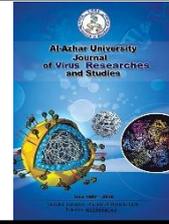




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### Evaluation of Risk Factors for Malignancy in a Solitary Thyroid Nodule

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#### Abstract

A solitary nodule may become cosmetically distressing to a patient and occasionally causes pressure symptoms. Less frequently, an autonomously hyperfunctioning single nodule may cause hyperthyroidism. However, in the greater proportion of patients, the major concern relates to the potential of malignancy within such a nodule. Aim of the work is to evaluate the prevalence of solitary thyroid nodules and evaluate the risk factors associated with the occurrence of malignancy. This a prospective study was carried out on 100 adults' patients with clinically palpable Solitary Thyroid Nodule presenting to the outpatient clinics in Al-Zahraa university Hospital from January 2021 to December 2021. Selected patients had clinically palpable STNs who succeeded to fulfill the inclusion criteria set for the study. Patients presenting with STNs and fulfilling the inclusion criteria will be selected, informed, included, categorized, and recorded for demographic variables. There are significant predictors of malignancy in STNs such as male gender, extreme of age, Solitary nodules Size between 2-4 cm, Microcalcifications, Hypoechoic pattern, Solid pattern, Ill-defined edges, and Increased intramodular vascularity and proved by FNAC. This study concluded female predominance was observed, peak incidence was in the age group 31-50 years. The most common presenting complaint was painless neck swelling.

**Keywords:** Risk Factors, Malignancy, Solitary Thyroid Nodule.

#### 1. Introduction

Solitary thyroid nodule (STN) is one of the common thyroid presentations, and approximately 8% of the adult population presents with clinically palpable thyroid nodules [1].

A proper history of the present illness represents an important part of the clinical assessment. This should be targeted to search for risk factors for thyroid cancer and other useful information that would help to formulate a diagnosis and start a management strategy. Special investigations are required in suspected

cases of familial disease such as familial MTC, MEN II, familial PTC, FAP, Cowden Disease, Gardner's Syndrome, and Carney's Syndrome [2].

Thyroid function testing, including serum TSH measurement, should be performed to identify underlying thyroid dysfunction but not to differentiate benign from malignant nodules [3].

Thyroid ultrasound is the first-line tool for the evaluation of patients with nodular thyroid disease. Evidence-based guidelines recommend thyroid ultrasounds for all

patients suspected of having thyroid nodules by either physical examination or another imaging study [4].

Thyroid FNA has high sensitivity and specificity in the diagnosis of papillary thyroid carcinoma, as well as other thyroid malignancies, including medullary and anaplastic thyroid carcinoma. The sensitivity, specificity, and accuracy of thyroid FNAC are significantly improved when FNAC is performed under ultrasound guidance [5].

The incidence of thyroid cancer continues to rise worldwide, mostly as a result of increased use of diagnostic imaging modalities and surveillance tools [6].

Medical and/or surgical management strategies of the thyroid nodules should be guided by clinical data together with the results of ultrasound evaluation and FNAC analysis if appropriate [7].

## 2. Patients and Methods

**Ethical Considerations:** This study was conducted according to the standards approved by Al-Azhar University's Research Ethics Committee. All participants signed the informed consent after a full explanation of the study details.

### 2.1 Inclusion Criteria

All selected patients presented with solitary thyroid nodule from age 21 years old to 60 years old which were diagnosed by personal data including age, sex, exposure of previous irradiation and clinical examination including symptoms (pain, hoarseness of voice, dysphagia, dyspnea, hemoptysis and other swelling) and signs (hardness, limited of mobility and other swelling) and investigated by preoperative preparation and thyroid hormone levels, ultrasound scan, FNAC and intraoperative findings as hardness of nodule and highly vascular then confirmed by histopathological examination of the biopsy taken.

### 2.2 Exclusion Criteria

Patients who refused to participate in the study, presence of preoperative vocal cord dysfunction, giant goiter, Grave's disease, retrosternal goiter, toxic goiter, and patients unfit for general anesthesia.

### 2.3 Operative procedure

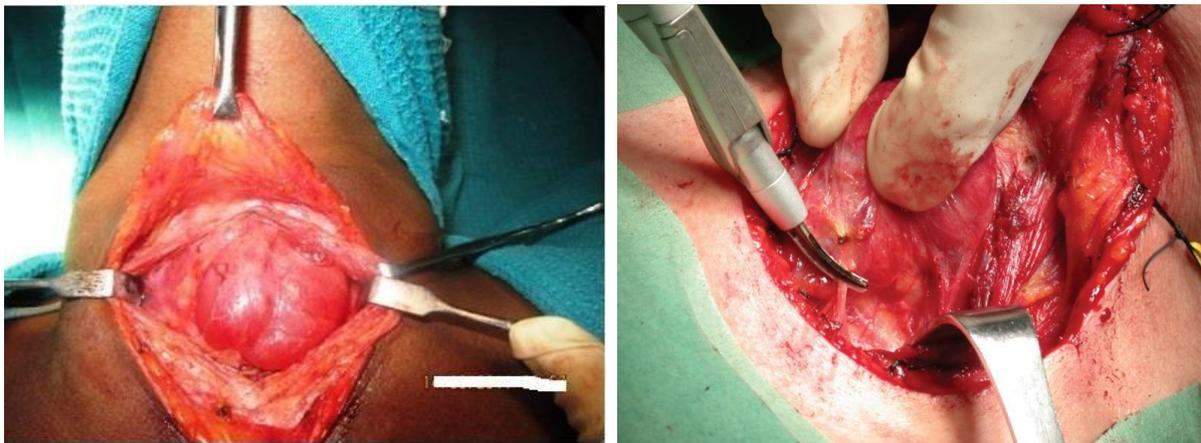
All-surgical procedures were performed under general anesthesia with endotracheal intubation. All operations were performed using a standardized capsular dissection technique through a collar incision. The lobe of the thyroid gland was progressively dissected away from strap muscles, its vascular pedicles were ligated with Vicryl 2/0 suture or coagulated and divided with HS. The thyroid lobe was progressively dissected off the trachea after the recurrent laryngeal nerves and parathyroid glands were identified and dissected off the thyroid capsule. After securing hemostasis, a suction drain was routinely put in the thyroid bed as a part of the study protocol to measure the amount of blood loss during the first 48 hours.

## 3 .Results

This study is a prospective cross-sectional study to evaluate the predictivity of different preoperative clinical findings and postoperative histopathological data of malignancy in patients with clinically palpable STNs presenting to outpatient clinics in Al-Zahraa Hospital from January 2021 to December 2021. Table. 1 shows age and sex distribution of benign and malignant nodule. Benign lesion was the most common lesion in both males and females. Malignancy was common in older age groups in both sexes. Table. 2 shows distribution of study subjects as per their clinical features. Swelling of the thyroid region was present in all cases. The next most common symptom was pain in 8% of the cases. Only one patient presented with hoarseness of voice, 4 cases with dyspnea

and 2 cases with palpable lymph node. Table. 2 shows Distribution of study subjects as per their Preoperative neck ultrasound findings include the increased vascularity and the irregular nodule margins, and to a lesser extent the microcalcification, hypoechoic nodule echogenicity in most malignant cases. This means that ultrasound is indicator for malignancy in STNs. Table. 4 shows distribution of study subjects as per their FNAC report. FNAC showed that majority

had follicular neoplasm followed by nodular goiter. Table. 5 shows accuracy rate of FNAC with histopathology as gold standard. The sensitivity of FNAC was found to be 96%. Table. 6 shows distribution of study subjects as per the histopathological report. Follicular adenoma was the most common histopathological finding in 50% of the cases. Malignancy was reported in 14% of the cases.



**Figure (1):** Shows 14 mm diameter of umbilical cord 3.2 mm diameter of the umbilical artery. 6.4 mm diameter of the umbilical vein.

**Table (1):** Age and sex distribution of benign and malignant nodule.

	Benign	Malignant	Total	Benign	Malignant	Total
21-30	1	0	1	20	0	20
31-40	1	0	1	10	3	13
41-50	2	2	4	35	5	40
51-60	1	2	3	10	1	11
61 and above	1	0	1	5	1	6
Total	6	4	10	80	10	90

**Table (2):** Distribution of study subjects as per their clinical features.

Signs and symptoms	Number	Percentage
welling thyroid region	100	100
Pain	8	8
Toxic symptoms	0	0
Dyspnea	4	4
Dysphagia	0	0
Regional palpable lymphnode	2	2
Hoarseness of voice	1	1
Hard consistency	4	4

**Table (3):** Distribution of study subjects as per their Preoperative neck ultrasound findings.

Nodule size	Malignant	Benign	Total
<2cm	0	22	22
2-4cm	6	44	50
>4cm	8	20	28
Nodule echogenicity			
Hypoechoic)	12	0	12
Isoechoic	2	39	41
Hyperechoic	0	47	47
Nodule calcification			
Microcalcifications	10	0	10
Coarse calcifications	2	1	3
Peripheral rim calcification	2	5	7
No calcification	0	80	80
Nodule color Doppler			
Intramodular vascularity	12	6	18
No intramodular vascularity	2	80	82
Nodule size			
<2cm	0	22	22
2-4cm	6	44	50
>4cm	8	20	28
Nodule margins			
Halo and regular)	0	80	80
No halo and regular	2	6	8
Halo and irregular	2	0	2
No halo and irregular	10	0	10

**Table (4):** Distribution of study subjects as per their FNAC report.

FNAC report	Number of patients
Follicular Neoplasm	56
Nodular Goiter	36
Papillary Carcinoma	8

**Table (5):** Accuracy rate of FNAC.

Result	True positive cases	False negative	False positive	Total
No. of cases	94	6	0	100

**Table (6):** Distribution of study subjects as per the histopathological report.

HPE report	Number
Papillary Carcinoma	8
Follicular variant of papillary carcinoma	2
Follicular carcinoma.	4
Follicular Adenoma	50
Nodular Goiter	36
Total	100

#### 4. Discussion

Solitary thyroid nodules represent a fairly common clinical problem, and differentiated thyroid cancer is becoming increasingly prevalent [8].

The clinical importance of STNs lies in the need to exclude thyroid cancer which occurs in 5-15% depending on age, gender, radiation exposure history, family history, and other factors [9].

Generally, only STNs over 1 cm should be evaluated, since they have a greater potential to be clinically significant cancers [10].

It is recommended that every patient with a palpable STN should undergo an FNAC [11]. Some clinical variables have been associated with a greater risk of malignancy, e.g., age, male gender, previous radiotherapy, a positive family history of thyroid cancer [12].

Our series was a prospective cross-sectional study to evaluate the predictivity for malignancy in (100) patients with clinically palpable STNs presenting to the outpatient clinics in El-Zhraa Hospital from June 2021 to December 2021.

Manmadha et al, prospective study of randomly selected patients with 75 clinically palpable, solitary thyroid nodule diagnosed and treated at Prathima Institute of Medical Sciences Karimnagar. Total duration of study was two years, from 2010 October to 2012 September [13].

Mohamed et al, A total of 83 patients with STNs who underwent hemithyroidectomy, total thyroidectomy, and total thyroidectomy with modified neck dissection in Ain Shams University Hospitals and Helwan University Hospital between September 2016 and December 2017 [14].

In Our series Benign lesion was the most common lesion in both males and females. Malignancy was common in older age groups in both sexes. the different age groups of benign and malignant patients We divided into five groups, and the results showed that there is higher risk from 41 to

60 years than the others, and the difference was not highly significant among age groups, this needs further investigation and larger number of patients to be accurate.

Manmadha et al, the youngest patient was 14 years old and the oldest was 65 years old. 80% of solitary nodules occurred during the age between 21-50 years. The highest incidence of 36% was recorded during the third decade of life, out of 75 patients, 65 were females and 10 were males. This gives a Female: Male ratio = 6.5:1. Solitary thyroid nodule is 6.5 times more common in women.

Mohamed et al, that most patients presenting with STN were females (n=64, 77.1%). Mean age was 36.96 years. By studying the age and sex as single predictor factors of malignancy, it was found that the being a male patient is highly significant single independent factor.

Although the most common age group of STNs is the third and fourth decades of life, but interestingly the malignancy is more common in the second decade [15].

In Our series according to clinical features of patients Swelling of the thyroid region was present in all cases. The next most common symptom was pain in 8% of the cases. Only one patient presented with hoarseness of voice, 4 cases with dyspnea and 2 cases with palpable lymph node. On examination the only finding was hard consistency in 4 cases. findings on local examination were not very specific to relate for malignancy, except for cases with lymphadenopathy and hardness which was later found to harbor malignancy by histopathological diagnosis.

Manmadha et al, All the patients had swelling and only single palpable nodule. Toxic symptoms were present in 2 patients. Clinical evidence of obstruction to airway or of the great veins of neck by a solitary thyroid nodule is rare. The presence of stridor, respiratory wheeze; engorgement of neck veins should be interpreted with caution and the possible existence of a

second pathology within the mediastinum or lungs should be considered while hoarseness of voice was present, only in one patient. On examination the only finding was hard consistency in 4 cases. In this study, 2 patients had regional lymph node enlargement, which on FNAC proved to be secondary deposits from papillary carcinoma. 14 patients had difficulty in swallowing and 6 patients, pain over the swelling, 3 patients had difficulty in breathing, which was mostly uncharacteristic, neither Exertional nor positional.

Clinical features such as nodule size and rapid growth rate giving rise to compression symptoms are also associated with an increased risk [16].

In Our series Preoperative neck ultrasound findings include the increased vascularity and the irregular nodule margins, and to a lesser extent the microcalcification, hypoechoic nodule echogenicity in most malignant cases. This means that ultrasound is indicator for malignancy in STNs.

Mohamed et al, findings include the increased vascularity and the irregular nodule margins, and to a lesser extent the microcalcification, hypoechoic nodule echogenicity, and being taller than wider. Similar results were reported by other studies.

Papini et al. evaluated the relative risk of malignancy of the main US features and showed that the presence of microcalcifications presented a higher specificity for malignancy [17]. Absent halo combined with the presence of spot microcalcifications and/or hypoechoic nodule echogenicity were the most predictive of malignancy (sensitivity 60% and specificity 93.5%) [18].

Hypoechoic STNs with irregular margins and microcalcifications increased the probability of malignancies [18]. Nodule vascularity has also been proposed to be of a diagnostic value, but many authors question this proposal [19]. Solid composition, central vascularity, greater

stiffness, and taller greater than wider in a transverse dimension are US characteristics having predictive value for malignancy on a lesser scale [20].

Workup of patients with STNs includes both US and FNA. Information obtained on the US includes tumor size, presence of solid versus cystic components, nodule definition, and calcifications [21].

US-detected calcifications were found to be a significant independent cancer predictor [22]. Taking individual risk factors in isolation and applying their risk of malignancy to patients is not always reliable [23].

A strong association is of note between calcifications and thyroid malignancy, particularly in patients with STNs [1]. Patients younger than 45 who have calcified STNs constitute a high-risk group, with a probability of harboring thyroid malignancy [24].

In Our series accuracy rate of FNAC with histopathology as gold standard. The sensitivity of FNAC was found to be 94%. FNAC showed that majority had follicular neoplasm followed by nodular goiter. No cases of MTC or Hurthle cell carcinoma were reported in our series.

Manmadha et al, Fine needle aspiration cytology represents a reliable method of providing a tissue diagnosis and is the investigation of choice for solitary thyroid nodule. In this study FNAC was a very dependable and an easy investigation without complications. It is the gold standard test for evaluating thyroid nodules mostly due to simplicity and easy availability of the tests. Amongst the FNAC reports, follicular neoplasm was the commonest to be reported with the inability to identify vascular/capsular invasion. Adenomatous goiter, presenting as a solitary nodule was next commonest eventuality. 4 cases were reported as papillary carcinoma with two of them showing deposits in the neck nodes. No report was possible in 5 cases. Total benign cases on FNAC were 66 accounting to a percentage of 88%. And total number of

malignant cases was 4 with a percentage of 5.33%. Similar findings were reported by Ashcraft et al and Campbell et al. [25].

Mohamed et al, that its sensitivity is 100% (no false negative cases), whereas its specificity is 54% (high false-positive cases). Which not similar for our study.

FNA is considered to be the most accurate, sensitive, specific, and cost-effective diagnostic tool in the preoperative evaluation of STNs [26].

In Our series the histopathological report. Follicular adenoma was the most common histopathological finding in 50% of the cases. Malignancy was reported in 14% of the cases. 8 cases were diagnosed preoperatively and were offered the confirmative treatment the rest 6 cases were diagnosed only on HPE reporting.

Manmadha et al, all resected specimens were submitted for histopathological examination. Histology proven malignancy in this series of study of solitary thyroid nodule is 11.4%, of which 75% (6 cases) were of papillary carcinoma and the rest 25% (2 cases) were of follicular carcinoma types.

Mohamed et al, it was found that the strongest independent factor in the study was the 'No halo and irregular Margin' in U/S, and that microcalcifications, hypoechoic, and taller nodules were highly suspicious factors for malignancy.

Genetic and/or environmental factors, such as living in an endemic goiter region and variations in iodine exposure, may affect thyroid cancer rates [27].

The increasing prevalence of thyroid cancer worldwide is partly attributed to increased detection by advanced diagnostic techniques [13]. In a study of 300 patients, 46.2% of STNs were malignant compared to 22.5% of MNGs. This was not the case in several other studies [15].

## 5. Conclusion

The utmost clinical importance of a solitary thyroid nodule is the exclusion of malignancy. STNs are fairly common lesions, frequently detected by modern imaging methods (mainly ultrasonography). These data substantively expand our un-worsening knowledge of STNs in adults by showing that advancing age increases the risk of thyroid nodule formation. The combination of FNA with clinical and US parameters may improve the diagnostic definition of palpable STNs. US has a sensitivity and specificity of 100% and 95% respectively, while FNAC has sensitivity, specificity, diagnostic accuracy, and positive predictive value of 94%, 99%, 99.2%, and 88.9% respectively. It is concluded from the present series that 12% of STNs are malignant, with female preponderance and a mean age of STN is 31-40 years. US findings should be the primary criterion used to decide the management of asymptomatic STNs. STNs and MNGs carry almost the same risk of thyroid malignancy.

FNAC is the gold standard for evaluation of solitary thyroid nodules with an accuracy of 94% in our study. Females are more commonly affected than males. 14% of solitary thyroid nodules were malignant. Suspect malignancy at extremes of age. Operative procedures in treatment of solitary thyroid nodule are justified, as they provide the specimen for correct diagnosis. high incidence of malignancy within clinically detected STN and the presence of the following factors increases the incidence of malignancy: microcalcification, ultrasonography showing solid echogenicity, and lymphadenopathy detected either clinically or by U/S. Therefore, we highly recommend treating STN with high degree of suspicion, and the patient should undergo further investigations by U/S and FNAC.

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