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Association of formation of urinary calculi with blood lipid levels.

Longlong Tang, Hesong Ye, Yuan Qin, Ming Yang, Wentao Gong, Qi He, Yang Shen and Qiyue Wang

Jiangsu Second Chinese Medicine Hospital, The Second Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing 210000, Jiangsu Province, China.

Keywords: urinary calculi; blood lipids; correlation.

Abstract. We aimed to analyze the composition of urinary calculi and its correlations with blood lipids such as triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Three hundred patients with urinary calculi treated from January 2020 to July 2021 were selected retrospectively into a urinary calculi group, while three hundred healthy individuals who received physical examination in our hospital during the same period were enrolled in a control group. Using the Spearman correlation analysis, we investigated the correlation between the composition of urinary calculi and dyslipidemia and explored the factors affecting urinary calculi through multivariate logistic regression analysis. The serum levels of TG and TC were significantly higher ($p<0.05$), the serum HDL-C level was significantly lower ($p<0.05$), while the serum LDL-C level displayed no significant difference ($p>0.05$) in the urinary calculi group compared with those in the control group. The proportion of uric acid calculi was significantly higher in urinary calculi patients with dyslipidemia than that in those with normal blood lipids ($p<0.05$). However, no significant difference was observed in the proportions of infectious calculi and calcium calculi between urinary calculi patients with dyslipidemia and those with normal blood lipids ($p>0.05$). Dyslipidemia was positively correlated with uric acid calculi ($p<0.05$) but not associated with infectious calculi or calcium calculi ($p>0.05$). TG was a risk factor for urinary calculi ($p<0.05$). The formation of urinary calculi is closely associated with blood lipid levels. Dyslipidemia, especially hypertriglyceridemia, can easily induce the formation of uric acid calculi.

Corresponding author: Hesong Ye. Jiangsu Second Chinese Medicine Hospital, The Second Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing 210000, Jiangsu Province, China. Email: yehsjscmu@shu-edu.cn

Asociación de formación de cálculos urinarios con niveles de lípidos en sangre.

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Palabras clave: cálculos urinarios, lípidos en sangre, correlación.

Resumen. Nuestro objetivo fue analizar la composición de los cálculos urinarios y sus correlaciones con los lípidos sanguíneos, como los triglicéridos (TG), el colesterol total (CT), el colesterol de lipoproteínas de baja densidad (LDL-C) y el colesterol de lipoproteínas de alta densidad (HDL-C). Trescientos pacientes con cálculos urinarios tratados desde enero de 2020 hasta julio de 2021 fueron seleccionados retrospectivamente e incluidos en el grupo de cálculos urinarios, mientras que trescientas personas sanas que recibieron un examen físico en nuestro hospital durante el mismo período se inscribieron en el grupo control. La correlación entre la composición de los cálculos urinarios y la dislipidemia se investigó mediante un análisis de correlación de Spearman, y los factores que afectan a los cálculos urinarios se exploraron mediante un análisis de regresión logística multivariable. Los niveles séricos de TG y TC fueron significativamente más altos ($p<0,05$), el nivel sérico de HDL-C fue significativamente más bajo ($p<0,05$), mientras que el nivel sérico de LDL-C no mostró diferencias significativas ($p>0,05$) en el grupo los cálculos urinarios en comparación con los del grupo control. La proporción de cálculos de ácido úrico fue significativamente mayor en los pacientes con cálculos urinarios y dislipidemia que en aquellos con lípidos sanguíneos normales ($p<0,05$). Sin embargo, no se observaron diferencias significativas en las proporciones de cálculos infecciosos y cálculos de calcio entre los pacientes con cálculos urinarios con dislipidemia y aquellos con lípidos sanguíneos normales ($p>0,05$). La dislipidemia se correlacionó positivamente con cálculos de ácido úrico ($p<0,05$), pero no se asoció con cálculos infecciosos o cálculos de calcio ($p>0,05$). TG fue un factor de riesgo para cálculos urinarios ($p<0,05$). La formación de cálculos urinarios está estrechamente relacionada con los niveles de lípidos en sangre. La dislipidemia, especialmente la hipertrigliceridemia, puede inducir fácilmente la formación de cálculos de ácido úrico.

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INTRODUCTION

Urinary calculi is one of the common urinary system diseases, with an annually steadily increasing prevalence rate, especially in young people, and the first attack rate is the highest among people aged 20-30 years old [1,2]. From a global view, urinary calculus presents a high prevalence rate in countries such as the United States, China, Thailand, and the United Kingdom, but is rare in Central America, South America, and Africa. Epidemiological data have manifested that the incidence rate of urinary calculi is 1-5% in China, and about 25% of such patients need to be hospitalized [3,4]. As people's working rhythm speeds up, their diet structure changes and their living standards improve, the incidence rate of urinary calculi is climbing each year. The formation of urinary calculi is exceptionally complicated and closely associated with abnormal lipid metabolism, insulin resistance, hyperglycemia, hypertension, obesity, etc.[5]. Blood lipids are essential substances for the primary metabolism of living cells, which widely exist in human bodies and can take part in energy metabolism [6]. According to a study [7], abnormal lipid metabolism is essential in forming urinary calculi. However, the correlations between blood lipids and urinary calculi remain unclear. Therefore, this study analyzed the composition of urinary calculi, and the correlations of urinary calculi with blood lipids were investigated to provide a theoretical basis for the clinical prevention and treatment of urinary calculi.

PATIENTS AND METHODS

General data

Three hundred patients with urinary calculi treated in our hospital from January 2020 to July 2021 were selected retrospectively into a urinary calculi group, while three hundred healthy individuals who received physical examination in our hospital during the same period were enrolled in a control group.

Inclusion criteria: 1) patients diagnosed as urinary calculi by B-ultrasound, kidney ureter bladder X-ray, intravenous pyelography, or computed tomography urography, 2) those whose medical history was complete, 3) those without blood diseases, 4) those without autoimmune diseases, 5) those with no cardiovascular diseases, and 6) those who were informed of this study and signed the informed consent. Exclusion criteria: 1) patients complicated with dysfunction of vital organs such as heart, liver, or lung, 2) those pregnant or breastfeeding, 3) those complicated with a malignant tumor, hypertension, or diabetes mellitus, 4) those with abnormal blood coagulation, 5) those with hyperparathyroidism, or 6) those with cognitive dysfunction.

Methods

Age, gender, BMI, smoking history, drinking history, and other general data of all the subjects were recorded after admission. Five ml of fasting peripheral venous blood was collected in the morning and placed in an aseptic vacuum blood collection tube. After centrifugation (Beijing Era Beili Centrifuge Co., Ltd., model: DT4-6D) at 3,000 rpm for 15 min to separate the serum, the serum levels of low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and total cholesterol (TC) were measured using an automatic biochemistry analyzer (Beijing Beiruida Pharmaceutical Technology Co., Ltd., model: SR95-SUNMATIK-9050). The criteria for dyslipidemia were those referred to in the *Chinese Guidelines for the Prevention and Treatment of Dyslipidemia in Adults (2016 Revision)*[8]. Urinary calculi samples were collected on the day of operation, which were washed with distilled water and dried naturally. Later, the composition of urinary calculi was analyzed using a LUMOS stand-alone FT-IR spectroscopy analyzer (Bruker, Germany).

Statistical analysis

The IBM SPSS 26.0 software was utilized for statistical analysis. The numerical data were expressed as n (%) and compared by the χ^2 test between groups. The measurement data were expressed as ($\bar{\chi} \pm s$) and compared by t-test between groups. Spearman's analysis was employed to analyze the correlation between urinary calculi composition and dyslipidemia. Besides, multivariate logistic regression analysis was adopted to explore the factors affecting urinary calculi. $p<0.05$ indicated that the difference was statistically significant.

RESULTS

Baseline clinical data

In the urinary calculi group, there were 190 males and 110 females, aged 18-67 years old, with an average age of 45.56±5.23 years old and a body mass index (BMI) of 24.51±3.34 kg/m^2. Two hundred of the patients had a smoking history, while 210 of them had a drinking history. In terms of urinary calculi type, there were 100 cases of kidney calculi, 190 cases of ureteral calculi, and ten cases of bladder calculi. In the control group, there were 189 males and 111 females, aged 18-68 years old, with a mean age of 45.51±5.45 years old and a BMI of 24.57±3.17 kg/m^2. Among them, 202 patients had a smoking history, while 209 had a drinking history. No significant differences were found in the age, gender, smoking history, BMI, drinking history and other general data between the two groups ($p>0.05$).

Composition of urinary calculi

The composition analysis results of the 300 patients with urinary calculi indicated 260 cases of calcium calculi (including 102 cases of calcium oxalate - calcium oxalate monohydrate/calcium oxalate dihydrate), 32 cases of calcium oxalate + calcium phosphate, 54 cases of calcium oxalate + hydroxyapatite, 54 cases of calcium oxalate + uric acid, and 18 cases of calcium oxalate + uric acid + calcium phosphate, 51 cases of infectious calculi (including 23 cases of hydroxyapatite + calcium oxalate, 14 cases of magnesium ammonium phosphate + calcium oxalate, four cases of hydroxyapatite + magnesium ammonium phosphate, two cases of ammonium urate, and eight cases of magnesium ammonium phosphate + uric acid), and 28 cases of uric acid calculi (including ten cases of uric acid calculi and 18 cases of uric acid + magnesium ammonium phosphate).

Serum levels of TG, HDL-C, TC and LDL-C

The serum levels of TG and TC were significantly higher, while the serum HDL-C levels were significantly lower in urinary calculus group than those in control group, showing statistically significant differences ($p<0.05$). However, the serum LDL-C levels in the urinary calculus group displayed no statistically significant differences in comparison with those in control group ($p>0.05$) (Fig. 1).

Multivariate logistic regression analysis results of factors affecting formation of urinary calculi

Multivariate logistic regression analysis was performed by incorporating the factors with significant differences above, revealing that TG was a risk factor for the formation of urinary calculi ($p<0.05$) (Table 1).

Composition of calculi in urinary calculi patients with normal blood lipids and dyslipidemia

The proportion of uric acid calculi in urinary calculi patients with dyslipidemia was significantly higher than in those with normal blood lipids, showing a statistically significant difference ($p<0.05$). However, there were no statistically significant differences in the proportions of infectious calculi and calcium calculi between urinary calculi patients with dyslipidemia and those with normal blood lipids ($p>0.05$) (Table 2).

Correlation between the composition of urinary calculi and dyslipidemia

Dyslipidemia was positively correlated with uric acid calculi ($p<0.05$), but not associated with infectious calculi or calcium calculi ($p>0.05$) (Table 3).

DISCUSSION

The reasons for the formation of urinary calculi are complicated, and are associated with various factors. According to a study[9], hyperglycemia, hypertension and abnormal lipid metabolism are risk factors for the formation of urinary calculi, and abnormal lipid metabolism is an important contributor to

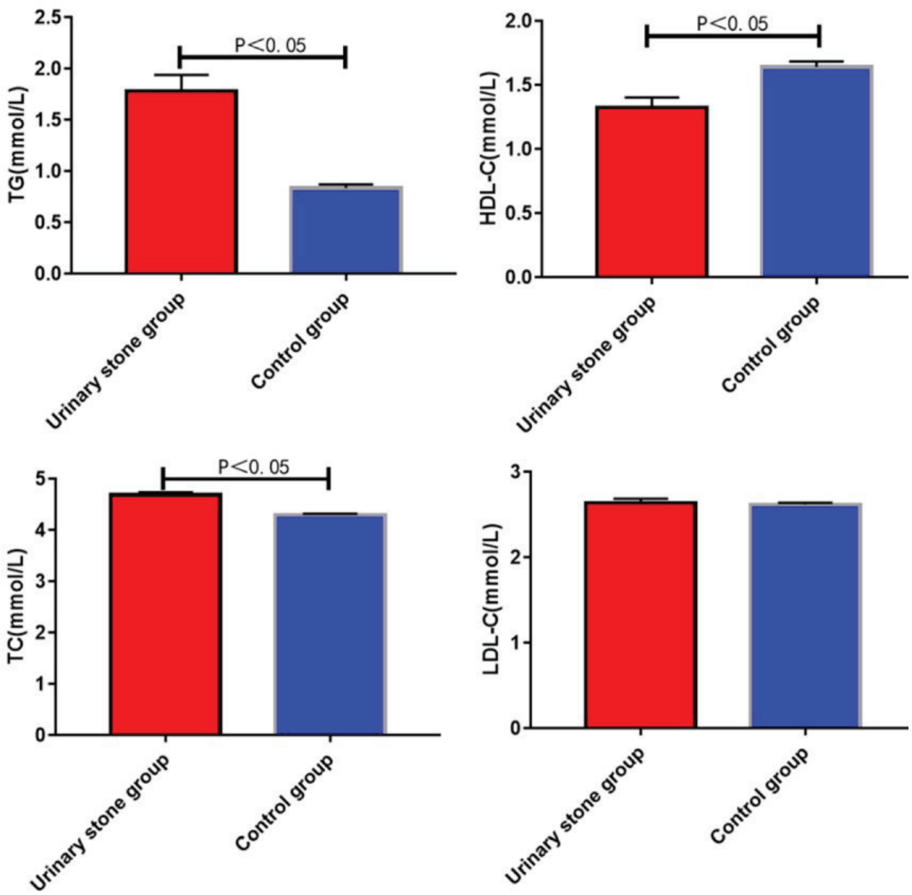

Fig. 1. Serum levels of TG, HDL-C, TC and LDL-C.

Table 1
Composition of calculi in urinary calculi patients with normal blood lipids and dyslipidemia (n(%)).

Group	n	Infectious calculi	Calcium calculi	Uric acid calculi
Normal blood lipids	210	39 (18.57)	180 (85.71)	8 (3.81)
Dyslipidemia	90	12 (13.33)	80 (88.89)	20 (22.22)
χ^2		1.225	0.550	25.241
P		0.268	0.459	<0.001

Tabla 2
Correlation between composition of urinary calculi and dyslipidemia.

Composition of urinary calculi	Dyslipidemia	
	r	p
Infectious calculi	0.082	0.647
Calcium calculi	0.056	0.834
Uric acid calculi	0.678	<0.001

Table 3
Logistic regression analysis results of factors affecting urinary calculi.

Variable	Partial regression coefficient	Standard error	Wald	P	95% CI	OR
Gender	-0.242	0.179	1.562	0.983	0.431-0.902	0.872
Age	0.243	0.154	1.872	0.871	0.672-1.325	1.128
BMI	-0.319	0.147	4.234	0.643	0.542-0.927	0.743
Smoking history	0.156	0.182	1.784	0.743	0.783-1.221	1.209
Drinking history	0.257	0.211	1.673	0.683	1.092-2.532	1.392
TG	0.811	0.305	12.298	0.004	1.547-5.092	2.345
LDL-C	0.041	0.098	0.345	0.823	0.811-1.243	1.112
HDL-C	0.209	0.174	1.205	0.645	0.745-1.562	1.532
TC	0.227	0.172	1.782	0.711	0.943-2.093	1.342

the formation of urinary calculi, which can increase the risk of urinary calculi by 25-30%. A previous study [10] suggested that elevated blood lipid levels will induce rising blood viscosity, leading to atherosclerosis (AS), affecting renal blood flow, and thereby facilitating the deposition of lithogenic substances in the blood to form calculi. The results of this study manifested that the serum levels of TG and TC were remarkably higher. In contrast, serum HDL-C level was dramatically lower in the urinary calculus group than those in the control group. Still, the serum LDL-C levels were not significantly different between the two groups, which was consistent with the study results of Besiroglu *et al.* [11]. These findings suggest that the formation of urinary calculi is associated with dyslipidemia. Moreover, the results of multivariate logistic regression analysis demonstrated that TG was a risk factor for urinary calculi, implying that dyslipidemia, especially hypertriglyceridemia, is more prone to the formation of urinary calculi. Hence, controlling blood lipids has important clinical significance for the prevention of urinary calculi.

For the 300 urinary calculi patients enrolled in this study, the high incidence age was 40-50 years old, with more males than females (the male-to-female ratio was 1.73). By analyzing the composition of urinary calculi, it was found that there were 260 cases of calcium calculi, 51 cases of infectious calculi, and 28 cases of uric acid calculi. It can be inferred that calcium calculi were the major components of calculi in the 300 patients. It is probably because the dietary structure of residents in this area is dominated by seafood, meat, and other high-protein and high-cholesterol foods. Excessive intake of such foods can result in the elevation of blood lipids and increased endogenous acid metabolites in urine, which boosts the excretion of urinary calcium, calcium oxalate, and uric acid, reduces citrate excretion, and lowers the reabsorption of calcium in urine, thereby inducing more calcium oxalate calculi. Among the 300 patients with urinary calculi in this study, the proportion of patients with infectious calculi was next only to those with calcium calculi; most were female. Infectious calculi are the results of infection caused by urease-producing bacteria in urine, and the major components include magnesium ammonium phosphate, apatite and so on [12]. It has been pointed out in a study [13] that urinary tract infection is one of the most common pathogenic factors of female urinary calculi, and the incidence rate of upper urinary tract infectious calculi in female is three times that in men. In the present study, uric acid calculi were the least common among the 300 patients with urinary calculi. Uric acid is not only the major composition of uric acid calculi, but also involved in the formation of calculi composed of other elements. Hyperuricemia-induced calculi are co-formed by a variety of components under different internal environments [14]. It has been revealed in a study [15] that patients with uric acid calculi have higher incidence rates of diabetes mellitus, poor glucose tolerance, and hypertriglyceridemia than normal people. The results of this study also demonstrated that the proportion of uric acid calculi in urinary calculi patients with dyslipidemia was dramatically higher than that in those with normal blood lipids. Still, there was no significant difference in the proportions of infectious calculi and calcium calculi between urinary calculi patients with dyslipidemia and those with normal blood lipids.

This suggested that dyslipidemia can easily lead to the formation of urinary calculi, especially uric acid calculi, which was further confirmed by the Spearman correlation analysis in this study. It is because elevated blood lipid levels can lead to lipid deposition, which damages the tubular excretory function, thus resulting in rising uric acid levels. Meanwhile, increased uric acid levels reduce lipoprotein esterase activity and TG decomposition. As a result, the blood TG level rises. In addition, high uric acid can cause increased excretion of urine, rising uric acid concentration in urine, and decreased urine PH, so it is more likely to induce the formation of uric acid calculi under the action of multiple factors [16-18]. Uric acid can reduce the protective activity of inhibitors against calcium oxalate crystal formation in urine, allowing the formation of calcium oxalate crystals and aggregation into stones. Therefore, hyperuricemia is related to uric acid-induced heterogeneous nucleation of calcium oxalate crystals [19].

Hence, in clinical treatment of urinary calculi, besides calculus treatment, attention should be paid to regulating the metabolism level in the body, effective control of blood lipids, reasonable diet, and more exercise, so as to lower the risk of recurrent urinary calculi.

In summary, the formation of urinary calculi is closely associated with blood lipid levels. Dyslipidemia, especially hypertriglyceridemia, can easily lead to the formation of uric acid calculi. Controlling blood lipids has important clinical significance for the prevention of urinary calculi. Regardless, this study is limited. This is a single-center retrospective study with a small sample size, so the results may be biased. In the future, we will perform multicenter prospective studies with larger sample sizes to clarify the specific mechanism.

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Conflicts of interest

The authors reported no potential conflict of interest.

ORCID numbers

- Longlong Tang (LT): 0000-0002-9951-3257
- Hesong Ye (HY): 0000-0002-8303-6468
- Yuan Qin (YQ): 0000-0003-1257-3984
- Ming Yang (MY): 0000-0002-8688-3611
- Wentao Gong (WG): 0000-0002-8891-0476
- Qi He (QH): 0000-0003-1987-0949
- Yang Shen (YS): 0000-0002-6329-9826
- Qiyue Wang (QW): 0000-0002-6593-9145

Authors' contribution

LT and HY designed the study; YQ, MY and WG conceived and supervised the study; QH and YS performed and analyzed the experiments; QW drafted the paper. All authors read and approved the final manuscript.

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