Original Article

Menorrhagia and Uterine Volume Associated with Lower Urinary Tract Symptoms in Patients with Adenomyosis

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Abstract

Background: Adenomyosis is a gynecological disorder with symptoms most presenting as dysmenorrhea and heavy menstrual bleeding. However, the presence of lower urinary tract symptoms (LUTS) among women with adenomyosis remains unclear. This study was designed to determine the prevalence of LUTS and factors related to the severity of these symptoms in this population.

Methods: From July 2016 to November 2016, a total of 298 untreated symptomatic adenomyosis patients and 280 age-matched controls were enrolled. Demographics, LUTS, pain symptoms, ultrasonographic uterine size, and serum CA125 level were recorded. LUTS were evaluated using the International Prostate Symptom Score (IPSS) questionnaire. Factors related to the severity of LUTS were detected using the logistic regression analysis presented as odds ratio (*OR*) and 95% confidence interval (*CI*).

Results: Compared with the control group, patients with adenomyosis had a greater IPSS total (4 [2–8] vs. 2 [0–3], $Z = -8.159$, $P < 0.001$), IPSS storage (2 [1–4] vs. 1[0–2], $Z = -7.361$ $P < 0.001$), and IPSS voiding (2 [0–4] vs. 0 [0–1], $Z = -7.194$, $P < 0.001$). Of the patients with adenomyosis, 30.2% had moderate-to-severe lower urinary tract symptoms (IPSS ≥8). The most prevalent LUTS were daytime frequency (40.9%), followed by nocturia (24.8%), weak stream (24.2%), and incomplete emptying (23.5%). In study group, patients with an IPSS total score ≥8 had higher proportion of menorrhagia (51.1% vs. 30.8%, $\chi^2 = 11.162$ $P = 0.025$) and larger uterine volumes (183.3 [109.8–273.8] cm^3 vs. 148.5 [96.4–262.7] cm^3, $Z = -1.441$, $P = 0.150$) compared to patients with an IPSS total score <8. On multivariate logistic regression analysis, patients with menorrhagia were associated with an increased risk of an IPSS total score ≥8 (*OR*: 2.309, 95% *CI*: 1.310–4.070, $P = 0.004$), an IPSS storage subscore ≥4 (*OR*: 2.422, 95% *CI*: 1.395–4.206, $P = 0.002$), and an IPSS voiding subscore ≥5 (*OR*: 1.971, 95% *CI*: 1.176–3.302, $P = 0.010$). However, patients with uterine volume more than 180 cm^3 had more than 2-fold risk of bearing IPSS total score ≥8 (*OR*: 2.437, 95% *CI*: 1.381–4.300, $P = 0.002$), IPSS storage subscore ≥4 (*OR*: 2.486, 95% *CI*: 1.433–4.314, $P = 0.001$), and IPSS voiding subscore ≥5 (*OR*: 2.700, 95% *CI*: 1.485–4.908, $P = 0.001$).

Conclusions: Lower urinary tract symptoms are prevalent in patients with symptomatic adenomyosis and greatly affect patients' quality of life. Menorrhagia and large uterine volume could be potential risk factors that increase the occurrence of moderate-to-severe LUTS.

Key words: Adenomyosis; International Prostate Symptom Score; Lower Urinary Tract Symptoms

Introduction

Adenomyosis is a gynecological disorder characterized by the benign invasion of endometrial glands and stroma into the myometrium causing uterine enlargement and asymmetric thickening of anterior and posterior myometrial walls.[1] The prevalence of adenomyosis is estimated 20–35%.[2-4] Broadly speaking, abnormal uterine bleeding, pelvic pain, and infertility are its three main symptoms that women with adenomyosis often present with and these seriously affect patients' quality of life (QOL). Conventionally, the diagnosis of adenomyosis is based on clinical findings and pathologic confirmation after hysterectomy. However, transvaginal sonography (TVS) and magnetic resonance imaging (MRI) have been shown to be accurate, noninvasive methods for detection.[5] Treatment options vary according to different symptoms and fall into the following categories: medical

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treatments, surgical procedures, radiologic or sonographic interventions, or combinations of these choices.[6]

During our clinical work, we notice that lower urinary tract symptoms (LUTS) are frequently happened on patients with adenomyosis which greatly affect their daily activities if left untreated.[7] However, there is currently a lack of precise data regarding the presence of urinary symptoms and their association with clinical status in women with adenomyosis. It is essential to appraise LUTS in patients with adenomyosis from which knowledge gained can be used to develop therapeutic and preventive strategies.

Methods

Ethical approval

This study was approved by the Institutional Review Board and Hospital Local Ethics Committee. All participants provided informed consent.

Study design and patients

This was a cross-sectional and case-control designed study. The patients with untreated adenomyosis were consecutively recruited between July 2016 and November 2016. None of the participants had undergone surgical or medical treatment for the disease before. All participants were in stable condition. The accuracy of the diagnosis of adenomyosis was later confirmed histologically on some women who subsequently underwent surgery (uterus or wedge-shaped excision). Inclusion criteria included women older than 18 years who had either transvaginal ultrasonography or MRI diagnosed as adenomyosis with a description of uterine size. We also invited age-matched subjects who underwent physical examinations at our hospital to serve as control group with a normal appearance of the uterine myometrium on transvaginal ultrasonography and had no history of endometriosis, adenomyosis, or uterine fibroids. Women were excluded if they were in a current urinary tract infection, bladder stone, inflammatory bladder lesions found on cystoscopic examination. Patients with preexisting neurological diseases, diabetes, arterial hypertension, thyroid dysfunction, pelvic organ prolapse and urinary incontinence due to childbirth factor and vaginal or urethral surgery, pregnant, had a concurrent pelvic mass, history of gynecologic cancer, concurrent use of medications known to interfere with bladder or sphincter function, such as anticholinergics, sympathomimetics, sympatholytics, narcotics, antidepressants, antipsychotics, and diuretics were also excluded from the study.

Assessment of urologic symptoms

Women enrolled were asked to complete the International Prostate Symptom Score (IPSS) questionnaire in a private room. Although originally developed to standardize the assessment of LUTS in elderly men with benign prostatic hyperplasia, it has been shown to be neither disease nor sex specific. Many urologists take IPSS into their daily practice and research of female LUTS with good feasibility and validity.[8,9] The IPSS consists of eight questions in three subcategories that constitute three subscores: three questions about storage symptoms, four questions about voiding symptoms, and one question about QOL.[10] Storage subscore includes (daytime frequency, urgency, and nocturia) scores from 0 to 5 points. The voiding subscore includes (incomplete bladder emptying, intermittency, weak urinary stream, and straining) scores from 0 to 5. The total scores range from 0 to 35. The QOL question scores range from 0 to 6. The severity of LUTS was classified as none or mild (IPSS <8), moderate (IPSS 8–19), or severe (IPSS ≥20).[11] Storage symptoms were defined as moderate or severe for a subscore of ≥4 points, while voiding symptoms were defined as moderate or severe for a subscore of ≥5 points.[12] The variables were dichotomized as none or mild and moderate or severe symptoms.

Demographics and clinical status

Demographic data such as age, body mass index (BMI), parity, visual analog scale scored from 0 to 10 for dysmenorrhea and pelvic pain, total IPSS scores, subscale scores, uterine volume, and CA125 level were recorded. Imaging findings describing uterine size were abstracted from official reports. Uterine volume measurements were made in 3 dimensions and calculated using the formula for an ellipsoid shape: $V = 0.5233 \times$ length $\times$ anteroposterior diameter $\times$ transverse diameter and recorded in cubic centimeters. The pictorial blood assessment chart (PBAC) was used to evaluate participants' menstrual blood loss, as described by Higham *et al*.[13] Patients with a PBAC score of >100, being equivalent to >80 ml blood loss in a cycle were considered menorrhagia.[14] When taking uterine volume into account, we used uterine volume with 180 cm^3 (approximately 10 weeks size gravid uterus) as dividing value based on sonographic evaluation of uterine volume by Sheth *et al*.[15]

Statistical analysis

The Statistical Package for Social Sciences for Windows, version 17.0 (SPSS, Chicago, IL, USA) was used for statistical analyses. Data were expressed as means and standard deviations (SD) or median and interquartile range (IQR) for numeric variables or counts and percentages for categorical variables. Numeric variables were compared using Student's *t*-test or nonparametric Mann-Whitney *U*-test, and categorical variables were compared using the Chi-square test or Fisher's exact test as appropriate. Multivariate regression analyses were used to determine factors associated with severity of LUTS evaluated by IPSS among patients with adenomyosis presented as odds ratios (*OR*s) and 95% confidence intervals (*CI*s). For all statistical tests, a $P < 0.05$ was considered statistically significant.

Results

In this study, we included 298 consecutive patients with untreated adenomyosis (study group) and 280 age-matched controls with a normal-appearing myometrium (control group). The demographic data were similar between the two groups as shown in Table 1. The mean age was 39.3 ± 6.4 years in

the adenomyosis group and 38.3 ± 5.4 years in the control group ($P = 0.225$). The average BMI was 22.2 ± 2.9 kg/m^2 for adenomyosis group and 22.0 ± 3.1 kg/m^2 for control group. Individual urinary symptoms and total and subscale IPSS scores between the adenomyosis and control groups are also summarized in Table 1. LUTS were significantly more prevalent in the adenomyosis group than that in the control group. Daytime frequency was the most prominent symptom followed by nocturia, weak stream, and incomplete emptying. A total of 40.9% of patients in the adenomyosis group reported increased daytime frequency compared with that of 22.5% in the control group. Patients from the adenomyosis group significantly more often complained about nocturia than those from the control group (24.8% vs. 7.5%, $P < 0.001$). A total of 23.5% of the patients in the adenomyosis group and 5.7% in the control group had incomplete emptying. Moreover, the adenomyosis group had a marked higher median total symptom score (4 [2–8] vs. 2 [0–3], $Z = –8.159$, $P < 0.001$), storage symptom score (2 [1–4] vs. 1 [0–2], $Z = –7.361$, $P < 0.001$), voiding symptom score (2 [0–4] vs. 0 [0–1], $Z = –7.194$, $P < 0.001$), and QOL score (2 [1–4] vs. 1 [0–2], $Z = –7.184$, $P < 0.001$).

Among the 298 adenomyosis patients, 90 (30.2%) had an IPSS ≥8 (moderate-to-severe LUTS), whereas 178 (59.7%) had an IPSS <8 (none or mild LUTS). Table 2 shows the comparisons of demographic and clinical parameters between the patients with none or mild and moderate-to-severe LUTS. No significant differences were observed for all the analyzed covariates between the two IPSS subgroups except for menorrhagia. Patients with moderate-to-severe urinary symptoms had higher proportion of menorrhagia (51.1% vs. 30.8%, $\chi^2 = 11.162$, $P = 0.025$) and larger mean uterine volumes (183.3 [109.8–273.8] cm^3 vs. 148.5 [96.4–262.7] cm^3, $Z = –1.441$, $P = 0.150$) though without statistical significance.

Further multivariate binary logistic regression analysis indicated that menorrhagia and large uterine volume were factors related to moderate-to-severe LUTS [Table 3].

Patients with heavy menstrual bleeding experienced more than a 2-fold increase in the odds of IPSS total ≥8 (*OR*: 2.309, 95% *CI*: 1.310–4.070, $P = 0.004$), IPSS storage subscore ≥4 (*OR*: 2.422, 95% *CI*: 1.395–4.206, $P = 0.002$), and an IPSS voiding subscore ≥5 (*OR*: 1.971, 95% *CI*: 1.176–3.302, $P = 0.010$). Of note, uterine volume over 180 cm^3 (about 10 gestation weeks) was associated with a higher risk of IPSS total score ≥8 (*OR*: 2.437, 95% *CI*: 1.381–4.300, $P = 0.002$), IPSS storage subscore ≥4 (*OR*: 2.486, 95% *CI*: 1.433–4.314, $P = 0.001$), and IPSS voiding subscore ≥5 (*OR*: 2.700, 95% *CI*: 1.485–4.908, $P = 0.001$). No association was found between severity of LUTS and age, BMI, parity, dysmenorrhea, pelvic pain, and serum CA125 levels.

Discussion

In this survey, we found that LUTS evaluated by IPSS were prevalent and variable in patients with symptomatic adenomyosis compared to those with normal appearance of the uterine myometrium which were similar with findings by other researchers. But *et al*.[16] revealed that women with

Table 1: Demographic and clinical characteristics of study group and control group

Variables	Adenomyosis group (n = 298)	Control group (n = 280)	Statistical value	P
Age (years)	39.3 ± 6.4	38.3 ± 5.4	1.216*	0.225
BMI (kg/m^2)	22.2 ± 2.9	22.0 ± 3.0	0.571*	0.568
Parity	1(0–1)	1(0–1)	–0.930†	0.352
Infertility	76 (25.5)	26 (9.3)	26.126‡	<0.001
Caesarean section	84 (28.2)	40 (14.3)	16.557‡	<0.001
Education status				
Primary	6 (2.0)	12 (4.3)	2.470‡	0.116
Secondary	28 (9.4)	24 (8.6)	0.120‡	0.729
High school	38 (12.8)	32 (11.4)	0.297‡	0.626
University	226 (75.8)	212 (75.7)	0.001‡	0.972
LUTS				
Frequency (≥8/daytime)	122 (40.9)	63 (22.5)	22.555‡	<0.001
Urgency (≥1/week)	52 (17.4)	24 (8.6)	9.964‡	0.002
Nocturia (≥2/night)	74 (24.8)	21(7.5)	31.575‡	<0.001
Incomplete emptying	70 (23.5)	16 (5.7)	36.016‡	<0.001
Intermittency	50 (16.8)	12 (4.3)	23.528‡	<0.001
Weak stream	72 (24.2)	20 (7.1)	31.240‡	<0.001
Straining	50 (16.8)	28 (10.0)	5.682‡	0.017
IPSS total	4 (2–8)	2 (0–3)	–8.159†	<0.001
IPSS storage	2 (1–4)	1(0–2)	–7.361†	<0.001
IPSS voiding	2 (0–4)	0 (0–1)	–7.194†	<0.001
Quality of life	2 (1–4)	1 (0-2)	–7.184†	<0.001

Numeric data are expressed as mean ± SD and/or median (IQR). Categorical data are expressed as number (percentage). *t; †Z; ‡χ^2 value. BMI: Body mass index. LUTS: Lower urinary tract symptoms; IPSS: International Prostate Symptom Score; SD: Standard deviation; IQR: Interquartile range.

Table 2: General characteristics of patients with mild (IPSS <8) and moderate-to-severe LUTS (IPSS ≥8) in study group

Characteristic	IPSS <8	IPSS ≥8	Statistical value	*P*
Patients, *n* (%)	208 (69.8)	90 (30.2)		
Age (years)	38.8 ± 6.3	40.5 ± 6.4	–1.498*	0.134
BMI (kg/m^2)	22.0 ± 3.0	22.7 ± 2.6	–1.326*	0.187
Parity	1 (0–1)	1 (0–2)	–2.117†	0.034
Caesarean section	64 (30.8)	20 (22.2)	2.267‡	0.132
Infertility	48 (23.1)	28 (31.1)	2.134‡	0.377
Education, university and above	168 (80.8)	66 (73.3)	2.060‡	0.846
Dysmenorrhea	8(6–9)	8 (6–10)	–1.182†	0.237
Pelvic pain	1 (0–5)	0 (0–5)	–0.062†	0.950
Menorrhagia	64 (30.8)	46 (51.1)	11.162‡	0.025
Uterine volume (cm^3)	148.5 (96.4–262.7)	183.3 (109.8–273.8)	–1.441†	0.150
CA125 (U/ml)	83.3 (45.8–151.0)	89.8 (46.8–162.1)	–0.762†	0.446
IPSS total	2 (1–4.8)	9 (9–14)	–13.770†	<0.001
IPSS storage	2 (1–3)	5 (4–7)	–11.371†	<0.001
IPSS voiding	0 (0–2)	5 (4–8)	–12.911†	<0.001
Quality of life	1 (1–3)	4 (3–5)	–9.358†	<0.001

Numeric data are expressed as *n* (%), mean ± SD and/or median (IQR). Categorical data are expressed as number (percentage). *t; †Z; ‡χ^2 value. BMI: Body mass index. LUTS: Lower urinary tract symptoms; IPSS: International Prostate Symptom Score; SD: Standard deviation; IQR: Interquartile range.

Table 3: Factors associated with severity of LUTS (moderate-to-severe versus none or mild) using multivariate logistic regression analysis in study group

Variables	IPSS total			IPSS storage			IPSS voiding		
	OR	95% *CI*	*P*	*OR*	95% *CI*	*P*	*OR*	95% *CI*	*P*
Age	1.034	0.995–1.074	0.092	1.026	0.988–1.065	0.185	1.001	0.962–1.042	0.958
BMI	1.067	0.981–1.160	0.129	0.980	0.903–1.065	0.635	1.054	0.966–1.151	0.236
Parity									
1	0.884	0.509–1.535	0.661	1.181	0.687–2.030	0.547	0.972	0.539–1.756	0.926
≥2	1.890	0.886–4.032	0.100	1.477	0.693–3.148	0.313	1.697	0.771–3.739	0.189
Infertility	1.162	0.656–2.058	0.607	0.852	0.481–1.508	0.582	1.408	0.778–2.550	0.258
Cesarean section	0.716	0.421–1.215	0.215	1.110	0.670–1.840	0.686	1.182	0.686–2.037	0.546
Education status	1.125	0.640–1.979	0.683	1.304	0.747–2.278	0.351	1.108	0.607–2.023	0.738
Menorrhagia	2.309	1.310–4.070	0.004*	2.422	1.395–4.206	0.002*	1.971	1.176–3.302	0.010*
Dysmenorrhea	1.047	0.953–1.150	0.342	1.024	0.936–1.120	0.608	0.981	0.892–1.079	0.690
Uterine volume									
>180 cm^3	2.437	1.381–4.300	0.002*	2.486	1.433–4.314	0.001*	2.700	1.485–4.908	0.001*
CA125	1.001	0.999–1.003	0.149	1.001	0.999–1.003	0.219	1.001	0.999–1.003	0.508

*Statistically significant. BMI: Body mass index; *OR*: Odds ratio; *CI*: Confidence interval; LUTS: Lower urinary tract symptoms; IPSS: International Prostate Symptom Score.

adenomyosis more often experienced overactive bladder symptoms particularly irritative symptoms in an adenomyosis group (23.3%) as compared with controls (7.8%) which significantly decreased their QOL.[16] Ekin *et al*.[17] also discovered that the frequency of urinary symptoms was significantly higher in the adenomyosis group than that in the control group including stress urinary incontinence, urgency, daytime frequency, urge urinary incontinence, and dyspareunia. Moreover, the irritative and obstructive symptoms evaluated by the Urogenital Distress Inventory scores of patients with adenomyosis could be improved by levonorgestrel-releasing intrauterine system treatment as well as menorrhagia and dysmenorrhea in their further study.[18] Then, we examined the severity of multiple specific LUTS experienced by women with adenomyosis and its related risk factors, which has not been addressed by previous studies. We noted that the presence of menorrhea and large uterine volume (more than 180 cm^3) were associated with moderate-to-severe LUTS. In general, the etiology of adenomyosis and its relationship with urinary tract symptoms remain unclear. Explanations include the physiological mechanisms with regard to bulk symptoms and neurogenic dysfunction, leading to urinary symptoms. Enlarged uterine volumes may increase intra-abdominal pressure and partially compress the bladder wall, leading to decreased cystometric capacity and bladder filling and increased sensation of urinary voiding at lower volumes. This may be true since similar connections with LUTS were noticed in women with uterine fibroids.[19] In addition, it has

been demonstrated that adenomyotic nodules highly express inflammatory and neurogenic factors such as interleukin-1β, corticotropin-releasing hormone, nerve growth factor, and SYN which may affect the neurons of the pelvic plexus that innervate the lower urinary tract, leading to urinary dysfunction.[20] Abnormal uterus smooth muscle contractility in adenomyosis might indirectly contribute to LUTS as well.[21] It is likely that in the case of adenomyosis, some other unidentified factors are present and not yet known to us.

The findings highlight the importance of pretreatment screening for specific LUTS in women with enlarged uterine volumes and menorrhagia which will help establish the severity and determine if additional evaluation or therapy is warranted. However, possible limitation concerns the use of self-reported questionnaires for assessing LUTS which introduces a potential response bias. Moreover, studies of large sample size from multicenter are required to verify these findings. Multicenter studies with large sample groups are required to clarify the etiology of urinary tract dysfunction that causes genitourinary symptoms.

In conclusion, adenomyosis is a chronic gynecological disorder with unknown features that decreases the QOL of affected women. We found a correlation between urinary tract dysfunction and adenomyosis, especially in patients with menorrhagia and large uterine volume. Future studies should further investigate the natural history of these symptoms and include objective bladder testing, such as uroflowmetry and urodynamics measurements in women with adenomyosis, and to determine the change in symptoms with treatment resulting in decreased uterine size or adenomyoma removal.

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Conflicts of interest

There are no conflicts of interest.

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