

Original Article

The Prevalence of Thyroid Dysfunction in an Iodine-Sufficient Area in Iran

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Background: The prevalence of hypothyroidism in Iran is unknown. The aims of the present study were to estimate the prevalence of overt and subclinical hypothyroidism among the adult population of Isfahan, a large metropolitan city in Iran, 15 years after universal salt iodization.

Methods: A cross-sectional survey was conducted from January 2006 through April 2006. The selection was conducted by stratified probability cluster sampling through household family members in Isfahan, Iran. Thyroid stimulating hormone (TSH) of 2523 men and women aged >20 years (mean: 39.0) was measured. Additional thyroid tests were done and serum levels of antithyroid antibodies were evaluated in individuals with elevated TSH. Elevated TSH with normal free T4 index (FT4I) at the second measurement was considered as subclinical and high TSH with low FT4I as overt hypothyroidism.

Results: The overall prevalence of hypothyroidism was 4.8% [95% confidence interval (CI) 3.7, 6.1] in men and 12.8% (95% CI 10.9, 14.6) in women; and 37.6% of hypothyroid men and women had positive antithyroperoxidase antibodies and/or antithyroglobulin antibody, while 19.3% of men and women were euthyroid. The mean (SE) of urinary iodine was 20.3 (0.55) µg/dL and 20.1 (1.37) µg/dL for euthyroid and hypothyroid individuals, respectively ($P=0.65$). Older age, female sex, and goiter were strongly associated with both overt and subclinical hypothyroidism.

Conclusion: Hypothyroidism appears to be common in Isfahan, Iran. The high prevalence of hypothyroidism in Isfahan may be due to autoimmunity with no correlation to iodine intake.

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Keywords: Adult • autoimmunity • hypothyroidism • iodine • Iran

Introduction

Hypothyroidism is a serious, often clinically neglected chronic condition, and may be associated with adverse health outcomes that can be avoided by levothyroxine treatment.¹ Both clinical and subclinical forms of hypothyroidism contribute to hyperlipidemia, hypercholesterolemia, cardiovascular, and psychiatric disease, especially in older

people.^{2,3} Controversy exists about the benefits of screening thyroid disorders in populations⁴ and some studies have reported its cost-effectiveness.⁵

The prevalence of subclinical hypothyroidism varies substantially from nation to nation,⁶ and its current prevalence ranges from 1% to 10%, approaching 20% in some reports.^{7,8} The higher prevalence rates are in women and with advancing age.⁶⁻¹¹ In a survey, the prevalence of subclinical hypothyroidism in men over the age of 74 (16%) was almost as high as it was in women of the same age (21%).⁸ Up to 75% of patients have only mildly elevated serum thyrotropin values,^{7,8} and 50% to 80% of patients have positive tests for antithyroperoxidase antibody (TPOAb), depending on age, gender, and serum thyrotropin levels. Goiter is twice as prevalent among patients with this condition as in the general population.⁷

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The prevalence and pattern of hypothyroidism depend on ethnic, geographic, and environmental factors including iodine intake status.^{12,13} After legislation of salt iodization of 40 parts per million in 1994, goiter was still endemic and urinary iodine concentration remained elevated in many provinces of Iran.¹⁴ In order to determine an appropriate strategy in the field of screening of thyroid disorders in Iran, 15 years after universal salt iodination, this study was conducted in 2006 to investigate the prevalence of hypothyroidism in the adult population aged >20 years in Isfahan, an iodine-sufficient area in the central part of Iran.^{15,16}

Materials and Methods

Study area

Our investigation was conducted in Isfahan, a very large metropolitan city situated in the center of Iran. Located 1,590 meters above sea level, it covers an area of approximately 107,000 km² between 30°42' and 34°30' N latitude and 49°36' and 55°32' E longitude, with a population of almost two million (1,986,542 in 2006, men: 1,017,940, women: 968,602). It is an iodine-sufficient area since 15 years ago. Of the inhabitants, 32.4% were <20 and 7.6% were aged 60 or older in 2006. The climate is dry with a quite wide temperature difference between summer and winter. The mean annual precipitation is 220 millimeters (reference period 2006). The population structure and socio-economic status of Isfahan are similar to the rest of the country. Private physicians and hospitals, district health centers, and government and university hospitals and clinics provide health services.

Subjects

A stratified, multistage probability cluster sample, with probability proportionate to size procedure, was used to obtain a representative sample of the population. The frame for the selection of the sampling units was based on the Isfahan zip code databank. The postal addresses of the starting points for the survey in each cluster were determined, using Isfahan zip code databank. A counterclockwise movement from this point was used to ensure a representative sample of households. Sample size was based on a prevalence of hypothyroidism of 3%, with precision of 0.7%, after accounting for a maximum nonresponse rate of 10%. A total of 1314 (50.5%) men and 1286 (49.5%) women aged >20 were

invited, and 97% (1275 men and 1248 women) responded. The subjects had a mean (SD) age of 39.0 (12.4) years (range: 20 – 86). From the total of 2,523 participants in the study, 170 (6.7%) participants had high serum TSH levels and were asked to refer to the Thyroid Clinic of Isfahan Endocrine and Metabolism Research Center (IEMRC). Of them, 53 (31.2%) refused the second invitation despite enormous efforts to increase the participation rate, while 117 took part (Figure 1). Men and women >20 years entered the study (inclusion criteria) if there was no evidence of neurologic, psychiatric, cardiac, hematologic, hepatic, renal, autoimmune and pulmonary diseases, active malignancy, or other chronic diseases, as determined by history, physical examination, and screening blood tests (exclusion criteria). The Medical Ethics Committee of Isfahan University of Medical Sciences approved the study protocol which complied with the current version of the Declaration of Helsinki, and all subjects gave their consent.

Data collection

Subjects were invited to IEMRC clinics for an interview and clinical examination. Seven trained general practitioners served as examiners. Before data collection began, the physicians thoroughly explained to subjects the purpose and procedure of the study and sought their consent. Overnight fasting blood samples were collected from all participants and palpation of the thyroid was performed. Serum specimens were stored at -20°C until tested for TSH concentration. Subjects with abnormal TSH results or any abnormality on physical examination were visited by an endocrinologist. Those with any suspicious findings in thyroid examination or TSH level and those who were known cases of thyroid disorders were recalled and second blood samples were obtained to measure thyroxine (T4), triiodothyronine (T3), serum TSH, T3 resin uptake (T3RU), anti-TPOAb, and antithyroglobulin antibody (TgAb). Serum TSH concentration was sent to all participants. The interval between the first examination and reininvitation was about two to three weeks. Autoantibodies were not measured in 57 overt hypothyroid patients, because they were on treatment with levothyroxine which may have decreased the level of thyroid autoantibodies.¹⁷ The same methodology was used for both the first and second visits. Serum TSH concentration was assayed by immunoradiometric assay (Kavoshyar

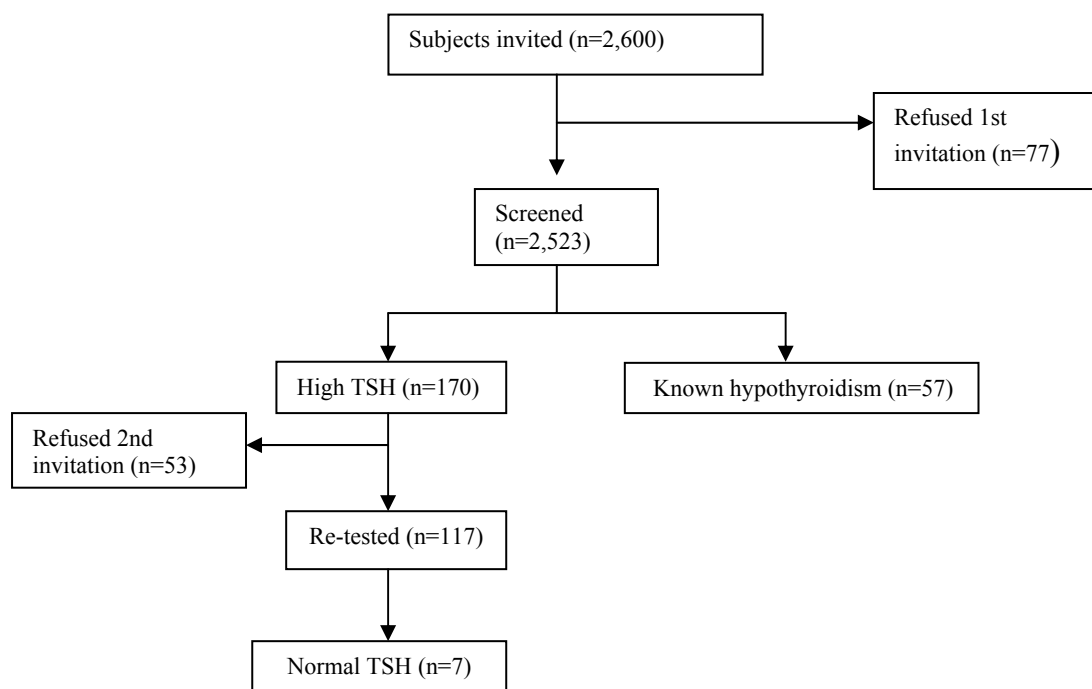


Figure 1. Design of the study.

Co., Tehran, Iran). Intra-assay and inter-assay coefficient of variation (CV) was 1.5% and 1.9%, respectively. The central 95% normal range for TSH was 0.3 – 4 mIU/L, calculated by the renouncement statistical methods¹⁸ as recommended by the manufacturer of the kit. Serum TPOAb and TgAb were measured with Rapid ELISA (Genesis Diagnostic Products Corp.). Intra-assay and inter-assay CV for TPOAb was 7% and 5%, respectively. It was less than 12% for TgAb. TPOAb and TgAb concentrations of more than 75 IU/mL and 100 IU/mL, respectively, were considered positive. Serum T4, T3, and T3RU were measured by radioimmunoassay (Kavoshyar Co., Tehran, Iran). T4 intra- and inter-assay CV was 4.7% and 4.9%, respectively. Normal range of T4 concentration was 4.5 – 12.0 µg/dL. T3 intra- and inter-assay CV was 5.2% and 3.9%, respectively. Normal range of T3 concentration was 80 – 190 ng/dL. T3RU intra- and inter-assay CV was 3.6% and 4.4%, respectively. Normal range of T3RU concentration was 25 – 35%. Free T4 index (FT4I) was calculated by T3RU*T4 and its normal range was 1.3 – 4.8 µg/dL.

Urinary iodine (UI) was measured in 710 (28.1%) participants who were randomly selected on the day of sampling using digestion method based on the modification of Sandell-Kolthoff reaction.¹⁹ Intra-assay and inter-assay CV for UI

was 1.25% and 2.2%, respectively. UI less than 10 µg/dL was considered as iodine deficiency and UI more than 30 µg/dL as iodine excess.²⁰

Laboratory findings and the final diagnosis were sent to the participated individuals in order to be observed by their own physician to start levothyroxine or adjust its dosage.

TgAb, TPOAb, T4, T3, T3RU, and TSH were also measured in 151 randomly selected euthyroid participants at the second visit.

Definitions

Thyroid status was defined as euthyroid (TSH level within the normal range, 0.3 – 4 mIU/L), overt hypothyroidism (TSH>4 mIU/L and low FT4I), subclinical hypothyroidism (TSH level>4 mIU/L and normal serum FT4I), overt hyperthyroidism (TSH level<0.3 mIU/L and high FT4I or T3), and subclinical hyperthyroidism (TSH level<0.3 mIU/L and normal FT4I and T3).¹² Thyroid size was graded according to World Health Organization classification to grade 0 (no palpable or visible), I (palpable but not visible), and II (visible).²¹

Statistical analysis

Statistical methods used included the Mann-Whitney U test, Chi-squared test, and stepwise binary logistic regression. Age-adjusted means were calculated and compared using general linear

models. Multiple logistic regressions were carried out with the SPSS for Windows (SPSS Inc., Chicago, IL, USA) to obtain the odds ratio (OR), accompanied by 95% confidence intervals (CI). We considered the following covariates in the multivariate-adjusted analyses: age, gender, and goiter status. All tests for statistical significance were two-tailed, with the level of significance set at $\alpha < 0.05$. TSH, UI, and TgAb results were transformed to logarithmic values before analysis because they showed a skewed distribution.

Results

Characteristics

When compared with general population of Isfahan (2006 census), the study population was slightly younger and had more high school and college graduates but had a similar gender distribution. Distributions of selected characteristics among 1275 men and 1248 women are shown in Table 1. Women had a lower educational level but a higher rate of goiter and nodules and were younger than men. The mean (SD) age was 40.7 (12.3) years for men and 37.4 (12.4) for women. Grade I and II goiters were present in 7.5% and 1.7% of men and 17.3% and 11.5% of women, respectively ($P < 0.001$). The mean (SD) TSH was 2.4 (5.8) mIU/L for men and 2.7 (3.7) for women. Of the women, 224 (18.0%) were menopause.

Prevalence

Of the 2523 studied subjects (1275 men and

1248 women), 2254 (89.3%) were euthyroid (1199 (94.0%) men and 1055 (84.5%) women), 72 (20 men and 52 women) had overt hypothyroidism, 147 (40 men and 107 women) had subclinical hypothyroidism, and 17 (two men and 15 women) had overt hyperthyroidism (Table 2). Fifty-seven subjects were already known to have primary hypothyroidism and were receiving levothyroxine at the first visit. Over 10% of the studied individuals aged 20 – 86 years had abnormal thyroid function tests (10.7%). There were 219 individuals (8.7%) with an elevated TSH concentration (hypothyroidism), most of whom were mildly hypothyroid. There were 42 participants (1.7%) with a low TSH concentration ($TSH < 0.3$ mIU/L). The remaining 2254 individuals (89.3%) had normal serum TSH concentrations ($0.3 \leq TSH \leq 4$ mIU/L). The prevalence of overt and subclinical hypothyroidism was 2.9% (95% CI: 2.24, 3.58) and 5.8% (95% CI: 4.95, 6.82), respectively. The prevalence rates were higher in women (4.2% for overt and 8.6% for subclinical hypothyroidism) than men (1.6% for overt and 3.1% for subclinical hypothyroidism) ($P < 0.001$). The prevalence of hypothyroidism was higher in older people compared to younger people (Table 3).

The UI and serum TSH concentrations were not significantly correlated ($r = 0.024$, $P = 0.520$). Serum TSH was significantly correlated with TPOAb (0.339 , $P < 0.001$) and TgAb ($r = 0.199$, $P < 0.001$). Serum TPOAb and TgAb showed a significant correlation ($r = 0.246$; $P < 0.001$) but serum TSH

Table 1. Age and age-adjusted means and proportions of selected characteristics among 1275 men and 1248 women, Iran, 2006.

Variables	Men	Women	Difference (95% CI)
	Mean (SE)	Mean (SE)	
Age (yr)	40.7 (0.35)	37.4 (0.35)	3.3 (2.34, 4.26)***
Serum TSH (mIU/L)	2.4 (0.14)	2.7 (0.14)	-0.3 (-0.68, 0.08)
Urine iodine ($\mu\text{g/dL}$)	20.0 (0.76)	20.6 (0.63)	-0.6 (-3.36, 0.56)
	No. (%)	No. (%)	
Education			
Primary or below	205 (16.1)	246 (19.8)	-3.7 (-6.68, -0.69)***
Secondary	621 (48.8)	627 (50.4)	-1.6 (-5.57, 2.25)
Matriculation or above	385 (30.2)	320 (25.7)	4.5 (1.00, 8.00)***
Unknown	62 (4.9)	50 (4.0)	0.9 (-0.76, 2.46)
Goiter status			
No	1157 (90.7)	888 (71.2)	19.5 (16.60, 22.60)***
Grade I	96 (7.5)	216 (17.3)	-9.8 (-12.30, -7.23)***
Grade II	22 (1.7)	144 (11.5)	-9.8 (-11.7, -7.90)***
Nodule			
No	1258 (98.7)	1203 (96.4)	2.3 (1.06, 3.48)***
Yes	17 (1.3)	45 (3.6)	—

Age-adjusted means were calculated using general linear models, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Table 2. Prevalence of thyroid abnormalities among 1275 men and 1248 women, Isfahan, Iran, 2006.

Thyroid status	Men	Women	Difference (95%CI)
	n (%)	n (%)	
Euthyroid	1199 (94.0)	1055 (84.5)	9.5 (7.11, 11.90)*
Subclinical hypothyroid	40 (3.1)	107 (8.6)	-5.5 (-7.26, -3.61)*
Overt hypothyroid	20 (1.6)	52 (4.2)	-2.6 (-3.90, -1.30)*
Subclinical hyperthyroid	9 (0.7)	16 (1.3)	-0.6 (-1.35, 0.20)
Overt hyperthyroid	5 (0.4)	16 (1.3)	-0.9 (-1.69, -0.40)*
Euthyroid sick syndrome	2 (0.2)	2 (0.2)	0.0 (-0.31, 0.31)

See Materials and Methods section for definition of thyroid status, * $P < 0.001$.

level was not correlated with age ($r=0.016$, $P=0.420$).

Risk factors

Overall, 15.9% of euthyroid, 39.5% of subclinical, and 43.0% of overt hypothyroid individuals had goiter. Grade I goiter was more than twice and grade II goiter was more than three times more prevalent among individuals with subclinical hypothyroidism as in euthyroid individuals. The prevalence of overt hypothyroidism in grade I and II goiter was 1.75 and 6.0 times higher than that in euthyroid individuals. In the total study population, men were more euthyroid than women ($P < 0.05$). Compared to nongoitrous individuals, goitrous individuals had a significant higher frequency of positive TPOAb (66.7 vs. 33.3%; $P < 0.001$) and positive TgAb (62.7 vs. 37.3 ; $P < 0.001$). Among individuals with either positive TPOAb or positive TgAb, 11 (9.2%) had overt hypothyroidism and 41 (34.5%) had subclinical hypothyroidism. About 37.6% of hypothyroid men and women had

positive TPOAb and/or TgAb, while 19.3% of men and women were euthyroid. Compared to individuals without antibodies, the risk of subclinical hypothyroidism was 2.6-fold higher in those with either TPOAb or TgAb (relative prevalence (RP) 2.6; 95% CI 1.76, 3.88) and risk of overt hypothyroidism was three times higher in those with either TPOAb or TgAb (RP 3.06; 95% CI 1.26, 7.42) (Table 3).

Of all the women, 224 (18.0%) were menopause and 27 were hypothyroid (12.1%), [20 (8.9%) had subclinical and seven (3.1%) had overt hypothyroidism]. The prevalence of hypothyroidism was not higher in menopausal women ($P=0.6$) (Table 3).

As expected, titer of serum TSH, TPOAb, and TgAb in hypothyroid patients, either overt or subclinical, was higher than euthyroid people. It was higher in patients with overt hypothyroidism in comparison to those with subclinical hypothyroidism. Serum T4 and FT4I in overt hypothyroid individuals was lower than euthyroid and subclinical hypothyroidism (data not shown).

Table 3. Prevalence rates of subclinical and overt hypothyroidism by selected characteristics.

Variables	At risk (n)	Subclinical hypothyroidism			Overt hypothyroidism			
		Cases (n)	Prevalence (%)	Relative prevalence (95%CI)	Cases (n)	Prevalence (%)	Relative prevalence (95% CI)	
Men	1275	40	3.1	1.00	5	0.4	1.00	
Women	1248	107	8.6	2.73 (1.92, 3.90)**	30	2.4	6.13 (2.39, 15.7)**	
Age (yr)	<30	691	29	4.2	1.00	8	1.2	1.00
	30-39	606	36	5.9	1.42 (0.88, 2.28)	26	4.3	3.71 (1.69, 8.12)*
	40-49	685	46	6.7	1.60 (1.02, 2.52)*	26	3.8	3.28 (1.49, 7.19)*
	50-59	391	28	7.2	1.71 (1.03, 2.83)*	8	2.0	1.77 (0.67, 4.67)
	≥60	150	8	5.3	1.27 (0.59, 2.72)	4	2.7	2.30 (0.70, 7.55)
Menopause	224	20	8.9	1.00	7	3.1	1.00	
Not menopause	1021	84	8.2	0.92 (0.58, 1.47)	45	4.4	1.42 (0.65, 3.09)	
Goiter status	No	2045	89	4.4	1.00	41	2.0	1.00
	Grade I	312	31	9.9	2.25 (1.54, 3.38)***	11	3.5	1.75 (0.91, 3.38)
	Grade II	166	27	16.3	3.70 (2.50, 5.58)***	20	12.0	6.0 (3.61, 10.00)***
Without antibodies	265	43	16.2	1.00	8	3.0	1.00	
Only TPOAb+	134	46	34.3	2.60 (1.76, 3.83)**	27	20.1	6.67 (3.12, 14.3)**	
Only TgAb+	135	41	30.4	2.30 (1.54, 3.43)**	24	17.8	5.89 (2.72, 12.8)**	
Both TPOAb and TgAb+	75	23	30.7	2.32 (1.47, 3.68)**	20	26.7	8.83 (4.05, 19.20)**	
Either TPOAb or TgAb+	119	41	34.5	2.61 (1.76, 3.88)**	11	9.2	3.06 (1.26, 7.42)**	

Total number of at risk is not the same for each variable because of missing values, * $P < 0.05$, ** $P < 0.001$, *** $P < 0.001$.

Table 4. Factors related to the prevalence of overt and subclinical hypothyroidism (stepwise binary logistic regression Model), significant adjusted odds ratios (95%CI).

Variables	Subclinical hypothyroidism	Overt hypothyroidism
Age (yr)		
<30	1.00	1.00
30–39	1.69 (1.009, 2.82)*	4.23 (1.88, 9.54)**
40–49	2.33 (1.42, 3.81)**	4.81 (2.12, 10.89)***
50–59	2.58 (1.48, 4.49)**	2.62 (0.96, 7.20)
≥60	1.96 (0.86, 4.48)	3.62 (1.32, 4.04)**
Gender		
Men	1.00	1.00
Women	2.52 (1.70, 3.73)***	2.31 (1.32, 4.04)**
Goiter status		
No	1.00	1.00
Grade I	2.35 (1.50, 3.67)***	1.79 (0.89, 3.61)
Grade II	4.36 (2.64, 7.22)***	6.97 (3.75, 12.97)***

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Multivariate logistic regression analyses of overt and subclinical hypothyroidism in relation to age, gender, and goiter status are shown in Table 4. Both overt and subclinical hypothyroid adults were more likely to be older, of female sex, and goitrous than those with euthyroid function.

Discussion

In this cross-sectional study of 2523 adults aged 20 – 86 years, we found that hypothyroidism was common in Isfahan, as 12.8% of women and 4.7% of men had hypothyroidism; however, most of them were mildly hypothyroid. These data are consistent with reports of the high prevalence of hypothyroidism in other iodine-sufficient populations.^{6,7,22–24} As in other studies in developed countries, hypothyroidism tends to increase with age and is more common in women, and people with goiter.^{6–9,22,23,25,26}

The prevalence of hypothyroidism in various studies from around the world shows a considerable variation and its current prevalence ranges from as low as 1% to as high as 20%^{7,8,27} for subclinical and 1 – 2% for overt hypothyroidism.⁶ Estimates of the prevalence of hypothyroidism depend upon methodological factors, classifications of hypothyroidism, and composition of the community examined by age, ethnicity, and gender, making comparisons between studies of limited values. Tunbridge et al.⁷ were the first to provide a reliable estimate of the prevalence of hypothyroidism in the general adult population. They found out that 10.3% and 0.3% were suffering from subclinical and overt hypothyroidism, respectively. Another study from Tehran, Iran, on individuals ≥ 20 years demonstrated that 0.35% of individuals were overt

and 2.2% were subclinical hypothyroid.²⁸ A study from five coastal areas of Japan, which has iodine-rich seaweed (kelp), showed that the prevalence of hypothyroidism was 0 – 9.7%.²⁹ Another study from northern Japan, where iodine intakes is high, revealed that 0.7% of men and 3.1% of women were overt hypothyroid.¹⁰ The prevalence of elevated TSH among Colorado men and women was 9.5%.⁸ The prevalence of subclinical hypothyroidism is about 5.3% in the USA and 5 – 10% in most countries in western Europe.^{7,8,27,30} Elevated serum TSH levels were found in 1.2% of men and women in Germany.¹¹ The prevalence of subclinical and overt hypothyroidism is higher in Isfahan than the values reported in Tehran,²⁸ and Germany,¹¹ but comparable with those of developed nations such as Denmark, Sweden, Italy, Japan, the USA, and the UK, in the same age group, whose overt hypothyroidism prevalence ranges from 1 – 2%⁶ and subclinical hypothyroidism prevalence ranges from 5 – 10%.^{5,7–10,27,31} Geographical differences in iodine intake, diverse study populations, or various definitions of disease between populations in Isfahan and other parts of the world might be possible explanations.

Consistent with prior studies,^{7,8,28,31} the prevalence of hypothyroidism was found to be higher in women than in men, and the difference was more evident in overt hypothyroidism where the rate for women was more than six times higher than that for men. Supporting the results of other studies,^{7,32} hypothyroidism was higher among goitrous individuals, after adjustment for other confounders, which is known to be associated with disturbances of the thyroid iodine metabolism.³³

In our study, the prevalence of hypothyroidism was not higher in menopausal women and people older than 60. However, too few individuals older

than 60 years of age were studied to comment on the effects of older age.

The median of UI in this study was in the range of sufficient iodine intake and the prevalence of hypothyroidism was not correlated with iodine intake status. No one had UI more than 100 µg/dL. According to previous reports, the UI that could induce subtle or reversible changes in pituitary-thyroid function in adults is higher than 100 µg/dL.³⁴

Another finding that requires further elaboration is the high prevalence of positive TPOAb and TgAb in hypothyroid individuals, supporting the results of other studies.^{35,36} Our study showed that positive TgAb and TPOAb either alone or combined, could significantly increase the risk of hypothyroidism, indicating that both should be considered as risk factors of hypothyroidism. In a study in China comparing the prevalence of hypothyroidism in three areas with different iodine intake, it was demonstrated that the prevalence of hypothyroidism and also rate of autoimmunity increased with higher iodine intake.³⁷ Some other studies have indicated that the prevalence of hypothyroidism increases with increasing iodine supply.^{38,39} However, the clinical implications of thyroid autoimmunity following correction of iodine deficiency are still unclear. In an individual subject, UI excretion reflects iodine intake over a short period of time before the collection and it has a day-to-day variability. It does not reflect the chronic supplementation of iodine during years.^{40,41} Therefore, the increased prevalence of antithyroid antibodies in our hypothyroid people may be due to individual susceptibility to chronic iodine supplementation as supported by other studies,^{5,38} or that other unknown factors have increased thyroid autoimmunity in our community.

Our study has several strengths and limitations. The strengths include a large sample consisting of men and women, sound representativeness of Isfahan population, and information on potential determinants of hypothyroidism. One limitation of our study was the possibility that TSH cut-offs used in this study may have understated health risk. The cut-offs are those recommended by the manufacturer of the kit and other studies.^{12,18} As a cross-sectional study, the present analysis is limited in its ability to elucidate causal relationships between risk factors and hypothyroidism. The 76.7% response rate for second invitation was high for such surveys but we

had no data to check for nonresponse bias. Minor differences in education and age between the study participants and the entire population of Isfahan could slightly limit the generalizability of our findings. Despite the above-mentioned limitations, the findings here add to our understanding of the epidemiology of hypothyroidism in Isfahan. Furthermore, this study provides new data from Isfahan, an iodine-sufficient area that has been under-represented in the previous studies.

In summary, hypothyroidism appears to be quite common in Isfahan. The high prevalence of hypothyroidism in Isfahan may be due to autoimmunity with no correlation to iodine intake.

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