Int J Clin Exp Med 2017;10(7):10890-10897
www.ijcem.com /ISSN:1940-5901/IJCEM0050968

Original Article

Prevalence, related lifestyle and metabolic risk factors of hypothyroidism in adults: across-sectional study in Gansu province, Northwestern China

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Received February 16, 2017; Accepted May 16, 2017; Epub July 15, 2017; Published July 30, 2017

Abstract: *Objective:* The objective of the cross-sectional epidemiological study is to investigate the prevalence and the possible related lifestyle, metabolic risk factors of hypothyroidism in adults of Gansu province, Northwest China. *Methods:* Every participant was asked to complete a questionnaire, anthropometric measurements and venous blood samples. *Results:* At the end of the study, 10071 adults in Gansu province were enrolled. The prevalence of hypothyroidism was 10.1% (overt hypothyroidism (OH): 1.5%, subclinical hypothyroidism (SCH): 8.7%). Female (12.1%) had a higher percentage when compared to male (7.5%). In multivariate logistic regression analysis, in addition to older age and female increased the odds, current or previous smoking history (*OR*: 0.467, 95% *CI*: 0.289, 0.754, *P*=0.002), salty taste preference (*OR*: 0.355, 95% CI: 0.162, 0.776, *P*=0.022) and a frequent seafood intake (*OR*: 0.148, 95% CI: 0.057, 0.385, *P*<0.001) were tended to be associated with reduced risk. In multivariate logistic regression analysis adjusted for sex, age, smoking, taste preference and seafood intake, positive TPO-Ab (*OR*: 2.419, 95% CI: 1.160, 5.043, *P*=0.018), positive Tg-Ab (*OR*: 1.976, 95% CI: 1.037, 3.768, *P*=0.039) and high TG (*OR*: 1.241, 95% CI: 1.044, 1.474, *P*=0.014) level were associated with increased risk of hypothyroidism. *Conclusions:* The prevalence of hypothyroidism in Gansu province was high, affecting approximately one in ten adults, and majority of which were SCH. Increasing age, female, positive TPO-Ab or Tg-Ab, and increased TG were associated with higher risk of hypothyroidism.

Keywords: Hypothyroidism, epidemiology, risk factor, protective factor

Introduction

Hypothyroidism is a common health problem in the world. It has been reported that hypothyroidism was associated with an increased risk of cardiovascular disease [1], heart failure [2], cognitive and motor impairments [3], and nonalcoholic fatty liver disease [4]. Hypothyroidism can be defined as an increase in serum thyrotropin (TSH), associated with decreased (overt hypothyroidism (OH)) or normal (subclinical hypothyroidism (SCH)) serum thyroid hormone levels [5]. The prevalence of hypothyroidism in the general population is 4.6% (OH for 0.3% and SCH for 4.3%) [6] to 23.5% (OH for 4.2% and SCH for 19.3%) [7]. The high prevalence of hypothyroidism maybe because of traditional risk factors such as sex, age, deficient iodine intake. A number of studies [8, 9] suggested that lifestyle factors were associated with increased prevalence of hypothyroidism. Recently, several animal experiments reported that lipotoxicity may have a contribution to the pathogenesis of thyroid dysfunction [10, 11].

In a developing and densely populated country like China, hypothyroidism has attracted people's attention for its high prevalence rate. However, less is known regarding the prevalence of hypothyroidism in Gansu province, which is located in the Northwest China. In this paper, we reported the prevalence of hypothyroidism in adults, and explored the related risk factors of hypothyroidism.

Methods

Participants

During the period June 2014 and May 2015, a cross-sectional, epidemiological study was conducted in seven major regions of Gansu province. Multi-stage stratified and Probability Proportionate to Size cluster sampling method was used to select participators (residing in that area for at least 5 years, aged 18 years and above) in this study. Exclusion criteria as following: pregnant women; Long-term use of estrogen or contraceptive drugs; taking glucocorticoids. Finally, 10071 male and female inhabitants were selected to participate in the large study.

Study procedure

Initially, all subjects gave informed consent before they participated in the study. Once informed consent was obtained, all participants were asked to complete a questionnaire to collect basic demographic information such as age, gender, education, lifestyle factors (smoking status, alcohol drinking, taste preferences and seafood intake), and thyroid diseases history. Then anthropometric measurements (height, weight, and blood pressure) were measured and venous blood samples (after 8 h of fasting) were drawn from all participants. Serum was stored at -20°C after obtaining samples and assayed for thyroid function, serum lipid levels, fasting plasma glucose (FPG) and uric acid (UA) within 1 week. A central certified laboratory performed the hematological and biochemical investigations.

Blood pressure was measured 3 times with a mercurial sphygmomanometer desk (GB3053-93YUYUE Co. Inc, Jiangsu, China) on the right upper arm after the participants had rested for minimal 5 minutes. Average value of the three readings was used for the study. Educational level was classified into four groups: illiteracy, primary school, secondary school, and undergraduate and above. Smoking habit was classified as currently or previously smoking and never. Alcohol drinking behavior was classified as moderate: 1-6 times/week; heavy: every day, and never. Taste preferences were divided into three groups of salt preferences: salty, average, and less salty. Frequency of seafood intake was assessed in three groups: frequent (≥3 times/week), occasional (<3 times/week), and never.

According to WHO, subjects were classified as BMI≤25 kg/m^2, BMI≥25 kg/m^2 (overweight), and BMI≥30 kg/m^2 (obesity). Systolic blood pressure was classified as SBP≥140 mmHg or not. Diastolic blood pressure was classified as DBP≥90 mmHg or not.

Laboratory methods

Assays for Thyroid Stimulating Hormone (TSH), total thyroxine (TT4), thyroglobulin antibodies (Tg-Ab) and thyroid peroxidase antibodies (TPO-Ab) were measured by a Chemiluminescent Microparticle immunoassay (CMIA) using the kit from Abbott with the instrument Immulite 2000 (Abbott Laboratories, USA). TSH had a normal reference range of 0.35 mIU/L to 4.94 mIU/L and functional detection limit of 0.01 mIU/L. TSH level above 100 IU/mL were recorded as 100 IU/mL. TT4 had a normal reference range of 62.68 nmol/L to 150.84 nmol/L. The working range for this method is 0.01 mIU/liter to 50 mIU/liter. The normal range for TPO-Ab in humans is <5.61 IU/ml, and for Tg-Ab is <4.11 IU/ml. Levels of TPO-Ab and Tg-Ab above 1000 IU/ml were recorded as 1000 IU/ml. Serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), FPG and UA were determined using the AU5400 automatic analyzer (Olympus, Beckman Coulter, USA).

Diagnostic criteria

Hypothyroidism was defined as follows: 1) Subjects with T4<62.68 nmol/L and TSH>4.94 mIU/L were classified as OH; 2) Normal serum T4 and TSH>4.94 IU/L was defined as SCH; 3) Subjects with antibody concentration for TPO-Ab≥30 IU/ml, and for Tg-Ab≥20 IU/ml were regarded as antibody positive.

Data analysis

Data were recorded on the computer twice by two independent individuals who were responsible for logic and consistency checks. The data analysis was performed with SPSS (version 17.0). Categorical variables were analyzed using Chi-squared test. Numeric variables were compared using one-way classification ANOVA if in normal distribution and Mann-Whitney U test or Kruskal-Wallis H test if not in normal distribution. Normal distribution variations are expressed as mean ± SD. Results of non-nor-

Table 1. Characteristics of study population by thyroid disease status

	No. Of Subjects (%)	OH		SCH	
		No. (%)	P	No. (%)	P
Total subjects	10071 (100)	147 (1.5)		873 (8.7)	
Sex			0.012		<0.001
Male	3591 (35.7)	39 (1.1)		222 (6.4)	
Female	6480 (64.3)	108 (1.7)		651 (10.4)	
Age at baseline, years			0.780		<0.001
≤45	2406 (23.9)	36 (1.5)		114 (4.7)	
46-55	3192 (31.7)	45 (1.4)		270 (8.5)	
56-65	2706 (26.9)	36 (1.3)		351 (13.0)	
≥66	1767 (17.5)	30 (1.7)		138 (7.8)	
Education			0.418		0.019
Illiteracy	1959 (19.5)	36 (1.8)		183 (9.3)	
Primary school	1959 (19.5)	33 (1.7)		195 (10.0)	
Secondary school	3465 (34.4)	45 (1.3)		345 (10.0)	
Undergraduateand above	1986 (19.7)	33 (1.7)		150 (7.6)	
TPO-Ab			<0.001		<0.001
Negative	8923 (88.6)	85 (1.0)		732 (8.2)	
Positive	1285 (11.4)	62 (5.4)		141 (12.3)	
Tg-Ab			<0.001		<0.001
Negative	8127 (80.7)	75 (0.9)		569 (7.0)	
Positive	1944 (19.3)	72 (3.7)		304 (15.6)	

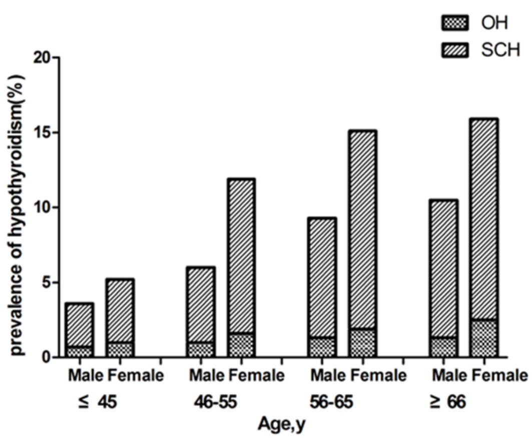

Figure 1. The prevalence of hypothyroidism in different gender and different age groups.

mal distribution are expressed as median (25th percentile, 75th percentile). Potential risk factors of hypothyroidism were analyzed by multivariate logistic regression analysis. *P* values <0.05 were considered statistically significant.

Results

The characteristics of study population by thyroid disease status are showed in **Table 1**. 10071 participants were enrolled in the study. Among all the subjects, 6480 (64.3%) were female, the mean age was 54.0 years (standard deviation 11.5, range 18-79 years), 54.1% had completed secondary school. The prevalence of hypothyroidism was 10.1%, which contained OH (1.5%) and SCH (8.7%). A larger proportion of females than males were found to be affected by OH and SCH. There was a significant difference in the prevalence of SCH in the four age groups, as well as in different educational levels. Compared to negative anti-thyroid antibodies, positive anti-thyroid antibodies group had much higher OH and SCH prevalence. Based on the above definitions of hypothyroidism, there were 1107 subjects (9.8%) with an elevated TSH concentration. Among those with an elevated serum TSH concentration, 927 subjects (83.7%) had a level between 4.94 and 10 mIU/L; 180 subjects (16.3%) had a value greater than 10 mIU/L. Positive TPO-Ab and TG-Ab were found in 18.1% and 10.6% of the adult population, respectively (not be shown in **Table 1** and be shown in Supplementary Data).

The prevalence of hypothyroidism in different gender and different age groups is shown in **Figure 1**, ranging from about 5.2% to 15.9% in female and from 3.6% to 10.5% in male. SCH was more common than OH.

Table 2. Clinical and laboratorial baseline characteristics of the participants with EU, SCH and OH

Variables	EU (M ± SD)	SCH (M ± SD)	OH (M ± SD)	*P* value
TSH (mIU/L)*	2.13 (1.39, 2.81)	6.50 (5.39, 9.00)[a]	9.42 (6.80, 33.26)[b,c]	<0.001
TT4 (nmol/L)	105.12±12.16	81.78±12.91[a]	48.16±10.81[b,c]	<0.001
TPO-Ab (IU/ml)*	0.03 (0, 0.34)	0.11 (0, 1.31)[a]	4.96 (0.59, 622.88)[b,c]	<0.001
Tg-Ab (IU/ml)*	1.18 (0.79, 2.23)	1.85 (0.96, 17.78)[a]	29.71 (0.84, 171.06)[b]	0.047
SBP (mmHg)	130.04±21.27	134.56±24.34	134.58±15.68	0.209
DBP (mmHg)	82.82±12.72	83.67±11.73	83.43±13.16	0.911
BMI (kg/m^2)	24.09±3.26	24.14±3.53	24.59±2.95	0.876
TC (mmol/L)	4.89±0.95	5.08±1.15	5.72±0.54[b]	0.043
TG (mmol/L)	1.63±0.99	1.79±0.90	2.26±0.70[b]	0.047
LDL-c (mmol/L)	3.17±0.84	3.36±0.92	4.17±0.51[b]	<0.001
HDL-c (mmol/L)	1.47±0.40	1.49±0.44	1.51±0.30	0.942
FPG (mmol/L)	5.41±1.32	5.66±1.72	6.24±2.94	0.087
UA (umol/L)	303.83±80.78	307.03±98.56	344.59±75.06	0.262

Note: *Mann-Whitney U test or Kruskal-Wallis H test; P: comparing the three groups, P<0.05; [a]comparing SCH and EU, P<0.05, [b]comparing OH and EU, P<0.05; [c]comparing OH and SCH, P<0.05.

Table 3. Risk factors of hypothyroidism in multivariate logistic regression analysis

Variables	*OR* (95% CI)	*P* value
Sex		0.022
Male	Referent	
Female	1.454 (1.055, 2.005)	
Age at baseline, years		<0.001
≤45	Referent	
46-55	2.025 (1.351, 3.035)	
56-65	2.981 (1.996, 4.451)	
≥66	3.105 (2.028, 4.752)	
Educational level		0. 868
Illiteracy	Referent	
Primary school	1.332 (0.683, 2.595)	
Secondary school	1.207 (0.605, 2.409)	
Undergraduate and above	1.127 (0.416, 3.050)	
Smoking habit		0.002
Never	Referent	
Current or previous	0.467 (0.289, 0.754)	
Alcohol drinking		0.085
Never	Referent	
Moderate	1.404 (0.899, 1.964)	
Heavy	0.284 (0.040, 2.083)	
Taste preference		0.022
Less Salty	Referent	
Average	0.849 (0.666, 1.082)	
Salty	0.355 (0.162, 0.776)	
Seafood intake		<0.001
Never	Referent	
Occasionally	0.715 (0.501, 1.019)	
Frequently	0.148 (0.057, 0.385)	

Clinical and laboratorial baseline characteristics of the participants with euthyroid (EU), SCH and OH are shown in **Table 2**. As is shown, the serum concentrations of TSH, T4, TPO-Ab and TG-Ab in patients with OH or SCH were significantly higher than EU subjects. Moreover, the means of serum TC, TG and LDL-C levels increased in OH when compared with EU patients. But the differences between SCH and EU did not reach statistical significance. No significant differences were found between the three groups on the means of SBP, DBP, BMI, FGP, HDL-C, and UA.

Multivariate logistic regression analysis, in which gender, age, educational level, lifestyle factors and related metabolic factors as the independent variables and whether hypothyroidism as the dependent variable, showed that age, gender, smoking habit, taste preference and seafood intake habit were independently associated with hypothyroidism. The results demonstrated that female (*OR*: 1.454, 95% CI: 1.055, 2.005, *P*=0.022) were independently risk factors of hypothyroidism and compared to younger adults (aged 18-45 years), older adults had great-

BMI (kg/m²)		0.614
<25	Referent	
25-30	0.790 (0.452, 1.383)	
≥30	1.192 (0.429, 3.309)	
SBP (mmHg)		0.880
<140	Referent	
≥140	0.952 (0.501, 1.807)	
DBP (mmHg)		0.463
<90	Referent	
≥90	0.909 (0.705, 1.173)	
Family history of thyroid diseases		0.795
No	Referent	
Yes	1.427 (0.098, 20.815)	
TPO-Ab positive	2.419 (1.160, 5.043)	0.018
Tg-Ab positive	1.976 (1.037, 3.768)	0.039
TC (mmol/L)	1.011 (0.861, 1.187)	0.894
TG (mmol/L)	1.241 (1.044, 1.474)	0.014
LDL-C (mmol/L)	1.008 (0.718, 1.337)	0.898
HDL-C (mmol/L)	0.763 (0.416, 1.397)	0.380
FPG (mmol/L)	0.947 (0.831, 1.078)	0.411
UA (umol/L)	1.001 (0.998, 1.004)	0.564

Note: Alcohol drinking: Moderate: 1-6 times/week; Heavy: every day, and never. Seafood intake: frequently: ≥3 times/week), occasionally: <3 times/week, and never.

er chances of being diagnosed as hypothyroidism (46-55 years: *OR*: 2.025, 95% CI: 1.351, 3.035, *P*=0.001; 56-65 years: *OR*: 2.981, 95% CI: 1.996, 4.451, *P*<0.001; 66 years and above: *OR*: 3.105, 95% CI: 2.028, 4.752, *P*<0.001). Positive TPO-Ab (*OR*: 1.976, 95% CI: 1.037, 3.768, *P*=0.039), positive Tg-Ab (*OR*: 2.419, 95% CI: 1.160, 5.043, *P*=0.018) and serum TG level (*OR*: 1.241, 95% CI: 1.044, 1.474, *P*= 0.014) were significantly associated with an increased risk of hypothyroidism. While current or previous smoking history (*OR*: 0.467, 95% CI: 0.289, 0.754, *P*=0.002), salty taste preference (*OR*: 0.355, 95% CI: 0.162, 0.776, *P*=0.022) and a frequent seafood intake (*OR*: 0.148, 95% CI: 0.057, 0.385, *P*<0.001) were found may have effects on protecting against hypothyroidism. However, educational level, alcohol drinking status, BMI, SBP, DBP, family history of thyroid diseases, serum levels of TC, LDL-C, HDL-C, FPG and UA were not significantly associated with hypothyroidism (**Table 3**).

Discussion

In this study, we assessed the prevalence of hypothyroidism in adults residing in Gansu province of China. Hypothyroidism was found to be a common clinical problem affecting 10.1% of the study population. This suggests that almost one-tenth of adults in Gansu province were hypothyroid, and SCH (8.7%) was much more common than OH (1.5%).

The prevalence of hypothyroidism has been reported from different countries recently and showed a considerable variation. A large cross-sectional study which contained ten cities in eastern and central China reported that the prevalence of OH and SCH were 1.1% and 16.7%, respectively [12]. Teng WP *et al*. showed the prevalence rates of OH in three different communities ranging from 0.3% to 2.0% and that of SCH ranging from 0.9% to 6.1% [13]. The prevalence figures for OH (1.5%) in our study were closely consistent with these earlier published data, the prevalence for SCH (8.7%) were much lower than the ten cities' study [12]. Our prevalence rate for SCH was also lower than the rate in a cross-sectional study conducted in the Xinjiang Autonomous Region, where also in northwest China [14]. Marwaha *et al.* reported the prevalence rates of OH and SCH in India are 3.5% and 8.02%, respectively [15]. Whereas the data from National Health and Nutrition Examination Survey (NHANES III) showed that OH and SCH were found in 0.3% and 4.3% of the U.S. population [6]. Diverse study populations, living environment, lifestyle factors, and iodine nutritional status among others and various definitions in other studies may account for the discrepancy of prevalence rate.

Previous studies had shown a predominance of hypothyroidism in female and the prevalence of hypothyroidism increased significantly with age [16, 17]. Investigation for an unselected population in Mid-Norway stated that the prevalence of hypothyroidism was 4.8% and 0.9% for female and male, respectively [17]. In the same study, only 1.54% of females less than 30 were hypothyroid, compared with 5.33% of those in their eighth decade. In males, the prevalence of hypothyroidism also increased with age. Our study showed that the prevalence of hypothyroidism in female are significantly higher than male (12.1% vs 7.5%, P<0.001). Multivariate logistic regression analysis proved that female and increasing age were independent risk factors for hypothyroidism. Degenerative changes occurring in the thyroid of old people and combined effect of estrogen [18] and progesterone in female may account for it.

Compared to subjects with negative thyroid antibodies, the prevalence of OH in people with positive thyroid antibodies was much higher, the same association can be found in SCH. Multivariate logistic regression analysis showed that positive Tg-Abor TPO-Ab were independent risk factors for the development of hypothyroidism. It had been found that autoimmunity played a dominant role in the occurrence of hypothyroidism [19, 20].

In our study, we found that current or previous smoking history habit was an independent lifestyle factor for hypothyroidism. Some previous researches had focused on the association between hypothyroidism and smoking habit and yielded conflicting results. Our findings indicated that smoking is negatively associated with hypothyroidism, which was consistent with previous findings [21, 22]. However, the results were at variance with finding that smoking increasing the risk of hypothyroidism [23] and analysis showed that there were no association between cigarette smoking and hypothyroidism [22]. A possible explanation for the protective effect of smoking is decreased thyroid iodide transport and organification in smokers protect against the development of autoantibodies [22, 24]. To fully illuminate the association between smoking and hypothyroidism, well-designed studies taking the amount and duration of smoking into consideration are indispensable.

In multivariate logistic regression analysis, we found that both a frequent consumption of seafood and salty taste preference were independent lifestyle factors for hypothyroidism. The consumption of seafood and salt are primary source of iodine. Although the implementation of mandatory universal salt iodization has been successfully carried out in China from 1995, dietary iodine deficiency remains a common cause of hypothyroidism [12]. The study conducted in Xinjiang Autonomous Region of China reported a higher incidence rate of OH in iodine-deficient population than in iodine-sufficient group (4.8% *vs* 2.8%) [14]. However, differing result, excessive iodine intake lead to hypothyroidism were also published [12, 13]. The protective effects of seafood and salt intake on the development of hypothyroidism might be explained by the increase of iodine intake. Gansu province located in the northwest China, far away from the sea, resulted in the lower iodine content of the local food and the lower frequency of seafood consumption. An in-depth assessment of the iodine nutritional status of the population should be conducted, which may help to clarify the prediction.

With regards to the relationship between hypothyroidism and alcohol consumption, a population-based case-control study reported that moderate alcohol consumption had a protective effect on overt autoimmune hypothyroidism [25]. In a prospective study by Effraimidis *et al.* [8], alcohol consumption of >10 units/week may protect against the development of OH. However, in present study, we did not find a significant relationship between alcohol consumption and hypothyroidism.

Recently, a study from China showed that TSH levels were positively correlated with BMI and DBP [26]. Cooper also reported that a higher BMI was associated with a higher frequency of hypothyroidism [27]. We did not find a significant correlation between hypothyroidism and BMI, as well as between hypothyroidism and DBP. Furthermore, we found that people who had a family history of thyroid disease were not significantly related with their development of hypothyroidism. The absence of specific symptoms of hypothyroidism and low awareness for hypothyroidism result in the low diagnosis rate may account for the phenomenon.

We found that serum TG were independent risk factors for the development of hypothyroidism. On one hand, notably, hypothyroidism has been regarded as a risk factor for lipid abnormalities, which may subsequently result in atherosclerosis [28]. On the other hand, recent studies had indicated that lipotoxicity seriously and extensively harmed human health by promoting the pathogenesis of metabolic diseases [29]. Jankovic *et al.* observed that in obese subjects who with hypertriglyceridemia and increased serum TSH concentrations, the TSH levels significantly decreased when the serum triglyceride levels decreased after a bariatric surgery

[30]. Their results suggested that hypertriglyceridemia might be positively associated with the presence of SCH. What's more, in an animal study [31], long term high-fat lard feeding could decrease the levels of serum thyroxine and increase the concentration of TSH. In our study, increased TG was found be possible risk factor for the development of hypothyroidism. To illustrate the mechanism of the phenomenon, further research should be conducted.

The strong point of this study is the large sample size. All the samples have been analyzed at a central laboratory. Further, the study population belongs to different regions of Gansu province, represents probably the population of Gansu. However, there are few limitations of this study. Firstly, the amount of salt uptake was not accurately. Secondly, urinary iodine in the study population was not measured.

In conclusion, the prevalence of hypothyroidism in Gansu province is high, and our screening program demonstrated that both lifestyle factors and metabolic factor were associated with the occurrence and development of hypothyroidism. However, as a cross-sectional study, the limitation is that it is not possible to evaluate whether the associations are casual. A prospective study with stronger study design should be taken for further research.

Acknowledgements

We acknowledge the support from Gansu Provincial Hospital, and researchers participated in the study for data collection, the local medical staff who contributed to the investigation and all participants enroll in this study.

Disclosure of conflict of interest

None.

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