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Selenium Status Associates with Thyroid Hormone and Thyroid Dysfunction in Older Chinese Adults

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Abstract

Selenium (Se) is physiologically essential for thyroid function. However, epidemiological studies on the association between Se status and thyroid function are limited and the results are inconsistent. Therefore, we explored this association in an elderly Chinese population sample. Participants in the cross-sectional study were people aged 65 years or older who provided fingernail and whole blood samples. Hyperthyroidism and hypothyroidism were defined by serum thyroid hormones concentrations, including thyroid stimulating hormone (TSH), total triiodothyronine (TT3), total thyroxine (TT4), free thyroxine (FT3), and free thyrotropin (FT4). Significant positive association was observed between whole blood and fingernail Se concentrations ($r = 0.672$, $P < 0.001$). Compared with the lowest Se quartile (Q1), the other

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Ethical Approval The study was approved by the Ethics Review Committee of National Institute for Environmental Health, Chinese Center for Disease Control and Prevention.

Informed Consent All participants provided their written informed consent prior to participating in the study.

Conflict of Interest The authors declare no competing interests.

fingernail Se quartile groups had lower TSH, higher FT3 and FT4 levels, and Q2 had higher TT3 levels after adjusting for covariates; the other whole blood Se quartile groups had lower TSH levels, Q2 had higher FT3, FT4 and TT3 levels, Q3 had higher FT3 levels, and Q4 had higher FT4 levels after adjusting for covariates. Compared with Q1, the adjusted odds ratios (OR) and 95% confidence intervals (95% CIs) of hypothyroidism for Q4 of whole blood Se was 0.141 (0.029,0.675), and the adjusted OR (95% CIs) of hyperthyroidism for Q2 and Q3 of fingernail Se were 4.121 (1.233,13.733) and 3.614 (1.095,11.926). Higher Se levels were significantly associated with lower TSH levels and higher levels of TT3, FT3 and FT4. Meanwhile, higher Se levels were associated with lower risk of hypothyroidism and higher risk of hyperthyroidism.

Keywords

Selenium; Fingernail; Whole blood; Thyroid hormone; Thyroid dysfunction

Introduction

Selenium (Se) is an essential trace element for human body, which plays an important role in maintaining thyroid function [1]. Se could regulate cell death and apoptosis of thyroid follicular cells [2], and affect thyroid hormone metabolism [3, 4]. Thyroid is the organ with the highest Se concentration in human body [5], where Se is presented in the form of selenoproteins such as glutathione peroxidases (GPXs) and iodothyronine deiodinases (DIOs) to perform biological functions [6]. GPXs can protect the thyroid from peroxidative damage by acting as antioxidants and modifying the redox status [7]. DIOs can catalyze the degradation of thyroxine (TT4) to triiodothyronine (TT3) and reverse triiodothyronine (rT3), which play critical roles in thyroid hormone metabolism [8].

The association between Se status and thyroid function has been explored in previous population-based studies, but the results are inconsistent. A cross-sectional study from China found that lower serum Se status was associated with higher prevalence of thyroid disease [9]. A case-control study from Iran showed that serum Se levels were significantly lower in newly diagnosed patients with Graves' disease (GD) and Hashimoto's thyroiditis (HT) than those in the euthyroid patients [10]. However, randomized controlled trials in the United Kingdom and New Zealand indicated that Se supplementation had no effect on thyroid hormone levels and thyroid function [11, 12]. Another European cross-sectional study further showed that plasma Se levels were not associated with thyroid function in healthy older men [13]. It is of note that previous studies have commonly measured serum or plasma Se to reflect Se status, few studies have measured whole blood Se and nail Se. Whole blood Se correlated well with serum and plasma Se [14, 15], and nail Se was a good biomarker of Se exposure over the past 6 months to 1 year [16]. Further studies are required to explore the association between Se and thyroid function using whole blood and fingernail Se.

The distribution of Se in soil is extremely uneven and site-specific, although China is one of the 40 Se-deficient countries in the world, there are also some high Se areas scattered in Se-deficient areas [17]. Meanwhile, there is a high prevalence of thyroid dysfunction in

older adults [18], whether Se status is associated with high risk of thyroid dysfunction need to be verified. Considering these factors, we explored the association between Se status and thyroid hormone levels and thyroid dysfunction in an older Chinese population, fingernail Se and whole blood Se were both measured.

Methods

Study Design and Participants

A cross-sectional study on 994 older adults aged 65 or older was carried out during the 2017-2018 follow-up from the Selenium and Cognitive Decline Cohort Study in four rural counties of China [19]. Residents were enrolled in the study if they met the following eligibility criteria: (a) had lived in the area for at least 30 years; (b) consumed local food and with no dietary supplement; (c) had no language communication problem; (d) agreed to complete a face-to-face interview and provide blood and fingernail samples. Statistical analysis was performed using data from 408 participants with fingernail Se status and thyroid hormone measurements, further analysis was performed for 400 of these participants who had additional whole blood Se measurements.

All participants provided their written informed consent prior to participating in the study. The study was approved by the Institute for Environmental Health and Related Safety, Chinese Center for Disease Control and Prevention.

Fingernail Se Measurement

During the interview, more than 1 g of fingernail samples was collected from each study participant, which were sealed in clean plastic ziplock bags and labeled with basic information. Fingernail samples were cleaned by ultrasound followed by soaking in HNO_3 and HClO_4 and digested on electric hot plate, then reduced by HCl prior to measurement. The Se concentration in fingernails was determined by atomic fluorescence method with the lowest detection limit of $0.065 \mu\text{g/L}$ and the recoveries of 90.0%-106.8%. Selenium standard stock solution of $1000 \mu\text{g/mL}$ (State Nonferrous Metals and Electronic Materials Analysis and Testing Center) was diluted to a concentration of $1000 \mu\text{g/L}$, intermediate standard solution was diluted to $5 \mu\text{g/L}$ with 5% HCl . The standard working solutions were diluted by the instrument automatically to concentrations 0.1, 0.2, 0.3, 0.5, 1.0, 2.0 and $5.0 \mu\text{g/L}$, corresponding to the content of the actual samples were 0.1, 0.2, 0.3, 0.5, 1.0, 2.0, $5.0 \mu\text{g/g}$. In addition, each sample was analyzed in parallel, and if the relative error of the parallel samples was more than 10%, the determination was repeated.

Whole blood Se Measurement

3 mL of early morning fasting venous blood was collected by the nurses using 5-mL purple top (EDTA) vacutainer tubes, and all samples were stored in polypropylene tubes at -80°C until laboratory analysis. Whole blood Se concentrations were determined by inductively-coupled plasma mass spectrometry (ICP-MS). The sample was accurately added to the centrifuge tube and 0.250 mL of concentrated nitric acid was added. After 1 hour of cold digestion, the sample was placed in a boiling water bath for 4 hours to clarify the sample. Finally, the sample was cooled to room temperature, diluted to 5.00 mL with deionized

water, shaken well and then tested. 1000 mg/L standard solution (National Research Center For Certified Reference Materials, NRCCRM, China), and 100 mg/L internal standard element reserve solution of scandium, germanium, indium, and bismuth (NRCCRM, China) were used as standards and internal standards. The internal standard solution was introduced online and the standard solution and sample diluent were measured. The determination values of standard substances were consistent with the certificate values. The limit of detection for Se was 0.54 $\mu\text{g/L}$. The relative standard deviation (RSD) of replicate analysis of samples was less than 10%. In order to monitor the detection procedure, blank samples were analyzed for every 20 samples in all batches; 10% duplicated samples were also included; the samples were reanalyzed if the two results differed by $> 10\%$.

Definition of Hyperthyroidism and Hypothyroidism

3 ml Non anticoagulant whole blood samples were centrifuged at 1500 \times g for 20 min within four hours to acquire serum samples. Serum thyroid hormones were measured by immunochemiluminometric assays (ICMA), including thyroid stimulating hormone (TSH), total triiodothyronine (TT3), total thyroxine (TT4), free triiodothyronine (FT3) and free thyroxine (FT4). The limit of detection (LOD) for TSH, TT3, TT4, FT3 and FT4 was 0.005 mIU/L, 0.1 ng/ml, 0.5 $\mu\text{g/dl}$, 0.2 pmol/L, and 2.5 pmol/L, respectively.

According to the reference interval for thyroid hormones established in the Chinese population [20], the reference interval for the five thyroid hormones are as follows for men: TSH (0.64-5.03 mIU/L), FT4 (12.8-20.6) pmol/L, FT3 (4.3-6.2) pmol/L, TT4 (64.2-135.1) nmol/L, and TT3 (1.2-2.3) nmol/L; and for women: TSH (0.77-5.66 mIU/L), FT4 (11.9-18.9) pmol/L, FT3 (3.8-5.5) pmol/L, TT4 (68.2-134.7) nmol/L, TT3 (1.2-2.2) nmol/L.

Hyperthyroidism was defined as TSH below the reference range and one of several other hormones above or within the reference range; Hypothyroidism was defined as TSH above the reference range and several other hormones below or within the reference range.

Covariates Analysis

Previous studies have shown that age, gender, smoking, alcohol consumption, and body mass index (BMI) were significantly associated with thyroid measures [21-23]. Therefore, these factors were considered as covariates in our study. Information on sociodemographic characteristics such as age, gender and lifestyle factors such as alcohol consumption and smoking were collected from standardized questionnaires. BMI was calculated as weight in kilograms divided by height in square meters. The effects of ethnicity was not considered in this study because 408 participants were from specific regions and population.

Statistical Analysis

Descriptive data were presented as mean \pm standard deviation and percentages. Analysis of variance (ANOVA) models or chi-square tests were performed to compare the differences in demographic variables among Se quartile groups. Scatter plot and Pearson correlation analysis were used to describe the correlation between whole blood Se and fingernail Se concentrations. Multivariate linear regression models were used to examine the association

between whole blood Se or fingernail Se and five thyroid hormones levels. Logistic regression models adjusting for covariates were performed to examine the association between whole blood Se levels or fingernail Se levels and the risk of hyperthyroidism or hypothyroidism.

Statistical analyses were performed using R version 4.3.0 (<http://www.R-project.org>). *P* values < 0.05 were considered as statistically significant.

Results

Characteristics of the Participants

A total of 408 participants were included in the fingernail Se study population, including 259 females (63.48%). The average age of participants was 73.82 ± 5.31 years old, and the average fingernail Se level was 0.50 ± 0.17 $\mu\text{g/g}$. The participants were divided into four quartile groups according to fingernail Se levels, as shown in Table 1. The fingernail Se level for each group was 0.28 ± 0.09 , 0.46 ± 0.03 , 0.55 ± 0.03 and 0.70 ± 0.08 $\mu\text{g/g}$, respectively. Lower rates of smoking and alcohol consumption, higher rates of female and hyperthyroidism, lower TSH levels, and higher TT3, FT3, and FT4 levels were observed in higher fingernail Se quartile groups ($P < 0.05$).

A total of 400 participants were included in the whole blood Se research population, including 253 females (63.25%). The average age of the participants was 74.31 ± 5.54 years old, and the average whole blood Se level was 117.56 ± 74.86 $\mu\text{g/kg}$. The participants were divided into four quartile groups according to whole blood Se levels, as shown in Table 2. Lower rates of smoking and hypothyroidism, higher rates of female, lower TSH levels, and higher TT3, FT3, and FT4 levels were observed in higher whole Se quartile groups ($P < 0.05$).

Whole blood Se and Fingernail Se

The scatter plot showed that there was a linear association between whole blood Se and fingernail Se concentrations in the 400 participants who had both whole blood Se and nail Se measured (Figure 1). Pearson correlation analysis showed that there was medium positive correlation between whole blood Se and fingernail Se, and the correlation was statistically significant ($r = 0.672$, $P < 0.001$).

Se and Thyroid Hormone Levels

Our results showed that the higher fingernail Se was associated with lower TSH, higher FT4, FT3 and TT3 levels, as shown in Table 3. Compared with the lowest fingernail Se quartile group (Q1), lower TSH and higher FT4 and FT3 levels were observed in the Q2, Q3 and Q4, TT3 levels were higher only in the Q2 (all $P < 0.05$), after adjusting for all covariates. No statistically significant association between fingernail Se and TT4 levels was observed in all models ($P > 0.05$).

Higher whole blood Se levels were associated with lower TSH, higher FT4, FT3 and TT3 levels, as shown in Table 4. Compared with the lowest whole Se quartile group (Q1), Q2 had higher FT3, FT4 and TT3 levels, Q3 had higher FT3 levels, and Q4 had higher FT4

levels (all $P < 0.05$), after adjusting for all covariates. No statistically significant association between whole blood Se and TT4 levels was observed in all models ($P > 0.05$).

Se and Thyroid Dysfunction

Logistic regression was employed to illustrate the association between Se and thyroid dysfunction (Table 5). Compared with the lowest Se quartile group (Q1), the risk of hypothyroidism was lower in the highest quartile group (Q4) of whole blood Se (OR = 0.141, 95%CI: 0.029, 0.675), and the risk of hyperthyroidism was higher in the Q2 and Q3 of fingernail Se (Q2: OR = 4.121, 95%CI:1.233, 13.733) (Q3: OR = 3.614, 95%CI:1.095, 11.926), after adjusting for all covariates.

Discussion

In this study, higher whole blood and fingernail Se levels were associated with lower TSH levels and higher FT3, FT4, and TT3 levels. For thyroid function, higher whole blood Se levels were associated with lower risk of hypothyroidism, while higher fingernail Se levels were associated with higher risk of hyperthyroidism. The results from two analysis using different Se bio-markers consistently suggested there was a close relationship between Se status and thyroid function.

Several previous studies supported our findings regarding the association between higher Se levels and lower TSH levels and higher TT3 and FT3 levels. Results from a randomized controlled trial showed that Se supplementation increased plasma Se levels but decreased serum TSH levels in a Danish population [24]. Similarly, a cross-sectional study found that higher plasma Se levels were associated with lower TSH levels in Latvian coastal fishermen and inland subjects [25]. Results from the 2011-2012 National Health and Nutrition Examination Survey (NHANES) in the United States indicated that FT3 and TT3 levels were significantly higher in women with increased serum Se levels [26].

However, there were also some studies that did not support our results. Se supplementation trials in older population in the United Kingdom and New Zealand did not observe any effect on thyroid hormones levels [11, 12]. In a study on older European men, no significant association was found between plasma Se levels and TSH, FT4, TT3, and TT4 levels [13]. The difference in the geologic distribution of Se and dietary patterns in different countries could partly explain the inconsistency [27, 28]. In addition, lower Se levels were associated with higher FT4 and FT3 levels in healthy postmenopausal women [29]. Although the age of our study participants was comparable to that of all other studies, gender differences were observed, and the differences between study results could also be explained by the sexual dimorphism in Se intake and metabolism [30].

Several previous studies reported that higher Se levels were associated with lower risk of hypothyroidism, which were consistent with our findings. Intervention study showed that combined inositol and Se therapy reduced the risk of developing hypothyroidism in patients with autoimmune thyroid disease (AITD) [31]. Another randomized controlled trial also found that Se supplementation could restore euthyroidism in subclinical hypothyroid patients with autoimmune thyroiditis (AIT) [32]. Moreover, Se intake was negatively

associated with subclinical hypothyroidism in a large Brazilian study cohort on 14,283 adult employees [33]. Higher serum Se levels were associated with lower risk of hypothyroidism in a cross-sectional study on 6,152 subjects in China [9]. A case-control study indicated that patients with autoimmune hypothyroidism had lower serum Se levels than health controls [34]. On the other hand, higher fingernail Se levels were associated with higher risk of hyperthyroidism in our study. However, a cross-sectional study in China suggested that Se deficiency may be a risk factor for hyperthyroidism, which was contrary to our findings [35]. To date, the research on the association between Se and hyperthyroidism are still limited. Therefore, further studies, especially the prospective cohort studies, are needed to verify the association between Se and thyroid dysfunction.

Although the biological mechanism underlying the association between Se and the thyroid function has not yet been fully understood, studies have indicated that Se exerts protective effects on the thyroid gland through inhibiting oxidative stress, attenuating fibrosis, and modulating the immune response. An *in vivo* mice study observed that the lack of selenoproteins in thyroid epithelial cells could result in more lipid peroxidation and nitrosative stress [36]. Another study showed that Se supplementation had the potential to improve the prognosis of AIT by altering the subset differentiation and function of CD4+T cells [37]. An animal study using rat models indicated that Se deficiency could lead to an active process of thyroid fibrosis in which inflammatory response and an excess of TGF-beta play a key role [38]. *In vitro* cellular experiment also showed that Se exerts protective effects against oxidative stress and cell damage in human thyrocytes and thyroid fibroblasts [39].

Our study has several strengths. Firstly, fingernail Se and whole blood Se were measured to evaluate the long-term and short-term Se status of participants, respectively. This ensured comparability of our results with other studies. Secondly, the consistent results from whole blood Se and fingernail Se analysis samples increased the reliability of our study conclusion. Thirdly, Se levels in our study subjects were distributed over a wide range because they came from four different rural areas in China, which allowed us to observe the association between Se and thyroid function more objectively.

Several limitations remain in our study. Firstly, like in other cross-sectional studies, causal associations between Se levels and thyroid hormone levels and thyroid dysfunction could not be confirmed, longitudinal studies are needed to verify our results. Secondly, some confounding factors which could affect results have not been taken into account, such as an individual's iodine status. Thirdly, our conclusions may not be applicable to younger population because our study was conducted only in older adults.

Conclusion

Our results suggest that higher Se levels were significantly associated with lower TSH levels and higher levels of TT3, FT3 and FT4. Meanwhile, higher Se levels were associated with lower risk of hypothyroidism and higher risk of hyperthyroidism. Further prospective studies are needed to confirm our findings and explore potential mechanisms.

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Data Availability

No datasets were generated or analyzed during the current study.

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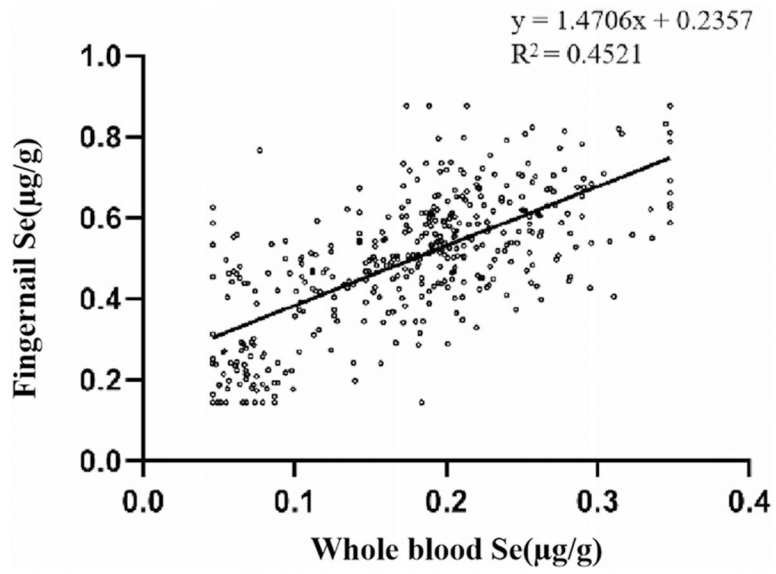


Fig. 1.
The association between whole blood Se and fingernail Se levels

Table 1

sample characteristics of fingernail Se population

Variable	Total population	Quartile groups of fingernail Se levels ($\mu\text{g/g}$)				P-Value
		Q1 (n= 102) 0.418	Q2 (n = 102) (0.418-0.507)	Q3 (n = 103) (0.507-0.607)	Q4 (n = 101) > 0.607	
Fingernail Se ($\mu\text{g/g}$)	0.50 \pm 0.17	0.28 \pm 0.09	0.46 \pm 0.03	0.55 \pm 0.03	0.70 \pm 0.08	< 0.001
Age (Years)	73.82 \pm 5.31	73.96 \pm 5.09	73.57 \pm 6.10	73.62 \pm 5.09	74.15 \pm 4.94	0.843
Female, n (%)	259 (63.48)	56 (54.90)	51 (50.00)	76 (73.79)	76 (75.25)	< 0.001
BMI(kg/m^2)	23.49 \pm 3.52	22.27 \pm 3.29	23.30 \pm 3.42	23.77 \pm 3.78	24.62 \pm 3.20	< 0.001
Smoking, n (%)	141 (34.56)	41 (40.20)	43 (42.16)	27 (26.21)	30 (29.70)	0.041
Alcohol consumption, n (%)	138 (33.82)	49 (48.04)	36 (35.29)	24 (23.30)	29 (28.71)	< 0.001
TH						
TSH (uIU/ML)	2.37 \pm 2.03	3.07 \pm 2.45	2.16 \pm 1.92	2.12 \pm 1.75	2.12 \pm 1.78	< 0.001
TT3 (nmol/L)	1.83 \pm 0.32	1.75 \pm 0.35	1.90 \pm 0.32	1.87 \pm 0.30	1.81 \pm 0.28	0.004
TT4 (nmol/L)	113.67 \pm 18.40	114.74 \pm 18.38	112.01 \pm 18.72	114.31 \pm 17.11	113.62 \pm 19.50	0.729
FT3 (pmol/L)	4.57 \pm 0.54	4.40 \pm 0.54	4.72 \pm 0.55	4.61 \pm 0.48	4.55 \pm 0.55	< 0.001
FT4 (pmol/L)	16.12 \pm 2.06	15.51 \pm 1.95	16.47 \pm 2.15	16.28 \pm 2.09	16.22 \pm 1.93	0.005
Hypothyroidism, n (%)	41 (10.05)	4 (3.92)	14 (13.73)	15 (14.56)	8 (7.92)	0.035
Hypothyroidism , n (%)	26 (6.37)	12 (11.76)	5 (4.90)	5 (4.85)	4 (3.96)	0.081

Data presented as mean \pm standard deviation or n (%)

Table 2

sample characteristics of whole blood Se population

Variable	Total population	Quartile groups of whole blood Se levels (µg/kg)				P-Value
		Q1 (n = 100) 116.153	Q2 (n = 100) (116.153 - 187.378)	Q3 (n = 100) (187.378 - 223.490)	Q4 (n = 100) > 223.490	
Whole blood Se(µg/kg)	117.56 ± 74.86	75.61 ± 21.12	160.47 ± 19.50	203.14 ± 10.21	271.02 ± 37.09	< 0.001
Age (Years)	74.31 ± 5.45	74.31 ± 5.45	73.60 ± 5.42	73.81 ± 5.43	73.80 ± 5.05	0.810
Female, n (%)	253 (63.25)	54 (54.00)	58 (58.00)	74 (74.00)	67 (67.00)	0.015
BMI(kg/m ²)	23.50 ± 3.51	22.56 ± 3.57	23.27 ± 3.44	23.72 ± 3.54	24.44 ± 3.26	0.002
Smoking, n (%)	141 (35.25)	37 (37.00)	46 (46.00)	29 (29.00)	29 (29.00)	0.035
Alcohol consumption, n (%)	136 (34.00)	40 (40.00)	38 (38.00)	24(24.00)	34 (34.00)	0.079
TH						
TSH(µU/ML)	3.37 ± 2.05	3.04 ± 2.44	2.12 ± 2.02	2.28 ± 1.94	2.03 ± 1.07	< 0.001
TT3(nmol/L)	1.84 ± 0.32	1.75 ± 0.36	1.93 ± 0.28	1.84 ± 0.30	1.83 ± 0.30	< 0.001
TT4(nmol/L)	113.75 ± 18.53	113.26 ± 19.66	116.35 ± 15.20	111.12 ± 18.74	114.27 ± 20.03	0.249
FT3(pmol/L)	4.58 ± 0.53	4.42 ± 0.52	4.73 ± 0.53	4.58 ± 0.50	4.58 ± 0.55	< 0.001
FT4(pmol/L)	16.13 ± 2.07	15.71 ± 2.01	16.44 ± 2.11	16.03 ± 2.11	16.35 ± 1.99	0.049
Hyperthyroidism, n (%)	40 (10.00)	6 (6.00)	14 (14.00)	11 (11.00)	9 (9.00)	0.286
Hypothyroidism, n (%)	25 (6.25)	12 (12.00)	6 (6.00)	5 (5.00)	2 (2.00)	0.029

Data presented as mean ± standard deviation or n (%)

Table 3

Fingernail Se and thyroid hormone levels β (95% CI)

		Quartile groups of fingernail Se levels ($\mu\text{g/g}$)				P-Value
		Q1 ($n = 102$) 0.418	Q2 ($n = 102$) (0.418 - 0.507)	Q3 ($n = 103$) (0.507 - 0.607)	Q4 ($n = 101$) > 0.607	
TSH						
Model 1	Reference		-0.907 (-1.457, -0.357)*	-0.952 (-1.501, -0.404)*	-0.954 (-1.506, -0.403)*	0.001
Model 2	Reference		-0.937 (-1.491, -0.384)*	-1.012 (-1.571, -0.452)*	-1.033(-1.603, -0.463)*	< 0.001
FT3						
Model 1	Reference		0.320 (0.174, 0.465)*	0.211 (0.066, 0.356)*	0.149 (0.003, 0.294)*	< 0.001
Model 2	Reference		0.297 (0.154, 0.441)*	0.218 (0.073, 0.363)*	0.158 (0.011, 0.306)*	< 0.001
FT4						
Model 1	Reference		0.963 (0.402, 1.523)*	0.776 (0.217, 1.335)*	0.711 (0.149, 1.273)*	< 0.001
Model 2	Reference		0.931 (0.364, 1.498)*	0.862 (0.290, 1.435)*	0.749 (0.166, 1.333)*	0.003
TT3						
Model 1	Reference		0.149 (0.063, 0.235)*	0.119 (0.033, 0.204)*	0.060 (-0.026, 0.147)	0.004
Model 2	Reference		0.131 (0.045, 0.216)*	0.083 (-0.004, 0.169)	0.029 (-0.059, -0.117)	<0.001
TT4						
Model 1	Reference		-2.737 (-7.813, 2.340)	-0.432 (-5.496, 4.632)	-1.118 (-6.208, 3.971)	0.729
Model 2	Reference		-3.215 (-8.352, 1.922)	-2.189 (-7.379, 3.001)	-2.844 (-8.130, 2.442)	0.154

Model 1: unadjusted; Model 2: age, gender, BMI, smoking and alcohol consumption were adjusted. * $P < 0.05$

Table 4

Whole blood Se and thyroid hormone levels β (95%CI)

		Quartile groups of whole blood Se levels ($\mu\text{g}/\text{kg}$)				P-Value
		Q1 (<i>n</i> = 100) 116.153	Q2 (<i>n</i> = 100) (116.153 - 187.378)	Q3 (<i>n</i> = 100) (187.378 - 223.490)	Q4 (<i>n</i> = 100) > 223.490	
TSH						
Model 1	Reference	-0.920 (-1.481, -0.359)*	-0.758 (-1.319, -0.197)*	-1.016 (-1.577, -0.456)*	0.001	
Model 2	Reference	-0.842 (-1.404, -0.281)*	-0.737 (-1.304, -0.170)*	-1.093 (-1.660, -0.526)*	< 0.001	
FT3						
Model 1	Reference	0.309 (0.163, 0.455)*	0.159 (0.013, 0.305)*	0.155 (0.009, 0.301)*	0.001	
Model 2	Reference	0.293 (0.150, 0.435)*	0.165 (0.021, 0.309)*	0.141 (-0.003, 0.285)	< 0.001	
FT4						
Model 1	Reference	0.739 (0.167, 1.311)*	0.328 (-0.244, 0.900)	0.642 (0.070, 1.241)*	0.049	
Model 2	Reference	0.695 (0.119, 1.270)*	0.375 (-0.206, 0.956)	0.627 (0.046, 1.208)*	0.034	
TT3						
Model 1	Reference	0.181 (0.094, 0.267)*	0.091 (0.005, 0.178)*	0.081 (-0.006, 0.167)	0.001	
Model 2	Reference	0.171 (0.086, 0.256)*	0.063 (-0.022, 0.149)	0.057 (-0.029, 0.143)	< 0.001	
TT4						
Model 1	Reference	3.086 (-2.059, 8.231)	-2.142 (-7.287, 3.003)	1.001 (-4.143, 6.146)	0.249	
Model 2	Reference	2.750 (-2.405, 7.906)	-3.648 (-8.850, 1.555)	0.106 (-5.309, 5.097)	0.032	

Model 1: unadjusted; Model 2: age, gender, BMI, smoking and alcohol consumption were adjusted. * $P < 0.05$

Table 5

Se and thyroid dysfunction

	Q1	Q2	Q3	Q4
	OR (95%CI)	OR (95%CI)	OR (95%CI)	OR (95%CI)
Whole blood Se and thyroid dysfunction				
hyperthyroidism	1 (Reference)	2.350 (0.828, 6.668)	1.518 (0.511, 4.511)	1.344 (0.434, 4.160)
hypothyroidism	1 (Reference)	0.603 (0.208, 1.747)	0.459 (0.148, 1.426)	0.141 (0.029, 0.675)*
Fingernail Se and thyroid dysfunction				
hyperthyroidism	1 (Reference)	4.121 (1.233, 13.733)*	3.614 (1.095, 11.926)*	1.649 (0.452, 6.020)
hypothyroidism	1 (Reference)	0.362 (0.117, 1.118)	0.382 (0.122, 1.195)	0.307 (0.089, 1.054)

age, gender, BMI, smoking and alcohol consumption were adjusted. * $P < 0.05$