






# Prevalence of Thyroid Nodules and Associated Clinical Characteristics: Findings from a Large Sample of People Undergoing Health Checkups at a University Hospital in Vietnam

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**Background:** Thyroid nodule is a common disorder normally detected by ultrasound. However, little is known about the population prevalence of thyroid nodules in a Vietnamese population. This study aimed to estimate the prevalence of thyroid nodules, its characteristics, and associated factors in a large number of people undergoing annual health checkups.

**Methods:** A retrospective, cross-sectional descriptive study was conducted, based on electronic medical records of people undergoing health checkups at the Health Checkup Department, University Medical Center at Ho Chi Minh City. All of the participants underwent thyroid ultrasonography, anthropometric measurements, and serum examinations.

**Results:** A total of 16,784 participants (mean age:  $40.4 \pm 12.7$  years, 45.1% female) were included in this study. The overall prevalence of thyroid nodules was 48.4%. The mean diameter of nodules was  $7.2 \pm 5.8$  mm. The prevalence of nodules with malignant characteristics was 36.9%. Women had a significantly higher prevalence of thyroid nodules than men (55.2% vs 42.9%,  $p < 0.001$ ). Advanced age, hypertension, and hyperglycemia were significantly associated with thyroid nodules in both genders. In men, significant factors also included increased body mass index. In women, these included increased total cholesterol and LDLc, hypertriglyceridemia, and hyperuricemia.

**Conclusion:** This study showed a high prevalence of TNs in Vietnamese people undergoing general health checkups. Importantly, the proportion of TNs with malignant risk was quite high. Therefore, screening for TNs should be added to annual health checkups to improve early detection of TNs, targeting those who have a high-risk profile based on factors identified in this study.

**Keywords:** thyroid nodules, malignant thyroid nodules, thyroid ultrasound, general health checkup

## Introduction

The thyroid gland is among the largest endocrine glands, consists of two connected lobes and weighs about 20–30 g in adults.<sup>1</sup> Thyroid nodules (TNs) are discrete lesions within the thyroid gland that are radiologically different from surrounding thyroid tissues.<sup>2</sup> In clinical practice, TNs are common both in patients and in the general population. Previous studies have revealed the prevalence of TNs ranging from 4–7% to 67%.<sup>1,3</sup> For example, in a recent study in China among nearly seven million participants, 36.9% of people going to health checkups were found to have TNs.<sup>4</sup> However, the high variation of prevalence of TNs reported in previous studies implies that TNs depend on context and population. Thus, investigating TNs in various populations and in different countries is helpful in evidence-based medicine.

Although TNs are common, they are often asymptomatic and not all patients who have TNs are in critical condition. This is because most asymptomatic TNs are benign, their level of thyroid hormone secretion is in the normal range and their risk of thyroid cancer is only about 0.45% to 13.0%. While only people who have nodules at a certain risk level should go for diagnostic assessment, detection of these thyroid lesions leads to concerns about malignancy for all patients.<sup>3,5</sup> Because the majority of nodules have no symptoms, in recent years, the use of ultrasound for general health checkups has been increasing to diagnose TNs early and identify nodules with high risk of thyroid cancer for fine needle aspiration cytology. Moreover, one of the most common strategies used to screen for TNs is the risk profile. Previous studies have shown that TNs could be associated with gender, advanced age, central obesity, hypertension, diabetes and fatty liver.<sup>6,7</sup>

In Vietnam, under the Labor Law, workers of all occupations are required to have a compulsory health checkup. In recent years, thyroid assessment has been added to health checkup in some hospitals in our country. However, to date, there have been a scarcity of published data of TNs prevalence and risk factors in Vietnam. The lack of such important evidence may result in the lack of TN assessment and thus the under-diagnosis or late-diagnosis of TN, especially thyroid cancer. This study aimed to investigate the prevalence of TNs and associated factors. Findings from this study can help in decision making with regard to whether or not TN screening should be added to annual health checkups.

## Methods

### Design and Setting

A retrospective, cross-sectional descriptive study was conducted at the Health Checkup Department at University Medical Center (UMC) at Ho Chi Minh City from July to December 2019. UMC is the biggest university hospital in the South of Vietnam. The hospital has an average of more than 50,000 people undergoing health checkups per year. This study was based on electronic medical records from all people undergoing health checkups during the study period.

This study was reviewed and approved by the Institutional Ethics Committees of the University Medical Center at Ho Chi Minh City. Because of the retrospective nature of this study and the fact that data collection was based on electronic medical records, written informed consent was waived. The data were anonymized and maintained with confidentiality in accordance with the Declaration of Helsinki.

### Participants and Data Collection

We extracted data from medical records for all people who had thyroid ultrasound. Background information including age, gender, height (cm), weight (kg), and body mass index (BMI) was collected. Data also included systolic blood pressure (SBP [mm/Hg]), and diastolic blood pressure (DBP [mm/Hg]) which were the average of two measures. Blood samples were obtained by venipuncture after an 8-hour fast in the morning. The following factors were also included: fasting blood glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc), triglycerides (TG) and uric acid (UA). Reference ranges of the blood tests were: 154–357  $\mu\text{mol/L}$  in females and 208–428  $\mu\text{mol/L}$  in males for UA, 3.9–5.2 mmol/L for TC,  $> 0.9$  mmol/L for HDLc,  $< 3.4$  mmol/L for LDLc and 0.46–1.88 mmol/L for TG. Fasting blood glucose results were divided into 3 categories, including  $< 5.6$  mmol/L, 5.6–6.9 mmol/L and  $\geq 7.0$  mmol/L. Hypertension was diagnosed with SBP  $\geq 140$  mmHg and/or DBP  $\geq 90$  mmHg or patients with a history of hypertension and receiving antihypertension medication.

High resolution thyroid ultrasound technique by Samsung's new generation HS 40 ultrasound machine with 12 MHz frequency probe was used. A thyroid ultrasound was performed when the patient was in the supine position with the neck fully extended. Thyroid nodules were defined as discrete lesions within the thyroid gland that are radiologically different from surrounding thyroid tissues.<sup>2</sup> The number of TNs was also recorded and classified as solitary thyroid nodule (STN) if there was only one TN or multiple thyroid nodules (MTNs) if there were two or more TNs. For each nodule, size (length, width and depth in millimeters), shape, location, echogenicity, and boundary were recorded. Suspicious features of malignant TNs included hypoechogenicity, irregular margins, microcalcifications, taller than wide shape, extrathyroidal invasion and metastatic cervical lymph node.<sup>8</sup>

## Data Analysis

Statistical analyses were performed using Stata software, version 16.0. Continuous data were described by mean and standard deviation (SD), while categorical data were described by counts and percentage. Differences in the prevalence of TNs between different groups were evaluated by Chi-square tests. Differences of mean values among individuals with or without TNs were evaluated by independent *t*-tests. Univariate binary logistic regression analysis was applied to identify factors associated with TNs. All tests were 2-sided, and a *p* value < 0.05 was considered statistically significant.

## Results

There were 31,395 people undergoing health checkups at UMC during the study period. Approximately 46.5% (n=14,611) were excluded because they did not undergo thyroid ultrasound examination. Finally, a total of 16,784 individuals were eligible and included in data analysis. Among these, the mean age was  $40.4 \pm 12.7$  years and 45.1% were female. Two thirds of participants (68.2%) had BMI in the normal range for Asian population and more than one fourth (26.8%) had hypertension (Table 1).

Nearly half (48.4%, n=8128) of people had TNs. The prevalence of TNs was significantly higher in females and those who were old, had hypertension, and increased blood glucose. In males, significant factors also included increased body

**Table 1** Participants' Characteristics Stratified by Thyroid Nodule and Gender (N=16,784)

Characteristics	Total n (%) (N = 16,784)	Thyroid Nodule n=8128, 48.4%	P value	Male n=9218 (54.9%)		Female n=7566 (45.1%)	
				Thyroid Nodule n=3950 (42.9%)	P value	Thyroid Nodule n=4178 (55.2%)	P value
<b>Gender</b>			<0.001				
Male	9218 (54.9)	3950 (42.9)					
Female	7566 (45.1)	4178 (55.2)					
<b>Age</b>			<0.001		<0.001		<0.001
< 30	3329 (19.8)	1129 (33.9)		475 (28.6)		654 (39.3)	
30–39	6132 (36.5)	2473 (40.3)		935 (31.5)		1538 (48.6)	
40–49	3701 (22.1)	2003 (54.1)		949 (45.0)		1054 (66.2)	
50–59	2165 (12.9)	1464 (67.6)		874 (61.9)		590 (78.2)	
60–69	890 (5.3)	647 (72.7)		427 (67.8)		220 (84.6)	
70–79	394 (2.3)	289 (73.4)		200 (68.0)		89 (89.0)	
≥ 80	173 (1.0)	123 (71.1)		90 (64.3)		33 (100)	
<b>BMI</b>			<0.001		<0.001		<0.001
< 18.5	899 (5.4)	366 (40.7)		70 (28.3)		296 (45.4)	
18.5–24.99	11,426 (68.2)	5567 (48.7)		2319 (42.0)		3248 (55.0)	
25–29.99	3976 (23.7)	1954 (49.1)		1385 (44.9)		569 (64.1)	
≥ 30	445 (2.7)	218 (49.0)		161 (47.9)		57 (52.3)	
<b>Hypertension</b>			<0.001		<0.001		<0.001
Yes	4500 (26.8)	2342 (52.0)		1711 (47.7)		631 (68.9)	
No	12,284 (73.2)	5786 (47.1)		2239 (39.7)		3547 (53.3)	
<b>TC</b>			0.722		0.036		<0.001
Increased	6981 (41.6)	3392 (48.6)		1867 (41.7)		1525 (60.8)	
Normal	9799 (58.4)	4734 (48.3)		2082 (43.9)		2652 (52.5)	
<b>LDL-c</b>			0.739		0.095		<0.001
Increased	7546 (45.0)	3665 (48.6)		2044 (42.0)		1621 (60.4)	
Normal	9234 (55.0)	4461 (48.3)		1905 (43.8)		2556 (52.4)	

(Continued)

**Table 1** (Continued).

Characteristics	Total n (%) (N = 16,784)	Thyroid Nodule n=8128, 48.4%	P value	Male n=9218 (54.9%)		Female n=7566 (45.1%)	
				Thyroid Nodule n=3950 (42.9%)	P value	Thyroid Nodule n=4178 (55.2%)	P value
<b>HDL-c</b>							
Decreased	1545 (9.2)	734 (47.5)	0.448	550 (44.8)	0.147	184 (58.2)	0.274
Normal	15,235 (90.8)	7392 (48.5)		3399 (42.6)		3993 (55.1)	
<b>Triglycerides</b>							
Increased	5647 (33.7)	2692 (47.7)	0.163	1965 (43.8)	0.068	727 (62.6)	<0.001
Normal	11,133 (66.3)	5434 (48.8)		1984 (41.9)		3450 (53.9)	
<b>Uric acid</b>							
Increased	4310 (25.7)	1983 (46.0)	<0.001	1492 (42.4)	0.502	491 (62.0)	<0.001
Normal	12,474 (74.3)	6145 (49.3)		2458 (43.1)		3687 (54.4)	
<b>Glucose</b>							
< 5.6 mmol/L	11,682 (69.6)	5305 (45.4)	<0.001	2084 (37.1)	<0.001	3221 (53.1)	<0.001
5.6–6.9 mmol/L	3982 (23.7)	2105 (52.9)		1300 (48.2)		805 (62.6)	
≥ 7.0 mmol/L	1120 (6.7)	718 (64.1)		566 (62.2)		152 (72.4)	

**Abbreviations:** BMI, body mass index; TC, total cholesterol; HDL-c, high-density lipoprotein cholesterol; LDL-c, low-density lipoprotein cholesterol.

mass index. In females, these included increased total cholesterol and LDLc, hypertriglyceridemia and hyperuricemia (Table 1).

Among participants with TNs, the proportion of MTNs was higher than that of STNs in both genders (59.9% and 40.1%, respectively). TNs were mainly located in both lobes (46.6%). Among the nodules located only in one lobe, 28.5% of nodules were in the right lobe, higher than the left lobe (23.8%) and the isthmus (1.1%). The mean nodular diameter was  $7.2 \pm 5.8$  mm and the majority of thyroid nodules had a diameter of less than 10 mm (77.4%). The mean diameter of the nodules in females was larger than that in males ( $7.7 \pm 6.2$  mm and  $6.7 \pm 5.4$  mm, respectively) (Table 2).

**Table 2** Sonographic Features of Thyroid Nodules (N=8128)

	Total, n (%)	Male, n (%)	Female, n (%)
<b>Number of nodules</b>			
1	3261 (40.1)	1689 (42.8)	1572 (37.6)
≥ 2	4867 (59.9)	2261 (57.2)	2606 (62.4)
<b>Location of nodules</b>			
Right lobe	2313 (28.5)	1167 (29.5)	1146 (27.4)
Left lobe	1937 (23.8)	999 (25.3)	938 (22.5)
Isthmus	88 (1.1)	37 (0.9)	51 (1.2)
Both lobes	3790 (46.6)	1747 (44.2)	2043 (48.9)
<b>Features suspicious for malignancy</b>			
Hypoechogenicity	2921 (35.9)	1076 (27.2)	1845 (44.2)
Irregular margins	269 (3.3)	99 (2.5)	170 (4.1)
Microcalcifications	295 (3.6)	149 (3.8)	146 (3.5)
Taller than wide shape	94 (1.2)	35 (0.9)	59 (1.4)

(Continued)

**Table 2** (Continued).

	Total, n (%)	Male, n (%)	Female, n (%)
Surrounding invasion	16 (0.2)	5 (0.1)	11 (0.3)
Any feature above	2996 (36.9)	1124 (28.5)	1872 (44.8)
<b>Nodule diameter</b> (mm, mean $\pm$ SD)	7.2 $\pm$ 5.8	6.7 $\pm$ 5.4	7.7 $\pm$ 6.2
<b>Subgroup of nodule diameter</b>			
< 5 mm	3330 (41.0)	1750 (44.3)	1580 (37.8)
5–9 mm	2960 (36.4)	1431 (36.2)	1529 (36.6)
10–14 mm	1072 (13.2)	466 (11.8)	606 (14.5)
15–19 mm	405 (5.0)	162 (4.1)	243 (5.8)
$\geq$ 20 mm	360 (4.4)	141 (3.6)	219 (5.2)

**Abbreviation:** SD, standard deviation.

**Table 3** Suggestive Malignant Characteristics of Thyroid Nodules in Ultrasound (N=8128)

TNs with Suggestive Malignant Characteristics	Right Lobe n (%)	Left Lobe n (%)	Isthmus n (%)
Hypoechogenicity	1941 (23.9)	1733 (21.3)	104 (1.3)
Irregular margins	163 (2.0)	108 (1.3)	8 (0.1)
Microcalcifications	160 (2.0)	141 (1.7)	10 (0.1)
Taller than wide shape	63 (0.8)	35 (0.4)	1 (0.0)
Extrathyroidal invasion	9 (0.1)	5 (0.1)	2 (0.0)

We found that among those with TNs, 36.9% (n=2998) had at least one malignant characteristic, including hypoechogenicity, irregular margins, microcalcifications, taller than wide shape, extrathyroidal invasion. This figure was more prevalent in females than in males (44.8% vs 28.5%, respectively) (Table 2). Hypoechogenicity was the most frequent sign of possible thyroid cancer on ultrasound. Additionally, other suspicious malignant characteristics of TNs were found to be less than 2% (Table 3).

## Discussion

### The Prevalence of Thyroid Nodules

The development of ultrasound with high-frequency probe has enabled the detection of very small TNs. Our study found that 48.4% of people undergoing annual health checkups had TNs. Many studies in other countries using similar study design have shown the prevalence of TNs ranging from 21.3% to 68%.<sup>4,6,7,9–15</sup> The difference in the prevalence of TNs among these studies can be attributed to many factors including selection criteria, gender, age, iodine diet and history of radiation exposure.<sup>16</sup> For example, studies with a majority of women (60–70%) and average age older than 50 had a significantly high rate of TNs (50–68%)<sup>9,11,12,14</sup> compared to our study. In contrast, studies that excluded people with a history of thyroid disease typically have a significantly lower prevalence of TNs (28–33%).<sup>10,13</sup> Our study population was those who underwent general health check-up, most of whom were in healthy condition with no symptoms. Thus, the prevalence in our study partly reflects the frequency of TNs in a general population. Moreover, given the high prevalence of TNs in previous studies and ours and the possible health related consequences of TNs, screening for TNs should be considered in health checkup.

### Thyroid Nodules and Associated Factors

In our study, the prevalence of TNs was higher in women than in men (55.2% vs 42.9%,  $p < 0.001$ ). Other studies also show similar findings, with 40.6–44.7% of TNs in women and 27.0–29.9% of TNs in men.<sup>4,6,7</sup> The prevalence of TNs in

pregnant and reproductive women was the highest,<sup>17</sup> suggesting that there may be a combined role of estrogen and progesterone. It can be assumed that estrogen may be involved in the growth and development of thyroid cells and tumors because estrogen affects TSH synthesis and both normal thyroid tissue and goiters express estrogen receptors.<sup>18</sup> Moreover, the prevalence of TNs increased with age in our data. This result is in line with earlier studies that indicated a positive correlation between age and the presence of TNs in both genders.<sup>6,12,18,19</sup> Thyroid nodules may be considered to be part of the natural aging process within the thyroid gland, which explains the trend of appearance of TNs with aging.<sup>18,20</sup> Previous studies have revealed that reactive oxygen species are precipitated with increasing age, leading to changes in the thyroid parenchyma and accumulation of abnormal cellular changes.<sup>21</sup>

In our study, BMI was positively associated with the appearance of nodules in males and females. However, the relationship between BMI and TNs appears to be inconsistent in findings from various studies. For example, Hongwei Guo did not find a difference in the proportion of nodules among different BMI groups in China.<sup>16</sup> In Panagiotou's study in Greece, BMI in people with TNs tended to be higher compared to those without TNs, although this difference was not statistically significant.<sup>14</sup> In contrast, several studies have reported significantly higher BMI in those with TNs.<sup>11,18</sup> On the other hand, being underweight (BMI <18.5 kg/m<sup>2</sup>) was considered a protective factor which reduced the risk of having TNs by 29% compared to those with normal BMI (p=0.045).<sup>22</sup> The association between BMI and TNs may depend on the differences in thyroid function and race, therefore more studies are needed to clarify this issue.<sup>16</sup> The main hypothesis for the association between obesity and TNs is insulin resistance since hyperinsulinemia stimulates proliferation and inhibits apoptosis in thyroid cells.<sup>23</sup> Moreover, high serum leptin concentration in obese individuals can cause an increase in TSH level, leading to the development of TNs.<sup>24</sup> Along with economic development, sedentary lifestyle and unhealthy diet have increased the proportion of obesity, especially those of working age who often undergo general health check-up.

Moreover, our finding that the prevalence of TNs in people with hypertension was significantly higher than those with no hypertension is consistent with a large body of literature. For example, Ayturk found that hypertension was an independent risk factor for TNs.<sup>25</sup> Hongwei Guo's study demonstrated a significantly higher proportion of nodules in people with hypertension, compared to those with normal blood pressure (51.1% vs 43.0%, p <0.001).<sup>16</sup> In the SPECT-China study, hypertension was a risk factor for developing TNs in both genders.<sup>11</sup> Similarly, the presence of hypertension in the elderly increased the risk of TNs by 63% compared to those with normal blood pressure (P=0.005).<sup>22</sup> In Moon's study in Korea, people with TNs had significantly higher mean systolic and diastolic blood pressure than the non-nodule group.<sup>6</sup> However, the relationship between blood cholesterol and TNs was different among the studies. In our study, the increase of total cholesterol, LDLc and hypertriglyceridemia was associated with having TNs in women, but not in men. We also found that HDLc was not associated with the presence of TNs in both genders. However, in the SPECT-China study, an increase in LDLc, a decrease in HDLc and an increase in triglycerides were risk factors for the development of TNs.<sup>11</sup> According to Moon's study, an increase in total cholesterol and LDLc were associated with having TNs, whereas an increase in triglycerides and a decrease in HDLc were associated with a decrease in the proportion of nodules.<sup>6</sup> There are also studies that did not find a difference in the proportion of TNs between different lipid groups.<sup>16</sup>

Our data showed that increased uric acid was associated with TNs in females (62.0% versus 54.4%, p <0.001), but not in males (p = 0.502). Liu's study showed that uric acid was a protective factor in men, but a risk factor in women.<sup>19</sup> Moon's research showed that the nodule group had significantly lower uric acid compared to the non-nodule group.<sup>6</sup> A decrease in uric acid can lead to an oxidation reaction, damaging the thyroid cells and the formation of TNs.<sup>26</sup> In women, estrogen promotes uric acid elimination, causing proliferation and inhibition of thyroid cell differentiation, leading to more TNs than in men.<sup>27</sup> Our study found that the percentage of people with TNs in fasting blood glucose 5.6–6.9 mmol/L group (52.9%) and fasting blood glucose ≥ 7 mmol/L group (64.1%) was significantly higher than in the normal blood glucose group (45.4%). This result was not found to be significant in previous studies.<sup>6,11</sup> Insulin resistance and hyperglycemia are independent risk factors for the development of goiter, but the exact molecular mechanisms and pathogenesis are still unknown,<sup>25</sup> despite insulin receptor overexpression in goiter and some thyroid carcinoma.<sup>28</sup> On the other hand, increased insulin receptors amplify the effects of IGF-II on tumor cells, including the formation and development of tumors.<sup>29</sup>



## Sonographic Features of Thyroid Nodules

We found that both males and females had a higher proportion of MTNs than STNs (59.9% and 40.1%, respectively). However, the proportion of multiple nodules in females was higher than in males (62.4% vs 57.2%). In other studies, the proportion of STNs was from 28.7% to 55% and that of MTNs was from 45% to 72.3%.<sup>7,10,13,15,18–20</sup> In areas with adequate iodine intake, the proportion of STNs usually stabilizes regardless of age, while that of MTNs increases with age.<sup>30</sup> Moreover, the majority of TNs (46.6%) were identified in both lobes in our study. The proportion of TNs in the right lobe was higher than that in the left lobe (28.5% and 23.8%, respectively). These findings were similar to previous studies where the STNs in the right lobe accounted for 38%–54%, the left lobe 21–47.4%, and the isthmus 0.4%–3.7%.<sup>10,13,20</sup> In a study by Shayeb et al, the proportion of TNs located in one and both lobes were 46.9% and 53.1%, respectively.<sup>15</sup> This confirms that most of TNs located in the right lobe can be explained by the natural difference in the size of the thyroid lobes as the right lobe is usually 20% larger than the left lobe.<sup>13,31</sup>

In this study, the mean diameter of TNs was higher in females than in males with more than three fourths of nodules having a diameter of  $\leq 10$  mm. International studies performed on people going for health checkups showed that most of TNs were small in size, with the percentage of people with a diameter of  $\leq 10$  mm ranging from 57% to 88%.<sup>6,10,12,13,15,19,20</sup> These data show that small and unpalpable nodules only detected by ultrasound are quite common in healthy people. Importantly, we found that TNs with at least one malignant characteristic were common with the dominance of hypoechogenicity. In addition, TNs with malignant characteristics were most frequently found in the right lobe. These findings are in line with previous studies where the proportion of hypoechoic nodules in a study of Bartolotta was 64.8%,<sup>10</sup> in Panagiotou's study was 32%,<sup>14</sup> and in a study of Shayeb et al was 50%.<sup>15</sup> In the SPECT-China study, the proportion of other features such as microcalcification (1.1%) and taller than wide shape (2.3%) was low.<sup>11</sup> Also, the proportion of nodules with irregular margin was 12.5%, according to a study by Shayeb et al.<sup>15</sup>

Our study highlights some important clinical implications. This is the first study in Vietnam to systematically analyze the prevalence of TNs and its characteristics in a large number of people undergoing general health checkup. Because people undergoing general health examination are mostly healthy and asymptomatic, our result partly reflects the frequency of TNs in the general population. Given the high prevalence of TNs and those with suspicious malignant characteristics, our study confirms the need for TNs screening in health checkup in Vietnam. The addition of TNS screening seems to be feasible since our results showed that the majority of TNs detected were  $\leq 1.0$  cm in size, thus confirming the role of thyroid ultrasound which is available even in primary care facilities. This study also found a relationship between TNs and many different anthropometric and metabolic parameters. The associated factors identified in this study could help clinicians in targeting high-risk patients who should be prioritized for routine thyroid ultrasound for early detection of TNs. Given the effective treatments available, early screening for TNs helps to decrease people's health burden and improve their quality of life. Moreover, our study may have implications in other related fields such as organ transplantation. Because TNs are common even in healthy individuals, a more rigorous donor evaluation approach is needed, such as considering fine needle aspiration (FNA) as the first step in evaluating TNs to rule out thyroid cancer in healthy donors.<sup>32</sup>

This study has several limitations. First, people who underwent health examinations at UMC may not represent the overall Vietnamese population. Further, there was a large number of people who did not receive thyroid ultrasound and were subsequently excluded from data analysis. These may affect the generalizability of our findings. Second, the nature of the cross-sectional study design used in our study prevents us from confirming the causal relationship between TNS and other factors. Moreover, the pathological mechanisms of the relationships need further investigation and explanation. Another limitation of our study was the lack of data about FNA. During a standard health checkup, we did recommend that those who had a high risk of malignancy should have FNA. However, not all patients did the FNA and data on the FNA were scarce. As recommended from a recent study, further studies investigating cytological characteristics of the TNs using FNA and standard classification systems such as the Bethesda System for Reporting Thyroid Cytopathology are needed.<sup>33</sup> Finally, the presence of TNs can be affected by numerous factors. However, our study was a retrospective study using electronic medical records and thus information on thyroid surgery history, current medications, iodine

consumption and thyroid function was not available. It would be helpful in future studies if longitudinal studies or nested case control studies can be used to follow-up these people for better understanding of TNs in Vietnamese population.

## Conclusion

This study showed a high prevalence of TNs in Vietnamese people undergoing general health check ups. The majority of TNs were less than 10 mm in diameter, mostly located in both lobes or the right lobe. Importantly, the proportion of TNs with malignant risk was quite high and hypoechogenicity was the most common malignant feature. Therefore, screening for TNs should be added into annual health checkup to improve early detection of TNs. For resource-limited settings like Vietnam, such screening program can be targeted to those who have a high-risk profile based on factors identified in our study such as old-age, female gender, obesity, hypertension, hyperglycemia, dyslipidemia, and hyperuricemia.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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The authors declare no conflicts of interest to declare that are relevant to the content of this article.

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