Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: informahealthcare.com/journals/irnf20

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To cite this article: Mehmet Inci, Abdullah Demirtas, Bahadir Sarli, Emrecan Akinsal & Numan Baydilli (2012) Association between Body Mass Index, Lipid Profiles, and Types of Urinary Stones, Renal Failure, 34:9, 1140-1143, DOI: 10.3109/0886022X.2012.713298

To link to this article: https://doi.org/10.3109/0886022X.2012.713298

Published online: 14 Aug 2012.

Renal Failure, 2012; 34(9): 1140–1143
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ISSN 0886-022X print/1525-6049 online
DOI: 10.3109/0886022X.2012.713298

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CLINICAL STUDY

Association between Body Mass Index, Lipid Profiles, and Types of Urinary Stones

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Abstract

Objective: The purpose of this study was to determine the differences in body mass index (BMI), levels of cholesterol, and levels of triglycerides (TGs) among urolithiasis patients with different stone compositions. *Materials and methods*: Forty-nine patients who had a diagnosis of nephrolithiasis and had undergone open surgery or percutaneous surgery were included, and patients without urolithiasis were randomly selected as controls. Urinary stones were collected and analyzed using infrared spectroscopy. Data relating to patient's age, BMI at diagnosis, serum total cholesterol (TC), high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol (LDL-C) were collected. The stone groups including calcium oxalate monohydrate-calcium oxalate dihydrate (COM-COD), COM, and uric acid were compared with one another and with the control group. In addition, the stone formers group (COM-COD, COM, uric acid, calcium phosphate, and mixed-type stones) was compared to the control group. *Results*: BMI, TC, and TG levels were significantly higher in stone formers compared with the control group; this association of BMI and TC with stone formation was more prominent in uric acid and COM-COD stone formers, but there was no such prominence for COM stones. LDL-C levels in COM-COD stone formers were significantly higher when compared with COM stone formers. *Conclusion*: Elevated BMI, hypercholesterolemia, and hyperlipidemia, which are leading components of metabolic syndrome, may be associated with different types of urinary stone formation.

Keywords: body mass index, hypercholesterolemia, hypertriglyceridemia, nephrolithiasis

INTRODUCTION

The prevalence of urinary tract stones is about 10–15% in Western countries and 20–25% in Middle Eastern countries.[1] Furthermore, besides its high prevalence, it results in loss of work time and elevated health costs due to its recurrence.[2] The most common types of kidney stones are calcium oxalate (CaOx), calcium oxalate monohydrate (COM), and calcium oxalate dihydrate (COD). Calcium phosphate (CaP), uric acid, and struvite stones are also seen. CaOx stones usually contain CaP on a limited scale, which forms the nidus of the stone.[3] The pathogenesis of nephrolithiasis is multifactorial and it is associated with age, gender, heredity, body habitus, geographical location, climate, diet, fluid intake, and drugs used.[4–7] Recently, it has been suggested that urolithiasis is an aspect of the metabolic syndrome (MetS) and that body mass index (BMI) and dyslipidemia are the major aspects of these syndrome. MetS may affect stone risk factors that cause the formation of different stone types including CaOx, CaP, or mixed stones (uric acid/CaOx or CaOx/CaP).[8] As for the mechanisms investigating the MetS with nephrolithiasis, several related factors have been revealed, including elevated excretion of uric acid, oxalate and calcium, lower urine pH, and decreased citrate excretion.[9] A link between MetS and nephrolithiasis has been suggested by previous studies,[8–10] and selected aspects of MetS, such as elevated BMI,[11–15] hypercholesterolemia,[13] hypertriglyceridemia,[16] type II diabetes,[17–20] coronary artery diseases,[13,20] body weight change,[14] and hypertension[13,21–23] have been directly related to an increased risk of nephrolithiasis. Different risk factors can be valid for different types of stones, and the types of urinary tract stones have not been evaluated in previous studies. The study is a risk factor analysis of

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Received 21 June 2012; Revised 29 June 2012; Accepted 6 July 2012

important aspects of MetS in terms of BMI and lipids in relation to urolithiasis and urolithiasis of different compositions.

The aim of this study is to investigate and define the relationship between different types of stones and BMI; the levels of cholesterol, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C); and low-density lipoprotein cholesterol (LDL-C) and to compare the patients' BMI and lipid parameters with the controls.

MATERIALS AND METHODS

In this case–control study, 49 patients (35 males and 14 females) who had been diagnosed with nephrolithiasis and undergone open surgery or percutaneous surgery in the urology clinic of the Erciyes University Medical Faculty (Kayseri, Turkey) between March 2009 and April 2010 were included. The stones extracted from the patients were gathered following the operation and analyzed with infrared spectroscopy. Calcium oxalate monohydrate-calcium oxalate dehydrate (COM-COD) stones were found in 27 patients, COM stones in 10 patients, uric acid stones in 8 patients, calcium phosphate stones in 2 patients, and mixed-type stones in 2 patients. Patients who had cardiovascular disease, diabetes mellitus,[24] hypertension,[25] metabolic syndrome,[26] neoplasm, malabsorption, drugs that could affect urate metabolism (allopurinol or a high-dose acetylsalicylate), chronic kidney disease (glomerular filtration rate <60 mL/min), thyroid and parathyroid disease, and patients taking antihyperlipidemic treatment were not included in this study. Subjects with chronic diarrhea, urinary tract infection, and patients taking medications, or treatment for renal stones (thiazide, alkali therapy) were also excluded. Fifty age- and sex-matched (36 males and 14 females) controls who presented to our clinic for a routine check-up, were understood not to have urinary tract stones by medical history and urinary ultrasonography, and were randomly selected and used as a control group. All exclusion criteria were applied to both stone formers and controls. Venous blood samples (6–8 mL) were collected from each subject in the morning between 8:00 a.m. and 9:00 a.m., after an overnight fast. In all patients, BMI, total cholesterol (TC), TG, HDL-C, and LDL-C were measured. In addition, a comparison was made between groups of patients with different stone composition and normal subjects in terms of these factors. In addition, the stone formers group was compared with the control group in aspect of these parameters. The study was approved by the Ethical Committee of the Mustafa Kemal University School of Medicine (Hatay, Turkey).

Statistical Analysis

The data obtained from the study were evaluated using the SPSS for Windows 15.0 (SPSS Inc., Chicago, IL, USA) statistical package program. The Student's *t*-test and Mann–Whitney *U* test were used to compare the variables between the stone formers and the controls. The Kruskal–Wallis and Mann–Whitney *U* tests were used in the comparison of patients with different types of stones (COM-COD, COM, and uric acid). Four patients with CaP stones ($n = 2$) and mixed-type stones ($n = 2$) were not included in the subgroup analyses. All results are presented as mean ± standard deviation. A p value of ≤ 0.05 was considered significant.

RESULTS

The clinical characteristics and laboratory values of the study population are shown in Table 1. There were significant differences when stone formers were compared with the control group in terms of BMI ($p < 0.01$), TC ($p < 0.05$), and TG levels ($p < 0.01$). In subgroup analyses of stone formers and controls, there were statistical differences between COM-COD stone formers and controls in terms of BMI ($p < 0.05$), TC ($p < 0.01$), and TG levels ($p < 0.01$). In addition, there were significant differences between uric acid stone formers and controls in the case of BMI ($p < 0.01$), TC ($p < 0.05$), and TG levels ($p < 0.01$). In the COM stone formers, there was no significant difference when compared with the control group in terms of BMI, TC, and TG. When COM-COD stone formers were compared with COM stone formers, the LDL-C level in COM stone formers was significantly lower than that of COM-COD stone formers ($p < 0.05$) (Table 1).

DISCUSSION

The major findings of this pilot study are as follows: (1) BMI and TC levels were significantly higher in stone formers than in normal subjects. Interestingly, such a

Table 1. Relation between laboratory values and stone type in subjects with kidney stones and controls.

	Control ($n = 50$)	Stone formers ($n = 49$)	COM-COD ($n = 27$)	COM ($n = 10$)	Uric acid ($n = 8$)
Age	50.5 ± 8.9	47.0 ± 10.0	49.0 ± 9.5	40.5 ± 10[a,e]	54.7 ± 9.9[d]
BMI (kg/m^2)	25.4 ± 3.3	28.8 ± 4.5[a]	28.1 ± 4.6[b]	27.7 ± 4.6	32.0 ± 3.5[a]
Total C (mg/dL)	195.4 ± 36.4	218.6 ± 45.7[b]	221.7 ± 38.3[c]	192.6 ± 45.9	234.1 ± 52.3[b]
HDL-C (mg/dL)	39.1 ± 7.5	39.7 ± 9.7	40.4 ± 10.7	41.0 ± 9.9	37.6 ± 8.4
LDL-C (mg/dL)	130.8 ± 34.2	132.4 ± 43.0	142.0 ± 40.1	105.2 ± 40.1[e]	133.0 ± 35.7
TG (mg/dL)	127.5 ± 63.8	243.6 ± 200.2[a]	213.6 ± 131.4[a]	192.8 ± 120.1	357.6 ± 395.7

Notes: BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride. [a]$p < 0.01$ (compared with control), [b]$p < 0.05$ (compared with control), [c]$p < 0.01$ (compared with control), [d]$p < 0.05$ (uric acid vs. COM), [e]$p < 0.05$ (COM-COD vs. COM).

difference was only recorded in patients with COM-COD stones and uric acid stones, but not in patients with COM stones. (2) LDL-C levels in COM-COD stone formers were significantly higher when compared with COM stone formers.

The composition of the stone has a vital importance in decision making concerning correct treatment and preventing recurrence.[27–29] However, previous epidemiological studies demonstrating the relationship between obesity/ MetS and nephrolithiasis are limited in that they lack stone analysis information due to epidemiological database limitations. If a preventive treatment is not applied, the rate of recurrence is ~10.5% in 1 year, 33% in 5 years, and 50% in 10 years.[30] Detection of the acquired and environmental factors that cause urinary tract stones can prevent the disease and decrease its morbidity. Although many studies have been conducted to investigate various factors relating to kidney stones, the type of stones has not been investigated in most studies. Thus, we focused on the relationship between the type of kidney stones and BMI, hyperlipidemia, and hypercholesterolemia, which are established components of the MetS.

Several etiologies have been proposed for the association between MetS and risk factors for uric acid stones. As described before, low urine pH is an important and the most prevalent component of uric acid stone development.[9] Overweight, obesity, and hyperlipidemia are associated with lower urine pH and increased urate excretion which in acid urine might cause uric acid stone formation.[16,31–35] Elevated uric acid excretion is a risk factor not only for the formation of uric acid stones but also for the formation of CaOx stones. The crystallographic properties of uric acid crystals are similar to CaOx crystals, which may contribute to heterogeneous nucleation and epitaxial crystal growth. This effect would explain the physicochemical mechanism by which uric acid affects CaOx crystallization. It is also called as "the silanization effect."[36–38] Previous studies showed correlation between BMI and urinary oxalate, calcium excretion.[32,33] Various studies relating to nephrolithiasis showed that elevated BMI was associated with lower urinary pH.[16,31–34] The formation of CaOx stones depends on urine pH; thus, a decrease in urine pH might result in a decrease in calcium phosphate crystals, and this might in turn cause an increase in the formation of CaOx stones.[39]

In a study that included 181 patients who had urinary tract disease, Hamano et al.[13] showed that there was a significant association between the formation of urinary CaOx stones and the important risk factors of coronary artery disease such as obesity, hypertension, hypercholesterolemia, and smoking. In an experimental study, Kajikawa et al.[40] suggested that a high-cholesterol diet induced elevated renal calcification and renal osteopontin (OPN) mRNA in rats. The researchers also reported that there could be some relationship between kidney stone formation and atherosclerosis, demonstrated by an elevated OPN expression in tissue. In another study, Tsujihata et al.[41] showed a decrease in renal crystal retention in rats with atorvastatin. In a study carried out on rats, Iba et al.[42] indicated that elevated TG levels resulted in elevated urinary uric acid and calcium excretion, and this ultimately led to renal stone formation. Garbachinsky et al.[9] suggested MetS associated with lipotoxicity—lipid accumulation in the kidney—causing changed renal structure and function. Lipotoxicity can result in an increased acid extraction, with decreased ammonia synthesis and ammonium excretion, resulting in a lower urinary pH.

In conclusion, by the stone formation analysis, we demonstrated that elevated BMI and hyperlipidemia, which are leading components of metabolic syndrome, may be associated with urinary stone formation and type of hyperlipidemia may differ between various types of stone formation. However, nephrolithiasis is a complex disorder, consisting of multiple related factors, and any potential relation between MetS and nephrolithiasis should be confirmed by further studies. In addition, future prospective studies with larger samples where urinary pH, urine concentrations of citrate, uric acid, calcium, and oxalate were determined. It is also necessary to compare the physical activity between stone formers and control groups since BMI might have an indirect effect on this.

***Declaration of interest*:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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