specificity	92.7%
Accuracy	86.6%

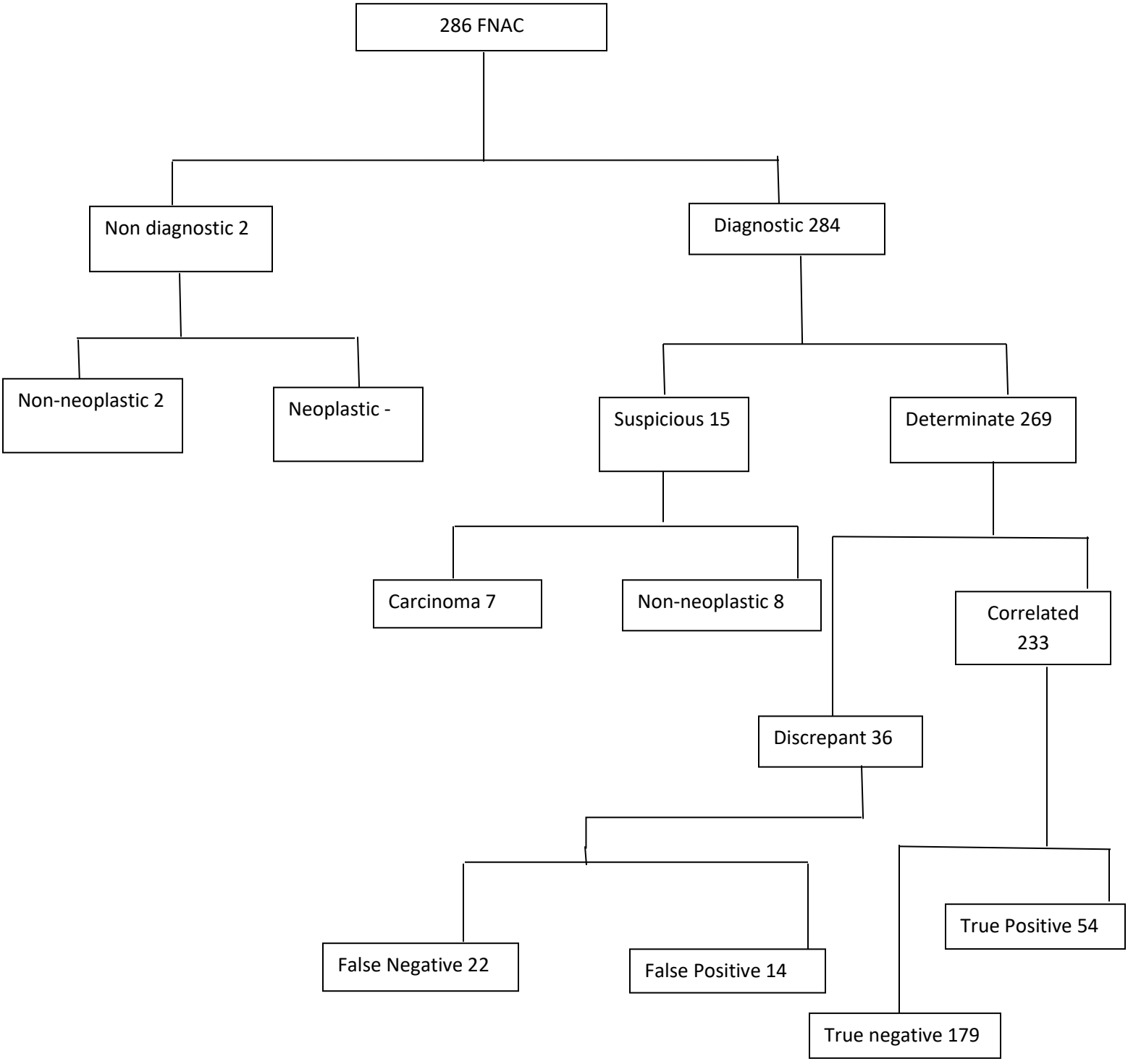

Figure 7: Diagram showing cyto-histologic correlation of 286 FNAC results, 2015-20, JMC, Jimma, Oromia, Ethiopia

6. Discussion

As can be inferred from various literatures age and sex are associated factors of thyroid lesions. The age group commonly affected with thyroid lesions in this study is 20-59 which accounts for 88.9% of the cases with average age of 34.8. This is in agreement with a study done in black lion hospital in which 85% of the patients with thyroid lesion fall under the age group 20-59 (21). Also other studies support this (16,27–30). Diseases of the thyroid are more common in women with female to male ratio of 4.1:1 with 468 (80.6%) cases seen in females. This is consistent with studies done in Kenya, Nigeria, Saudi Arabia and Spain with variable ratios reflecting different study populations (19,27,29,31). High ratio of thyroid lesions in female sex was suggested to be from level of hormonal variation after puberty and this study does seem to validate this scientific explanation (34).

Recent retrospective study done in the same hospital shows 155 (64.8%) patients presenting with thyroid lesions were living in rural areas surrounding Jimma while the rest 84 (35.2%) are mainly from Jimma town (15). This is in agreement with this study which depicts 353 (60.8%) patients who came from surrounding areas with variable distance from Jimma town and 208 (35.8%) from Jimma town.

Non-neoplastic thyroid lesions constitute 432 (74.3%) of overall cases. NCG by itself accounts for 417 (71.8%) of overall thyroid lesions. This is consistent with a study done in SPHMMC (Addis Ababa) in which 152 (68.4%) of the cases were NCG (32). Previously done clinical study in the same hospital also shows NCG as the most prevalent pattern of thyroid disease accounting for 74.6 % of cases (33). This picture is also found to be a consistent finding when compared to similar studies done in Uganda (20) that showed NCG to be the commonest consisting of 90 (65.7%), Yemen 164 (63.1%) (28) and Bangladesh 81 (75%) of the cases (34).

Inflammatory lesions of thyroid (thyroiditis) represent twelve (2.1%) of the cases with female to male ratio of 5:1 and a mean age at presentation of 34.8 $\pm$ 11.4 with 8/581 (1.3%) of the overall thyroid lesions being chronic lymphocytic thyroiditis/Hashimotos thyroiditis. Two studies done in India show frequency of Lymphocytic thyroiditis at 30 (2%) and 37 (1%) with mean age of 40$\pm$ 10 which is in agreement with this study (5,35). A study done in Italy also shows the frequency to be 54 (1.4%) of the cases (36).

Neoplastic diseases of the thyroid were found to be 149 (25.6%) constituting the second most common thyroid lesion in the study with female to male ratio of 5:1. Benign neoplasms were seen in 54 (9.3%) of the cases with follicular adenoma being the most common 42 (77.8%) followed by 7 cases of hurthle cell adenoma (12.9%), NIFTP 5 cases (9.3%) and 1 case (1.8%) of well differentiated tumor of uncertain malignant potential (WDTUMP). This figure is comparable with similar study conducted by Tsegaye B and Ergete W. in Addis Ababa (21) in which 164 (21%) were thyroid neoplasms in which 100 (60.9%) were adenomas. Study done in Western Kenya (31) indicates occurrence of benign neoplasms to be 51 (13.1%) which is comparable with this study. A retrospective study done in Zaria, Nigeria (19) shows frequency of 36 (12.1%) benign neoplasms with similar female to male ratio of 5:1, with follicular adenoma constituting thirty-three (91%) of the cases. A slight variation in the frequencies can be due to different sample sizes and duration of the study. Similar study done in Pakistan (27) shows a total of 255 (26%) neoplastic lesions which is consistent with the current study, however, among the benign neoplasms follicular adenomas account for 67 (65.9%) cases which is lower than the figure seen in the current study. This can be explained by the strict histopathologic criteria employed in the study in classifying benign thyroid neoplasms in the aforementioned study which was technically difficult to employ in the current study.

Among the 581 biopsies Ninety-five (16.4% of total cases and 63.8% of all thyroid neoplasms) cases were malignant with female to male ratio of 2.65: 1 and mostly are seen in the age group 20-29 accounting for 26 (27.4%) of cases. Study conducted in black lion hospital found significantly lower numbers of thyroid malignancy, in which only 64 (8.2%) of the cases were malignant (21). Similar figures are also reported from study done Gonder Hospital which shows frequency of thyroid malignancy to be 62 (7.3%) (6).

There is overall predominance of malignant thyroid neoplasms over the benign counterparts in this study. As the study hospital is the largest tertiary referral hospital in the southwestern part of the country, most cases are referral cases with suspected malignancy. This can contribute to the higher incidence of cancers in the hospital and this is also a reflection of increasing prevalence of thyroid cancer in the region and mandates larger scale studies to determine the underlying causes and associated factors. However, such figures are also seen in other studies.

Histopathological study from Ibadan, Nigeria shows Seventy-six (43.7%) cases were benign and 98 (56.3%) cases were malignant (37). Study conducted in Saudi Arabia also showed the predominance of thyroid carcinoma in which seventy-four (91.4%) cases of malignant neoplasms were found (38). Another study in Pakistan shows 153/255 (60%) of the neoplastic thyroid lesions were malignant, which is similar with the current study (13).

Among the malignant thyroid neoplasms Papillary thyroid carcinoma was the most common with frequency of Sixty-nine (72.6%) cases with female to male ratio of 2.8:1, mean age at presentation of 35.6 and 30 (78.9%) cases have a 1–5 year history of symptoms. This figure is similar with the study conducted in black lion hospital which shows 49 (76.9%) cases to be papillary thyroid carcinoma (21). Similar predominance of papillary thyroid carcinoma is reported in other literatures with variable proportions (4,10,11,39). Papillary thyroid carcinoma was the most common malignancy in study done in Nigeria which accounts for 98 (56.3%) cases with peak incidence in the 3rd decade (40). Another study done in Saudi Arabia shows papillary thyroid carcinoma to be the most common malignancy accounting for 105 (74%) of cases with mean age of 37.5 years (41). Study conducted in Ireland from consecutive 1003 thyroidectomy specimens 261 were malignant in which papillary carcinoma accounted for 75.1% of cases (34). Large scale study in Sao Paulo, Brazil which shows 9607 (72%) cases of papillary carcinoma and similar study done in USA shows 28,414 (86%) cases (11).

Only Fourteen (14.7%) cases of Follicular carcinoma are seen in this study with mean age of 36.9 and presenting within 1 year of development of symptoms in 8 (57.4%) cases. This is in agreement with study conducted in Gonder in which eighteen (29%) of the cases turn out to be follicular (6). However, this is contrary to the finding of a study done in Harare, Zimbabwe, in which follicular carcinoma was the most common malignancy seen in 60 (70%) patients (4). This shows that follicular carcinomas may be a reflection of a more severe iodine lack in certain populations or indeed a reflection of some etiological differences for this tumor in the different populations.

Medullary carcinoma is still relatively uncommon with only three (0.5%) cases identified in this study which is in agreement with findings from two studies in Addis Ababa in which only one and two cases were found(21,33), Port-Harcourt, Nigeria (one case), Yemen (two cases) (28) as well as reports from Pakistan (four cases). (27) Only one case of Anaplastic thyroid carcinoma was identified in this study (A 70-year-old male patient) which is in harmony with other reports of rare incidence of this disease entity (10,11,13,29).

Diagnostic sensitivity and specificity of FNAC in this study are 71% and 92.7% respectively. These figures are slightly higher than similar study done by W. Ergete and D. Abebe in which the sensitivity and specificity were 67% and 84.7% respectively (42). Similar study done in Tanzania shows 66.7% sensitivity and 92.5% specificity (25). Even lower sensitivity of FNAC (61.5%) in diagnosing malignancy is reported in Uganda (24). This is also in harmony with other studies in which in areas with a high prevalence of multinodular goiter, the sensitivity for detecting malignancy is relatively low whereas specificity is high (43).

Among 286 FNAC's cyto-histologic correlation was achieved in 233 (86.6%) cases. Such concordance rate is in agreement with study done in Tikur Anbesa hospital in which 274 cases (82%) were correlated (42). Similarly Indian correlation study shows 80.2% and study conducted in USA shows 88% correlation (26).

False negative and false positive results account for 22 (8.2%) & 14 (5.2%) respectively. This is in agreement with an Egyptian study in which the false negative and false positive rates were 7.2% and 5.8 % respectively (23). Similar figures are also seen in a study conducted to determine discordance rate between thyroid cytology and histopathology in USA in which 8% false negative and 4% false positive results were found (18). The overall reported false-negative rates range from 1–11%. According to various literatures it is difficult to establish the true frequency of false-negative results, since only a small percentage (approximately 10%) of patients with benign cytologic findings undergo surgery. However, all reports agree that if all patients with thyroid FNA would also have histologic examinations, the true false-negative rate would be below 5% (3,8,34,44).

Diagnostic accuracy of FNAC in this study was 86.6% with Negative predictive value of 89.1% and Positive predictive value of 80%. Accuracy is slightly higher than a study done in Tikur Anbesa Hospital which shows 82% diagnostic accuracy (42). A Study done in Tanzania to assess the cytohistologic correlation of thyroid lesions shows accuracy of 81.4% with NPV of 86% and PPV of 75% (25). Similar study conducted in Uganda shows diagnostic accuracy, NPV & PPV of 85.9%,93.9% & 47% respectively (24). Study done in USA shows diagnostic accuracy of FNAC to be 86.8% with NPV & PPV of 90% & 85.4% respectively (34).

With regard to the risk of malignancy in suspicious or indeterminate groups seven out of fifteen suspicious cases (46.7%) correlated with histopathologic diagnosis of thyroid carcinoma. Thus, there is a significant probability that a cytologically indeterminate lesion could be neoplastic, and there is a good chance that this lesion will be malignant. This is in agreement with study done in Addis Ababa showing four out of seven suspicious cases (57%) turning out to be malignant and a study done in USA in which 19 out of 40 suspicious cases (47%) were indeed malignant (34,42).

7. Conclusion

Most of the thyroid lesions are seen between the ages of 20 and 59 with female to male ratio of 4.1:1.

Nodular colloid goiter is by far the commonest thyroid lesion.

Neoplastic thyroid diseases are not rare entities and thyroid malignancy is found to be more common than benign neoplasms.

Papillary thyroid carcinoma is the most frequent malignancy.

Cyto-histologic correlation is achieved in 86.6% of the cases.

Overall sensitivity and specificity of FNAC is 71% and 92.7% respectively with diagnostic accuracy of 86.6%.

8. Recommendation

Thyroid malignancy which is found to be more prevalent than benign neoplasms in this study requires further extensive studies to reveal the factors behind such figures.

Proper clinical and pathologic evaluation of all goiters is mandatory not to overlook underlying malignancies.

Public health campaigns need to be carried out to raise public awareness about the benefits of early health service seeking once a neck mass has been noticed.

The application of strict reporting protocol for FNAC interpretation is likely to decrease the rates of false negative and false-positive FNAC diagnoses.

More detailed study needs to be undertaken to assess the discordance rate of FNAC and their underlying causes.

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