

Metabolic Syndrome in patients with Urinary Tract Stone Disease: A Hospital based Single Center Study

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ABSTRACT

Introduction

Patients with urinary tract stones (UTS) are at increased risk of developing metabolic syndrome (MetS). Assessment for MetS could be useful for patients presenting with UTS. We assessed the prevalence of MetS and each of its components in patients with UTS. Correlation of 24-hour urinary, serum calcium and uric acid levels with components of MetS were also done.

Methods

A cross-sectional study was conducted at Tribhuvan University Teaching Hospital, Institute of Medicine from August 2021 to July 2022. After the approval from the Institutional Review Committee, 118 consenting adult patients with unilateral or bilateral UTS who fulfilled inclusion criteria were studied.

Results

Thirty-five (29.7%) stone formers had MetS. Among them, 23 (65.7%) were males, and 12 (34.3%) females. The mean body mass index of patients with MetS was 25.96 ± 4.62 kg/m². In patients with MetS, 24 (68.8%) had high blood pressure and impaired plasma FBS. Twenty-one (60.0%) patients had increased serum triglyceride levels, and 54.3% had reduced HDL-cholesterol. Systolic blood pressure had a significant correlation with hypercalciuria ($P=0.01$) and hyperuricemia ($P=0.046$). Serum triglyceride levels were significantly correlated with hypercalcemia ($P=0.045$). The mean estimated glomerular filtration rate (eGFR) of the study population was 83.48 ± 32.37 mL/min/1.73 m².

Conclusion

Urinary tract stone disease are associated with metabolic syndrome. Assessment for metabolic syndrome should be considered in patients with urinary tract stone disease.

Keywords

Hypercalciuria; hypercalcemia; hyperuricemia; hypertension; metabolic syndrome; Renal stone disease

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INTRODUCTION

Metabolic syndrome (MetS), also known as syndrome X and insulin resistance syndrome comprises glucose intolerance, high blood pressure, dyslipidemia, and central obesity. It is associated with increase risk of atherosclerotic cardiovascular diseases (CVD) and increases mortality in the general population.¹ It has become a major public health problem due to its high prevalence of around 20–25% globally.²

A significant association has been demonstrated between urinary tract stone (UTS) and MetS.³ Higher concentration of serum uric acid (UA) is found in patients with UA stones. Serum UA levels were positively correlated with body mass index, systolic and diastolic blood pressure, High-density lipoprotein-cholesterol, triglyceride, and fasting blood sugar,⁴ thus increasing the risk of diabetes mellitus⁵ and hypertension⁶. Since patients with UTS are at increased risk of developing MetS, a stone is likely a "symptom" of an underlying, perhaps covert, metabolic derangement in idiopathic stone formers.

This increased risk has both individual and health policy implications given the associated adverse cardiovascular outcomes. Strong evidence for routine assessment for MetS in patients with UTS is still inadequate. This study aimed to estimate the prevalence of MetS and each of its component in patients with UTS and also study correlation of 24-hour urinary and serum calcium and uric acid levels with components of MetS.

METHODS

This was a single-center, quantitative, cross-sectional study conducted at Tribuvan University Teaching Hospital (TUTH), Institute of Medicine (IOM) from August 2021 to July 2022. The study protocol was approved by the Institutional Review Committee (IRC) of the IOM. A group of 118 consenting adult patients with unilateral or bilateral UTS defined as hyperechoic lesions in the urinary tract by ultrasonography (USG) or hyperdense foci on computed tomography (CT) scan were included in the study. Patients with congenital renal abnormalities, Autosomal dominant polycystic

kidney disease (ADPKD), advanced chronic kidney disease with eGFR of <30 ml/min/1.73m², metabolic bone disorder or taking treatment for osteoporosis, proven metabolic causes of stone disease like primary hyperoxaluria, complication of calculus disease like calculus pyelonephritis, pyonephrosis or perinephric abscess were excluded from the study. Patients with major debilitating diseases like cancer and pregnant women were also not included.

Sample size for the study was calculated using formula $n = z^2pq/d^2$ keeping 95% confidence interval, 9% error, and the prevalence of 46.3%.⁷ Participants were enrolled by convenience sampling technique. Data was collected using interview and examination method. A standard proforma was used to collect the data. All patients underwent measurement of waist circumference (WC), systolic (SBP) and diastolic blood pressure (DBP), fasting blood sugar (FBS), serum triglycerides (TG), serum high density lipoprotein(HDL) cholesterol, serum uric acid (UA), serum calcium, ECG, renal function test (RFT), and 24-hour urinary calcium and uric acid. The International Diabetic Federation (IDF) criteria for defining MetS⁸ was used to categorize patients into patients with and without MetS.

The prevalence of MetS and each of its components, the relationship between 24-hour urine and serum calcium, and uric acid levels and MetS components, the estimation of glomerular filtration rates (eGFR), and changes in electrocardiograms (ECG) of the patients were recorded in a single referral hospital setup. Version 25.0 of SPSS software was used to evaluate the variables. Categorical variables such as sex, MetS, GFR stages, and CVD were expressed as percentages. Continuous variables such as age and individual components of MetS were described as mean and standard deviation. A Student's t test was used to compare blood and urine biochemical indices among patients with MetS. The Chi square test and Fischer's exact test were employed to find out the association between urinary biochemical indices and individual components of MetS. Pearson's correlation was used to analyze the relationship between serum UA, serum calcium, urine UA and urine calcium with metabolic components. A p value of < 0.05 was considered significant.

Table 1. Prevalence of individual components of metabolic syndrome among study participants syndrome

Metabolic component	With MetS (n=35)	Without MetS (n=83)
WC (M≥90cm; F≥80cm)	35(100%)	4(4.8%)
SBP (≥130 mmHg)	24(68.6%)	23(27.7%)
DBP (≥85 mmHg)	24(68.6%)	23(27.7%)
TG (≥ 150 mg/dL mg/dl)	21(60.0%)	18(21.7%)
HDL (<40 mg/dL mg/dl)	19(54.3%)	35(42.4%)
FBS (≥ 100 mg/dL mg/dl)	24(68.6%)	38(45.8%)

Table 2. Comparison of urinary biochemical indices in patients with and without metabolic syndrome

Urinary biochemical indices	MetS		p-value
	Present (n=35)	Absent (n=83)	
Urine uric acid level			
≥4.46 mmol/Day	4(11.4%)	11(13.3%)	0.53
<4.46 mmol/Day	31(88.6%)	72(86.7%)	
Urine calcium level			0.32
≥7.5 mmol/Day	18(51.3%)	18(51.3%)	
<7.5 mmol/Day	17(48.6%)	17(48.6%)	

RESULTS

Out of 118 cases, 85 (72.0%) were males and 33 (28.0%) were females, with a male to female ratio of 2.57:1. The median age of the study participants was 46 years, with a minimum age of 19 years and a maximum age of 77 years. Thirty-five (29.7%) of the patients had MetS. Among them, 23 (65.7%) were males and 12 (34.3%) females. Fifteen (42.9%) of the patients with MetS were below 40 years of age, 17 (48.5%) were between 40-60 years of age and 3 (8.5%) were above 60 years of age. The mean body mass index (BMI) of patients with MetS was 25.96 ± 4.62 kg/m². In patients with MetS, 24 (68.8%) had high BP and impaired plasma FBS. Twenty-one (60.0%) patients had increased serum triglyceride level, and 54.3% had reduced HDL-cholesterol. (Table 1)

Among the patients with MetS, 4 (11.4%) had hyperuricosuria and 18 (51.3%) had hypercalciuria. However, the urinary biochemical indices in patients with and without MetS did not show any statistical significance as shown in Table 2.

In patients with UTS diseases, prevalence of various stages of CKD based on eGFR among patients with and without MetS is shown in Table 3.

This study did not find any difference in ECG changes between patients with and without MetS.

We did not find any statistically significant correlation between hyperuricosuria and individual components of MetS. However, hypercalciuria was correlated with SBP which was statistically significant (Pearson's coefficient = 0.234; P = 0.01)

Table 3. CKD stages in patients with and without metabolic syndrome

eGFR	With MetS (n=35)	Without MetS (n=83)
I	16 (45.7%)	41(49.4%)
II	12 (34.2%)	23 (27.7%)
III	5 (14.2%)	10 (12.0%)
IV	1 (2.8%)	3 (3.6%)
V	1(2.8%)	6 (7.2%)

(Figure 1). We did not find a significant correlation of other components of MetS with hypercalciuria. We found a significant correlation of hyperuricemia with SBP (Pearson's coefficient = 0.184; P = 0.046) (Figure 2). and not with other components of MetS. Similarly, serum TG levels had shown a statistically significant correlation with hypercalciuria (Pearson's coefficient = -0.185; P = 0.045). (Figure 3)

DISCUSSION

Our study showed that UTS was more common in males than females, with a male to female ratio of 2.6:1, which is in agreement with studies done by Shokouhi et al, and Rayhan et al, both showing a ratio of 2.7:1.^{9,10} Increased incidence in males has been attributed to increased dietary protein intake and muscle mass, which increases the excretion of phosphates and reduces urinary citrate concentration. The lower risk of stone formation in women has been attributed to estrogens, which may also help to prevent the formation of calcium stones by keeping urine alkaline and raising protective citrate levels.¹¹

Sedentary lifestyle habits, increased intake of animal proteins and salted foods, and lack of exercise lead to obesity, HTN, T2DM, and dyslipidemia. These cause an increased risk of developing UTS and CVD.¹² In this study, 35 (29.7%) UTS patients had MetS, which is in accordance with the study done by Rendina et al. in 2008 in southern Italy, in which 31% of the studied population with renal stones had MetS.¹³

A study done by McCarron et al. in 1995 showed an increased urinary excretion of oxalate, calcium, and uric acid in subjects weighing more than 120 kg compared to subjects weighing less than 100 kg.¹⁴ Ekeruo reported a greater prevalence of hypercalciuria, hyperoxaluria, and hyperuricosuria in an obese population of stone formers compared to a non-obese population.¹⁵ A similar result was observed in this study as the majority of the studied population had obesity (72.9%) and 4 (11.4%) of the patients with MetS had hyperuricosuria and 18 (51.3%) had hypercalciuria.

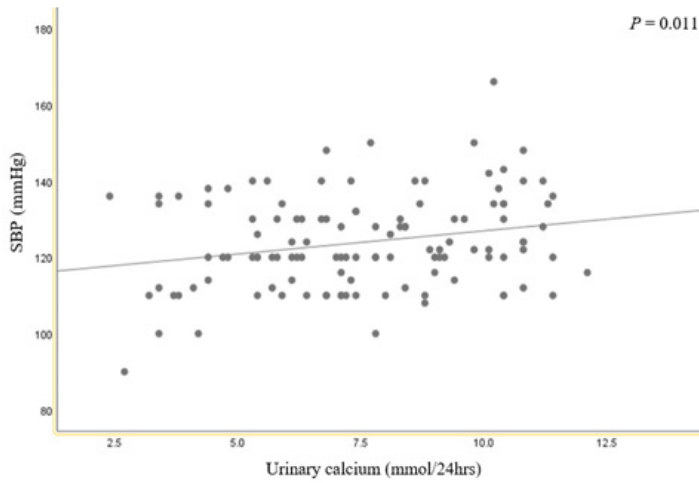


Figure 1. Correlation of SBP with 24 hour urinary calcium (n = 118)

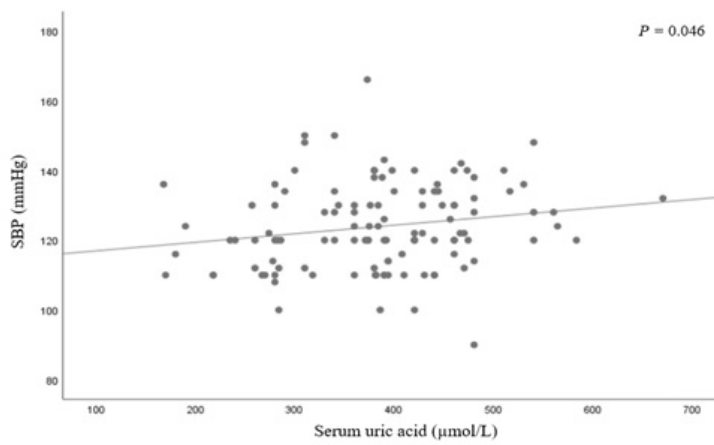


Figure 2. Correlation of SBP with serum uric acid (n = 118)

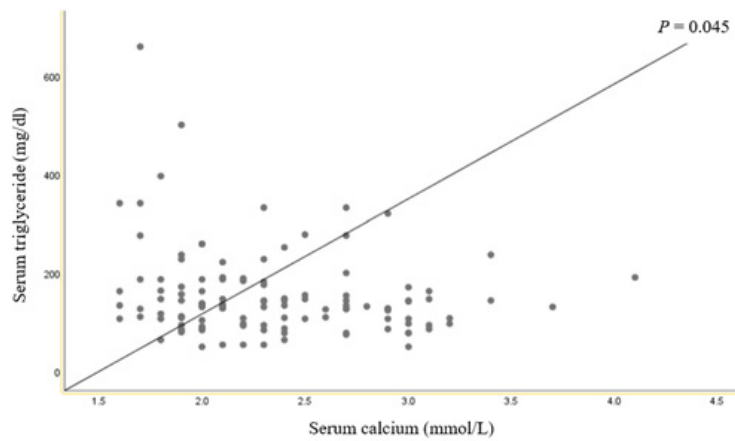


Figure 3. Correlation of serum TG with serum calcium (n = 118)

Several investigators have proposed that hypercalciuria might be the mechanism linking UTS and HTN.¹⁶ The possibility that renal damage caused by stones might contribute to HTN has also been suggested.¹⁷ In this study, this correlation between hypercalciuria and SBP was statistically

significant with a P-value of 0.011. Reduction in endothelial nitric oxide bioavailability by UA is likely to be involved in the mechanism of development of HTN.¹⁸ In this study, there was a statistically significant correlation between serum UA and SBP with a p-value of 0.046. This result is in accordance

with the study done by Sara et al. in 2015.¹⁹

Previous studies have reported a positive correlation of insulin resistance and hyperglycemia with hypercalciuria and the formation of Ca-based stones.²⁰ A study done by Shui-Dong et al. suggested that patients who were diagnosed with UTS were at an increased risk for developing DM.²¹ In this study, 52.5% had high FBS. However, a statistically significant correlation between glucose levels and hypercalciuria could not be observed.

Hypercalcemia decreases cholesterol catabolism and stimulates lipid synthesis.²² In present study, a statistically significant correlation between TG concentration and the concentration of serum calcium was identified with a p-value of 0.045. A similar finding was reported by Rolf et al. in 1999.²³

We observed that the majority of the patients (18, 51.3%) with MetS had hypercalciuria. This result is in accordance with the study done by Raina AF et al. in 2017, which reported hypercalciuria accounting for 60.8% of the main cause of UTS.²⁴ They also reported that 25.8% of their patients with UTS had hyperuricosuria. In the previous studies, calcium stones were the most common type of UTS, comprising 78–80% of all stones removed from patients with UTS in developed countries.^{3,25} The presence of UA stones was less common, accounting for only 5 to 10% of all kidney stones.²⁶ In this study, the chemical composition of stones was not done due to the unavailability of a facility at our center. However, in reference to the above data, it is reasonable to speculate that the majority of our study patients had calcium-based stones as most of them had hypercalciuria.

Frequent stone recurrence, combined with urinary tract infection, obstruction, and frequent urological interventions, are responsible for the loss of renal function.²⁷ Moreover, percutaneous and extracorporeal urological methods for the treatment of renal stones may also lead to chronic deterioration of renal function.²⁸ In this study, the prevalence of each stage of CKD was higher in patients without MetS than in patients with MetS, and only one in the MetS group had progressed to end-stage CKD.

The main limitations of this study were the cross-sectional design, small sample size, hospital-based study, and absence of dietary data. However, the observed findings can be utilized for further work in order to make decisions on prevention and treatment strategies to reduce cardiovascular events, recurrence of UTS, and preserve eGFR.

CONCLUSION

Patients with UTS were more likely to have MetS. The most common stone types were speculated to be calcium-based. Hyperuricosuria, hypercalciuria, and serum calcium all had positive strong correlation

with SBP and serum TG level. We suggest that all patients presenting with UTS should be screened for MetS. A larger multi center study is recommended to have final answer.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

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