



# Histopathological pattern of thyroidectomy specimens at South Egypt Cancer Institute: A cross sectional study

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## Abstract:

**Background:** Thyroid disorders are considered a major health problem all over the world and in our society in Egypt. All over time there were a number of classifications and updates about thyroid pathology. The objective of the present study is to apply the latest World Health Organization (WHO) update about thyroid neoplasm. Overall, the new classification is helpful in the new knowledge of pathology, clinical behavior, and tumor genetics that help in patient management to avoid overdiagnosis and overtreatment of patients with indolent thyroid tumors that cause no harm to patients.

**Aim of the work:** Microscopic evaluation of all thyroidectomy specimens enrolled at South Egypt Cancer Institute from the period of Jan 2008 to Dec 2018 in the light of new WHO classification with emphasis on criteria of the borderline tumor in the form of evaluation of the pattern either follicular or papillary pattern, assessment of presence or absence of papillary nuclear features and assessment of capsular or vascular invasion.

**Results:** Out of 590 thyroidectomy specimens, 462 (78.3%) were females and 128 (21.7%) were males. The studied cases included 315 hyperplastic cases (53.4%), 53 inflammatory cases (9%), and 222 (37.6%) neoplastic cases. 11 cases fulfilled the borderline criteria (1.9%) 9 cases of noninvasive follicular tumor with papillary like nuclear features (NIFTP) & only 2 cases of well differentiated follicular tumor of uncertain malignant potential WDTUMP.

**Conclusion:** Thyroid lesions show female predominance with a female to male ratio of 3.72 to 1. The peak incidence for thyroid lesions is commonly seen in fourth decade. Non-neoplastic cases outnumber neoplastic cases. The introduction of the borderline category in thyroid tumor classification will open a new era for pathologists in the diagnosis of thyroid nodules that have equivocal microscopic features.

**Keywords:** follicular patterned thyroid nodule, borderline group, hyperplastic, neoplastic, WHO classification.

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## Introduction:

The thyroid gland is considered one of the most important controlling glands in our bodies. Thyroid disorders range between congenital, hormonal, inflammatory, hyperplastic and neoplastic [1]. There is an aggressive management of indolent thyroid nodules sometimes [2]. After total thyroidectomy and neck dissection, the microscopic examination may reveal a well-defined follicular neoplasm with some atypia. This makes the decision for the written final pathological report and post-operative management difficult and not understood [2]. The molecular studies showed that most of these lesions have RAS mutations that is seen in the follicular pattern thyroid tumor including follicular

adenoma rather than BRAF mutation seen in papillary thyroid carcinoma [3].

The World Health Organization recently published a new classification of thyroid tumors containing significant revisions [4].

The major modifications are seen in the follicular-derived neoplasms. A "borderline" tumor group has been added to the current classification. This includes follicular tumor of uncertain malignant potential (FTUMP), well differentiated tumor of uncertain malignant potential (WDTUMP) and noninvasive follicular tumor with papillary-like nuclear features (NIFTP). The microscopic features FTUMP is well defined follicular patterned tumor with questionable

capsular or vascular invasion and total absence of papillary-like nuclear features, while WDTUMP is composed of well-defined follicular shaped tumor with both questionable capsular/vascular invasion and papillary like nuclear features. On the other hand, NIFTP is characterized by a well-defined follicular tumor without any capsular/vascular invasion or papillary-like nuclear features [5].

Overall, the new classification is helpful in the new knowledge of pathology, clinical behavior and tumor genetics that aid in patient management to avoid overdiagnosis and overtreatment of patients with indolent thyroid tumors that may cause no harm to patients [6].

#### *Aim of the study:*

Microscopic evaluation of all thyroidectomy specimens enrolled in SECI from the period of Jan 2008 to Dec 2018 in the light of new WHO classification with emphasis on the criteria of borderline tumor by:

- Evaluation of the thyroid lesion pattern either papillary or follicular
- Assessment of papillary nuclear features score
- Assessment of capsular or vascular invasion

## **Material and Method:**

### *Study cohort*

A retrospective cross-sectional study has been conducted in the department of pathology at South Egypt Cancer Institute (SECI). All cases registered as goiter or thyroid nodules within the study period from January 2008 to December 2018 have been collected from the departmental records. All H&E stained slides for thyroid lesions have been retrieved and reviewed. The cases have been grouped into a hyperplastic, inflammatory and neoplastic groups. The study was approved by institutional ethics committee number 17100586.

### *Inclusion criteria*

1. Thyroid lesions for patients who were presented with thyroid enlargement, who underwent any type of thyroid operation (i.e. lobectomy, subtotal thyroidectomy, or total thyroidectomy).
2. Patient age from 11 years old to 80 years old

### *Exclusion criteria*

Thyroid tumors that are not derived from follicular and parafollicular cells such as lymphoma and metastasis.

### *Pathological evaluation*

1. Evaluation of all hyperplastic, inflammatory and neoplastic thyroid lesions was done according to the WHO classification 4th edition.
2. All slides for thyroid neoplasm were reviewed according to 2017 World Health Organization (WHO) Classification of tumors of the thyroid and its revised criteria 2018 to confirm the type and to identify cases that fulfill the criteria of borderline follicular tumors and rare variants of papillary thyroid carcinoma.

\*Criteria for NIFTP: well defined follicular neoplasm with absence of capsular and vascular invasion with papillary nuclear features score 2-3, no necrosis, no mitosis and no papillae.

\*Criteria for WDTUMP: well-defined follicular neoplasm with questionable capsular or vascular invasion and questionable papillary nuclear features

\*Criteria for FTUMP: well defined follicular neoplasm without any papillary nuclear features and with questionable capsular or vascular invasion

3. Apply Turin criteria described for insular carcinoma.

-Presence of solid/trabecular/insular growth pattern.

-Absence of conventional papillary nuclear features.

-Presence of at least one of the following: convoluted nuclei, mitotic activity  $>$  or  $=$  3/10HPF or tumor necrosis.

4. Evaluate difference between Hashimoto's thyroiditis and lymphocytic thyroiditis:

Both are considered different phases of immune mediated thyroid disorder generally known as "Autoimmune thyroiditis".

\*For both Hashimoto's thyroiditis and lymphocytic thyroiditis:

The common dominator is the presence of lymphocytic infiltration of thyroid gland with germinal center formation.

\*For Hashimoto's thyroiditis:

Combination of:

1-Epithelial cell destruction. Thyroid cells are packed with mitochondria with acidophilic cytoplasm and called Askanazy cells

2-Lymphoid cellular infiltration accompanied by actual lymphoid follicles formation and germinal center formation.

3-Fibrosis

### *Data collection*

All available clinicopathological data of the patients included in the study has been retrieved from the database system and patients' paper notes. Clinicopathological information include age, gender, presentation, capsular invasion, vascular invasion, nature of specimen obtained and gross picture of the lesion.

### *Statistical analysis*

Data analysis was carried out using SPSS version 20 (SPSS Inc., Chicago, IL, USA). Categorical data were presented as frequencies and percentages. Continuous data were reported as means  $\pm$  standard deviation and/or median and range (min-max).

## **Results:**

This study includes 590 thyroidectomy specimens. Female predominance was noted with a female to male ratio of 3.72:1. The age of the studied cases ranges from 12 to 80 years old with a mean age of  $40.5 \pm 10$  years and median age of 39 years (Table1).

Non-neoplastic thyroid lesions include hyperplastic and inflammatory thyroid lesions and both accounted

for 368 cases (62.4%). Colloid nodular goiter (Figure 1) is the most common non-neoplastic hyperplastic thyroid lesions and accounts for 315 cases (53.4% of the whole

reviewed specimens), 252 females and 66 males (Table1).

Table (1): Frequency of different thyroid lesions

Types & Subtypes of variables			Frequency	Percent%	Total
<b>Gender</b>	Male		128	21.7%	590
	Female		462	78.3%	
<b>Different thyroid lesions</b>	Hyperplastic		315	53.4%	590
	Inflammatory		53	9%	
	Neoplastic		222	37.6%	
<b>Non-neoplastic lesions</b>	Colloid nodular goiter		315	53.4%	368(62.4%)
	Hashimoto thyroiditis		40	6.8%	
	Autoimmune thyroiditis		11	1.9%	
	Lymphocytic thyroiditis		2	0.3%	
<b>Neoplastic lesions</b>	Benign neoplastic lesions	Follicular adenoma	50	8.5%	51(8.7%)
		Hurthle cell adenoma	1	0.2%	
	Borderline neoplastic lesions	NIFTP	9	1.5%	11(1.8%)
		WDTUMP	2	0.3%	
	Malignant neoplastic lesions	PTC	123	20.8%	160(27.1%)
		MTC	11	1.9%	
		FTC	10	1.7%	
		Anaplastic C	9	1.5%	
		Insular C	6	1%	
		Hurthle c. C	1	0.2%	

Fifty three cases are inflammatory thyroid lesions, 40 cases (6.8%) of Hashimoto thyroiditis (Figure 2), 11 cases (1.9%) of autoimmune thyroiditis and 2 cases (0.3%) of lymphocytic thyroiditis (Table1). Most of non-neoplastic cases are found in the 4th decade of life (Table 2).

As regards the neoplastic thyroid lesions, they represent 37.6% of all cases (Table 1).

After strict application of the new WHO classification of follicular patterned thyroid tumor (2017) and the revised criteria (2018), we classified thyroid neoplasms into benign, borderline and malignant. 11 cases out of 50 previously diagnosed as follicular adenoma are fulfilled the criteria of the new category (borderline). Table 1 represents the frequency of benign neoplastic category after revision which are 52 cases (8.8%) including 50 cases of follicular adenoma (8.5%) and only one case of Hurthle cell adenoma (0.2%). One case of follicular adenoma with bizarre nuclei was detected in our study as a rare variant (Figure 3). Most of benign cases are found in the age group 31-40 years with female predominance (Table 2).

The borderline neoplastic lesions represent 11 cases (1.9%); 9 noninvasive follicular neoplasm with papillary-like nuclear features (NIFTP) (Figure 4) and 2 cases of well-differentiated tumor of uncertain malignant potential (WDTUMP) (Figure 5). Table 3

shows the different clinicopathological variables of the new category.

Papillary thyroid carcinoma is considered the most common neoplastic lesion and accounts for 123 cases out of 160 cases, most cases are seen in the age group from 51 to 60 years 72.4% (89 cases) are females (Table 2). Two cases are of rare variants of papillary thyroid carcinoma include the hobnail variant and the oncocytic variant (Figure 6).

Eleven cases are of medullary thyroid carcinoma representing 6.9% with male predominance (Table1, 2).

Follicular thyroid carcinoma follows papillary thyroid carcinoma and medullary thyroid carcinoma in frequency and represent 10 cases (6.3% of malignant neoplastic cases), commonly seen in older age groups from 6th to 7th decades with female predominance (Table 2). Undifferentiated thyroid carcinoma (anaplastic carcinoma) accounts for 9 cases (5.6%) mostly between 51 and 70 years with also female predominance (Table 2). Six cases of poorly differentiated carcinoma (Insular carcinoma) fulfill the Turin criteria which represent 1% of studied cases and are much more in females and commonly seen in 7th decade (Table 2).

Only one case of Hurthle cell carcinoma is seen in a male aged 69 years old (Table 2).

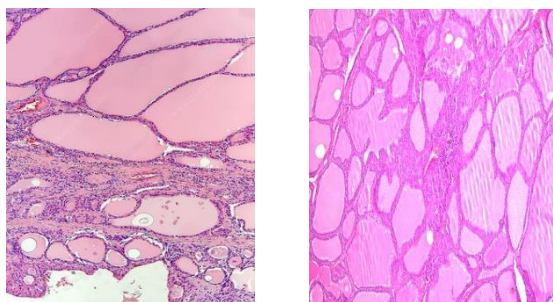
Table (2): Age groups and gender distribution among different thyroid lesions:

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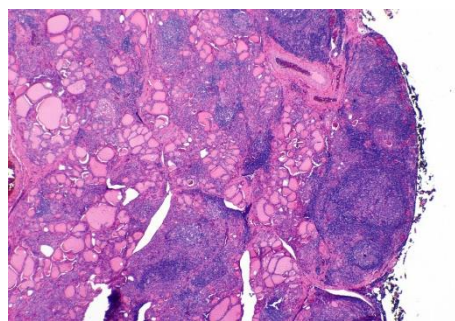
Table (3): Different clinicopathological variables seen among the 11 reviewed follicular adenoma cases

Sex	Age	Capsular invasion	Vascular invasion	Gross Picture	Papillary nuclear features	Type of operation	Year of diagnosis	New category
Male	52	No	No	Firm greyish white nodule 1.5x1.5 cm	Score 3	Right hemi thyroidectomy	2016	NIFTP
Female	24	No	No	Well defined firm greyish white nodule 2x1.5 cm	Score 2	Right hemi thyroidectomy	2012	NIFTP
Female	35	No	No	Well defined nodule firm grey tan 1x1.5 cm	Score 2 to 3	Total thyroidectomy and bilateral neck dissection	2016	NIFTP
Female	38	No	No	Well defined soft tan nodule in left lobe 3x1 cm	Score 2 to 3	Total and left neck dissection	2011	NIFTP
Female	41	No	No	Homogenous cut section	Score 2 to 3	Right thyroidectomy	2010	NIFTP
Female	43	No	No	Well defined firm greyish white nodule 1.5x1.5 cm	Score 2 to 3	Left hemi thyroidectomy	2016	NIFTP
Female	45	No	No	Homogenous cut section	Score 2 to 3	Near total thyroidectomy	2008	NIFTP
Female	45	No	No	Well defined firm greyish white nodule 2x2.5 cm	Score 2 to 3	Total thyroidectomy and bilateral neck dissection	2012	NIFTP
Female	46	No	No	Small well defined firm grey white nodule in right lobe and near total replacement of left lobe by large hard nodule 4x4x3 cm	Score 2 to 3	Total thyroidectomy and bilateral neck dissection	2014	NIFTP
Female	36	Questionable	Questionable	Homogenous cut section	Questionable	Total thyroidectomy	2009	WDTUMP
Male	38	Questionable	Questionable	Homogenous cut section	Questionable	Total thyroidectomy	2009	WDTUMP

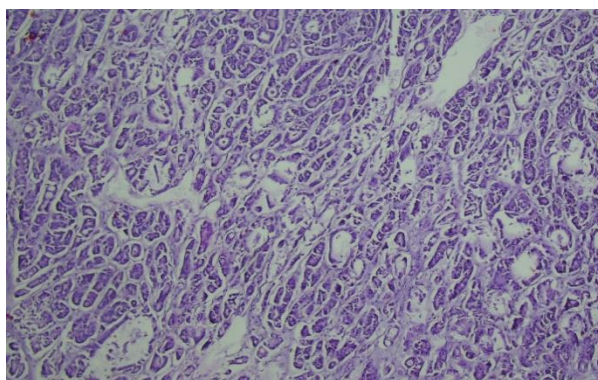
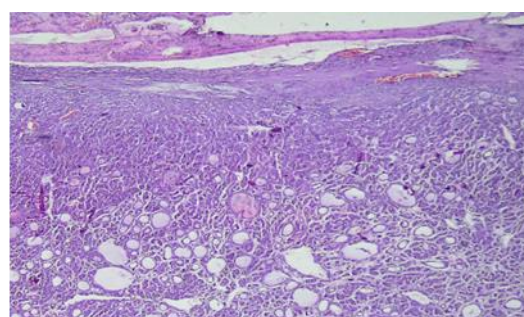
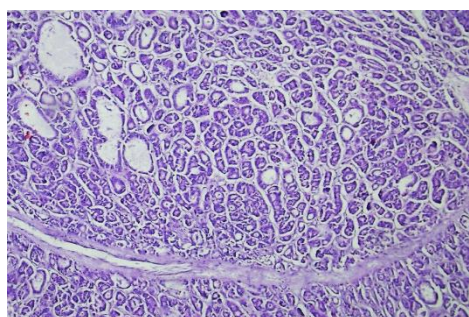




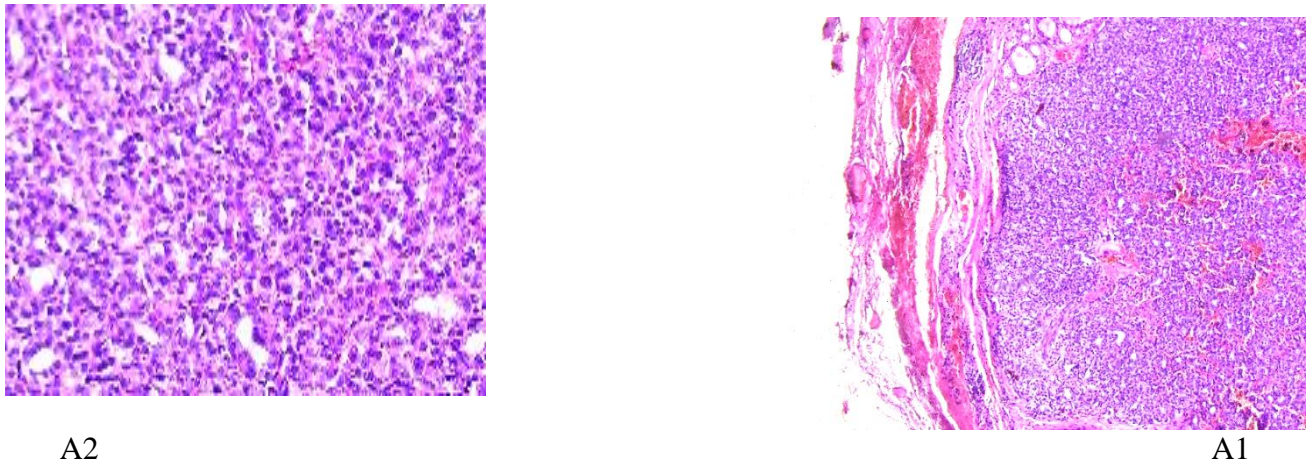
**Figure (1):** Colloid nodular goiter, magnification x10



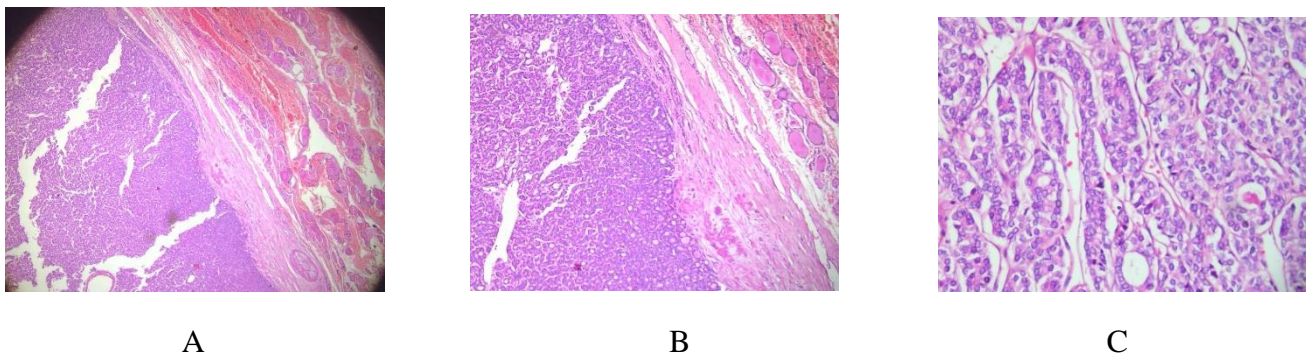
**Figure (2):** Hashimoto thyroiditis, magnification x4.



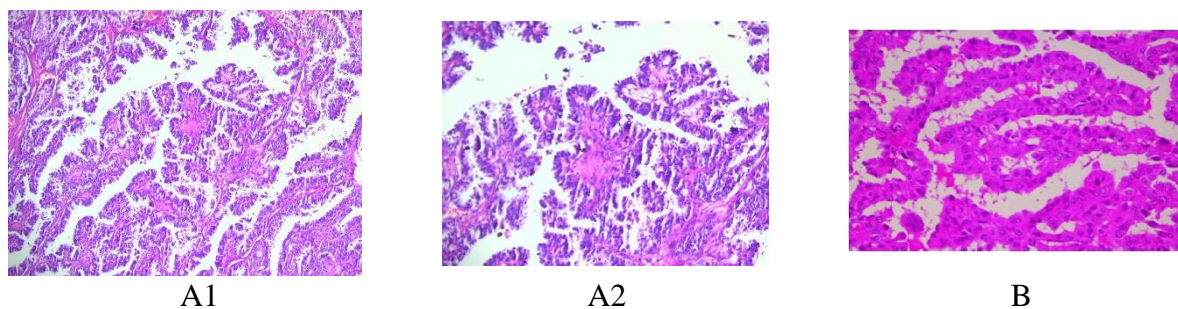
**Figure (3):** Follicular adenoma with bizzare nuclei magnification x4, x10 & x400



**Figure 4:** NIFTP (A1) show capsulated follicular patterned tumor without any invasion of capsule, magnification x4. (A2) show closely backed follicles, magnification x10.



**Figure 5:** WDTUMP (A) show capsulated follicular patterned tumor, magnification x 4 (B) show questionable capsular invasion, magnification x 10 (C) show questionable papillary nuclear features, magnification x 40



**Figure 6:** PTC and its rare variants reviewed in this study  
A1, 2: hobnail PTC variant x10 & x20.  
B: oncocytic PTC variant



## Discussion:

Thyroid gland lesions are common worldwide. The great concern is given to them as thyroidectomy may offer a cure in many cases. In 11 years of the present study duration, 590 thyroidectomy specimens were encountered. The age group ranged from 11 to 80 years old with a mean age of 40.5 years old. The most common age group was the fourth decade. This is similar to other studies; Rajagopal et al, 2021 who reported a mean age of 40 years similar to our study [7], Fahim et al., 2014 from Pakistan found a mean age of 32 years. Padmom et al, 2020 found their cases between 40-50 years old with a mean age of 45 years [8].

Colloid nodular goiter was the most common thyroid lesion in the present study which represented 53.4% of all studied cases. This finding was consistent with that reported by Solomon et al., 2015 [9]. Sheela and Sreedevi, 2018 and Vamitha, 2020 reported that colloid nodular goiter represented 56.9% and 54% of their studied cases respectively [10,11]. However, the study of Padmavathi and Jyothi, 2018 showed a percentage of 37.2% of the 211 thyroid specimens over 5 years were colloid nodular goiter [12].

In our study females formed the majority of the cases (78.3%) which was in keeping with other studies reported from India by Kartthick, 2019 [13] and from Al-Madinah by Albasri et al., 2014 [14], while Parthipa and Vamitha, 2020 reported that in their 145 thyroidectomy specimens 90.1% were female [11]. This was explained by excess estrogen receptors and increased incidence of autoimmune diseases among females [10].

In our study, non-neoplastic thyroid lesions outnumbered neoplastic lesions. These findings were consistent with most recent studies on thyroidectomy specimens [8,10].

The mean age for colloid nodular goiter observed in our study was commonly in the fourth decade (31-40 years old) that was in keeping with many studies [12,14]. This can be explained by that in both males and females the prevalence of nodular goiter declines with age and this finding fits the observation that lean body mass (known to decline with age) is the major determinant of thyroid size [16].

The next most common non-neoplastic lesion in our study was Hashimoto's thyroiditis which accounted for 40 cases and represented 6.8% with female predominance. This was in accordance with the study done by Magdalene et al., 2017 who reported that Hashimoto thyroiditis represented 10.6% [17]. Most cases encountered in the fourth decade are similar to many other studies as this age is a common age group for autoimmune disease [8,9].

Despite of great advances in the understanding of thyroid tumors, there are problems and unanswered questions" stated Drs. Meissener and Warren more than 50 years ago [18]. This reflects the struggles most of pathologists have lived over the past years. That led to difficulty for proper thyroid tumor classification especially the indolent lesions which in turn led to difficult management and follow-up of patients [19].

Benign thyroid tumors are common, and although malignant tumors are relatively rare, they represent the most common endocrine malignancies [10]. The WHO published its fourth edition on the histological classification of thyroid tumors in 2017 and revised certain criteria 2018. The major modifications are concerned with encapsulated follicular patterned tumor. A borderline category is included within the new classification which included NIFTP, WDTUMP and FTUMP. The main criteria for such group are to evaluate the pattern, papillary nuclear features and capsular or vascular invasion. Another modification includes adoption of "Turin criteria" for diagnosis of insular carcinoma. Histopathological classification of thyroid tumors is essential for further therapy and prognosis.

Neoplastic thyroid lesions in our study accounted for 222 cases which represented 37.6% of all included cases and that was keeping with the study of Padmom et al, 2020 [8].

Malignant lesions in our studied cases predominate, which was similar to many recent studies [8,11]. This could be explained by the presence of many risk factors for malignant thyroid including environmental/lifestyle factors (e.g., radiation, iodine intake, and nitrates), as well as comorbidities (e.g., chronic lymphocytic thyroiditis), and perhaps a complex multiplication of these factors were considered possible causes for a true increase in thyroid cancer incidence [20]. However, early detection by modern diagnostic techniques might play role in increasing the incidence of thyroid tumors [21]. All these factors are common in our locality.

Believing that H&E stained slides are very important for the pathologist, we strictly applied in our study the new WHO classification of follicular patterned thyroid tumor (2017) and the revised criteria (2018).

The NIFTP cases (nine cases) were seen in the age group 41-50 years old and met the criteria required for its diagnosis. The absence of a papillary structure was recently applied as a rigid diagnostic criterion for NIFTP [22]. This criterion was previously suggested in the study by Cho et al which showed that a cutoff of less than 1% papillae could give rise to diagnostic discrepancies and lead to a misclassification of biologically more aggressive variants of PTC as NIFTP [22].

That is why recent studies advise extensive sampling of the whole nodule and careful examination to rule out any evidence of invasion at the periphery of the tumor, any abnormal papillary structure, solid areas, necrosis or mitosis. Concerning two cases of WDTUMP in our study, Alam et al., 2018 reported one case of WDTUMP out of 100 thyroidectomy cases in their study [15].

None of the revised follicular adenoma met the criteria of FTUMP. However, Padmavathi and Jyothi, 2018 reported seven cases of FTUMP [12].

Malignant thyroid neoplasm accounted for 160 cases (27.1%) and that was quite similar to the study done by Parthipa and Vamitha, 2020 who reported that 20% of their studied cases were malignant [11].



On the other hand, our results were in discordant to many studies like that done by Alam et al., 2018 (16%), and by Solomon et al., 2015 (12.6%) [9,15]. This might be due to a different number of thyroidectomy specimens reviewed between our study and the study of Alam et al., 2018 (100 cases) [15].

The most predominant histological type of malignant thyroid neoplasm observed in our study was papillary carcinoma similar to most recent studies. Papillary thyroid carcinoma was commonly seen in the sixth decade. Alam et al reported the range group between 20-50 years old [15] while Parthipa and Vamitha documented the age group between 31-40 years who included only 145 cases in their study. The older age was more documented in many studies for PTC mostly due to prolonged exposure to malignant thyroid risk factors required.

In our study, we had two cases of rare variants of papillary thyroid carcinoma, hobnail variant and oncocyctic variant. The hobnail variant is very aggressive and may show transformation to poorly differentiated thyroid carcinoma or undifferentiated thyroid carcinoma [19].

Medullary thyroid carcinoma represented 1.9% of cases in our study (11 cases) and was commonly seen in the seventh decade. Solomon et al reported 6 cases of MTC but were presented at the age of fifty [9].

In our study, follicular thyroid carcinoma followed MTC in incidence (10 cases) and was commonly seen in the age group between 51-70 years. This was much higher than the study done by Parthipa and Vamitha who reported only 2 cases of FTC (11) and Sheela and Sreedevi who reported 4 cases of FTC [10]. This higher incidence might be explained by different geographical location and environmental factors as follicular thyroid carcinoma was more common in iodine-deficient areas and although many iodination programs had been introduced in our country, there were areas like New Valley still had iodine deficiency [23].

9 cases of undifferentiated carcinoma (Anaplastic carcinoma) (1.5%) were included and were commonly seen in the age group between 51-70 years old. Both studies of Alam et al, 2018 [15] and Solomon et al, 2015 [9] reported only one case of anaplastic carcinoma at age of seventy.

After strict application of Turin criteria [19], we had 6 cases of poorly differentiated carcinoma (Insular carcinoma) and that represented 1% of studied cases and were commonly seen in the age group between 61-70 years old. Sheela and Sreedevi reported only one case of insular carcinoma in their study in the age group between 50-59 years old [10].

Thus, the present study gives valuable epidemiological and demographic information about the various types of thyroid disorders that were diagnosed in the last 10 years from 2008 to 2018 in the pathology department of South Egypt Cancer Institute and also applies the strict criteria of the new WHO classification for thyroid tumors 4th edition.

## Conclusion:

Thyroid gland is considered the most important endocrine organ. Thyroidectomy may have both therapeutic and diagnostic value. Thyroid lesions show female predominance.

Peak incidence for thyroid lesions is commonly seen in the fourth decade. Non-neoplastic cases outnumber neoplastic cases. Colloid nodular goiter was the most frequent non-neoplastic lesion. The most common benign tumor was Follicular adenoma. Although borderline lesions are not representing a high incidence in our study, they are very important for diagnosis to avoid over-diagnosis or overtreatment and hazards of radioactive iodine.

Histopathologic examination is still the mainstay for a definite diagnosis.

**Disclosure statement:** The Authors have no conflict of interest.

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