



# Thyroid incidentaloma in Isfahan, Iran — a population-based study

Częstość występowania *incidentaloma* tarczycy w Isfahanie, Iran — badanie populacyjne

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## Abstract

**Introduction:** Thyroid nodules not detected in palpation but diagnosed following a radiological procedure or during surgery are called thyroid incidentalomas.

We designed this study to investigate the prevalence of sonographic thyroid incidentaloma in Isfahan, Iran, for the first time.

**Material and methods:** By a multistage cluster sampling method, 2523 adults were selected randomly. From this group, 2045 had normal thyroid examination. 234 out of the 2045 were selected randomly for thyroid sonography. Thyroid stimulating hormone (TSH), urinary iodine concentrations (UIC) and antithyroid antibodies were measured.

**Results:** The prevalence of thyroid incidentaloma was 13.2% [Confidence interval (CI) 95% = 8–18]. The average age of subjects with and without incidentaloma was 46.1 (12.4) and 38.4 (12.1), respectively ( $P = 0.002$ ). It was more prevalent in females than in males (19% vs. 10%) [Odds ratio (OR) = 2.59, CI 95% = 1.17–5.76,  $P$  value ( $P$ ) = 0.01]. Median UIC in the incidentaloma group (14  $\mu\text{g}/\text{dl}$ ) was significantly lower than in the group of subjects without nodules (20  $\mu\text{g}/\text{dl}$ ) (OR = 0.9, CI 95% = 0.91–0.99,  $P = 0.02$ ). There was no difference in the levels of TSH and antithyroid antibodies between the two groups ( $P > 0.05$ ).

Mean diameter of nodules was 8.14 (3.43) mm.

**Conclusions:** The prevalence of thyroid incidentaloma was 13.2% in Isfahan. It was higher in females than males and increased with age. (Pol J Endocrinol 2008; 59 (4): 316–320)

**Key words:** thyroid nodule, ultrasonography, Iran, adult

## Streszczenie

**Wstęp:** *Incidentaloma* to guzki tarczycy niewykrywalne palpacyjnie, lecz zdiagnozowane przypadkowo podczas badania obrazowego lub zabiegu chirurgicznego. Celem badania było określenie po raz pierwszy częstości *incidentaloma* wykrywanych w badaniu sonograficznym w populacji irackiego miasta Isfahan.

**Materiał i metody:** Metodą wielostopniowego losowania zespołowego wybrano grupę 2523 dorosłych osób. Spośród 2045 osób, u których nie stwierdzono zmian w badaniu palpacyjnym, wytypowano losowo 234 osoby do badania sonograficznego tarczycy. Oznaczono u nich również stężenie hormonu tyreotropowego (TSH, *thyroid stimulating hormone*), stężenie jodu w moczu (UIC, *urinary iodine concentration*) oraz przeciwciała przeciwtruczycowe.

**Wyniki:** *Incidentaloma* tarczycy wykryto u 13,2% badanych (95% przedział ufności [CI] = 8–11). Średni wiek osób, u których wykazano obecność guzków wynosił 46,1 ( $\pm$  12,4) lat, natomiast osób bez guzków — 38,4 ( $\pm$  12,1) lat ( $p = 0,002$ ). *Incidentaloma* występowały częściej u kobiet niż u mężczyzn (19 vs. 10%; iloraz szans [OR] = 2,59; 95% CI = 1,17–5,76;  $p = 0,01$ ). Obie grupy nie różniły się pod względem stężeń TSH i przeciwciał przeciwtruczycowych ( $p > 0,05$ ).

Średnica guzków wynosiła średnio 8,14 ( $\pm$  3,43) mm.

**Wnioski:** Częstość *incidentaloma* tarczycy w populacji Isfahanu wynosiła 13,2%; była większa u kobiet niż u mężczyzn i wzrastała z wiekiem. (Endokrynol Pol 2008; 59 (4): 316–320)

**Słowa kluczowe:** guzki tarczycy, ultrasonografia, Iran, osoby dorosłe

## Introduction

Thyroid nodule is a common problem. Approximately 4–10% of people in the United States have a palpable thyroid nodule [1]. In a study, in Los Angeles, 67% of 97 persons with no past or family history of thyroid

disease had thyroid nodules in sonography (regardless of thyroid examination status) [2].

Thyroid nodules are mostly benign. However, their diagnosis, treatment and follow up are essential to rule out thyroid cancer [3].



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The most common method to diagnose thyroid nodule is palpation. This detection depends on various factors such as its size and location and the patient's neck anatomy. The diagnosis may be underestimated, especially when the nodule diameter is less than 1 cm [4]. Nodules not diagnosed by patients nor physicians but detected during radiological procedures, neck and thoracic surgeries or whole body nuclear scan are called thyroid incidentalomas [5].

Sonography is a radiological procedure that can reveal many small impalpable nodules (> 3 mm) [6]. Sonography can also detect predictors of malignant nodules such as hypoechogenicity and calcification [7].

The prevalence of thyroid microcarcinoma, detected incidentally in surgery or autopsy, is 0.5% to 28.4% [8, 9]. Therefore, the correct approach to thyroid incidentaloma is important.

The prevalence of thyroid incidentaloma has been reported to be 13.4% in Seoul [10], 14.8% in the Gdansk, Sopot and Gdynia agglomeration [11] and 18.5% in Taipei [12].

We designed this study to investigate the prevalence of thyroid incidentaloma and its clinical, biochemical and sonographic characteristics in a population-based study in Isfahan, a big centrally located city in Iran, with two million [1 986,542 in 2006 (men 1 017,940, women 968,602)].

## Material and methods

In a cross sectional study, 2600 Isfahani adults (> 20 years) were selected by multistage cluster sampling method. At the first stage, we selected 40 blocks on the city map randomly.

Then, we asked the Post Office for the addresses of all the homes in each block.

We then selected 960 addresses from the list (24 homes in each block) at random. In this way, 2600 adult people were invited to take part in the study. 2523 out of the 2600 people, mean age 39 (12.4) years, range: 20–86 years, 1275 males (50.5%) and 1248 females (49.5%), accepted our invitation and came for examination and testing at the Isfahan Endocrine and Metabolism Research Center (IEMRC), according to a preplanned appointment between January and April 2006 (positive invitation response rate 97%).

Demographic data and history of thyroid disorders and medications were obtained for each person and thyroid examination was carried out. Their past medical documents were observed carefully.

Of the 2523 studied cases, 2045 subjects had normal thyroid in physical examination. From these outwardly normal cases, 300 were invited, randomly, for sonography. However, just 234 out of the 300 invited people came for sonography. The mean age of people who

underwent sonography was 39.4 (12.4) years with a range of 20–71 years.

This study was in accordance with the ethical standards of the IEMRC and Isfahan University of Medical Sciences committees on human experimentation, and with the 3rd edition of the Guidelines on the Practice of Ethical Committees in Medical Research issued by the Royal College of Physicians of London.

TSH concentration was measured in all 234 people, urinary iodine concentration in 200 people and antithyroid peroxidase antibody (Anti TPO) and antithyroglobulin antibody (Anti Tg) in 40 out of 234 people.

Normal range of TSH concentration was 0.3–4 mU/L.

Anti Tg and Anti TPO measurements greater than 100 IU/ml and 75 IU/ml, respectively, were considered as positive. The normal range of urinary iodine concentration was 10–30  $\mu\text{g}/\text{dl}$  and those outside this range were supposed to be abnormal (UIC < 10  $\mu\text{g}/\text{dl}$  was defined as urinary iodine deficiency, and UIC > 30  $\mu\text{g}/\text{dl}$  was considered as iodine excess).

TSH concentration was measured by IRMA (Kavoshyar kits, Tehran, Iran) (Intra-assay and inter-assay coefficient variation (CV) were 1.5% and 1.9%, respectively). Anti TPO and Anti Tg were measured by Rapid Enzyme-Linked Immunosorbent Assay (ELISA) (Genesis Diagnostic Company). Intra-assay and inter-assay CV for Anti TPO were 7% and 5%, respectively, and less than 12% for Anti Tg. Urinary iodine level was assayed by digestion method.

Thyroid ultrasonography was performed by HS-2000 Honda ultrasound equipment with a 7.5 megahertz (MHZ) linear probe. Sonographers were blind of thyroid physical examination status. People were examined in a supine position with hyper-extended neck by one of two radiologists. Transverse (X), sagittal (Y) and anteroposterior (Z) lengths of right and left lobes were measured and volumes (V) calculated by three-dimensional ellipsoid formula ( $V = \pi/6 \times X \times Y \times Z$ ) and expressed in millilitres [13]. The sum of the volumes of both lobes was taken as the thyroid volume (TV).

The isthmus was not taken into account in thyroid volume calculation. Thyroid volume, number of nodules (if any), the greatest diameter and echogenicity of the nodule, as well as its calcification, were reported.

## Statistical analysis

Anti Tg, Anti Tpo, TSH and urinary iodine concentration were not normally distributed and were recorded as median (range) and compared by Mann-Whitney test in the groups with and without incidentaloma.

Normally distributed data (age, nodule size and thyroid volume) were recorded as mean and standard deviation. They were compared between the two groups by *t*-test.

**Table I.** Comparison between characteristics of adult Isfahani population with and without thyroid incidentaloma in 2006  
**Tabela I.** Porównanie parametrów demograficznych i laboratoryjnych dorosłych mieszkańców Isfahanu, u których wykryto lub niewykryto incidentaloma tarczycy w 2006 roku

Characteristics	With Nodule (n = 31)	No Nodule (n = 203)	P-Value
Female	16 (51.6%)	68 (33.5%)	0.01
Age (year)	46.1 (12.4)	38.4 (12.1)	0.02
Parity History in females	15 (93.7%)	40 (58.8%)	0.001
TSH [mU/L]	1.9 (0.3–4.8)	1.8 (0.1–5.2)	0.5
Anti TPO [IU/ml]	3.6 (0.7–23)	3.8 (1–555)	0.6
Anti Tg [IU/ml]	4.5 (1–221)	9.1 (2–756)	0.6
Abnormal TSH	2 (6.4%)	6 (2.9%)	0.5
Positive Anti TPO Ab	**0 (0%)	*2 (15.4%)	0.1
Positive Anti Tg Ab	**1 (3.7%)	*2 (15.4%)	0.2
Urinary iodine	£14 (2–40)	§ 20 (1.8–42)	0.02
Iodine deficiency	5 (18.5%)	30 (17.3%)	0.5
Thyroid Volume [ml]	11.9 (5.7)	9.8 (3.7)	0.001

\*27 out of 31 had Anti TPO and Anti Tg measurement; \*\*13 out of 203 had Anti TPO and Anti Tg measurement; £ 27 out of 31 had urinary iodine measurement; § 173 out of 203 had urinary iodine measurement; Data were recorded as number (percent) or median (range) or mean (standard deviation); TSH — Thyroid Stimulating Hormone, Anti Tg Ab — Anti Thyroglobulin antibody, Anti TPO Ab — Anti Thyroid Peroxidase antibody

Chi-square test was used to compare the two groups in terms of gender and parity history.

To compare the data of males and females, we entered age as a covariate in Uni-variate general linear model.

Fisher exact test was used to compare abnormal TSH levels, positive Anti Tg and Anti TPO.

Statistical analysis was carried out using SPSS software, version 13. P-values less than 0.05 were considered statistically significant.

## Results

The characteristics of the 234 adults with normal thyroid examination who underwent sonography are shown in Table I.

Mean age of these people was 39.4 (12.4) years with the range of 20–71 years. Mean age of males was 40.7 (11.8) years vs. 37.1 (13.1) years for females (OR = 1.02, CI 95% = 1–1.05, P = 0.04).

The thyroid nodule prevalence following sonography in 234 people with normal thyroid examination was 13.2% (CI 95% = 8–18). The prevalence of thyroid incidentaloma in our study was higher in females than males. However, it was not statistically significant (19% vs. 10%, respectively, P = 0.05).

We entered age as covariate in the analysis and found that the prevalence of thyroid incidentaloma was higher in women after adjusting for age (OR = 2.59, CI 95% = 1.17–5.79, P = 0.01).

In women with thyroid incidentaloma, parity history was higher than in those without (OR = 11.1, CI 95% = 1.39–89.3, P = 0.001).

Twenty-eight percent of women with parity history and 4% of those without had thyroid incidentaloma (OR = 11.1, CI 95% = 1.39–89.3, P = 0.001). The mean of the parity numbers was 3.4 (2) and 3 (1.7) in people with and without incidentaloma, respectively (P = 0.4).

TSH level was not significantly different between the healthy and incidentaloma groups [1.9 mU/L (0.3–4.8) vs. 1.8 mU/L (0.1–5.2), P = 0.5].

Abnormal TSH concentrations in two people with thyroid incidentaloma was 4.7 mU/L and 5.2 mU/L. In the healthy group, it was 0.1mU/L in one person and between 4.2 mU/L and 5.1 mU/L in five people.

The median urinary iodine concentration was 18.3 µg/dl. Its range was 1.8–42 µg/dl. In the incidentaloma group, 5 people (18.5%) were iodine deficient (UIC < 10 µg/dl), 20 (74%) were normal and 2 (7.4%) had iodine excess (UIC > 30 µg/dl). In those without nodules, iodine deficiency, sufficiency and excess were observed in (n = 30) (17.3%), (n = 112) (64.8%) and (n = 31) (17.9%) people, respectively. Urinary iodine status was not different between the two groups (P = 0.2).

The sonographic characteristics of thyroid nodules in the people with thyroid incidentaloma are shown in Table II.

None of the thyroid incidentalomas in our population had a diameter of more than 1.5 cm. A nodule diameter of between 1–1.5 cm was observed in only 23.8% of patients.

## Discussion and conclusions

The prevalence of thyroid incidentaloma was 13.2% in our study (CI 95% = 8–18), which was similar to pre-

**Table II. Characteristics of nodule in Isfahani adults with thyroid incidentaloma in 2006\*****Tabela II. Charakterystyka guzków incidentaloma tarczycy wykrytych u dorosłych mieszkańców Isfahanu w 2006 roku**

Nodule Characteristics	n (%)
Multiple nodule	9 (29%)
Single nodule	22 (71%)
Hypoechogenicity	18 (58%)
Both hyper- and hypoechogenicity	9 (29%)

\*Mean and standard deviation of nodule diameter was 8.14 (3.43) ml

vious studies; 13.4% in Seoul [10]. 8% in the Gdańsk, Sopot and Gdynia agglomeration [11] and 18.5% in Taipei [12]. None of the nodules had a diameter of more than 1.5 cm. We can indirectly conclude that the physical examination in our study was done precisely. As was expected, thyroid incidentaloma was observed more often in older people (OR = 1.05, CI 95% = 1.02–1.08, P = 0.02). Age has also been considered a risk factor for thyroid nodule development in other studies [5, 11, 12]. By entering age as covariate in data analysis, the prevalence of thyroid incidentaloma was higher in females than males (OR = 2.59, CI 95% = 1.17–5.79, P = 0.01). This was in accordance to some other studies [11, 14].

A history of parity was observed more frequently in women with thyroid incidentaloma (93.7% vs. 58.8%). However, 28% of women with delivery history had thyroid nodules. Just 4% of nulliparus women (with no delivery history) had nodules, in our study. These findings are similar to a study conducted in Germany, in which it was reported that 25.1% of women with a history of parity had thyroid incidentalomas [15]. This could be due to the increased need for iodine during pregnancy.

In the present study, the number of deliveries had no correlation with the presence of thyroid incidentaloma. It is contrary to a Chinese study, which reported a positive correlation [14].

TSH levels were not significantly different between the healthy and incidentaloma groups [1.9 (0.3–4.8) mU/L vs. 1.8 (0.1–5.2) mU/L, P = 0.5]. Thyroid function was normal in patients with thyroid nodule [16, 17].

There was no significant difference between healthy subjects and those with incidentaloma with regard to auto-immune markers (Anti Tg & Anti TPO), in the present study. However, as antithyroid antibodies were measured in only 13 out of 203 healthy people, this conclusion may not be accurate.

The median level of urinary iodine concentration was significantly lower in the incidentaloma group

(OR = 0.9, CI 95% = 0.91–0.99, P = 0.02), although both groups were iodine sufficient. Urinary iodine concentrations were 14  $\mu\text{g}/\text{dl}$  and 20  $\mu\text{g}/\text{dl}$  in people with and without thyroid incidentalomas, respectively. Thyroid nodule prevalence is higher in iodine deficient areas [4].

It seems that lower urinary iodine concentration in the incidentaloma group could explain the development of nodules. However, urinary iodine concentration reflects the iodine intake on the day of urinary collection. It cannot be interpreted as the long-term status of iodine intake, which could have an effect on thyroid nodule development [18].

In another study, performed on 4649 people, thyroid volume was 11.9 ml in areas with mild iodine deficiency. This increased to 13.5 ml in areas of moderate iodine deficiency [19]. In the present study, thyroid volume was higher in the incidentaloma group [11.9 (5.7) ml vs. 9.8 (3.7) ml, OR = 1.1, CI 95% = 1.02–1.21, P = 0.001].

According to the published data, there is a correlation between thyroid volume and iodine intake status [20]. However, greater thyroid volume among people with incidentaloma could be expected.

In our study, multinodular goitre was observed in 29% of subjects in the incidentaloma group. This result is higher than in some similar studies. In Taipei it was 3% [12] and in the Gdańsk, Sopot and Gdynia agglomeration it was 12% [11]. However, it was lower than that reported in Turkey (48%) [9].

In our study, 58% of thyroid incidentalomas were hypoechogenic, and 29% were both hypo & hyperechogenic (multiple nodules). In Italy, reported levels are 58% and 8%, respectively [21].

In conclusion, the prevalence of thyroid incidentaloma was 13.2% in Isfahan. It was more prevalent in women and older people, and it increased with parity history. In the incidentaloma group, the thyroid volume was higher and urinary iodine concentration was lower than in the group of healthy subjects.

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