The Egyptian Journal of Hospital Medicine (October 2019) Vol. 77 (6), Page 5906-5910

The Prevalence of Thyroid Cancer in Patients with Multinodular Goiter

Mansour Mohamed Kabbash, Hassan Ahmed Abdallah, Anwar A. El Shenawy, Mostafa Mohamed Sayed Mohamed*

Department of General Surgery, Faculty of Medicine, Aswan University, Egypt

***Corresponding author:** Mostafa Mohamed Sayed Mohamed, **Mobile:** (+20) 1144376088, **Email:** tantawy_wael@yahoo.com

ABSTRACT

Background: Thyroid cancer is the most common endocrine carcinoma, as it accounts for almost 90% of all endocrine malignancies. The incidence of thyroid carcinoma is about 1-3 cases in every 100,000 population. During the last 30 years, the rate of thyroid cancer incidence has increased worldwide.

Objective: The aim of this work was to determine the frequency of thyroid carcinoma in multinodular goiter in patients undergoing thyroidectomy to make a strategy to perform total thyroidectomy (TT) as a rule of treatment.

Patients and methods: This retrospective study included the medical charts and surgical data of a total of 50 patients who underwent surgery for goiter at General Surgery Department, Aswan University Hospital between 2015 and 2018.

Results: The present study showed that the frequency of papillary carcinoma was 6% of all thyroid diseases (from 50 patients), 60% of incidental thyroid carcinoma as the frequency was high in the 4th decade of life. The present study showed that the frequency of follicular carcinoma was 2% of all thyroid diseases (one case), 20% of ITC. Patient was in the 4th decade. The present study showed that the frequency of undifferentiated thyroid cancer was 2% of all thyroid diseases. **Conclusion:** It could be concluded that, according to the finding of this study, total thyroidectomy is the preferred method in benign thyroid disease for which surgery is indicated. The advantages of TT include reduction of recurrence rate, achieves a permanent cure of thyroid disorders.

Keywords: Thyroid Cancer, Multinodular Goiter, CT, MRI, PET scan.

INTRODUCTION

Multinodular goiter (MNG) is defined as an enlarged thyroid gland with multiple nodules. Patients with MNG may undergo surgery to address goiter enlargement, which can cause compressive symptoms or cosmetic concerns; thyrotoxicosis; indeterminate cytology and suspicious or diagnosed malignancy [(1)].

According to the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) Program, TC represents 3.4% of all cancers diagnosed yearly. By 2030 TC, would become the fourth leading cancer diagnosis, following breast, prostate and lung carcinomas [(2)].

The more frequent use of sensitive diagnostic procedures, including ultrasound, Doppler examination, imaging techniques like CT scan, MRI or PET scanning, and biochemical markers, has increased the detection of many types of cancer [(3)].

Ultrasound-guided fine needle aspiration (FNA) is used to evaluate the thyroid nodule.

This technique of good sensitivity is simple, minimally invasive, rapid, and the complications are rare and minor (hematoma at the point of puncture, pain, vagal discomfort). It has improved the selection of patients who are candidates for surgery [(4)].

As far as the thyroid is concerned, ultrasound and cytology examinations have identified an increasing number of small, asymptomatic thyroid cancers. Finally, the incidental discovery of preclinical thyroid tumors at pathology examination may be more frequent because of the increased use of enlarged surgical excision (total or subtotal thyroidectomy) for non-malignant thyroid diseases [(3)].

The optimal surgical procedure for MNG patients remains a subject of debate, due to not only the increasing prevalence of incidental thyroid carcinoma (ITC) among these patients but also the incidence of TC in recurrent goiter. Total thyroidectomy is the clear procedure of choice for the treatment of most TCs; however, there is currently no surgical recommendation for MNG management that takes into account the prevalence of ITC [(5)].

Optimal oncologic treatment for thyroid cancer involves preoperative lymph node evaluation with ultrasound and compartment-oriented dissection of pathologically cancerous nodes. Hence, there are clear advantages to having a cancer diagnosis prior to proceeding with any surgery as a second operation obviously carries additional risks, costs, and stress for the patient [(6)].

The aim of this work was to determine the frequency of thyroid carcinoma in multinodular goiter in patients undergoing thyroidectomy to make a strategy to perform total thyroidectomy as a rule of treatment in any patient with multinodular goiter planned to be operated.

PATIENTS AND METHODS

This retrospective study included the medical charts and surgical data of a total of 50 patients who underwent surgery for goiter, attending at General Surgery Department, Aswan University Hospital between 2015 and 2018.

Ethical consideration:

This study followed all regulations of the Ethical Committee of Faculty of Medicine, Aswan University. Written informed consent of all the subjects

Received:23/08/2019
Accepted:23/09/2019

was obtained; included the required information about this study.

Inclusion criteria:

- Patients undergoing total thyroidectomy.
- Age between 18 and 75 years.
- Both genders.

Exclusion criteria:

- History of neck irradiation.
- Recurrent goiter.
- Family history of thyroid cancer.
- Evidence of malignancy.
- Suspicion of malignancy during the preoperative fine needle aspiration biopsy (FNAB).

All patients were subjected to preoperative and postoperative evaluation in the form of clinical, biochemical, radiological, operative and pathological studies.

Demographic characteristics of the patients, previous medical history, thyroid hormone profiles, thyroid ultrasonography (US) findings, FNAB findings, thyroid scintigraphy findings, surgical techniques, early postoperative complications, and histopathological diagnoses were recorded.

The included subjects were divided into two groups according to the final histopathological examination of the surgical specimens; **Group A (ITC group)** consisted of 5 patients with incidental thyroid carcinoma and **Group B (**MNG group**)** consisted of consisted of 45 patients with Multinodular goiter.

Statistical analysis

The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science **(SPSS 25).** Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

Descriptive statistics: Frequency and percentage of non-numerical data.

Analytical statistics: Fisher's exact test was used to examine the relationship between two qualitative variables when the expected count is less than 5 in more than 20% of cells.

P- value: level of significance:
-P>0.05: Non significant (NS).
-P< 0.05: Significant (S).
-P<0.01: Highly significant (HS).

RESULTS

This study included 50 patients subjected for thyroidectomy for benign thyroid disease.
All patients subjected to preoperative and postoperative evaluation in the form of clinical, biochemical, radiological, operative and pathological studies.

Table (1): Demographic data for whole study group.

		N	%
Group	Benign	45	90.0%
	Cancer	5	10.0%
Sex	Male	8	16.0%
	Female	42	84.0%
Age (years)	< 20	1	2.0%
	20 – 30	10	20.0%
	30 – 40	12	24.0%
	40 – 50	14	28.0%
	>50	13	26.0%
Residence	Rural	27	54.0%
	Urban	23	46.0%

The incidence was much more common in females (42 patients) than males (8) with ratio (6.25:1). The age ranges from 18 to 75 years with mean of age was 40.72 years. The highest age incidence was found to be in the fifth decade of life (14 patients) and much less below 20 years (1 patient). The incidence was more in rural areas (27 patients) than urban areas (23 patients).

Table (2): Symptoms & Signs for whole study group

		N	%
Symptoms & Signs	Swelling	12	24.0%
	Swelling, pressure symptoms	27	54.0%
	Swelling, toxic symptoms	6	12.0%
	Swelling. Pain refers to the ear	2	4.0%
	Swelling, retrosternal ext.	2	4.0%
	Swelling, retrosternal ext., pressure symptoms	1	2.0%

	N	%
Swelling	50	100.
Pressure symptoms	28	56.0
Toxic symptoms	6	12.0
Pain refers to the ear	2	4.0
Retrosternal extension	3	6.0

It was found that all patients presented with thyroid swelling, 28 patients with pressure symptoms, 6 patients with toxic symptoms, 3 patients with retrosternal extension and 2 patients with pain referred to the ear.

Table (3): Post-operative diagnosis for whole study group

Post-operative diagnosis	No change in preoperative diagnosis	45	90.0%
	Papillary thyroid cancer	3	6.0%
	Follicular thyroid cancer	1	2.0%
	Undifferentiated thyroid cancer	1	2.0%

The histopathological examination of the removed gland shows 5 cases had thyroid cancer, 3 cases had papillary thyroid cancer, 1 patient had follicular thyroid cancer and 1 patient had undifferentiated thyroid cancer.

Table (4): Complications for whole study group.

		N	%
Complications	No	39	78.0%
	Haemorrhage	1	2.0%
	Infection	4	8.0%
	Hypoparathyroidism	2	4.0%
	Recurrent laryngeal n. injury	1	2.0%
	External laryngeal nerve injury	2	4.0%
	Recurrence	1	2.0%

In this study, the most frequent complication is infection (4 cases) then hypoparathyroidism (2 cases) and externa laryngeal n. injury (2 cases), then recurrent laryngeal n. injury (1 case) and recurrence (1 case).

Table (5): Comparison between patients with benign thyroid disease and patients with thyroid cancer according to sex and age.

		Group				***Monte Carlo (Fisher's Exact) test of significance***	
		Benign **(**MNG**)** ***(n=45)***		***Cancer*** **(**ITC**)** ***(n=5)***			
		N	***%***	***N***	***%***	***P-Value***	***Sig.***
Sex	*Male*	*7*	*15.6%*	*1*	*20.0%*	*1.00*	*NS*
	Female	*38*	*84.4%*	*4*	*80.0%*		
Age	*<20 YRS*	*1*	*2.2%*	*0*	*0.0%*	*0.368*	*NS*
	20 – 30	*10*	*22.2%*	*0*	*0.0%*		
	30 – 40	*9*	*20.0%*	*3*	*60.0%*		
	40 – 50	*13*	*28.9%*	*1*	*20.0%*		
	>50	*12*	*26.7%*	*1*	*20.0%*		

In cancer group: male patients (20%) and female patients (80%), while in benign group male patients (15.6%) and female patients (84.4%) with P-value 1.00 which is non-significant. The highest age incidence in cancer group was found to be in the fourth decade (60%) while in benign group, the highest age incidence was in the fifth decade (28.9%).

Table (6): Comparison between patients with benign thyroid disease and patients with thyroid cancer according to Symptoms & Signs.

		Group				Monte Carlo (Fisher's Exact) test of significance	
		Benign (n=45)		Cancer (n=5)			
		N	%	N	%	P-Value	Sig.
Symptoms & Signs	Swelling	12	26.7%	0	0.0%	0.012	S
	Swelling, pressure symptoms	25	55.6%	2	40.0%		
	Swelling, toxic symptoms	6	13.3%	0	0.0%		
	Pain refers to the ear	1	2.2%	1	20.0%		
	Swelling, retrosternal ext.	1	2.2%	1	20.0%		
	Swelling, retrosternal ext., pressure symptoms	0	0.0%	1	20.0%		

It was found that all thyroid cancer cases presented with neck swelling without toxic symptoms, (2 cases) with pressure symptoms with one of them had retrosternal extension, (1 case) with pain referred to the ear.

Table (7): Sex and age distribution of thyroid cancer cases.

		Cancer group	
		N	%
Sex	Male	1	20.0%
	Female	4	80.0%
Age (years)	<20 YRS	0	0.0%
	20 – 30	0	0.0%
	30 – 40	3	60.0%
	40 – 50	1	20.0%
	>50	1	20.0%

The incidence was much more common in females (4 patients) than males (1 patient). The highest age incidence was found to be in the fourth decade (3 patients)

DISCUSSION

This study included 50 patients subjected to thyroidectomy for benign thyroid disease. All patients were subjected to preoperative and postoperative evaluation in the form of clinical, biochemical, radiological, operative and pathological studies.

In this study, the female (42) to male (8) ratio for the patients subjected to thyroid surgery was (6.25:1) and the age ranged from 18 to 75 years, with mean age of 40.72 years. The highest age incidence was found to be in the fifth decade of life (14 patients) and much less below 20 years (1 patient). These were similar to the results of **Askitis *et al.* [7].** They study 228 cases of thyroidectomy specimens, 182 females and 46 males with female: male ratio 4:1, and the age ranges from 11 to 80 years, with a median age of 50 years.

In this study the incidental carcinoma was found in 5 out of 50 patients (10%). Non-malignant thyroid diseases were 45 cases (90%). These results were similar to the results of **Miccoli *et al.* [8],** when they study 998 cases underwent thyroidectomy for benign thyroid disease and final histopathology revealed ITC in 104 patients (10.4%) and this group included 71 females and 33 males with a mean age of 48.5 years (range 21-79 years). Also **Costamagna *et al.* [9]** study 646 cases underwent thyroid surgery and Final histopathology revealed ITC in 53 patients (9.3%). This group included 46 women and 7 men with a mean age of 56.7 years (range 25-82 years).

Different results obtained by **Askitis *et al.* [7];** in their study, 228 cases underwent total thyroidectomy and final histopathological examination revealed ITC in 33 cases (14.5%). These little different result may be due to they select the cases only underwent total thyroidectomy.

In a study of 2306 patients by **Kaliszewski *et al.* [5],** among the 2306 MNG patients, ITC was detected in 49 (2.12%). In another study including 90 patients, **Bhuiyan *et al.* [10]**, ITC was detected in (11.1%) reaching that the incidence of an incidental carcinoma among patients undergoing thyroidectomy for MNG is higher than anticipated.

The present study showed that the frequency of Papillary carcinoma was 6% of all thyroid diseases (from 50 patients), 60% of incidental thyroid carcinoma as the frequency was high in the 4th decade of life.

The results of **Askitis *et al.* [7],** showed that papillary thyroid carcinoma had the highest incidence from 228 cases, 11.8% of thyroid diseases, 81.8% of incidental thyroid carcinoma (27/33), mean age at 33 years.

The results of **Miccoli *et al.* [8]** showed that papillary carcinoma was observed in 95.2% of all ITC (99/104).

The present study showed that the frequency of follicular carcinoma was 2% of all thyroid diseases (one case), 20% of ITC. Patient was in the 4th decade.

The results of **Askitis *et al.* [7]**, they state that follicular carcinoma was the second common thyroid malignancy and was observed in 4 patients from 228 (1.8% of thyroid diseases) and 12.1% of ITC (4/33).

Nanjappa *et al.* [11], also found the follicular carcinoma had the incidence of 2.6% of ITC. **Miccoli *et al.* [8],** found that follicular carcinoma was the second common thyroid malignancy and was observed in 4 patients from 104 patients had ITC (3.8%).

The present study showed that there was one case had undifferentiated thyroid cancer (2% of thyroid diseases, 20% of ITC) in the 6th decade of life, but no cases of anaplastic, medullary thyroid cancer or lymphoma.

The results of **Askitis *et al.* [7],** were 2 cases had undifferentiated thyroid cancer representing 6.1% of ITC.

Nanjappa *et al.* [11], study 187 cases underwent thyroidectomy for benign thyroid disease and found no cases of anaplastic, medullary thyroid cancer or lymphoma.

Finally, according to the finding of this study, we favor total thyroidectomy as the preferred method in benign thyroid disease for which surgery is indicated. The advantages of TT include reduction of recurrence rate, achieves a permanent cure of thyroid disorders.

The avoidance of rare possibilities of transformation from well differentiated to undifferentiated carcinoma and avoidance of second operation.

CONCLUSION

The data were collected, revised and summarized then results were tabulated with the final conclusion was:

A correct preoperative assessment, with a careful selection of nodules for fine-needle aspiration cytology on the basis of ultrasound pattern, could better address the choice of surgical procedure. The non-irrelevant incidence of incidental thyroid cancer , the eventuality of multifocality and bilaterality and the possible occurrence of relapse, support that total thyroidectomy without residuum is a valuable option for treating benign thyroid conditions such as multinodular goiter.

The results of this study confirm that the frequency of ITC in patients undergoing surgery for benign thyroid diseases is not negligible. Our data also indicate that the possibility of missing a malignant neoplasm exists in cases of large nodules in the context of multinodular goiter. This finding may provide support for the recommendation to perform multiple FNAC not only in dominant nodules, but also in all other nodules appearing suspicious at clinical examination or at US.

When an incidental cancer is diagnosed after hemi-thyroidectomy, a radicalization with central neck dissection could be considered.

RECOMMENDATIONS

To surgeons:

Identification of incidental thyroid carcinoma requires proper diagnostic tools, including ultrasonography, reliable FNAC technique and proper pathological examination. In experienced hand, pre-operative FNAC& FNAB diagnosis plays a crucial role in the diagnosis of thyroid nodules.

Frozen section evaluation at the time of surgery is highly recommended to aid in determining the extent of operation.

After the result of our study, we highly recommend total thyroidectomy rather than hemi or subtotal thyroidectomy in patient undergoing surgery for benign thyroid disease.

To researchers:

It is recommended to consider the developing molecular histochemical markers of thyroid carcinoma in further studies and evaluate their sensitivity & specificity aiming at clarifying suspicious (indeterminate) fine needle aspiration (FNAC & FNAB) results.

To hospitals:

Hospitals should play more attention to the archiving system which should be computerized.

REFERENCES

1. **Lin Y, Wu H, Yu M *et al.* (2016):** Patient outcomes following surgical management of multinodular goiter Does multinodularity increase the risk of thyroid malignancy? Medicine, 95(28):e4194.
2. **Rusinekm D, Chmielik E, Krajewska J *et al.* (2017):** Current advances in thyroid cancer management. Are we ready for the epidemic rise of diagnosis?. Int J Mol Sci.,18:1817-22.
3. **Pellegriti G, Frasca F, Regalbuto C *et al.* (2013):** Worldwide increasing incidence of thyroid cancer: update of epidemiology and risk factors. Journal of Cancer Epidemiology, 2013:965212.
4. **Dionigi G (2017):** Surgery for benign thyroid disease in 2018 Gland Surg., 7(2):239-241.
5. **Kaliszewski K, Strutyńska-Karpińska M, Zubkiewicz-Kucharska A *et al.* (2016):** Should the Prevalence of Incidental Thyroid Cancer Determine the Extent of Surgery in Multinodular Goiter?. PLoS ONE, 11(12): e0168654.
6. **Schneider DF, Cherney Stafford LM, Brys N *et al.* (2017):** Gauging the Extent of Thyroidectomy for Indeterminate Thyroid Nodules: An Oncologic Perspective, Endocr Pract., 23(4): 442–450.
7. **Askitis D, Efremidou EI, Karanikas M *et al.* (2013):** Incidental thyroid carcinoma diagnosed after total thyroidectomy for benign thyroid diseases incidence and association thyroid disease type and laboratory markers. https://www.ncbi.nlm.nih.gov › pmc
8. **Miccoli P, Minuto MN, Galleri D *et al.* (2006):** Incidental thyroid carcinoma in large series of consecutive patients operated on for benign thyroid disease. ANZ Journal of Surgery, 76:123-126.
9. **Costamagna D, Pagano L, Caputo M *et al.* (2013):** Incidental cancer in patients surgically treated for benign thyroid disease. Our experience at a single institution. Giomale di Chirurgia, 34(1-2):21-6.
10. **Bhuiyan MMZU, Machowski A (2015):** Nodular thyroid disease and thyroid malignancy: experience at Polokwane Mankweng Hospital Complex, Limpopo Province, South Africa. SAMJ: South African Medical Journal, 105(7):570–572.
11. **Nanjappa N, Kumar A, Swain SK *et al.* (2013):** Incidental thyroid carcinoma. Indian Journal of Otolaryngology and Head and Neck Surgery, 65(1):37-39.