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Frequency of Thyroid Cancer in Sonographically and Clinically Isolated Thyroid Nodules in Thyroidectomy Patients

Dr. Mohammad Omar Farook[1*], Dr. Mohammad Jamal Hussain[2], Dr. Kazi Shah Alam[3]

[1]Senior Consultant (ENT), General Hospital, Rangamati, Bangladesh
[2]Associate Professor and Head, Department of ENT & Head- Neck surgery, Rangamati Medical College, Bangladesh
[3]Associate Professor, Department of ENT, National Institute of ENT, Dhaka, Bangladesh

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***Corresponding author:** Dr. Mohammad Omar Farook
Senior Consultant (ENT), General Hospital, Rangamati, Bangladesh

Abstract **Original Research Article**

***Background*:** Thyroid nodules are common in areas with low iodine levels, in women, and in patients undergoing neck irradiation. Thyroid nodules can be detected and evaluated using high-resolution ultrasonography (US). US are used to assess the size and characteristics of thyroid nodules, as well as the presence of lymph node metastasis in the neck. It also makes guided fine-needle aspiration possible (US-FNA). ***Methods*:** A prospective cross-sectional study carried out at General Hospital, Rangamati during the period from January 2021 to January 2022. Total 87 patients include who were clinically and sonographycally diagnosed as solitary thyroid nodule. Nodules were excluded from this part of the study if images were not available for review. All the patients treated surgically, and histopathological examination carried out. Data were analyzed by standard statistical methods. Results were analyzed by proper test of significance. ***Results*:** Females predominated at 64(73.6%), 50(57.5%) had solitary nodules, 79(90.8%) were euthyroid, 29(33.3%) had nodules measuring 1.0-1.9 cm, 13(14.9%) were malignant, and 53(60.9%) underwent hemi-throidectomy. Calcification and intranodular vascularity in ultrasonography findings were statistically significant ($p < 0.05$). Thyroid activity 100% of euthyroid tumors were malignant, while 66 (89.2%) were benign. ***Conclusion*:** The incidence of thyroid cancer was discovered to be 14.9% using sonography. Thyroid nodule size has a nonlinear effect on cancer risk. A 2.0 cm threshold is detected, after which cancer risk remains unchanged. All of the euthyroid tumors were malignant.

Keywords: Thyroid nodules, euthyroid, ultrasonography, nodule size, malignant.

INTRODUCTION

Thyroid nodules are found in 50-65% of healthy people, with the majority being asymptomatic and discovered by chance [1]. The vast majority are benign and do not require treatment, with less than 5% being malignant [1]. Thyroid nodules are more common in areas with low iodine levels, in women, and in patients undergoing neck irradiation. A thyroid nodule can cause compressive symptoms or hyperthyroidism in rare cases, necessitating treatment [1]. One way to describe the single thyroid nodule is as an isolated growth within of a normally impalpable gland. The patient frequently discovers the enlargement by accident, or a family member, acquaintance, or neighbor calls her attention to it. The nodule may also be encountered as an incidental finding when a patient is examined for some unrelated disease. About 70% of discrete thyroid swellings are clinically isolated. A nodule may be adenoma, cyst, multinodular goitre, thyroiditis or thyroid carcinoma [2].

These small nodules are increasingly detected by neck ultrasound and parallel the rising incidence of small differentiated thyroid cancer over the last two decades [3]. The rate of detection of thyroid nodules and carcinomas has increased with the widespread use of ultrasonography (US), which is the mainstay for the detection and risk stratification of thyroid nodules as well as for providing guidance for their biopsy and nonsurgical treatment [4]. Palpable thyroid nodules occur in about 6% of women and 2% of men with higher prevalence in the elderly and iodine-deficient areas. However, the great majority of thyroid nodules are impalpable and asymptomatic with an estimated prevalence of 20–76% in the general population [5]. Differentiated thyroid carcinoma (DTC), a malignant proliferation of the follicular cells of the thyroid gland, accounts for 90% of all thyroid cancers and is

increasing threefold each decade [6] to become the fourth most common malignancy by 2030 [7]. Despite its high prevalence among endocrine malignancies, it has an excellent prognosis (survival rate at 10 years of 80–95%) and a high chance of definitive cure [8].

Inclusion of thyroid ultrasound in the routine diagnostic workup greatly increased the number of thyroid nodules detected [9, 10]. According to epidemiological studies, a prevalence of up to 65% of the adult population can be expected [11]. If we base the rate of malignancy (ROM) of these nodules on data from current guidelines, between 7 and 15% of the nodules bear a malignancy) [12, 13].

Thyroid ultrasonography (USG) is the most reliable method for detecting thyroid nodules, and with the advances in imaging methods, it is being used more frequently in patients with GD. Nodular lesions may be found in GD with thyroid USG in the preoperative period [14].

As recently highlighted in several studies, the diagnosis of a thyroid nodule frequently causes great distress in patients due to a fear of malignancy [15]. Despite guidelines' recommendations to discharge patients with a low suspicion of malignancy, many of their attending physicians share the patients' concerns about the dignity of their thyroid nodule(s).

MATERIALS AND METHODS

Simple random sampling of prospective cross-sectional study was done. The study was carried out at General Hospital, Rangamati during the period from January 2021 to January 2022. This study includes 87 patients admitted with clinically and sonographycally diagnosed as solitary thyroid nodule. Nodules were excluded from this part of the study if images were not available for review. All patients underwent thyroid sonography as part of their evaluation, and those patients with one or more thyroid nodules larger than 1 cm diameter who had ultrasound-guided FNA are the subject of this report. Patients whose serum TSH was normal or elevated were advised to have ultrasound-guided FNA of all nodules larger than 1 cm in maximal diameter. If the serum TSH was less than 0.5 μU/ml, patients had thyroid scintigraphy to identify autonomously functioning nodules, which were not aspirated. Calcitonin measurements were not routinely performed. Thyroid ultrasonography was performed by one of three radiologists, each with special expertise in thyroid sonography, using a 5- to 15-MHz transducer. For each nodule, the following sonographic characteristics were recorded: size, parenchymal composition, echogenicity, presence or absence of a halo, margin appearance, presence or absence of calcifications, type of calcifications, and presence or absence of other nodules larger than 1 cm in the gland. Size was recorded as three orthogonal dimensions. All the patients treated surgically, and histopathological examination carried out. Data were analyzed by standard statistical methods. Results were analyzed by proper test of significance.

Data Analysis

The study coordinators performed random checks to verify data collection processes. Completed data forms were reviewed, edited, and processed for computer data entry. Frequencies, percentages were used for descriptive analysis. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0.

RESULTS

Almost two third (65.5%) patients belonged to age <45 years, 64(73.6%) were female, 50(57.5%) had solitary nodules, 79(90.8%) were euthyroid, 29(33.3%) was nodules size 1.0-1.9 cm, 13(14.9%) were malignant and 53(60.9%) was operation performed by hemi-throidectomy (Table 1). In ultrasound findings, calcification and intranodular vascularity were statistically significantly ($p<0.05$) but number of nodules, consistency, echogenicity and margins were not statistically significantly ($p>0.05$) between malignant and benign nodules (Table 2). Table 3 shows the pathological diagnosis of the 87 patients with thyroid nodules included in the study. The results show that 13 out of 87 nodules (14.9%) were diagnosed as malignant, including anaplastic, follicular, medullary, and papillary carcinomas. Papillary carcinoma was the most common malignant diagnosis, accounting for 9.2% of all nodules. The majority of the nodules (74 out of 87, 85.1%) were diagnosed as benign, including different types of adenomas, cystadenomas, granulomatous thyroiditis, and nodular hyperplasia. Follicular adenoma was the most common benign diagnosis, accounting for 42.5% of all nodules (Table 3). Age, sex, number of nodules, thyroid function and size of nodules were not statistically significantly ($p>0.05$) between malignant and benign nodules (Table 4). Age, sex, number of nodules and type of malignant were not statistically significantly ($p>0.05$) between two groups (Table 5).

Table 1: Demographic characteristics of the study patients (n=87)

Demographic characteristics	Number	Percentage
Age (years)		
<45	57	65.5
≥45	30	34.5
Sex		
Female	64	73.6

Demographic characteristics	Number	Percentage
Male	23	26.4
Number of nodules		
Solitary	50	57.5
Multiple	37	42.5
Thyroid function		
Euthyroid	79	90.8
Hyperthyroid	6	6.9
Hypothyroid	2	2.3
Size of nodules (cm)		
1.0-1.9	29	33.3
2.0-2.9	26	29.9
3.0-3.9	19	21.8
≥4	13	14.9
Diagnosis		
Benign	74	85.1
Malignant	13	14.9
Type of operation		
Total throidectomy	23	26.4
Near total	2	2.3
Subtotal	9	10.3
Hemi-throidectomy	53	60.9

Table 2: Ultrasound features in malignant and benign nodules (n=87)

Ultrasound findings		Malignant(n=13)	Benign(n=74)	Total	P value
Number of nodules	Solitary	10	40	50	0.124
	Multiple	3	34	37	
Consistency	Solid	8	25	33	0.147
	Cystic	1	16	17	
	Mixed	4	33	37	
Echogenicity	Hypo	10	35	45	0.118
	Hyper	2	16	18	
	Iso	1	23	24	
Margins	Well defined	8	56	64	0.286
	Ill defined	5	18	23	
Calcification	Macro	4	67	71	0.001
	Micro	9	7	16	
Intranodular Vascularity	Present	5	10	15	0.028
	Absent	8	64	72	

Table 3: Pathological diagnosis of the studied patients (n=87)

Pathological diagnosis	Number	Percentage
Malignant		
Anaplastic carcinoma	1	1.1
Follicular carcinoma	2	2.3
Medullary carcinoma	2	2.3
Papillary carcinoma	8	9.2
Benign		
Atypical adenoma	1	1.1
Cystadenoma	2	2.3
Follicular adenoma	37	42.5
Follicular cystadenoma	2	2.3
Hurthle cell adenoma	1	1.1
Granulomatous thyroiditis	1	1.1
Nodular hyperplasia	27	31.0
Papillary adenoma	3	3.4

Table 4: Comparison between pathological diagnosis with clinical characteristics (N=87)

Variables	Malignant (n=13)	Benign(n=74)	P value
Age			
<45	6 (46.2%)	51 (68.9%)	0.111
≥45	7 (53.8%)	23 (31.1%)	
Sex			
Female	10 (76.9%)	54 (73.0%)	0.766
Male	3 (23.1%)	20 (27.0%)	
Number of nodules			
Solitary	5 (38.5%)	45 (60.8%)	0.075
Multiple	8 (61.5%)	29 (39.2%)	
Thyroid function			
Euthyroid	13 (100.0%)	66 (89.2%)	
Hyperthyroid	0 (0.0%)	6 (8.1%)	0.461
Hypothyroid	0 (0.0%)	2 (2.7%)	
Size of nodules (cm)			
1.0-1.9	4 (30.8%)	25 (33.8%)	
2.0-2.9	3 (23.1%)	23 (31.1%)	
3.0-3.9	3 (23.1%)	16 (21.6%)	0.812
≥4	3 (23.1%)	10 (13.5%)	

Table 5: Size of thyroid nodules with clinical characteristics in malignant patients (N=13)

Variables	Size of nodules <2.0 cm (n=4)	Size of nodules ≥2.0 cm (n=9)	P value
Age			
<45	2 (50.0%)	4 (44.4%)	0.853
≥45	2 (50.0%)	5 (55.6%)	
Sex			
Female	3 (75.0%)	7 (77.8%)	0.913
Male	1 (25.0%)	2 (22.2%)	
Number of nodules			
Solitary	2 (50.0%)	3 (33.3%)	0.569
Multiple	2 (50.0%)	6 (66.7%)	
Type of malignant			
Anaplastic carcinoma	0 (0.0%)	1 (11.1%)	
Follicular carcinoma	0 (0.0%)	2 (22.2%)	0.307
Medullary carcinoma	0 (0.0%)	2 (22.2%)	
Papillary carcinoma	4 (100.0%)	4 (44.4%)	

DISCUSSION

In this study showed that almost two third (65.5%) patients belonged to age <45 years, 64(73.6%) were female, 50(57.5%) had solitary nodules, 79(90.8%) were euthyroid, 29(33.3%) was nodules size 1.0-1.9 cm, 13(14.9%) were malignant and 53(60.9%) was operation performed by hemi-throidectomy. El-Gammal *et al.,* [4] demographic characteristics of 87 patients with thyroid nodules were aged less than 45 years and most of them were women. More than half of the patients had solitary nodules with normal function.in terms of thyroid function, majority were euthyroid which is 90.91%. About 28.18% of the patients had nodular sizes less than or equal to 4 cm. The prevalence of cancer was 15.45% in this study. Total thyroidectomy was the most common surgical operation performed which is 60.91% followed by hemi thyroidectomy. In addition, high-resolution ultrasound can detect thyroid nodules in 19–67% of randomly selected individuals with higher frequency in women and the elderly [16. The increase in the use of thyroid ultrasound imaging by radiologists, endocrinologists, and head and neck surgeons has led to the discovery of large numbers of asymptomatic thyroid nodules, which may occur in 50% or more of adults [17], as well as a rapid increase in the diagnosis of thyroid cancer. Reynolds *et al.,* [18] reported that thyroid cancer was more common in older age groups than in younger age groups. Chen *et al.,* [19] reported that thyroid cancer was common among the age group of less than 45 years. A recent study reported similar data with a high incidence of malignancy in women [20]. On the other hand; Paul *et al.,* [21] reported that the incidence of malignancy is higher in men. Rashid *et al.,* majority (90.42%) case was operation by hemi-throidectomy followed by subtotal thyroidectomy was 5(2.65%) and total thyroidectomy was 13(6.91%).

In ultrasound findings, Calcification and intranodular vascularity were statistically significantly

(p<0.05) but number of nodules, consistency, echogenicity and margins were not statistically significantly (p>0.05) between malignant and benign nodules. El-Gammal *et al.,* [4] ultrasonographic criteria of benign and malignant nodules there were statistically significant ultrasound data predicting malignancy in thyroid nodules such as microcalcification (*P* = 0.002), ill-defined edges (*P* = 0.0003), increased intranodular vascularity (*P* = 0.0008), size below 2 cm (*P* = 0.0063), solid consistency (*P* = 0.002), and hypoechogenicity (*P* = 0.004).

In this study observed age, sex, number of nodules, thyroid function and size of nodules were not statistically significantly (p>0.05) between malignant and benign nodules. El-Gammal *et al.,* [4] reported that the prevalence of cancer among female patients aged greater than or equal to 45 years had bilateral nodules with normal function. As regards nodular sizes, the cases with a nodular size of 1.0–1.9 cm were more prevalent among cancer patients than in benign cases. All cancer cases had euthyroid after adjusting for confounding factors; the size of the nodules (1.0–1.9 cm) and age were still predictors of cancer in the studied cases. Nodular size had 2.5 times prediction of cancer while age had about 0.5 times. Witczak *et al.,* [20] reported that there was no statistically significant difference between patients with benign diseases than those with malignant diseases regarding different age groups. In a recent study published by Jaheen and Sakr [21] that has been no significant difference between both sexes regarding the incidence of malignancy. Moreover, Jang *et al.,* [22] found no statistically significant difference in the incidence of thyroid malignancy between men and women. The size of the nodule up to 2 cm was statistically significant in predicting cancer and beyond 2 cm there is no significant increase in the percentage of malignancy. Also, thyroid nodules 1.0–1.9 cm in diameter provided baseline cancer risk for comparison (29.4% risk of cancer). The overall prevalence of cancer in nodules 2.0–2.9 cm was 23.5%; in nodules 3.0–3.9 cm, 23.5%; and in nodules 4.0 cm, 23.5%. This was statistically significant (P = 0.032). Kamran *et al.,* [23] reported that greater nodule size influences cancer risk, although the increase in absolute risk between small (1.0–1.9 cm) and large (4.0 cm) nodules is modest. Notably, a threshold effect is detected at ∼2.0 cm in nodule diameter. Thereafter, larger nodule size imparts no further malignant risk, even if 4.0 cm or larger [23]. Kuru *et al.,* [24] reported that nodule size greater than or equal to 4 cm was an independent factor associated with malignancy. Carrillo *et al.,* [25] reported that nodules greater than or equal to 4 cm were significantly more likely to contain malignancy. On the other hand, Albuja-Cruz *et al.,* [26] reported that a nodule size greater than or equal to 4 cm is not associated with a higher prevalence of malignancy overall. Cavallo *et al.,* [27] reported that the risk of malignancy is inversely related to the nodule size.

In present study observed age, sex, number of nodules and type of malignant were not statistically significantly (p>0.05) between two groups. El-Gammal *et al.,* [4] there were no significant relationships between nodular size with age, sex, or numbers of nodules. On the other hand, there were significant relationship between nodular size and types of cancers, where all cancer cases having a nodular size of 1.0–1.9 cm were diagnosed as papillary carcinoma while papillary carcinoma constituted about 58.3% of cancer cases having larger sizes (≥2 cm). Frates *et al.,* [28] reported that the incidence of malignancy in solitary thyroid nodules is higher than that of multinodular goiter (P = 0.01). Kamran *et al.,* [23] reported that increasing nodule size was associated with a lower proportion of papillary carcinomas (P < 0.01). Rashid *et al.,* [2] reported 100% malignant thyroid nodules are papillary carcinoma.

CONCLUSION

In conclusion, sonographically, the incidence of thyroid cancer was found to be 14.9%. The size of a thyroid nodule has a nonlinear effect on cancer risk. A threshold of 2.0 cm is detected, beyond which cancer risk remains unchanged.

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