Association of Body Mass Index, Waist Circumference, and Waist-Stature Ratio With Urine Composition in Patients With Urolithiasis

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Keywords. nephrolithiasis, obesity, abdominal obesity, urine composition, relative supersaturation

Introduction. This study was aimed to evaluate the correlation of body mass index (BMI), waist circumference (WC), and waist-stature ratio (WSR) with urinary composition in urolithiasis patients.

Materials and Methods. Medical reports of 1410 urolithiasis patients referred to a tertiary in Tehran, from 2010 to 2015, were reviewed. Collected data included WC, BMI, and WSR, 24-hour urine composition, and the first-morning urine pH. Urinary relative supersaturation of calcium oxalate, calcium phosphate, and uric acid were calculated. Linear correlation and logistic regression models were used for study analyses.

Results. A total of 511 records were reviewed. In the women, supersaturation of calcium oxalate significantly correlated with BMI, WC, and WSR. Supersaturation of uric acid significantly correlated with WC. Using regression analyses, BMI and WSR were associated with greater supersaturation of calcium oxalate abnormality, which persisted after adjustment for confounding factors (odds ratio, 1.080; 95% confidence interval, 1.001 to 1.166 for BMI; odds ratio, 1.053; 95% confidence interval, 1.001 to 1.108 for WSR). Larger WC accompanied abnormal values for supersaturation of calcium oxalate; however, the model was marginally significant (odds ratio, 1.032; 95% confidence interval, 1.000 to 1.065; \( P = .05 \)) in multivariable analysis. In the men on the other hand, none of the obesity indexes were associated with the supersaturation measures.

Conclusions. Although both obesity and abdominal obesity correlated with supersaturation of calcium oxalate, mostly by changes in urine volume and pH in women, none of those indexes showed significant correlation with urine composition in the men population of our study.

INTRODUCTION

Urolithiasis is a common highly recurrent disease and its prevalence is increasing worldwide in parallel to obesity.1 According our previous study, the incidence rate of disease in Iran was 136 per 100 000 population in 2008.2 Because of the treatment costs and the effect of the disease on quality of life, and also its risk of progress to chronic kidney disease,3 urolithiasis should be considered as a health priority.

Epidemiological studies revealed a significant relationship between obesity and urolithiasis incidence.4 Studies also showed that obesity affects the type of urinary calculus. Many attempts have been made to find out the pathophysiology of this relationship.5 Some studies have shown
some association between the obesity and urinary metabolites. Two studies by Taylor and colleagues and Eisner and colleagues showed that higher a body mass index (BMI) was associated with higher urinary calcium, oxalate, uric acid, sodium, phosphate levels and also a lower urinary pH,\textsuperscript{6,7} which are all in favor of kidney stone formation. In contrast, some studies had controversial results.\textsuperscript{8} There are also studies which have illustrated a relationship between urinary metabolites and metabolic syndrome measures other than BMI, and therefore, contemplated urolithiasis as a systemic disease.\textsuperscript{9}

Different indexes have been used to define obesity and to quantify its severity. The most commonly used index is BMI, which is a measure of weight adjusted for height and is routinely used in many epidemiological studies. However, BMI is an imperfect measure of body's fat.\textsuperscript{10} Compared to BMI, abdominal obesity is more indicative of the amount of body fat and also more related to chronic diseases and is one of the criteria that lead to the diagnosis of the metabolic syndrome.\textsuperscript{10,11} Waist circumference (WC) and waist-stature ratio (WSR) are two indexes to measure abdominal obesity.\textsuperscript{10} Although the association between obesity and urinary calculus incidence is documented, few studies have evaluated the relationship between the 24-hour urine composition and abdominal obesity indexes.\textsuperscript{12} Since former studies have shown that abdominal obesity is strongly related to chronic systemic diseases such as urolithiasis, the aim of current study was to evaluate the correlation between not only obesity index (BMI), but also abdominal obesity indexes (WC and WSR), with urinary metabolic abnormalities in urolithiasis patients.

**MATERIALS AND METHODS**

**Study Design and Study Population**

In this cross-sectional study, we reviewed the medical reports of 1410 patients with urolithiasis, referred to the Preventive Clinic for Urolithiasis Patients from 2010 to 2015. This clinic is housed within Labbafinejad Hospital in Tehran, Iran. The study protocol was approved by the local ethics committee.

Patients’ records were included if the patients had kidney or ureteral calculi and visited for their initial metabolic stone workup within the age of 18 to 70 years; if their BMI was greater than 18.5 kg/m\textsuperscript{2}; if they had at least one 24-hour urine analysis result collected properly, with 24-hour urine creatinine greater than 800 mg for men and greater than 600 mg for women;\textsuperscript{7} and if their anthropometric data were available. Patients were excluded if they were pregnant or lactating; if they had cystinuria, inflammatory bowel disease, chronic kidney disease, hepatic disease, thyroid or parathyroid disease, or immunologic diseases; or if they had a history of ileal or colonic resection, bariatric surgery, or struvite calculi. We also excluded patients with primary hyperoxaluria or those who were treated with any medication influencing 24-hour urine constituents including potassium citrate, hydrochlorothiazide, vitamin B6, vitamin C, and calcium supplements.

**Anthropometric and Demographic Data**

Patients’ demographic (age, sex, and family history of lithiasis) and anthropometric (body weight, height, and WC) data were collected by the physicians. Weight, height, and WC were measured according to the standard protocols,\textsuperscript{13,14} and BMI (kg/m\textsuperscript{2}) and WSR were calculated. The patients were categorized, using the BMI, as normal, overweight, and obese based on 1998 clinical guidelines.\textsuperscript{15}

**Laboratory Tests**

All patients presented to our clinic had been asked to do a complete workup including 2 consecutive 24-hour urine collections with a 1-week interval and a fasting morning urine sample. Urine parameters such as volume and levels of creatinine, phosphate, calcium, oxalate, citrate, sodium, potassium, magnesium, and uric acid were measured, using standard methods as published previously.\textsuperscript{16} Urine pH was measured in fasting morning samples using a dipstick method. The LithoRisk software (Biohealth, Italy) was used to calculate urinary relative supersaturation of calcium oxalate (COSS), calcium phosphate (CPSS), and uric acid (UASS).\textsuperscript{17} The average 24-hour urine variables were analyzed if two 24-hour urine collection results were available.\textsuperscript{18} Abnormal 24-hour urine compositions were also defined as follows: volume less than 2000 mL, calcium greater than 200 mg/24 h, magnesium less than 80 mg/24 h, oxalate greater than 40 mg/24 h, citrate less than 320 mg/24 h,\textsuperscript{19} uric acid greater than 600
mg/24 h, sodium greater than 200 mEq/24 h, and potassium less than 40 mEq/24 h. Supersaturation values were considered abnormal as stated by the LithoRisk software cutoffs as follow: COSS greater than 5, CPSS greater than 2, and UASS greater than 1. Fasting urine pH less than 5.5 was also considered abnormal. Kidney or urethral calculi, if available, were analyzed using chemical analysis. Compositions greater than 50% were considered as the calculus type. Calculi with no composition greater than 50% were defined as mixed calculi.

**Statistical Analyses and Sample Size**

In order to evaluate the correlation of BMI with the first outcomes by the Fisher transformation, given the probability of type I error of 0.05, power of 0.80, and correlation coefficient of 0.25, the required sample size were estimated to be 123 patients.

As primary analyses showed a significant difference between the men and the women in terms of urine composition, all analyses were stratified by sex to avoid biased results. Age, BMI, WC, and WSR were treated as continuous numerical variables. Normality test was performed for all numerical continuous variables, and nonparametric analyses were used for all variables without normal distribution. The Linear association between obesity indexes and urine composition were assessed using the Pearson and Spearman correlation tests, for parametric and nonparametric analyses, respectively. The difference between the men and the women was analyzed using the independent samples t test for numerical variables and the chi-square test for categorical variables. Logistic regression models were used to determine the odds ratio (OR) and 95% confidence interval (CI) of urine composition abnormality occurrence with regards to obesity indexes, considering age and family history as confounding factors. Statistical analyses were performed using the SPSS software (Statistical Package for the Social Sciences, version 19.0, IBM Corp, New York, NY, USA). A P value less than .05 was set as significance.

**RESULTS**

Of 1410 records in our database, 511 met the inclusion criteria. Demographic and anthropometric data of the patients are presented in Table 1. The women had significantly higher BMI and WSR compared to the men. Considering BMI cutoffs, 79.5% of the patients were categorized as overweight or obese. Compared to the men, there were more obese but fewer overweight patients among the women (Table 1).

Urine composition and abnormalities are depicted in Table 2. The men had significantly higher creatinine, calcium, sodium, magnesium, oxalate, phosphorus, COSS, and UASS levels, while they had significantly lower citrate values, compared to the women. In addition, the men had

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Women (n = 153)</th>
<th>Men (n = 358)</th>
<th>All (n = 511)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>46.52 ± 11.18</td>
<td>45.92 ± 11.18</td>
<td>46.10 ± 11.45</td>
<td>.58</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>74.75 ± 13.59</td>
<td>82.52 ± 13.59</td>
<td>80.19 ± 14.18</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.59 ± 0.07</td>
<td>1.71 ± 0.07</td>
<td>1.68 ± 0.09</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>29.73 ± 4.00</td>
<td>28.02 ± 4.00</td>
<td>28.53 ± 4.43</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Body mass index categories</td>
<td></td>
<td></td>
<td></td>
<td>0.03</td>
</tr>
<tr>
<td>Normal</td>
<td>28 (18.3)</td>
<td>77 (21.5)</td>
<td>105 (20.5)</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>60 (39.2)</td>
<td>172 (48.0)</td>
<td>232 (45.4)</td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>65 (42.5)</td>
<td>109 (30.4)</td>
<td>174 (34.1)</td>
<td></td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>95.79 ± 11.28</td>
<td>97.75 ± 11.28</td>
<td>97.16 ± 11.95</td>
<td>.11</td>
</tr>
<tr>
<td>Waist-stature ratio</td>
<td>0.61 ± 0.07</td>
<td>0.57 ± 0.07</td>
<td>0.58 ± 0.07</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Family history of calculi</td>
<td>87 (56.9)</td>
<td>201 (56.1)</td>
<td>288 (56.4)</td>
<td>.88</td>
</tr>
<tr>
<td>Calculus composition†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium oxalate</td>
<td>37 (78.7)</td>
<td>106 (79.1)</td>
<td>143 (79.0)</td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td>7 (14.9)</td>
<td>20 (14.9)</td>
<td>27 (14.9)</td>
<td></td>
</tr>
<tr>
<td>Calcium phosphate</td>
<td>1 (2.1)</td>
<td>2 (1.5)</td>
<td>3 (1.7)</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>2 (4.3)</td>
<td>6 (4.5)</td>
<td>8 (4.4)</td>
<td>.99</td>
</tr>
</tbody>
</table>

*Values are mean ± standard deviation and count (percentage).
†Stone composition data were available for 181 patients (47 women and 134 men).
significantly higher abnormal values of calcium, sodium, citrate, oxalate, and UASS, whereas they showed lower rate of low magnesium compared to the women (Table 2).

The linear association between obesity indexes and urine composition are shown in Tables 3 and 4. In the women, only urine creatinine and COSS had significant positive correlations with all indexes of obesity (BMI, WC, and WSR; Table 3). The results for the men showed a significant negative correlation...
between all indexes of obesity and urine pH. On the other hand, the results showed significant positive correlations between all indexes of obesity and urine creatinine, sodium, potassium, citrate, and phosphorus values. The only obesity index which correlated with calcium in the men was BMI (Table 4).

Tables 5 and 6 show the results of logistic regression models in the women and the men, respectively. In the women, a higher BMI was associated with a higher likelihood of COSS abnormal values (OR, 1.089; 95% CI, 1.012 to 1.173), which persisted after adjustment for potential confounding factors (OR, 1.080; 95% CI, 1.001 to 1.166; Table 5). Regarding abdominal obesity, larger WC accompanied with a higher frequency of volume, pH, citrate, and COSS abnormalities. However, in multivariable analyses, WC had marginally significant associations with volume (OR, 1.035; 95% CI, 1.000 to 1.071, \( P = 0.052 \)) and COSS (OR, 1.032; 95% CI, 1.000 to 1.065, \( P = 0.051 \)). There was no association between WC and citrate in multivariable analyses. Also, in patients with greater WSR, higher odds of abnormal volume (OR,
1.064; 95% CI, 1.014 to 1.116), pH (OR, 1.066; 95% CI, 1.013 to 1.121), and COSS (OR, 1.055; 95% CI, 1.009 to 1.104) were observed, which was similar in the multivariable models.

The results of regression analyses in the men yielded different findings (Table 6). Higher BMI increased the odds of abnormality in levels of calcium (OR, 1.103; 95% CI, 1.038 to 1.171) and sodium (OR, 1.073; 95% CI, 1.014 to 1.136), while decreased the odds of abnormality of magnesium level (OR, 0.938; 95% CI, 0.887 to 0.991), which all persisted in adjusted analysis models. Since 24-hour urine calcium content was shown to be affected significantly by dietary factors, further adjustments were made for 24-hour sodium and phosphorus levels, as a surrogate for dietary intake.7

The effect of BMI on urinary calcium disappeared after adjustments (OR, 1.062, 95% CI, 0.992 to 1.136). The OR of oxalate abnormality was only increased by WC increment, which disappeared after adjustment for confounding factors. The OR of pH abnormality was increased by all indexes of obesity; however, the association between WSR and pH also disappeared after the adjustment.

DISCUSSION

Our study population had a higher rates of overweight and obese patients than a normal population according to the national reports (27% to 38.5% overweight and 12.6% to 25.9% obesity).21 The rate of obesity and overweight was also higher than our previous results in 2010 (37.1% overweight and 13.6% obesity).22 The results showed that the linear correlation between obesity indexes and urine composition was different in the women and the men (Tables 3 and 4). Although many urinary metabolites showed correlation with all obesity indexes in the men, we did not find any correlation between COSS and obesity indexes in this group. This finding can be explained by concurrent increase of both promoters and inhibitors of stone formation, as previously discussed by Taylor and colleagues.6 However, in the women, COSS was the only variable which positively correlated with all obesity indexes. The negative correlation of obesity indices with both volume and pH is the reason for such correlation between obesity indexes and COSS. This difference between men and women is consistent with the results of Taylor

Table 6. Analysis of Association of Obesity Indexes in Male Patients With Urine Composition Abnormal Findings*

<table>
<thead>
<tr>
<th>Urine Parameter</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Body Mass Index</td>
<td>Waist Circumference</td>
<td>Waist-Stature Ratio†</td>
</tr>
<tr>
<td></td>
<td>Unadjusted Model</td>
<td>Adjusted Model</td>
<td>Unadjusted Model</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>1.139 (1.053 to 1.231)</td>
<td>1.123 (1.038 to 1.123)</td>
<td>1.034 (1.008 to 1.060)</td>
</tr>
<tr>
<td>Volume</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>1.103 (1.038 to 1.171)</td>
<td>1.102 (1.036 to 1.172)</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>1.073 (1.014 to 1.136)</td>
<td>1.072 (1.013 to 1.135)</td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td>0.886 (0.834 to 0.942)</td>
<td>0.898 (0.845 to 0.956)</td>
<td>0.953 (0.933 to 0.974)</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.938 (0.887 to 0.991)</td>
<td>0.942 (0.890 to 0.997)</td>
<td></td>
</tr>
<tr>
<td>Citrate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxalate</td>
<td></td>
<td>1.021 (1.002 to 1.041)</td>
<td></td>
</tr>
<tr>
<td>Uric acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium oxalate supersaturation</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Calcium phosphate supersaturation</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Uric acid supersaturation</td>
<td></td>
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</tbody>
</table>

*Adjusted model included age and positive family history. Ellipses indicated not significant.
†All odds ratios were calculated for each 0.01 unit increase in waist-stature ratio.
and colleagues which showed that the magnitude of the correlation between kidney calculus incidence and obesity may be greater in women compared to men. Our findings may address the reason for the difference between men and women in their urinary metabolites and obesity relationship.

The other noticeable finding was the association between many dietary urinary metabolites (sodium, potassium, and magnesium) and BMI in the men in our study. However, in the women, the only dietary factor which was correlated with obesity was urine volume. This finding suggests that the difference between men and women’s urinary contents and volume may be the result of the different dietary pattern and lifestyle. Further studies with concentration on dietary habits in both sexes are needed to evaluate this hypothesis.

Our findings revealed correlations between BMI and some specific urinary metabolites, while other urinary metabolites showed some association with abdominal obesity indexes, but not BMI. This emphasizes the difference between BMI and abdominal obesity indexes’ accuracy in interpreting the results of every study related to this field. Body mass index is an index to screen body weight status (underweight, normal weight, overweight, and obese). Although it is highly correlated with abdominal obesity, it is not an accurate measure of the body fatness. In contrast, WC and WSR are better correlated with body fatness. Since the correlation between urine metabolites and BMI means that the metabolites are correlated to the body weight, the correlation between urine metabolites and WC or WSR, but not BMI, reveals that urinary metabolites are mostly correlated with body fat rather than body weight.

No correlation was found between UASS and obesity in the men. In the women, however, WC was the only index that had correlation with UASS. Since WC was correlated with pH but not uric acid in the female participants, this correlation could be explained by the effect of WC on pH rather than uric acid. In favor of our results, Taylor and colleagues agreed that the effect of BMI on UASS is via the effect of lower pH rather than higher uric acid. The correlation between body size and urinary pH is suggested to be secondary to insulin resistance.

Although UASS and WC were correlated in the women, the odds of UASS abnormality were not increased by WC or other indexes. The previous reports regarding the correlation between UASS and obesity are scarce and controversial, and none of them studied the effect of abdominal obesity on UASS. Only a recent study by Pigna and coworkers reported that pH and UASS were correlated to visceral fat in male stone formers. Further studies in this field are warranted.

Citrate is another urinary metabolite which was previously reported to be inversely related to insulin resistance. On the other hand, estrogen increases the urinary citrate levels, and therefore, high urinary citrate levels in the men with high obesity indexes may be due to higher estrogen level in obese men. This finding is consistent with the results Negri and colleagues found in their research.

Another remarkable finding in our study was the correlation between the urinary calcium and BMI in the men. The OR of calcium abnormality was raised by increasing BMI; however, the model became nonsignificant after adjusting for dietary sodium and phosphorus. Although insulin resistance is proposed to be the basis for the correlation between body size and urinary calcium excretion, based on our results, the correlation seems to be due to dietary rather than metabolic effect of insulin resistance in our study.

Our study had strength and limitations which should be mentioned. Major strengths were measuring and applying various abdominal obesity indexes instead of using only BMI as a body fat index, using relative supersaturations, physician-measured anthropometric data, and examining obesity indexes as continuous variables to more accurately define the relationship between increasing body size and relative supersaturation. Limitations include cross-sectional design, lack of dietary intake data, and using dipstick rather due to lack of access to pH-meter for pH measurements.

CONCLUSIONS

Although both obesity and abdominal obesity are positively correlated with COSS mostly by changes in urine volume and pH in women, none of those indexes showed significant correlation with urine composition in men population of our study. Further studies in this context with dietary intake assessment are warranted.

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CONFLICTS OF INTEREST
None declared.

REFERENCES


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