

# Correlation of metabolic syndrome and urolithiasis: A prospective cross-sectional study

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## Abstract

**Background:** Correlation between urolithiasis and metabolic syndrome has been demonstrated in the literature. This study assessed the association of metabolic syndrome and its components with urolithiasis in Indian patients.

**Methods:** A cross-sectional prospective observation study included patients aged > 18 years with urolithiasis. Demographic details, body mass index (BMI), waist circumference, blood pressure, and laboratory parameters were examined.

**Results:** Total 1200 patients with urolithiasis were divided into two groups (with [ $n = 208$ ] and without metabolic syndrome [ $n = 992$ ]). The mean age of total population was 47.26 (14.68) years with 721 males and 479 females. The mean height, weight, BMI were significantly different between both groups ( $P < 0.001$ ). Proportion of obese (BMI > 25) patients, proportion of patients with hyperuricemia, waist circumference, blood pressure, triglyceride, fasting blood sugar (FBS) levels were significantly higher in patients with metabolic syndrome; however, high density lipoprotein (HDL) levels were significantly reduced in metabolic syndrome group ( $P < 0.001$ ). A significantly increasing trend in mean waist circumference, triglycerides, FBS, systolic blood pressure and diastolic blood pressure and a decreasing trend in mean HDL with increase in number of metabolic components were observed ( $P < 0.001$ ). Female patients were 19.6 times more likely to develop metabolic syndrome than male patients ( $P < 0.001$ ). Increasing waist circumference, triglycerides, FBS, blood pressure were associated with increased risk of metabolic syndrome ( $P < 0.05$ ). Decreasing HDL was associated with reduced risk of metabolic syndrome. Patients with hyperuricemia were 5.68 times more likely to exhibit metabolic syndrome ( $P = 0.006$ ).

**Conclusion:** This study indicates the presence of a significant association of metabolic syndrome and its components with urolithiasis.

**Keywords:** Hyperuricemia, metabolic syndrome components, obesity, risk, urolithiasis

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## INTRODUCTION

Urolithiasis is one of the most common urological disorder with a significant burden worldwide with a prevalence

of around 5%–10% and more commonly reported in men than women.<sup>[1]</sup> Urolithiasis is also common in India and is often complicated with comorbidities. Metabolic

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syndrome is a general metabolic condition commonly seen worldwide and has been reported to be increasing in last few decades. It is a group or combination of central obesity, hyperglycemia, dyslipidemia, and hypertension and hence has an increased risk of cardiovascular disease.<sup>[2]</sup> It has been known that obesity is a contributing factor for the development of urolithiasis. A recent systematic review and meta-analysis has demonstrated a significant association between urolithiasis and metabolic syndrome.<sup>[3]</sup> However, there is a limited data available from India on the association of urolithiasis with metabolic syndrome and its components. This paper reports results of a study that evaluated the correlation between metabolic syndrome and urolithiasis in Indian patients.

## METHODS

This was a cross-sectional prospective observation study conducted at <Mahatma Gandhi Medical College and Research Institute Hospital> between January 2017 and December 2018. The study protocol was reviewed and approved by the Institutional Ethics Committee. The study was conducted in accordance with approved protocol and the ethical principles that have their origin in the Declaration of Helsinki. A written informed consent was obtained from each study participants before participation in the study.

Eligible patients were of either sex aged more than 18 years and had a confirmed diagnosis of urolithiasis. Each patient underwent detailed evaluation and following data was collected: Demographic details, body mass index (BMI), waist circumference, blood pressure, laboratory parameters. Of the total patients with urolithiasis patients were divided into two groups based on metabolic syndrome (with and without metabolic syndrome). The diagnosis of metabolic syndrome was based on the following criteria: (a) increased waist circumference ( $\geq 90$  cm for men and  $\geq 80$  cm for women); (b) hypertriglyceridemia (triglycerides  $\geq 150$  mg/dl); (c) low High-density lipoprotein cholesterol (HDL-C) (HDL-C;  $< 40$  mg/dL in men and  $< 50$  mg/dL in women); (d) systolic blood pressure (SBP)  $\geq 130$  mmHg and/or diastolic  $\geq 85$  mmHg; and (e) fasting glucose  $\geq 110$  mg/dL. Metabolic syndrome was defined as the presence of three or more of these five criteria.

Statistical analyses were performed using IBM SPSS Statistics 23.0 Desktop-US. Categorical variables are reported as number (percentage) and continuous variables as mean (standard deviation [SD]). Categorical variables (gender, BMI status, serum uric acid status) analyzed using Chi-square test and continuous variables (age, height, weight, waist

circumference, SBP, diastolic blood pressure [DBP], triglycerides, HDL and fasting blood sugar [FBS]) were analyzed using a nonparametric test, Mann–Whitney U-test. Correlation analysis between quantitative variables were done using Spearman's correlation coefficient. Univariate logistic regression analysis was performed using binomial logistic regression. The Wald test was used to determine statistical significance for each of the independent variable. Odds ratio was interpreted to predict the risk of metabolic syndrome development in urolithiasis patients.

## RESULTS

A total of 1200 patients with a confirmed diagnosis of urolithiasis were included in the study. Of these 1200 patients, 208 (17.33%) patients were also diagnosed with metabolic syndrome. Table 1 summarizes the demographics and baseline characteristics. The mean (SD) age of total population was 47.26 (14.68) years. In total 721 (60.08%) patients were males and 479 (39.91%) were females [Table 1]. Overall, age and sex were comparable between patients with and without metabolic syndrome. The mean height and weight were significantly ( $P < 0.001$ ) different between both groups. Distribution of patients according to BMI significantly ( $P < 0.001$ ) differed between both groups. Overall, 581 (43.12%) patients were obese (BMI  $> 25$ ). Among patients without metabolic syndrome 39.4% of patients were obese; however, of the metabolic syndrome group 91.3% of patients were obese ( $P < 0.001$ ). Waist circumference was significantly ( $P < 0.001$ ) higher in patients with metabolic syndrome (99.82 cm) than those without metabolic syndrome (83.48 cm). SBP and DBP, triglyceride levels, and FBS levels were significantly ( $P < 0.001$ ) higher in patients with metabolic syndrome than those without metabolic syndrome; however, HDL levels were significantly reduced in metabolic syndrome group ( $P < 0.001$ ). Serum levels of phosphorous, calcium and magnesium were in normal range in both the groups. Proportion of patients with elevated serum uric acid levels was significantly higher in metabolic syndrome group than in nonmetabolic syndrome group.

When the correlation was evaluated among patients with urolithiasis, weight was found to have positive correlation with height, waist circumference, triglyceride, SBP, and DBP. Waist circumference had positive association with triglycerides, SBP, and DBP; however, a negative correlation between HDL and triglycerides was observed [Table 2].

Among patients with metabolic syndrome, a significant positive correlation of weight with height, waist circumference, SBP and DBP was observed. Waist circumference had positive correlation with triglycerides

**Table 1: Baseline characteristics of study population**

Characteristics	Total patients (n=1200)	Patients without metabolic syndrome (n=992)	Patients with metabolic syndrome (n=208)	$\chi^2$ , P
Age (years)	47.26 (14.68)	47.35 (14.84)	46.80 (13.91)	P=0.636
Gender, n (%)				
Male	721 (60.08)	604 (60.90)	117 (56.30)	$\chi^2=1.542$ ,
Female	479 (39.91)	388 (39.10)	91 (43.80)	P=0.214
Height (cm)	162.17 (8.10)	162.82 (7.96)	159.6 (8.05)	P<0.001
Weight (kg)	68.27 (11.30)	66.24 (10.55)	77.98 (9.61)	P<0.001
BMI (kg/m <sup>2</sup> ), n (%)				
Underweight (<18.5)	5 (0.41)	5 (0.50)	0 (0)	$\chi^2=189.217$ ,
Normal (18.5-22.9)	300 (25)	300 (30.20)	0 (0)	P<0.001
Overweight (23-24.9)	314 (26.17)	296 (29.80)	18 (8.70)	
Obese (>25)	581 (43.17)	391 (39.40)	190 (91.3)	
Waist circumference (cm)	86.31 (9.40)	83.48 (6.52)	99.82 (9.28)	P<0.001
SBP (mmHg)	128.36 (8.93)	126.17 (7.98)	136.44 (8.83)	P<0.001
DBP (mmHg)	82.25 (6.84)	80.79 (5.59)	89.18 (7.91)	P<0.001
Triglycerides (mg/dL)	139.51 (17.78)	134.71 (13.49)	160.40 (17.80)	P<0.001
HDL (mg/dL)	47.97 (9.21)	49.43 (8.66)	40.97 (8.49)	P<0.001
FBS (mg/dL)	97.34 (14.69)	95.40 (12.96)	106.56 (18.48)	P<0.001
Serum phosphorus (mg/dL), n (%)				
Normal (2.5-4.5)	1200 (100)	992 (100)	208 (100)	-
Elevated (>4.5)	-	-	-	
Serum uric acid (mg/dL), n (%)				
Normal (3-7)	1122 (93.50)	943 (95.10)	179 (86.10)	$\chi^2=22.93$ ,
Elevated (>7)	78 (6.50)	49 (4.90)	29 (13.90)	P<0.001
Serum calcium (mg/dL), n (%)				
Normal (100-300)	1200 (100)	992 (100)	208 (100)	-
Elevated (>300)	-	-	-	
Serum magnesium (mg/dL), n (%)				
Normal (1.7-2.2)	1200 (100)	992 (100)	208 (100)	-
Elevated (>2.2)	-	-	-	

Data shown as mean (SD), unless otherwise specified. BMI: Body mass index, HDL: High density lipoprotein, FBS: Fasting blood sugar, DBP: Diastolic blood pressure, SBP: Systolic blood pressure, SD: Standard deviation

**Table 2: Correlation between parameters among patients with urolithiasis (n=1200)**

Parameter 1	Parameter 2	Correlation coefficient	P
Height	Weight	0.412	<0.001
Weight	Waist circumference	0.643	<0.001
	Triglyceride	0.501	<0.001
	SBP	0.383	<0.001
	DBP	0.302	<0.001
	Triglyceride	0.614	<0.001
Waist circumference	SBP	0.430	<0.001
	DBP	0.414	<0.001
Triglyceride	HDL	-0.326	<0.001

DBP: Diastolic blood pressure, SBP: Systolic blood pressure, HDL: High-density lipoprotein

and DBP, whereas had a negative correlation with FBS. A significant positive correlation was observed between HDL and FBS; however, a significant negative correlation was observed between triglycerides and FBS [Table 3]. When the correlation was evaluated among patients without metabolic syndrome a significant positive correlation was observed between weight and height, waist circumference and triglycerides. Waist circumference was also positively correlated with triglycerides [Table 4].

As the number of metabolic components increased, a significant increasing trend in mean waist circumference,

triglycerides, FBS, SBP and DBP ( $P < 0.001$ ) and a significant decreasing trend in mean HDL ( $P < 0.001$ ) were observed [Table 5]. The univariate logistic regression analysis showed that female patients were 19.6 times (1/0.051) more likely to develop metabolic syndrome than male patients ( $P < 0.001$ ). Increasing waist circumference, triglycerides, FBS, DBP and SBP were associated with increased risk of metabolic syndrome in patients diagnosed with urolithiasis ( $P < 0.05$ ). Decreasing HDL was associated with reduction in the likelihood of exhibition of metabolic syndrome in patients with urolithiasis. Patients with elevated serum uric acid were 5.68 times more likely to exhibit metabolic syndrome than patients with normal serum uric acid levels ( $P = 0.006$ ) [Table 6].

## DISCUSSION

The key parameters depicting metabolic syndrome include overweight, arterial hypertension and disturbances of the carbohydrate metabolism.<sup>[4]</sup> However, the link between urolithiasis and metabolic syndrome has suggested a possible role of multiple metabolic risk factors in the development of urolithiasis.<sup>[3,5]</sup> Increased BMI, body weight, waist circumference and major weight gain has

been shown to be independently associated with higher risk of renal stone formation.<sup>[6-8]</sup>

The present study was conducted to assess the correlation between metabolic syndrome and urolithiasis in Indian patients. The mean age of total population was 47.26 years with 60.08% of males. Significantly lower mean height and higher weight were observed in patients with metabolic syndrome. Distribution of patients according to BMI significantly ( $P < 0.001$ ) differed between both groups. Overall, 581 (43.12%) patients were obese (BMI >25). Among patients without metabolic syndrome 39.4% of patients were obese; however, in the metabolic syndrome group, 91.3% of patients were obese ( $P < 0.001$ ). Waist circumference was significantly higher in patients with metabolic syndrome (99.82 cm) than those without metabolic syndrome (83.48 cm) ( $P < 0.001$ ). SBP and DBP, triglyceride levels, and FBS levels were significantly higher in patients with metabolic syndrome than those without metabolic syndrome; however, HDL levels

were significantly reduced in metabolic syndrome group ( $P < 0.001$ ). These observations suggest that metabolic risk factors are predominantly present in urolithiasis patients with metabolic syndrome.

Several studies attributed the increased incidence of uric acid stone formation in the obese population to the production of more acidic urine as compared to nonobese patients.<sup>[7,9]</sup> An increased incidence of urolithiasis of up to 75% has been seen in patients who are overweight or obese.<sup>[10]</sup> The present study observations corroborate this hypothesis. Obesity is associated with impaired carbohydrate tolerance and inappropriate calcium response to glucose ingestion. Another reason could be relationship of obesity with changes in the environment of urine leading to urinary stone formation.<sup>[11,12]</sup>

A study by Pak *et al.* concluded that stone-forming patients with diabetes mellitus have a high prevalence of uric acid stones.<sup>[13]</sup> Taylor *et al.* study reported increased risk of stone diseases in diabetes patients.<sup>[6]</sup> The present study also reported incidence of diabetes in urolithiasis patients with metabolic syndrome. Insulin resistance has been correlated to the reduction in renal ammonium production and low urinary pH, resulting into formation of urolithiasis.<sup>[14]</sup> Moreover, direct correlation between low urinary pH and number of metabolic syndrome risk factors as well as inverse correlation between degree of insulin resistance and urinary pH have been shown in a cross-sectional study performed by Maalouf *et al.*<sup>[12]</sup> Various recent studies reported the varying percentage of patients with metabolic syndrome in the range of 11.5%–38.3% with higher prevalence of urolithiasis among them as compared to patients without metabolic syndrome. A systematic review and meta-analysis by Besiroglu *et al.*<sup>[4,15-18]</sup> confirmed the strong association of metabolic syndrome with urolithiasis with a 1.4-fold increase.<sup>[3]</sup>

A recent study by Nejatnamini *et al.* reported that individuals with metabolic syndrome have higher uric acid

**Table 3: Correlation between parameters among patients with metabolic syndrome (n=208)**

Parameter 1	Parameter 2	Correlation coefficient	P
Height	Weight	0.654	<0.001
Weight	Waist circumference	0.349	<0.001
	SBP	0.328	<0.001
	DBP	0.330	<0.001
Waist circumference	Triglyceride	0.350	<0.001
	FBS	-0.383	<0.001
	DBP	0.396	<0.001
Triglyceride	FBS	-0.383	<0.001
HDL	FBS	0.301	<0.001

HDL: High-density lipoprotein, FBS: Fasting blood sugar, DBP: Diastolic blood pressure, SBP: Systolic blood pressure

**Table 4: Correlation between parameters among patients without metabolic syndrome (n=992)**

Parameter 1	Parameter 2	Correlation coefficient	P
Height	Weight	0.505	<0.001
Weight	Waist circumference	0.586	<0.001
	Triglyceride	0.406	<0.001
Waist circumference	Triglyceride	0.494	<0.001

**Table 5: Comparison of parameters according to the number of metabolic components present**

Parameters	Number of metabolic components present						P
	0 (n=187)	1 (n=467)	2 (n=266)	3 (n=151)	4 (n=108)	5 (n=21)	
Age (years)	46.35 (15.39)	48.56 (14.57)	46.34 (14.14)	45.97 (15.29)	46.83 (13.99)	49.33 (15.52)	0.215
Height (cm)	162.09 (8.16)	161.68 (8.16)	162.54 (7.81)	161.83 (8.57)	163.53 (7.66)	164.43 (8.11)	0.202
Weight (kg)	67.85 (11.41)	68.09 (11.00)	68.76 (10.98)	68.95 (12.63)	67.78 (11.60)	67.71 (9.93)	0.895
Waist circumference (cm)	31.92 (1.56)	32.31 (2.18)	33.88 (2.52)	37.45 (4.32)	38.71 (3.91)	41.43 (2.5)	<0.001
Triglycerides (mg/dL)	130.22 (8.49)	131.87 (11.42)	139.21 (15.77)	153.23 (19.85)	165.55 (14.32)	163.57 (5.82)	<0.001
HDL (mg/dL)	53.33 (6.96)	50.15 (7.86)	47.78 (9.20)	44.62 (8.91)	36.97 (5.57)	34.57 (2.04)	<0.001
FBS (mg/dL)	90.13 (6.99)	94.20 (11.26)	99.53 (15.37)	102.32 (17.08)	106.20 (19.88)	122 (7.77)	<0.001
SBP (mmHg)	119.14 (2.80)	127.56 (8.37)	129.17 (7.42)	133.44 (8.72)	136.94 (7.03)	137.14 (4.63)	<0.001
DBP (mmHg)	78.61 (3.47)	81.03 (5.90)	81.77 (6.10)	85.96 (7.93)	88.61 (8.37)	88.57 (3.58)	<0.001

Data shown as mean (SD). HDL: High density lipoprotein, FBS: Fasting blood sugar, DBP: Diastolic blood pressure, SBP: Systolic blood pressure, SD: Standard deviation

**Table 6: Univariate logistic regression analysis**

Parameters	OR	95% CI	P
Sex	0.051	0.020-0.132	<0.001
Waist circumference	1.978	1.574-2.486	<0.001
Triglyceride	1.085	1.055-1.115	<0.001
HDL	0.831	0.789-0.876	<0.001
FBS	1.123	1.090-1.156	<0.001
SBP	1.076	1.019-1.137	0.009
DBP	1.156	1.075-1.244	<0.001
Elevated serum uric acid	5.686	1.643-19.679	0.006

OR: Odds ratio, CI: Confidence interval, HDL: High density lipoprotein, FBS: Fasting blood sugar, DBP: Diastolic blood pressure, SBP: Systolic blood pressure

levels.<sup>[19]</sup> Another study by Zhang *et al.* showed that uric acid as an independent risk factor of metabolic syndrome, and its higher concentrations increased the risk of metabolic syndrome.<sup>[20]</sup> The present study observations showed that proportion of patients with hyperuricemia were significantly higher in metabolic syndrome group than in nonmetabolic syndrome group. These observations are parallel to the study by Strohmaier *et al.* who reported hyperuricemia in 37% of patients with urolithiasis.<sup>[21]</sup>

As discussed earlier, number of metabolic components responsible for metabolic syndrome affects severity of renal stone disease. In addition to obesity, other metabolic disorders like diabetes mellitus, hypertension and dyslipidemia also play a role in increased severity of kidney stone disease. Kohjimoto *et al.* observed 1.8 times larger odds of recurrent formation of stones as well as the formation of multiple stones in patients with four metabolic traits compared to those with zero traits.<sup>[22]</sup> The present study also found similar results. As the number of metabolic components increased, a significant increasing trend in mean waist circumference, triglycerides, FBS, SBP, and DBP ( $P < 0.001$ ) and a significant decreasing trend in mean HDL ( $P < 0.001$ ) were observed in urolithiasis patients with metabolic syndrome.

In the present study, univariate logistic regression analysis showed that female patients were 19.6 times (1/0.051) more likely to develop metabolic syndrome than male patients ( $P < 0.001$ ). This might be due to the high prevalence of cardiometabolic risk factors such as hypertension, increased waist circumference, concomitant increases in hypertriglyceridemia and fasting glucose in females.<sup>[23]</sup> Furthermore, hormonal regulation of body weight and adiposity in females could contribute to the high risk of metabolic syndrome. A meta-analysis by Kuk and Ardern suggested that abdominal obesity was the dominant MetS feature in women.<sup>[23]</sup>

The present study reported that rise in metabolic components (such as increasing waist circumference,

triglycerides, FBS, blood pressure) was directly associated with increased risk of metabolic syndrome in patients diagnosed with urolithiasis ( $P < 0.05$ ). However, decreasing HDL was associated with reduction in the likelihood of exhibition of metabolic syndrome in patients with urolithiasis. These results are in concordance with other previous studies.<sup>[5,16,21]</sup>

Present study also reported that patients with elevated serum uric acid were 5.68 times more likely to exhibit metabolic syndrome than patients with normal serum uric acid levels ( $P = 0.006$ ). These results indicate the strong association between hyperuricemia and risk of metabolic syndrome in patients with urolithiasis.<sup>[14,24]</sup> A study by Maalouf *et al.* reported that increased uric acid excretion appears to be commonly related to insulin resistance, which further relates with obesity.<sup>[12]</sup> Zhang *et al.* study showed that hyperuricemia is an independent risk factor of metabolic syndrome.<sup>[20]</sup> Nejatinamini *et al.* study depicted the role of serum uric acid as one of the determinants of the metabolic syndrome. They concluded that with one unit increase of serum uric acid, the odds of developing metabolic syndrome approximately doubled.<sup>[19]</sup> Other previous studies have also shown that individuals with high uric acid levels have 1.6 times higher odds of developing metabolic syndrome. The mechanism involved in this association may include reduction in endothelial nitric oxide bioavailability by uric acid or hyperinsulinemia reduces urinary uric acid excretion by the effect of insulin on urinary tubules leading to hyperuricemia.<sup>[25-27]</sup>

## CONCLUSION

The present study observations suggest that hypertension, diabetes mellitus, hypertriglyceridemia, hyperuricemia, and reduced HDL were prominently associated with the increased risk of developing metabolic syndrome in patients with urolithiasis. Therefore, presence of metabolic syndrome and its components are significantly associated with urolithiasis in Indian patients.

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## Conflicts of interest

There are no conflicts of interest.

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