Association between Decreased Thyroid Stimulating Hormone and Hyperuricemia in Type 2 Diabetic Patients with Early-stage Diabetic Kidney Disease

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Research

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Abstract

Background

Serum uric acid (SUA) is associated with the development of diabetic kidney disease (DKD). Thyroid hormones can regulate metabolism and insulin resistance. The relationship between SUA and thyroid function is still uncertain.

Methods

254 type 2 diabetic patients with early-stage DKD were enrolled in current study and were further classified as high SUA group (SUA > 360 μmol/L, n = 126) and normal SUA group (SUA ≤ 360 μmol/L, n = 128). 85 control subjects were recruited as control group. The clinical characteristics were obtained via face-to-face surveys and medical records.

Results

Compared with normal SUA group and control group, high SUA group exhibited the increased SUA, free triiodothyronine and free thyroxine levels, and the decreased thyroid stimulating hormone (TSH) level (P < 0.017 for all), and no significant difference was detected in these parameters between normal SUA group and control group. Furthermore, the increased creatinine (β = 2.049, P < 0.001), triglycerides (β = 10.068, P < 0.001), urinary albumin-to-creatinine ratio (β = 0.262, P = 0.001), fasting blood glucose (β = 5.280, P = 0.003) and fasting insulin (β = 1.440, P = 0.034) levels, and the decreased TSH (β = -24.906, P < 0.001) level were independently correlated with higher SUA level in type 2 diabetic patients with early-stage DKD. Notably, decreased TSH retained a significant association (odds ratio = 1.654, P = 0.002) with hyperuricemia in type 2 diabetic patients with early-stage DKD.

Conclusions

TSH is negatively correlated with SUA, and decreased TSH is an independent risk factor for hyperuricemia in type 2 diabetic patients with early-stage DKD. These results indicate that thyroid hormones, TSH in particular, might participate in regulating uric acid metabolism in patients with early-stage DKD.

1. Background

The prevalence of type 2 diabetes mellitus (T2DM) is greatly increasing, and many patients suffer from diabetes-related complications. Diabetic kidney disease (DKD), one of the major microvascular complications of diabetes, is the main cause of end-stage renal disease and is associated with high morbidity and mortality.

In human beings, uric acid (UA) is the end product in purine metabolism, and approximately 70% of UA is eliminated through the kidney [1]. The increased serum uric acid (SUA) has been reported to be correlated with the progression of insulin resistance [2], metabolic syndrome [3], and T2DM [4]. Recently, SUA has been documented to cause the development of microvascular diseases and thereby renal injury in DKD by several reported effects, including inducing the endothelial dysfunction [5], causing the inflammatory cascades [6], activating the profibrotic cytokine [7], and increasing the activity of the renin-angiotensin aldosterone system [6]. Therefore, the elevated SUA has been regarded as one of the major predictors of DKD.

Accumulating evidence has indicated that thyroid hormones can regulate metabolism and insulin resistance [8]. Thyroid dysfunction can worsen glucose metabolism and induce hyperglycemia in patients with T2DM, promoting the risk of diabetic complications. Hyperglycemia decreases the level of thyroid stimulating hormone (TSH) and reduces the conversion of thyroxine to triiodothyronine in the peripheral tissues [9]. There have been several studies about the relationship between SUA and thyroid function. However, the results were conflicting. Some studies supported that there was a higher risk of hyperuricemia in patients with hypothyroidism [10] or with subclinical hypothyroidism [11] relative in comparison to the general subjects. On the other hand, a linear relationship between free thyroxine (FT4) and SUA was observed in a large-scale cross-sectional clinical study in individuals without overt thyroid dysfunction [12]. Moreover, a recent study has also demonstrated that the decrease of SUA by the treatment of febuxostat or allopurinol led to the increase of TSH in patients with gout [13].

To the best of our knowledge, studies of the relationship between SUA and thyroid hormones in patients with DKD have been few in number, with incomplete information regarding the underlying interaction. Therefore, in the present study, we aimed to investigate the possible association between thyroid hormones and SUA in type 2 diabetic patients with early-stage DKD.

2. Methods

2.1. Study population

The study protocol was approved by the Medicine and Pharmacy Ethics Committee of Beijing Chao-Yang Hospital, Capital Medical University. Written informed consent was obtained from each subject.

The participants aged from 18 to 80 years were recruited consecutively from May 2017 to March 2019 in a group of outpatients at the Department of Endocrinology, Beijing Chao- Yang Hospital, Capital Medical University, Beijing, China.

Patients were diagnosed with T2DM as defined by the World Health Organization (WHO) criteria, and were diagnosed with early-stage DKD according to urinary albumin-to-creatinine ratio (UACR) [14]. Subjects were selected in line with both results of UACR from two urine samples collected on different days in one month were in 30 ~ 300 mg/g [14]. Hyperuricemia was defined as the SUA level > 360 μmol/L [15].

People with primary glomerulonephritis or kidney diseases caused by secondary conditions other than diabetes, with gout or medicines that influence UA metabolism, with history of thyroid diseases or medicines that influence thyroid function, and with infection, malignancies, autoimmune disease, hypertension, congestive heart failure or pregnancy were excluded from all groups.

The following exclusion criteria for type 2 diabetic patients with early-stage DKD were applied: known type 1 and other specific types of diabetes (e.g., genetic defects of the β-cell, genetic defects in insulin action, diseases of the exocrine pancreas, endocrineopathies, drug- or chemical induced diabetes, infections, uncommon forms of immune mediated diabetes, or other genetic syndromes associated with diabetes) according to the WHO classification of diabetes mellitus. Moreover, people with recent acute diabetic complications, including ketoacidosis, hyperosmolar nonketotic diabetic coma and lactic acidosis, were also excluded from the study. In addition, none of the control participants had a history of glycometabolism abnormality.

254 type 2 diabetic patients with early-stage DKD were enrolled for the study, and were further divided into high SUA group (SUA > 360 μmol/L, n = 126) and normal SUA group (SUA ≤ 360 μmol/L, n = 128). 85 control subjects were recruited as control group.

2.2. Measurements of clinical parameters

A standard questionnaire was used to collect information about the participants' health status and medications. Height and weight were measured without shoes and in light clothing to the nearest 0.1 cm and 0.1 kg, respectively, by the same trained group. Body mass index (BMI) was calculated as weight (kg) / [height (m)]^2. Blood pressure was measured using a calibrated standard mercury sphygmomanometer. All readings were measured from the non-dominant arm after a 5-min resting period with the patients in the sitting position.

Fasting blood samples were collected in the morning after an 8-h overnight fast. Random spot urine samples were obtained after 24 hours without physical exercise. UACR was determined as the mean of measurements of two urine samples obtained on different days in one month. Blood and urine analyses were conducted in the Central Laboratory of Beijing Chao-Yang Hospital, Capital Medical University.

Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), fasting blood glucose (FBG), creatinine (CR) and UA in serum were detected using a Dade-Behring Dimension RXL Autoanalyzer (Dade Behring Diagnostics, Marburg, Germany). Fasting insulin (FINS) was estimated on a Beckman Access 2 (Fullerton, CA, USA). Glycated hemoglobin (HbA1c) was measured by high-performance liquid chromatography using the HLC-723G7 analyzer (Tosoh Corporation, Japan). Insulin resistance was determined using the following method: homeostasis model assessment of insulin resistance (HOMA-IR) = FINS (mIU/L) * FBG (mmol/L) / 22.5. The estimated glomerular filtration rate (eGFR) was calculated using the Chinese modification of diet in renal disease (MDRD) equation: eGFR (ml/min/1.73 m^2) = 175 × (serum creatinine) $^{-1.234}$ × (age)$^{-0.179}$ × (0.79 for female) [14]. Urinary creatinine was detected by enzymatic method (SIEMENS, Germany, BNProSpec);

urinary albumin was measured by scattering turbidimetry (Abbot, America, c16000). Free triiodothyronine (FT3), FT4 and TSH were measured by electrochemiluminescence immunoassay (ECLIA) using an Abbott Architect i2000 (Abbott Diagnostics, Abbott Park, IL, USA). The reference intervals for FT3, FT4 and TSH were 2.30 ~ 4.20 pg/ml, 0.89 ~ 1.76 ng/dl and 0.55 ~ 4.78 μIU/ml, respectively.

2.3. Statistical analysis

All analyses were performed using Statistical Package for Social Sciences version 20.0 (SPSS, Inc., Chicago, IL, USA). The normality of the data distribution was verified using the Kolmogorov-Smirnov test. Normally distributed data were expressed as the means ± standard deviations. Non-normally distributed data were expressed as medians with 25th and 75th percentiles. Comparisons of the clinical and biochemical markers in three groups were performed using one-way ANOVA and Kruskal-Wallis H test. Proportions were analyzed using the chi-squared test. The associations between clinical parameters and thyroid hormones and SUA in type 2 diabetic patients with early-stage DKD were examined using Pearson's or Spearman's correlation coefficient analyses. Variables with a *P*-value < 0.05 in Pearson's or Spearman's correlation coefficient analyses were retained for the multiple stepwise regression analyses. All tests were two-sided, and a *P*-value < 0.05 was used to indicate statistical significance for the results. However, given the multiple comparison performed, statistical significance at the 0.017 (0.05 divided by the times of comparison) should be used.

3. Results

3.1. Clinical characteristics of study participants in three groups

The study cohort included 254 type 2 diabetic participants with early-stage DKD consisting of high SUA group and normal SUA group, and 85 control participants as control group. The clinical characteristics of all study participants are listed in Table 1. The participants in three groups were similar in gender, age, systolic blood pressure (SBP), and diastolic blood pressure (DBP) ($P > 0.05$ for all). A significant trend was observed for BMI, TC, HDL-C, LDL-C, TG, FBG, HbA1c, FINS, HOMA-IR, CR, eGFR, UACR, FT3, FT4, TSH and SUA in three groups ($P < 0.01$ for all). High SUA group had the significantly increased levels of BMI, TG, FBG, HbA1c, HOMA-IR, CR, FT3 and FT4, and the significantly decreased level of eGFR compared with normal SUA group and control group ($P < 0.017$ for all). The levels of BMI, TG, FBG, HbA1c and HOMA-IR were significantly elevated in normal SUA group than those in control group ($P < 0.017$ for all), and no significant difference was detected in CR, eGFR, FT3 and FT4 between normal SUA group and control group ($P > 0.017$ for all). Both high SUA group and normal SUA group exhibited the significantly higher levels of TC, LDL-C, FINS and UACR, and the significantly lower level of HDL-C than control group ($P < 0.017$ for all), and there was no significant difference in these parameters between high SUA group and normal SUA group ($P > 0.017$ for all). Furthermore, compared with normal SUA group and control group, high SUA group was with a higher SUA level (Fig. 1) and a lower TSH level (Fig. 2) ($P < 0.017$ for both). However, no significant difference was observed in SUA and TSH between normal SUA group and control

group ($P > 0.017$ for both). The decreased TSH in high SUA group might indicate the possible association between thyroid function and uric acid metabolism in type 2 diabetic participants with early-stage DKD.

Table 1
Clinical characteristics of study participants in three groups

Parameters	High SUA group (n = 126)	Normal SUA group (n = 128)	Control group (n = 85)	*P*
Gender (M/F)	82/44	72/56	52/33	0.353
Age (years)	51.86 ± 10.68	53.89 ± 11.13	51.35 ± 10.77	0.177
BMI (kg/m^2)	26.99 ± 5.33‡†	25.09 ± 3.83†	23.58 ± 3.05	< 0.001
SBP (mmHg)	117.98 ± 9.63	118.32 ± 8.28	118.28 ± 11.82	0.956
DBP (mmHg)	68.83 ± 8.75	67.86 ± 7.38	68.55 ± 7.84	0.618
TC (mmol/L)	4.90 ± 1.30†	4.72 ± 1.33†	4.33 ± 0.61	0.003
HDL-C (mmol/L)	1.03 ± 0.25†	1.11 ± 0.31†	1.54 ± 0.33	< 0.001
LDL-C (mmol/L)	2.78 ± 0.87†	2.70 ± 1.07†	2.39 ± 0.46	0.006
TG (mmol/L)	2.20 (1.54, 3.01)‡†	1.55 (1.05, 2.33)†	0.78(0.62,1.12)	< 0.001
FBG (mmol/L)	9.30 ± 2.41‡†	7.92 ± 2.57†	5.02 ± 0.34	< 0.001
HbA1c (%)	9.06 ± 2.07‡†	8.45 ± 1.90†	5.57 ± 0.39	< 0.001
FINS (mIU/L)	15.40(10.98,20.03)†	14.70(9.23,18.20)†	8.70(5.37,12.40)	< 0.001
HOMA-IR	5.51 (4.66, 7.53)‡†	4.67 (3.06, 6.46) †	1.99 (1.26, 2.76)	< 0.001
CR (μmol/L)	73.22 ± 21.66‡†	59.95 ± 14.85	61.97 ± 11.29	< 0.001
eGFR (mL/min/1.73 m^2)	111.06 ± 34.75‡†	134.84 ± 35.83	128.70 ± 30.71	< 0.001
UACR (mg/g)	37.98(33.88,90.02)†	37.76(33.23,52.48)†	3.45 (1.79, 5.29)	< 0.001
FT3 (pg/ml)	3.63 ± 0.50‡†	3.46 ± 0.41	3.47 ± 0.37	0.004
FT4 (ng/dl)	1.34 ± 0.20‡†	1.25 ± 0.16	1.23 ± 0.14	< 0.001
TSH (μIU/ml)	1.54 (1.10, 2.25) ‡†	2.03 (1.29, 3.05)	2.03 (1.33, 2.95)	< 0.001

Parameters	High SUA group (n = 126)	Normal SUA group (n = 128)	Control group (n = 85)	*P*
SUA (μmol/L)	420.30 ± 65.31‡†	280.09 ± 65.04	274.64 ± 67.60	< 0.001

3.2. Correlation between clinical parameters and thyroid hormones and SUA in type 2 diabetic participants with early-stage DKD

Then, the Pearson's or Spearman's analyses were performed to assess the underlying association between thyroid function and uric acid metabolism in 254 type 2 diabetic participants with early-stage DKD including individuals in high SUA group and normal SUA group. The results showed that SUA was positively correlated with BMI (r = 0.351, P < 0.001), TG (r = 0.386, P < 0.001), FBG (r = 0.200, P = 0.001), FINS (r = 0.257, P < 0.001), HOMA-IR (r = 0.406, P < 0.001), CR (r = 0.593, P < 0.001), UACR (r = 0.252, P < 0.001), FT3 (r = 0.220, P < 0.001) and FT4 (r = 0.355, P < 0.001), and was negatively associated with HDL-C (r = -0.293, P < 0.001) and eGFR (r = -0.491, P < 0.001) in type 2 diabetic participants with early-stage DKD (Table 2). Moreover, SUA was negatively correlated with TSH (r = -0.346, 95% confidence interval: -0.457 to -0.211, P < 0.001) in type 2 diabetic participants with early-stage DKD (Fig. 3). These findings suggested that decreased TSH was associated with elevated SUA in type 2 diabetic participants with early-stage DKD.

Table 2
Correlation between clinical parameters and SUA in type 2 diabetic patients with early-stage DKD (n = 254)

Parameters	*r*	*P*
Age (years)	-0.113	0.072
BMI (kg/m^2)	0.351	< 0.001
SBP (mmHg)	0.108	0.087
DBP (mmHg)	0.071	0.257
TC (mmol/L)	0.025	0.687
HDL-C(mmol/L)	-0.293	< 0.001
LDL-C (mmol/L)	0.003	0.967
TG (mmol/L)	0.386	< 0.001
FBG (mmol/L)	0.200	0.001
HbA1c (%)	0.053	0.398
FINS (mIU/L)	0.257	< 0.001
HOMA-IR	0.406	< 0.001
CR (μmol/L)	0.593	< 0.001
eGFR (mL/min/1.73 m^2)	-0.491	< 0.001
UACR (mg/g)	0.252	< 0.001
FT3 (pg/ml)	0.220	< 0.001
FT4 (ng/dl)	0.355	< 0.001
TSH (μIU/ml)	-0.346	< 0.001

3.3. Multiple regression analysis of clinical parameters and thyroid hormones correlated with SUA in type 2 diabetic participants with early-stage DKD

Furthermore, to explore the role of thyroid function in uric acid metabolism, the multiple stepwise regression analysis was performed to determine which parameters were independently correlated with SUA in type 2 diabetic participants with early-stage DKD. The results showed that after adjusting for the confounders, the increased CR (β = 2.049, P < 0.001), TG (β = 10.068, P < 0.001), UACR (β = 0.262, P = 0.001), FBG (β = 5.280, P = 0.003) and FINS (β = 1.440, P = 0.034), and the decreased TSH (β = -24.906, P < 0.001) were independently related to higher SUA in type 2 diabetic participants with early-stage DKD (Table 3). The model had an adjusted R-squared value of 0.574 (F = 57.792 and P < 0.001).

Table 3
Multiple regression of parameters associated with SUA in type 2 diabetic patients with early-stage DKD

Parameters	*β*	SE	95% CI	Standardized *β*	*P*
Constant	150.129	26.107	98.709 ~ 201.550		< 0.001
CR (mIU/L)	2.049	0.257	1.543 ~ 2.555	0.415	< 0.001
TSH (μIU/ml)	-24.906	3.733	-32.258 ~ -17.553	-0.286	< 0.001
TG (mmol/L)	10.068	1.774	6.574 ~ 13.562	0.244	< 0.001
UACR (mg/g)	0.262	0.076	0.113 ~ 0.411	0.182	0.001
FBG (mmol/L)	5.280	1.735	1.862 ~ 8.698	0.143	0.003
FINS (mIU/L)	1.440	0.675	0.111 ~ 2.769	0.111	0.034

3.4. Logistic regression analysis of clinical parameters and thyroid hormones associated with hyperuricemia in type 2 diabetic patients with early-stage DKD

Subsequently, to further clarify the role of TSH in uric acid metabolism, the logistic regression analysis of the associations between the anthropometric parameters and the thyroid hormones and hyperuricemia in type 2 diabetic patients with early-stage DKD was analyzed, and the adjusted results were shown in Table 4. TG, CR, FBG and TSH were independently associated with hyperuricemia in type 2 diabetic patients with early-stage DKD. Elevated SUA was positively associated with TG [odds ratio (OR) = 0.799, $P < 0.006$], CR (OR = 0.936, $P < 0.001$), and FBG (OR = 0.822, $P = 0.002$). Notably, decreased TSH with an OR of 1.654 ($P = 0.002$, 95% confidence interval: 1.218 to 2.247) was associated with hyperuricemia in type 2 diabetic patients with early-stage DKD.

Table 4
Logistic regression of parameters associated with hyperuricemia in type 2 diabetic patients with early-stage DKD

	β	SE	OR	95% CI	*P*
TG (mmol/L)	-0.224	0.082	0.799	0.680 ~ 0.938	0.006
CR (μmol/L)	-0.066	0.014	0.936	0.911 ~ 0.961	< 0.001
FBG (mmol/L)	-0.196	0.063	0.822	0.727 ~ 0.931	0.002
TSH (μIU/ml)	0.503	0.156	1.654	1.218 ~ 2.247	0.002

4. Discussion

Hyperuricemia is one of the characteristics of metabolic syndrome which is based on insulin resistance [16]. Metabolic syndrome and insulin resistance might present obesity, hypertriglyceridemia, low HDL-C,

hyperglycemia, hyperinsulinemia and hyperuricemia [16]. In present study, subjects with hyperuricemia in type 2 diabetic patients with early-stage DKD had increased BMI, TG, FBG, HbA1c, HOMA-IR and SUA values compared with subjects with normal SUA level in type 2 diabetic patients with early-stage DKD and the controls. The levels of BMI, TG, FBG, HbA1c and HOMA-IR were significantly elevated in subjects with normal SUA level in type 2 diabetic patients with early-stage DKD than those in the controls. Type 2 diabetic patients with early-stage DKD in both high SUA group and normal SUA group exhibited the higher levels of TC, LDL-C and FINS, and the lower level of HDL-C than the control subjects. Furthermore, SUA was positively associated with BMI, TG, FBG, FINS and HOMA-IR, and was negatively correlated with HDL-C in type 2 diabetic patients with early-stage DKD. After adjusting for the confounders, increased TG, FBG and FINS were independently related to higher SUA in type 2 diabetic patients with early-stage DKD. Our findings suggested that type 2 diabetic patients with early-stage DKD were with higher insulin resistance than the controls, and that subjects with hyperuricemia presented further increased insulin resistance compared with subjects with normal SUA level in type 2 diabetic patients with early-stage DKD.

Accumulating evidence has demonstrated that SUA is independently associated with DKD in type 2 diabetic patients [17]. Hyperuricemia plays an important role in the development of DKD, and there is evidence that the reduction in SUA value benefits the progression of DKD [18]. In the early state of DKD, eGFR might present a reduction after a momentary elevation, and UACR shows increase; with the development of the renal injury, serum CR will elevate eventually [19]. Our present study indicated that type 2 diabetic patients with early-stage DKD exhibited higher UACR level than control subjects. Participants with hyperuricemia in type 2 diabetic patients with early-stage DKD had the higher CR value, and the lower eGFR value compared with participants without hyperuricemia in type 2 diabetic patients with early-stage DKD and the controls. Moreover, SUA was positively associated with CR and UACR, and was negatively related with eGFR in type 2 diabetic patients with early-stage DKD. After adjusting for the confounders, the increased CR and UACR were independently related to the elevated SUA in type 2 diabetic patients with early-stage DKD. Our results suggested that patients with hyperuricemia might present more severe renal injury than patients with normal SUA level in type 2 diabetic patients with early-stage DKD, and that hyperuricemia might be associated with DKD.

Importantly, we reported for the first time in present study that FT3 and FT4 were higher, and TSH was lower in patients with hyperuricemia in type 2 diabetic patients with early-stage DKD compared with patients with normal SUA level in type 2 diabetic patients with early-stage DKD and in the controls. SUA was positively associated with FT3 and FT4, and was negatively correlated with TSH in type 2 diabetic patients with early-stage DKD. In addition, the multiple regression analysis showed that after adjusting for the confounders, the decreased TSH was independently related to the higher SUA in type 2 diabetic patients with early-stage DKD. The logistic regression analysis presented that the reduction of TSH was associated with hyperuricemia in type 2 diabetic patients with early-stage DKD. Our findings suggested an association between thyroid function, TSH in particular, and UA metabolism in type 2 diabetic patients with early-stage DKD.

The association between SUA and thyroid function has been assessed in several previous studies which provided controversial results. An increase in hyperuricemia rates was observed in patients with hypothyroidism [10] and in patients with subclinical hypothyroidism [11] compared to the general individuals, but no relationship between hypothyroidism and hyperuricemia was found in these studies. Moreover, another research reported no relationship between SUA and thyroid hormones in patients with thyroid dysfunction [20]. However, the majority of previous studies are consistent with our findings. A previous large-scale cross-sectional study documented a linear association between FT4 and SUA in general subjects [12]. The risk of hyperuricemia was also significantly increased in individuals with higher FT4 level [12]. Additionally, a recent study also demonstrated that the decrease of SUA by the treatment of febuxostat or allopurinol exerted effects on the elevation of TSH in patients with gout [13]. It is possible that these conflicting results are due to the poly-pharmacotherapy or other confounding variables of the study populations, such as species, gender, age and health condition of the subjects. These discrepancies might also be caused by differences in the assays used by the different researches.

It has been speculated that the negative relationship between SUA and TSH in current research might be due to insulin resistance [21]. Hyperuricemia is one of the manifestations of insulin resistance, and the excessive TSH and the insufficient thyroxine and triiodothyronine contribute to insulin resistance [22]. There may be a compensatory reduction in TSH (the most sensitive index in thyroid hormones) which leads to the elevation of thyroxine and triiodothyronine, and further contributes to overcome insulin resistance. We hypothesize that the decreased TSH in type 2 diabetic patients with early-stage DKD according to the increase of SUA in our study might have reflected a compensatory result to counterbalance the increased insulin resistance which was indicated by the higher SUA.

There are some limitations in the present study. Firstly, the participants recruited in the current cohort were limited to type 2 diabetic patients with early-stage DKD individuals; hence, our results may not be directly applicable to other subjects. Secondly, the current study was one single center research, and the sample size in the study was relatively small; therefore, the findings of the present research might not have been powerful enough to account for potentially confounding factors in the analyses, and the results of our study might have been improperly influenced by some outliers. Thirdly, our study is a cross-sectional study which could not determine the existence of a causal relation but rather provides evidence for the link between the decrease of TSH and the probability of being hyperuricemia in type 2 diabetic patients with early-stage DKD. Our present research certainly provides possible hypotheses to be confirmed and extended by future prospective cohort and mechanistic studies. A follow-up study will be necessary to evaluate whether thyroid function independently related to hyperuricemia in type 2 diabetic patients with early-stage DKD eventually.

5. Conclusions

The current findings suggest that TSH is negatively correlated with SUA, and decreased TSH is an independent risk factor for hyperuricemia in type 2 diabetic patients with early-stage DKD. These results indicate that thyroid hormones, TSH in particular, might participate in regulating uric acid metabolism in

patients with early-stage DKD. Future studies involving the underlying mechanism and intervention strategies are highly warranted.

Abbreviations

BMI
Body mass index; CI:Confidence interval; CR:Creatinine; DBP:Diastolic blood pressure; DKD:Diabetic kidney disease; eGFR:Estimated glomerular filtration rate; FBG:Fasting blood glucose; FINS:Fasting insulin; FT3:Free triiodothyronine; FT4:Free thyroxine; HbA1c:Glycated hemoglobin; HDL-C:High-density lipoprotein cholesterol; HOMA-IR:Homeostasis model assessment of insulin resistance; LDL-C:Low-density lipoprotein cholesterol; MDRD:Modification of diet in renal disease; OR:Odds ratio; SBP:Systolic blood pressure; SE:Standard error; SUA:Serum uric acid; TC:Total cholesterol; TG:Triglycerides; TSH:Tthyroid stimulating hormone; T2DM:Type 2 diabetes mellitus; UA:Uric acid; UACR:Urinary albumin-to-creatinine ratio; WHO:World Health Organization

Declarations

Ethics approved and consent to participate

The study was approved by the Medicine and Pharmacy Ethics Committee of Beijing Chao-Yang Hospital, Capital Medical University, Beijing, China. Written informed consent was obtained from all patients.

Consent for publication

All the participants gave consent for direct quotes from their interviews to be used in this manuscript.

Availability of data and material

The data used to support the findings of this study are available from corresponding author upon request.

Competing interests

The authors declare that they have no conflicts of interest.

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Authors' contributions

YX conceived the study; XF wrote the manuscript; JH and YP collected and read the literature; and YX read and corrected the manuscript. All authors read and approved the final manuscript.

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No.

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Figures

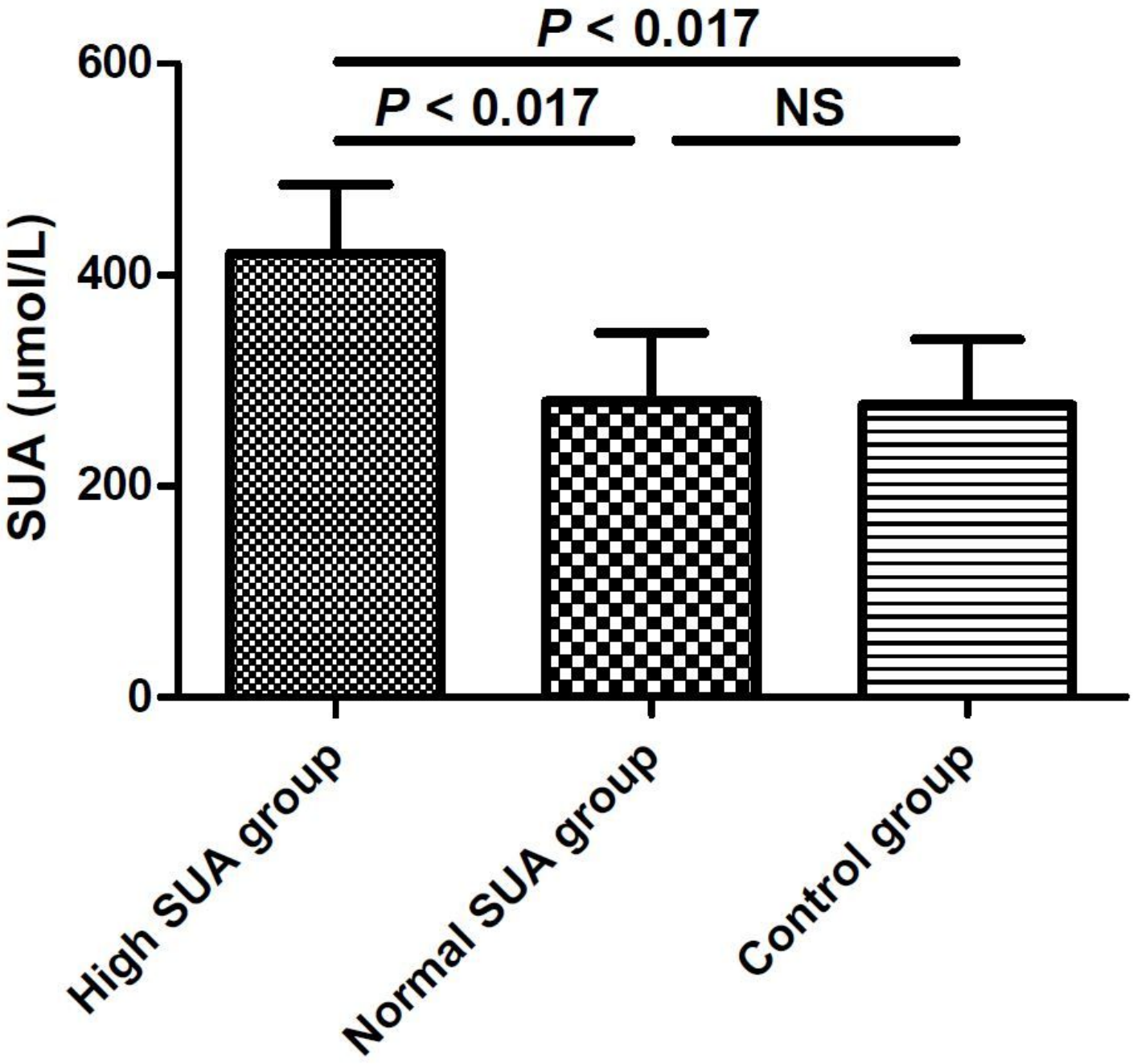

Figure 1

SUA level measured in all study participants The values are expressed as the means ± standard deviations. High SUA group, subjects with hyperuricemia in type 2 diabetic patients with early-stage diabetic kidney disease (n = 126); Normal SUA group, subjects with normal SUA level in type 2 diabetic patients with early-stage diabetic kidney disease (n = 126); Control group, control subjects (n = 85); SUA, serum uric acid.

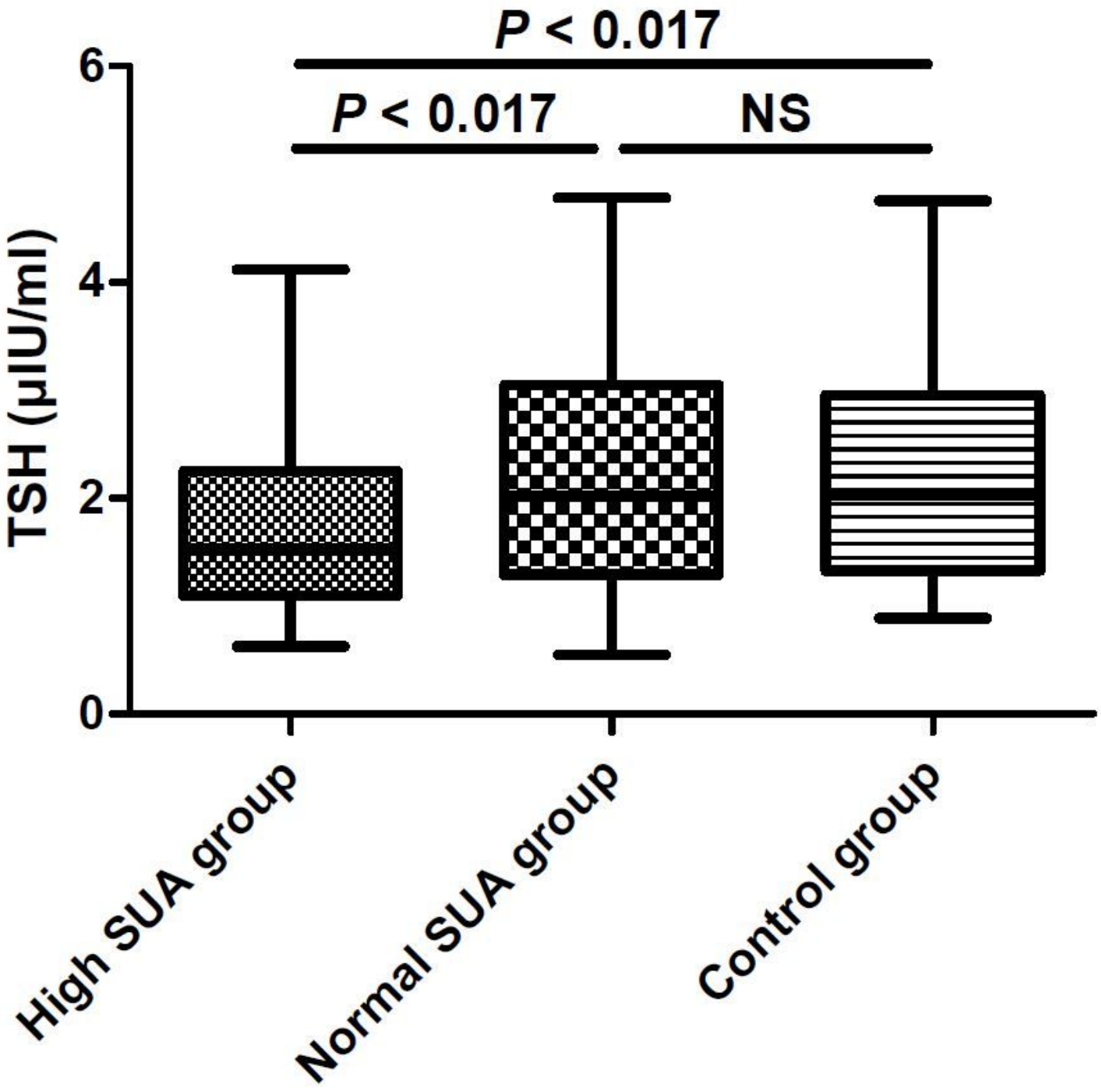

Figure 2

TSH level measured in all study participants The values are expressed as the medians (25th and 75th percentiles). High SUA group, subjects with hyperuricemia in type 2 diabetic patients with early-stage diabetic kidney disease (n = 126); Normal SUA group, subjects with normal SUA level in type 2 diabetic patients with early-stage diabetic kidney disease (n = 126); Control group, control subjects (n = 85); TSH, thyroid stimulating hormone.

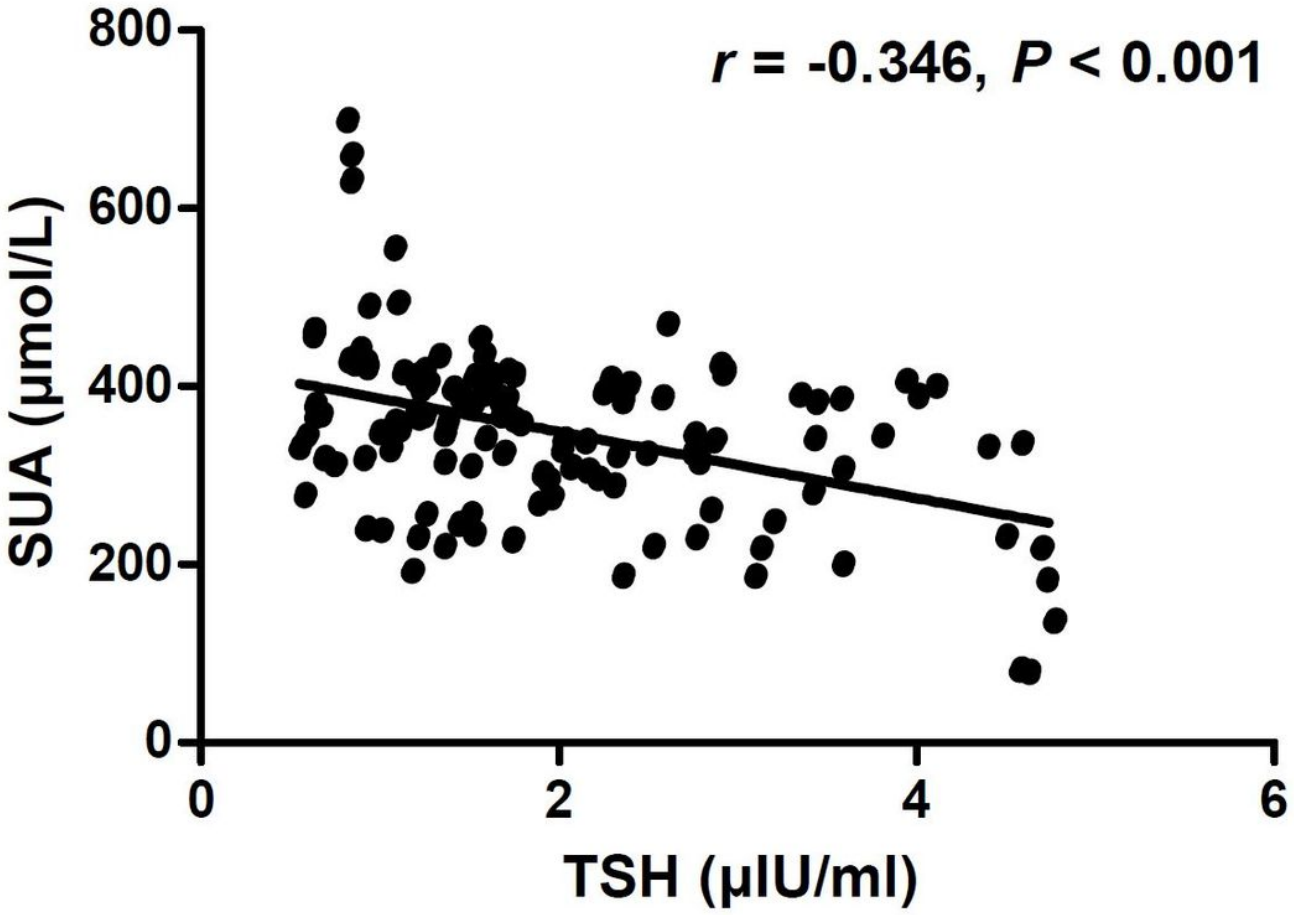

Figure 3

Correlation between TSH and SUA in type 2 diabetic patients with early-stage DKD TSH, thyroid stimulating hormone; SUA, serum uric acid; DKD, diabetic kidney disease (n = 254)