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Secondary provoked vestibulodynia in sexually-active women with recurrent uncomplicated urinary tract infections
J Sex Med. 2013 Sep; 10 (9): 2265-73. doi: 10.1111/jsm.12242. Epub 2013 Jul 22.

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ABSTRACT

INTRODUCTION. Uncomplicated recurrent urinary tract infections (rUTIs) associated with uropathogenic Escherichia Coli (UPEC) are common among healthy, reproductive-aged women. Provoked vestibulodynia (PVD) is a major reason of sexual pain in premenopausal women.

AIM. To assess prevalence and predictors of secondary PVD in a cohort of Caucasian-European, heterosexual, sexually active, reproductive-aged women seeking medical help for rUTIs as their primary complaint.

METHODS. Clinical and psychometric variables for 60 consecutive patients with rUTIs were considered. Patients were assessed with a thorough medical and sexual history, a number of psychometric instruments, and a specific physical examination. Urinalysis and self-collected urine cultures from the previous 12 months were also examined.

MAIN OUTCOME MEASURE. Descriptive statistics and logistic regression models were used to test the associations between secondary PVD and sociodemographic and clinical variables.

RESULTS. Mean age was 34.2 years (median: 33 years; range: 21–42). Secondary PVD was found in 36 of 60 patients (60%). Women with PVD had a higher prevalence of urinary tract infections (UTIs) over the previous 12 months (χ^2: 4.54; $P = 0.03$) and suffered more frequently from UPEC-related rUTIs (χ^2: 5.92; $P = 0.01$) than those without PVD. Moreover, women with PVD showed significantly lower scores on Female Sexual Function Index domains (all $P \leq 0.01$), as compared with PVD-negative women. UPEC-related rUTIs (odds ratio [OR]: 3.1; $P = 0.01$), 6 or more UTIs over the previous 12 months (OR: 2.8; $P = 0.01$), and treatment with 3 or more antibiotics throughout the same period (OR: 2.1; $P = 0.04$) emerged as independent predictors of PVD.

CONCLUSIONS. Three of 5 Caucasian-European, heterosexual, sexually active women of reproductive age complaining of rUTIs as their primary disorder also suffer from secondary PVD. Uncomplicated UPEC-related rUTIs are more frequently associated with secondary PVD than are UTIs caused by different uropathogens.

INTRODUCTION

Vulvodynia is a chronic vulvar pain condition of uncertain etiology [1] that affects up to 16% of American women [2]. No specific prevalence data are available for the European population. Vestibulodynia, formerly known as *vulvar vestibulitis syndrome* (VVS), represents the most common form of vulvodynia [3,4] and is the most frequent cause of dyspareunia in young women [2,5]. Provoked vestibulodynia (PVD) is a condition in which pain is triggered by simple physical contact, touch, pressure, or stretching of the tissue around the vaginal opening, eventually resulting in an inability to engage in both coital and noncoital sexual attempts [4,6]. PVD is often acquired, and dyspareunia may appear after a period of pain-free sexual intercourse [7,8].

The etiology of PVD is heterogeneous and multifactorial: One of the most credible theories, originally developed for VVS, suggests that PVD may represent a chronic local inflammatory condition with a wide variety of causes [9]. Infections have been discussed extensively as possible causes of acquired PVD [10]. Many women with PVD have a history of vulvovaginal candidiasis [11]. Likewise, unambiguous literature also suggests a link between PVD and recurrent yeast vulvovaginal infections or genital human papillomavirus (HPV) infection [12-14]. Conversely, analysis of the potential pathophysiologic correlations between PVD and uncomplicated recurrent urinary tract infections (rUTIs) has been scant [12,15,16]. It is necessary to differentiate between women's sexual pain disorders that are potentially associated with the presence of urinary tract infections (UTIs)and those associated with interstitial cystitis/bladder pain syndrome, which has been discussed extensively in the literature [17,18].
UTIs are extremely common clinical entities affecting women throughout the life span [19]. Acute uncomplicated UTIs are among the most commonly encountered bacterial infections in women [20], with a reported incidence of 0.5 to 0.7 episode per woman each year [21]. Roughly 25% to 35% of women between the ages 20 and 40 have experienced an uncomplicated UTI [20], and a subset of these women complains of rUTIs. Sixty percent of rUTIs in women are post coital [19-21;22,23]. Uropathogenic *Escherichia coli* (UPEC) is the pathogen that causes uncomplicated UTIs in 75% to 90% of cases because UPEC has special features that allows it take advantage of the bladder environment [23,24].

AIMS

Given the significant prevalence of female sexual dysfunction in the context of urologic disorders [25] and the growing clinical observation of sexual complaints from women with rUTIs, we sought prevalence and predictors of PVD in a cohort of consecutively treated, Caucasian-European, heterosexual, sexually active women of reproductive age presenting for outpatient urologic evaluation of rUTIs as the primary disorder.

METHODS

Patients

From January 2009 to June 2012, demographic and clinical variables for 60 consecutively treated, Caucasian-European, heterosexual, sexually active women of reproductive age seeking medical help for rUTIs at the same urologic outpatient clinic were considered for this exploratory, prospective analysis. RUTIs were defined as 4 or more episodes that were documented by laboratory reports from the same local laboratory during the previous 12 consecutive months.
Patients were assessed with a thorough medical and sexual history, including use of combined hormonal contraception (CHC) during the previous 6 months. Health-significant comorbidities were scored with the Carlson Comorbidity Index (CCI) [26]. We used the *International Classification of Diseases, Ninth Revision, Clinical Modification* because its coding algorithms were used to define the 17 comorbidities that constitute the most widely used CCI. Eligible women met the following criteria:

- Were no younger than 18 and no older than 42 years of age
- Complained of bacterial rUTIs
- Had no significant menstrual cycle disorders and no history of dysmenorrhea or alteration of bleeding profile (especially not a period of amenorrhea longer than3 months at the onset of rUTIs), as defined by menstrual history during the previous 3 months
- Were not suffering presently and had not suffered in the past from genital herpes or HPV as well as lichen planus, Paget disease, and vulvar carcinoma
- Were not suffering presently and had not suffered in the past from any neurologic disease, which was also ruled out with the CCI compilation

- Had never received previous vulvar or vaginal surgery or vulvar treatments (any type)
- Did not suffer from introital dyspareunia before the onset of rUTIs.

Estimated body mass index (BMI), defined as weight in kilograms by height in square meters, was considered for each patient. For BMI, we used the cut-offs proposed by the US National Institutes of Health [27]: normal weight (18.5–24.9), overweight (25.0–29.9), obese (30.0–34.9).

Urinalysis and self-collected urine cultures from the previous 12 months were considered to classify the most frequently observed uropathogens. For the purpose of this study, only urine cultures obtained through clean-catch samples (void after cleaning) were considered for the analyses. In all cases, urine specimens were sent almost immediately to the local microbiology laboratory, where they were immediately inseminated on culture plates. Bacterial counts of urine specimens were estimated in the local laboratory using routine methods. The microbiologic definition of UTI was 10^5 or more colony-forming units per milliliter from midstream.

For the purpose of this analysis, patients were stratified according to their relationship status, which was defined as *stable sexual relationship* if the woman had the same sexual partner for 12 or more consecutive months or *no stable sexual relationship.* Likewise, patients were segregated according to their educational status into a low educational level (LL) group, which included patients with an elementary or secondary school education, and a high educational level (HL), which considered women with either a high school degree and/or a university or postgraduate degree.

Prevalence of lower urinary tract symptoms (LUTS) was analyzed in all subjects. To provide a frame of reference for interpreting voiding dysfunction, all subjects completed the American Urological Association Symptom Index (AUA-SI) [28], a validated 7-question, self-administered questionnaire with 3 questions dedicated to investigating filling symptoms and 4 entries assessing voiding symptoms.

The Female Sexual Function Index (FSFI) [29,30] was completed for all cases. Patients were also invited to answer 2 general assessment questions (GAQs) addressing sexual pain, with response options including *yes* or *no*: (1) “Over the past 4 weeks, have you experienced discomfort or pain during or after vaginal penetration?” (2) “Over the past 4 weeks, have you experienced pain in your vagina/genital area during or after sexual activity without penetration (eg, masturbation, oral sex)?”

All patients underwent a detailed physical examination of the external genitalia that was carried out by 2 independent physicians (A.S. and A.G. or R.E.N.). This exam included standard vulvar pain mapping with a cotton-tipped swab palpation [31]. Gentle pressure was applied systematically to the different parts of the vulva to assess the extent and the characteristics of pain. The test was performed at the 2, 4, 5, 6, 7, 8, 10, and 12 o’clock positions. When pain was reported, patients were asked to quantify it with a Visual Analog Scale (VAS; minimum of 0, maximum of 10) [32].

Literacy problems and other reading and writing problems were excluded for all patients. Data collection followed the principles outlined in the Declaration of Helsinki. All patients signed an informed consent agreeing to share their own anonymous information for future studies.

Main Outcome Measures

The primary end point of the present study was to evaluate whether rUTIs are frequently associated with secondary PVD (ie, the clinical manifestation of PVD following the onset of rUTIs) in women attending an outpatient clinic. PVD was defined as the triggering of pain by simple physical contact with or pressure to the vulvar vestibule without local visible findings at physical examination; clinically, vulvar pain results in the inability to engage in both coital and noncoital sexual attempts. The secondary end point was to assess potential predictors of PVD among women suffering from rUTIs.

Statistical Analyses

Data are presented as mean (median; range). The statistical significance of differences in means and proportions was tested with the 2-tailed *t* test and the Pearson χ^2 test, respectively. Univariable (UVA) and multivariable (MVA) logistic regression models tested potential predictors associated

with acquired PVD. Statistical tests were performed using MedCalc v.12.3.0 (MedCalc Software, Mariakerke, Belgium). All tests were 2-sided, with a significance level set at 0.05.

RESULTS

Table 1 lists patients' medical characteristics and descriptive statistics of the sample. Almost 77% of patients suffered from UPEC-related rUTIs, with other uropathogens almost equally distributed.
Table 2 details patients' sociodemographic and psychometric characteristics and descriptive statistics. Based on AUA-SI scores, women did not report clinically significant voiding dysfunction. Conversely, mean FSFI total score for the whole cohort of women was below the cut-off value for normality (ie, 26.55) previously suggested by Wiegel et al [33]; overall, 65% of women had an FSFI total score below the cut-off for normality (Table 2).
Based on patients' sexual histories, GAQs, and physical examinations, acquired PVD was found in 36 patients (60%), with 100% agreement among the physicians. Table 3 stratifies patients' characteristics according to positivity for PVD. Patients with and without PVD did not differ in terms of age, categorized BMI values, categorized CCI scores, history of CHC over the previous 6 months, educational levels, rates of stable sexual relationships, and mean AUA-SI scores. Conversely, women with PVD had higher numbers of UTIs over the previous 12 consecutive months and suffered more frequently from UPEC-related rUTIs than those without PVD (all $P \leq 0.03$). Moreover, patients with UPEC-related rUTIs complained of PVD more frequently than those with rUTIs associated with other uropathogens (32 of 46 [69.6%] vs 4 of 14 [28.6%] women, respectively; χ^2: 5.908; $P = 0.015$). More PVD patients had been treated with 3 or more different antibiotics over the previous 12 months than had PVD-negative women, although the difference did not reach statistical significance. Patients with PVD more frequently reported having first sexual intercourse at a younger age than those without sexual pain. Moreover, women complaining of PVD showed significantly lower scores for the FSFI total score and for the sexual desire, arousal, lubrication, satisfaction, and pain domains (all $P \leq 0.01$) than PVD-negative women. As expected, mean VAS score was higher for patients with PVD than for those without PVD.
At UVA, UPEC-related rUTIs and 6 or more UTIs over the previous 12 months were significantly associated with a higher risk of having PVD; conversely, women aged 23 or older at first sexual intercourse (vs 17 or younger) were protected from the risk of having PVD (all $P \leq 0.04$). No clear association emerged at UVA between PVD and any other variables (Table 4).
Similarly, at MVA, UPEC-related rUTIs, 6 or more UTIs over the previous 12 months, and treatment with 3 or more antibiotics over the previous 12 months emerged as independent predictors of PVD (all $P \leq 0.04$) (Table 4). In contrast, women aged 23 or older at first sexual intercourse (vs 17 or younger) were inversely associated with the risk of having PVD ($P = 0.01$). No clear association was found between PVD and any other variables at MVA (Table 4).

DISCUSSION

We tested prevalence and predictors of PVD in a relatively small cohort of consecutively treated, Caucasian-European, heterosexual, sexually active women of reproductive age seeking medical help for rUTIs as their primary disorder. Our findings show that 3 of 5 patients with rUTIs also suffered from secondary PVD, which emerged clinically as an acquired de novo disorder. We observed that PVD was significantly more frequent in women with uncomplicated UPEC-related rUTIs than in those with UTIs associated with other uropathogens. In the absence of adequate longitudinal studies, it cannot be assumed that UTIs were the cause of PVD; however, in terms of daily practice, these findings are of major importance because rUTIs are highly prevalent in women of any age [19-21]. In particular, 25% to 35% of women between the ages of 20 and 40 have experienced an uncomplicated UTI [20], with UPEC responsible for the vast majority [23,24].

Current results confirm previous observations that women with LUTS as a primary complaint may also suffer frequently from sexual dysfunction [18,25,34-37] that, for most, is either unknown or misunderstood by their urologists and/or gynecologists [34,38]. The clinical urgency of our findings lies in the fact that PVD, thought to be the most common form of chronic dyspareunia, has particularly high prevalence among young, reproductive-aged women [1]. Its onset is frequently associated with deleterious consequences for sexual function, well-being, and relationships, and its management is particularly difficult in young women with potential futures as sexual partners and as parents [39]. Moreover, notwithstanding the significant psychological distress known to be associated with vulvodynia [40], available data suggest that women reported a number of barriers related to seeking help for PVD [39]. This finding is even more true if the primary disorder is a urologic problem (ie, rUTI) that is considered to be of limited impact *quo ad vitam.*

The importance of the clinical conclusions of this study are further supported by the findings that the highest number of UTI episodes and the number of different types of antibiotic used emerged as independent predictors of PVD. These results are even more important given the possibility that repeated antibiotics (and, at least sometimes, abused antibiotic treatments) may promote the onset of recurrent vulvovaginal candidiasis, with a severe local inflammation process and a consequently greater risk of vulvodynia [11]. The potential association between *postmenopausal* sexual pain disorders and rUTIs, especially post coital, is potentially related to estrogen deficiency, which may affect genital arousal and vaginal lubrication as well as hypertonicity of the pelvic floor and greater susceptibility to urethral trauma and infections. The picture for premenopausal women is less clear.

Previous experimental evidence suggested that neuropathic pain mechanisms might be involved in vestibulodynia, formerly known as VVS [32,41,42]. Women with VVS were shown to have a significant increase in the number of intraepithelial nerve endings compared with controls [43,44]. An interesting murine model demonstrated that after 3 rounds of vulvar yeast infection—or a single, long (14- to 21-day), fully resolved infection with *Candida albicans*—mice become hypersensitive to touch in the vulvar area [45]. In the same experimental model, the allodynic mice displayed a significant increase in vulvar nerve fiber density, including peptidergic sensory and sympathetic fibers. Even more interesting, live yeast were not required to support the inflammatory status because injections of the yeast cell wall glucanzymosan produced the same chronic pain syndrome [45].

Recently, a significant correlation between recurrent vulvovaginal candidiasis and PVD was confirmed in women [11]. To our knowledge, our findings are among the first to support the clinical association between bacterial rUTIs and PVD [16]. As previously noted, we consider this observation clinically relevant because rUTIs are common among young, sexually active, and otherwise healthy women who have anatomically and physiologically intact lower urinary tracts [46]. Among those women, most of these infections are caused by UPEC [23,24,47], and the infections are truly new and not persistent [48]; fecal flora acts as an optimal reservoir for the same microbial strain that may subsequently recolonize the introitus and then the bladder and eventually may cause rUTI [49]. A second contributing possibility is that *E. coli* may cross the colonic mucosa (especially in those women complaining of irritable bowel syndrome and/or obstructive constipation, which can be associated with the so-called leaky gut syndrome) and may get into the blood stream and then into the bladder mucosa.

Moreover, it may be hypothesized that rUTIs trigger pelvic floor overactivity (more specifically, of the levator ani), thus eventually "narrowing" the vaginal introitus and predisposing the area to both microabrasion of the vestibular mucosa and microtrauma of the urethral area; in this context, the former condition could contribute to the onset of PVD, whereas the latter could predispose the bladder to further UTI. Speculatively, we think that UPEC per se may be able to act as a pathogen capable of causing damage at the level of the peripheral tissue (ie, the vestibule) including triggering the release of pro-inflammatory mediators and activating the cascade of events that induce and support the phenomenon of neurogenic inflammation, which has been recognized as the basis of vestibulodynia [10].

Our findings also suggest that secondary PVD was more frequently observed in women who had their first sexual intercourse at a younger age, possibly confirming previous studies. First, sexual pain may start from adolescence, with pain extending beyond intercourse to nonsexual contexts [50]. Second, the undisputed association between UTIs and recent sexual intercourse [51] may start with adolescence and puberty, with a consequent cascade of deleterious events for a woman's sexual health. Third, whereas age at first intercourse had already emerged as a well-established risk factor for HPV infection [52], analysis of the far more widespread problem of UPEC-related rUTIs and their devastating consequences for women's sexual health has been scant in the literature.

Interestingly, the association between VVS and CHC use was reported in women who had used CHC for a significantly longer period than their healthy counterparts [53]. Age at the beginning of CHC usage emerged as one of the predictors for VVS [53]. Similarly, Greenstein et al [54] showed that a significantly higher number of patients who were treated for VVS at the investigators' clinic had a history of low-dose estrogen compared with those women who used high-dose estrogen oral contraceptives. Our findings did not confirm these results because PVD was present equally in women with and without use of CHC, and CHC did not emerge as a significant predictor of PVD in patients with rUTIs.

Our study is not devoid of limitations. The study reports the results of a cross-sectional analysis conducted with a relatively small, homogenous cohort of women; therefore, these findings may be optimal for this cohort of same-race heterosexual women but would deserve external validation with an independent, larger sample. We used some GAQs, and we requested that patients complete the FSFI, both targeting the last 4 weeks before assessment; however, it is unclear whether the responses would be appropriate if sexual activities were not attempted. Our analyses lacked precise data about the actual frequency of sexual intercourse and the frequency of penetrative vaginal or anal intercourse. Moreover, we lacked comprehensive information about the use of vaginal lubricants or moisturizers and the type of condom used, if any. Although we could rule out genital candidiasis and yeast infections at the time of physical examination, we lacked precise data about the potential impact of recurrent vulvovaginal candidiasis; similarly, we lacked specific real-time culture to exclude any other vaginal pathogen that was not considered in the urine samples [11,16]. We lacked data about the local hormonal milieu, which clearly emerged as a key factor in promoting urogynecologic and women's sexual health [55-57]. In addition, this analysis lacked a careful evaluation of bowel function, with particular focus on the prevalence of constipation and the presence of typical irritable bowel syndrome [58,59]. Finally, the study lacked psychometric evaluation of pain-associated sexual distress.

CONCLUSIONS

These clinical findings show that 3 of 5 Caucasian-European, heterosexual, sexually active women of reproductive age complaining of rUTIs as the primary disorder also suffer from secondary PVD. Moreover, PVD is significantly more frequent in women with uncomplicated UPEC-related rUTIs than in those with UTIs associated with other uropathogens. The lack of longitudinal data prevents us from assuming that UTIs were the cause of acquired PVD. Given the high prevalence of rUTIs in women of any age and particularly in sexually active women of reproductive age, these findings emphasize the importance of investigating sexual health among women with urologic complaints and vice versa.

ACKNOWLEDGMENTS

The authors thank Dragonfly Editorial for reviewing the language in this manuscript.

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Table 1

Patients' medical characteristics and descriptive statistics (N = 60)

Age, y		
Mean (median)	34.2	(33)
Range	21–42	
BMI, kg/m^2		
Mean (median)	22.2	(24.0)
range	18.5–27.0	
BMI, n (%)		
Normal weight	42	(70.0)
Overweight	11	(18.3)
Class ≥1 obesity	7	(11.7)
CCI score		
Mean (median)	0.2	(0.0)
Range	0-2	
CCI, n (%)		
Score 0	54	(90.0)
Score ≥1	6	(10.0)
OC, n (%)	21	(35)
No. of UTI episodes (prior 12 mo), n (%)		
4	42	(70.0)
5	10	(16.7)
≥6	8	(13.3)
Uropathogens in urine cultures, n (%)		
Escherichia coli	46	(76.7)

Enterococcus faecalis	5	(8.3)
Staphylococcus spp	4	(6.7)
Ureaplasma urealyticum	2	(3.3)
Klebsiella, Proteus, Serratia	3	(5)
No. of different types of antibiotic over the prior 12 mo, n (%)		
1	39	(65.0)
2	11	(18.3)
≥3	10	(16.7)

Keys: BMI, body mass index; CCI, Charlson Comorbidity Index; OC, oral contraceptive; UTI, urinary tract infection.

Table 2

Patients' sociodemographic and psychometric characteristics and descriptive statistics (N = 60)

Educational status, n (%)		
LL	2	(3.3)
HL	58	(96.7)
Current relationship status, n (%)		
No stable sexual relationship	7	(11.7)
Stable sexual relationship ≥12 mo	53	(88.3)
Age at first intercourse, y		
Mean (median)	19.2	(18)
Range	12-35	
Age at first intercourse, n (%)		
≤17 y	21	(35)
18-22 y	28	(46.7)
≥23 y	11	(18.3)
AUA-SI, mean (median)	12.3	(13)
FSFI domains, mean (median)		
Desire	4.4	(4.5)
Arousal	4.4	(4.4)
Lubrication	3.2	(3.0)
Orgasm	4.2	(4.3)
Satisfaction	4.1	(4.0)
Pain	3.8	(3.5)
Total score	24.8	(25.0)
FSFI total score <26.55, n (%)	39	(65.0)

Keys: LL, low educational level; HL, high educational level; AUA-SI, American Urological Association Symptom Index; FSFI, Female Sexual Function Index.

Salonia A. Clementi MC. Graziottin A., Nappi RE. Castiglione F. Ferrari M. Capitanio U. Damiano R. Montorsi F.
Secondary provoked vestibulodynia in sexually-active women with recurrent uncomplicated urinary tract infections
J Sex Med. 2013 Sep; 10 (9): 2265-73. doi: 10.1111/jsm.12242. Epub 2013 Jul 22.

Table 3

Patient segregation according to positivity for provoked vestibulodynia (N = 60)

	PVD+		PVD−		*P* value*	95% CI
No. of patients (%)	36	(60.0)	24	(40)		
Age, y						
Mean (median)	34.2	(34)	33.6	(33)	0.47	−2.27, 1.07
Range	21–39		22–42			
BMI, kg/m^2						
Mean (median)	21.4	(23)	22.7	(24)	0.10	−0.26, 2.86
Range	18.5–27.0					
CCI, n (%)						
Score 0	32	(88.9)	22	(91.7)	0.93 (χ^2: 0.007)	−17.49, 19.43
Score ≥1	4	(11.1)	2	(8.3)		
CHC, n (%)	14	(38.9)	7	(29.2)	0.62 (χ^2: 0.245)	−17.3, 33.9
No. of UTI episodes (prior 12 mo), n (%)						
4	21	(58.3)	21	(87.5)	0.03 (χ^2: 4.54)	3.6, 49.34
5	8	(22.2)	2	(8.3)		
≥6	7	(19.4)	1	(4.2)		
Rates of uropathogens in urine cultures, n (%)						
Escherichia coli	32	(88.9)	14	(58.3)	0.01 (χ^2: 5.92)	5.98, 53.71
Other uropathogens	4	(11.1)	10	(41.7)		
No. of different types of antibiotic over the prior 12 mo, n (%)						
1	21	(58.3)	18	(75)	0.08 (χ^2: 3.11)	−0.5, 38.48
2	6	(16.7)	5	(20.8)		
≥3	9	(25.0)	1	(4.2)		
Educational status, n (%)						
LL	1	(2.8)	1	(4.2)	0.66 (χ^2: 0.19)	−11.05, 18.59
HL	35	(97.2)	23	(95.8)		

Current relationship status, n (%)						
No stable sexual relationship	3	(8.3)	4	(16.7)	0.56 (χ^2: 0.34)	−10.1, 30.14
Stable sexual relationship ≥12 mo	33	(91.7)	20	(83.3)		
Age at first intercourse, n (%)						
≤17 y	17	(47.2)	4	(16.7)	0.005 (χ^2: 7.76)	9.05, 54.35
18 – 22 y	17	(47.2)	11	(45.8)		
≥23 y	2	(5.6)	9	(37.5)		
VAS, mean (median)	7.3	(7.0)	1.8	(2.0)	<0.001	−6.16, −4.84
AUA-SI, mean (median)	13.3	(13)	12.5	(13)	0.22	−2.09, 0.49
FSFI domains, mean (median)						
Desire	2.5	(3.0)	4.3	(4.0)	<0.001	1.41, 2.19
Arousal	4.0	(4.0)	4.6	(4.0)	0.01	0.13, 1.07
Lubrication	3.0	(3.0)	3.6	(4.0)	0.006	0.18, 1.02
Orgasm	4.1	(4.0)	4.4	(4.2)	0.16	−0.12, 0.72
Satisfaction	2.7	(3.0)	4.6	(4.4)	<0.001	1.51, 2.29
Pain	1.8	(2.0)	4.8	(4.6)	<0.001	2.61, 3.39
Total score	19.4	(20.0)	26.3	(27.0)	<0.001	6.23, 7.57

Keys: BMI, body mass index; CCI, Charlson Comorbidity Index; CHC, combined hormonal contraception; UTI, urinary tract infection; LL, low educational level; HL, high educational level; VAS, Visual Analog Scale; AUA-SI, American Urological Association Symptom Index; FSFI, Female Sexual Function Index.
*P value according to χ^2 test or 2-tailed independent t test, as indicated.

Table 4

Logistic regression models predicting provoked vestibulodynia (N = 60)

Predictor	Univariable analysis		Multivariable analysis	
	OR	*P* value	OR	*P* value
Age	0.98	0.48	0.96	0.56
BMI	1.23	0.87	1.27	0.67
CCI (0 vs ≥1)	1.02	0.65	1.16	0.73
CHC use	1.15	0.45	1.05	0.53
Educational status (HL vs LL)	0.89	0.27	0.94	0.33
Stable relationship status	0.90	0.68	0.93	0.54
Age at first intercourse, ≥23 y vs ≤17 y	0.47	0.04	0.51	0.03
Uropathogens, UPEC vs others (any type)	2.8	0.03	3.1	0.01
No. of UTI episodes (prior 12 mo), ≥6 vs ≤5	2.6	0.02	2.8	0.01
No. of types of antibiotic (prior 12 mo), ≥3 vs ≤2	1.8	0.06	2.1	0.04

Keys: OR, odds ratio; BMI, body mass index; CCI, Charlson Comorbidity Index; OC, oral contraceptive; LL, low educational level; HL, high educational level; UTI, urinary tract infection; UPEC, uropathogenic *Escherichia coli.*