

Incidence of Malignancy in Egyptian Patients with Cold Thyroid Nodule(S): Retrospective Study

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ABSTRACT

Background: this study was to evaluate the incidence of malignancy in Egyptian patients with cold thyroid nodule(s) after total thyroidectomy and histopathological analysis and the final result in our study was the incidence of malignancy in Egyptian patients with cold thyroid nodule(s) was (20%).

Aim: the aim of the work was to evaluate the incidence of malignancy in Egyptian patients with cold thyroid nodule either solitary thyroid nodule or dominant cold nodule in multi-nodular goiter through retrospective study. **Materials and Methods:** the study was carried out on 30 Egyptian patients suffering from cold nodule(s) in the thyroid gland. Patients were managed at Al- Azhar University hospital; Cairo; Egypt. The study was controlled retrospectively. Ethical approval from the local Ethics Committee of Surgery Department was obtained.

Results: according to the descriptive statistics of our study, the total number of cases was thirty patients, twenty-six of them were females and four were males, also the mean age of studied group was (37.87). The final results of post-operative histopathological examination were twenty-four cases diagnosed as benign and six malignant cases.

Conclusion: in this retrospective study the final results of histopathological examination were 24 benign cases (80%) and 6 cases were malignant (20%). So in our study the incidence of malignancy in Egyptian patients with cold thyroid nodule(s) was (20%).

Keywords: Incidence of malignancy, cold, thyroid, nodule(s), retrospective study.

INTRODUCTION

Thyroid nodules are often found on the gland, with a prevalence of 4-7%. The majority of nodules does not cause any symptoms and are non-cancerous. Non-cancerous cases include simple cysts, colloid nodules, and thyroid adenoma. Malignant nodules which only occur in about 5% of nodules include follicular, papillary, medullary carcinoma and metastases from other sites ⁽¹⁾.

Nodules are more likely in females, those who are exposed to radiation, and in those who are iodine deficient. When a nodule is present, thyroid function tests are performed and reveal whether a person has a normal amount of thyroid hormones "euthyroid" or an excess of hormones, usually secreted by the nodule, causing hyperthyroidism ⁽²⁾.

When thyroid function tests are normal, an ultrasound is often used to investigate the nodule, and provide information such as whether the nodule is fluid-filled or a solid mass, and whether the appearance is suggestive of a benign or malignant cancer. A needle aspiration biopsy may then be performed, and the sample undergoes cytology, in which the appearance of cells is viewed to determine whether they resemble normal or cancerous cells ⁽³⁾.

Cold nodule is a scintigraphy evidence (hypo functional district node) on the thyroid. Cold nodes produce little or no hormones triiodothyronine (T3) and thyroxine (T4). To put it differently, cold node is a part of thyroid nodule, not representing in scintigraphy ⁽⁴⁾.

The most common neoplasm affecting the thyroid gland is a benign adenoma, usually presenting as a painless mass in the neck. Malignant thyroid cancers are most often carcinomas, although cancer can occur in any tissue that the thyroid consists of including C-cells and lymphomas. Cancers from other sites also rarely lodge in the thyroid. Radiation of the head and neck presents a risk factor for thyroid cancer, and cancer is more common in women than men, occurring at a rate of about 2:1 ⁽⁵⁾.

In most cases, thyroid cancer presents as a painless mass in the neck. It is very unusual for thyroid cancers to present with other symptoms. Most malignant thyroid cancers are papillary, followed by follicular, medullary, and thyroid lymphoma ⁽⁶⁾.

Because of the prominence of the thyroid gland, cancer is often detected earlier in the course of disease as the cause of a nodule. A radioactive iodine uptake test can help reveal the activity and location of the cancer and metastases.

With the exception of the rare Anaplastic thyroid cancer, which carries a very poor prognosis, most thyroid cancers carry an excellent prognosis and can even be considered curable⁽⁷⁾.

AIM OF THE STUDY

Evaluate the incidence of malignancy in Egyptian patients with cold thyroid nodule either solitary thyroid nodule or dominant cold nodule in multi-nodular goiter through retrospective study.

MATERIALS AND METHODS

This retrospective study was conducted in Surgery Department, Al-Azhar University Hospital (Al Hussein University Hospital) in the period between July 2017 and March 2018. The study was carried out on 30 Egyptian patients suffering from cold nodule(s) in the thyroid gland. All patients underwent total thyroidectomy and histopathological examination was done. **The study was approved by the Ethics Board of Al-Azhar University.**

Inclusion criteria:

- Patients with cold thyroid nodules.
- Patients with solitary cold thyroid nodule.
- Patients with dominant cold thyroid nodule.

Exclusion criteria:

- Patients with recurrent goiter.
- Patients with pure thyroid cyst.
- Patients with hot nodule(s) in the thyroid gland.
- Patients refuse to do surgical intervention.

Methods:

All patients had been subjected to the followings:

I. Preoperative assessment

A- Full clinical assessment.

B- Routine laboratory studies:

Blood samples were collected using conventional venipuncture and when it was necessary to use tourniquet to assist venipuncture

it was removed for thirty seconds before collecting the samples.

- All hematological parameters (CBC, kidney function, liver function, RBS, PT, PTT, INR).
- Fasting blood samples were used for measurement of serum calcium and the results were corrected to an albumin level of 4 g/dl by adding or subtracting 0.09 mg/dl for every 0.1 g/dl deviation in albumin.

C- Thyroid profile

Namely free T3, free T4, TSH were assayed by microparticle enzyme immunoassay on the AX SYM.

D- Neck ultrasonography

Neck ultrasonography was done for detection of gland texture, retrosternal extension, and cervical lymphadenopathy.

E- Chest and thoracic inlet X ray

Was done for detection of any tracheal deviation or compression, retrosternal extension and for lung assessment before anesthesia.

F- Thyroid scan when indicated

Was done for detection of the nature of the toxic gland and the nature of the nodules (hot - warm - cold).

G- Fine needle aspiration cytology (FNAC)

When indicated (cold nodule on thyroid scan or dominant of multinodular goiter or solitary thyroid nodule). Any case which was proved to be positive by FNAC was excluded from this study as total thyroidectomy is not a matter of debate in all kinds of thyroid cancer.

H- Referral to ENT specialist

For indirect laryngoscope to determine the mobility of the vocal cords and also for medicolegal reasons.

- All patients were informed that they have to take postoperative medications (hormonal replacement) for life with no chances for recurrence.
- Also patients were informed about all possible complications of total thyroidectomy.

II. Operative technique

All patients underwent total thyroidectomy. The procedure was carried out under general anesthesia.

RESULTS

Table (1): Demographic features of the studied patients

Variables		Patients	Studied patients (n= 30)
Age (years)	Range		20 – 64
	Mean ± SD		36.87 ± 12.79
Sex	Female		26 (86.7%)
	Male		4 (13.3%)

This table shows that the age range of the studied cases was from 20-64 years old (mean age 36.87 years). 26 patients were females (86.7%) and 4 patients were males (13.3%).

Table (2): Ultrasound findings of thyroid gland of the studied patients

Variables		Patients	Studied patients (n= 30)	
			N	%
Ultrasound findings	Dominant nodule		2	7%
	Lymph node enlargement		1	3%
	Solid nodules		16	53%
	Cystic nodule		11	37%

This table shows ultrasound findings of thyroid gland of the studied patients. It shows that 2 (7%) cases with dominant nodules, 16 (53%) cases with solid nodules, 11 (37%) cases with cystic nodule and 1 (3%) case with nodule associated with lymph node enlargement.

Table (3): Diagnosis of thyroid nodules according to nodularity in the studied patients

Variables		Patients	Studied patients (n= 30)	
			n	%
Diagnosis	Multi-nodular		24	80%
	Solitary nodule		6	20%

This table shows diagnosis of thyroid nodules by ultrasound in this study, the results described as follows: 24 cases were multi-nodular (80%), 6 cases are solitary nodules (20%).

Table (4): Diagnosis of thyroid nodules by paraffin in the studied patients

Variables		Patients	Studied patients (n= 30)	
			N	%
Thyroid nodule	Benign		24	80%
	Malignant		6	20%

This table shows diagnosis of thyroid nodules by paraffin in this study, the results described as follows: 24 cases were benign (80%), 6 cases are malignant (20%).

Table (5): Histo-pathological reports of studied patients

Variables		Patients	Studied patients (n= 30)	
			N	%
Histo-pathological reports	Colloid goiter		20	67%
	Follicular adenoma		5	17%
	Follicular carcinoma		1	3%
	Papillary carcinoma		3	10%
	Medullary carcinoma		1	3%

This table shows the histo-pathological reports of studied patients. It shows that 20 (67%) cases have colloid goiter, 5 (17%) cases have follicular adenoma, 3 (10%) cases have papillary carcinoma, 1 (3%) case have follicular carcinoma and 1 (3%) case have medullary carcinoma.

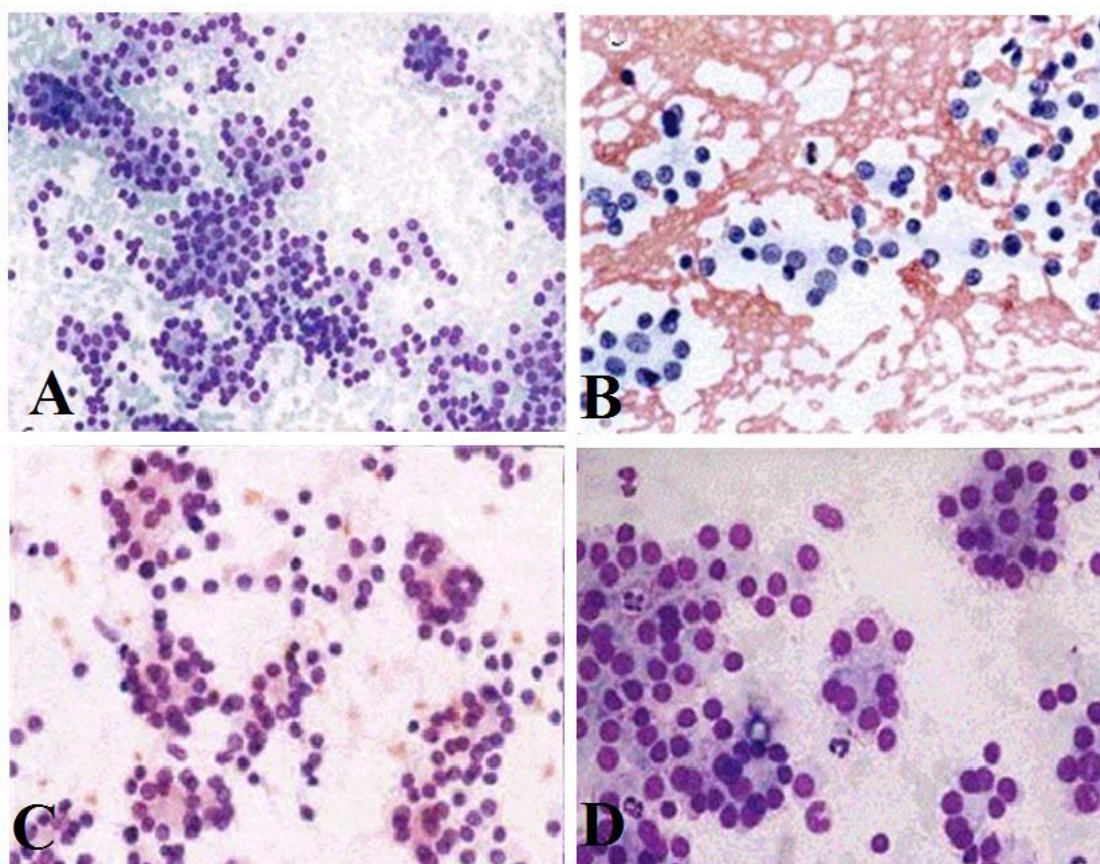


Figure (1): A. Follicular neoplasm, B. Cellular smears of single cells, C. micro-follicular cell clusters or rosettes in a repetitive manner, D. some nuclear hyperchromasia.

DISCUSSION

Thyroid carcinoma is a relatively rare tumor, but it represents the most frequent form of cancer of endocrine glands. It represents 1% of human neoplasia and its annual incidence is estimated worldwide from 0.5% to 10:100,000 subjects in the world population. Such incidence is increased if cases of occult carcinoma are taken into consideration. This occult carcinoma is a non evident neoplasia, occurring with cervical nodal disease, or accidentally detected in a thyroid that has been removed for pathology or during an autopsy⁽⁸⁾.

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. In addition, high resolution ultrasound (US) can detect thyroid nodules in 19-67% of randomly selected individuals with higher frequency in women and elderly⁽⁹⁾. The clinical importance of thyroid nodules rests with the need to exclude thyroid cancer, depending on age, sex, radiation exposure, family history of thyroid malignancy, other associated syndromes, and other factors. Differentiated thyroid cancer, which includes papillary and follicular cancer, comprises

the vast majority (90%) of all thyroid cancer. In the United States, the incidence of thyroid cancer is on the rise. Almost the entire change has been attributed to an increase in the incidence of papillary thyroid cancer (PTC). Moreover, 49% of the rising incidence consisted of cancers measuring 1 cm or smaller and 87% consisted of cancers measuring 2 cm or smaller. This tumor shift may be due to the increasing use of neck US and early diagnosis and treatment⁽¹⁰⁾. Patients with MNG have the same risk of malignancy as those with STN. However, one large study revealed that a solitary nodule had a significantly higher likelihood of malignancy than did non-solitary nodule ($p < 0.001$), although the risk of malignancy per patient was the same and independent of the number of nodules⁽¹¹⁾.

MNG has historically been thought of as a benign condition with a low risk of associated malignancy, and may be present in up to 4% of the population in iodine sufficient countries. However, recent studies have suggested that the incidence of malignancy in patients with MNG approaches that of patients with STN⁽¹²⁾.

In the current study, in an attempt of detecting the incidence of malignancy in Egyptian patients with cold thyroid nodule(s), by

retrospectively analyzing each patient's demographic and clinical data, FNA, and US features. It was found that out of 30 patients with cold thyroid nodule(s), 6 had thyroid cancer on histopathology (20%). The range of thyroid cancer in MNG patients varied widely from 1% to 31%, with an average of 1% - 14%. The difference in the reported rates of malignancy among patients with MNG in the above studies undoubtedly reflects difference in the selection criteria used for analysis, as well as geographic differences in the population studied⁽¹³⁾.

In the present study, no significant difference in age was found between patients with benign disease and those with malignant disease. The median age was 36 years and 37 years, respectively.

Several authors reported that detection of malignancy did not correlate with patient's gender, which is in accordance with the current findings. Other studies however, reported higher rates of thyroid carcinoma in male patients. Especially in patients with follicular neoplasm (BIII, BIV)⁽¹⁴⁾.

While some authors reported that older age is an independent risk factor of malignancy, others, in accordance with our findings, found no correlation with age in patients with solitary or multiple nodules. In a study by Luo. Age lost its significance as an independent risk factor for thyroid malignancy when included in a multivariate analysis, suggesting that age is not a very strong independent risk factor for malignancy and will likely not be helpful in predicting the risk of malignancy in a given patient. On the other hand, some investigators found that older age is significantly correlated with the presence of benign neoplasms in thyroid nodules. This wide contradiction is probably due to differences in patients selection and numbers of the study population⁽¹⁵⁾.

Though history of previous radiation exposure and presence of family history of thyroid cancer are well established thyroid cancer risk factors. No significant difference could be detected regarding family history of thyroid cancer, previous radiation exposure, or history of previous thyroid surgery in the present study. This may be attributed to incomplete or inaccurate data of patients' records in the present retrospective study.

None of the patients when reviewing their records had hoarseness of voice. Some patients presented with dyspnea or dysphagia not related to systemic cause, or disfigurement caused by neck mass, and others was discovered incidentally on physical examination, color Doppler evaluation of the carotid artery, or imaging studies performed for unrelated reasons.

Differentiated thyroid carcinoma rarely cause airway obstruction, vocal cord paralysis or esophageal symptoms at their clinical presentation. Hence, the absence of local symptoms does not rule out a malignant tumor⁽¹⁶⁾.

In this study all patients underwent to preoperative radionuclide scanning which revealed cold nodule(s).

In a large study of patients with thyroid nodule(s) who underwent preoperative radionuclide scanning and all patients underwent surgery regardless of the functional status of a nodule, 84% were cold, 10.5 % were warm and 5.5 % were hot. Thyroid cancer was found in 16% of cold nodule(s), 9 % of warm nodules and 4 % of hot nodules⁽¹⁷⁾.

Tc-99m is trapped but not organified by the thyroid, therefore nodules not demonstrated on Tc-99m scanning must be rescanned with ¹¹²³I to determine if they are adenomas or carcinomas that have the ability to trap Tc-99m. There is discrepancy of tracer uptake in thyroid neoplasms when comparing ¹¹²³I with Tc-99m. Any hot nodule on Tc-99m scintigraphy should be rescanned with ¹¹²³I for better recognition of the risk of malignancy⁽¹⁸⁾.

Tc-99m doesn't penetrate the sternum well and therefore it is not useful in assessing retrosternal extension, or detection of pulmonary metastasis.

Thallium-201 is another isotope that produces very little radiation exposure and is of value in imaging thyroid carcinoma.

Its uptake is not affected by thyroid hormones or iodinated medication. It can be used in follow up of patients with papillary and follicular carcinoma, that fail to concentrate radioactive iodine and it can detect recurrent medullary carcinoma, and useful in detection of metastatic thyroid carcinoma⁽¹⁹⁾.

The imaging modality of choice for the investigation of thyroid nodule is high resolution US, especially when combined with FNA, which has been proven to be an important and widely accepted, cost-effective, simple, safe and accurate method for triaging patients with thyroid nodules either to surgical intervention or follow-up⁽²⁰⁾.

Some researches adopted The Thyroid Imaging Reporting And Data System (TIRADS) classification in differentiating benign from malignant nodules, and it showed a very successful and reliability in predicting thyroid malignancy. Unfortunately, this could not be done in the present study, as most of the US reports in this study gave either only one dimension of thyroid nodule (the largest), or when describing three dimensions, they did not discriminate the anteroposterior diameter (A) from the transverse one (T), and so it could not be decided whether it is a nodule with $A/T > 1$ or $A/T < 1$ ⁽²¹⁾.

In our study the ultrasound findings of thyroid gland of the studied patients. It shows that 2 (7%) cases with dominant nodules, 16 (53%) cases with solid nodules, 11 (37%) cases with cystic nodule and 1 (3%) case with nodule associated with lymph node enlargement.

In our study the studied patients were classified into two groups according to the nodularity by ultrasound finding as follows: 24 cases were multi-nodular (80%), 6 cases are solitary nodules (20%).

Fine needle aspiration (FNA) has an essential role in the evaluation of euthyroid patients with thyroid nodule(s). It reduces the rate of unnecessary thyroid surgery for patients with benign nodules and triages patients with thyroid cancer to appropriate surgery. Before the routine use of FNA, the percentage of surgically resected thyroid nodules that were malignant was 14%. With current thyroid FNA practice, the percentage of resected nodules that are malignant surpasses 50%⁽²²⁾.

Some reviews concluded that the usefulness of FNA in detecting malignancy is mainly confined to STN, and this utility is questionable when it comes to MNG. Moreover, there are few series that have studied FNA in MNG⁽²¹⁾, and they are all contradicting. In our study the diagnosis of solitary thyroid nodules by FNAC as follows: 4 cases were follicular nodule (67%), 2 cases are malignant nodule (33%). Cytopathological examination is the corner stone in appraising the malignant potential of a given thyroid nodule.

In our study the final histopathological examination was 24 cases were benign (80%), 6 cases are malignant (20%). The histo-pathological reports of studied patients show that 20 (67%) cases have colloid goiter, 5 (17%) cases have follicular adenoma, 3 (10%) cases have papillary carcinoma, 1 (3%) case have follicular carcinoma and 1 (3%) case have medullary carcinoma.

CONCLUSION

We concluded that the incidence of malignancy in Egyptian patients with cold thyroid nodule(s) (20%). The histo-pathological reports of studied patients show that 20 (67%) cases have colloid goiter, 5 (17%) cases have follicular adenoma, 3 (10%) cases have papillary carcinoma, 1 (3%) case have follicular carcinoma and 1 (3%) case have medullary carcinoma.

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