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Association between lower urinary tract symptoms and polycystic ovary syndrome

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SUMMARY

OBJECTIVE: The aim of this study was to analyze the association between lower urinary tract symptoms and polycystic ovary syndrome.

METHODS: A total of 180 women were enrolled in this prospective study. Demographic data, body mass index, waist circumference, modified Ferriman–Gallwey scores, biochemical parameters, ultrasonographic findings, and maximum urinary flow rate (Q max) were analyzed. In addition, the Beck Depression Inventory, Beck Anxiety Inventory, and Bristol Female Lower Urinary Tract Symptom Scored Form questionnaires were evaluated for each subject.

RESULTS: The mean age of patients was calculated as 23.78±3.04 years, which was similar for both groups (p=0.340). Body mass index, waist circumference, Beck Depression Inventory, Beck Anxiety Inventory, Bristol Female Lower Urinary Tract Symptom Scored Form, and modified Ferriman–Gallwey scores were significantly higher in group 2 (p<<0.001). Hyperandrogenism, lipid profile, and glucose metabolism disorders were more frequent in group 2 (p<<0.05). Bladder capacity (Q max), bladder wall thickness, and post-void residual volume values were similar in both groups (p>>0.05).

CONCLUSION: In our study, a close relationship was observed between polycystic ovary syndrome and lower urinary tract symptoms. In this context, we think that a detailed urinary system evaluation of women with polycystic ovary syndrome is extremely important.

KEYWORDS: Lower urinary tract symptoms. Women. Polycystic ovary syndrome.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is an endocrinological disorder that occurs in women of reproductive age[1]. Approximately 6–20% of women in this period are affected. Two-thirds of the criteria for oligomenorrhea or amenorrhea, clinical or biochemical signs of hyperandrogenism, and polycystic ovarian morphology, known as the Rotterdam consensus, are considered diagnostic[2]. Today, PCOS syndrome is one of the most complex health problems that require intense attention by healthcare professionals due to its multifactorial etiopathogenesis and progression and its consequences in different medical disciplines[3].

Clinical analyses have shown that PCOS is closely associated with various organic pathologies such as impaired glucose tolerance, hyperinsulinemia, insulin resistance, dyslipidemia, hyperandrogenism, and obesity. Given the high prevalence and multisystemic impact of PCOS, the importance of multidisciplinary treatment modalities has recently been increasingly recognized[4].

Lower urinary tract symptoms (LUTS) are characterized by three main symptoms[1]: storage symptoms, such as urgency, frequency, nocturia, and urge incontinence[2]; voiding symptoms, such as poor and/or intermittent stream; and[3] post-voiding symptoms, such as the feeling of incomplete emptying[5]. LUTS exceeds the critical threshold, quality of life is impaired, level of physical activity is decreased, and psychological condition is negatively affected[6]. Large-scale epidemiological studies have reported that, on average, 84% of women suffer from at least one of the lower urinary tract symptoms in their lifetime[7].

PCOS leads to several psychogenic, physical, and metabolic problems and thus affects the dynamics of many different systems. Urinary system dynamics are affected quite seriously by psychogenic and organic factors. To have a healthy voiding physiology, it is critical that physical and mental health be within normal limits. This study aimed to thoroughly analyze the association between PCOS and LUTS through a multi-dimensional evaluation of organic and psychological factors.

METHODS

A total of 90 patients of reproductive age who were diagnosed with PCOS for the first time were enrolled at Tokat Gaziosmanpaşa University, Medical School, and the same number of healthy

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volunteers were included in the study. Prior to this prospective study, approval was obtained from the local ethics committee of our hospital (date: 13.08.2020/Tokat Gaziosmanpasa University approval number: 20-KAEK-216).

The diagnosis of PCOS was made in the presence of clinical or biochemical hyperandrogenism, anovulation or oligomenorrhea, the polycystic appearance of the ovaries on ultrasound, and at least 2 of these 3 major criteria. Healthy volunteers were identified as group 1 and women with PCOS as group 2. A detailed history was obtained from all patients, and a physical examination was performed. Body mass index (BMI) was calculated for each patient after measuring weight and height. Patients with a BMI of 30 kg/m^2 or more were classified as obese. In addition, waist circumference was calculated. Accordingly, a waist circumference of 88 cm and above were classified as high risk. Hirsutism is assessed with the modified Ferriman–Gallwey score (mFG)[1]. The extent of lower urinary tract symptoms in each case included in the study was analyzed using the Bristol Female Lower Urinary Tract Symptom (BFLUTS) questionnaire. After several studies with large series, the use of BFLUTS with 34 questions was replaced by BFLUTS-SF (scoring form) with 19 questions, which is an easy-to-use form that provides clearly measurable results for clinicians with better reproducibility. This scoring system includes 5 categories. BFLUTS-SF includes 4 questions defining filling symptoms (BFLUTS-FS), 3 questions defining voiding symptoms (BFLUTS-VS), 5 questions about signs of incontinence (BFLUTS-IS), 2 questions analyzing sexual function (BFLUTS-sex), and finally, 5 questions assessing the quality of life of those affected (BFLUTS-QoL)[8,9]. Because sexual dysfunction was not examined in this study, BFLUTS sex was not considered. In this regard, the BFLUTS-SF was reliably used in our study by excluding 2 questions analyzing sexual functioning. The distribution of responses among cases in the PCOS and control groups was statistically compared. In addition, the Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI) were applied to the patients in both groups to better assess the psychological state of the patients[10].

Hormone analysis determined the levels of dehydroepiandrosterone sulfate (DHEA-S), LH, FSH, prolactin, and estradiol. As for the lipid profile, triglyceride, LDL, and HDL levels were measured. The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) score was used to monitor glucose metabolism. Bladder ultrasonography was also performed in all patients to determine bladder capacity, residual urine volume after urination (PVR), and bladder wall thickness (BWT). The patients' maximum urinary flow rate (Q max) was also measured by a uroflowmetry test.

Diagnosis of PCOS based on the 2003 Rotterdam ESHRE/ASRM consensus criteria. Detailed medical history research was done on healthy volunteers. Only nulliparous women aged 18–49 years with no history of pelvic surgery were included in this study. In addition, patients diagnosed with a neurological or endocrine disease or metabolic disorder, patients taking medications for chronic diseases, patients with cancers of the genitourinary system, and patients with urinary tract infections were excluded from the study.

Statistical analysis of data was performed with the SPSS program (version: 22.0, SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented with median (minimum–maximum) and mean±standard deviation (SD) as a function of the normality distribution of the data for numeric variables. Descriptive statistics for categorical variables were presented as numbers and percentages (%). Testing of the normality distribution of the data for the selection of statistical tests was performed using the Kolmogorov–Smirnov test. The Mann–Whitney U test was used to compare numerical measurements between two independent research groups. Power analysis was performed to select the sample size, and it was decided to take a total of 90+90 patients for 5% error and 90% power.

RESULTS

The mean age of the patients was reported as 23.78±3.04 years, which was similar for both groups (p=0.340). A total of 33 (18.3%) patients were obese, and 41 (22.8%) had a high waist circumference. The mean BMI of patients in group 2 was calculated at 27.9±7.26 kg/m^2, and their waist circumference was 87.67±9.73 cm. These values were significantly higher compared to group 1 (p<<0.001). A total of 6 (3.3%) subjects had severe hirsutism. The mean mFG score in group 2 was 16.12±5.79, which was significantly higher than in group 1 (p<0.001). The BDI and BAI scores of patients in group 2 were 16.5±9.48 and 16.48±9.59, respectively. The psychological condition of the patients in group 2 was negatively affected based on these scoring systems (p<0.001).

A total of 42 (23.3%) subjects had impaired glucose metabolism. While only 8 (4.4%) cases in group 1 had impaired glucose metabolism, the mean HOMA-IR score was calculated to be 1.58±0.78. This score was significantly lower compared to group 2 (p<0.001). Also, abnormalities in lipid profile were more frequent in group 2 (for triglyceride, p< 0.001; for LDL, p=0.036; for HDL, p=0.021). The levels of DHEA-S and LH were significantly higher in patients in group 2 compared to those in group 1 (p<<0.001 and p=0.039, respectively). There was no statistically significant difference between groups in FSH, prolactin, and estradiol levels (p>0.05).

The mean BFLUTS-SF total scores of groups 1 and 2 were 15.59±11.06 and 27.78±14.18, respectively, except for the analysis of sexual function. The scores were significantly higher in group 2 (p<<0.001). Similarly, all categories of this scoring system for the analysis of filling, voiding, incontinence, and quality of life were significantly higher in patients in group 2 (p<0.001) (Figure 1). In addition, no significant difference was found between groups in bladder capacity, BWT, PVR, and Q max (p>0.05) (Table 1).

Correlation analysis was used for the cases in group 2. A high level of significant positive correlation was found between BMI, waist circumference, and BFLUTS-SF parameters; a moderate level of positive correlation was found between the mFG scores and BFLUTS-SF parameters. Similarly, a high level of significant positive correlation was found between the BDI and BAI scores and the BFLUTS-SF parameters. On the contrary, moderate and high levels of positive correlation were significantly found between HOMA-IR, DHEA-S, and the BFLUTS-SF parameters; a moderate level of positive correlation was significantly found between triglyceride levels and the BFLUTS-SF parameters. While weak and moderate levels of negative correlation were significantly found between the HDL levels and the BFLUTS-SF parameters, weak and moderate levels of positive correlation were found in terms of the LDL levels (Table 2).

DISCUSSION

Clinical findings vary according to age groups in PCOS cases. Patients often present with ovulation problems such as menstrual irregularities or infertility. Other clinical implications include endothelial damage, obesity, insulin resistance, and hyperandrogenism, which are closely associated with inflammatory processes in the pathogenetic pathways of PCOS[1]. For healthy maintenance of voiding physiology, anatomic factors must be in perfect harmony with neuroendocrine pathways. When this dynamic is disrupted in any way, LUTS occur. Inflammatory responses and metabolic effects of these processes lead to some consequences for the dynamics of the lower urinary system in PCOS[11-13]. This situation has a significant negative impact on the quality of life of patients with PCOS. Nevertheless, to our knowledge, there are few studies on this topic in the literature. Our study addresses the different aspects of the changes that occur in the bladder dynamics of patients with PCOS.

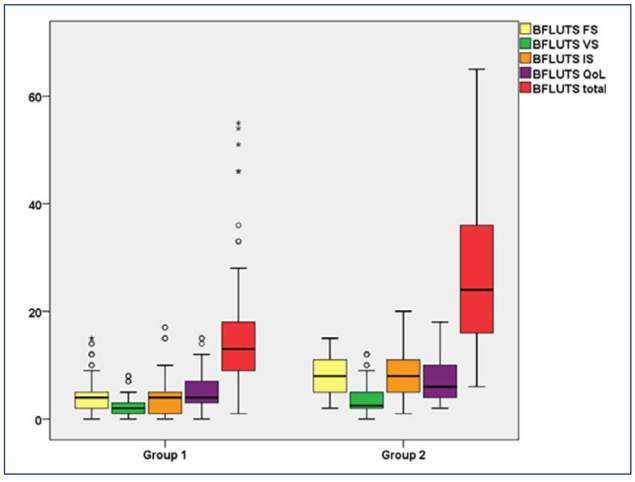

Figure 1. Distribution of voiding symptom scores between research groups.

Studies have shown that hyperandrogenism is present in more than 80% of PCOS cases. Recent studies emphasize both the microscopic and clinical implications of changes in androgen hormone levels on the urinary system. In an experimental study, Çayan et al.[14] examined rats undergoing oophorectomy. They reported that androgen and estrogen deprivation decreased bladder capacity and compliance, and function improved after hormone therapy. In a similar study, Tek et al.[15] assessed the effects of testosterone therapy on bladder functions in orchidectomized rats, reporting an elevation in bladder capacity and smooth muscle/collagen content following testosterone therapy. Antonio et al.[16] reported that pelvic floor muscle strength was evaluated in a clinical study of 79 patients diagnosed with 36 PCOS. They reported that although pelvic floor muscle strength was higher in patients with PCOS, these values did not present a statistically significant correlation. Yet, the urinary incontinence ratio was recorded at a statistically significant high level in PCOS cases. In another study, Sahinkanat et al.[11] reported a correlation between bladder symptoms, such as pelvic pain, nocturia, or urinary urgency, and testosterone levels in women with PCOS. However, in the same study, no statistical correlation was found between ultrasonographic findings such as bladder capacity, PVR, and testosterone level. Similarly, our study also showed an increase in the frequency of LUTS with elevated testosterone levels. On the contrary, no significant difference was found in Qmax, PVR, bladder capacity, and BWT.

The prevalence of obesity in PCOS is approximately 30–70%, which is quite high compared to the normal population[17]. Obesity leads to the formation of oxidative stress in the urethral mucosa, a reduction in the amount of collagen, and a loss of urethral elasticity[18]. Any increase in intra-abdominal pressure, in addition to these histopathologic changes, leads to an increase in lower urinary system symptoms in obese patients[12]. In a large series by Lai et al.,[19] researchers examined lower urinary system symptoms in subjects and found a direct relationship between obesity and overactive bladder, frequency, urinary incontinence, and stress incontinence. Our study showed a higher prevalence of obesity in patients with PCOS compared with the control

Table 1. Comparison of demographic data, modified Ferriman–Gallwey, Beck Depression Inventory, Beck Anxiety Inventory, of Bristol Female Lower Urinary Tract Symptom Scored Form values, bladder measurements, uroflowmetry test scores, and biochemical parameters between groups.

	Group 1 (n=90) Median (min–max) (Mean±SD)	Group 2 (n=90) Median (min–max) (Mean±SD)	p-value
Age (year)	23 (19–33) (23.5±2.78)	23.5 (19–34) (24±3.28)	0.340
BMI (kg/m^2)	22 (16–35) (23.4±3.68)	25 (16–45) (27.9±7.26)	**<0.001***
Waist circumference (cm)	77.5 (57–99) (76.06±10.87)	86.5 (60–106) (87.67±9.73)	**<0.001***
mFG score	7 (1–25) (7.96±5.72)	19 (7–28) (16.12±5.79)	**<0.001***
BDI	9 (1–30) (8.97±5.19)	15 (2–39) (16.5±9.48)	**<0.001***
BAI	7 (1–30) (7.94±4.79)	17 (1–39) (16.48±9.59)	**<0.001***
BFLUTS-FS	4 (0–15) (4.39±3.18)	8 (2–15) (8.76±3.41)	**<0.001***
BFLUTS-VS	2 (0–8) (2.11±2.03)	2.5 (0-12) (3.63±2.78)	**<0.001***
BFLUTS-IS	4 (0–17) (4.12±3.86)	8 (1–20) (7.98±4.14)	**<0.001***
BFLUTS-QoL	4 (0–15) (4.97±3.48)	6 (2–18) (7.41±4.12)	**<0.001***
BFLUTS-SF total	13 (1–55) (15.59±11.06)	24 (6–65) (27.78±14.18)	**<0.001***
Bladder capacity (cc)	400 (300–670) (410.6±71.7)	400 (300–750) (402.9±69.7)	0.313
PVR (cc)	10 (0–65) (14.67±16.9)	10 (0–60) (16.47±16.2)	0.198
Q max (mL/s)	31 (15–40) (29.8±5.99)	30 (14–40) (28.9±6.2)	0.157
BWT (mm)	2 (0.3–7.1) (2.59±1.31)	2.3 (0.4–7.1) (2.71±1.4)	0.556
FSH (mIU/mL)	3.8 (2–7) (3.87±0.97)	4 (2–8) (4.46±1.5)	0.064
LH (mIU/mL)	6.1 (1.9–9) (6.22±1.25)	7 (2.1–10) (7±2.14)	**0.039***
LH/FSH	1.45 (0.51–2.57) (1.46±0.44)	1.75 (0.57–3.3) (1.7±0.69)	**0.044***
HOMA-IR	1.5 (0.5–3.9) (1.58±0.78)	2.5 (0.5–4.4) (2.31±1.13)	**<0.001***
Prolactin (mIU/L)	17.5 (4–35) (17.5±5.29)	20 (4–45) (20.8±6.99)	0.089
DHEA-S (mg/Dl)	161 (65–500) (176.9±109.6)	302.5 (80–640) (289.3±159.6)	**<0.001***
Estradiol (pg/Ml)	56.5 (30–130) (66.2±28.6)	60 (27.8–149) (71.4±37.8)	0.132
Triglyceride (mg/dL)	123 (60–285) (131.3±51.5)	157.7 (70–360) (178.8±79.5)	**<0.001***
HDL (mg/dL)	41 (21–78) (42.1±10.7)	35 (21–72) (36±9.37)	**0.021***
LDL (mg/dL)	132 (80–192) (131.1±26.9)	145 (70–200) (146.8±28.5)	**0.036***

Data are presented as mean±minimum–maximum numbers and as mean±standard deviation. Mann–Whitney U test was used. BMİ: body mass index; mFG: modified Ferriman–Gallwey; BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; BFLUTS-FS: Bristol Female Lower Urinary Tract Symptom-Filling Symptoms; BFLUTS-VS: Bristol Female Lower Urinary Tract Symptom-Voiding Symptoms; BFLUTS-IS: Bristol Female Lower Urinary Tract Symptom- Incontinence Symptoms; BFLUTS-QoL: Bristol Female Lower Urinary Tract Symptom- Quality of Life; BFLUTS-SF: Bristol Female Lower Urinary Tract Symptom- Scored Form; PVR: Post-void residual volume; Q max: Maximum urinary flow rate; BWT: Bladder wall thickness; FSH: Follicle Stimulating Hormone; LH: Luteinizing Hormone; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; DHEA-S: Dehydroepiandrosterone Sulfate; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein. *Bold values indicate statistically significant (p<0.05).

group. On the contrary, lower urinary symptoms were found to be directly related to increased waist circumference and BMI in patients with PCOS.

Broad meta-analyses have found that metabolic syndrome is 3.35 times more common in PCOS[19]. Metabolic disorders have a significant impact on bladder dynamics. Lee et al.[20]

Table 2. Correlation analysis results between age, body mass index, waist circumference, Ferriman–Gallwey Score, Beck Depression Inventory, Beck Anxiety Inventory, voiding symptom scores, bladder measurements, and biochemical parameters for group 2 (n=90).

		BFLUTS FS	BFLUTS VS	BFLUTS IS	BFLUTS QoL	BFLUTS SF Total	Bladder Capacity	PVR	Qmax	BWT
Age	r	-0.273	-0.176	-0.266	-0.152	-0.244	0.157	-0.217	-0.096	-0.208
	p	0.116	0.208	0.121	0.199	0.137	0.114	0.093	0.274	0.102
BMI	r	0.742*	0.708*	0.723*	0.710*	0.733*	-0.294*	0.457*	0.123	0.220*
	p	<0.001	<0.001	<0.001	<0.001	<0.001	0.003	<0.001	0.248	0.037
WC	r	0.739*	0.703*	0.725*	0.707*	0.731*	-0.299*	0.437*	0.116	0.214*
	p	<0.001	<0.001	<0.001	<0.001	<0.001	0.002	<0.001	0.278	0.043
FG Score	r	0.575*	0.550*	0.582*	0.508*	0.589*	-0.258*	0.424*	0.137	0.261*
	p	<0.001	<0.001	<0.001	<0.001	<0.001	0.014	<0.001	0.199	0.013
BDI	r	0.740*	0.711*	0.728*	0.700*	0.730*	-0.293*	0.450*	0.103	0.226*
	p	<0.001	<0.001	<0.001	<0.001	<0.001	0.003	<0.001	0.332	0.033
BAI	r	0.727*	0.703*	0.714*	0.702*	0.715*	-0.288*	0.430*	0.094	0.215*
	p	<0.001	<0.001	<0.001	<0.001	<0.001	0.006	<0.001	0.380	0.042
FSH	r	0.040	0.062	0.009	0.004	0.016	0.285*	-0.177	0.205	-0.026
	p	0.707	0.559	0.936	0.972	0.884	0.007	0.096	0.053	0.806
LH	r	-0.070	-0.065	-0.043	-0.033	-0.073	0.186	0.092	-0.113	-0.179
	p	0.509	0.543	0.687	0.756	0.492	0.079	0.389	0.290	0.092
LH/ FSH	r	-0.019	-0.029	0.029	0.051	0.004	-0.081	0.242*	-0.270*	-0.125
	p	0.861	0.784	0.786	0.631	0.970	0.448	0.021	0.010	0.240
HOMA-IR	r	0.719*	0.712*	0.738*	0.675*	0.705*	-0.297*	0.416*	0.062	0.183
	p	<0.001	<0.001	<0.001	<0.001	<0.001	0.004	<0.001	0.561	0.084
Prolactin	r	-0.224	-0.168	-0.196	-0.130	-0.195	-0.007	-0.289	0.250	-0.058
	p	0.054	0.114	0.064	0.221	0.066	0.950	0.053	0.060	0.585
DHEA-S	r	0.736*	0.691*	0.680*	0.738*	0.702*	-0.301*	0.459*	0.122	0.234*
	p	<0.001	<0.001	<0.001	<0.001	<0.001	0.004	<0.001	0.251	.026
Estradiol	r	0.178	0.244	0.269	0.152	0.175	-0.125	0.251*	0.112	0.122
	p	0.107	0.096	0.063	0.216	0.106	0.062	0.031	0.294	0.095
Triglyceride	r	0.667*	0.601*	0.648*	0.655*	0.641*	-0.210	0.257*	0.102	0.130
	p	<0.001	<0.001	<0.001	<0.001	<0.001	.057	0.022	.337	.223
HDL	r	-0.607*	-0.493*	-0.601*	-0.470*	-0.584*	0.210*	-0.198	0.111	-0.054
	p	<0.001	<0.001	<0.001	<0.001	<0.001	0.021	0.079	0.296	0.612
LDL	r	0.587*	0.494*	0.536*	0.569*	0.545*	-0.156	0.235*	-0.110	0.013
	p	<0.001	<0.001	<0.001	<0.001	<0.001	0.055	0.041	0.303	0.902

*Statistically significant (Spearman's correlation coefficient: p<0.05). WC: Waist circumference; mFG: modified Ferriman–Gallwey; BMI: body mass index; BDI: Beck Depression Inventory; BAI: Beck Anxiety Inventory; BFLUTS-FS: Bristol Female Lower Urinary Tract Symptom-Filling Symptoms; BFLUTS-VS: Bristol Female Lower Urinary Tract Symptom-Voiding Symptoms; BFLUTS-IS: Bristol Female Lower Urinary Tract Symptom- Incontinence Symptoms; BFLUTS-QoL: Bristol Female Lower Urinary Tract Symptom- Quality of Life; BFLUTS-SF: Bristol Female Lower Urinary Tract Symptom- Scored Form; PVR: Post-void residual volume; Q max: Maximum urinary flow rate; BWT: Bladder wall thickness; FSH: Follicle Stimulating Hormone; LH: Luteinizing Hormone; HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; DHEA-S: Dehydroepiandrosterone Sulfate; HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein.

reported bladder dysfunction in their study on experimental animals after the creation of metabolic syndrome. The same study indicated injury in bladder smooth muscle mitochondria, the elevation of interstitial tissue leukocytes, and intense neutrophil infiltration around the endothelium. In a similar study, Tong et al.[21] highlighted the presence of findings indicating detrusor overactivity in 62.5% of rats exposed to metabolic syndrome. In our study, insulin resistance and dyslipidemia were detected commonly in women with PCOS. Besides, it was concluded that such metabolic disorders are associated with the severity of LUTS.

Psychogenic problems are also quite common in women with PCOS. Previous comprehensive studies indicate a depression rate of 28–64% in patients with PCOS. On the contrary, anxiety disorders are significantly more common in PCOS (34–57%) than in the general population[22]. In a series of 100 women followed for at least 6 months, Heidari et al.[23] concluded that there was a direct association between depressive disorders and irritability symptoms, obstructive symptoms, and urodynamic test results. However, in the same study, no association was found between obsessive-compulsive disorder and LUTS. Our study concludes that anxiety and depression scales are severely impaired in women with PCOS. The study also suggests that depression and anxiety scale scores correlate with LTUS severity.

The main limitations of our study were the performance of the analyses in a single center, the limited number of cases in a similar geography, the impossibility to assess sexual function, and the inability to perform an invasive urodynamic examination. On the contrary, although PCOS is a very common pathology, the urinary system dynamics of this patient group are mostly ignored by health professionals. In this prospective study, we believe that associating PCOS with urinary system dynamics will make important contributions to the medical literature.

CONCLUSION

According to the results of our study, a strong association was found between PCOS and LUTS. Moreover, an association was found between the severity of LUTS and the psychological problems observed in patients with PCOS, hyperandrogenism, obesity, impaired glucose, and lipid profile.

AUTHORS' CONTRIBUTIONS

EK: Conceptualization, Data curation, Formal Analysis, Investigation, Resources, Writing – original draft, Writing – review & editing. **SG:** Conceptualization, Data curation, Formal Analysis, Writing – original draft, **FE:** Writing – original draft, Writing – review & editing.

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