



Clinical Characteristics and Evaluation of Diagnostic and Management Approaches among Iraqi Patients with Solitary Thyroid Nodules

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Original Article

Summary

Despite the fact that the vast majority of thyroid nodules are benign, early diagnosis is of great importance to classify them and rule out any risk of malignancy. The solitary thyroid nodule (STN) is a frequent condition, its prevalence ranges from 4 to 7% of the general population, increases with age, and is more frequent in women than in men. Appropriate and diagnostic and treatment approaches is a serious concern for patients and surgeons, due to the fear that it could be a malignant neoplasm. We aimed to assess the validity of diagnostic methods and treatment of solitary thyroid nodules among group of Iraqi patients Hence we consecutively included 60 patients during a period of 24 months who were presented with solitary thyroid nodules seeking for treatment. Findings of the study showed that STN was more frequent in females than males in a ratio of 5 to one. Out of the 60 patients, 51 were surgically treated, 9 cases treated by aspiration and followed up. Unfortunately, 3 cases (5.0%) were malignant. In conclusion, STN are common in females and its incidence increases with the advancing age. Appropriate diagnostic method and following the standard guidelines is so beneficial for proper management and outcomes.

Keywords: *Thyroid diseases, Solitary Thyroid Nodules, Diagnosis, Management*

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1. INTRODUCTION

Thyroid gland is a small soft organ (weighing 25-40 g) which is located on the front surface of the neck and lies on the tracheal rings. The gland is named so because it is located in front of the thyroid cartilage of the larynx. It has two lobes (left and right), which are interconnected by an isthmus. The thyroid gland has a huge impact on the functioning of all organs. The lack or excess production of thyroid hormones manifests itself differently in everyone, depending on which organ in a person is more vulnerable (1,2). Thyroid disorders remain the most common endocrine diseases after diabetes worldwide, And every year the number of patients with these disorders increases (3). Thyroid nodules are rather common. About 4-7% of the adult population has palpable and clinically detectable nodules. Only, 8-16% of these nodules harbor thyroid cancer But nodules that incidentally found by ultrasonography suggest a prevalence of 19-67% . The detection of thyroid nodules has risen several folds with the advent of imaging tools, particularly ultrasound (4). According to the American Thyroid association (ATA), thyroid nodules defined as a discrete lesion within the thyroid gland, radiologically distinct from the surrounding thyroid parenchyma (5) The solitary thyroid nodule (STN) is a frequent condition its prevalence, increases with age, and is more frequent in women than in men (4,5) . The diagnosis and treatment of STN is a serious concern for patients, due to the fear that it is a malignant neoplasm. Its main problem consists in the selection of malignant nodules, whose frequency oscillates between 5-16% of all STNs and their treatment is surgical resection. The diagnosis of benign STN is necessary to avoid unnecessary surgical excision and reduce morbidity and the economic cost of indiscriminate surgery of all STN (3–6). Thyroid nodules are usually benign tumors that are very common in clinical practice. They develop due to excessive replication of thyroid cells. Nodules that are small in size and located some distance from sensitive structures such as the trachea are usually asymptomatic (meaning they are not felt by patients and do not cause health problems), they may not even be noticed. However, some thyroid nodules can cause symptoms such as shortness of breath (choking) or – only in the case of hot nodules – hyperthyroidism (overactive thyroid) (3–5,7). Benign nodules are classified based on their ability to produce hormones compared to healthy thyroid tissue. They are differentiated into three categories: hot, cold, and indifferent (or "normal") nodules. Hot nodules are more active than normal thyroid tissue and therefore produce more hormones. On

the other hand, cold nodules are masses of tissue with no real capacity to produce thyroid hormones compared to normal thyroid tissue. Normal or indifferent nodules cannot be differentiated from healthy tissue by their hormone-producing capacity. Most thyroid nodules are cold nodules (approx. 50-85%), while only 10% of nodules are "hot" and about 40% are indifferent. Hot nodules can cause significant metabolic imbalance and dysregulation of various processes in the body. As long as these nodules remain small, the effects may not be serious, however, excessive hormonal overproduction can lead to the development of hyperthyroidism (8). Despite the fact that the vast majority of thyroid nodules are benign, early diagnosis is of great importance to classify them and rule out any risk of malignancy. In addition, diagnostic approaches help to recognize the different types (hot, cold or indifferent) in order to decide the most appropriate treatment. Scintigraphy is a commonly used instrument to classify them (4,9). The palpation of the thyroid can reveal the presence of thyroid nodules in ten percent of women and two percent of men. If ultrasonography was performed, the prevalence of thyroid nodules might be as high as fifty percent or even higher. Even though it accounts for only one percent of all cancers, thyroid carcinoma is the most common form of endocrine malignancy. To ensure that patients who appear with thyroid nodules are managed effectively and are not over- or under-treated, it is consequently essential to have a clear diagnostic strategy (10). In most cases, the detection of a clinically isolated harmless thyroid nodule has been interpreted as a strong recommendation for surgery due to the fact that this condition is regarded as a very suspicious marker of cancer. There has been a large amount of variation in the reported incidence of cancer in these cases, ranging anywhere from 3% to 36% (11) Over the past twenty years, there has been a shift in the treatment approach for thyroid nodules. The conventional method of eliminating all thyroid nodules has given way to diagnostic testing that is more reliable and cost effective. This testing allows for the surgical treatment of thyroid nodules that are most likely to be cancerous, while treating benign thyroid nodules in a more conservative manner. Since the single nodule is the most common indicator of thyroid cancer, there is a need for approaches that are low-cost, straightforward, and risk-free to correctly identify those nodules that have to be managed surgically due to malignancy (12). Since the clinical features alone are not conclusive, many different types of studies have been employed to try to answer this dilemma; however, each research method still has its own

set of limitations. Determining the functional condition of the nodule by measuring its capacity to concentrate radioiodine was one of the first procedures developed, and it has proven to be one of the most useful. Because the majority of 'cold' swellings (80%) are benign, routine isotope scanning is unnecessary and inappropriate for distinguishing benign from malignant lesions (13,14). B-mode ultrasonography and serum human thyroglobulin levels are two of the other approaches that have been developed to identify between benign and malignant nodules (15,16). The majority of medical centers now use fine needle aspiration as a standard practice. The tissue that is collected during fine needle aspiration is then analyzed cytologically. Nodules can be categorized according to their characteristics, such as whether they are benign, inflammatory, cystic, or malignant, with the assistance of an experienced pathologist. In numerous cases of ambiguous lesions, the use of diagnostic molecular techniques on aspirated thyroid cells was beneficial in differentiating benign from malignant thyroid nodules. As a result, more efforts to enhance existing procedures and develop new ways are required (17–19). However, accurate history taking and risk profiling, as well as regular palpation, monitoring of thyroid function tests such as TSH, free T3 and free T4, possibly monitoring of tumor markers (TG and calcitonin) are just as important as thyroid ultrasound and scintigraphy. With the help of the last mentioned studies, on the basis of the echostructure and the dynamics of the contrast agent, it is already possible to determine quite accurately how high the individual risk is and, accordingly, how much therapy is needed. If there is uncertainty, additional data can be obtained using a fine needle biopsy. Therefore, we aimed in the current study to address the clinical characteristics of solitary thyroid nodules among Iraqi patients and to evaluate the current diagnostic and management approaches.

2. PATIENTS and METHODS

This was a prospective study conducted during a period of 24 months. A total of 60 patients presented with solitary thyroid nodule (STN) were consecutively enrolled during the study period. Diagnostic procedures and surgical interventions were in accordance with the standard protocols followed in our practice at our hospital. Among the studied group, 40 patients performed thyroid scan. According to the findings of thyroid scanning, these patients categorized as, “cold”, “warm or hot” nodules subgroups. For the purpose of this study, the

standard definitions of nodules were applied. Fine needle aspiration cytology (FNAC) was performed for 55 patients, of them 50 were performed by an expert professional cytologist at our hospital. The researchers performed the remaining 5 FNACs. A fine needle with a 22 gauge and a disposable plastic syringe of 10 milliliters capacity were used to aspirate cytological samples. The findings of cytological examination were reported by the staff of our hospital labs in collaboration with cytologists and the surgeons (the researchers). Thyroid cytology revealed either “benign” : (Thy 2) when the examined thyroid tissue showed normal epithelia cells with different RBCs amount or colloid. Malignant (Thy 5) was identified when the thyroid tissue showed on cytology, criteria of malignancy such as high cellularity, varied shape , size and nuclear structure. Suspicion was denoted for the thyroid tissue that showed high cellularity and sheets of follicular cells, this was categorized as “Thy 3 & 4) , however, malignancy was suspected in cytological diagnosis. This category also called indeterminate.

When the aspirate was insufficient for the cytology study, it was assigned as “inadequate, insufficient or Thy 1). Out of the original 60 patients, 9 were not fit for surgery while 51 patients were managed surgically. Their surgical, final histopathological studies , thyroid scanning and FNAC were compared. Statistical analysis and procedures, performed using the SPSS software for windows, version 27. Categorical variables expressed as frequencies and proportions and were compared with chi-square test or Fisher’s exact test accordingly. Scale variables presented as mean and standard deviation and were compared with parametric tests. All statistical tests and analysis performed at a level of significance of 0.05 or less to be considered as significant

3. RESULTS

A total of 60 patients who had a solitary thyroid nodule and met the inclusion criteria were enrolled, with a mean age of 35.4 ± 6.2 (range: 20 – 71) years. Age distribution revealed that 45% aged between 20 – 30 years, and the frequency distribution of the age groups decreased with advancing age. Females were the most affected group than men with a female to male ratio of almost 5.67 to one (51/9). Clinically, all of the cases had neck swelling, however, the majority of them, (75.0%) did not have any associated pain. There were 9 cases (15%) with difficulty swallowing, and 4 cases had difficulty swallowing and dyspnea. Two patients presented with lymphadenopathy on the right side of the neck (**Table 2 and Figure 1**). Tests of

thyroid function using T3, T4, and TSH were normal in 54 out of 60 cases (90%), low in 4 cases (6.7%), and elevated in 2 cases (3.3%), (**Figure 2**). Isotopic scanning of the nodules performed in 40 cases, of them hot nodules found in 2 cases (5%), warm nodules in 6 (15%) and cold in majority of these cases 32/40 (80%). In total, sixty patients who were diagnosed with thyroid nodules underwent ultrasound, in 43 cases the nodules were solid while cystic nodules in the remaining 17 cases. Furthermore, ultrasonography showed that among males, solid and cystic nodules found in 77.8% and 22.2%, respectively, while among females they were found in 70.6% and 29.4%, respectively, (**Table 2**). The procedures and operations performed for the patients are shown in (**Table 3**), where lobectomy + isthmusectomy performed in 34 cases (56.6%), bilateral subtotal thyroidectomy in 15%, total thyroidectomy in 6.7%, isthmusectomy in 5%, and Nodulectomy in only one case (1.7%). Aspiration only was performed in 9 cases (15%). Cytological findings of the studied group revealed that 47 cases with benign, one case was suspicious, two cases malignant, and five cases were insufficient and 5 cases were not eligible for cytology. Among the 51 cases that were surgically treated, histology studies revealed 3 carcinomas and 48 non-carcinomas cases, Histopathology revealed 42 cases of colloid nodules with focal fibrosis and bleeding or cystic degeneration, 5 cases of follicular adenomas, 1 case of Hashimoto's thyroiditis, 2 cases of papillary carcinoma and 1 case of follicular carcinoma (**Table 4**). It is worth mentioning that the surgeon did a second lobectomy to remove more of the malignant lobe after discovering that the cancer had spread to the opposite lobe. Furthermore, the confirmed carcinoma cases included two females aged 30-40 years and one male within the age group, 50-60 years (**Table 5**). Despite the low number of carcinoma cases but the proportional distribution indicated that at older age higher risk of carcinomas among males compared to females.

Table 1. Baseline characteristics of the studied group (N=60)

Variable	No.	%	
Age (year)	≤ 30	27	45.0
	31 - 40	14	23.3
	41 - 50	11	18.3
	> 50	8	13.3
Mean (SD)	35.4 (6.2)		
Gender	Male	9	15.0
	Female	51	85.0
	Female: Male ratio	5.7	-
Presentation/ finding	Painless cervical swelling	45	75.0
	Difficult Swelling	9	15.0
	Difficult Swelling + Dyspnea	4	6.7
	Palpable lymph node	2	3.3

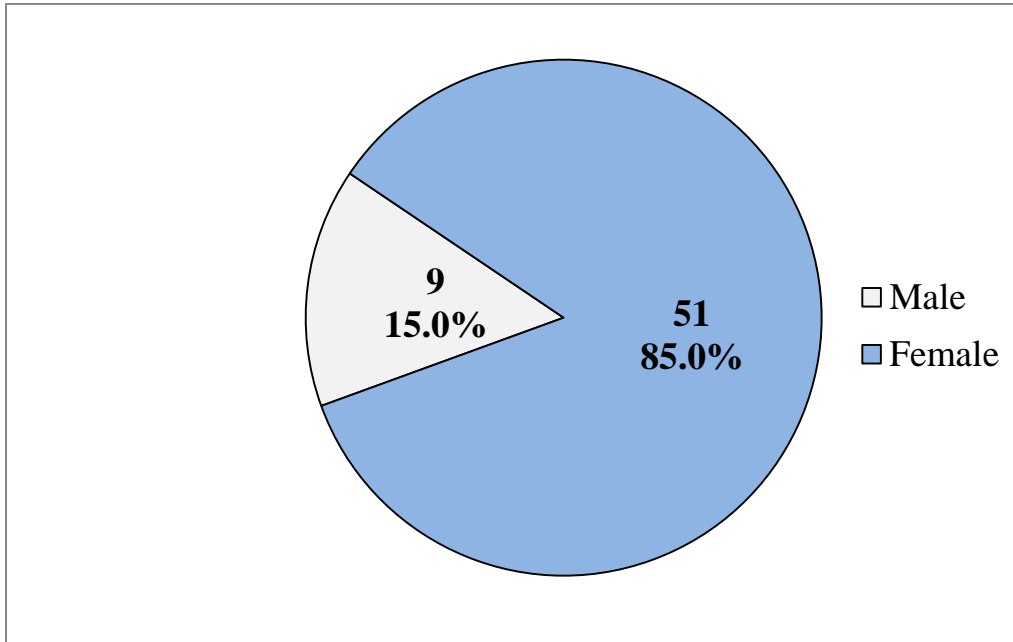


Figure 1. Pie-chart showing gender distribution and female to male ratio of the studied group showing the dominant female gender (Female to male ratio = 5.67)

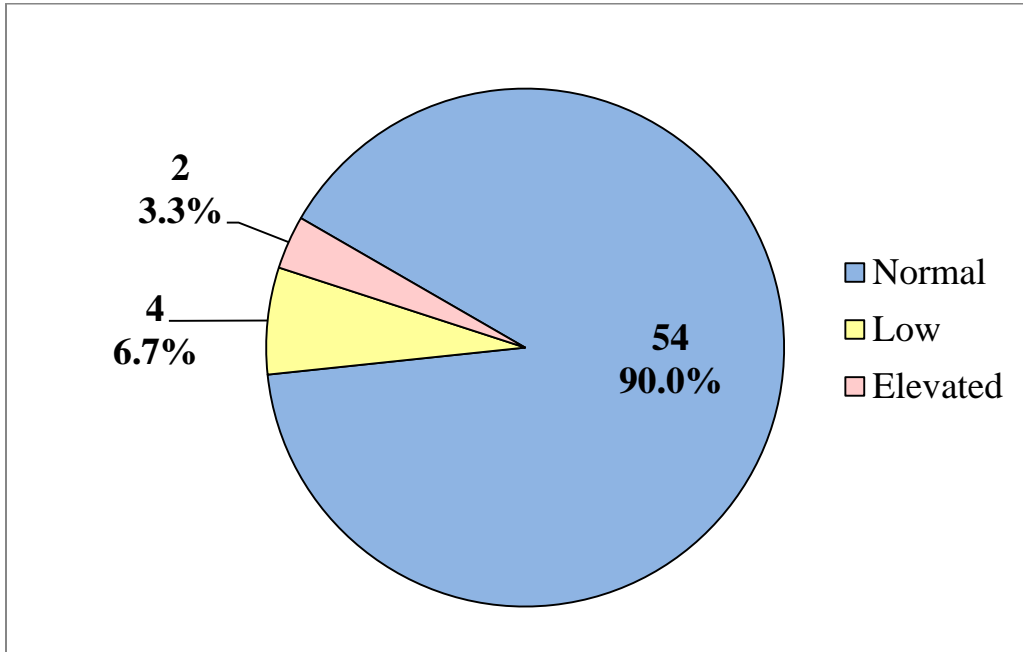


Figure 2. Pie-chart showing the thyroid function tests of the studied group showing the dominant female gender (N=60)

Table 2. Findings of Isotopic Scanning and ultrasonography

Variable		No.	%	
Scanning of the nodules (for 40 cases only)	Hot	2	5.0	
	Warm	6	15.0	
	Cold	32	80.0	
Ultrasound findings	Male (n=9)	Solid nodule	7	77.8
		Cystic nodule	2	22.2
	Female (n=51)	Solid nodule	36	70.6
		Cystic nodule	15	29.4

Table 3. Distribution of procedures and operations performed for the studied group

Type of Operations	No.	%
Lobectomy + isthmusectomy	34	56.6
Bilateral Subtotal Thyroidectomy	9	15.0
Total Thyroidectomy	4	6.7
Isthmusectomy	3	5.0
Nodulectomy	1	1.7
Aspiration only	9	15.0
Total	60	100.0

Table 4. Cytological and histopathological findings of the studied group

Findings		No. of cases	%
Cytological findings	Benign	47	78.4
	Suspicious	1	1.7
	Malignant	2	3.3
	Insufficient	5	8.3
	Not eligible for FNAC	5	8.3
Total		60	100.0
Histopathological findings of Surgically treated cases (N=51)	Colloid nodule	42	82.4
	Follicular adenoma	5	9.80
	Hashimoto's thyroiditis	1	1.96
	Papillary carcinoma	2	3.92
	Follicular carcinoma	1	1.96
Total		51	100.0

Table 5. Age and gender distribution of cases with malignant STNs (n=3)

Age (year)*	Male		Female		Total	
	No.	%	No.	%	No.	%
30 - 40	0	0.0	2	3.9	2	3.3
50 - 60	1	11.1	0	0.0	1	1.7
Total	9	15.0	51	85.0	60	100.0

*none of the cases in other age groups had malignant STNs

4. DISCUSSION

A solitary thyroid nodule affects 68.4% of people between the ages of 21 and 40, making this age range the most likely to be affected. According to Gupta et al. (18) 44% were between the ages of 21 and 40. Dorairajan and Jayashree (20) reported 44% between the ages of 21 and 40. According to the findings of Messaris and colleagues (21), the prevalence of palpable thyroid nodule was highest between the ages of 21 and 40 years (42.8%), and it dropped with increasing age until it was lowest in those over 80 years old . It is likely that an increased incidence of multiple nodularity is to blame for the lower prevalence of solitary thyroid nodules in people of advanced age (22). In our study, the incidence of solitary thyroid nodules was more than five times higher in females than in males, with a ratio of five to one. The female to male ratio was found to be 11-1 by Manoj Gupta (18). Findings from large population based study found higher prevalence of thyroid nodules among females compared to male and that advancing age, hypertension, hyperglycemia were significantly associated with thyroid nodules in both genders (23). According to Tunbridge et al. (24), the ratio of females to males who had the condition was 6 to 1. Concerning the various procedures for scanning the thyroid, 80% of these scintiscans revealed the presence of a nonfunctioning (cold) nodule, 15% of the total scans indicated the presence of isofunctioning (warm) nodules, and only 5% of the total scans indicated the presence of hyperfunctioning (hot) nodules. According to Kummar and colleagues (19), 81.1% of the samples were cold, 8.5% warm, and 12.4% hot. Hot nodules are more active than normal thyroid tissue and therefore produce more hormones. On the other hand, cold nodules are masses of tissue with no real capacity to produce thyroid hormones compared to normal thyroid tissue. Previous studies referred that most thyroid nodules are cold nodules almost 50-85%, while only 10% of nodules are "hot" and about 40% are indifferent. Hot nodules can cause significant metabolic imbalance and dysregulation of various processes in the body. As long as these nodules remain small, the effects may not be serious, however, excessive hormonal overproduction can lead to the development of hyperthyroidism (8). In our series of patients who had thyroid ultrasound scanning, 28.4% of the nodules were cystic lesions, while 71.6% of the cases were solid lesions. According to Shukri (25), 33% of the cases were cystic while 67% of the lesions were solid. According to

De Los Santos (26), cystic lesions made up 32% of cases, whereas solid lesions made up 68% of cases. The incidence of malignancy was found to be 5.1% in our research, however in other studies , the rate of malignancy in incidental thyroid nodules is much vary and may reach up to 24% (27,28).

5. CONCLUSIONS

Female gender and advancing age are the more important factors for higher rates of solitary thyroid nodules. No differences between both genders regarding the sonographic findings and histopathological approval of malignancy. Clinical and epidemiological characteristics of the Iraqi patients with solitary thyroid nodules more likely to be close to that in other countries. Hence, The following guidelines seem to be useful in the management of patients with a solitary thyroid nodule

Ethical Clearance:

Ethical issues were taken from the research ethics committee. Informed consent was obtained from each participant. Data collection was in accordance with the World Medical Association (WMA) declaration of Helsinki for the Ethical Principles for Medical Research Involving Human Subjects, 2013 and all information and privacy of participants were kept confidentially.

Conflict of interest: Authors declared none

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