

Incidence of Thyroid Cancer in Long Standing Multinodular Goiter: Prospective Study

Manee Mahmood Ali¹, Aqeel Shakir Mahmood¹, Warkaa M Al-Wattar^{2*}

¹Department of Surgery, Baghdad Medical College, University of Baghdad, Baghdad, Iraq

²Department of Oral Pathology, College of Dentistry, Mustansiriyah University, Baghdad, Iraq

ABSTRACT

Introduction: Multi-nodular goiter is a common presentation of many thyroid diseases. Thyroid nodules are present in 4%-7% of the people on neck palpation. Multi-nodular goiter was thought to be at a low risk for malignant changes, as compared to its single nodule, but many studies showed a significant risk.

Aim: To determine the incidence of thyroid cancer in longstanding multinodular goiter after histopathological examination of thyroid specimens following near total or total thyroidectomy.

Patients and Methods: This prospective, observational study was done in the surgical Department of Baghdad Teaching Hospital, by our team in the first surgical unit-second floor, over a period of twenty five months from December 2014 to January 2017. All the patients with multinodular goiter were evaluated and they were offered surgery by near total or total thyroidectomy. The specimens were sent for histopathological examination to assess the incidence and the types of various types of thyroid cancer in Multi-nodular goiter.

Results: Among the 147 Multi-nodular goiter cases which were studied, 19 (12.9%) cases had a thyroid malignancy. Papillary carcinoma constitutes 74% of the cases and it was the most common type of malignancy observed.

Conclusions: Multinodular goiter could be assign of different types of thyroid malignancy. The most common type was papillary carcinoma.

Key words: Multinodular, Goiter, Thyroductomy

HOW TO CITE THIS ARTICLE: Manee Mahmood Ali, Aqeel Shakir Mahmood, Warkaa M. Al-Wattar*, Incidence of thyroid cancer in long standing multinodular goiter: Prospective study, J Res Med Dent Sci, 2018, 6 (5):217-222

Corresponding author: Warkaa M. Al-Wattar

e-mail ✉: a_warkaa@yahoo.com

Received: 18/08/2018

Accepted: 20/09/2018

INTRODUCTION

Embryology

Thyroglossal duct develops from the median bud of the pharynx and its vestigial remnant is foramen cecum that presents at tongue base. This hollow structure migrates caudally and passes near and sometimes through, the developing hyoid cartilage. The parathyroid glands develop from the third and fourth pharyngeal pouches and thymus also develops from the third pouch and when it descends; it takes the associated parathyroid gland with it which explains why the inferior parathyroid nerve which arises from the third pharyngeal pouch normally lies inferior to the superior gland. The developing thyroid lobes fuse with the structures that arise in the fourth pharyngeal pouch, i.e. the superior parathyroid gland and the ultimobranchial body.

Parafollicular cells (C cells) which arise from the neural crest reach the thyroid via the ultimobranchial body [1].

Surgical anatomy

The normal thyroid gland weight is about 20 g–25 g and the functional unit is the lobule that is supplied by a single arteriole and composed of 24-40 follicles lined by cuboidal epithelium. The follicle contains colloid in which thyroglobulin is stored. The arterial supply is rich, and extensive anastomoses occur between the main thyroid arteries and branches of the tracheal and esophageal arteries.

There is an extensive lymphatic network within the thyroid gland but some lymph channels pass directly to the deep cervical nodes, the subcapsular plexus drains mainly to the central compartment and paratracheal nodes and nodes on the superior and inferior thyroid veins (level 4 VI), and from there to the deep cervical (levels II, III, IV and V) and mediastinal groups of nodes (level VII) [1].

Goiter

The normal thyroid gland is not palpable but generalized enlargement of the thyroid gland is known as goiter (from the Latin guttur=the throat). Thyroid nodules are found in 4%-7% of the people on neck palpation. An

isolated swelling in one lobe with no palpable abnormality elsewhere is termed a solitary nodule while swellings with evidence of abnormality elsewhere in the gland are termed dominant nodule. An increased incidence of thyroid cancer (usually follicular type) has been reported from endemic areas so dominant or rapidly growing nodules in long-standing goiters should always be subjected to aspiration cytology [1].

Thyroid cancer

The infinite majority of primary malignancies are carcinoma derived from the follicular cells, which are classified by Dunhill histologically as differentiated and undifferentiated and the differentiated carcinomas are subdivided into follicular and papillary. Lymphoma and medullary cancers make up the remainder of primary malignancies. Metastases to the thyroid, most commonly from kidney and breast, are rare. Direct invasion by upper aerodigestive squamous cancer is a rare but lethal event. Lymph node and blood-borne metastases to bone and lung occur and may be the mode of presentation [2].

Types of thyroid carcinoma

A. Benign: Include Follicular adenoma

B. Malignant: Include

1. Primary: Which are subdivided into:

- i. Follicular epithelium-differentiated and Follicular Papillary
- ii. Follicular epithelium-undifferentiated and Anaplastic
- iii. Parafollicular cells, Lymphoid cells and Medullary Lymphoma

2. Secondary: includes Metastatic and Local infiltration [3]

The incidence of thyroid carcinoma is high in endemic goitrous areas, possibly due to TSH (Thyroid Stimulation Hormone) stimulation. Malignant lymphomas sometime develop in autoimmune thyroiditis due to lymphocytic infiltration in the autoimmune process [1].

Anaplastic thyroid carcinoma is a highly aggressive, which is undifferentiated carcinoma that may arise on top of normal or abnormal thyroid. Making the diagnosis by Fine Needle Aspiration (FNA) of the thyroid with a long-standing history of multinodular goiter is not uncommon [4].

Thyroid cancer is a relatively rare (less than 1% of all human tumors), but represents the most frequent form of cancer of the endocrine glands (90% of all endocrine cancers) [5]. The American Cancer Society estimates that 17000 new cases of thyroid cancer are diagnosed annually in the United States, thyroid cancer represents 3.8% of all new cancer cases in the United States and that 1300 thyroid cancer-related deaths occur annually [6,7]. It may present either as a solitary nodule or as a

dominant nodule in a Multinodular Goiter. Multinodular goiter was thought to be at a low risk for malignancy as compared to a solitary thyroid nodule [8-10]. However, various studies have reported a 7%-17% incidence of thyroid cancer in multinodular goiter [1,2,9]. The incidence of the thyroid cancer ranges from 0.9%-13% in different parts of world [11]. Such an incidence increases further if cases of occult carcinoma also take into consideration. The exposure to ionizing radiation and the availability of more sensitive diagnostic techniques may be the possible explanations for a worldwide increase in the incidence of thyroid carcinoma [8,12]. Thyroid carcinoma occurs at all ages [13]. Most of the cases diagnosed between the 5th and 6th decade of life [14]. It is found frequently in females more than males, male to female ratio is 1:2.7, but the ratio of cancer associated mortality is 1:2 indicating that the thyroid cancer is slightly more aggressive in men [6].

Geographical studies show marked differences in incidence of thyroid cancer ranging, For example, from 6% of population in Hawaii and Iceland to less than 1.5 in Denmark and England [15]. A recent report from Iraq showed that thyroid cancer in 2000-2005 was 5 folds of that 1990-2000 [16].

Surgical treatment

Patients with large, locally aggressive or metastatic differentiated thyroid cancer need total thyroidectomy, with excision of adjacent involved structures if necessary, and suitable nodal surgery is followed by radioiodine ablation with long-term TSH suppression. Now a day, treatment guidelines prefer routine near total or total thyroidectomy for patients with multinodular goiter, which is necessitating an early reoperation and second lobectomy following a diagnostic first lobectomy with routine central compartment node dissection for all tumors greater than 1 cm. Total thyroidectomy facilitates the use of radioiodine for postoperative scanning to detect and subsequently ablate metastases results in lower thyroglobulin levels. An undetectable serum thyroglobulin is increasingly used as a marker for a cure. While this policy may reduce the rate of reoperation for recurrent disease, it is unlikely to improve an existing 99% survival in low risk patients and exposes patients to increased risk of recurrent laryngeal nerve injury, hypoparathyroidism and later development of second cancers. Local recurrence, in either the thyroid bed or contralateral lobe, should be exceptionally rare after total lobectomy, particularly in low risk cases. Total thyroidectomy is recommended for tumors greater than 2 cm and those with nodal involvement or metastases and lobectomy for the remainder [17].

PATIENTS AND METHODS

This prospective, observational study was done in the Surgical Department of Baghdad Teaching Hospital by

our team in the first surgical unit–second floor, over a period of twenty five months from December 2014 to January 2017.

All the patients with goiter were examined clinically and sonologically. The patients with multinodular goiter who subsequently operated with near total or total thyroidectomy were selected for the study. Those with lobectomy or subtotal thyroidectomy were excluded from our study. After detailed history taking, none of those patients had a history of radiation exposure to the neck or a family history of a thyroid cancer. The distribution in regards of age and gender was based on patient’s records and histopathology reports. During the pre-operative assessment, all the selected patients underwent clinical examination, biochemical investigations, including the thyroid function test and serum calcium levels, thyroid ultrasonography and vocal cords examination. CT scan of the neck was done to those with retrosternal Goiter. FNA was performed only in those with a suspicious thyroid nodule, which was detected during the clinical examination and on neck ultrasonography.

The data collections were done according to the agreement of the teaching board in the Iraqi Board of Medical specialty. All the selected cases of multinodular goiter, and total thyroidectomy were performed following the identification and preservation of the recurrent laryngeal nerves and the parathyroid glands. After surgery, all the thyroid specimens were sent for a Histopathological examination in our hospital or private laboratories. Microsoft Excel 2010 and IBM SPSS (software platform offers statistical package for social sciences) version 15 was used in statistical data analysis.

RESULTS

In our prospective study, we had 147 cases of multinodular goiter. Of these 133 (90.5%) were females and 14 (9.5%) were males, with an obvious female predominance. Female to male ratio of patients with goiter is (9.5:1). The age of the majority of the patients with multinodular goiter was 3rd and 4th decades of life (Figure 1 and Table 1). The most common presenting complaint was anterior neck swelling for more than a year.

The patients underwent surgery as a treatment based on the suspicious findings during the diagnostic work-up

and the compressive symptoms due to long standing goiter. Most of the cases had near total thyroidectomy and the specimens were sent to a histopathological evaluation. The histopathology of the specimens revealed that 19 patients had a malignant focus and so the incidence of cancer in patients with long-standing multinodular goiter was 12.9% in our study (Figure 2).

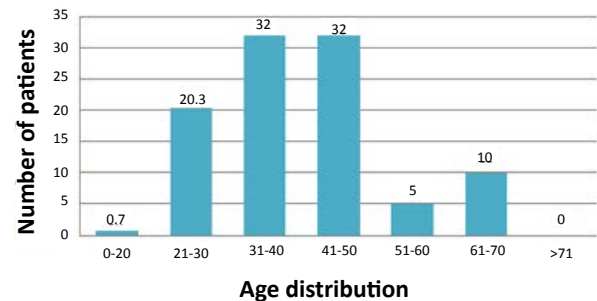


Figure 1: Age Distribution of patients with multinodular goiter

Table 1: Distribution of cases with multinodular goiter among age groups for both females and males

Gender	Number and percentage	Age groups							
		0-20	21-30	31-40	41-50	51-60	61-70	>71	
Female	No	133	-	28	41	46	5	13	-
	%	90.4	-	22	32	36	0.3	9.7	-
Male	No	14	1	6	6	1	2	2	-
	%	9.6	-	4.4	4.4	0.8	1.6	1.6	-
Total	No	147	1	47	47	47	7	1	-
	%	100	0.7	32	32	32	5	10	-

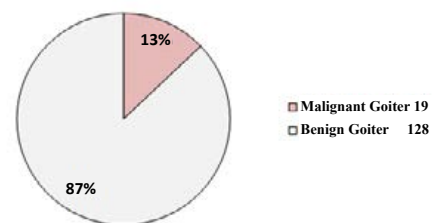


Figure 2: Incidence of CA thyroid in patients with multinodular goiter

128 cases with multinodular goiter were benign. 118 are females and 10 are males (Table 2). Of the 19 patients with multinodular goiter and thyroid cancer, 15 (79%) were females and 4 (21%) were males. Female to male ratio of patients with cancer is (3.7:1) (Figure 3). The most common age group for the presentation of thyroid

Table 2: Distribution of cases with multinodular goiter without thyroid cancer among age groups for both females and males

Gender	Number and percentage	Age groups							
		0-20	21-30	31-40	41-50	51-60	61-70	>71	
Female	No	118	-	24	40	40	2	12	-
	%	92	-	20.5	34	34	1.5	10	-
Male	No	10	1	1	5	1	1	1	-
	%	18	10	10	50	10	10	10	-
Total	No	128	1	25	45	41	3	13	-
	%	100	0.7	20	35	32	2.3	10	-

cancer was 41-50 (31%) years in our study (Figure 4 and Table 3).

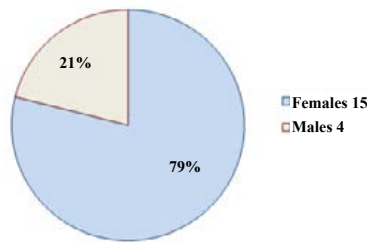


Figure 3: Sex distribution of patients with CA thyroid

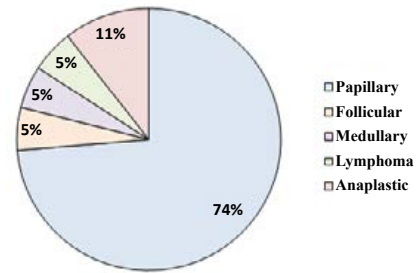


Figure 5: Distribution of different types of CA thyroid

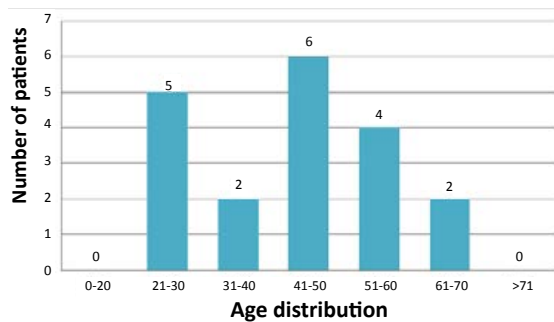


Figure 4: Age distribution of patients with CA thyroid

Among the malignancies, papillary carcinoma (74%) was the commonest type which was observed in 14 out of 19 patients with thyroid cancer in our study. Anaplastic carcinoma was found in 2 patients (11%), follicular, medullary carcinoma and lymphoma were found in one patient (5%) for each (Figure 5 and Table 4).

DISCUSSION

In multinodular goiter, surgery is offered for cosmeses, the pressure symptoms, and thyrotoxicosis and for the suspicion of malignancy [10]. Multinodular goiter was thought to have a low risk for the development of thyroid cancer compared to a solitary thyroid nodule [8-10]. In our study the incidence of thyroid cancer in patients with multinodular goiter was highly consistent with studies conducted in Iraq by Al Hashimi et al. and Benzarti et al. [16,17]. ul Haq et al. reported an 8% incidence of malignancy in multinodular goiter in his study [11]. Prades et al. from France, however, reported quite a high incidence; 12.2% [18-20]. The annual incidence of thyroid cancer differs considerably in different regions of the world and is increasing in some European countries, USA and Canada [21]. Several possible causes for the increase in the incidence of thyroid cancer; including exposure to ionizing radiation, sex hormones and iodine deficiency [22,23]. Thyroid carcinoma represents 1% of

Table 3: Distribution of cases with multinodular goiter with thyroid cancer among age groups for both females and males

Gender	Number and percentage	Age groups							
		0-20	21-30	31-40	41-50	51-60	61-70	>71	
Female	No	15	-	4	1	6	3	1	-
	%	79	-	26	7	40	20	7	-
Male	No	4	-	1	1	-	1	1	-
	%	13	-	25	25	-	25	25	-
Total	No	19	-	5	2	6	4	2	-
	%	100	-	26	10.5	32	21	10.5	-

Table 4: Distribution of cases with thyroid cancer among age groups for both females and males

Type of thyroid cancer	Gender	No	Age groups						
			0-20	21-30	31-40	41-50	51-60	61-70	>71
Papillary	Female	13	-	4	1	5	3	-	-
	male	1	-	-	-	-	1	-	-
Follicular	Female	-	-	-	-	-	-	-	-
	male	1	-	-	1	-	-	-	-
Medullary	Female	-	-	-	-	-	-	-	-
	male	1	-	1	-	-	-	-	-
Lymphoma	Female	1	-	-	-	-	-	1	-
	male	-	-	-	-	-	-	-	-
Anaplastic	Female	1	-	-	-	1	-	-	-
	male	1	-	-	-	-	-	1	-
Total		19	-	5	2	6	4	2	-
%		100	-	26	10.5	32	21	10.5	-

all the malignancies and it is the commonest endocrine tumors [11]. The incidence of thyroid cancer has increased by up to five-fold during the last 60 years [8,24]. A recent report from Iraq showed that thyroid cancer in 2000-2005 was 5 folds of that reported between 1990-2000. The rise in the number of malignant thyroid tumors, especially papillary carcinoma may also be due to stress, or changing type of diet, or to exposure of Iraqi people to depleted Uranium or other pollutants. This again needs further studies to prove [16]. Females with multinodular goiter have more risk of thyroid cancer in our study possibly due to Iodine deficiency, hormonal factors, lactation suppressant drugs and fertility medications [11]. The majority of the thyroid cancers are well-differentiated cancers of follicular cell origin. These include papillary, follicular and Hurthle cell carcinomas. While papillary thyroid carcinoma is the commonest histologic form in most parts of the world [25], this was consistent with the observations made by Benzarti *et al* [17]. A thyroid nodule should raise the suspicion of malignancy. If it was a dominant nodule in the multinodular goiter, hard, irregular, fixed, rapidly growing, associated with cervical lymphadenopathy and recurrent laryngeal nerve palsy. In our study; there was high male incidence for malignancy with long standing multinodular goiter. This availability of better and more sensitive diagnostic techniques is thought to be responsible for the increasing incidence of thyroid cancer [8,12]. Total removal of the thyroid gland eliminates the possibility of the transformation of a differentiated cancer to an undifferentiated type [26] and associated with more effective use of postoperative diagnostic and therapeutic radioactive iodine [27]. Recently, there is an obvious change in the surgical attitude towards more extensive surgery mostly due to the increase in the incidence of thyroid carcinoma in patient with multinodular goiter [16].

CONCLUSIONS

The risk of thyroid cancer in a long standing multinodular goiter is not as low as it was thought previously. The risk of occult malignancy and the possibility of transformation of a differentiated cancer to an undifferentiated type is quite significant.

ACKNOWLEDGEMENT

The authors would like to thank Baghdad University and Mustansiriyah University, Iraq for their support to accomplish this work.

CONFLICT OF INTEREST

There is no conflict of interest.

REFERENCES

1. Baily H, Love M. Short Practice of Surgery. City

Lewis 1977.

2. Dunhill TP. Carcinoma of the thyroid gland. *BJs* 1931; 19:83-113.
3. Cole WH, Majarakis JD, Slaughter DP. Incidence of carcinoma of the thyroid in nodular goiter. *J Clin Endocrinol* 1949; 9:1007-11.
4. Maatouk J, Barklow TA, Zakaria W, *et al*. Anaplastic thyroid carcinoma arising in long-standing multinodular goiter following radioactive iodine therapy. *Acta Cytol* 2009; 53:581-3.
5. Landis SH, Murray T, Bolden S, *et al*. Cancer statistics, 1998. *CA: Cancer J Clin* 1998; 48:6-29.
6. Wu XC, Chen VW, Steele B, *et al*. Cancer incidence in adolescents and young adults in the United States, 1992-1997. *J Adolesc Health* 2003; 32:405-15.
7. Jemal A, Siegel R, Ward E, *et al*. Cancer statistics, 2007. *CA: Cancer J Clin* 2007; 57:43-66.
8. Memon W, Khanzada TW, Samad A, *et al*. Incidence of thyroid carcinoma in multinodular goiters. *Rawal Med J* 2010; 35:65-7.
9. Gandolfi PP, Frisina A, Raffa M. The incidence of thyroid carcinoma in multinodular goiter: Retrospective analysis. *Acta Biomed* 2004; 75:114-7.
10. Pedomallu R, Pedomallu SB, Rama Rao K, *et al*. Incidence of occult carcinoma in multinodular goitre which was diagnosed on the basis of the histopathological findings. *Internet J Surg* 2008; 17.
11. ul Haq RN, Khan BA, Chaudhry IA. Prevalence of malignancy in goiter-A review of 718 thyroidectomies. *J Ayub Med Coll Abbottabad* 2009; 21:134-6.
12. Cerci C, Cerci SS, Eroglu E, *et al*. Thyroid cancer in toxic and non-toxic multinodular goiter. *J Postgrad Med* 2007; 53:157.
13. Adams CW, Symmers WS. Systemic pathology. Churchill Livingstone 1978.
14. Greene FL. American Cancer Society. *AJCC Cancer Staging Manual* 2002; 6.
15. Scott GC, Meier DA, Dickinson CZ. Cervical lymph node metastasis of thyroid papillary carcinoma imaged with fluorine-18-FDG, technetium-99m-pertechnetate and iodine-131-sodium iodide. *J Nucl Med* 1995; 36:1843-5.
16. Al-Hashimi HM. Thyroid nodules in Iraq. *Postgrad Med J* 1972; 48:80-2.
17. Benzarti S, Miled I, Bassoumi T, *et al*. Thyroid surgery (356 cases): Risks and complications. *Rev Laryngol Otol Rhinol (Bord)* 2002; 123:33-7.

18. Alagić-Smailbegović J, Kapidzić A, Sutalo K, et al. Surgical treatment of thyroid gland diseases. *Med Arh* 2005; 59:241-3.
19. Prades JM, Dumollard JM, Timoshenko A, et al. Multinodular goiter: Surgical management and histopathological findings. *Eur Arch Otorhinolaryngol* 2002; 259.
20. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. *JAMA* 2006; 295:2164-7.
21. Sakoda LC, Horn-Ross PL. Reproductive and menstrual history and papillary thyroid cancer risk: The San Francisco bay area thyroid cancer study. *Cancer Epidemiol Biomarkers Prev* 2002; 11:51-7.
22. Dal Maso L, La Vecchia C, Franceschi S, et al. A pooled analysis of thyroid cancer studies. V. Anthropometric factors. *CCC* 2000; 11:137-44.
23. Whelan SL. Patterns of cancer in five continents. WHO, International Agency for Research on Cancer and International Association of Cancer Registries 1990.
24. Townsend CM, Beauchamp RD, Evers BM, et al. *Sabiston Textbook of Surgery E-Book*. Elsevier Health Sci 2016.
25. Hussain N, Anwar M, Nadia N, et al. Pattern of surgically treated thyroid diseases in Karachi. *Biomedica* 2005; 21:18-20.
26. Sarda AK, Bal S, Kapur MM. Near-total thyroidectomy for carcinoma of the thyroid. *Br J Surg* 1989; 76:90-2.
27. Mazzaferri EL, Young RL. Papillary thyroid carcinoma: A 10 year follow-up report of the impact of therapy in 576 patients. *Am J Med* 1981; 70:511-8.