ORIGINAL ARTICLE

The Prevalence of Subclinical Thyroid Nodules Diagnosed by Ultrasound in Asymptomatic Iranian Population

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ABSTRACT

Background: Different diagnostic methods have estimated different prevalence rates for thyroid nodules. Ultrasonography is a useful imaging method for evaluating thyroid gland.
Aim: To evaluate the prevalence of subclinical thyroid nodules in an Iranian population by ultrasound method.
Methods: This study performed from December2017 to May2018 on 103 patients attended to the Radiology Departments. All patients underwent an ultrasound screening of thyroid gland(GEE6 model device with 7-12 MHz probe).A checklist ofdemographic data and nodule's characteristics including number, size, shape, echogenicity, vascularity, calcification and cystic changes was recorded. Patients with palpable thyroid nodules, patients with known thyroid problems and those who referred for thyroid ultrasonography, were excluded from the study.
Results: The number of patients with subclinical thyroid nodulesformed 17.48% of the studied population. Thyroid nodules were detected in 21.54% of women and 10.53% of men.Moreover, 60% of subclinical thyroid noduleswere unilateral and 35% were bilateral. The mean number of subclinical thyroid nodulesdetected in patients was 3.39±2.93.There was no significant difference between the mean number of patients with cystic changes in their subclinical thyroid nodulesand patients without any cystic changes in their nodules.
Conclusion: The prevalence of subclinical thyroid nodulesin the studied population was lower than the similar studies. More studies with bigger sample size is recommended.
Keywords: Thyroid, thyroid nodule, ultrasound

INTRODUCTION

Thyroid nodule is one of the most common diseases of the thyroid gland. It is designated as an abnormal growth of thyroid cells which is found as a lump within the gland. Palpation is the most usable screening method for detecting thyroid nodules. The prevalence of palpable thyroid nodules is different all over the world and it is about 4-7% in the global population.Detection of thyroid nodules by palpitation depends on various factors such as size and location of the nodule and the anatomy of neck. Thyroid nodules may be undetectable by palpatation, especially when their diameter isless than 1 cm[(1,2)]. However palpation remains the most common screening method to detect thyroid nodules. technical Progression has increased the validity and sensitivity ratein many methods of imaging that detect subclinical nodules in organs like adrenal, pituitary and thyroid glands[(3,4)].

Ultrasonography is a useful imaging method for evaluating thyroid gland.Ithas an important role in the detection of subclinical thyroid nodules, which are unpalpable during physical examination. The term subclinical thyroid nodules(STNs) defines as the presence of newly diagnosed focal thyroid mass lesions seen on imaging such as ultrasound, computed tomography, magnetic resonance imaging and the more advanced positron emission tomography. Ultrasonography is the gold standard for study of thyroid nodules[(1)].

Most of thyroid nodules are benign and less than 5% are malignant[(5,6)]. The ultrasound method can diagnose one or more nodules in 19-46 percent of general population with clinically normal thyroid, especially in people over 50 years old[(3,7–9)].

Fifty percent of detected thyroid nodules by sonography cannot be palpated on physical examination, but they have the same risk of malignancy as palpable nodules.The risk of malignancy in these nodules is about 1.5–10%[(9,10)].

Since iodine deficiency is endemic in Iran, this study was designed to evaluate the prevalence of STNs in asymptomatic Iranian subjects using high-resolution ultrasonography.

MATERIALS AND METHODS

Studied population: This cross-sectional study was done from December 2017 to May 2018, on patients attended to the Radiology Departments of our two university teaching hospitals in Khuzestan Province-Iran for a purpose other than ultrasonography of thyroid gland. The samples were selected randomly.
Ethical consideration: This study was approved by the Ethics Committee of the Ahwaz Jundishapur University of Medical Sciences (Moral Code: IR.AJUMS.REC.1397.378). The aim of the study was explained for all the samples and informed consent was gathered from all of them.Patient were advised that they could exit the study whenever they wished.
Practical methods: All of the patients underwent an ultrasound screening of thyroid gland (GEE6 model device with 7-12 MHz probe).A checklist of demographic data and nodule's characteristics including number, size, shape, echogenicity (based on Hypoechoic, Hyperechoic, and Isoechoic states), vascularity, micro-calcification, and cystic changes was designed. The checklist was completed and registered for each patient by the researcher. Patients had

access to the doctor at any time of the study. Inclusion criteria included patients aged more than 16 years who attended to the Radiology Departments for Ultrasound scans for a purpose other than that of Thyroid gland. Exclusion criteriaincluded patients with palpable thyroid nodules in physical examination, patients with known thyroid problems and diseases and patients referred for doing thyroid ultrasonography.

Statistical analysis: For data analysis, mean and standard deviation were used in quantitative variables and frequency and percentage in qualitative ones. Chi-square test and t-test were used to compare the frequency of variables and their means. All analyses were performed using the SPSS version 22. Statistical significance was set at p-value less than 0.05.

RESULTS

The mean age of the studied samples was 36.81±15.583 (range 15-88) years old. The patient's demographic information can be seen in Table 1.

The number of female patients was significantly higher than males (P<0.05) and the number of patientswith STNs was significantly lower than healthy ones (P <0.05).

Additionally, most of the patients were hospitalized in different parts of the hospitals and the number of these patients was significantly more than those who were referred to the hospital'sradiology departments as outpatients (P<0.05).

The mean age of patients with STNs was 41.5±18.912 years old and there was no significant differencebetween the mean age ofnormalsubjects and those with STNs.Furthermore, there was no significant difference between the mean age of subjects based on their gender (Table 2). The number of patients with the diagnosis of STNs was determined based on age groups, that showed the higher frequency of patients aged 25-35 years old (38.89%).

The prevalence ofSTNsin women was significantly higher than men. STNs were detected in 21.54% of women, and 10.53% of men. It should be noted that the number of patient without STNs was higher in both sex(P< 0.0001)(Table 3). There was a significant difference between the locations of STNs in the studied patients, so that the right and bilateral lobes were the most common locations of STNs (Table 3).

The number of patients with STNsand the O and Ablood types was more than patients with other types of blood group, but no significant difference was found between the prevalence of STNsand types of blood group (P= 0.22). However there was a significant difference between types of Rh in patients with STNs, that indicates more prevalence of patients with negative type of Rh.

Although the mean number of STNsin the right lobe was higher than other areas, there was no significant difference between the mean numbers of STNs in the three areas studied. Additionally, the mean number of STNsdiagnosed in patients was 3.39±2.93. The diameter of each nodule was also recorded for each patient, and in assessments for patients with more than one nodule, if the sizes of the nodules were close (difference wasbetween 1 to 2 millimeters), their mean size was considered. If the difference of the nodules's size was more than 3 mm, the largest nodule was considered as the size of the patient's nodule;therefore the mean diameter of STNsin the patients was 7.50±3.254mm.

The number of patients with well-defined border nodules (14 patients) and ill-defined border nodules (4 patients)were significantly different (P<0.0001). The mean size of noodules with ill defined border was higher than the nodules with well defined border, but there was no significant difference between the mean sizes of nodules in both groups.

There was no significant difference in the mean number of patients with cystic changes intheir STNs compare to the patients without any cystic change. There was only one patient withmicro-calcificationsin his STNs, and in the rest of the cases, this complication was not reported. There was a significant difference between the echogenicity of STNsbased on Hypoechoic, Hyperechoic, and Isoechoic states. The frequency of STNswithHypo echogenicity was significantly higher than Hyper and Iso echogenicity.

The frequency of thyroid nodules with vascularity was significantly lower than non-vascular nodules. In addition, vascular patternin all ofthem was peripheral type (Table 4).

In the group of patients with STNs, people with history of radiotherapy or exposing to ionizing radiations and positive familial history of thyroid disease were significantly less than those with negative records. Additionally, in patients with noSTNs, those with a history of radiation exposure and positive familial history of thyroid disease were significantly less than those with negative records (P<0.05).

Table 1. Patient's demographic information

Variable			Number	Percent	P-value
Gender	Female		65	63.11%	<0.0001*
	Male		38	36.89%	
Blood Groups	A		36	34.95%	0.85
	B		24	23.30%	
	AB		18	17.48%	
	O		25	24.27%	
	Rh	+	85	82.52%	<0.0001*
		-	18	17.48%	
Existence of nodule	Yes		18	17.48%	<0.0001*
	No		85	82.52%	
Admission status	Hospitalized		93	90.29	<0.0001*
	Outpatient		10	9.71	

Table 2. The mean age of studied population based on gender and samples status

Age		Mean±SD	P-value
According to Gender	Male	39.75±18.822	0.681
	Female	42.0±19.616	
Sample status	With STN	41.50±18.912	0.162
	Without STN	35.86±14.649	

STN= Subclinical Thyroid Nodule

Table 3. Prevalence of STNs based on gender and location

Prevalence		Number	Percent	P-value
According to Gender	Male	4	22.22%	< 0.0001*
	Female	14	77.78%	
Female	With STN	14	21.54%	< 0.0001*
	Without STN	51	78.46%	
Male	With STN	4	10.53%	< 0.0001*
	Without STN	34	89.47%	
According to Location of STN	Right lobe	8	40%	0.041
	Left lobe	4	20%	
	Bilateral	7	35%	
	Isthmus	1	5%	

STN= Subclinical Thyroid Nodule

Table 4. The prevalence of cystic changes, echogenicity, micro-calcification and vascularity

Variable		Number	Percent	P-value
Cystic Changes	Yes	8	44.44%	0.98
	No	10	55.56%	
Existence of micro calcification	Yes	1	5.56%	<0.0001
	No	17	94.44%	
Echogenicity	Hypoechoic nodule	12	66.67%	0.008*
	Hyperechoic nodule	3	16.66%	
	Isoechoic nodule	3	16.66%	
Existence of vascularity	Yes	4	22.22%	<0.0001*
	No	14	77.78%	

DISCUSSION

The number of patients with STNs was significantly lower than healthy subjects and it was 17.48% of the subjects participated. A study conducted by Rad et al. revealed an incidence of 19.6% of STNs[11] and another study done by Tomimori et al., reported STNs in 17% of patients, which were in line with the incidence of STNs in our study (17.48%)[12]

Steele et al. reported that STNs were seen in 9.4% of their patients[13].In the study by Karaszewski et al., the prevalence of STNs detected by ultrasonography was reported 14.8%[14]. Min and his colleagues noted positive STNs findings in 13.4% of Korean population[15]. Carroll reported thatSTNswas found in 13% of patients who had been referred for carotid ultrasonography[16].

Many other studies indicated slightly higher prevalence of STNs ranging from 21 up to 28.3%[5,17–20].

SaneiTaheri and his colleagues conducted a study from september2005 to may2006 in Iran. They reported the prevalence of 52.5% of STNs in their patients[21], which is significantly higher than our result. We think that despite the superiority of number of patients they had studied, this difference may be due to the fact that iodine deficiency has beendecreasing since the five nation-wide surveys were performed in Iran from 1990[22].

In a study done by Guth et al, in Germany they reported 68% prevalence of STNs[23].In another study performed by Ezzat et al., the prevalence of STNs detected by ultrasonography was reported 67%[7].The variability of these studies may be due to several factors such as differences in iodine intake in populations, age and sex of the population examined, inclusion in the study of subjects with known thyroid disease, size of the thyroid lesions considered to be a nodule and technology that has been used(operator, probe frequency). other possible reasons could be Genetic and demographic factors.

There was a significant difference between the number of male and female patients participating in the study, with the females significantly more than the males. Among the patients with STNs, 78.78% were female. Our result was in line with many studies[7,13,14,18,21]. The prevalence of STNs was significantly higher in females (21.54%), than males (10.53%). This has been also reported by studies done by T. Rago et al. in Italy, Olusola Bella et al. in Nigeria, Kamran et al. in Pakistan and Mohammadi et al. in Iran[5,17,19,24]. It is known that the prevalence of STNs in females is four times more than that of males[25], this might also explain the increase in prevalence of STNs in our female patients.

According to the results, the mean age of patients with STNs was 41.5 ± 18.912 years old. There were no significant differences between mean age of patients according to their gender. In the present study, although the mean age in patients with STNs was higher than the normal group, this difference was not statistically significant. Our results were in keeping with the the results of observation conducted by Sanei et al., they noted that there was no difference between the mean age of patients with and without nodule, they also reported that regarding the prevalence of nodules, there was not any difference

between the patients aged less and higher than 60 years [21].However many previous studies reported that the incidence of STNs increases with age[13,14,19,23,26].

There was a significant difference between the locations of STNs. As the right lobe and bilateral were, respectively, the most prevalent sites. This result was in line with the previous reports[17,19,20,27].It might be because of the native size-difference between right and left lobes of thyroid gland, that the right lobe was supposed to be 1.2 folds larger than the left[20,28,29]. In total, 60% of STNs were unilateral and 35% were bilateral which is on apar with many previous studies[13,18,21]. According to the results, although the mean number of STNs in the right lobe was higher than other areas, there was no significant difference between the mean number of nodules in the three areas studied. Furthermore, the mean number of STNs detected in patients was 3.39±2.93.

There was a significant difference between the number of patients with well defined border nodules and those with ill defined border nodules. the number of nodules with well defined border were significantly higher than ill defined border nodules. Additionally, although the mean size of STNs was higher in ill defined border group, it had no statistically significant difference with the group of nodules with well defined border. Our results was in line with the study conducted by Sudhir et al. in UAE which reported that out of 15 patients with STNs, eleven had well-defined border while ill-defined bordes were found in four patients[18].

Out of 18 patients with STNs in our study, 8 patients had STNs with cystic changes(44.44%). There was no significant difference between the mean number of patients with and without cystic changes in their STNs. There are many studies in line with our results[19,20,25,30].Inconsistent with the results of the study, Olusola Bella et al., reported that most of the nodules detected in their patients were cystic[19]. Sudhir et al. noted that among their patients, ten (31.25%) were reported to have solid nodules whereas two (6.25%) of them were having cystic nodules[18].

Among the patients with STNs, there was only one case with micro-calcification (5.55%), and in the rest of the cases, this complication was not reported. Boniface et al. reported two cases with micro-calcifications(1.58%)[20]. Sudhir et al. noted that micro-calcification had been found in the ultrasound of 5 patients(15.6%)[18]

There was a significant difference between the echogenicity of STNs, so that the frequency of hypoechoic nodules(66.67%) was significantly higher than Hyperechoic (16.66%) and Isoechic ones(16.66%). In the study done by Saneei et al., they noted that 73.3% had Hypoechoic and 23.7% had Hyperechoic nodules[21].Rago et al. reported that a diffuse thyroid hypoechogenicity was found in 12 patients, they noted that all of them had circulating thyroid autoantibodies positive test and also 5 of them had overt or subclinical hypothyroidism[5].Sudhir et al.stated that in their study, 50% of patients had hypoechoic nodules while 12.5% had hyperechoic nodules[18]. Also Rad and his colleagues reported in their study that 32% of nodules they've found were hypoechoic and 16% were hyperechoic[11].Results of these studies were in line with ours. However there were studies that found a predominance of isoechoic or hyperechoic nodules too[24,27,30,31,32].

The existence of vascularity in STNs (4 cases) was significantly lower than those with non-existence of vascularity. in addition, vascular pattern in each of these 4 cases was peripheral type.

although the number of patients with STNsand the O and A blood types was more than the other types of blood group, but no significant difference was found between the prevalence of STNs in different types of blood group. however, there was a significant difference between types of Rh in patients with STNs, that indicates more prevalence of patients with negative type of Rh.

CONCLUSION

According to the resultsthe prevalence of STNs is 17.48%.The prevalence of STNs in women was significantly higher than men. The prevalence of STNs in the studied population was lower than the similar studies, which may be because ofthe smallernumber of subjects that wereevaluated in this study,so studies with a larger sample size, normal gender distribution and longer period of studyare suggested, to obtain more precisely results.

Acknowledgment: This study was approved in Ahvaz Jundishapur University of Medical Sciences (AJUMS). The study was financially supported by AJUMS (Grant.No: GP95214).

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