Risk Management and Healthcare Policy

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ORIGINAL RESEARCH

The Relationship Between Thyroid Function Status and Serum Uric Acid Levels Based on a Restricted Cubic Spline Model: A Cross-Sectional Study

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Purpose: To date, no comprehensive studies have examined the relationship between various thyroid function statuses and thyroid hormone levels with uric acid levels. This study aims to analyze the correlation between thyroid disease and hyperuricemia.

Patients and Methods: Data from individuals undergoing health screenings in the Taiyuan area were collected. The data were categorized by thyroid disease type, thyroid function indices (FT4, FT3, and TSH), and serum uric acid (SUA) levels, followed by statistical analysis.

Results: The analysis indicated that the prevalence rates were as follows: clinical hyperthyroidism (CHyper) at 0.9%, subclinical hyperthyroidism (SCHyper) at 0.7%, clinical hypothyroidism (CHypo) at 0.8%, subclinical hypothyroidism (SCHypo) at 13.7%, and hyperuricemia at 16.9%. Further analysis revealed that the prevalence of hyperuricemia increased with higher FT4 and FT3 levels but decreased with lower TSH levels. However, logistic regression analysis showed that after adjusting for covariates, thyroid disease status, including CHyper, SCHyper, CHypo, and SCHypo, was not significantly correlated with hyperuricemia. Among the thyroid function indices, only FT4 had a statistically significant effect on the risk of hyperuricemia (OR 1.028, 95% CI 1.011–1.045). Additionally, the restricted cubic spline (RCS) was employed to assess the dose-response relationship between thyroid function indicators (FT4, FT3, and TSH) within the normal reference range and the risk of hyperuricemia. The FT4 level exhibited a positive relationship with the risk of hyperuricemia (nonlinear test χ^2 was 0.26, $P > 0.05$). When FT4 exceeded 16.85 pmol/L, higher levels of FT4 became a risk factor for hyperuricemia.

Conclusion: Thyroid disease status does not significantly affect hyperuricemia. However, within the normal range, the FT4 level demonstrates a positive dose-response relationship with the risk of hyperuricemia.

Keywords: hyperuricemia, hyperthyroidism, hypothyroidism, thyroid hormone, restricted cubic spline

Introduction

With the growing emphasis on health among the population, screenings for thyroid diseases have become more prevalent, leading to an elevated detection rate of thyroid dysfunction. This encompasses clinical hyperthyroidism (CHyper), subclinical hyperthyroidism (SCHyper), clinical hypothyroidism (CHypo), and subclinical hypothyroidism (SCHypo). Thyroid hormones play a pivotal role in metabolism, and imbalances can give rise to metabolic disorders.[1] Serum uric acid (SUA), a by - product of purine metabolism, is influenced by thyroid hormones. Elevated SUA levels can stem from increased production or decreased excretion, resulting in conditions such as hyperuricemia (HUA). HUA is a disorder that can impact all physiological systems and serves as an independent predictor of metabolic syndrome, which has garnered increasing

Received: 4 June 2025
Accepted: 5 September 2025
Published: 23 September 2025

attention. HUA can initiate local inflammation and tissue damage and is associated with various health problems, including gout, chronic kidney disease, hypertension, cardiovascular diseases, and diabetes.[2] In 1955, Kuzell et al[3] first documented the relationship between CHypo and uric acid, after which there has been a growing focus on the effect of thyroid hormones on uric acid. Although numerous studies have explored the effects of different thyroid function states on uric acid, the findings have been inconsistent. One study indicated that in males, neither CHyper nor CHypo was associated with HUA; however, in females, CHypo was not associated with HUA, while CHyper might increase the risk of HUA.[4] Previous research has reported a high prevalence of HUA in both CHyper and CHypo.[5,6] There have been relatively few studies on the relationship between subclinical thyroid dysfunction and uric acid, and their conclusions have also been inconsistent. One study demonstrated that neither SCHyper nor SCHypo was significantly associated with SUA levels.[7] However, Zhang et al observed a significantly higher risk of HUA in the SCH population.[8] There is limited evidence from recent studies, and no studies have comprehensively analyzed the relationship between different thyroid function states and uric acid levels.

Therefore, this study analyzes data from medical examination centers to investigate the relationship between thyroid diseases and uric acid levels under different thyroid function states (including CHyper, SCHyper, CHypo, and SCHypo), as well as the associations among the levels of three thyroid hormones (FT3, FT4, and TSH). To further clarify the potential association between thyroid diseases and uric acid, it may be necessary to emphasize thyroid function testing in populations with hyperuricemia, offering novel perspectives for the prevention and treatment of hyperuricemia.

Materials and Methods

Research Object

The study did not cause harm to the human body, did not involve sensitive personal information or commercial interests, and used anonymized data; therefore, it is exempt from patient consent. This study was conducted in accordance with the Declaration of Helsinki, and the procedure was approved by the Institutional Review Board of Taiyuan City Central Hospital. The data of health examinations performed at the Shangning Health Examination Center of Taiyuan from October 2020 to October 2021 were obtained for this study. Data were collected for 119,463 examinations.

The inclusion criteria were as follows: (1) SUA, thyroid function, and other important physical examination data were complete and available for review; and (2) the latest physical examination data, in the event of repeated physical examination records being available.

The exclusion criteria are as follows: (1) a history of severe liver or kidney dysfunction or cancer; (2) a history of taking medications that affect thyroid hormones and uric acid within the past three months; (3) a history of consuming iodine-containing drugs or contrast agents within the past three months; and (4) pregnancy or lactation.

Finally, the data of 16,808 examinations were analyzed (Figure 1).

Data Collection and Definitions

In each examination, a trained professional medical examiner meticulously recorded each examinee's sex, age, and past medical history, (including a history of malignant tumors, thyroid disease, and thyroid surgery. The examiner also measured each examinee's height, weight, and body mass index (BMI). After a sitting period of approximately 15 minutes, the medical examiner used a unified electronic sphygmomanometer to measure each examinee's blood pressure and recorded the systolic blood pressure (SBP) and diastolic blood pressure (DBP). Fasting venous blood was collected in the morning following an 8-hour fast. The levels of SUA, fasting plasma glucose (FPG), total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), alanine aminotransferase (ALT), aspartate aminotransferase (AST), and estimated Glomerular Filtration Rate (eGFR) were measured using a Hitachi 7600 automatic biochemistry analyzer (provided by Hitachi High-Tech Diagnostics (Shanghai) Co., Ltd). Serum levels of FT4, FT3, and TSH were measured using a Maccura i3000 automatic chemiluminescence immunoassay analyzer (manufactured by Sichuan Maccura Biotechnology Co., Ltd).

The euthyroidism (Euthy) reference values were as follows: 12.06 pmol/L $\leq$ FT4 $\leq$ 23 pmol/L; 3.3 pmol/L $\leq$ FT3 $\leq$ 7.3 pmol/L; and 0.3 mIU/L $\leq$ TSH $\leq$ 4.3 mIU/L. The CHyper reference values were as follows: TSH < 0.3 mIU/L, and FT4 > 23 pmol/L or FT3 > 7.3 pmol/L. The CHypo reference values were as follows: TSH > 4.3 mIU/L, and FT4 < 12.06 pmol/L or FT3

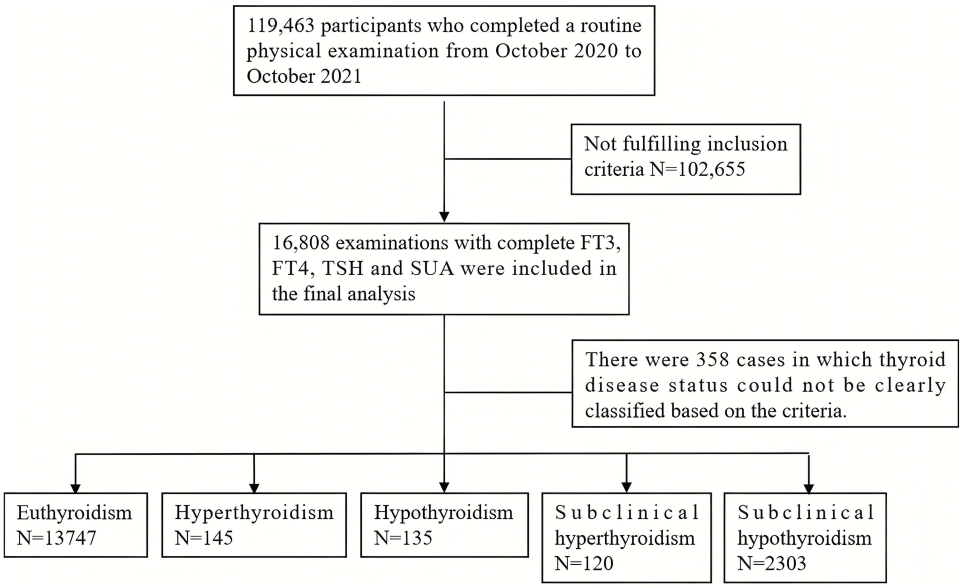

Figure 1 Study design.

< 3.3 pmol/L. The SCHyper reference values were as follows: TSH < 0.3 mIU/L, with both FT4 and FT3 within the normal range. The SCHypo reference values were as follows: TSH > 4.3 mIU/L, with both FT4 and FT3 within the normal range. In accordance with the Guidelines for the Diagnosis and Management of Hyperuricemia and Gout in China (2019),[9] SUA > 420 μmol/L in both males and females was defined as HUA.

Statistical Methods

Data was analyzed using SPSS version 26.0 and R version 4.4.2. Normally distributed data is presented as mean and standard deviation (SD), and compared using the independent samples *t*-test or one-way ANOVA for multiple groups. Non-normally distributed data is shown as median and interquartile range [M (Q1, Q3)], with the Mann–Whitney *U*-test for group comparisons. Count data is given as number and percentage, analyzed with the χ^2 test. Correlations between normally distributed bivariate variables were assessed with the Pearson correlation test, and the Spearman test for non-normally distributed variables. Multivariate logistic regression was applied to study the relationship between thyroid dysfunction types and SUA levels, with three models to adjust for covariates. Odds ratios (ORs) and 95% confidence intervals (CI) were calculated. The restricted cubic spline (RCS) method was used to model the dose-response relationship between FT4, FT3, TSH, and HUA risk in normal thyroid function. Statistical significance was set at $P < 0.05$.

Results

Study Population Characteristics

A total of 16,808 examinations with complete FT4, FT3, TSH, SUA, and biochemical data were screened. Out of these, there were 145 cases of CHyper (0.9%), 135 cases of CHypo (0.8%), 120 cases of SCHyper (0.7%), 2,303 cases of SCHypo (13.7%), and 2,839 cases of HUA (16.9%). The examinees consisted of 9,805 females (58.3%) and 7,003 males (41.7%), with an average age of 49.03 ± 13.35 years. General information is provided in Table 1.

Comparison of the Prevalence of HUA Among Different Thyroid Function Statuses and Three Levels of Thyroid Function

The SUA level was similar between the Euthy and CHyper groups, but lower in the CHypo, SCHypo, and SCHyper groups compared to the Euthy group ($P < 0.05$) (Table 1). The prevalence of HUA varied across thyroid status groups: 17.2% in Euthy, 15.9% in CHyper, 10.4% in CHypo, 10.0% in SCHyper, and 13.6% in SCHypo (Table 2).

https://doi.org/10.2147/RMHP.S536398

Table 1 Basic Characteristics of People with Different Thyroid Status

Variables		Euthy (n = 13,747)	CHyper (n = 145)	CHypo (n = 135)	SCHyper (n = 120)	SCHypo (n = 2303)
Gender [n (%)]	Male	6023 (43.80%)	51 (35.20%) *	30 (22.20%) **	24 (20.00%) ***	653 (28.40%) ***
	Female	7724 (56.20%)	94 (64.80%)	105 (77.80%)	96 (80.00%)	1650 (71.60%)
Age ($\bar{x} \pm s$, years)		48.66±13.23	48.39±13.33	51.86±13.49**	48.69±11.1	51.48±13.82**
BMI ($\bar{x} \pm s$, kg/m^2)		24.71±3.56	23.64±3.02**	25.6±3.84**	23.77±2.76***	24.73±3.49
SBP ($\bar{x} \pm s$, mmHg)		121.67±17.32	125.81±17.77**	123.55±19.27	122.11±16.17	124.12±18.61**
DBP ($\bar{x} \pm s$, mmHg)		73.04±11.3	73.6±10.28	73.62±11.49	73.42±11.26	73.7±11.35**
UA ($\bar{x} \pm s$, mmol/L)		332.08±95.62	327.51±89.75	310.67±87.39**	304.74±80.16**	320.32±90.38**
ALT [M(Q1,Q3), mmol/L]		17 (13,26)	21 (15,30) **	16.5 (12.00,22.25)	17 (12,27)	17 (13,25)
AST [M(Q1,Q3), mmol/L]		19 (16,23)	20.5 (17.0,25.0)*	20 (18,24) **	18 (16,22)*	20 (17,24) **
TG [M(Q1,Q3), mmol/L]		1.41 (0.97,2.10)	1.28 (0.86,1.86) **	1.47 (1.00,2.43)	1.37 (0.98,1.99)	1.49 (1.02,2.19) **
TC ($\bar{x} \pm s$, mmol/L)		4.91±0.98	4.24±1.03**	5.23±1.14**	4.74±0.88	5.05±1.01**
HDL-C $\bar{x} \pm s$, mmol/L)		1.39±0.29	1.29±0.28**	1.42±0.29	1.37±0.26	1.42±0.28**
LDL-C ($\bar{x} \pm s$, mmol/L)		2.85±0.81	2.38±0.79**	2.97±0.90	2.72±0.74	2.93±0.82**
FPG ($\bar{x} \pm s$, mmol/L)		5.64±1.37	5.87±1.31*	5.63±1.25	5.66±1.21	5.57±1.23*
eGFR ($\bar{x} \pm s$, mL/min/1.73m^2)		116.72±32.72	125.72±36.68**	109.42±32.58*	117.08±27.59	109.74±32.07***

Notes: Compared with Euthy group, ***$P < 0.001$, **$P < 0.01$, *$P < 0.05$.
Abbreviations: Euthy, euthyroidism; CHyper, hyperthyroidism; CHypo, clinical hypothyroidism; SCHyper, subclinical hyperthyroidism; SCHypo, subclinical hypothyroidism.

Table 2 Prevalence of HUA in Different Thyroid States

Group	Non-HUA [n (%)]	HUA [n (%)]
Euthy	11350 (82.6)	2397 (17.4)
CHyper	122 (84.1)	23 (15.9)
CHypo	121 (89.6)	14 (10.4)*†
SCHyper	108 (90.0)	12 (10.0)*†
SCHypo	1986 (86.4)	317 (13.6)*‡

Notes: *Compared with Euthy group, $P < 0.05$; †Compared with CHyper group, $P < 0.05$; ‡Compared with SCHyper group, $P < 0.05$.
Abbreviation: HUA, hyperuricemia.

The FT4, FT3, and TSH levels were categorized into four groups based on quartile ranges. Statistical analysis revealed that the prevalence of HUA rose with increasing FT4 levels, with rates of 12.10%, 14.90%, 18.30%, and 23.30% for quartiles 1 through 4, respectively. Similarly, the prevalence of HUA increased with higher FT3 levels, at 9.30%, 12.90%, 17.20%, and 29.20%, respectively. In contrast, the prevalence of HUA gradually decreased as TSH levels increased, with rates of 19.30%, 18.90%, 16.50%, and 13.80%, respectively (Figure 2).

Correlation Analysis of FT4, FT3 and TSH with SUA in People with Different Thyroid Function Statuses

Spearman's test was utilized to examine the correlations between thyroid function parameters and SUA levels in a non - normally distributed population. In both the general and euthyroid groups, FT4 and FT3 showed positive correlations with SUA, whereas TSH exhibited a negative correlation with SUA ($P < 0.05$). In the CHyper group, no significant correlations were identified ($P > 0.05$). In the SCHyper group, only FT3 demonstrated a positive correlation with SUA ($P < 0.05$), while TSH and FT4 did not ($P > 0.05$). In the CHypo group, FT3 was positively correlated with SUA ($P < 0.05$), but no significant

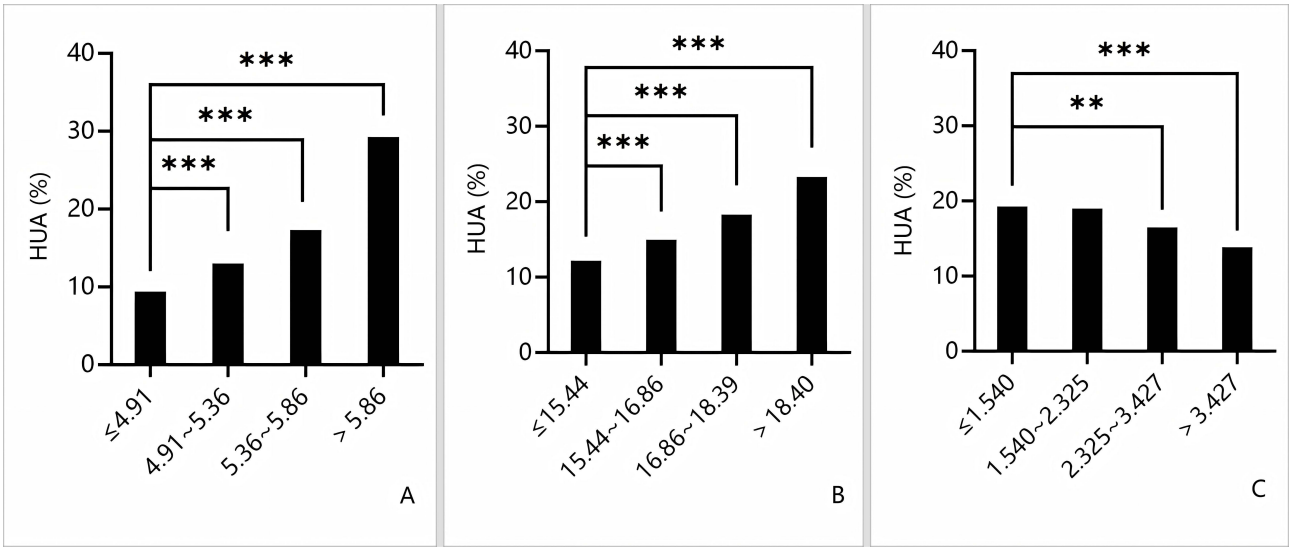

Figure 2 There were prevalence of HUA at different levels of thyroid function, and the first quantile level group was compared with the other groups. (**A**) represents the relationship between FT3 quartile levels and the prevalence of HUA. (**B**) represents the relationship between FT4 quartile levels and the prevalence of HUA. (**C**) represents the relationship between TSH quartile levels and the prevalence of HUA. Compared with the first quantile, ***$P < 0.001$, **$P < 0.01$.

correlations were observed for TSH and FT4 ($P > 0.05$). In the SCHypo group, FT4 and FT3 were positively correlated with SUA ($P < 0.05$), but TSH was not ($P > 0.05$) (Table 3).

Multivariate Logistic Regression Analysis of Thyroid Function and Risk of HUA

Univariate analysis (Model 1) indicated that TSH decreased the risk of HUA, while FT4 and FT3 increased it, both with statistical significance ($P < 0.05$). After adjusting for sex, age, and BMI in Model 2, the effect of TSH became non-significant ($P > 0.05$). In Model 3, which included additional covariates such as SBP, DBP, TG, TC, ALT, AST, and eGFR, only FT4 was found to significantly increase the risk of HUA ($P < 0.05$) (Table 4).

The study examined the correlation between thyroid function and the risk of HUA. Initially, both CHypo, SCHypo, and SCHyper were found to reduce the risk of HUA compared to euthyroid individuals ($P < 0.05$), whereas CHyper did not significantly alter the risk of HUA ($P > 0.05$). However, after adjusting for covariates, no type of thyroid disease was found to significantly influence the risk of HUA ($P > 0.05$) (Table 4).

Dose–Response Curve for Each Index and Risk of HUA in the Euthy Group

RCS was utilized to analyze the dose-response relationship between thyroid function indicators (FT4, FT3, and TSH) within the normal reference range and the risk of HUA.

The Akaike information criterion (AIC) value for the model was the smallest when 7 TSH nodes were selected (AIC = 13,050.27). The results indicated that the risk of HUA was highest when TSH was 1.25 mIU/L, and it then decreased with increasing TSH levels (nonlinear test, $\chi^2 = 10.74$, $P = 0.057$). At a TSH level of 2.10 mIU/L, the OR for the risk of

Table 3 Correlation Analysis of Various Thyroid Function Indicators with SUA

Variables	Total Population		Euthy		CHyper		CHypo		SCHyper		SCHypo	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
TSH	−0.07	0.000	−0.06	0.000	0.01	0.885	−0.09	0.307	0.08	0.390	−0.02	0.472
FT3	0.26	0.000	0.27	0.000	0.06	0.447	0.21	0.016	0.25	0.005	0.17	0.000
FT4	0.16	0.000	0.16	0.000	−0.01	0.914	0.11	0.220	−0.09	0.336	0.14	0.000

https://doi.org/10.2147/RMHP.S536398

Table 4 Logistic Regression of Risk of HUA

Variables		Model 1		Model 2		Model 3	
		OR (95% CI)	P	OR (95% CI)	P	OR (95% CI)	P
Thyroid hormone-related indicators	TSH	0.975 (0.961–0.989)	0.001	1.000 (0.989–1.011)	0.954	0.992 (0.980–1.005)	0.223
	FT3	1.212 (1.169–1.257)	0.000	1.040 (1.011–1.070)	0.006	1.015 (0.982–1.050)	0.366
	FT4	1.063 (1.050–1.076)	0.000	1.026 (1.010–1.042)	0.001	1.028 (1.011–1.045)	0.001
Thyroid disease statuses	Euthy	1.0		1.0		1.0	
	CHyper	0.908 (0.580–1.421)	0.674	1.335 (0.786–2.267)	0.284	1.511 (0.849–2.687)	0.160
	CHypo	0.557 (0.320–0.971)	0.039	0.829 (0.432–1.592)	0.574	0.669 (0.344–1.305)	0.239
	SCHyper	0.535 (0.294–0.973)	0.041	1.248 (0.644–2.421)	0.512	1.215 (0.600–2.458)	0.589
	SCHypo	0.758 (0.667–0.860)	0.000	1.219 (1.050–1.414)	0.009	1.136 (0.974–1.326)	0.104

Notes: Model 1: Univariate model of HUA; Model 2: Adjustment for age, sex, and BMI; Model 3: Adjusting for age, sex, BMI, SBP, DBP, TG, TC, ALT, AST, and eGFR.

HUA was 1 (Figure 3A). However, after adjusting for sex, age, BMI, SBP, DBP, TG, TC, ALT, AST, and eGFR, there was no significant association between TSH and HUA risk (nonlinear test, χ^2= 0.72, P = 0.396) (Figure 3B).

With six nodes, the FT3 model exhibited the lowest AIC at 14208.55. The results indicated a "J"-shaped nonlinear relationship between FT3 and HUA risk (nonlinear test, χ^2= 13.68, P = 0.008), with the risk increasing as FT3 levels rose. At 5.33 pmol/L, FT3's OR for HUA risk was 1, and above this level, the risk increased sharply (Figure 3C). However, after adjusting for the aforementioned covariates, the ORs for HUA were greater than 1 regardless of the FT3 level, and no significant dose-response trend was found (nonlinearity test, χ^2= 3.33, P = 0.068) (Figure 3D).

The FT4 model with four nodes exhibited the lowest AIC value (AIC = 14,658.77). The results indicated a linear dose-response relationship between FT3 levels and the risk of HUA (nonlinear test, χ^2= 5.49, P = 0.064). The risk of HUA increased with higher FT4 levels. At a FT4 level of 16.85 pmol/L, the odds ratio (OR) was 1 (Figure 3E). After adjusting for covariates, a positive linear relationship persisted (nonlinear test, χ^2 = 0.26, P = 0.610). For FT4 levels below 16.85 pmol/L, the OR for HUA risk was less than 1, and above this level, the OR exceeded 1 (Figure 3F).

Discussion

The recent epidemiological data from the TIDE cohort, a multicenter study conducted in China, indicates that the prevalence of CHyper among Chinese adults is 0.98%, SCHyper is 0.44%, CHypo is 1.02%, SCHypo is 12.93%, and HUA is 17.7%.[10,11] The data for our study were obtained from physical examinations of the population in Taiyuan, Shanxi, China. The analysis indicated that the prevalence of CHyper was 0.9%, SCHyper was 0.7%, CHypo was 0.8%, SCHypo was 13.7%, and HUA was 16.9%, which is basically consistent with the results reported for the TIDE study. HUA is a metabolic disorder characterized by abnormally high levels of SUA, primarily due to either increased production or decreased excretion of SUA.[12] Numerous studies have reported that elevated SUA levels are a significant contributing factor to cardiovascular diseases, including myocardial infarction, stroke, and heart failure.[13–17] Only 20% of the body's uric acid (SUA) is ingested through the diet, while 80% is produced by the catabolism of purines.[18] Therefore, it is necessary to identify additional factors that affect uric acid metabolism, as this is of significant importance for reducing the disease burden.

In this study, qualitative and quantitative analyses were conducted to examine the prevalence of HUA across various thyroid function states. The qualitative analysis revealed that the prevalence of HUA among individuals with CHyper was higher than that among those with CHypo, but it was not significantly different from the prevalence among individuals with Euthy. However, the HUA rate in the SCHypo population was higher than that in the SCHyper population. Further quantitative analysis revealed that the prevalence of HUA increased in tandem with rising levels of FT4 and FT3, yet the prevalence of HUA gradually diminished as TSH levels increased. This differs from the outcomes reported in certain earlier studies. A study conducted by Giordano et al[5] indicated that individuals with hyperthyroidism and those with hypothyroidism exhibit a higher prevalence of HUA compared to the general population.

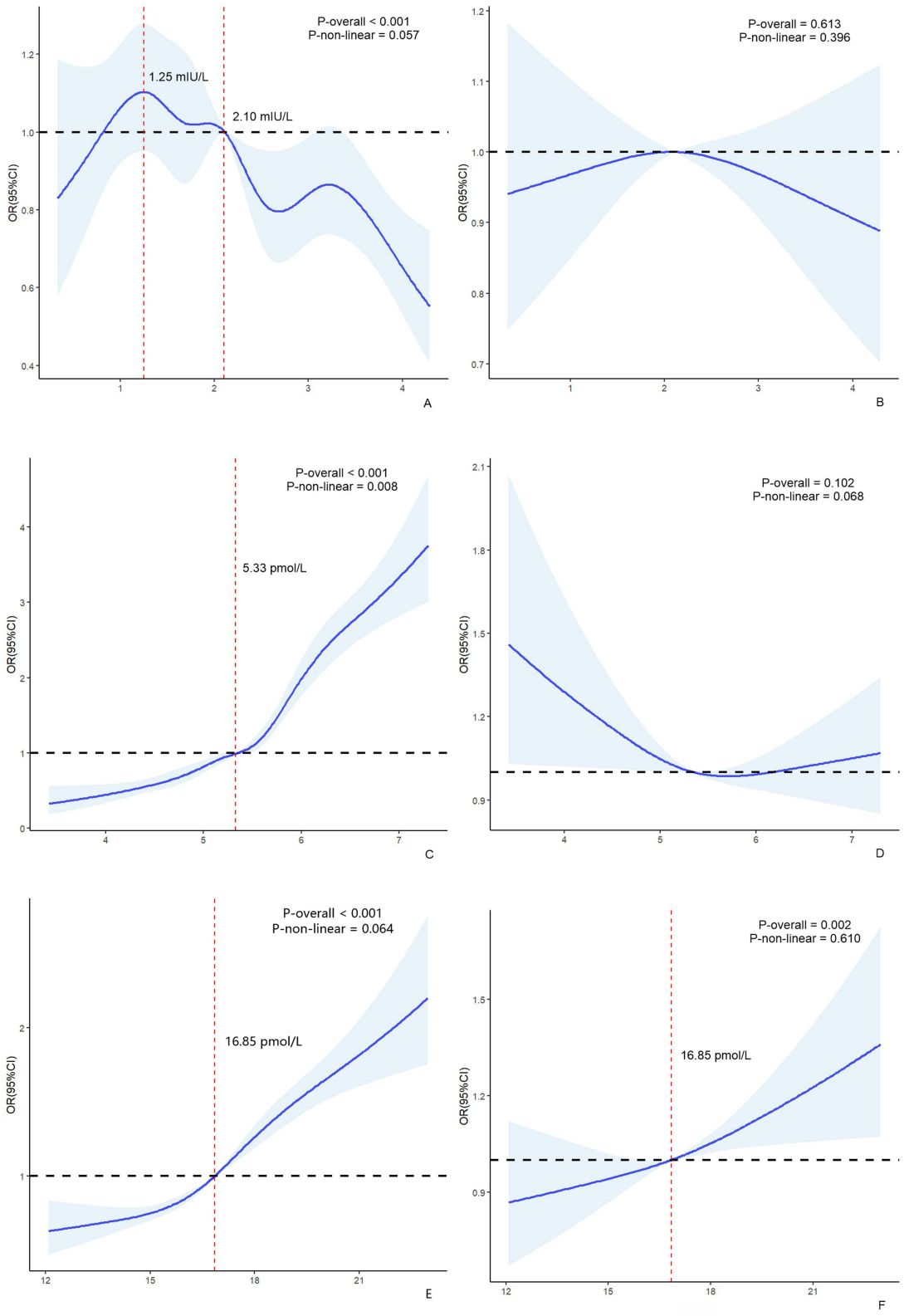

Figure 3 Using the restricted cubic spline (RCS) method, the dose-response relationship between thyroid function indicators within the normal range and the risk of HUA was analyzed. (**A** and **B**) represent the dose-response relationship between TSH and the risk of HUA occurrence before and after adjusting for covariates, respectively. (**C** and **D**) represent the dose-response relationship between FT3 and the risk of HUA occurrence before and after adjusting for covariates, respectively. (**E** and **F**) represent the dose-response relationship between FT4 and the risk of HUA occurrence before and after adjusting for covariates, respectively.

https://doi.org/10.2147/RMHP.S536398

Currently, the connection between thyroid disorders and uric acid levels is a subject of debate. Research suggests that there is no substantial link between T4 or TSH levels and SUA in cases of hyperthyroidism or hypothyroidism.[19] However, another study revealed that hyperthyroid patients have elevated SUA levels, with hyperthyroidism being a risk factor for HUA in both males and females.[20] Our research indicates that among individuals with hyperthyroidism, encompassing both SCHyper and CHyper, there is no significant correlation between FT3, FT4, and TSH levels and SUA. Moreover, logistic regression analysis revealed that neither SCHyper nor CHyper has a statistically significant effect on the risk of HUA.

However, some studies suggest an association between hypothyroidism and the prevalence of HUA.[21] A large cohort study involving 11,446 participants concluded that SCHypo significantly increases the risk of HUA.[8] However, our findings indicate that although FT3 and FT4 levels positively correlate with SUA in SCHypo or CHypo populations, logistic regression analysis did not establish a direct link between these conditions and the development of HUA. However, our logistic regression analysis of thyroid hormone levels and the risk of HUA indicated that only FT4 was associated with the risk of HUA.

We further analyzed the relationship between thyroid hormone levels and serum uric acid levels in individuals with normal thyroid function (euthyroid). When traditional logistic regression is applied to the study of etiological inferences and dose-response relationships, it is necessary to assume that the relationship between the variables is linear. However, in actual clinical studies, a purely linear relationship is uncommon. Previous studies often group continuous variables and then convert them into categorical variables to observe possible nonlinear relationships between independent and dependent variables. This method, however, results in the loss of some information during grouping, and different outcomes may be observed depending on the number of groups and nodes selected. The RCS model integrates quantitative data with outcome events, and the outcomes can illustrate the impact of minor quantitative alterations in the independent variable on the OR value of the dependent variable through a continuity curve. This approach overcomes the limitations of the Ln (OR) method, which only provides linear estimates for the effect of continuous variables on dependent variables. It also enables the continuous representation of a nonlinear dose–response relationship.[22,23] Based on the aforementioned research conclusions, we have determined that Euthy may also influence the occurrence of HUA. Therefore, the use of RCS, in conjunction with a logistic regression model, was employed to fit the dose-response relationship between FT3, FT4, TSH, and the risk of HUA. This approach allowed for a more intuitive observation of the changes in the relationship between thyroid function and HUA, as well as the inflection points for each hormone level when the trend changes. The study's findings indicated that, both before and after adjusting for covariates, there was a positive linear relationship between FT4 levels and the risk of HUA. Specifically, the risk of HUA rose with increasing FT4 levels when they exceeded 16.85 pmol/L. These results align with previous research conducted by Ye[7] and more recent work by Chao.[24]

The effects of thyroid hormones on uric acid levels may occur through various pathways. Previous research has indicated that FT4 might influence uric acid concentrations in the body by enhancing the turnover of purine nucleotides.[5,6] Another hypothesis suggests that thyroid dysfunction may be associated with reduced uric acid clearance. Lippi et al[25] found that e-GFR was decreased and increased in subjects with TSH>2.5 μIU/mL and TSH<0.2 μIU/m, respectively. They suggested that TSH levels may be an independent predictor of e-GFR. A recent study examined the correlation between HUA and e-GFR across various thyroid function statuses. The findings corroborated those of Lippi et al, indicating that e-GFR was notably diminished in both male and female subjects with a TSH level exceeding 2.5 μIU/mL.[15] However, these conflicting studies cannot be fully explained by the aforementioned mechanism. Recently, Laclaustra[26] suggested that reduced sensitivity to thyroid hormones may explain the conflicting reports in previous studies. A recent study examined the correlations between the TFQI, TSHI, and TT4RI with SUA. The TFQI, TSHI, and TT4RI all reflect the sensitivity of the thyroid gland's center. The TFQI's value ranges from −1 to 1; positive values suggest decreased thyroid hormone sensitivity, while negative values suggest increased thyroid hormone sensitivity. A TFQI value of 0 signifies normal thyroid hormone sensitivity. Elevated TSHI and TT4RI values might suggest reduced central sensitivity to thyroid hormones. Furthermore, the correlation between FT3/FT4 and SUA, which indicates sensitivity to peripheral thyroid hormones, was also examined. The results of the study showed that impaired central

and peripheral sensitivity to thyroid hormones (increased TFQI, TT4RI, TSHI, and PTHQI and decreased FT3/FT4 ratio) were associated with elevated SUA levels in a Chinese euthyroid population.[27]

This study possesses several positive attributes. Firstly, the sample size incorporated is larger than that of numerous previous studies. Secondly, this study examined the relationship between various thyroid disease statuses, an array of thyroid hormone-related indicators, and uric acid from multiple dimensions, a task not undertaken in prior studies. Finally, to more accurately describe the relationship between the two, this study employed a range of statistical methods for a comprehensive analysis. However, it is important to note that this study also has its limitations. First, this is a cross-sectional study, with data sourced from the physical health screening at the health examination center. Further prospective studies are needed to verify causal relationships. Second, we did not collect data on dietary habits that may affect SUA levels; however, Shanxi is a non-coastal city with a shortage of seafood and a predominantly high carbohydrate diet. Additionally, we established the levels of serum FT4, FT3, TSH, and SUA based on a single measurement, and thus, the diagnoses are not definitive. Finally, since the population in this study was from China, it is uncertain whether our findings are applicable to other ethnic groups.

Conclusion

Thyroid disease status does not have a significant effect on HUA. However, FT4 levels within the normal range exhibit a positive dose-response relationship with the risk of HUA, with a cutoff value of 16.85 pmol/L. This indicates that monitoring FT4 levels, even in individuals without apparent thyroid disease, could be beneficial for evaluating the risk of HUA. Individuals with FT4 levels nearing or surpassing 16.85 pmol/L may require more frequent monitoring of their uric acid levels or preventive strategies for HUA or gout, particularly if they possess additional risk factors.

Acknowledgments

We want to acknowledge the staff of Shangning Health Examination Center of Taiyuan. We also want to acknowledge the colleagues who participated in this current study.

Disclosure

The authors report no conflicts of interest in this work. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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