

The Prevalence of Differentiated Thyroid Cancer in Multinodular Goiter versus Single Thyroid Nodule in Karbala

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Received: 27 May 2026; **Accepted:** 22 June 2026; **Published:** 18 July 2026

Abstract: Background: Thyroid cancer is the most common cancer affecting the endocrine system, accounting for approximately 1% of all human cancers, thyroid cancer occurs in 5–15% of cases with thyroid nodules depending on age, sex, radiation exposure history, family history, and other factors.

Objectives: to determine the prevalence of differentiated thyroid cancer in patients with multinodular goiter (MNG) and single thyroid nodule undergoing surgery in Karbala city.

Methods: a prospective study that was conducted at Imam Al-Hussain medical city and Safeer Al-Hussain hospital, Karbala, Iraq, over a period of twelve months starting from 1st of December 2021 to 1st of December 2022. During this period a total of 100 patients (88 female and 12 male) undergo thyroid surgery for different causes have been enrolled in the study.

Results: The overall prevalence of differentiated thyroid cancer was (19%), there is a strong relationship between nodularity and pathology types .which shows 16 (66.7) of patients with follicular adenoma, 9 patients (60%) with papillary thyroid cancer, and all patients 4(100%) with follicular thyroid cancer were single thyroid nodule, while 45 (84.9) of patients with colloid goiter and all patients with thyroiditis were multi nodular.

Conclusions: the prevalence of malignancy was significantly higher in single thyroid nodule than multi nodular goiter, with papillary thyroid cancer being the most common histological subtype. But, the prevalence of malignancy in multi nodular goiter was also quite high and cannot be underestimated, ultrasonography and Fine Needle Aspiration Cytology are both important tools that predicting malignancy in suspicious thyroid diseases (nodular).

Keywords: Multi nodular goiter, papillary thyroid cancer, solitary thyroid nodule, follicular thyroid cancer.

Introduction: Thyroid cancer is the most common cancer affecting the endocrine system, accounting for approximately 1% of all human cancers. it has annual incidence of (0.5-10 /100000) people worldwide(1). Differentiated thyroid cancer (DTC) is increasing in incidence with mostly excellent prognosis. The appearance of DTC depends on age, sex, family history, radiation exposure and many other factor(2). DTC occurs in 7–15% of patients with thyroid surgery. In the

year 2014, approximately 63,000 new cases of DTC were diagnosed in the US, Compared to 2009 with only 31,200 new cases. In Germany there are about 6000 new cases of DTC per year. The growing incidence of thyroid cancer and the tumor shift to diagnosis of smaller tumors is due to the increased usage of diagnostic methods, such as ultrasound of the neck(3). Differentiated thyroid cancer includes papillary and follicular cancer that derive from thyrocytes and

express the sodium iodine symporter. DTC represents the majority (90%) of all types of thyroid cancer (4). Papillary thyroid carcinoma (PTC) is the most common form of DTC.

Follicular thyroid carcinoma (FTC) is a malignant tumor, histologically derived from follicular thyroid cells, showing transcapsular or vascular invasion and missing the typical nuclear signs of papillary carcinoma. In the traditional classification of FTC there are two groups: minimally invasive and widely invasive (5,6,7).

Thyroid nodules are a common clinical problem. Epidemiologic studies have shown the prevalence of palpable thyroid nodules to be approximately 5% in women and 1% in men living in iodine-sufficient parts of the world(8,9).

In contrast, high-resolution ultrasound (US) can detect thyroid nodules in 19–67% of randomly selected individuals with higher frequencies in women and the elderly(10). The clinical importance of thyroid nodules rests with the need to exclude thyroid cancer which occurs in 5–15% depending on age, sex, radiation exposure history, family history, and other factors(11,12).

Fine needle aspiration cytology (FNAC) is the clinical procedure of choice for evaluating whether a nodule is benign or malignant(13). It is a simple, safe and most accurate method for selecting the patients who will need surgical resection or follow-up. Ultrasound-guided FNA (USgFNA) has improved diagnostic accuracy compared to FNA by palpation(14,15).

Both the European Thyroid Association and the American Thyroid Association have issued clinical practice guidelines and recommendations as to how to evaluate thyroid nodules. Nodules that are usually 1.0 cm or greater in dimension and are nonfunctioning require further evaluation by FNA. If the TSH is suppressed, then radionuclide scintigraphy is indicated to rule out a functioning nodule. Nodules that are less than 1.0 cm but have suspicious ultrasound characteristics also require further investigation. These characteristics are: hypoechogenicity, microcalcifications, irregular margins, intranodular vascularity and regional lymphadenopathy(16,17).

The diagnostic cornerstone of thyroid nodules remains the ultrasound examination. It should be performed in any case of known or suspected thyroid nodules or cervical lymphadenopathy to assess if further diagnostic is needed. Sonographic patterns suspicious of malignancy are microcalcifications, irregular margins, solid consistency, hypoechogenicity, extrathyroidal extension (ETE) and a tall shape rather than a wide one(18). The ultrasonographic features of thyroid cancer (19)

Aim of the Study

Is to determine the prevalence of differentiated thyroid cancer in patients with multinodular goiter (MNG) and single thyroid nodule undergoing surgery in Karbala city

Methods

This prospective study was conducted at Imam Al-Hussain medical city and Safeer Al-Hussain hospital, Karbala, Iraq, over a period of one year starting from 1st of December 2021 to 1st of December 2022. During this period a total of 100 patients (88 female and 12 male) undergo thyroid surgery for different indications have been enrolled in the study. All the patients have accepted to participate in this study and their verbal consent has been taken.

Most patients had preoperative assessment by history and examination, with standard pre-operative assessment which include evaluation, ultrasonography (US) of the thyroid and neck, fine-needle aspiration cytology (FNAC) of the thyroid nodule, and FT3, FT4, TSH, and TSH, also thyroid antibody titer, all patients underwent checking of vocal cord mobility, serum calcium, In addition to routine investigations before surgery such as CBC, virology, ECG, and sometimes echo study.

Patients were divided in to two groups according to nodularity whether single thyroid nodule or multinodular goiter, with the help of thyroid ultrasound.

We used special questioner regarding information from the patients like radiation exposure or family history of thyroid diseases.

All patients' data have been recorded in the study paper and collected.

Regarding ultrasound and FNAC most of them done in different clinic not in one clinic, some of them in private clinic and some of them in private hospital and the others in our hospital.

The ultrasound report use the TIRAD for classification of thyroid nodules.

The FNAC report used the Bethesda scoring for thyroid nodules.

All patients admitted to the hospital and were euthyroid before the operation.

Inclusion criteria :

- Age between 14-65years.
- Patients with hypothyroidism and enlarged gland.
- Patients with hyperthyroidism and goiter.
- Patients with suspected nodule.
- Exclusion criteria

- Thyroidectomy due to metastatic cancer from other organs.
- Undifferentiated thyroid cancer.

Surgery was either total or near total (leaving only 1gm of thyroid tissue in one side) or sometimes lobectomy with isthmusectomy.

All the patients are discharged either within 24 hours to 48 hours post-surgery.

The final histopathological report received either from the senior during follow up visit or sent by the patient through the phone after a period of 10 days to 3 weeks.

Statistical Analysis:

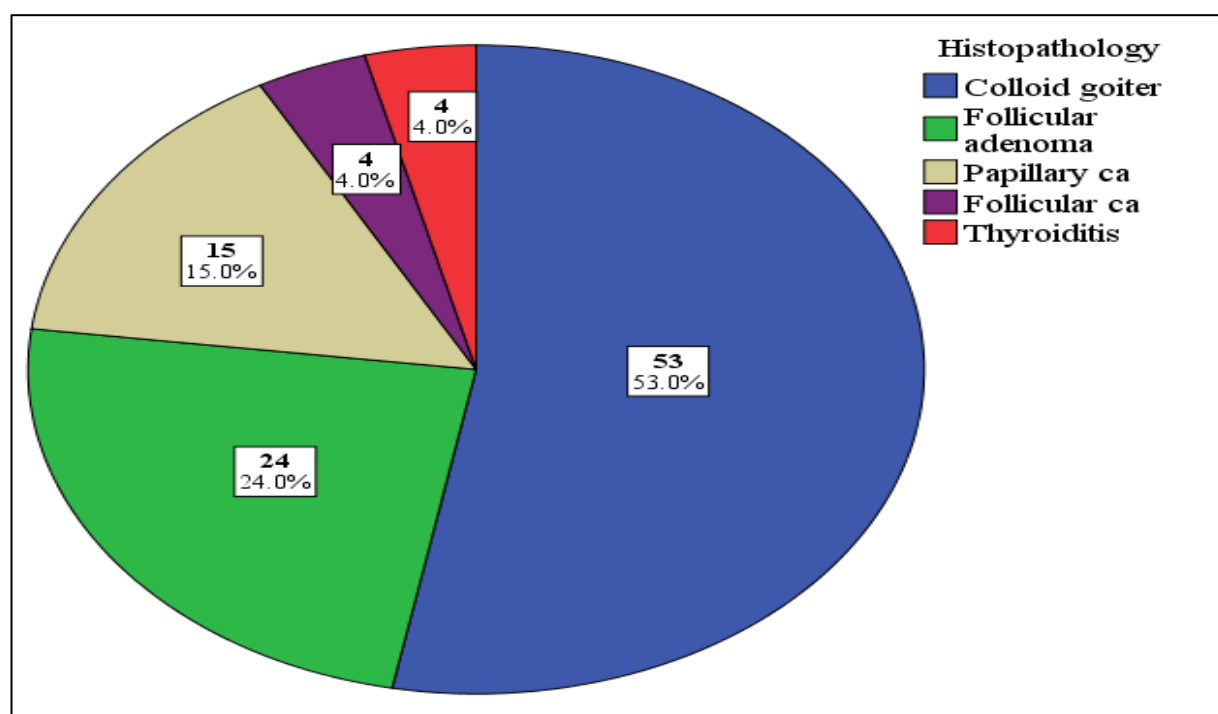
Statistical analysis was performed using IBM® SPSS® version 23 for Windows. Chi-square test was used to analyze the association between categorical variables,

Fisher's Exact test was used instead of the former when needed. Independent Samples T-test and analysis of variables (ANOVA) were used to test the statistical significance of the difference between two variable or more, respectively.

Results

This study enrolled 100 patients; 12 males and 88 females, their overall mean age was 41.1 ± 10.6 years, while males' mean age was 43.4 ± 10.2 years, while females mean age was 40.8 ± 1.7 years. The most frequently observed pathology was colloidal goiter with 53 (53%) cases, followed by follicular adenoma with 24 (24%) cases, while there were 15 (15%) patients with papillary carcinoma, and four (4%) patients with follicular carcinoma, and four (4%) with thyroiditis, as shown in Figure-1

Figure-1: Distribution of the study sample according to histopathology



There was no statistically significant difference in mean age between pathology types, however it can be observed that patients with follicular adenoma and papillary ca had lower age group, with 37.5 ± 10.6 years and 37.57 ± 11.77 years, respectively. The gender

distribution showed no significant statistical association with pathology type, probably due to low number of males in the current study. There were only five smokers; two with colloidal goiter and three with papillary carcinoma. As shown in Table 5

Table 5: Distribution of basic characteristics of the study group according to histopathology

Variables	Colloid goiter	Follicular adenoma	Papillary ca	Follicular ca	Thyroiditis	P-value
Age (years) Mean± SD	43.53±9.7	37.5±10.6	37.57±11.77	44.5±16.68	40±3.9	0.105

Male/ Female ratio	5/48	3/21	4/11	0/4	0/4	0.444
Smokers/ nonsmokers	2/51	0/24	3/12	0/4	0/4	0.134

There were statistically significant differences between pathology types according to TIRADS and Bethesda scores, as patients with papillary and follicular ca had significantly higher scores compared to other pathologies, with mean of 4 ± 0.8 , 3.5 ± 0.6 for TIRADS, and 4.5 ± 0.9 , 4 ± 0.0 for Bethesda, respectively. Patients with TIRADS >3 and the

histopathology showed colloid goiter were only two (3.8%), six (25%) with follicular adenoma, 10 (66.7%) with papillary ca, two (50%) with follicular ca, and nil in patients with thyroiditis. There were no patients with Bethesda scores >3 with colloid goiter, three (12.5%) with follicular adenoma, 13 (86.7%) with papillary ca, four (100%) all cases with follicular ca, and no case with thyroiditis. As shown in Table 6.

Table-6: Distribution of histopathology types according to ultrasonography TIRAD and Bethesda scoring system

Variables	TIRADS			Bethesda scoring system		
	Mean	SD	Score>3 No. (%)	Mean	SD	Score>3 No. (%)
Colloid goiter	2.5	0.6	2 (3.8%) out of 53 patients	2.2	0.4	0 (0.0%) out of 53 patients
Follicular adenoma	3.0	1.0	6 (25.0%) out of 24 patients	2.6	0.7	3 (12.5%) out of 24 patients
Papillary ca	4.0	0.8	10 (66.7%) out of 15 patients	4.5	0.9	13 (86.7%) Out of 15 patients
Follicular ca	3.5	0.6	2 (50.0%) out of 4 patients	4.0	0.0	4 (100.0) out of 4 patients
Thyroiditis	2.8	0.5	0 (0.0%) out of 4 patients	2.5	0.6	0 (0.0) Out of 4 patients
P-value	<0.001		<0.001	<0.001		<0.001

There was statistically significant association between pathology and nodularity, as 16(66.7%) cases of follicular adenoma, nine (60%) of papillary ca, and all cases of follicular ca were single nodular, while 45

(84.9%) of colloid goiter and all cases of thyroiditis were multinodular, as shown in Table-7. The percentages of papillary ca and follicular ca among patients with single nodular goiter were 24.3% and 10.8%, respectively,

while the percentage of papillary ca among patients with multinodular goiter was 9.5%.

Table-7: Distribution of histopathology results according to thyroid nodularity

Histopathology	Single nodular goiter	Multi nodular goiter	P-value
	Number (%)	Number (%)	
Colloid goiter	8(15.1%)	45(84.9%)	<0.001
Follicular adenoma	16(66.7%)	8(33.3%)	
Papillary ca	9(60%)	6(40%)	
Follicular ca	4(100%)	0(0)	
Thyroiditis	0(0)	4(100%)	
Total	37 (37.0%)	63 (63.0%)	

Cases with single nodular goiter had higher TIRADS and Bethesda scores, and 14(70%) of TIRADS or Bethesda scores >3 had single nodular goiter, while age, gender

and smoking showed no statistically significant difference according to thyroid nodularity, as shown in Table-8.

Table-8: Distribution of study variables according to thyroid nodularity

Variables		Single nodular goiter	Multi nodular goiter	P-value
		Number (%)	Number (%)	
Age (year) mean± SD		38.39±12.91	42.68±8.81	0.082
Gender	Male	4(33.3)	8(66.7)	1.0
	Female	33(37.5)	55(62.5)	
Smoking		1 (20.0)	4 (80.0)	0.649
TIRADS> 3		14(70)	6(30)	<0.001
FNA> 3		14(70)	6(30)	<0.001

Discussion

The prevalence of thyroid cancer is increasing worldwide. This study is the first study in Karbala city regarding differentiated thyroid cancer prevalence among patients with multinodular goiter and single thyroid nodule.

The overall prevalence of differentiated thyroid cancer was (19%) ,which is slightly higher in comparison in what was published in 2020 in Yemen which shows cancer prevalence was (13.8) in thyroid nodules , with mean age 37.5 (30) . but in a study in Spain published at 2011 showed that the risk of thyroid malignancy in

thyroid nodules was (24.9) (20).

Of these (19%) , papillary thyroid cancer was 15 (79%) with female to male (11:4) which is more predominant than follicular thyroid cancer which is only 4 (21%) and all of them were females , which may be due to small sample number.

Regarding TIRAD score , patients with PTC and FTC shows higher score than other pathologies with mean of 4 ± 0.8 , 3.5 ± 0.6 for TIRADS respectively with p-value $< (0.001)$, which is equal to what was published in November 2022(21).

Regarding Bethesda scoring patients with PTC and FTC shows higher score than other pathologies with mean score 4.5 ± 0.9 , 4 ± 0.0 for Bethesda, respectively with p-value $> (0.001)$.

Our study shows that the most common histopathology was colloid (53%), and the second most common pathology was follicular adenoma (24%), which is agreed to one study in Baghdad Medical City 2018(22).

Our study shows that patients with thyroid malignancy have higher TIRAD score and higher Bethesda score, patients with thyroid cancer and TIRAD more than 3 were 10(66%) for PTC and 2 (50%) for FTC.

Patients with PTC and Bethesda score more than 3 were 13 (86.7%) and patients with FTC and Bethesda score more than 3 were 4 (100%).

From this we noticed that FNAC was more accurate than Ultrasound for diagnosis of thyroid malignancy from other thyroid diseases, which agree to what was published in 2019 in Pakistan Medical journal (23), and it could be operator dependent.

Patients with papillary thyroid cancer (PTC) and patients with follicular adenoma shows lower age with regard to other pathologies with mean age 37.5 ± 10.6 years and 37.57 ± 11.77 years, respectively , which agreed to what was published in Journal of Korean society of surgery in 2012 (24).

Our study shows that there is a strong relationship between nodularity and pathology types .which shows 16 (66.7) of patients with follicular adenoma, 9 patients (60%) with papillary thyroid cancer, and all patients 4(100%) with follicular thyroid cancer were single thyroid nodule, while 45(84.9) of patients with colloid goiter and all patients with thyroiditis were multi nodular. The percentages of papillary ca and follicular ca among patients with single nodular goiter were 24.3% and 10.8%, respectively, while the percentage of papillary ca among patients with multi nodular goiter was 9.5%, which is agreed to what was published in USA in 2006 (25), also it agreed to meta-analysis study in USA in 2012 (26). But some studies shows similar rate

of malignancy among MNG and STN (27).

Conclusion

1. We conclude that the prevalence of malignancy was significantly higher in STN than MNG, with PTC being the most common histological subtype. But, the prevalence of malignancy in MNG was also quite high and cannot be underestimated. It would be practically wise to keep this in mind while evaluating patients with MNG and ample effort should be made to pre-operatively identify any malignant focus, so that appropriate therapeutic protocol can be planned.

2. Ultrasonography and Fine Needle Aspiration Cytology are both important tools that predicting malignancy in suspicious thyroid diseases (nodular).

Recommendations

1. Patients with solitary thyroid nodule are more prone to thyroid malignancy than multi nodular goiter.
2. Thyroid nodule in young age should be treated carefully and properly.
3. Larger sample is needed to be more informative.

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