



St. Paul Hospital Millennium Medical College
Post Graduate Study Program

**Rate and risks of follicular thyroid carcinoma in patients
With cytologic diagnosis of follicular neoplasia.**

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ABSTRACT

Background: Studies have shown that the risk of malignancy in follicular neoplasms is as high as 30%. Often, surgery is recommended for such lesions, not for therapeutic purposes but as a diagnostic method, leading to increased hospital costs and related morbidities. Recent studies have suggested that tumour size predicts malignant potential of these follicular neoplasms.

Objective: The aim of this study is to evaluate the rate of FTCs among the patients who have cytologic diagnosis of follicular neoplasm and to determine the clinical features of follicular thyroid carcinoma in comparison with thyroid follicular adenoma and other benign thyroid pathology.

Method: A Comparative cross-sectional study design on patients who have histopathologic diagnosis of follicular adenoma and follicular carcinoma with respect to the clinical features in follicular neoplasms was reviewed from medical records retrospectively from January 2015 to December 2019, at St Paul's Hospital Millennium Medical college, Addis Ababa, Ethiopia. subjects were identified from the hospital log books (admission, discharge and operation) and individual patient charts was reviewed for the study variables. The data was collected by trained final year medical students. After data was collected and data was analysed using SPSS software. The analyzed data presented using charts, tables, and graphs and described using texts.

Result: A total of 135 patients undergoing thyroidectomy for follicular neoplasm and suspected for follicular neoplasm in the study period. Among this the record of 110 patients retrieved for analysis.

Among those operated for follicular neoplasia 78 (70.9%) of them found to be benign and 32 (29.1%) of them are found to be malignant after biopsy. From those benign disease 48 (43.6%) of them are follicular adenoma and 28 (25.5%) of them are benign nodular goitre. Those diagnosed to be malignant after biopsy shares 21 (19.1%) of the case is follicular carcinoma and 11 (10%) of the patients are papillary carcinoma.

Size of the mass greater than or equal to 4 cm with p value of 0.012 is strongly associated with the prevalence of follicular carcinoma than follicular adenoma. The associated symptoms of shortness breath also associated with diagnosis of follicular carcinoma.

Conclusion: Lesions larger than or equal to 4 cm in diameter and lesion associated with other added symptoms like shortness of breath, and difficulty of swallowing diagnosed as suspicious for follicular neoplasm by FNA cytology are associated with an increased risk of the presence of a malignant tumour.

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ACRONYM

AUS/ FLUS = Atypia of unknown significance / follicular lesion of unknown significance

FN/SFN = Follicular neoplasm or suspicious for follicular neoplasm

FNAC = Fine needle aspiration cytology

FTC = Follicular thyroid carcinoma

PTC = Papillary thyroid carcinoma

HT = Hemi thyroidectomy

TT = Total thyroidectomy

HBP's = Hepatobiliary and pancreatic surgery

EBS = Endocrine and breast surgery

SPHMMC= Saint Paul hospital millennium medical college

MPH = Master of public health

1. INTRODUCTION

Background

Follicular thyroid carcinoma (FTC) is the second most common thyroid malignancy after papillary thyroid carcinoma (PTC). The reported incidence of FTC is highly variable ranging from 10% to 32% of differentiated thyroid carcinoma. However, there are marked geographical variations in the relative proportions of FTC, likely due to difference in dietary iodine content. Indeed, in iodine deficient areas the relative rate of FTC tends to be even higher, up to 40% of the cases of differentiated thyroid carcinoma (1). In Ethiopia one study shows a 7.3% of thyroid malignancy prevalence among those with thyroid nodules & the papillary and follicular carcinoma accounts for 45.2% and 29% respectively (2).

The rate of malignancy in cytologic diagnosis of follicular neoplasm is 12% and 47.5% in study done in two different areas and from which follicular carcinoma account 9% and 26.5% respectively (3,4).

Lesions larger than 4 cm in diameter, fixed lesions, solitary nodules, lesions in younger age or older age and lesion with previous history of radiation exposure diagnosed as follicular neoplasm or suspicious for follicular neoplasm by FNA cytology are associated with an increased risk of malignancy (3, 5).

Identification of capsular or vascular invasion is necessary to achieve a definitive diagnosis of follicular carcinoma. However, FNAC has limited value in the presence of indeterminate cytologic findings and unable to identify capsular or vascular invasion. FNAC can show abundant follicular epithelial cells in sheets with crowding and overlapping of cells, micro follicle formation, and scant or no colloid which can be visible on both follicular adenoma and follicular carcinoma (6).

Statement of the problem

The incidence of FTCs varies across the globe reflecting the population studied the environmental factors the method of study, and the iodine status of the area. Studies in Ethiopia (2) and some parts of Africa (7,8) have found follicular thyroid carcinoma as second common type of differentiated carcinomas of the thyroid gland.

The risks that are associated with increased risk of malignancy has different result in different study, but younger age or older age, larger nodular size, fixity of nodule and previous history of radiation exposure are associate risks with incidence of malignancy (3,4,5,10).

In study done in Arizona, America, of the 219 patients, 184 (84%) underwent thyroidectomy for benign disease (benign colloid nodule in 12, follicular adenoma in 130, and other benign diagnoses in 42), Only 35 (16%) patients have malignancy. However, nine of these cases were incidental papillary tumors that did not involve the primary nodule. Therefore, the index nodule was benign in 193 patients (88%) and malignant in 26 (12%).

Of the 26 cancers in the index nodule, 3 were papillary cancer, 4 were follicular variant of papillary carcinoma, and only 19 (9% of the total group) were true follicular carcinomas. In this study lesion larger than 4 cm in diameter, fixed lesions and lesions in younger patients are associated with an increased risk of malignancy (3).

In other study done in Seoul, Korea, of 215 patients with follicular neoplasm 102 (47.4%) of patients had malignancy consisting of 29(13.5%) papillary carcinoma, 57 (26.5%) follicular carcinoma, 7% hurtle cell carcinoma and 1% is medullary carcinoma. In this study there is higher of malignancy and follicular carcinoma this is because they exclude cytologic diagnosis of suspicious for follicular neoplasm. In the same study they try to asses risks of being male gender, nodule size and age, only age <20 and >70 shows increased risk of malignancy (4).

Thyroid lesions that are follicular neoplasm or suspicious for follicular neoplasm present a challenge. Malignant cells are found in only 10 to 15% of these nodules. Conversely, 85% of patients in this subgroup undergo an unnecessary operation (3).

Significance of the study

Studies have shown that the rate of follicular carcinoma in follicular neoplasms is ranging from 9% to 26.5% (20, 21). Often, surgery is recommended for such lesions, not for therapeutic purposes but as a diagnostic method, leading to increased hospital costs and related morbidities (9).

The aim of this study is to review the actual rate of follicular thyroid carcinoma in a tertiary referral centre in Ethiopia and to determine the clinical risks that are associated with malignancy since there are no enough studies on this topic. This research project also aims to contribute an input for the management plan for follicular neoplasm.

2. LITERATURE REVIEW

Thyroid nodules can be caused by a simple overgrowth of “normal” thyroid tissue, fluid-filled cysts, inflammation (thyroiditis), or a tumour either benign or malignant. The clinical importance of thyroid nodule rests with the need to exclude thyroid cancer which occurs in 7-15% of cases depending on age, sex, radiation exposure history, family history and other factors (11).

The reported frequency of cancer in nodular goitre varies widely from 4 to 20% and it is generally thought to be more common in Solitary thyroid nodule than in Multinodular goitres (12).

In one study done in Nigeria, Kanu, There were 160 multinodular goitres during the study period, out of which 24 (15.0%) had histologically diagnosed cancer and one out of the thirteen patients with solitary thyroid nodule (7.6%) had carcinoma. The ages of the patients with carcinoma ranged from 16 to 65 years, with a mean age of 38.8 years. Eighteen (72%) were females, and 7(28%) were males. Six out of the 25 cases of carcinoma were detected preoperatively by fine needle aspiration cytology. Well differentiated follicular carcinoma was the predominant histological type in 13 (52%) cases, followed by papillary in ten (40%), medullary carcinoma in one (4%) and anaplastic carcinoma in one (4%) patient. This is consistent with the findings elsewhere in endemic goitrous regions (12)

Thyroid carcinoma are derived from the follicular epithelial cell and the variance include papillary carcinoma, follicular carcinoma, hurthel cell carcinoma and anaplastic carcinoma.

Follicular thyroid carcinoma (FTC) is the second most common thyroid cancer after papillary carcinoma, but it is ranked first in producing distant metastases among thyroid carcinomas (13).

Follicular adenoma and follicular carcinoma of the thyroid gland are tumours of follicular cell differentiation that consist of a micro follicular architecture with follicles lined by cuboidal epithelial cells. A follicular adenoma is a benign encapsulated tumor of the thyroid gland. It is a firm or rubbery, homogeneous, round or oval tumor that is surrounded by a thin fibrous capsule. A follicular adenoma is a common neoplasm of the thyroid gland. The ratio of follicular adenoma to follicular carcinoma in surgical specimen is approximately 5:1 (6, 11).

Follicular carcinoma has microscopic features that are similar to a follicular adenoma. However, a follicular carcinoma tends to be more cellular with a thick irregular capsule, and often with areas of necrosis and more frequent mitoses. The tumor is surrounded by a variable, thick, fibrous connective tissue capsule that contains

smooth muscle-walled vessels. Either capsular or lymphovascular invasion is sufficient for the diagnosis of follicular carcinoma (6, 14).

A follicular carcinoma cannot be distinguished from a follicular adenoma based on cytologic features alone. It is distinguished from a follicular adenoma on the basis of capsular invasion, vascular invasion, extra thyroidal tumor extension, lymph node metastases, or systemic metastasis. Capsular invasion is defined as tumor extension through the entire capsule. A follicular neoplasm with tumor invasion into but not through the entire capsule is considered a follicular adenoma (6,11). Vascular invasion is defined as tumor penetration into a large calibre vessel within or outside the capsule. Vascular invasion occurs when tumor cells within vessels are (14):

- Within or beyond the capsule,
- Identified by direct extension into the vessel,
- lined by endothelial cells,
- Associated with thrombus ,
- Not freely floating within the vascular space, and
- Having a morphology that is identical to the cells within the tumor.

Patients with a follicular adenoma or a follicular carcinoma usually present with a thyroid nodule. Patients with follicular carcinoma may rarely present with lung or bone metastases identified on an imaging study (6).

Fine Needle Aspiration Cytology

Fine needle aspiration cytology (FNAC) is a valuable and cost-effective pre-operative investigation for thyroid nodules in adults. The results can reassure that a nodule is benign, triage patients for diagnostic surgery, or provide a definite diagnosis of some thyroid malignancies enabling one-stage therapeutic surgery. Accordingly, optimum cytology specimens should have at least six follicles each containing at least 10 to 15 cells from at least two aspirates (9, 15 and 16).

Fine needle aspiration cytology in patients with a follicular adenoma and patients with a follicular carcinoma is characterized by abundant follicular epithelial cells in sheets with crowding and overlapping of cells, microfollicle formation, and scant or no colloid. According to the Bethesda system for reporting thyroid cytopathology, this cytologic appearance is classified as follicular neoplasm or suspicious for follicular neoplasm. A fine needle aspiration cytology specimen consistent with a follicular neoplasm accounts for 20% of all fine needle aspiration cytology results and has a 15%–30% risk of malignancy (6,9). The differential diagnosis for a patient with a thyroid nodule and a fine needle aspiration cytology result consistent with a follicular neoplasm is a follicular adenoma, adenomatous hyperplasia, follicular carcinoma, follicular variant of papillary carcinoma, and classic papillary carcinoma (6).

A study done in turkey in a total of 98 consecutive patients with follicular neoplasm on FNAC were included in the study. Total or near total thyroidectomy was performed in 78 patients (80%) and thyroid lobectomy was performed in 20 patients (20%). Thyroid cancer was diagnosed in 26 patients (27%). Papillary cancer was the most common cytologic findings (20 patients 77%) and 6 patients (23%) had a diagnosis of follicular carcinoma (10).

The study mentioned above regarding to the clinical and sonographic risk factors shows the mean nodule size was slightly larger in malignant nodules than in benign nodules. The mean age was similar in patients with malignant disease and those with benign disease. In patients with older than 45 years, the risk of malignant neoplasm did not increase. Male sex was not predictive for thyroid cancer. The presence of Solitary nodule was not predictive for malignancy. Solid echo structure, presence of microcalcifications, and hypoechoic nodules on ultrasonography were predictive for malignancy (10).

Several studies investigated clinical, ultrasonographic, and cytologic criteria to predict malignancy in follicular lesions. Some of these Studies have suggested that the cases diagnosed as follicular neoplasm with a lower risk of malignancy can be managed by close follow-up and repeated FNAC. However, the topic of risk factors predicting malignancy in thyroid nodules with a diagnosis of follicular neoplasm is still controversial (10).

On ultrasound examination of the thyroid gland high suspicion of malignancy is warranted with a solid hypoechoic nodule or a solid hypoechoic component in a partially cystic nodules with one or more of the following features: irregular margins (specifically defined as infiltrative, microlobulated, or spiculated), micro calcifications, taller than wide shape, disrupted rim calcification with a small extrusive hypoechoic soft tissue component, or evidence of extra thyroidal extension (10, 17).

Treatment of a patient with a follicular neoplasm

A patient with a FNAC consistent with a follicular neoplasm should, at minimum undergo a diagnostic thyroid lobectomy and isthmusectomy. Patients with a follicular neoplasm and a prior history of head or neck radiation or nodular disease involving the contralateral lobe of the thyroid gland should be treated with a definitive total thyroidectomy. Frozen section examination has not been helpful for intraoperative decision-making because it rarely distinguishes a follicular adenoma from carcinoma (6).

When surgery is considered for patients with a solitary, cytological indeterminate nodule, thyroid lobectomy is the recommended initial surgical approach. This approach may be modified based on clinical or sonographic characteristics and patient preference (6).

Because of increased risk for malignancy, total thyroidectomy may be preferred in patients with indeterminate nodules that are cytologically suspicious for malignancy, positive for known mutations specific for carcinoma, sonographically suspicious, or large (>4 cm), or in patients with familial thyroid carcinoma or history of

radiation exposure, if completion thyroidectomy would be recommended based on the indeterminate nodule being malignant following lobectomy (11).

Completion thyroidectomy is preferably performed within the first week of initial surgery or 3 months later to avoid operation during the period of maximal scarring. Delay in performing completion thyroidectomy beyond 6 months following initial thyroidectomy may be associated with a higher risk of metastases and reduced survival (6)

In solitary small low-risk lesions, Hemi thyroidectomy thanks to its lower complication rates is still the safest standard of care, avoiding unnecessary morbidity. In our series in HT patients a lower mean hospital stay and costs were also reported. TT should be recommended in case of Multinodular disease or in presence of thyroiditis that might be associated with a higher risk of cancer. Even if a more conservative surgical approach might be suggested in FN patients, more prospective randomized trials are requested to achieve a better preoperative diagnostic accuracy reducing the amount of unnecessary surgical operations with a diagnostic aim (18).

3. OBJECTIVES

General objective

To determine the rate and risks of follicular thyroid carcinoma in patients with cytologic diagnosis of follicular neoplasia.

Specific Objective

- To determine the rate of follicular adenocarcinoma
- To identify the clinical risks associated with follicular adenocarcinoma

4. METHODS AND MATERIALS

Study area

The study was conducted in SPHMMC which is found in Gulele kifle ketema, North west Addis Ababa, Ethiopia. Addis Ababa city has estimated population of 5 million.

St Paul's Hospital Millennium Medical College was established, first as a Hospital in 1968 by Emperor Haile-Selassie, St. Paul's had been serving the people for more than 5 decades now. In 2007, with the aim of providing better healthcare services to its patients and producing skilled healthcare professionals, it opened a Medical School with a unique integrated curriculum and admission criteria.

The department of surgery is among the oldest department in the college, providing different subspecialty services. One of the subspecialty is endocrine and breast surgery which is managing most of the thyroid problem including the thyroid follicular carcinoma. Goitre is also one of the most common indications for patient admission in the surgical ward it accounts for 22% of elective general surgery admission in SPHMMC from 2013 to 2016 GC.

Study Design

A comparative cross sectional study design was conducted in patients who has been treated and hospitalized at SPHMMC, Addis Ababa, Ethiopia with a Diagnosis of Thyroid Follicular neoplasm from January 1, 2015 to December 31, 2019 GC.

Source population

All Patients with cytologic diagnosis of follicular neoplasm, hospitalized and treated in SPHMMC was the source population for this study.

Study population

Patients who have cytologic diagnosis of follicular neoplasm in the study period from January1, 2015 to December 31, 2019 and who fulfil the inclusion criteria.

Sample size and Sampling technique

Taking the margin of error 5%, Confidence interval 95% and 9% proportion from previous study as described in the literature review and using the sample size calculation formula,

$$N = z^2 p (1-p) / d^2 \Rightarrow (1.96)^2 0.09 \times 0.91 / 0.0025 = 125$$

Patients will be identified from operation log book which undergone an operation for diagnosis of follicular neoplasm and this will serve as sampling frame and randomly will be selected using excel.

Inclusion Criteria

Patients with cytologic diagnosis of follicular neoplasm or suspicious for follicular neoplasm and those undergone thyroidectomies was included in the study.

Exclusion criteria

- Patients with diagnosis of hurtle cell neoplasm
- Patients who didn't have a post thyroidectomy biopsy result.
- Patients who had inconclusive biopsy result.

Variables

Independent variable;

- Age
- Sex
- Clinical factors: 1. Duration of swelling
2. Size of the mass
3. Consistency of the mass
4. Nodularity of the mass
5. Fixity of the mass

Dependent variable;

- Presence of Thyroid follicular carcinoma.

Data collection

The socio demographic data, clinical factors and biopsy result was collected from patient medical record with aid of data collection format. Medical interns was trained as data collector and the principal investigator was responsible for monitoring data collection process and data analysis.

Among the patients who met the inclusion/exclusion criteria was selected and data extraction formats which are having inconsistent, incomplete data and that can't be completely filled with the available information in the patient's chart was differed from analysis. So that the quality of the data collected was satisfactory.

Data analysis

The arranged data was entered and statistically analysed using statistical package for social science (SPSS). Univariate associations between the presence of cancer and categorical variables was evaluated with use of the X2 test or Fisher's exact test. Associations was assessed jointly by using stepwise multivariate logistic regression. The odds ratio of malignancy was evaluated by logistic regression analyses. Confidence interval of 95% and p-value < 0.05 was statistically significant cut off point.

Ethical consideration

Ethical clearance of this research is obtained from SPHMMC research directorate office. Patients wasn't required to provide informed consent since the study was rely on the patients' medical records. The effort to protect the confidentiality of the study was made by the principal investigator.

Dissemination plan for results

The final written report of the research will be submitted to the Department of general surgery and the college research directorate.

5. Results

A total of 135 patients undergoing thyroidectomy for follicular neoplasm and suspected for follicular neoplasm in the study period. Among this the record of 110 patients retrieved for analysis.

The Age of patients' ranges from 17-60 years and the mean age was 43.63 years. 65 (59.1 %) of the patients age is less than 45 years and 45 (40.9%) of the patients are aged greater than or equal to 45 years. Of the 110 patients, 98 (89.1%) were Females and 12 (10.9%) were male (F: M = 9:1). 58 (52.7%) of the patient is coming from the Addis Ababa, the remaining of the patients are from outside of Addis Ababa.

Table 1. Sociodemographic table.

		Frequency	Percent
Age	< 45 years	65	59.1
	>=45 years	45	40.9
Gender	Female	98	89.1
	Male	12	10.9
Address	Addis Ababa	58	52.7
	Outside of Addis Ababa	52	47.3

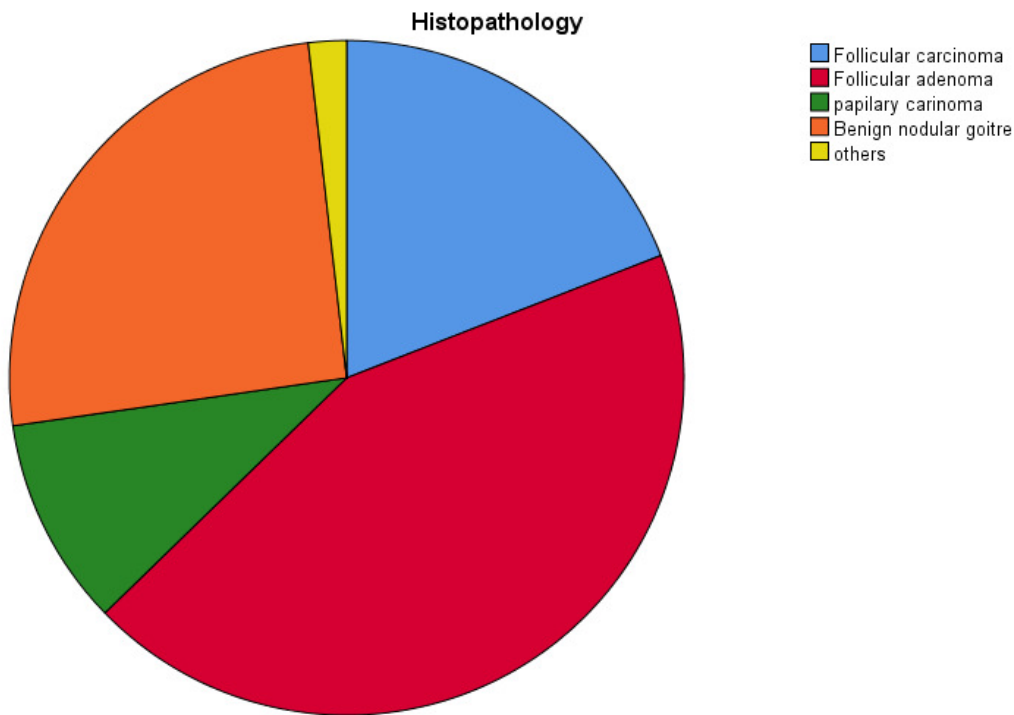
Among those operated for follicular neoplasia 78 (70.9%) of them found to be benign and 32 (29.1%) of them are found to be malignant after biopsy. From those benign disease 48 (43.6%) of them are follicular adenoma and 28 (25.5%) of them are benign nodular goiter. Those diagnosed to be malignant after biopsy shares 21 (19.1%) of the case is follicular carcinoma and 11 (10%) of the patients are papillary carcinoma.

A total of 69 cases (Follicular adenoma = 48 + Follicular carcinoma =21), (62.7%) were consistent with FN. Thus, the FNAC diagnostic accuracy for FN is 62.7%.

Table 2: Post op biopsy Histopathology diagnosis:

Histopathology		Number of patients	Percent
Benign	Follicular adenoma	48	43.6%

	Nodular colloid goiter	28	25.5%
	Other	2	1.8%
	Total	78	70.9%
Malignant	Follicular carcinoma	21	19.1%
	Papillary carcinoma	11	10%
	Total	32	29.1%



The duration of anterior neck swelling ranges from 1 year to 40 years and the mean duration of swelling is 5.66 years. 45 (40.9%) of the patient present in less than 2 years of anterior neck swelling. 33 (30%) of the patient present between 2 years and 5 years of duration, and the remaining 12.7 % and 13.6 % of the patients present within 6 to 10 years and greater than 10 years respectively.

The size of the mass in largest diameter ranges from 1 cm to 12 cm and the mean size of the mass is 4.91 cm. Among the 110 patients 53 (48.2%) of them present with less than 4 cm size of mass and 57 (51.8%) of them present with greater and equal to 4 cm size.

Most of the patients (80%) have no other associated symptoms, from those present with associated symptoms 13 (11.8%) present with shortness of breath, 5 (4.5%) present with voice change, 2 (1.8%) with recent increment of size and 1 (0.9%) is with difficulty of swallowing.

90.9 % of the patient have firm consistency of the mass, 95 % of them have mobile and 85.5% of the mass with multiple nodularity.

From the operation type done for the patients Lobectomy and isthmusectomy accounts 40 (36.4%) of the patient, near total thyroidectomy 30 (27.3%) of the patients, Dunhill's thyroidectomy 20 (18.2%), subtotal thyroidectomy 9 (8.2%) and total thyroidectomy 9 (8.2%) of the patient. 69.4% of surgery is done for benign thyroid pathology

Table 3: The relationship between the histopathologic diagnosis and type of operation done

		Operation done					
		Lobectomy + Isthmusectomy	Subtotal Thyroidectomy	Dunhills Procedure	Near total Thyroidectomy	Total Thyroidectomy	Total
Histopathology	Follicular carcinoma	7	1	3	7	2	20
	Follicular adenoma	19	3	9	13	3	47
	papillary carcinoma	3	0	3	4	1	11
	Benign nodular goiter	10	5	5	6	2	28
	others	1	0	0	0	1	2
Total		40	9	20	30	9	108

Bivariate analysis

Table 4: Association of the independent variable with Malignant and benign thyroid pathology at bivariate analysis

	Variables	Range of variable	Benign	Malignant	p-value	OR
1	Gender	Male	6	6		
		Female	70	28	0.021	5.566
2	Associated symptoms	Voice change	1	4	0.005	
		Shortness of breath	5	8	0.012	24.15
		Difficulty of swallowing	0	1	0.002	9.508
		Recent increment of size	1	1	1.00	
3	Size	< 4 cm	45	8		
		>= 4cm	31	26	0.021	0.262
4	Consistency	Soft	4	0	1.00	
		Firm	72	28	0.99	
		Hard	0	6	0.99	

Gender of female ($p = 0.021$), from associated symptoms voice change ($p = 0.05$), shortness of breath ($p = 0.012$), difficulty of swallowing (0.002) and size $\geq 4\text{cm}$ ($p = 0.021$) are significantly associated with being malignant thyroid pathology.

Multivariate analysis

Table 5: multivariate analyses of categorical predictor variables that correlated with histopathologic diagnosis of follicular carcinoma.

S.N	Variables	Variables range	Follicular carcinoma rates	p-value	OR
1	size	$\geq 4\text{cm}$	18 (85.7%)	0.012	18.22
2	Associated Symptoms	Shortness of breath	6 (30%)	0.019	0.439

As a finding of this study size of the mass greater than or equal to 4 cm with p value of 0.012 is strongly associated with the prevalence of follicular carcinoma and the associated symptoms of shortness breath also associated with diagnosis of follicular carcinoma.

6. Discussion

The cytological diagnosis of follicular neoplasm has continued to be a frustrating entity for pathologists, surgeons, and patients. As it is difficult for management decision and difficult to differentiate benign from malignant lesion. The FNA diagnostic accuracy of follicular neoplasm in this study is 62.7% which is lower than the study done in Korea (69.5%) (4).

In this study 32 (29.1%) of the cases being malignant, which is a bit higher when compared with other studies (3,10), but it is in the range of the Bethesda System for reporting cytopathology which gives the risk of malignancy for FNA diagnosis of follicular neoplasm is 15-30% (9) and it recommends to have surgical lobectomy for this class of FNA diagnosis. But despite of this in this study only for 37% of the patient's lobectomy is done, for 63% of the patients the surgery is more than lobectomy among this 36% of patients undergone near total and total thyroidectomy which is thought to have more complication and morbidities related to the surgery.

The American Thyroid Association (ATA) recommends total thyroidectomy for lesions larger than 4 cm, when the biopsy is suspicious for papillary carcinoma or shows marked atypia, in patients with family history of thyroid carcinoma, and in patients with a history of radiation exposure (recommendation rating: A). For all other nodules including Follicular neoplasm and suspicious for follicular neoplasm, the ATA recommends thyroid lobectomy (recommendation rating: C) (11). Despite of this in this study 69.4 % of surgery is done for benign pathology from this 42.5 % of operation is more than lobectomy.

Follicular thyroid carcinoma was the most common cytologic finding (21 of 32 patients [65%], of whom 11 [35%] were diagnosed as having the papillary carcinoma) where as in the other studies the papillary carcinoma was the most common type from the malignant lesion (10). This study revealed 19.1% rate of follicular carcinoma and it is more than two times higher than the study done in Arizona (9%) (3).

Several studies investigated clinical, ultrasonographic, and cytologic criteria to predict malignancy in follicular lesions (3,10,17). However, the topic of risk factors predicting malignancy in thyroid nodules with a diagnosis of follicular neoplasm is still controversial.

This study assesses clinical predictor for malignancy and specifically for Follicular carcinoma. Being female is more associated with malignant thyroid pathology and has 5.5 times more likelihood of having malignancy than males.

Associated symptoms other than swelling shows strong association with risk of malignancy in this study unlike to the other studies. Shortness of breath and difficulty of swallowing is more related to malignancy rate than the other associated symptoms.

Size of the thyroid nodule is the most studied clinical predictor for malignancy in many studies (3,10,17), this study also found strong association between size and rate of malignancy. A size of ≥ 4 cm thyroid nodule is more associated with rate of malignancy with p value of 0.021 and with follicular carcinoma with p value of 0.012 and OR of 18.22.

On this current study, Age has no significant association with risk of malignancy unlike to other studies which reveal age greater than 45 has more risk for presence of malignant tumour (10).

Conclusion And Recommendation

On the basis of this study, it concludes that lesions larger than or equal to 4 cm in diameter, lesions in female and lesion associated with other added symptoms like shortness of breath, and difficulty of swallowing diagnosed as suspicious for follicular neoplasm by FNA cytology are associated with an increased risk of the presence of a malignant tumor.

Accordingly, this study suggests that smaller lesions, particularly for those without other associated symptoms has minimal chance of being malignant so should be managed with lobectomy and isthmusectomy and to follow the biopsy result for subsequent management.

To increase the predictability of malignancy from diagnosis of follicular neoplasm it may need more study on sonographic features of the nodules and cytopathological analysis of the tissue other than the clinical predictors.

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8. ANNEXES

Data collection format / Questionnaire

This data collection format is going to extract data from the patient medical record chart. And I the data collector assure the data filled below is complete and consistent.

Name of data collector.....

Signature

ID		
Socio demographic	Age	
	Gender	1. Male 2. Female
	Address	1. AA 2. Oromiya 3. Amhara 4. SNPPR 5. Other
	Occupation	1. House wife 2. Farmer 3. Student 4. Private business 5. Government Employee 6. Unemployed
	Religion	1. Orthodox 2. Muslims 3. Protestant 4. Other
	Marital status	1. Single 2. Married 3. Divorced 4. Widowed
	Ethnicity	1. Oromo 2. Amhara 3. Tigre 4. Gurage 5. Others
	Education level	1. Illiterate 2. Primary school 3. Secondary school 4. College level
28		

Clinical factors	Duration of swelling	
	Associated symptoms	1. Voice change 2. Shortness of breath 3. Difficulty of swallowing 4. Resent increment of size 5. None
	Consistency	1. Soft 2. Firm 3. Hard
	Fixity of the mass	1. Fixed 2. Mobile
	Size	
	Nodularity	1. Solitary 2. Multiple 3. Diffuse
Cytopathology	Preoperative FNAC	1. Follicular neoplasm 2. Suspicious for follicular neoplasm
Histopathology	Post op biopsy	1. Follicular carcinoma 2. Follicular adenoma 3. Papillary thyroid carcinoma 4. Benign nodular goitre 5. Others
Operation done	1. Lobectomy + isthmusectomy 2. Subtotal thyroidectomy 3. Dunhill's procedure 4. Near total thyroidectomy 5. Total thyroidectomy	