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Original Research Article

The correlation between metabolic syndrome and calcium urolithiasis

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ABSTRACT

Background: Urolithiasis affects about 12% of the global population. This study helps us to find the correlation between metabolic syndrome, its components and the risk of calcium stone urolithiasis.
Methods: A cross-sectional study was conducted on 140 patients who underwent surgery for urolithiasis and whose stones were calcium-containing. A group of subjects who never had a history of urolithiasis was taken as control. Various anthropometric and biochemical parameters were studied to estimate and compare the prevalence of metabolic syndrome in both the groups.
Results: The study showed that the central obesity of the study population was higher. However, even though prevalence of hypertension was more in the stone group compared to the control population, this difference was not statistically significant. On analysis of biochemical parameters like fasting blood sugar, triglycerides and HDL, abnormal triglycerides and HDL were significantly higher in the stone group when compared to the control. On consideration of all parameters as per international diabetes federation (IDF) definition, prevalence of metabolic syndrome in stone group was 40% which was higher than the control group with 25% and the difference was statistically significant. While summing up the number of parameters of metabolic syndrome an individual has in each group it is evident that the proportion of patients in the stone group had a greater number of parameters compared to the control group.
Conclusions: This study could conclude that there is a significant correlation between calcium urolithiasis and metabolic syndrome.

Keywords: Urolithiasis, Metabolic syndrome, Calcium stones

INTRODUCTION

Metabolic syndrome is the simultaneous occurrence of hyperglycemia, hyperlipidemia, hypertension and visceral obesity. It is a chronic disease associated with high mortality. It substantially increases the risk of development of cardiovascular events and type 2 diabetes.[1] The underlying cause of the metabolic syndrome is a disorder in energy utilization and storage. Over a period of time, numerous definitions of metabolic syndrome have been proposed by various expert groups. However, the new IDF definition is universally considered as most acceptable as it includes the important concepts of the Metabolic syndrome and relies on the common laboratory investigations, considers ethnicity and is less restrictive than the other classifications.

The prevalence of urolithiasis is increasing globally and is observed across age, gender and race. Various factors influence the development of urolithiasis also including dietary habits, fluid intake, climate, occupation, education level and genetic and metabolic diseases. The prevalence of urolithiasis is estimated to be between 2-20%.[2] However due to variations in socioeconomic status and geographic locations, the prevalence and incidence have changed in different countries or regions over the years. In 2015, 22.1 million cases occurred resulting in 16,100 deaths.[3] The incidence of urolithiasis is increasing and with the increasing need for medical and surgical intervention, there is a significant burden on the patient and economy.

The identification of common, modifiable risk factors for kidney stones may result in new approaches to the treatment and prevention of urolithiasis. Metabolic syndrome and nephrolithiasis present similar epidemiological characteristics. An increased incidence of urolithiasis of greater than 75% is seenin overweight and obese patients compared to their normal counterparts.[4] An increased risk for urolithiasis has been noticed to have a positive correlation with the epidemic of metabolic syndrome.

Objectives

Objectives were to investigate the relationship between metabolic syndrome and calciumstone formation.

METHODS

A retrospective observational study was conducted on 140 patients who underwent surgery for urolithiasis and whose stones were calcium containing. All patients who attended outpatient department or admitted in the department of urology with a history of a surgery/procedure for urolithiasis (Open nephrolithotomy, percutaneous nephrolithotomy and ureterorenoscopy) and whose stones were detected to have calcium oxalate content > 70 % was enrolled in the study. We randomly selected 140 patients without any history of urolithiasis as control.

Patients with history of primary hyperparathyroidism, chronic diarrheal syndromes, intestinal malabsorption syndromes, complete distal renal tubular acidosis, primary hyperoxaluria, recurrent or active urinary tract infections, history of kidney transplantation, patients on ongoing 5α reductase inhibitor therapy, liver disease, primary gout, any debilitating chronic illness, or calculated creatinine clearance of less than or equal to 50ml/min was excluded from the study. Height, weight, waist circumference, blood pressure of the patient was measured, and a fasting blood sample was drawn to estimate the blood glucose, serum total cholesterol, high density lipoprotein (HDL) cholesterol, and triglycerides using enzymatic methods using an autoanalyzer.

Metabolic syndrome was defined according to the IDF consensus worldwide definition.

The IDF defined metabolic syndromeas the presence of Central obesity ie, Increased waist circumference >90 cm for men and >80 cm in women (according to ethnic criteria for South Asians-Indians) plus any two of the following-Elevated triglycerides (≥150 mg/dl), reduced HDL cholesterol (<40 mg/dl in men and <50 mg/dl in women), hypertension (≥130/>85 mmHg) and impaired fasting glucose (≥100 mg/dl).

Statistical analysis

The data was digitised using a data entry sheet created on Epi Data and analysed using SPSS 23.0, a proprietary software of IBM Inc. The baseline sociodemographic and clinical correlates of both the groups was assessed and compared. The treatment details and the clinical outcomes of both the groups was compared using tests of means or tests of proportions. The difference in characteristics between the two groups, was assessed using Chi Square test. Odds ratio (95% confidence interval) was calculated to evaluate the strength of association. Binary logistic regression was done, and adjusted odds ratios was calculated to account for possible confounding factors. P<0.05 was taken as statistically significant.

Ethical considerations

Study was conducted only after approval from institutional ethical committee. A written informed consent was taken from all the patients included in the study.

Sample size

The sample size was calculated as shown below:

n= (Za+Zb)2pqx^2/2

Za/2 = the Z value of a errorZ b= the Z value of b error,

d=minimum clinically relevant effect size p1=% the character in the standard group,

p2=p1+d or p1-d depending on whether we want to increase the p2 or decline it) p=average percentage of character= p1+p2/2

If we take the percentage of hypertension among the stone positive subjects as p and a minimum clinically relevant effect size of 20% is taken, then minimum sample size required is 87 each in study and control group. We increased the sample size to 140 in each group.

RESULTS

Both groups are comparable in terms of gender since male and femaledistribution were almost similar in both groups.

The mean age in stone group was 49.65±12.78 years and in control group was 51.2±11.62 years. There was no significant difference between the groups, hence the groups are comparable in terms of age.

It is evident that waist circumference was significantly higher in stone group with 89.69±10.78 cm compared to control group with 86.72±9.07 cm (Table 1).

When comparing systolic and diastolic blood pressure between 2 groups it was evident that systolic blood pressure was significantly different between groups (Table 2).

The mean FBS value was significantly higher in stone group 124.4±45.88 mg/dl compared to control group 111.78±41.65 mg/dl. When comparing the HDL values, it is evident that the mean value was lower in stone group 45.3±10.28 compared to control group 53.34±11.59 and the difference was statistically significant (Table 3).

In the present study the abnormal waist circumference (≥90 in male, ≥80 in female) was more in stone group (60.7%) compared to control group (45%) and the difference was statistically significant (Table 4).

In the present study the abnormal triglyceride (≥150 mg/dl) was more in stone group (34.3%) compared to control group (21.4%) and the difference was statistically significant (Table 5).

In the present study the abnormal HDL (<40 mg/dl in the male, <50 mg/dl in the female) was more in the stone group (43.6%) compared to the control group (22.1%) as well as the difference was statistically significant (Table 6).

In the present study the hypertension (≥130/85 mmHg) was more in stone group (41.4%) compared to control group (35%) but the difference was not statistically significant (Table 7).

In the present study the FBS (≥100 mg/dl) was more in the stone group (60.0%) compared to control group (51.4%) but difference was not statistically significant (Table 8).

The prevalence of metabolic syndrome in stone group was 40% which was higher than the control group with 25% and the difference was statistically significant (Table 9).

Table 1: Mean distribution of waist circumference.

Variables	Group	N	Mean	SD	Mean difference (95% C.I.)	Unpaired t test p value
Waist circumference	Stone	140	89.693	10.7816	2.97 (0.63 to 5.32)	0.013
	Control	140	86.721	9.0673		

Table 2: Comparison of blood pressure.

Variables	Group	N	Mean	SD	Mean difference (95% C.I.)	Unpaired t test p value
SBP	Stone	140	129.164	14.6791	4.4 (1.02 to 7.7)	0.011
	Control	140	124.800	13.7098		
DBP	Stone	140	77.750	10.9690	-1.01 (-3.5 to 1.49)	0.429
	Control	140	78.757	10.2976		

Table 3: Comparison of biochemical parameters (Mean values).

Variables	Group	N	Mean	SD	Mean difference (95% C.I.)	Unpaired t test p value
FBS	Stone	140	124.414	45.8833	12.64 (2.33 to 22.95)	0.016
	Control	140	111.779	41.6510		
Triglycerides	Stone	140	137.693	48.1607	0.38 (-9.09 to 9.85)	0.937
	Control	140	137.314	30.3427		
HDL	Stone	140	45.300	10.2807	-8.04 (-10.6 to -5.46)	<0.001
	Control	140	53.336	11.5880		

Table 4: Comparison of abnormal waist circumference.

Waist circumference	Stone		Control		Chi square test p value
	N	%	N	%	
Normal	55	39.3	77	55	0.008
Abnormal	85	60.7	63	45	
Total	140	100	140	100	

Table 5: Comparison of abnormally elevated triglycerides.

TG	Stone		Control		Chi-square test p value
	N	%	N	%	
Normal	92	65.7	110	78.6	0.016
Abnormal	48	34.3	30	21.4	
Total	140	100	140	100	

Table 6: Comparison of abnormally lower HDL values.

HDL	Stone		Control		Chi-square test p value
	N	%	N	%	
Normal	79	56.4	109	77.9	<0.001
Abnormal	61	43.6	31	22.1	
Total	140	100	140	100	

Table 7: Comparison of abnormally high blood pressure values.

BP	Stone		Control		Chi-square test p value
	N	%	N	%	
Normal	82	58.6	91	65	0.268
Hypertension	58	41.4	49	35	
Total	140	100	140	100	

Table 8: Comparison of abnormally high fasting blood sugar values.

FBS	Stone		Control		Chi-square test p value
	N	%	N	%	
Normal	56	40	68	48.6	0.149
Abnormal	84	60	72	51.4	
Total	140	100	140	100	

Table 9: Comparison of prevalence of metabolic syndrome.

Metabolic syndrome	Stone		Control		Chi-square test p value
	N	%	N	%	
Yes	56	40	35	25	0.007
No	84	60	105	75	
Total	140	100	140	100	

Table 10: Comparison of number of parameters of metabolic syndromebetween groups.

Number of parameters present	Stone		Control		Chi-square test p value
	N	%	N	%	
0	15	10.7	26	18.6	0.004
1	34	24.3	51	36.4	
2	28	20	28	20	
3	21	15	14	10	
4	27	19.3	9	6.4	
5	15	10.7	12	8.6	
Total	140	100	140	100	

The number of parameters taken into consideration for diagnosing metabolic syndrome were five (WC, TG, HDL, blood pressure and FBS). While sum up the number of parameters an individual having in each group it is evident that the proportion of patients in stone group had a greater number of parameters compared to control group. It was statistically significant.

DISCUSSION

Metabolic syndrome is simultaneous occurrence of hyperglycemia, hyperlipidemia, hypertension, and visceral obesity. It is chronic disease associated with high mortality. It substantially increases risk of development ofcardiovascular events and type 2 diabetes.[1]

Large scale epidemiologic studies have shown an increased prevalence of kidney stones in patients with lifestyle-related diseases such as hypertension[5], diabetes mellitus, obesity and dyslipidemia. Taken together these inter-related risk factors are termed metabolic syndrome.[6,7] Studies have shown that metabolic syndrome and its components are associated with increase rate of nephrolithiasis.

Although the exact pathophysiological mechanisms metabolic syndrome and nephrolithiasis are unclear, metabolic syndrome has been associated with changes in urinary constituents, including lower urinary pH, decreased citrate excretion, and increased uric acid and calcium excretion leading to increased risk of uric acid and calcium stone formation.[8,9] Conditions that are associated with insulin resistance, such as obesity the metabolic syndrome and T2DM are associated with increased risk of stone formation. Insulin resistance leads to reduced renal ammonia production, resulting in more acidic pH, creating a favorable environment for calcium oxalate and uric acid stone formation. Since 80% of kidney stones consist of calcium oxalate studies exploring the relationship between urinary risk factors for calcium stone formation and features of the metabolic syndrome are critical.[10]

Therefore, in this study, we aimed to investigate the relationship between calcium stone urolithiasis and the components of metabolic syndrome. We retrospectively studied anthropometric and biochemical values of 140 subjects with known calcium urolithiasis and compared it with a group of 140 subjects without stone disease. The age and sex of the sample taken in both the subsets was comparable without significant discrepancies. The gender wise distribution of stone group 59.3% males (n=87) and females 41.7% (n=53). Similarly in the control group without stone the distribution was 57.9% males (n=81) and females 42.1% (n=59). The mean age in stone group was 49.65±12.78 years and in control group was 51.2±11.62 years.

On analyzing the various anthropometric values, it was evident that the waist circumference was significantly higher in stone group (89.69±10.78 cm) compared to control group (86.72±9.07 cm). This points to correlation between abdominal obesity and urolithiasis. (Unpaired t test p=0.013). Similarly, when comparing systolic and diastolic blood pressure between two groups it was evident that the mean systolic blood pressure of the stone group was significantly higher (Unpaired t test p=0.011).

On comparing various biochemical parameters between the two groups, the mean FBS value was significantly higher in stone group (124.4±45.88 mg/dl) compared to control group (111.78±41.65 mg/dl) **(**Unpaired t test p=0.016). When comparing the HDL values, it is evident that the mean value was lower in stone group 45.3±10.28 compared to control group 53.34±11.59 and the difference was statistically significant (Unpaired t test p<0.01). However, the level of triglycerides in both groups did not differ significantly.

On comparing the percentage abnormality of various parameters in both the groups following findings were noted. The study showed abnormal waist circumference (≥90 cm in male, ≥80 cm in female) was more in stone group (60.7%) compared to control group (45.0%) and the difference was statistically significant (Chi square test p=0.008). This implies that a higher risk of calcium stone urolithiasis in men and women with stone disease compared to the normal population. According to studies conducted by Sarica and colleagues, obese patients excrete more urinary stone-forming risk factors such oxalate, calcium, and citrate.[11]

In idiopathic calcium stone disease, Parvin and colleagues discovered that oxalate plays the most significant role as a urinary stone risk factor, followed by calcium and uric acid, and that the adjusted body weight values are a stronger and more important predictor of calcium stone formation.

A number of epidemiologic investigations have examined the connection between nephrolithiasis and hypertension. Cross-sectional studies have shown that hypertensive patients have nephrolithiasis more frequently than normotensive patients do, the pathologic relationship between hypertension and stone disease is still unclear. Additionally, some prospective studies revealed that patients with hypertension may develop stones.[6,12] Eisner and colleagues' study has proven that hypertensive patients had higher calcium excretion.[13] Hypocitraturia, which develops in hypertensive patients because of acidosis, is another potential explanation. However, in our study on analyzing both groups the hypertension (≥130/85 mmHg) was more in stone group (41.4%) compared to control group (35%). But this difference was not statistically significant enough to draw a conclusive correlation (Chi square test p=0.268).

In our study, while considering various laboratory parameters it is observed that prevalence of abnormally elevated triglyceride levels (≥150 mg/dl) was more in stone group (34.3%) compared to control group (21.4%) and the difference was statistically significant (Chi square p=0.016). Also, the abnormally low HDL (<40 mg/dl in male, <50 mg/dl in female) was more in stone group (43.6%) compared to control group (22.1%) and the difference was statistically significant (Chi square p<0.001). These findings show a significant correlation between dyslipidemia and calcium stone urolithiasis.

According to Taylor and colleagues, patients with diabetes have a greater chance of having kidney stones and a higher rate of stone episodes than patients without diabetes.[6] This correlation existed regardless of age/BMI.

Meydan and colleagues' cross-sectional study evaluated incidence of kidney stone disease in diabetes and agematched non-diabetic participants. Nephrolithiasis significantly more common in diabetic people (21% among 321 vs. 8% among 115).[14] In order to demonstrate the connection between urolithiasis and diabetes, Lieske and colleagues compared 3,561 stone-formers with 3,561 age- and gender-matched control patients in case-control community-based study.[15] According to their findings, stone formers had 22% higher chance of developing diabetes and higher % of stone formers were diabetic. In our study when comparing fasting blood sugar (≥100 mg/dl) it was more in stone group (60%) compared to control group (51.4%) but the difference was not statistically significant (Chi square test p=0.149).

The IDF defines metabolic syndrome as the presence of Central obesity, that is, Increased waist circumference >90 cm for men and >80 cm in women. (According to ethnic criteria for South Asians-Indians) plus any two of the following-Elevated triglycerides (≥ 150 mg/dl), reduced HDL cholesterol (<40 mg/dl in men and <50 mg/dl in women), hypertension (≥130/>85 mmHg) and impaired fasting glucose (≥100 mg/dl).

While taking into consideration of this globally accepted and validated definition of metabolic syndrome, the prevalence of metabolic syndrome in stone group was 40% which was higher than the control group with 25% and thedifference was statistically significant (p=0.007).

West et al did an extensive study on correlation between the metabolic syndrome and calcium stone disease.[16] From 1988 to 1994, they collected health and dietary information on 33,994 men, women, and kids. They discovered that 4.7% of all persons over the age of 20 reported having kidney stones. From 3% with zero MS traits to 7.5% with three traits to 9.8% with five traits, the prevalenceof stones rose with the number of MS features. Two or more features significantly enhanced the probability of stones after controlling for confounders. The likelihood of stone increased roughly twofold when four or more features were present.

The number of parameters taken in to consideration for diagnosing metabolic syndrome were five (WC, TG, HDL, blood pressure and FBS). While summing up the number of parameters an individual having in each group, it is evident that the patients in stone group had a greater number of deranged metabolic parameters compared to control group. This observation was statistically significant (p=0.004).

Limitations

The study has certain limitations. Even though, the aim of the study was to analyze the correlation between calcium stone urolithiasis and metabolic syndrome, there are multitude of factors which affect stone formation which we could not take into consideration. Various anatomical and functional patient factors like uretero-pelvic obstruction, calyceal diverticulum, vesicoureteral reflux, recurrent urinary tract infections, renal tubular acidosis and horseshoe shaped kidney can increase propensity for stone formation in a normal otherwise healthy individual. These factors could not be outrightly ruled out in our study. Similarly various environmental and occupational factors that can influence stone formation could also be not taken into consideration.

CONCLUSION

This study was designed to investigate the relationship between various components of metabolic syndrome and calcium stone formation. The various anthropometric and biochemical parameters of metabolic syndrome (as per the IDF definition of metabolic syndrome) was studied separately and as a constellation of parameters in a population of calcium stone formers and compared with a control population with no history of calcium stone formation. The study showed that the average waist circumference, blood pressure, blood sugar and dyslipidaemia was higher among the stone formers when comparing with the non-stone formers. After considering all the parameters of metabolic syndrome, the prevalence of metabolic syndrome in the stone group was 40% which was higher than the non-stone formers (25%). While summing up the number of parameters of metabolic syndrome (as per IDF definition) an individual has in each group, it is evident that the proportion of patients in the stone group had a greater number of parameters compared to the control group. The study could draw a positive correlation between various components of metabolic syndrome and calcium urolithiasis. Urolithiasis is the most common cause of outpatient and inpatient patient burden in a urology department. With a global epidemic of metabolic syndrome and its tremendous impact on the healthcare, it is prudent to understand its implications on urolithiasis. The propensity of recurrent stone formation in individuals with metabolic syndrome and the risk for undergoing multiple surgeries for stones necessitates to adopt effective preventive measures by educating the vulnerable population.

It recommended to do a complete metabolic every patient presenting with urolithiasis to assess the risk for metabolic syndrome and educate them regarding various lifestyle modification to prevent recurrent stone formation that may risk renal failure.

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