The correlation between metabolic syndrome and lower urinary tract symptoms in females

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Aim: To evaluate the association between lower urinary tract symptoms (LUTS) and metabolic syndrome (MS) in women.

Materials and methods: A total of 155 women with LUTS were included in the study. LUTS were evaluated using the International Prostate Symptom Score (IPSS) and the Bristol Female Lower Urinary Tract Symptoms (BFLUTS) questionnaire. Besides total IPSS, voiding and storage IPSS were calculated separately. Diagnosis of MS was made according to the consensus report of the International Diabetes Foundation. The patients were classified into 3 groups: those without MS (group 1), those with 3 risk factors of MS (group 2), and those with more than 3 risk factors of MS (group 3). The groups were compared regarding IPSS and BFLUTS data.

Results: Of the patients, 37.4% (n = 58) had MS, while 62.6% (n = 97) did not. There were significant differences between group 1 and group 3 regarding BFLUTS-FS (filling symptoms), BFLUTS-QoL (quality of life), storage IPSS, and total IPSS. However, concerning BFLUTS-VS (voiding symptoms), BFLUTS-sex, and voiding IPSS, there was not any difference among the 3 groups.

Conclusion: The results of our study have shown that women with more than 3 MS components might have more storage symptoms than women without MS.

Key words: Female, lower urinary tract symptoms, metabolic syndrome

1. Introduction
Metabolic syndrome (MS) has a combination of risk factors that increase the risk of developing cardiovascular disease and type 2 diabetes (1–4). Those risk factors are glucose intolerance, atherogenic lipid profile, hypertension, and abdominal obesity (5–8). The prevalence of MS is increasing worldwide. MS is seen in 10% of persons with normal glucose tolerance, in 50% of those with abnormal glucose tolerance, in 50% of those with normal glucose tolerance, and in 80% of type 2 diabetics (9). For people over age 30, the prevalence of MS in Turkey is 27% for men and 38.6% for women (10).

Lower urinary tract symptoms (LUTS) represent a collection of symptoms associated with bladder filling (storage) and voiding. Storage symptoms include urgency, nocturia, and frequency; voiding symptoms consist of poor stream, hesitancy, terminal dribbling, and incomplete voiding (11). Age-related structural and functional changes in the lower urinary tract can cause LUTS in aging women (12). Nowadays, MS and its components are accepted as a major health problem, especially in modern societies (13). The syndrome has effects on all systems just as in the urinary tract (14). The increase observed in frequency and severity of the patients’ LUTS is thought to be related to MS components. Multiple studies demonstrated a strong independent association between LUTS and MS components in men (15,16). However, not as many studies investigated the same topic in women (17,18). In the present study, we aimed to evaluate the association between LUTS and MS in our female patients.

2. Materials and methods
Between January and July 2011, 155 women who applied to our outpatient urology clinic with LUTS were included in this study. Our urology clinic is a tertiary referral center located in the capital city of Turkey, Ankara. Patients with neurological disease, pelvic organ prolapse, previous pelvic surgery, and urinary tract infection were excluded from the study. Informed consent was obtained from each patient.
A detailed medical history was obtained initially and systemic diseases such as diabetes mellitus and hypertension were asked about in particular. LUTS were evaluated using Turkish validated versions of the International Prostate Symptom Score (IPSS) and the Bristol Female Lower Urinary Tract Symptoms Index Scored Form (BFLUTS-SF). For the IPSS, each symptom was graded from 0 (not at all) to 5 (always) by symptom frequency. Scores of these individual symptoms are aggregated to form a total symptom score range of 0 to 35. To discriminate between voiding and storage symptoms, the voiding IPSS (incomplete emptying, intermittency, weak stream, and straining) and the storage IPSS (frequency, urgency, and nocturia) were calculated separately besides the total IPSS. Nocturia was assessed as the number of times the patient arose at night to urinate after falling asleep. The BFLUTS-SF questionnaire comprises 3 subscales: filling symptoms (BFLUTS-FS), voiding symptoms (BFLUTS-VS), and incontinence symptoms (BFLUTS-IS), with the addition of single subscales for sexual function (BFLUTS-sex) and quality of life (BFLUTS-QoL). Blood pressures, body weights, body heights, and waist circumferences of all patients were measured. Body mass index (BMI) was calculated as body weight divided by the square of body height. Blood tests including serum glucose, triglyceride, high-density lipoprotein cholesterol (HDL-C), and insulin were performed. Blood samples were collected from the patients after one night of fasting. Fasting serum insulin levels were measured using the radioimmunoassay method (MP Biomedical and Diagnostics, San Diego, CA, USA). Metabolic syndrome diagnosis was made according to the consensus report of the International Diabetes Foundation (IDF) (19). According to IDF 2005 criteria of MS, central obesity was defined by waist circumference of women of >80 cm and 2 of the 4 factors mentioned in the IDF 2005 criteria (triglyceride > 150 mg/dL, HDL-C < 50 mg/dL, blood pressure > 130/80 mmHg, and fasting blood sugar > 100 mg/dL).

The results were given as means ± standard deviations. Two groups were compared using Student’s t-test. Multiple comparisons were performed by one-way ANOVA and Tukey tests. P-values lower than 0.05 were considered significant.

3. Results
Of the 155 patients, 24.2% (n = 58) had MS, while 75.8% (n = 97) did not. Furthermore, 55% of patients with MS had 3 components and 45% had more than 3. Mean age, waist circumference, BMI, fasting blood glucose, triglyceride, filling IPSS, and 3 subscales of BFLUTS (FS, IS, QoL) of patients with MS were significantly higher than those of patients without MS. However, mean serum HDL-C level of patients with metabolic syndrome was significantly lower than in patients without MS. Mean serum insulin level, voiding IPSS, and the other subscales of BFLUTS (VS, sex) were not significantly different between the patients with and without MS (Table 1).

Table 1. The clinical and laboratory data of women in 2 groups.

<table>
<thead>
<tr>
<th></th>
<th>Non-MS group (n = 97)</th>
<th>MS group (n = 58)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>42.01 ± 12.1</td>
<td>50.6 ± 11.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>BFLUTS-FS</td>
<td>6.72 ± 3.8</td>
<td>8.4 ± 3.6</td>
<td>0.006</td>
</tr>
<tr>
<td>BFLUTS-VS</td>
<td>2.71 ± 2.5</td>
<td>2.8 ± 2.9</td>
<td>0.86</td>
</tr>
<tr>
<td>BFLUTS-IS</td>
<td>3.9 ± 3.7</td>
<td>6.5 ± 5.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>BFLUTS-sex</td>
<td>0.6 ± 1.04</td>
<td>0.8 ± 1.3</td>
<td>0.23</td>
</tr>
<tr>
<td>BFLUTS-QoL</td>
<td>4.8 ± 4.3</td>
<td>6.8 ± 5.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Voiding IPSS</td>
<td>3.8 ± 4.6</td>
<td>4.8 ± 5.6</td>
<td>0.25</td>
</tr>
<tr>
<td>Storage IPSS</td>
<td>5.1 ± 3.8</td>
<td>6.9 ± 4.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Total IPSS</td>
<td>8.9 ± 7.3</td>
<td>11.7 ± 9.1</td>
<td>0.03</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.8 ± 4.1</td>
<td>30.5 ± 4.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>91.9 ± 19.9</td>
<td>110.0 ± 16.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>85.2 ± 16.6</td>
<td>117.5 ± 44.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>48.1 ± 10.8</td>
<td>39.9 ± 8.6</td>
<td>0.0001</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>102.6 ± 54.0</td>
<td>167.9 ± 88.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>Insulin (µIU/mL)</td>
<td>9.6 ± 8.3</td>
<td>13.3 ± 13.0</td>
<td>0.053</td>
</tr>
</tbody>
</table>

* Student’s t-test
The patients were then classified into 3 groups: those without MS (group 1), those with 3 risk factors of MS (group 2), and those with more than 3 risk factors of MS (group 3). The groups were compared regarding the 5 subscales of BFLUTS, voiding, filling, and total IPSS. There was a significant difference between group 1 and group 3 in regard to BFLUTS-FS, BFLUTS-QoL, filling IPSS, and total IPSS, while there was not between group 1 and group 2 or between group 2 and group 3. There were significant differences between group 1 and group 2 and between group 1 and group 3 in regard to BFLUTS-IS, while there was not between group 2 and group 3. However, in regard to BFLUTS-VS, BFLUTS-sex, and voiding IPSS, there was not any difference among the 3 groups (Table 2).

4. Discussion
A growing number of recent studies have underscored the association between LUTS and MS components in males (15,16,20,21). In a study including 158 patients with LUTS secondary to benign prostatic hyperplasia, Hammerstein et al. found that patients with the components of MS had bigger prostates than those without, and the annual increase in prostate volumes was also higher. In addition, annual prostate volume increase was positively correlated with obesity, fasting insulin levels, and systolic blood pressure, and negatively correlated with HDL-C levels (22). Kupelian et al. supported the presence of a link between MS and LUTS. In the Boston Area Community Health study, they reported that MS was associated with symptoms of voiding rather than filling (23).

The prevalence of LUTS is getting higher in women. In the longitudinal report of Wennberg et al., a marked increase was observed in LUTS of women over a period of 16 years (24). Results of the EPIC study were parallel with theirs and demonstrated that LUTS were prevalent in both men and women, with storage LUTS being more prevalent than voiding (25).

Tai et al. evaluated the effect of MS components on LUTS in their study with 850 type 2 diabetic women (17). They detected moderate to severe LUTS in 36.7% of patients and the increase in both total and storage symptom scores was greater than that of voiding in patients with MS compared to those without. Finally they concluded that the increase in symptom scores of patients with 4 or 5 components of MS was significant. Similarly, in our study, storage IPSS and BFLUTS-FS of patients with LUTS and more than 3 components of MS were significantly higher than in both the patients with 3 or fewer MS components and those without MS. In another recent study, MS correlated highly with overactive bladder in female patients (26). In the study of Hong et al., significant differences were observed in LUTS depending on the presence or absence of MS in females, but not in males. The authors underscored the sex differences in the morbidity rate of MS and its effect on LUTS (27).

### Table 2. BFLUTS and IPSS data of women in 3 groups.

<table>
<thead>
<tr>
<th></th>
<th>Non-MS (group 1) (n = 97)</th>
<th>MS 3 risk factors (group 2) (n = 32)</th>
<th>MS &gt;3 risk factors (group 3) (n = 26)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BFLUTS-FS</td>
<td>6.72 ± 3.8</td>
<td>8.1 ± 3.5</td>
<td>8.8 ± 3.8</td>
<td>0.02</td>
</tr>
<tr>
<td>BFLUTS-VS</td>
<td>2.71 ± 2.5</td>
<td>2.6 ± 3.0</td>
<td>3.0 ± 2.8</td>
<td>0.80</td>
</tr>
<tr>
<td>BFLUTS-IS</td>
<td>3.9 ± 3.7</td>
<td>6.3 ± 5.6</td>
<td>6.7 ± 6.1</td>
<td>0.002</td>
</tr>
<tr>
<td>BFLUTS-sex</td>
<td>0.6 ± 1.04</td>
<td>0.7 ± 1.0</td>
<td>1.0 ± 1.5</td>
<td>0.26</td>
</tr>
<tr>
<td>BFLUTS-QoL</td>
<td>4.8 ± 4.3</td>
<td>6.4 ± 5.1</td>
<td>7.3 ± 5.6</td>
<td>0.03</td>
</tr>
<tr>
<td>Voiding IPSS</td>
<td>3.8 ± 4.6</td>
<td>3.8 ± 5.4</td>
<td>6.1 ± 5.8</td>
<td>0.11</td>
</tr>
<tr>
<td>Storage IPSS</td>
<td>5.1 ± 3.8</td>
<td>5.8 ± 4.1</td>
<td>8.2 ± 5.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Total IPSS</td>
<td>8.9 ± 7.3</td>
<td>9.6 ± 8.3</td>
<td>14.3 ± 9.5</td>
<td>0.009</td>
</tr>
</tbody>
</table>

* One-way ANOVA
  1 Significant difference between groups 1 and 3 (P = 0.03, Tukey test).
  2 Significant differences between groups 1 and 2 and between groups 1 and 3 (P = 0.024 and P = 0.012, respectively, Tukey test).
  3 Significant difference between groups 1 and 3 (P = 0.045, Tukey test).
  4 Significant difference between groups 1 and 3 (P = 0.002, Tukey test).
  5 Significant difference between groups 1 and 3 (P = 0.006, Tukey test).
MS components have been thought to cause and increase storage and voiding symptoms both in men and women as a result of several pathophysiological pathways. One of the possible pathophysiological pathways associated with MS components is structural and functional bladder disorder caused by chronic bladder ischemia secondary to microvascular atherosclerosis (17,28). Bladder overactivity, fibrosis, neuropathy, and decreased bladder compliance as a result of arterial insufficiency were shown in rabbit models (29). In addition, long-term hyperglycemia-induced damage and viability reduction in parasympathetic pelvic ganglion neurons are the other possible mechanisms. Animal studies also supported that hypothesis; elevated serum glucose levels increased neuronal apoptosis in parasym pathetic neurons more than in sympathetic pairs (30,31). This unbalanced loss in autonomic neurons leads to sympathetic overactivity, and thus voiding symptoms secondary to bladder neck obstruction and decreased bladder contractility might develop. All these studies emphasize the association between MS components and LUTS.

The results of our study have shown that women with more than 3 MS components might have more storage symptoms than women without MS. Our results and their underlying mechanisms need to be supported by future studies with larger patient population.

References


