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Original Research Article

Obesity and metabolic evaluation of 24 hour urinary analysis of adult stone formers, a case control study

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ABSTRACT

Background: Urinary tract stone (Urolithiasis) is a common problem nowadays. Frequencies of urolithiasis vary from region to region: 1-5% in Asia, 5-9% in Europe, 13% in North America. Urolithiasis is believed to be due to imbalance & crystallisation of minerals inside urine, which act as the focus for more sedimentation and finally the formation of a stone within the urinary tract. The comorbidities associated with urinary stones includes: renal colic, urinary tract infection, hydronephrosis, obstruction of the collecting system, renal parenchymal damage which ultimately leads to renal failure and even death. The aim of this study was to assess the relationship between obesity and the metabolic evaluation of 24 hour urinary analysis of stone formers.
Methods: A case-control study was carried out on 70 patients aged ≥20 years with urolithiasis that were without any comorbidities treated between January 2014 to January 2015. We performed 24 hour urinary analysis on urolithiasis patients and classified them as being of low weight (body mass index; BMI: <18.5, 8 men, 5 women), normal weight (BMI: 18.5-24.9, 19 men, 7 women), overweight (BMI: 25-29.9, 30 men, 12 women) or obese (BMI≥30, 12 men, 7 women).140 healthy normal weight sex and age-matched controls were also included in the study in the ratio of 1:2.
Results: There was a statistically significant difference in the prevalence of obesity between the urolithiasis group and the control group ($p<0.05$).The correlation analysis revealed a significant positive relationship between BMI and the serum calcium, uric acid, urinary calcium, uric acid and citrate, and there was an inverse relationship between BMI and urinary pH ($p<0.05$). The frequency of urinary stone risk factors was increased with BMI ($p<0.05$).
Conclusions: The positive relationship between Obesity and the risk factors for urolithiasis was evident from this study. To understand the mechanism of urolithiasis in obese patient's further research is required.

Keywords: 24 hour urinary analysis, Saleem SM, Stone formers, Urolithiasis and obesity

INTRODUCTION

Urinary tract stone (Urolithiasis) is a common problem nowadays. Scientists have even found evidence of Urolithiasis in Egyptian mummy several thousand years ago.[1] Frequencies of urolithiasis vary from region to region: 1-5% in Asia, 5-9% in Europe, 13% in North America.[2-3] Urolithiasis is believed to be due to imbalance and crystallisation of minerals inside urine, which act as the focus for more sedimentation and finally the formation of a stone within the urinary tract.[4]

The comorbidities associated with urinary stones includes: renal colic, urinary tract infection,

hydronephrosis, obstruction of the collecting system, renal parenchymal damage which ultimately leads to renal failure and even death. Studies in the past have documented about the multifactorial causation of urolithiasis which include hypercalciuria, hypocitraturia, hyperuricosuria, hyperoxaluria, and hypomagnesuria.[1]

Many studies attribute low fluid intake, high or low urinary pH, dietary habits, sedentary life-style, high body mass index, environmental factors, genetic factors and even the hardness of water as a potential risk factor for development of urolithiasis.[5-9]

Urinary stones are of many types but the most common include calcium oxalate stones (80%), followed by struvite stones (10-15%), Uric acid and calcium phosphate stones, each with (5-10%) incidence rates in general population.

As it is well known that the prevalence of nephrolithiasis varies with age, gender, and race.[10-12] To our knowledge, there is no such information about the effect of obesity on urolithiasis in Kashmir division. This study aims to describe metabolic evaluation of 24 hour urinary constituents among adult ≥20 year's stone formers and obesity as a risk factor for urolithiasis.

METHODS

A Case control study was carried out on 70 patients aged ≥20 years with calcium oxalate stones that were without any comorbidity treated between January 2014 to January 2015. We performed 24 hour urinary analysis on these 70 urolithiasis patients having calcium oxalate stones and classified them as being of low weight (body mass index; BMI: 18.5, 8 men, 5 women), normal weight (BMI: 18.5-24.9, 19 men, 7 women), overweight (BMI: 25-29.9, 30 men, 12 women) or obese (BMI≥30, 12 men, 7 women). 140 healthy normal weight sex and age-matched controls were also included in the study.

Patients with single or recurrent episodes of urolithiasis of calcium oxalate type were included in the study. Episodes of stone formation were confirmed from history of the patients. Pregnant women and patients with urine output <1000ml/24 hour were excluded from the study. Prior ethical clearance from the hospital ethical committee was sought out and only those patients who gave written informed consent were included in the study. Demographic data from patients were collected, namely age and sex.

Anthropometric data included height, weight, hip circumference, waist circumference. Blood was analysed for lipid profile and Urine was collected for 24 hours in each patient and 10 ml sample of this urine was stored at 20°C before analysing for urinary constituents by spectrophotometer. Mean body mass index of study participants was analysed, and 24-hour urinary constituent's results were compared between stone formers and healthy controls.

The number of past urolithiasis episode in each patient were confirmed by personal history and available medical records. Metabolic diagnosis consisted of following categories: Hypercalciuria males: >7.5 mmol (300 mg)/24 hour, females: >6.25 mmol (250mg)/24 hour, Hyperoxaluria 0.46mmol (40mg)/24 hour, Hyperuricosuria: >4.46mmol (750 mg)/24 hour, Hypomagnesuria: <3 mmol/24 hour and Hypocitraturia: <1.56 mmol (300mg)/24 hour.

Statistical analysis

Statistical analysis was done using SPSS statistical software v 20.0.Data was presented by mean±Standard Deviation (±S), Group Comparison was done by t-test, Chi-square test was adopted to test enumeration data. p <0.05 was considered statistically significant.

RESULTS

Demographic and anthropometric analysis between underweight, normal weight, overweight and obese patients with urolithiasis and relation to recurrent stone formation are summarized in Table 1.

Table 1: Characteristics of patients with urolithiasis and frequency of stone formers according to BMI.

	Non Obese		Obese		
	Low Weight	**Normal Weight**	**Over Weight**	**Obesity**	**Total**
BMI range	<18.5	18.5-24.9	25-29.9	>30	
No. of Patients	10	29	19	12	n=70
No. of Male/Female	6/4	21/8	12/7	8/4	47/23
Age(Years)	50 ±12.3	48±11.5	52 ±13.2	48 ±15.3	50±13.7
Weight (Kgs)	46±4.2	67±8.4	78±8.2	87±6.4	69±6.8
Height (Cms)	154±5.4	154±6.2	154±5.2	154±5.1	154±5.9
Stone Formers (%)	1/10 (10%)	9/29 (31.03%)	13/19 (68.42%)	8/12 (66.66%)	31/70 (44.28%)

Males outnumber the females in the study group with mean age of the study participants being 50±13.7, weight 69±6.8 and height 154±5.9. The incidence of recurrent stone formers was 44.28% in the total study participants with 66.66% among obese patients, 68.42% among over weight patients and only 10% among underweight stone formers.

Table 2: 24 Hour urinary abnormalities in cases and controls.

Parameters	Stone patients N=70	Controls n=140	P-value
	Mean±SD	Mean±SD	
Calcium	9.41±2.07	5.04±0.44	<0.001*
Magnesium	2.66±0.54	3.74±0.30	<0.001*
Oxalate	41.58±5.45	33.78±2.85	<0.001*
Uric Acid	4.37±0.21	2.42±0.49	<0.001*
Citrate	1.32±0.18	1.93±0.32	<0.001*
Phosphate	42.32±1.87	41.08±0.67	<0.001*
Urine Volume	2.60±0.59	1.59±0.15	<0.001*

Table 3: Comparison between stone formers and controls according to BMI.

	BMI	Control % [n=140]	Stone formers % [n=100]
Low weight	<18.5	21 (15)	10 (10)
Normal weight	18.5-24.9	84 (60)	29 (29) *
Over weight	25-29.9	27 (19)	19 (19) *
Obesity	≥30	8 (6)	12 (12) *
Total		140	100

[*= p<0.5]

Our analysis shows positive correlation of obesity with urolithiasis. On metabolic evaluation of 24 hour urinary constituents in present study group of 70 patients with urolithiasis, 52 (75%) patients were having hypercalciuria as predominant urinary abnormality with Mean±SD 9.41±2.07which was persistently higher in comparison to control group and was statistically significant. The second most common urinary abnormality seen was Hypocitraturia found in 49 (70%) stone formers with Mean±SD of 1.32±0.18. Increased concentrations of uric acid were seen in 21 (30 %) stone formers.

Significant increase in urinary phosphate and oxalate concentrations were raised in stone formers in 31 (45%) and 37 (52%) patients with Mean±SD of 42.32±1.87 and 41.58± 5.45 respectively.

Table 4: Results of the 24-hour urine parameters and the serum parameters according to the BMI.

	Low weight	Normal weight	Over weight	Obesity	P-Value
24 hour urinary analysis					
pH	7.2±0.85	6.5±0.55	6.5±0.72	6.5±0.62	0.0004
Volume (ml)	2321±780	2399±988	2668±1288	2100±1480	0.7867
Calcium (mg)	109±50.2	159±88.8	185±110	188±13.8	0.0162
Uric Acid (mg)	352±115.4	540±192.6	632±235.4	690±332.1	<0.0001 *
Oxalate (mg)	18±10.4	32±14.2	34±17.3	26±14.2	0.4220
Citrate (mg)	255±138.6	380±215.	410±220.5	488±218.8	0.0042
Urea (gm)	16±4.5	16±3.2	23±4.6	28±7.4	<0.0001*
Serum					
Uric Acid (mg/dl)	3.6±0.84	5.2±1.44	5.8±1.66	5.6±1.38	<0.0001 *
Calcium (mg/dl)	8.6±0.62	8.8±1.05	9.2±0.51	9.4±0.20	0.0012
Phosphorus (mg/dl)	3.5±0.82	3.6±0.82	3.7±0.62	3.9±0.32	0.4326

Hypomagnesuria was seen in 45 (45%) stone formers and was not seen in the control group (Table 2). The comparison between the control group and stone formers with respect to BMI is shown in (Table 3). The chi-square test shows no significant difference in underweight stone formers but shows statistically significant difference in over weight stone participants ($p < 0.05$).

While comparing the values of the risk factors of obesity and 24 hour urinary and serum analysis, Serum uric acid value of the stone formers, calcium and urinary uric acid, urea and Citric acid showed a positive correlation to the BMI (Table 4).

DISCUSSION

The incidence of Kidney stone varies in different parts of the world, however, in Asia stone forming belt has been reported to stretch across Sudan, Saudia Arabia, UAE, Iran, Sindh province of Pakistan, Northern India, Myanmar, Thailand and Indonesia. The effect of stone geography on the incidence of stone formation may be direct through its effect on temperature whereby high temperatures increase perspiration which may result in concentrated urine or in our population it could be attributed to high intake of animal protein and sodium in the form of salt tea, which in some studies have shown increases urinary calcium and uric acid concentrations and lowers urinary citrate concentration.

The present study was undertaken to determine the relation of urolithiasis with obesity and to estimate 24 hour metabolic disturbances on the urinary lithogenic profile of patients with urolithiasis. The study analysis revealed that the patients with urolithiasis had hypocitraturia, hypercalciuria and hyperoxaluria as the predominant abnormality in 24 hour urinary analysis.

This result is in agreement with published data by Kumar et al, Orazaki et al, Tafekli et al, BabicIvanic et al.[13-16] All have reported the incidence of hypercalciuria to be very high in stone formers. Many large epidemiologic studies have also demonstrated that the most common metabolic abnormality in patients with urolithiasis is hypercalciuria.[17,18] Hypercalciuria is a multifactorial disorder however in our subjects high frequency of it may be due to consumption of diet rich in animal protein which contributes to hypercalciuria. Increase in calcium excreation on intake of dietary sodium is well established.

Every 100 mmol increase in dietary sodium results in approximately in a 25mg rise in urinary calcium. The adverse effects of a high salt intake also contribute to bone loss. Henceforth increase urinary calcium concentrations are an important factor in pathogenesis of urinary stone formation. In the present study, hypocitraturia was the second most common abnormality. Numerous studies have shown that low urinary citrate is a potential cause for calcium urolithiasis. Mean urinary citrate concentration was less in patients as compared to normal individuals and it was statistically significant.

In our patients high percentage of hypocitraturia (60%) was noted which was in accordance with findings of Kumar et al and Esen et al where hypocitraturia respectively was noted in (55%) and (44.9%) of stone formers. In the present study, analysis were designed to test our hypothesis that patients with urinary stones and an increased BMI (overweight/obese) have different urinary risk lithogenic profiles than patients with urolithiasis and normal age sex matched controls.[13,19] However, we did find a significant difference between these two groups.

Studies have demonstrated that an increased BMI is related with changes in the biochemical components of urine, including phosphate, oxalate, uric acid and citrate Negri et al reported that uric acid and oxalate were significantly higher in the urine samples of obese patients, and Taylor et al showed a positive relationship between BMI and urinary excretion of oxalate, calcium, uric acid, urea, citrate, sodium, phosphate and potassium.[21-25] However these studies only demonstrated that obese patients are more predisposed to urolithiasis than those within the normal weight range. A limitation of this study was the relatively small sample size of obese and overweight patients. Similarly, there was a disproportion in the numbers of patients with hyperuricemia and those with normouricemia. Further work needs to be done in patients with hyperuricemia, but without urinary stones, to establish whether they are predisposed to urolithiasis and, if so, how it can be prevented.

CONCLUSION

The positive relationship between Obesity and the risk factors for urolithiasis was evident from this study. To understand the mechanism of urolithiasis in obese patient's further research is required.

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