

## Incidental thyroid carcinoma

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### *Abstract:*

**Background:** thyroid carcinoma is the most common endocrine carcinoma as it accounts for almost 90% of all endocrine malignancies. The term incidental denoted malignant tumors of the thyroid gland detected by post-operative biopsy results of the resected specimens resected from benign thyroid diseases. Among the incidental thyroid malignancies, papillary carcinoma is the commonest pathological type.

**Objectives :** To determine the incidence of incidental thyroid carcinoma and to insist on accurate preoperative diagnostic work up of patients with thyroid diseases.

**Patients & Methods:** A prospective study, which was conducted during the period from March 2013 to April 2014 at Baghdad teaching hospital first surgical unit by the same team of surgeons. Ninety nine patients were referred for surgical treatment of goiters, 4 patients who had a known malignant diagnosis by FNAC were excluded from the study, the remaining 95 patients were evaluated for the presence of the cancer by post-operative pathological exam. The surgical operations performed were total lobectomy with isthmusectomy, subtotal, near total or total thyroidectomy.

**Results:** incidental thyroid carcinoma was found in 18 patients (18.9%), 15 patients with non-toxic MNG (15.7%), 2 patients with solitary thyroid nodule (2.1%) and one patient (1.1%) with toxic MNG. Out of 18 patients with incidental thyroid carcinoma, 15(83.3%) aged >45 and the remaining 3 (16.7%) aged <45, only one male had ITC and the remaining patients were females.

**Conclusions:** It can be concluded that the incidence of incidental thyroid carcinoma in our study is relatively high so a more radical surgical treatment in the management of patients with presumably benign thyroid disease is recommended.

**Keywords:** incidental thyroid carcinoma, micro-papillary carcinoma, total thyroidectomy.

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### **Introduction:**

Thyroid carcinoma is the most common endocrine carcinoma as it accounts for almost 90% of all endocrine malignancies. During the last 30 years, the rate of thyroid carcinoma incidence has increased worldwide, with average increases of 48.0% in men and 66.7% in women. (1,2).

The term “incidental” denoted malignant tumors of the thyroid gland detected by post-operative biopsy of surgical specimens resected for benign disease. The incidence of incidental thyroid carcinoma ranges from 3–16 % in different series.(3,15,16) Among the incidental thyroid malignancies, papillary carcinoma is the commonest pathological type. Micropapillary variant is the most common subtype among papillary carcinoma as described by many studies (3,15,16).

Although it is traditionally considered that the incidence of incidental thyroid carcinoma is higher in solitary nodular goiter (SNG) compared to multi-nodular goiter (MNG), it is not significantly different (4,15).

Incidental thyroid carcinoma is found more often in euthyroid patients, although a hyper functioning thyroid cannot be considered a protective factor against differentiated thyroid carcinoma. (3,4).

Papillary thyroid microcarcinoma (PTMC) is defined as a tumor that measures less than or equal to one centimeter in diameter(5,6). It is often undetected in the clinical examination and found incidentally after thyroidectomy performed for other reasons. Taking into account the presentation, PTMC can be divided into “incidentally detected” and “occult.” The term incidental refers to a tumor found during a thyroid surgical intervention for benign disease or during an autopsy. (7)

PTMC was defined as “occult” when it was undetected at clinical examination and indirectly diagnosed because of the presence of enlarged metastatic cervical lymph nodes or distant metastasis (7).

The indication of total thyroidectomy for treatment of well-differentiated thyroid carcinoma is not unanimous, and when total thyroidectomy is performed for benign thyroid diseases, it is even more controversial. Many authors support the indication of total thyroidectomy for non-malignant thyroid diseases. The rationale for this approach is the diffuse involvement of the thyroid observed in multinodular goiter, chronic thyroiditis and Graves’s disease(9).

The incidence of thyroid cancer varies from 7.5 to 13 % in multinodular goiter.( 10,11,12) The presence of multiple nodules decreases the diagnostic value of fine needle aspiration

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biopsy, and incidental thyroid cancer is frequent histological finding in multinodular goiter.(10,11,12) The incidence of regrowth of thyroid tissue after partial or less than total or near thyroidectomy for multinodular goiter is between 12 and 20 percent, and is dependant on the initial volume of diseased tissue as well as the extend of resection. In general, about half of patients who develop recurrence of benign goiter require surgical resection. (9,11,12)

FNAC was found to have missed malignancy in an average of 7.2% of cases (range 1-13%) when the final histological results were obtained after thyroidectomy. (13,14).

#### Patients and methods:

This prospective study was conducted during the period from March 2013 to April 2014 at Baghdad teaching hospital, first surgical unit (second floor) by the same team of surgeons. Ninety nine patients were referred for surgical treatment of thyroid disease. Four patients who had a known malignant diagnosis by FNAC were excluded from the study. The remaining 95 patients were evaluated for the presence of thyroid cancer by postoperative histopathological results. All patients underwent preoperative thyroid ultra sound, thyroid function test, FNAC, CXR and laryngoscopy to evaluate the motility of the vocal cords. A solitary or multinodular toxic goiter were diagnosed in patients presenting with nodular thyroid and suppressed TSH with or without overt elevation of T3 and/or T4. A thyroid was considered non-toxic and multinodular when it had 2 or more nodules and the patient had normal TSH level.

Surgical operations performed were total lobectomy with isthmusectomy, sub-total thyroidectomy, near-total or total thyroidectomy. In all cases the surgical procedure was carried out through a median collar incision, while respecting the integrity of the anterior neck muscle; a sternotomy was needed in only one patient with large retrosternal extension.

The identification of the recurrent laryngeal nerves and the parathyroid gland was systematically carried out.

The resected biopsies were sent for histopathological exam at learning laboratories in medical city complex and in Al-

Sharjah private laboratory. Any patient who diagnosed with incidental carcinoma by post operative histopathological exam and operated with less than total or near total thyroidectomy, they underwent a completion total thyroidectomy.

The study protocol was approved by the local committee of the scientific council of surgery. Written consent were obtained from all patients prior to participate in the study and prior to perform the operation.

**Statistical analysis:** Was performed by using the statistical package for social sciences (SPSS) software for windows version 20. Data of all patients were entered and analyzed with appropriate statistical tests. Age of the patients was presented as mean  $\pm$  standard deviation (SD) and range in years in addition, age was categorized into two groups (< 45 and  $\geq$ 45) years according to the latest TNM classification. Other variables were presented as frequencies (Number of patients) and percentages (%). Cross-tabulation of age group, sex, diagnosis and thyroid profile against the final diagnosis (ITC or benign) was performed, Chi square test was used to assess the significance (P.value) of the differences between these variables. Level of significance (P.value) of  $\leq$  0.05 was considered significant and  $>$  0.05 was not. Finally all findings and results were presented in tables with an explanatory paragraph for each.

#### Results:

Out of ninety five patients who underwent surgical treatment of thyroid disease; 79(83.2%) were female and 16 (16.8%) were male with a mean age of 40.5years (range 16-65 years). Preoperative diagnosis of these patients was: nontoxic MNG (n=65; 68.4%), solitary thyroid nodule (n=18; 18.9 %), toxic multinodular goiter (n=8; 8.5%), toxic nodule (n=2; 2.1%) and diffuse goiter (n=2; 2.1%), (Table 1).

The surgical procedures performed included: 47 near total thyroidectomy (49.5%), 34 total thyroidectomy (35.8%) and 11 total lobectomy and isthmusectomy (11.6%), 3 subtotal thyroidectomy (3.1%) . (Table 1).

**Table 1: preoperative diagnosis and surgical treatment**

Preoperative diagnosis	Total thyroidectomy No. (%)	Near total thyroidectomy No. (%)	Total Lobectomy No. (%)	subtotal No. (%)	Total No. (%)
Non toxic Multinodular goiter	29 (30.6%)	33 (34.7%)	0 (0.0)	3 (3.1%)	65 (68.4%)
Solitary thyroid nodule	2 (2.1%)	5 (5.2%)	11 (11.6%)	0 (0.0)	18 (18.9%)
Toxic multinodular goiter	3 (3.2%)	5 (5.2%)	0 (0.0)	0 (0.0)	8 (8.4%)
Toxic nodule	0 (0.0)	2 (2.1%)	0 (0.0)	0 (0.0)	2 (2.1%)
Diffuse goiter	0 (0.0)	2 (4.3%)	0 (0.0)	0 (0.0)	2 (2.1%)
<b>Total</b>	<b>34 (35.8%)</b>	<b>47 (49.5%)</b>	<b>11 (11.6%)</b>	<b>3 (3.1%)</b>	<b>95 (100%)</b>

The post operative pathological examination of the surgical specimens showed the presence of incidental thyroid carcinoma in 18 cases (18.9%) of total number of patients, 17 of them were female (94.4%) and one was male (5.6%) with a mean age of 35 years (range from 22-48 years).

The incidentally detected carcinomas were of micropapillary histotype in 10 cases (55.6%), papillary histotype in 4 cases (22.2%), papillary carcinoma with follicular variant in 3 cases (16.7%), in the remaining case (5.5%) the histotype was follicular carcinoma.

The distribution of incidentally detected thyroid carcinomas according to the pre-operative diagnosis and thyroid profile is summarized in (Table 2):

Fifteen patients with nontoxic MNG (15.7%), 2 patients with solitary thyroid nodule (2.1%) and one patient with toxic MNG (1.1%) and there is no significant correlation had been found between the diagnosis and the type of the lesion P. value 0.38.

**Table 2. Incidental thyroid carcinoma incidence and correlation related to preoperative diagnosis.**

Preoperative diagnosis	Number of cases (%)	ITC No. (%)	% ITC of the whole series
MNG	65 (68.4%)	15 (83.3%)	(15.7%)
Solitary thyroid nodule	18 (18.9%)	2 (11.1%)	(2.1%)
Toxic MNG	8 (8.5%)	1 (5.6%)	(1.1 %)
Toxic nodule	2 (2.1%)	0 (0.0)	0
Diffuse goiter	2 (2.1%)	0 (0.0)	0
<b>Total number</b>	<b>95 (100%)</b>	<b>18 (100%)</b>	<b>18.9%</b>
<b>P value =0.38</b>			

Total and near total thyroidectomy was the most commonly performed surgical procedure. Out of 18 patients 15 patients underwent total and near total thyroidectomy at the time of initial surgery. Two cases, initially treated by total lobectomy and isthmectomy, the other one treated by subtotal thyroidectomy, in these three patients who underwent less than total or near total thyroidectomy, a completion total thyroidectomy was performed.

The pathological specimen in two cases showed a papillary histotype and no sign of disease in the other one.

As it is shown in table 3, out of the 18 patients with ITC, 15 (83.3%) aged < 45 years and the remaining 3 (16.7%) aged ≥ 45 years, on the other hand only one male had ITC and the remaining 17 were females, however there was no statistically significant differences in age and gender in between those with ITC and benign lesions, in both comparison, P>0.05.

**Table 3. Correlation of type of ITC with age and gender.**

Variable	Group		Total (No.=95)	P.value*
	Benign (No.=77)	ITC (No.= 18)		
<b>Age group</b>				
< 45	64 (83.1)	15 (83.3)	79 (83.2)	0.72 NS
≥45	13 (16.9)	3 (16.7)	16 (16.8)	
<b>Gender</b>				
Male	15 (19.5)	1 (5.6)	16 (16.8)	0.31 NS
Female	62 (80.5)	17 (94.4)	79 (83.2)	

NS; not significant

Out of 18 patients with incidental thyroid carcinoma; 17 patients in euthyroid state (94.4%) and only one patient with toxic state (5.6%). Among those with benign lesions toxic goiter reported in 9 (11.7%) and euthyroid in 68 (88.3%), however, the difference was statistically not significant, P=0.73

**Table 5. Correlation between Thyroid function and ITC.**

Thyroid function	ITC n (%)	Benign n (%)	Total
Toxic	1 (5.6)	9 (11.7)	10 (10.5)
Euthyroid	17 (94.4)	68 (88.3)	85 (89.5)
<b>Total</b>	<b>18 (100.0)</b>	<b>77 (100.0)</b>	<b>95 (100.0)</b>
<b>P.value = 0.73 NS</b>			

The postoperative complications (recurrent laryngeal nerve palsy and hypocalcaemia) were reported in 14 patients (14.7%) included:

Temporary change in voice in 6 patients (6.3%)

Permanent unilateral recurrent nerve palsy in one patient (1.05%)

Transient symptomatic hypocalcemia in 6 patients (6.3%)

Permanent hypocalcemia in one patient (1.05%)

Permanent bilateral recurrent nerve palsy didn't occur in any patient.

According to the operation performed, the postoperative complications can be subdivided as follows total thyroidectomy was complicated by: 2 patients of temporary change in voice and one with permanent recurrent laryngeal nerve palsy together with 3 patients of symptomatic transient hypocalcemia and one patient of definitive one, while near-total thyroidectomy was complicated by: 3 patients of temporary change in voice and 3 patients of symptomatic transient hypocalcemia, one case of temporary change in voice was reported in patient who underwent subtotal thyroidectomy.

Table 6. Postoperative complications according to surgical treatment.

Surgical treatment	Temporary change in voice	Permanent unilateral nerve palsy	Transient hypocalcemia	Permanent hypocalcemia
Total thyroidectomy	2 (2.1%)	1 (1.05%)	3 (3.15%)	1 (1.05%)
Near total thyroidectomy	3 (3.15%)	0 (0.0)	3 (3.15%)	0 (0.0)
Subtotal thyroidectomy	1 (1.05%)	0 (0.0)	0 (0.0)	0 (0.0)
Total	6 (6.3%)	1 (1.05%)	6 (6.3%)	1 (1.05%)

### Discussion

Papillary carcinoma which accounts for some 85% of malignant thyroid carcinoma is the most common histotype of thyroid cancer. Its prognosis is good with a mortality rate below 5% at 10 years after diagnosis. (5,15) Papillary thyroid microcarcinoma is a particular variant of papillary carcinoma and it is characterized by a small diameter, low level of aggression and a very low frequency of distant metastases, this type of tumor often remains clinically unknown and in fact the papillary thyroid microcarcinoma is also the most common malignant thyroid tumors detected incidentally.(15)

The incidence of malignancy in patients undergoing surgery for benign thyroid disease is quite relevant, ranges from 3-16% in different series. (3,15,16), Miccoli et al found in their study 10.4% of incidental thyroid carcinoma (16), Smith et al found in their study 15.6% of incidental thyroid carcinoma (17), another study by Bradley et al showed an incidence of 12%(18). In our study incidental thyroid carcinoma was diagnosed in 18.9% of patients. FNAC was not ultrasound guided and only the dominant nodule was aspirated, also the vast majority of patients in this study had multinodular goiter, which decreases the diagnostic value of FNAC (10,12,15), perhaps these were the reasons for the high incidence. Hence the need to select the nodules for FNAC on the basis of their vascular patterns, sonographic features, and not just their size.(3,15,16) The availability of ultrasound guided FNAC, the limitation of cytology and the cytologist's expertise are factors that probably explain the worldwide difference in the incidence. (13,18) Our data suggest that age and sex cannot be considered as indicators of risk of thyroid carcinoma P value>0.05, similar observations have been reported in other studies (3,15,16).

In our study, the incidence of carcinoma in MNG was not significantly different from carcinoma in solitary thyroid nodule. So multinodularity cannot be considered as certain indicator of benign thyroid disease. (3,18)

The analysis of the size of the tumor showed that the majority of incidental thyroid carcinoma (55.6%) were microcarcinoma (tumor size less than 1 cm), and (22.2%) of ITC exceed one cm in diameter. The relatively high incidence of this papillary thyroid carcinoma more than one cm could be justified by the fact that needle aspiration cytology is not always adequate in detecting cancers. Thus, it would be more appropriate to take

multiple samples of tissue from larger nodules by performing a greater number of needle aspirations.(15,16)

In our study, there was no significant difference in the incidence of cancer between toxic and non toxic goiter (p value=0.73), and this result is matched with other studies,(16,19,20) therefore, hyperthyroidism cannot be considered a protective factor against thyroid carcinoma.(16,20) The finding of this study favors a more radical aggressive therapeutic management in patient with presumably benign thyroid disease, though this remains a controversial issue. We consider total or near-total thyroidectomy as the procedure of choice for the management of nodular disease. The advantage of this approach include the elimination of the frequently observed multifocal/bilateral papillary thyroid microcarcinoma, thereby reducing recurrence rates, the avoidance of the rare possibility of transformation from well differentiated to undifferentiated carcinoma. (3,21) Performing total/near-total thyroidectomy at the time of the initial surgery avoids the risk of reoperation which is associated with an increased morbidity, obviously the avoidance of a second operation is preferable for both the patient and the surgeon.(11,12,21) Additional advantages of total/near-total thyroidectomy are the possibility of better monitoring of treated patient by thyroglobulin measurements to detect residual or recurrent disease and increase the yield of postoperative radioactive iodine therapy.(12,15,21) Interestingly, hormone replacement therapy will be required in most patients (>50%) following more limited thyroid resection (i.e, lobectomy or subtotal thyroidectomy) thereby eliminating the theoretical advantage of less radical thyroid surgery.( 15,18,21)

### Conclusion:

This study shows the frequency of incidental thyroid carcinoma is significant in patients operated for benign thyroid disease. Also the incidence of ITC is not significantly different between patients presenting with toxic or nontoxic solitary thyroid nodule and MNG. FNAC is fairly inconclusive especially in patients with MNG. However, a larger study is needed to draw definite conclusions.

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