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Predictors of Thyroid Disorders among Men and Women: A Population-Based Study

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In Brief

Thyroid is a butterfly-shaped gland in the lower front of the neck, below the larynx and above the clavicle, which produces triiodothyronine and thyroxine hormones that are essential for body metabolism, heat production, proper growth, orientation, and cell growth (1).

Thyroid dysfunction (TD) is one of the most common chronic endocrine disorders with different prevalence rates across different populations. In Iran, the prevalence of clinical hyperthyroidism was reported as 0.32%—0.44% in women, and 0.2% in men (2). The prevalence of TD increased with age, being most prevalent in premenopausal women, with a women-to-men ratio of at least 4 to 1 (3).

A 2019 study demonstrated that the prevalence of hypothyroidism and hyperthyroidism was 9.47% and 1.19%, respectively. Moreover, body mass index (BMI), hypertension, type 2 diabetes, smoking, sleep disorders (sleep apnea), and comorbidities were significantly associated with hypothyroidism (4, 5). Since the prevention and identification of the risk factors associated with TD have not been seriously focused by sex, the present study aims to identify the prevalence and strength of the predictors TD among men and women aged 40 to 70 years in the Persian Kharameh Cohort Study in southern Iran. Although previous studies have shown some of these risk factors, this study has been conducted to identify the strong predictors of TD, both common and specific, in both sexes.

This demographic study has been performed with a large sample size (representative of the cohort performed in Kharameh) using the participants' comprehensive and accurate information and medical records to simultaneously evaluate all the possible covariables associated with TD by sex, eventually reducing the burden of these disorders and the costs imposed on the society.

This cross-sectional study was performed on the data of the Persian Kharameh Cohort Study. The Kharameh Cohort Study was a part of the Prospective Epidemiological Study Designs in Iran (PERSIAN) and its rationale, objectives, and design have already been published. The target population of this study included all 40 to 70 year-old people in Kharameh. At first, the participants were requested to complete an informed consent form. Then, interviews and measurements were performed by trained staff and the required data were collected (6).

Mean and standard deviation were used to represent the quantitative variables, while frequency and percentage were used to express the qualitative variables. The nor-

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↑What is "already known" in this topic:
The present study is the first to examine the prevalence and strength of predictors of thyroid dysfunction (TD) among men and women aged 40 to 70 years in the Persian Kharameh Cohort Study in the south of Iran.

→What this article adds:
This cross-sectional study was conducted on 10,663 people aged 40 to 70 years who participated in phase 1 of the Persian Kharameh Cohort Study. The total prevalence of TD was 6.8%—10% in women and 2.9% in men. The strongest risk factors for TD included age in women and smoking in men.

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mality of the quantitative variables was assessed using the Shaffer test and the related statistical graphs, including histogram and box plot. Differences between the subgroups were compared using the chi-square test. In addition, multiple logistic regression was used to statistically model the factors associated with TD. The interaction between the covariables was evaluated in the multiple logistic regression modeling. All data analyses were performed using SPSS 26.0 software, and $P < 5\%$ were considered statistically significant.

The mean age of the participants was 57.5 (8.2) years—59.7 (8.9) years in men and 55.8 (7.2) years in women. Among the study participants, 5944 (55.7%) were women and 9493 (89%) were married. More detailed information related to demographic and clinical features and sleep patterns are presented in Table 1.

The prevalence of TD was 6.8% (95% CI = 6-7)—10% (95% CI = 9.03-10.80) in women and 2.9% (95% CI = 2.40-3.40) in men. Additionally, the prevalence of this condition was 6.5% (95% CI = 5.60-7.30), 7.3% (95% CI = 6.20-8.30), 6.9% (95% CI = 6.10-7.90), and 6.7% (95% CI = 5.80-7.70) in people younger than 51 years, 51-57 years, 58-64 years, and 64 years and older, respectively.

Considering the interaction between sex and diabetes ($P = 0.006$), the results of multiple logistic regression modeling to determine the risk factors associated with TD have been presented by sex:

TD Among Women

The results of multiple logistic regression model showed that age, smoking, diabetes, hypertension, sleep medication use, BMI, and education level were associated

Table 1. Univariate comparison of demographics, clinical variables, and comorbidities according to the TD status (n = 10,663)

	Variable		Mean (SD) or N (%)	Thyroid Disease		*P* Value	OR (95% CI)
				Present (n=730)	Absent (n=9933)		
Demographics	Age (years)	Q1 (≤50)	3155 (29.6)	205 (6.5)	2950 (93.5)	0.687	1
		Q2(51-57)	2438 (22.9)	178 (7.3)	2260 (92.7)	0.238	1.13 (0.92 to 1.39)
		Q3(58-64)	2620 (24.6)	182 (6.9)	2438 (93.1)	0.497	1.07 (0.87 to 1.32)
		Q4(>64)	2450 (23.0)	165 (6.7)	2285 (93.3)	0.723	1.03 (0.84 to 1.28)
	Gender	Male	4719 (44.3)	137 (2.9)	4582 (97.1)	≤0.001	1
		Female	5944 (55.7)	593 (10.0)	5351 (90.0)		3.70 (3.06 to 4.48)
	Education level	Illiterate	5587 (52.4)	381 (6.8)	5206 (93.2)	0.909	1
		Literate	5076 (47.6)	349 (6.9)	4727 (93.1)		0.99 (0.85 to 1.15)
	Marital status	Married	9493 (89.0)	716 (6.8)	9771 (93.2)	0.557	1
		Single	1170 (11.0)	14 (8.0)	162 (92.0)		0.84 (0.48 to 1.47)
Clinical	BMI (kg/m^2)	<30	8728 (82.00)	533 (6.1)	8213 (93.9)	≤0.001	1
		≥30	1910 (18.00)	196 (10.2)	717 (89.8)		1.75 (1.48 to 2.08)
	Age at the first pregnancy (years)	<18	3372 (59.9)	252 (7.5)	3120 (92.5)	0.484	1
		18-35	2168 (38.5)	158 (7.3)	2010 (92.7)	0.797	0.97 (0.79 to 1.19)
		>35	94 (1.7)	10 (10.6)	84 (89.4)	0.255	1.47 (0.75 to 2.87)
	Hypertension	No	8122 (76.2)	476 (5.9)	7646 (94.1)	≤0.001	1
		Yes	2541 (23.8)	254 (10.0)	2287 (90.0)		1.78 (1.52 to 2.09)
	Diabetes	No	9064 (85.0)	574 (6.3)	8490 (93.7)	≤0.001	1
		Yes	1599 (15.0)	156 (9.8)	1443 (90.2)		1.59 (1.32 to 1.92)
	Lupus	No	10648 (99.9)	728 (6.8)	9920 (93.2)	0.319	2.09
		Yes	15 (0.1)	2 (13.3)	13 (86.7)		(0.74 to 9.30)
	Smoking	No	7958 (74.6)	72 (2.7)	2633 (97.3)	≤0.001	3.29
		Yes	2705 (25.4)	658 (8.3)	7300 (91.7)		(2.57 to 4.22)
Sleep pattern	Sleep duration (hours)	<7	6607 (62.0)	474 (7.2)	6133 (92.8)	0.087	1
		≥7	4056 (38.0)	256 (6.3)	3800 (93.7)		0.87 (0.74 to 1.02)
	Night work	No	9418 (88.3)	690 (7.3)	8728 (92.7)	≤0.001	1
		Yes	1245 (11.7)	40 (3.2)	1205 (96.8)		2.38 (1.72 to 3.29)
	Nap during the day (minutes)	No	4030 (37.8)	254 (6.3)	3776 (93.7)	0.084	1
		Yes	6633 (62.2)	476 (7.2)	6157 (92.8)		1.14 (0.98 to 1.34)
	Sleeping pills use	No	9736 (91.3)	640 (6.6)	9095 (93.4)	≤0.001	1
		Yes	928 (8.7)	90 (9.7)	838 (90.3)		1.52 (1.21 to 1.92)

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Table 2. Statistical modeling on the relationship between age, smoking, diabetes, hypertension, sleeping pills use, body mass index and education and TD using stepwise multiple logistic regression in women and men (n = 10,663)

	Variable		N (%)	*P* Value	OR (95% CI)
Female	Age	Q1 (≤50)	2329 (39.2)	-	Ref
		Q2 (51-57)	944 (15.9)	≤0.001	2.00 (1.57 to 2.55)
		Q3 (58-64)	1842 (31.0)	0.253	1.14 (0.91 to 1.42)
		Q4 (>64)	829 (13.9)	≤0.001	2.00 (1.52 to 2.64)
	Smoking	No	5741 (96.6)	0.022	Ref
		Yes	203 (3.4)		1.87 (1.09 to 3.20)
	Diabetes	No		0.006	Ref
			4809 (80.9)		1.34 (1.11 to 1.63)
		Yes	1135 (19.1)		
	Hypertension	No	4092 (68.8)	0.002	Ref
		Yes	1852 (31.2)		1.34 (1.14 to 2.74)
	Sleeping pills use	No	5320 (89.5)	0.021	Ref
		Yes	624 (10.5)		1.34 (1.04 to 1.73)
	BMI (kg/m^2)	<30	4392 (73.9)	0.025	Ref
		≥30	1550 (26.1)		1.23 (1.02 to 1.49)
	Education	Illiterate	3755 (63.2)	0.041	Ref
		Educated	2189 (36.8)		0.81 (0.66 to 0.99)
Male	Age (years)	Q1 (≤50)	826 (17.4)	-	Ref
		Q2 (51-57)	1494 (31.7)	0.030	1.81 (1.06 to 3.11)
		Q3 (58-64)	778 (16.5)	0.045	0.51 (0.26 to 0.98)
		Q4 (>64)	1621 (34.4)	0.009	2.08 (1.19 to 3.62)
	Smoking	No	2502 (53.0)	≤0.001	Ref
		Yes	2217 (47.0)		3.00 (1.97 to 4.57)
	Hypertension	No	4030 (85.4)	0.010	Ref
		Yes	689 (14.6)		1.77 (1.14 to 2.74)
	BMI (kg/m^2)	<30	4354 (92.3)	0.785	Ref
		≥30	363 (7.7)		1.08 (0.59 to 2.00)
	Sleeping pills use	No	4415 (93.6)	0.803	Ref
		Yes	304 (6.4)		0.91 (0.43 to 1.90)
	Diabetes	No	4255 (90.2)	0.311	Ref
		Yes	464 (9.8)		0.72 (0.39 to 1.34)
	Education	Illiterate	2887 (61.2)	0.018	Ref
		Educated	1832 (38.8)		0.62 (0.42 to 0.92)

with TD among women (Table 2). The odds of TD was 2 folds higher in women aged 51 to 57 and older than 64 years compared with those younger than 50 years (odds ratio [OR] = 2, 95% CI = 1.57-2.55; OR = 2.00, 95% CI = 1.52-2.64). Besides, Female smokers also had 87% higher odds of developing TD compared with nonsmokers (OR = 1.87, 95% CI = 1.09-3.20). Moreover, women with diabetes and hypertension had 34% higher odds of having TD compared with nondiabetic and non-hypertensive participants (OR = 1.34, 95% CI = 1.11-1.63; OR = 1.34, 95% CI = 1.14-2.74). Women who used sleep medications had 34% higher odds of having TD compared with nonusers (OR = 1.34, 95% CI = 1.04-1.73). In addition, women with BMIs ≥30 kg/m^2 were 23% more likely to have TD compared with those with BMIs ≤30 kg/m^2 (OR = 1.23, 95% CI = 1.02-1.49). Finally, literate women had 19% lower odds of having TD compared with illiterate women (OR = 0.81, 95% CI = 0.66-0.99) (Table 2).

TD Among Men

The results of multiple logistic regression model demonstrated that age, smoking, hypertension, and education level were associated with TD among men (Table 2). Men aged 51 to 57 years were 81% more likely to have TD compared with those aged younger than 50 years (OR = 1.81, 95% CI = 1.06-3.11). Men aged 64 years also had a 2-fold higher odds of having TD compared with men younger than 50 years (OR = 2.08, 95% CI = 1.19-3.62). In addition, those men who smoked had a 3-fold higher odds of having TD compared with nonsmokers (OR = 3.00, 95% CI = 1.97-4.57). Moreover, men suffering from hypertension were 77% more likely to develop TD compared with non-hypertensive men (OR = 1.77, 95% CI = 1.14-2.74). Finally, literate men had 94% lower odds of having TD compared with illiterate men (OR = 0.62, 95% CI = 0.42-0.92) (Table 2).

This population-based study used the data of the first phase of the Persian Kharameh Cohort Study in order to investigate the prevalence and predictors of TD among 10,666 participants by sex. According to the results, the risk factors of TD that were common among men and women were age, smoking, hypertension, and education level. Based on the strength of the association or odds ratio, age in women and smoking in men were identified as stronger predictors. Moreover, diabetes, BMI ≥30 kg/m^2, and use of sleeping pills were found to be other predictors only among women.

The overall prevalence of TD was 6.8%, being 10% among women. Shakeri et al reported the prevalence of TD as 8% among women, which was relatively consistent with the results of the present study. This could result from the improved diagnostic methods and increased prevalence of these disorders. In the present study, the prevalence of TD was 2.9% among men. Shakeri et al reported this measure to be 3.3% among men in Iran, which was consistent with the results of the current study

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(7).

According to the present study findings, men and women aged ≥64 years were twice more likely to develop TD compared with those in their 50s. Similarly, Chaker et al demonstrated that the prevalence of TD increased with age and was higher among the elderly population (≥60 years) (8). This may be due to the fact the thyroid tissue gradually develops fibrosis and atrophy over time, resulting in a reduction in the volume and size of the thyroid gland. On the other hand, limited salt intake reduces elderly individuals' iodine intake through iodized salt. Moreover, gastrointestinal conditions and malabsorption decrease the gastrointestinal absorption of iodine in these people. The absorption of circulating iodine by the thyroid gland is also lower in elderly people (9).

Based on the findings of the present study, the odds of having TD were 19% lower in literate women than in illiterate women and 34% higher in women with diabetes. The findings obtained by Gholampour et al and Amouzegar et al supported the results of the present study regarding the higher prevalence of TD among illiterate and diabetic women (10, 11). Generally, diabetes and TD are both associated with endocrine and hormonal problems. In this context, the lack of blood glucose control can lead to TD. Patients with TD have impaired insulin metabolism and impaired glucose tolerance, making diabetes difficult to control and increasing insulin requirements (12).

The findings of the present study indicated that hypertension, as another common risk factor among both men and women, might lead to a 34% and 77% elevation in TD prevalence in men and women, respectively. Stabouli et al (2010) found that hypertension could lead to TD and that hypertensive people were more likely to develop TD. Rivas et al also found that hypertension could be a risk factor for TD, because thyroid hormones have known effects on the cardiovascular system and blood pressure regulation (13).

In the present study, women with BMIs ≥30 kg/m^2 were 23% more likely to have TD compared with those with BMIs <30 kg/m^2. In the same line, Schmid et al (2015) showed that overweight (25%) and obese (55%) people were at an increased risk of TD (21). Since overweight and obesity cause changes in the body metabolism and TD has been found to be associated with overweight and obesity, the relationship between TD and overweight and obesity is complicated (14).

In the present study, smoking was a common risk factor for both men and women, but a stronger predictor among men. Based on the results, the odds of having TD was 87% higher in female smokers than in nonsmokers, while it was 3 folds higher in male smokers than in nonsmoker men. Consistently, Taylor et al and Cho et al concluded that smoking was a risk factor for TD. Smoking increases the endocrine function of the thyroid gland, leading to elevated serum levels of T3 and T4 hormones. Accordingly, from a pathophysiological point of view, tobacco can significantly affect the development of TD (15, 16).

Finally, the present study findings indicated that those women who used sleep medications were 34% more likely to have TD compared with non-user women. Leso et al also conducted a study in 2020 and stated that night shifts and sleep disturbances could increase the risk of TD (1). In the same line, Sheikh et al reported that sleep disorders doubled the odds of developing TD, which might be due to the fact that using sleep medications can impair the sleep time and, subsequently, result in TD (17, 18).

The study results indicated a high prevalence of TD among the study population, especially women. The common risk factors associated with TD in both women and men include age, smoking, hypertension, and illiteracy. Among the identified risk factors, the strongest were age in women and smoking in men. Furthermore, BMI ≥30 kg/m^2, diabetes, and the use of sleep medication were found to be the predictors of TD only among women. The use of sleep medication was reported as a predictor of TD in women for the first time in the present study. Therefore, the results of this population-based study with a large sample size can contribute to the establishment of effective interventions and programs aimed at reducing the prevalence of TD. One of the limitations of this study was the lack of separation of TD from each other. It is suggested that future studies investigate the risk factors of TD separately between hyperthyroidism and hypothyroidism in women and men.

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Authors Contribution

H.G. is the leading author and guarantor. Z.M., A.R., and M.Gh.J. designed the study and drafted and revised the manuscript. Z.M., A.R., and M.Gh.J. contributed to interpreting the data and drafting and revising the manuscript. All authors approved the submitted version of the manuscript.

Conflict of Interests

The authors declare that they have no competing interests.

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