

Association between endometriosis and lower urinary tract symptoms

Iwona Gabriel, M.D., Ph.D.,^{a,b} Allison F. Vitonis, S.M.,^{a,c} Stacey A. Missmer, Sc.D.,^{c,d,e} Ayòtundé Fadayomi, M.B.B.S., M.P.H.,^{c,f} Amy D. DiVasta, M.D., M.M.Sc.,^{c,g} Kathryn L. Terry, Sc.D.,^{a,c,d} and Vatche A. Minassian, M.D., M.P.H.^a

^a Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Boston, Massachusetts; ^b Department of Gynecology, Obstetrics and Oncological Gynecology, Medical University of Silesia, Bytom, Poland; ^c Boston Center for Endometriosis, Boston Children's Hospital and Brigham and Women's Hospital, Boston, Massachusetts; ^d Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts; ^e Department of Obstetrics, Gynecology and Reproductive Biology, Michigan State University College of Human Medicine, Grand Rapids, Michigan; ^f Department of Anesthesiology and Perioperative Medicine, University of Massachusetts Memorial Medical Center, Worcester, Massachusetts; and ^g Division of Adolescent and Young Adult Medicine, Department of Medicine, Boston Children's Hospital, Boston, Massachusetts

Objective: To determine if women with endometriosis experience lower urinary tract symptoms (LUTSs) more often than those without.

Design: Cross-sectional analysis at enrollment in a longitudinal cohort.

Setting: Enrollment at 2 academic hospitals and from the local community.

Patient(s): This analysis included 1,161 women with (n = 520) and without (n = 641) surgically confirmed endometriosis who were enrolled in the Women's Health Study: from Adolescence to Adulthood between 2012 and 2018.

Intervention(s): Not applicable.

Main Outcome Measure(s): Prevalence of LUTSs, including stress incontinence, urgency and frequency, straining with urination, incomplete bladder emptying, hematuria, dysuria, and bladder pain using standardized questionnaires.

Result(s): The primary outcomes were that women with endometriosis reported the following more often than those without: difficulty passing urine (7.9% vs. 2%; crude odds ratio [OR], 4.14 [95% confidence interval {CI}, 2.19–7.80]; adjusted OR [aOR], 4.31 [95% CI, 2.07–8.95]); still feeling full after urination (18.8% vs. 4.7%; crude OR, 4.73 [95% CI, 3.08–7.25]; aOR, 4.67 [95% CI, 2.88–7.56]); having to urinate again within minutes of urinating (33.1% vs. 17.0%; crude OR, 2.41 [95% CI, 1.83–3.18]; aOR, 2.49 [95% CI, 1.81–3.43]), dysuria (11.7% vs. 4.9%; crude OR, 2.55 [95% CI, 1.62–4.01]; aOR, 2.38 [95% CI, 1.40–4.02]); and pain when the bladder is full (23.0% vs. 4.9%; crude OR, 5.79 [95% CI, 3.82–8.78]; aOR, 6.04 [95% CI, 3.74–9.76]). For the secondary outcomes, among female participants with endometriosis, we observed that the odds of LUTS did not differ by the revised American Society for Reproductive Medicine stage (I/II vs. III/IV) or duration of endometriosis-associated symptoms.

Conclusion(s): Women with surgically confirmed endometriosis were more likely to report LUTS than those without. (Fertil Steril® 2022;117:822–30. ©2022 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Endometriosis, lower urinary tract symptoms, stress urinary incontinence, dysuria



DIALOG: You can discuss this article with its authors and other readers at <https://www.fertsterdialog.com/posts/33733>

Received August 22, 2021; revised December 28, 2021; accepted January 4, 2022; published online January 31, 2022.

I.G. has nothing to disclose. A.F.V. has nothing to disclose. S.A.M. reports grant from the J Willard & Alice S Marriott Foundation for the submitted work; grants from AbbVie, DoD, NIH, and Marriott Family Foundation; honoraria from University British Columbia and WERF; meeting and travel support from 34th Annual Meeting of the European Society of Reproduction and Embryology (ESHRE) 2018 Invited speaker, 3rd Annual Conference of the Canadian Society for the Advancement of Gynecologic Excellence (CanSAGE) 2018, Endometriosis Research Now—Patient Conference Endometriosis UK 2018, 4th Upper Egypt Assisted Reproduction Conference (UEARS 2019) Invited speaker, International Federation of Fertility Societies (IFFS) World Congress, ESHRE 2019 (and 2020 virtual), International Association for the Study of Pain (IASP) 4th World Congress on Abdominal and Pelvic Pain (WCAPP) 2019, National Endometriosis Network UK Meeting 2019; personal fees for advisory boards from AbbVie and Roche; and unpaid society leadership for SWHR, WERF, WES, ASRM, and ESHRE. A.F. has nothing to disclose. A.D.D. has nothing to disclose. K.L.T. has nothing to disclose. V.A.M. has nothing to disclose.

K.L.T. and V.A.M. should be considered similar in author order.

Supported by the J. Willard and Alice S. Marriott Foundation.

Reprint requests: Iwona Gabriel, M.D., Ph.D., Department of Obstetrics and Gynecology, Brigham and Women's Hospital, 75 Francis Street, Boston, Massachusetts 02115 (E-mail: igabriel@partners.org).

Fertility and Sterility® Vol. 117, No. 4, April 2022 0015-0282

Copyright ©2022 The Authors. Published by Elsevier Inc. on behalf of the American Society for Reproductive Medicine. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

<https://doi.org/10.1016/j.fertnstert.2022.01.003>

The prevalence of endometriosis is approximately 10% among women of reproductive age (1, 2). Common symptoms include dysmenorrhea, dyspareunia, chronic pelvic pain, and infertility (3). Endometriosis studies have documented coexisting comorbidities for which pain is a hallmark of presentation including migraine (4), interstitial cystitis (5), and irritable bowel syndrome (6, 7). Women with endometriosis report a significant negative impact of the disease on their quality of life, daily activities, and work productivity (8, 9). The same pattern of adverse outcomes on

personal, social, and professional life is observed in women with lower urinary tract symptoms (LUTSs) (10–12). Healthy bladder function or the lack thereof in girls and young adult women has been receiving renewed attention (13). Lower urinary tract symptoms include urinary frequency, urgency, nocturia, and urinary incontinence (14). One in 3 women across all ages reports LUTS (15). The prevalence of urinary incontinence in childhood and young adolescence ranges between 5% and 15% (16) and increases over the life span (15, 17). The promotion of bladder health and prevention of LUTS are crucially important for girls and young women because they may have long-lasting debilitating effects (18).

We previously reported that pain with urination and more frequent urination were associated with menstrual pain presence and severity in girls and women with endometriosis (7, 19). However, whether women with endometriosis are more likely to have LUTS is unknown. Thus, using data collected among the participants of the Women's Health Study: from Adolescence to Adulthood (A2A), we evaluated the association between endometriosis and LUTSs. Specifically, we hypothesized that women with endometriosis experience LUTSs more often than those without.

MATERIALS AND METHODS

Study Population

The A2A cohort and data collection methods have been described previously (4, 7, 19). The A2A is an ongoing longitudinal cohort study that enrolled premenopausal females older than the age of 7 years oversampled for those with surgically confirmed endometriosis. Participants were enrolled from 2012 to 2018. Participants with endometriosis were enrolled from Boston Children's Hospital (BCH) and Brigham and Women's Hospital (BWH) and were eligible if they were female and 7–55 years of age and had a surgical diagnosis of endometriosis at 1 of the 2 participating hospitals or had a prior surgical diagnosis elsewhere but were receiving follow-up treatment at 1 of these 2 hospitals. Participants without endometriosis were females aged 7–55 years and recruited from clinics at BCH and BWH and from the local Boston community through local advertisements, online postings, and word of mouth. These participants had never received a surgical diagnosis of endometriosis. This study is a joint project between BCH and BWH, with the overall aim of investigating endometriosis across the life span. Participants were recruited from Gynecology and Adolescent Medicine clinics within the 2 tertiary care centers as well as from the surrounding community via local advertisements, online postings, and word of mouth. The BCH and BWH Institutional Review Board approved the study. Informed consent was obtained, with parental consent/participant assent for girls aged <18 years.

Of the 1,549 participants enrolled in the A2A cohort, the analytic sample for this study was restricted to participants who completed a standardized questionnaire at entry to the study (20, 21) including questions regarding LUTSs. Lower urinary tract symptom-related questions included “have you experienced the following in the last 3 months: loss of urine when coughing, sneezing, or laughing (stress urinary

incontinence); difficulty passing urine; blood in the urine; still feeling full after urination (postvoid urgency); and having to urinate again within minutes of urinating (frequency)?” Pain-related severity questions included “how much pain (numeric rating scale [NRS], 0–10) do you usually have when the bladder is full and during urination (dysuria)?” We dichotomized participants as <5 vs. ≥ 5 on the 0–10 NRS (22). Other questions in the World Endometriosis Research Foundation (WERF) and Endometriosis Phenome and Biobanking Harmonization Project (EPHect)-compliant questionnaire included those related to medical history, lifestyle, current and previous medications, anthropometrics, environmental exposures, symptom experience, and current and past treatments and were described in detail by Vitonis et al. (21).

Participants were excluded if they did not complete the LUTS questions on the questionnaire ($n = 350$) or if they self-reported frequent bladder infections ($n = 39$). The final study group included 1,161 participants.

Exposure

The primary exposure of this study was laparoscopically diagnosed endometriosis. For the secondary exposure, we sought to evaluate the stage (defined by the revised American Society for Reproductive Medicine [rASRM]) or duration of endometriosis as an exposure in relation to LUTSs.

Outcome

The outcomes were LUTSs, including stress urinary incontinence, difficulty passing urine, blood in the urine, still feeling full after urination, having to urinate again within minutes of urinating, pain when the bladder is full, and dysuria. Together, these symptoms describe LUTSs.

Covariates

The demographic, lifestyle, and anthropometric characteristics of the participants considered as potential confounding factors included age (years), body mass index (BMI), race (White/non-White), parity (nulliparity/multiparity), educational status (middle school/ high school, college/graduate school), working status (yes/no), presence of acyclic pelvic pain in the past 3 months (yes/no), dysmenorrhea in the past 3 months (none; mild, medication never or rarely needed; moderate, medication usually needed; severe, medication and bed rest needed; and not cycling in the past 3 months), and current hormone use (yes/no). Age was also categorized as younger than 18 years old, between 18 and 25 years, and older than 25 years. The BMI was calculated from self-reported weight and height. Endometriosis stage was defined according to the rASRM classification (23). The duration of symptoms was derived from the questionnaires as time since the first symptoms were experienced to the date of questionnaire completion.

Statistical Analysis

Demographics were compared by endometriosis and LUTS status. We estimated the association between endometriosis

and the presence of stress urinary incontinence, difficulty passing urine, blood in the urine, still feeling full after urination, having to urinate again within minutes of urinating, pain when the bladder is full, and dysuria by calculating crude

and adjusted odds ratios (aORs) and 95% confidence intervals (CIs) using unconditional logistic regression. Age, BMI, race, and parity were included a priori in the adjusted logistic regression model as known risk factors for urinary

TABLE 1

Demographic characteristics among the participants of the Women's Health Study: from Adolescence to Adulthood with and without endometriosis.

Patient characteristics	Participants without endometriosis (n = 641)	Participants with endometriosis (n = 520)
Age category, n (%)		
<18 years	34 (5.3)	217 (41.7)
18–25 years	374 (58.3)	202 (38.8)
>25 years	233 (36.3)	101 (19.4)
Body mass index		
Mean (SD)	24.1 (5.8)	24.7 (5.6)
Median (IQR)	22.6 (14–66)	23.2 (16–56)
Missing, 2		
Race, n (%)		
White	464 (72.4)	467 (89.8)
Black or African American	41 (6.4)	14 (2.7)
Asian	88 (13.7)	3 (0.6)
More than 1 race	33 (5.2)	18 (3.5)
Other	15 (2.3)	18 (3.5)
Hispanic ethnicity, n (%)		
No	582 (91.5)	472 (92.9)
Yes	54 (8.5)	36 (7.1)
Missing, 17		
Parous, n (%)		
Nulliparous	575 (90.7)	491 (95.0)
Multiparous	59 (9.3)	26 (5.0)
Missing, 10		
Education/working status, n (%)		
Middle/high school	27 (4.2)	184 (35.4)
College/graduate school	134 (20.9)	124 (23.8)
Working	433 (67.6)	157 (30.2)
Other	47 (7.3)	55 (10.6)
Menstrual pain in the past 3 months, n (%)		
None	103 (16.1)	3 (0.6)
Mild, medication never or rarely needed	243 (37.9)	17 (3.3)
Moderate, medication usually needed	139 (21.7)	92 (17.8)
Severe, medication and bed rest needed	45 (7.0)	194 (37.5)
Not cycling	111 (17.3)	211 (40.8)
Missing, 3		
Acyclic pelvic pain in the past 3 months, n (%)		
No	550 (86.5)	181 (35.3)
Yes	86 (13.5)	332 (64.7)
Missing, 5		
Currently using hormones, n (%)		
No	372 (58.0)	104 (20.0)
Yes	269 (42.0)	416 (80.0)
Time between surgery and questionnaire completion, n (%)		
Surgery at < 90 days before questionnaire	n/a	88 (16.9)
Surgery at 91–365 days before questionnaire	n/a	48 (9.2)
Surgery at >365 days before questionnaire	n/a	191 (36.7)
Surgery performed after questionnaire	n/a	193 (37.1)

Note: IQR = interquartile range; n/a = non applicable; SD = standard deviation.

Gabriel. Urinary symptoms in endometriosis. *Fertil Steril* 2022.

TABLE 2

Associations between endometriosis and lower urinary tract symptoms reported at study enrollment.

Lower urinary tract symptom	Participants without endometriosis (n = 641)		Participants with endometriosis (n = 520)		Crude OR (95% CI)	aOR (95% CI) ^d
	No	Yes	No	Yes		
Stress urinary incontinence	544 (84.9%)	97 (15.1%)	433 (83.3%)	87 (16.7%)	1.13 (0.82–1.54)	1.25 (0.86–1.80)
Difficulty passing urine	628 (98.0%)	13 (2.0%)	479 (92.1%)	41 (7.9%)	4.14 (2.19–7.80)	4.31 (2.07–8.95)
Blood in the urine	632 (98.6%)	9 (1.4%)	498 (95.8%)	22 (4.2%)	3.10 (1.42–6.80)	1.82 (0.70–4.76)
Still feeling full after urination	611 (95.3%)	30 (4.7%)	422 (81.2%)	98 (18.8%)	4.73 (3.08–7.25)	4.67 (2.88–7.56)
Having to urinate again within minutes of urinating	532 (83.0%)	109 (17.0%)	348 (66.9%)	172 (33.1%)	2.41 (1.83–3.18)	2.49 (1.81–3.43)
Pain (severity of pain when the bladder is full ≥ 5) ^{a,b}	600 (95.1%)	31 (4.9%)	391 (77.0%)	117 (23.0%)	5.79 (3.82–8.78)	6.04 (3.74–9.76)
Dysuria (severity of pain with urination ≥ 5) ^{a,c}	599 (95.1%)	31 (4.9%)	447 (88.3%)	59 (11.7%)	2.55 (1.62–4.01)	2.38 (1.40–4.02)
One or more of the above symptoms vs. any of the above	424 (66.2%)	217 (33.8%)	229 (44.0%)	291 (56.0%)	2.48 (1.96–3.15)	2.46 (1.86–3.25)

Note: aOR = adjusted odds ratio; CI = confidence interval; OR = odds ratio.

^a Dichotomized from a 0–10 numeric rating scale.^b Ten patients with no response.^c Eleven patients with no response.^d Multivariable unconditional logistic regression model adjusted for age, body mass index, race, and parity, and current hormone use.

Gabriel. Urinary symptoms in endometriosis. Fertil Steril 2022.

incontinence. Secondary analyses were performed restricted to the exposed group (women with endometriosis) to investigate if the effect of endometriosis on LUTS was modified by the rASRM stage (stage I/II vs. III/IV) or duration of the participant's symptoms (<2, 2–4, or >5 years). Analyses were completed using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

A total of 1,161 women with endometriosis (n = 520) and without (n = 641) were included in the study population. Table 1 presents the demographic, menstrual, and acyclic pain symptom characteristics by endometriosis status. The mean age of women with endometriosis was 20.8 years (± 6.7), whereas the mean age of women without endometriosis was 25.4 years (± 7.0). The median BMI was similar in both groups (23.2 vs. 22.6 kg/m²). Most participants in both groups were White, non-Hispanic, and nulliparous. Five times more participants with endometriosis experienced acyclic pelvic pain in comparison with those without (65% vs. 13%). Lower urinary tract symptom was common overall and was reported by 43.8% of participants. Of those with surgically confirmed endometriosis, 291 women (56%) reported any LUTS compared with 217 women (34%) of those without endometriosis. Endometriosis was associated with a statistically significantly greater odds of LUTS compared with women without endometriosis (Table 2). The odds of difficulty passing urine (aOR, 4.31; 95% CI, 2.07–8.95), having to urinate again within minutes of urinating (aOR, 2.49; 95% CI, 1.81–3.43), and feeling full after urination (aOR, 4.67; 95% CI, 2.88–7.56) were twofold to fivefold higher for women with endometriosis than for those without. Furthermore, the likelihood of pain when the bladder is full (severity of at least 5 on the 0–10 NRS) (aOR, 6.04; 95% CI, 3.74–9.76) and that of pain with urination/dysuria (severity of at least 5 on the 0–10 NRS) (aOR, 2.38; 95% CI, 1.40–4.02) were greater for women with endometriosis than for those without.

Of 520 women with endometriosis, 418 had defined stage of disease on the basis of the rASRM staging system, and the odds of LUTS were not different between stages I/II and III/IV (Table 3). However, only 24 women with endometriosis were categorized as rASRM stage III/IV. The odds of LUTS did not vary by the duration of endometriosis symptoms (<2, 2–5, and >5 years) (Table 4).

DISCUSSION

Overall, we observed that LUTSs were common and reported by >40% of participants similar to other reports (24, 25). Women with endometriosis were more likely to experience various LUTSs, including difficulty passing urine, having to urinate again within minutes of urinating, or still feeling full after urination, than those without endometriosis. It is important to note that neither the rASRM stage of endometriosis nor duration of endometriosis-associated symptoms was associated with LUTS.

Previous reports of LUTS and endometriosis focused solely on the potential voiding difficulties resulting from the extensive pelvic surgery for advanced endometriosis. For example, Riiskjaer et al. (26) showed that common lower

TABLE 3

Association between the revised American Society for Reproductive Medicine stage and lower urinary tract symptoms among women with surgically confirmed endometriosis (of 520 participants with endometriosis, 418 had the revised American Society for Reproductive Medicine stage data).

Lower urinary tract symptom	Endometriosis stage I–II (n = 394)		Endometriosis stage III–IV (n = 24)		Crude OR (95% CI)	aOR (95% CI) ^d
	No	Yes	No	Yes		
Stress urinary incontinence	330 (83.8%)	64 (16.2%)	21 (87.5%)	3 (12.5%)	0.74 (0.21–2.54)	0.78 (0.21–2.96)
Difficulty passing urine	353 (89.6%)	41 (10.4%)	24 (100%)	0 (0%)	–	–
Blood in the urine	375 (94.2%)	19 (4.8%)	22 (91.7%)	2 (8.3%)	1.79 (0.39–8.20)	3.18 (0.54–18.5)
Still feeling full after urination	317 (80.5%)	77 (19.5%)	20 (83.3%)	4 (16.7%)	0.82 (0.27–2.48)	0.82 (0.25–2.62)
Having to urinate again within minutes of urinating	260 (66.0%)	134 (34.0%)	22 (91.7%)	2 (8.3%)	0.18 (0.04–0.76)	0.18 (0.04–0.82)
Pain (severity of pain when the bladder is full ≥ 5) ^{a,b}	298 (77.0%)	89 (23.0%)	17 (77.3%)	5 (22.7%)	0.98 (0.35–2.74)	0.88 (0.30–2.60)
Dysuria (severity of pain with urination ≥ 5) ^{a,c}	333 (86.5%)	52 (13.5%)	21 (95.4%)	1 (4.6%)	0.30 (0.04–2.32)	0.33 (0.04–2.60)
One or more of the above symptoms vs. any of the above	174 (44.2%)	220 (55.8%)	15 (62.5%)	9 (37.5%)	0.48 (0.20–1.11)	0.42 (0.17–1.05)

Note: aOR= adjusted odds ratio, CI= confidence interval; OR = odds ratio.

^a Dichotomized from a 0–10 numeric rating scale.

^b Seven patients with no response.

^c Nine patients with no response.

^d Adjusted for age, body mass index, race, parity, current hormone use, and time since surgery.

Gabriel. Urinary symptoms in endometriosis. *Fertil Steril* 2022.

urinary symptoms like urgency, frequency, straining to pass urine, or hesitancy did not change 1 year after pelvic surgery for advanced endometriosis. More recently, Roman et al. (27) found no dysuria and need of bladder catheterization after complex surgery for endometriosis. Another study from our research group presented data investigating 2 of the common LUTS complaints: more frequent urination (when experiencing pain during menses) and pain with urination (during menstrual pain) in adolescents and adults with endometriosis (7). Frequent urination was more common among adults than adolescents with endometriosis. Pain with urination during menstrual pain was prevalent among both adolescents and adults with endometriosis, occurring in approximately half the sample. The results reported here expand on this work with respect to inclusion criteria, sample size, and outcomes of interest.

A higher prevalence of LUTSs among women with endometriosis may be related to changes in pelvic sensation because both of these disorders result in alterations in local innervation. Prior studies have shown that pelvic innervation is altered in endometriosis-affected women with a higher density of autonomic, sensory C and A delta nerve fibers detected within endometriotic lesions (28). The central neural control pathways may overlap between endometriosis and bladder function, based on the model presented for pain stimulation by endometriosis and neurologic basis for the overactive bladder (29, 30). On the other hand, the surgical management of endometriosis may decrease pelvic and bladder innervation. For example, rectal shaving of deep infiltrating endometriosis leads to bladder atony in 2% of patients (31). In addition, modified communication on a cellular

level in both disorders is present. The nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), and glial-derived neurotrophic factor are acting as messengers between the peripheral effector tissue and the nerves that innervate it. The NGF and BDNF are abundantly expressed in the urothelium and the sensory afferents innervating the bladder (32). The urinary ratios of NGF/creatinine and BDNF/creatinine were shown to be significantly higher in women with overactive bladder vs. healthy controls (32). The BDNF is 2.5 times higher in patients with overactive bladder than healthy controls (33). Interestingly, the BDNF is also elevated in women with endometriosis across all stages of disease in the absence of any hormone therapy (34). On the other hand, the NGF is expressed in both eutopic and ectopic endometrial tissue of women with endometriosis (35), stimulating neuronal migration and axon growth. It is proven that the NGF is markedly up-regulated in nerve fibers associated with the areas of inflammation and is excitatory to terminals of sensory nerve fibers. The NGF may often be found at the invasion front of the endometriotic lesion (36) leading to higher innervation. Thus, our findings may also result from the inflammatory state resulting from endometriotic lesions and giving symptoms similar to overactive bladder through an elevated NGF level.

The strengths of our study include a large sample size of adolescent and young women who completed a detailed questionnaire at the time of enrollment with validated questions to assess endometriosis and LUTSs. The analysis of the symptoms at enrollment, in women both with and without surgically confirmed endometriosis, allows comparison of the prevalence of women having urinary tract issues.

TABLE 4

Logistic regression analysis of the duration of endometriosis symptoms and each LUTS outcome (of 520 participants with endometriosis, 477 had a known duration of symptoms).

Lower urinary tract symptoms	Endometriosis < 2 years (n = 143)		Endometriosis 2–4 years (n = 193)			Endometriosis ≥ 5 years (n = 141)		
	No	Yes	No	Yes	aOR (95% CI) ^d	No	Yes	aOR (95% CI) ^d
Stress urinary incontinence	121 (84.6%)	22 (15.4%)	162 (83.9%)	31 (16.1%)	1.04 (0.56–1.94)	110 (78.0%)	31 (22.0%)	1.25 (0.65–2.41)
Difficulty passing urine	133 (93.0%)	10 (7.0%)	174 (90.2%)	19 (9.8%)	1.34 (0.58–3.06)	132 (93.6%)	9 (6.4%)	0.94 (0.34–2.58)
Blood in the urine	137 (95.8%)	6 (4.2%)	182 (94.3%)	11 (5.7%)	1.34 (0.46–3.96)	137 (97.2%)	4 (2.8%)	1.11 (0.26–4.66)
Still feeling full after urination	117 (81.8%)	26 (18.2%)	158 (81.9%)	35 (18.1%)	0.94 (0.53–1.68)	114 (80.9%)	27 (19.1%)	0.84 (0.44–1.61)
Having to urinate again within minutes of urinating	106 (74.1%)	37 (25.9%)	129 (66.8%)	64 (33.2%)	1.50 (0.91–2.46)	86 (61.0%)	55 (39.0%)	1.56 (0.91–2.46)
Pain (severity of pain when the bladder is full ≥ 5) ^{a,b}	101 (74.3%)	35 (25.7%)	147 (77.4%)	43 (22.6%)	0.90 (0.53–1.54)	111 (79.9%)	28 (20.1%)	0.82 (0.45–1.52)
Dysuria (severity of pain with urination ≥ 5) ^{a,c}	118 (86.1%)	19 (13.9%)	169 (89.4%)	20 (10.6%)	0.70 (0.35–1.39)	121 (87.7%)	17 (12.3%)	0.86 (0.40–1.82)
One or more of the above symptoms vs. any of the above	66 (46.2%)	77 (53.8%)	91 (47.2%)	102 (52.8%)	0.98 (0.63–1.54)	56 (39.7%)	85 (60.3%)	1.10 (0.66–1.84)

Note: aOR= adjusted odds ratio, CI= confidence interval.

^a Dichotomized from a 0–10 numeric rating scale.

^b Seven patients with no response.

^c Six patients with no response.

^d Adjusted for age, body mass index, race, parity, current hormone use, and time since surgery.

Gabriel. Urinary symptoms in endometriosis. *Fertil Steril* 2022.

The limitations of the study include the possibility of misclassified symptom reporting skewed toward overreporting of LUTS; however, there are no data suggesting that those with endometriosis would overreport more than those without. Hence, nondifferential misclassification, should it exist, would bias the association between endometriosis and LUTS toward the null, not away from it. Additionally, there is the potential for misclassification of endometriosis status among our comparison group because some participants may have asymptomatic endometriosis or have had symptoms resolved by empiric treatment (e.g., oral contraceptives), thus avoiding surgery for definitive diagnosis. This would also lead to nondifferential misclassification and drive results to the null, resulting in an underestimate, not overestimate, of associations. The likely community prevalence of undiagnosed endometriosis is <2% (37, 38), and the characteristics of this small proportion of undiagnosed girls and women will be diluted among the true endometriosis-free participants. It is important to note, however, that although this study has high internal validity, these results may not be generalizable to other populations. Specifically, these results are limited to the demographic characteristics of our study population, who are mainly young adult nulliparous, non-Hispanic White women. Furthermore, because this analysis is cross-sectional, the temporality of the exposure with respect to the outcome is difficult to assess. Therefore, we are unable to assess whether endometriosis leads to an increase in LUTSs or if LUTSs precede endometriosis diagnosis. Longitudinal studies with data on LUTSs before endometriosis diagnosis are needed to evaluate the temporality of this association.

CONCLUSION

For all women of reproductive age, it is important to recognize that LUTSs are common. Women with surgically confirmed endometriosis are more likely to report several LUTSs than those without. We propose that LUTSs should be concurrently addressed during the course of initial diagnosis and subsequent management of endometriosis.

Acknowledgments: The authors thank the participants and their families who made this research possible.



DIALOG: You can discuss this article with its authors and other readers at <https://www.fertstertdialog.com/posts/33733>

REFERENCES

- Shafir AL, Farland LV, Shah DK, Harris HR, Kvaskoff M, Zondervan K, et al. Risk for and consequences of endometriosis: a critical epidemiologic review. *Best Pract Res Clin Obstet Gynaecol* 2018;51:1–15.
- Ghiasi M, Kulkarni MT, Missmer SA. Is endometriosis more common and more severe than it was 30 years ago? *J Minim Invasive Gynecol* 2020;27:452–61.
- Zondervan KT, Becker CM, Missmer SA. Endometriosis. *N Engl J Med* 2020;382:1244–56.
- Miller JA, Missmer SA, Vitonis AF, Sarda V, Laufer MR, DiVasta AD. Prevalence of migraines in adolescents with endometriosis. *Fertil Steril* 2018;109:685–90.
- Wu CC, Chung SD, Lin HC. Endometriosis increased the risk of bladder pain syndrome/interstitial cystitis: a population-based study. *Neurourol Urodyn* 2018;37:1413–8.
- Schomacker ML, Hansen KE, Ramlau-Hansen CH, Forman A. Is endometriosis associated with irritable bowel syndrome? A cross-sectional study. *Eur J Obstet Gynecol Reprod Biol* 2018;231:65–9.
- DiVasta AD, Vitonis AF, Laufer MR, Missmer SA. Spectrum of symptoms in women diagnosed with endometriosis during adolescence vs adulthood. *Am J Obstet Gynecol* 2018;218:324.e1–11.
- Soliman AM, Coyne KS, Zaiser E, Castelli-Haley J, Fuldeore MJ. The burden of endometriosis symptoms on health-related quality of life in women in the United States: a cross-sectional study. *J Psychosom Obstet Gynaecol* 2017;38:238–48.
- Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, de Cicco Nardone F, de Cicco Nardone C, et al. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril* 2011;96:366–73.e8.
- Krhot J, Gärtner M, Mokris J, Horcicka L, Svabik K, Zachoval R, et al. Effect of severity of urinary incontinence on quality of life in women. *Neurourol Urodyn* 2018;37:1925–30.
- Caruso S, Brescia R, Matarazzo MG, Giunta G, Rapisarda AMC, Cianci A. Effects of urinary incontinence subtypes on women's sexual function and quality of life. *Urology* 2017;108:59–64.
- Lin KY, Siu KC, Lin KH. Impact of lower urinary tract symptoms on work productivity in female workers: a systematic review and meta-analysis. *Neurourol Urodyn* 2018;37:2323–34.
- Lowder JL, Bavendam TG, Berry A, Brady S, Fitzgerald CM, Fok CS, et al. Terminology for bladder health research in women and girls: prevention of lower urinary tract symptoms transdisciplinary consortium definitions. *Neurourol Urodyn* 2019;38:1339–52.
- Markland A, Chu H, Epperson CN, Nodora J, Shoham D, Smith A, et al. Occupation and lower urinary tract symptoms in women: a rapid review and meta-analysis from the PLUS research consortium. *Neurourol Urodyn* 2018;37:2881–92.
- Minassian VA, Bazi T, Stewart WF. Clinical epidemiological insights into urinary incontinence. *Int Urogynecol J* 2017;28:687–96.
- Minassian VA, Drutz HP, Al-Badr A. Urinary incontinence as a worldwide problem. *Int J Gynaecol Obstet* 2003;82:327–38.
- Coyne KS, Sexton CC, Bell JA, Thompson CL, Dmochowski R, Bavendam T, et al. The prevalence of lower urinary tract symptoms (LUTS) and overactive bladder (OAB) by racial/ethnic group and age: results from OAB-POLL. *Neurourol Urodyn* 2013;32:230–7.
- Lukacz ES, Bavendam TG, Berry A, Fok CS, Gahagan S, Goode PS, et al. A novel research definition of bladder health in women and girls: implications for research and public health promotion. *J Womens Health (Larchmt)* 2018;27:974–81.
- DiVasta AD, Zimmerman LA, Vitonis AF, Fadayomi AB, Missmer SA. Overlap between irritable bowel syndrome diagnosis and endometriosis in adolescents. *Clin Gastroenterol Hepatol* 2021;19:528–37.e1.
- De Graaff AA, D'Hooghe TM, Dunselman GAJ, Dirksen CD, Hummelshoj L. The significant effect of endometriosis on physical, mental and social wellbeing: results from an international cross-sectional survey. *Hum Reprod* 2013;28:2677–85.
- Vitonis AF, Vincent K, Rahmioglu N, Fassbender A, Buck Louis GM, Hummelshoj L, et al. World Endometriosis Research Foundation Endometriosis Phenome and Biobanking Harmonization Project: II. Clinical and covariate phenotype data collection in endometriosis research. *Fertil Steril* 2014;102:1223–32.
- Allaire C, Williams C, Bodmer-Roy S, Zhu S, Arion K, Ambacher K, et al. Chronic pelvic pain in an interdisciplinary setting: 1-year prospective cohort. *Am J Obstet Gynecol* 2018;218:114.e1–12.
- Revised American Society for Reproductive Medicine classification of endometriosis: 1996. *Fertil Steril* 1997;67:817–21.
- Erekson E, Hagan KA, Austin A, Carmichael D, Minassian VA, Grodstein F, et al. Outpatient evaluation and management visits for urinary incontinence in older women. *J Urol* 2019;202:333–8.
- Yang E, Lisha NE, Walter L, Obiedin-Maliver J, Huang AJ. Urinary incontinence in a national cohort of older women: implications for caregiving and care dependence. *J Womens Health (Larchmt)* 2018;27:1097–103.
- Riskjaer M, Greisen S, Glavind-Kristensen M, Kesmodel US, Forman A, Seyer-Hansen M. Pelvic organ function before and after laparoscopic bowel resection for rectosigmoid endometriosis: a prospective, observational study. *BJOG* 2016;123:1360–7.

27. Roman H, Tuech JJ, Huet E, Bridoux V, Khalil H, Hennetier C, et al. Excision versus colorectal resection in deep endometriosis infiltrating the rectum: 5-year follow-up of patients enrolled in a randomized controlled trial. *Hum Reprod* 2019;34:2362–71.
28. Miller EJ, Fraser IS. The importance of pelvic nerve fibers in endometriosis. *Womens Health (Lond)* 2015;11:611–8.
29. As-Sanie S, Harris RE, Napadow V, Kim J, Neshewat G, Kairys A, et al. Changes in regional gray matter volume in women with chronic pelvic pain: a voxel-based morphometry study. *Pain* 2012;153:1006–14.
30. Minassian VA, Gabriel I. Urinary tract. In: Berek JS, Berek DL, editors. *Berek & Novak's gynecology*. Philadelphia, PA: Wolters Kluwer; 2020:702.
31. Marty N, Touleimat S, Moatassim-Driss S, Millochau JC, Vallee A, Stochino Loi E, et al. Rectal shaving using plasma energy in deep infiltrating endometriosis of the rectum: four years of experience. *J Minim Invasive Gynecol* 2017;24:1121–7.
32. Antunes-Lopes T, Pinto R, Barros SC, Botelho F, Silva CM, Cruz CD, et al. Urinary neurotrophic factors in healthy individuals and patients with overactive bladder. *J Urol* 2013;189:359–65.
33. Alkis O, Zumurutbas AE, Toktas C, Aybek H, Aybek Z. The use of biomarkers in the diagnosis and treatment of overactive bladder: can we predict the patients who will be resistant to treatment? *Neurourol Urodyn* 2017;36:390–3.
34. Wessels JM, Kay VR, Leyland NA, Agarwal SK, Foster WG. Assessing brain-derived neurotrophic factor as a novel clinical marker of endometriosis. *Fertil Steril* 2016;105:119–28.e1–5.
35. Morotti M, Vincent K, Brawn J, Zondervan KT, Becker CM. Peripheral changes in endometriosis-associated pain. *Hum Reprod Update* 2014;20:717–36.
36. García-Solares J, Dolmans MM, Squifflet JL, Donnez J, Donnez O. Invasion of human deep nodular endometriotic lesions is associated with collective cell migration and nerve development. *Fertil Steril* 2018;110:1318–27.
37. Zondervan KT, Cardon LR, Kennedy SH. What makes a good case-control study? Design issues for complex traits such as endometriosis. *Hum Reprod* 2002;17:1415–23.
38. Missmer SA. Why so null? Methodologic necessities to advance endometriosis discovery. *Paediatr Perinat Epidemiol* 2019;33:26–7.

Asociación entre endometriosis y síntomas del tracto urinario inferior.

Objetivo: Determinar si las mujeres con endometriosis experimentan más a menudo síntomas del tracto urinario inferior (STUI) en comparación con aquellas mujeres sin endometriosis

Diseño: Análisis transversal al momento de enrolar una cohorte longitudinal

Escenario: Enrolamiento en 2 hospitales académicos y en la comunidad local

Paciente(s): Este análisis incluyó a 1161 mujeres con ($n = 520$) y sin ($n = 641$) endometriosis confirmada quirúrgicamente que fueron enroladas en el Estudio de Salud de la Mujer: de la Adolescencia a la Edad Adulta entre 2012 y 2018

Intervención(es): No aplicable

Medida(s) de resultado principal(es): Prevalencia de STUI, incluida la incontinencia de orina de esfuerzo, urgencia y frecuencia miccional, vaciamiento vesical incompleto, hematuria, disuria y dolor vesical, mediante cuestionarios estandarizados

Resultado(s): Los resultados primarios fueron que las mujeres con endometriosis reportaron con más frecuencia que aquellas sin endometriosis, lo siguiente: dificultad para orinar (7,9 % frente a 2 %, razón de probabilidad (OR) 4,14, intervalo de confianza (IC) 2,19–7,80; OR ajustada [ORa] 4,31 [IC del 95 %, 2,07–8,95]); sensación de vejiga llena después de orinar (18,8 % frente a 4,7 %; OR 4,73 [IC 95 %, 3,08–7,25]; ORa, 4,67 [IC 95 %, 2,88–7,56]); necesidad de volver a orinar minutos después de orinar (33,1 % frente a 17,0 %; OR 2,41 [IC 95 %, 1,83–3,18]; ORa 2,49 [IC 95 %, 1,81–3,43]), disuria (11,7 frente a 4,9 %; OR 2,55 [IC 95 %, 1,62–4,01]; ORa 2,38 [IC 95 %, 1,40–4,02]) y dolor cuando la vejiga está llena (23,0 % frente a 4,9 %; OR 5,79 [IC 95 %, 3,82–8,78]; ORa 6,04 [IC 95 %, 3,74–9,76]). Para los resultados secundarios, entre las mujeres participantes con endometriosis, observamos que las probabilidades de STUI no diferían según el estadio revisado de la Sociedad Estadounidense de Medicina Reproductiva (I/II frente a III/IV) o la duración de los síntomas asociados con la endometriosis.

Conclusión(es): Las mujeres con endometriosis confirmada quirúrgicamente fueron más propensas a informar STUI que aquellas sin endometriosis