#### **ORIGINAL ARTICLE**



# Lower Urinary Tract Symptoms in Greek Women After Menopause: The LADY Study

Irene Lambrinoudaki<sup>1</sup> · Nikoletta Mili<sup>1</sup> · Areti Augoulea<sup>1</sup> · Eleni Armeni<sup>1</sup> · Panagiotis Vakas<sup>1</sup> · Konstantinos Panoulis<sup>1</sup> · Nikolaos Vlahos<sup>1</sup> · Themistoklis Mikos<sup>2</sup> · Grigorios Grimbizis<sup>2</sup> · Alexandros Rodolakis<sup>3</sup> · Stavros Athanasiou<sup>3</sup>

Received: 2 August 2023 / Accepted: 15 November 2023 / Published online: 27 January 2024 © The International Urogynecological Association 2024

#### Abstract

**Introduction and hypothesis** The genitourinary syndrome of menopause (GSM), apart from symptoms related to vulvovaginal atrophy (VVA), also consists of lower urinary tract symptoms (LUTS). Based on the common embryological origin of the genital and lower urinary system, the presence of estrogen receptors, and the high prevalence of VVA and LUTS in the menopausal population, the two conditions can coexist. This study is aimed at investigating the prevalence and risk factors of LUTS in a sample of Greek peri- and postmenopausal women.

**Methods** Four hundred and fifty (450) women, aged 40–70 years, attending three outpatient gynecology clinics for routine examination, completed a structured interview and responded to a validated questionnaire (International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms, ICIQ-FLUTS).

**Results** Urinary urgency or frequency affected 51.6% and dysuria 43.6% of the participants. Mild urgency or frequency was described by 25.6%, moderate by 14.4%, and severe by 11.6% of the women. Mild dysuria was reported by 26.26%, moderate by 5.8%, and severe by 11.6%. Age, weight, BMI, and number of pregnancies and abortions correlated with a higher ICIQ-FLUTS score. Women with moderate/severe symptoms of VVA, such as irritation, a burning sensation, and pruritus of the vulva or vagina, had a higher ICIQ-FLUTS score than women without such symptoms (beta coefficient 2.42, CI 1.204, 3.635, p < 0.001).

**Conclusions** Lower urinary tract symptoms are very common among peri- and postmenopausal women and are linked to symptoms of VVA. Our data support the need for prompt evaluation of women transitioning to menopause, as these symptoms compromise the quality of life.

Keywords LUTS · Genitourinary syndrome of menopause · Vulvovaginal atrophy · Postmenopause

Irene Lambrinoudaki and Nikoletta Mili contributed equally to this work

Handling Editor: Catherine Matthews Editor in Chief: Maria A. Bortolini

Irene Lambrinoudaki ilambrinoudaki@med.uoa.gr

- <sup>1</sup> Second Department of Obstetrics and Gynecology, Medical School, National and Kapodistrian University of Athens, Aretaieio Hospital, Athens, Greece
- <sup>2</sup> First Department of Obstetrics and Gynecology, Medical School, Aristotle University of Thessaloniki, Papageorgiou Hospital, Thessaloniki, Greece
- <sup>3</sup> First Department of Obstetrics and Gynecology, Medical School, National and Kapodistrian University of Athens, Alexandra Hospital, Athens, Greece

# Introduction

The Genitourinary Syndrome of Menopause (GSM) is a relatively novel term, defined by the Society for the Study of Women's Sexual Health (ISSWSH) and the Board of Trustees of The North American Menopause Society (NAMS) [1]. Apart from the classical symptoms of vulvovaginal atrophy (VVA), GSM also consists of lower urinary tract symptoms (LUTS) such as urinary urgency, frequency, and lower urinary tract pain, as well as urinary incontinence (UI) and voiding dysfunction [1]. The symptoms attributed to GSM can affect not only well-being but also the health-related quality of life [2, 3].

Embryologically, both the genital and lower urinary tract originate from the primitive urogenital sinus [4].

Tissue-specific analyses have demonstrated the presence of estrogen receptors (ERs) as well as progesterone receptors (PRs) in the squamous epithelium of both the proximal and distal urethra in areas of the bladder trigone and in certain pelvic floor muscles [4]. Consequently, postmenopausal estrogen deprivation leads to atrophy of the urethral epithelium, loss of periurethral collagen, and decreased sensitivity of urethral smooth muscle [5]. Thus, progressively after the menopausal transition, the function of the lower urinary tract becomes less efficient, triggering bothersome LUTS.

The prevalence of LUTS is particularly high with increasing age, affecting 10.5% of women at the age of 30–39 years to about 26% at the age of 70–79 years. Affected women report a lower quality of life and a negative impact on productivity, sleep, and sexual satisfaction [6]. Nevertheless, despite the extent of the problem, the majority of patients remain reluctant to seek medical help and to receive treatment [7]. This paradox is caused by stigma and shame surrounding urogynecological conditions. Limited health education on the cause and any available treatment options lead to the belief of many women that such symptoms come with the menopause and they have to bear with them [8].

Given the strong mediating effect of estrogen deficiency with regard to the development of LUTS following the menopausal transition, the efficacy of hormonal options, and nonhormonal alternatives has been explored. Concerning hormone treatment (HT), both systematic and local hormone therapy has been used to alleviate these symptoms [9]. Several studies indicate that only vaginal hormonal preparations have positive effects on LUTS, and that systemic HT may have a negative impact on UI [10]. The therapeutic effects of topical hormone therapy subside when the treatment is no longer used [11]. Current research has been shifted on the effect of laser therapy on collagen remodeling and the more sustainable amelioration of GSM and LUTS. Although the effects of laser treatments appear promising in alleviating GSM symptoms [12-14], its efficacy compared with sham treatment still remains controversial, as more RCTs are needed to draw final conclusions [14, 15]. Taking into consideration the high prevalence of urinary symptoms and the burden to the quality of life of aging woman, primary prevention practices should be aimed at identifying the most appropriate type of treatment according to the individual components of GSM, to offer appropriate individualized therapeutic strategies. Therefore, the aim of this study was to explore the prevalence of LUTS, risk factors and the interrelation between LUTS and symptoms of VVA in a group of Greek peri- and postmenopausal women attending routine gynecological screening.

#### **Materials and Methods**

The LADY (EpidemioLogical charActeristics of prevalent anD new genitourinarY syndrome of menopause cases in Greece) study was aimed at evaluating features related to the diagnosis of GSM in Greek women. The protocol was approved by the University Ethics Committee of Aretaieion Hospital, National and Kapodistrian University of Athens (224/18-06-2020). For the purposes of this study, all peri- or postmenopausal women who were visiting for the first time any of the three participating outpatient gynecological clinics for assessment and advice on climacteric symptoms in Greece between November 2020 and June 2022 were invited to participate in a structured face-to-face interview.

Inclusion criteria consisted of age between 40 and 70 years, and a peri- or postmenopausal status. GSM was diagnosed in women who experienced at least two bothersome vaginal symptoms or the presence of  $\geq 1$  symptom and one clinical sign corresponding to GSM. Postmenopause was defined in women with a history of at least 12 months of amenorrhea. Perimenopause was defined in those with bothersome menopausal symptoms and evidence of menstrual irregularity over the last 12 months. Four hundred and fifty (450) women agreed to participate, and signed informed consent. There was no statistically significant difference between responders and nonresponders with regard to age, anthropometric, or demographic characteristics.

During the first clinic consultation, anthropometric and demographic data, lifestyle, personal, obstetrical/gynecological history, as well as any intake of medications, were recorded. We measured height and weight, and calculated the body mass index as weight (kg) divided by height [2]  $(m)^2$ . Immediately thereafter, a trained gynecologist completed a gynecological evaluation.

In a structured face-to-face interview during their outpatient clinic visit, women were offered the option to complete the translated Greek version of the International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms (ICIQ-FLUTS) questionnaire [16]. Further questions included enquiry regarding the presence and severity of vulvovaginal symptoms (vaginal dryness, irritation, burning sensation, pruritus of the vulva or vagina, decreased lubrication during sexual activity, dyspareunia, postcoital bleeding), previous GSM diagnosis, previous or concurrent GSM treatment, and documentation of any previous consultation on vaginal health with their health care provider.

#### **ICIQ-FLUTS** Questionnaire

This questionnaire is aimed at evaluating the presence of female LUTS and the impact on quality of life during the previous 4 weeks. The questionnaire consists of 12 items assessed on a five-point Likert scale [16, 17]:

- 1. Nocturia
- 2. Urgency
- 3. Bladder pain
- 4. Frequency
- 5. Hesitancy
- 6. Straining
- 7. Intermittency
- 8. Urge urinary incontinence
- 9. Frequency of urinary incontinence
- 10. Stress urinary incontinence
- 11. Unexplained urinary incontinence
- 12. Nocturnal enuresis

The sum of the scores corresponding to the questions 1 to 4 added together correspond to the filling symptoms subscale. The sum of the scores corresponding to the questions 5, 6, and 7 added together correspond to the voiding symptoms subscale. The sum of the scores corresponding to the questions 8 up to 12 added together corresponds to the incontinence symptoms subscale. Every question has a second element corresponding to the severity of the symptom assessed. The total ICIQ-FLUTS score was estimated after the addition of the mean value of the score that corresponded to each of the questions.

#### **Statistical Analysis**

Statistical Analysis was performed using R version 4.2.2. The analysis was performed on all patients who had an ICIQ-FLUTS score evaluation.

Initial statistical analysis was based on descriptive statistics to provide an overview of all study data. Categorical variables were described by absolute and relative frequencies (based on the number of available data). For continuous variables we present mean values  $\pm$  standard deviation (SD), median, minimum and maximum values. All tests performed were two-sided and the significance level was set to  $\alpha = 0.05$ .

The relationship between baseline characteristics and the ICIQ-FLUTS score was assessed using the one-way analysis of variance (ANOVA) parametric test for categorical variables and the independent samples *t* test for continuous variables.

The main analysis focused on the investigation of independent factors affecting the ICIQ-FLUTS score. A multivariate generalized linear model was used. The dependent variable was the ICIQ-FLUTS score. The parameters tested for inclusion in the model were age, educational level (none/primary, secondary, higher/tertiary/postgraduate title), area of permanent residence (urban, rural), marital status (single, married, divorced/widowed), employment status (unemployed/household, working, retired), body mass index (BMI), smoking status (nonsmoker, current/ex-smoker), alcohol consumption (none, low, moderate/high), age at menarche, menopause, number of pregnancies, number of abortions, osteoporosis treatment (yes, no), treatment for thyroid disease (yes, no), treatment for cardiovascular disease (yes, no), statins (yes, no), irritation, burning sensation, pruritus of vulva or vagina (absent/mild, moderate/severe), dyspareunia (absent/mild, moderate/severe), postcoital bleeding (absent/mild, moderate/severe). The selection of the final independent variables was based on the Akaike information criterion and a backward selection procedure with a threshold of 0.05. The magnitude of association between the resulting independent variables and ICIQ-FLUTS score was expressed as odds ratios followed by corresponding confidence interval (95% CI).

## Results

### **Study Population**

The sample population was retrieved after carefully screening an original cohort of 614 women, of whom 164 did not agree to participate in the study. Of the 450 women enrolled in the study, 449 were included in the final analysis (1 woman was excluded because of incomplete data in the ICIQ-FLUTS questionnaire).

Our sample population consisted of women with a mean age of  $58.25 \pm 6.8$  years and 93% of them were postmenopausal. The majority of women were married and resided in a metropolitan area. Eighty-seven percent of the participants had a secondary or higher education and 46% were employed. The detailed demographic characteristics and gynecological history of our study population as well as the ICIQ-FLUTS score are presented in Table 1.

Only 39 individuals (8.7%) were presently undergoing some form of treatment for VVA symptoms. More specifically, 5.8% were using simple measures such as vaginal lubricants and moisturizers, 2.4% were using topical estrogens, 0.9% were under systemic hormone replacement therapy (HRT), and 0.7% were using other forms of treatment. Fifty women (11.11%) had used at least one treatment option in the past but had eventually stopped the therapy. Among those, over the counter products were once again the most commonly utilized therapeutic options (68% of past treatment users), topical estrogens had been prescribed to a mere 18% and HRT to 6% of women who had previously received treatment, whereas other forms of treatment had been used by 1.1%.

#### Prevalence of Lower Urinary Tract Symptoms

In our study urinary urgency or frequency affected 51.6% of the participants. Mild urgency or frequency was described by 25.6%, moderate by 14.4%, and severe by 11.6% of the

**Table 1** Patients' gynecological history and demographic charac-<br/>teristics in relation to the International Consultation on Inconti-<br/>nence Questionnaire Female Lower Urinary Tract Symptoms (*ICIQ-FLUTS*) score

		Mean ICIQ- FLUTS score	p value*
Age, years, mean $\pm$ SD	$58.28 \pm 6.8$		
Body mass index, mean $\pm$ SD	$27.3 \pm 4.9$		
Educational level, n (%)			0.032
None/primary education	52 (11.58)	10.21 (6.9)	
Secondary education	168 (37.42)	8.80 (6.3)	
Higher education/tertiary educa- tion/postgraduate title	229 (51.00)	7.83 (5.9)	
Area of permanent residence, <i>n</i> (%)			0.032
Urban	398 (88.64)	8.24 (6.2)	
Rural	51 (11.36)	10.24 (6.0)	
Marital status, n (%)			0.243
Single	34 (7.58)	7.59 (6.0)	
Married	341 (75.95)	8.33 (6.0)	
Divorced/widowed	74 (16.47)	9.50 (7.2)	
Employment status, $n$ (%)			0.014
Employed	207 (46.10)	7.66 (5.7)	
Unemployed/household	105 (23.39)	9.83 (7.0)	
Retired	137 (30.51)	8.65 (6.3)	
Smoking status, n (%)			0.878
Never	293 (65.26)	8.44 (6.2)	
Former/current	156 (34.74)	8.53 (6.3)	
Alcohol intake, n (%)			0.223
None	305 (67.93)	8.60 (6.7)	
Low	132 (29.40)	7.95 (5.0)	
Moderate/high	12 (2.67)	11.00 (5.3)	
Number of life births, $n$ (%)			<0.001
0	25 (5.57)	7.36 (5.4)	
1	56 (12.47)	7.11 (5.5)	
2	142 (31.63)	7.32 (5.3)	
3	96 (21.38)	8.47 (5.5)	
≥4	130 (28.95)	10.52 (7.5)	
Number of vaginal deliveries, <i>n</i> (%)			0.004
0	109 (24.28)	7.14 (5.3)	
1	62 (13.81)	7.73 (6.3)	
2	198 (44.10)	8.67 (6.0)	
≥3	80 (17.82)	10.36 (7.3)	
Number of Cesarean sections, $n(\%)$			0.457
0	363 (80.85)	8.65 (6.3)	
1	50 (11.13)	7.74 (5.6)	
≥2	36 (8.02)	7.67 (5.9)	
Number of abortions, n (%)			0.002
0	281(62.58)	7.80 (5.7)	
1	80 (17.82)	8.65 (6.2)	
≥2	88 (19.60)	10.45 (7.4)	

Bold indicates statistical significance which was set at the level of p-value <0.05

\*One-way ANOVA

**Table 2**Pearson correlation of patients' characteristics with the Inter-<br/>national Consultation on Incontinence Questionnaire Female Lower<br/>Urinary Tract Symptoms (*ICIQ-FLUTS*) score

	r	p value
Age (years)	0.116	0.014
Height (cm)	0.021	0.655
Weight (kg)	0.151	0.001
BMI (kg/m <sup>2</sup> )	0.155	0.001
Age at menarche (years)	0.091	0.054
Number of pregnancies	0.261	<0.001
Number of abortions	0.241	<0.001

Bold indicates statistical significance which was set at the level of p-value <0.05

women. Mild dysuria was reported by 26.26%, moderate by 5.8%, and severe by 11.6%.

#### **Factors Affecting LUTS Presence**

Age, weight, and higher BMI correlated with a higher ICIQ-FLUTS score. The number of pregnancies as well as the number of abortions also had a positive correlation with a higher ICIQ-FLUTS score (Table 2). In the linear regression model higher BMI (ß 0.131, 95% CI 0.016, 0.247) and the number of pregnancies (\$ 0.0578, 95% CI 0.156, 0.999) were associated with an ICIQ-FLUTS score increase (Table 3). Almost one third of the women included in this study (28.22%) were receiving treatment for cardiovascular disease (CVD). CVD treatment is associated with the presence of dysuria (OR 2.279, 95% CI 1.394, 3.726, p < 0.001). It is also associated with the severity of dysuria (OR 2.295, 95% CI 1.434, 3.673, p < 0.001) and urinary frequency (OR 1.563, 95% CI 1.035, 2.362, p < 0.033). Further adjustment for the use of HRT did not change the significance of the observed associations.

# Lower Urinary Tract and Vulvovaginal Atrophy Symptoms

Women who suffered from irritation, a burning sensation, or pruritus of the vulva or vagina had a higher ICIQ-FLUTS score ( $10.4 \pm 7.4$ ) than those who did not report any of those symptoms ( $7.7 \pm 5.5$ ; Table 4). In the linear regression model, irritation, a burning sensation, or pruritus of the vulva or vagina was also related to a higher ICIQ-FLUTS score ( $\beta$  2.42, 95% CI 01.204, 3.635). In addition, as shown in Fig. 1a, women with moderate or severe symptoms had a higher ICIQ-FLUTS score than those who presented none or mild irritation, burning, **Table 3** Linear regression model for the presence of independent fac-tors affecting the International Consultation on Incontinence Ques-tionnaire Female Lower Urinary Tract Symptoms (*ICIQ-FLUTS*)score.

	ß	SE	95% CI	p value
Area of permanent residenc	e			
Urban	_	_	_	
Rural	1.660	0.898	-0.104, 3.425	0.065
BMI (kg/m <sup>2</sup> )	0.131	0.059	0.016, 0.247	0.025
Total number of life births	0.578	0.214	0.156, 0.999	0.007
Number of abortions	0.494	0.291	-0.078, 1.065	0.090
Irritation, burning sensation, pruritus of the vulva or vagina				
Absent/mild	_	_	_	
Moderate/severe	2.420	0.619	1.204, 3.635	<0.001

Selection of final variables for inclusion in the model was done based on the Akaike information criterion

Variables considered for inclusion in the model were age, educational level (none/primary, secondary, higher education/tertiary education/ postgraduate), area of permanent residence, marital status (single, married, divorced/widowed), employment status (unemployed/household, working, retired), BMI, smoking status (nonsmoker, ex/current smoker), alcohol consumption (none, low, moderate/high), menarche, menopause, total gravidity, number of abortions, treatment for osteoporosis, treatment for thyroid disease, treatment for cardiovascular disease, statin use, as well as the symptoms vaginal dryness, irritation, burning sensation, pruritus of the vulva or vagina, dyspareunia, postcoital bleeding (absent/mild, moderate/severe)

Bold indicates statistical significance which was set at the level of *p*-value

SE standard error, CI confidence interval

or pruritus. We also found that gravidity also affects the ICIQ-FLUTS score in symptomatic women. In particular, women with an obstetrical history of more than four pregnancies and the presence of irritation, a burning sensation, and pruritus had a significantly increased ICIQ-FLUTS score (Table 1 and Fig. 1b).

## Discussion

The results of our study indicate that LUTS affect one out of two Greek peri- and postmenopausal women, greatly interfering with their everyday life and activity. In addition, symptoms such as pruritus of the vulva or vagina, local irritation or a burning sensation appear to be most significantly associated with the severity of LUTS. The experience of bothersome LUTS was associated not only with vaginal dryness but also with BMI and the number of deliveries.

The prevalence of LUTS in different studies varies because of discrepancies in assessed symptoms, definitions, and different questionnaires, as well as because of the variations in the reproductive status of the evaluated women. In the Japan Nurse's Health study overactive bladder (OAB), **Table 4** Evaluation of the International Consultation on Incontinence Questionnaire Female Lower Urinary Tract Symptoms (*ICIQ-FLUTS*) score according to symptoms of vulvovaginal atrophy (N = 449)

	Ν	Mean ICIQ- FLUTS score (SD)	p value*
Vaginal dryness			0.2
Yes	185	8.89 (6.1)	
No <sup>a</sup>	264	8.17 (6.3)	
Irritation, burning sensation, pruri- tus of the vulva or vagina			<0.001
Yes	128	10.42 (7.4)	
No	321	7.69 (5.5)	
Reduced lubrication during sexual activity			0.6
Yes	169	8.64 (5.9)	
No	280	8.37 (6.5)	
Dyspareunia			0.4
Yes	130	8.89 (6.2)	
No	319	8.30 (6.3)	
Postcoital bleeding			0.3
Yes	15	10.07 (6.4)	
No	434	8.41 (2.6)	

Bold indicates statistical significance which was set at the level of p-value

\*t test

<sup>a</sup>In all categories "No" includes patients with absence of the corresponding symptom or presence to a mild degree

stress urinary incontinence (SUI), and mixed urinary incontinence (MUI) were present in 9.5%, 13.9%, and 2.1% of women with a mean age of 46.5 years respectively [18]. In an Australian Study that included women aged 25–80 years, the overall prevalence of any UI was 41.7% [19]. Ohta et al. [20], recruited 10,000 Japanese women aged between 40 and 90 years, with a mean age of  $55.9 \pm 9.4$  years and found that 21.7% had UI and 20.0% had frequent urination.

The LADY study showed that the presence of LUTS was associated with age, weight, BMI, as well as the number of deliveries. The association between an experience of LUTS in older women of higher weight as well as multiparity is not surprising, and has been previously repeatedly documented in women of young and more advanced reproductive age [21–24]. More studies were aimed at determining if specifically, the menopausal transition period is associated with the development of UI symptoms. In a number of studies, the climacteric appears to be the main period of life where women are at risk of developing UI [25, 26]. Nagai et al. in the Japan Nurse's Health study, found that a significant increase in OAB prevalence was observed in the 45- to 54-year age group, indicating a nonlinear association with age [18]. Findings from the SWAN study have shown that



Irritation, burning sensation, pruritus of vulva or vagina

Moderate

Mild

Fig. 1 a Mean International Consultation on Incontinence Questionnaire (ICIQ) score according to the severity of the irritation, burning sensation, pruritus of the vulva or vagina. b Mean ICIQ score

Absent

the peri-menopausal status is associated with developing UI (early peri-menopause: HR 1.34, 95% CI 1.04, 1.68; late peri-menopause: HR 1.52, 95% CI 1.12, 2.05). A decrease in incontinence symptoms was found postmenopause (HR 0.57, 95% CI 0.34, 0.95) [27]. Factors that coincide and can be related to the menopause, such as aging, weight gain, nonrestorative sleep, depression, and anxiety, seem to be related to developing LUTS postmenopause rather than estrogen decline [28, 29].

Moreover, we found a significantly higher burden of LUTS in women who experience certain GSM symptoms,

by symptom of irritation, burning sensation, pruritus of the vulva or vagina, and by gravidity

Severe

namely irritation, a burning sensation or pruritus, but no link with VVA, as opposed to those without any symptoms, in this large sample of Greek peri- and postmenopausal women. Cagnacci et al., in the ANGEL study, evaluated 518 women (aged 40–55 years) and reported that more than 75% of the participants were distressed owing to LUTS. Similar to our findings, the ANGEL study did not reveal a consistent association of LUTS with VVA, after controlling for the presence of recurrent urinary tract infections. Among VVA symptoms only dyspareunia was associated with OAB [30]. In the Genisse study, among 430 postmenopausal women



Fig. 1 (continued)

with a mean age of 58.1 years, the risk of GSM diagnosis was significantly higher in women with SUI (OR 3.30; 95% CI 1.52, 7.15; p=0.001); MUI (OR 8.43; 95% CI 1.12, 63.69; p=0.01); OAB (OR 18.44; 95% CI 1.11, 307.50; p=0.002) [31].

The involvement of estrogens in LUTS management is contentious. Although biochemical studies show that estrogens have a favorable effect on the lower urinary tract, some clinical investigations show either benefits, mostly concerning OAB symptoms, or worsening, primarily in SUI symptoms [21, 32]. Results from a 2012 Cochrane review showed that systemic oral estrogens had a negative impact on UI independently of hysterectomy history and progestogen use (risk ratio [RR] 1.32, 95% CI 1.17 to 1.48). The same study concluded that topical estrogens may have beneficial effects on UI (RR 0.74, 95% CI 0.64 to 0.86) [33]. Data from large studies, such as the Women's Health Initiative (WHI) and the Nurse's Health Study advised against the prescription of systemic hormone therapy to treat UI [34-36]. These findings in combination with the peak of UI in perimenopause when hormone therapy is mainly prescribed, raise the question whether this peak could be iatrogenic.

On the other hand, some data support the use of topical estrogen therapy mainly for OAB. In a study that evaluated the urodynamic effects of vaginal estriol in women with GSM and OAB, there was significant improvement in first desire to void and maximum cystometric capacity [37]. In a randomized control trial (RCT) of 59 women, when compared with oxybutynin, vaginal estrogen appeared to be equally beneficial in reducing the frequency of day-time voids [38]. In addition, another RCT supports the notion that a combination of vaginal estrogen cream and

antimuscarinics could potentially constitute a therapy for postmenopausal women with OAB [39]. Nevertheless, in another study aimed at comparing the efficacy of antimuscarinics alone versus in combination with local estrogens for OAB, no synergistic effect was found [40].

Research conducted on animals suggests that androgens, such as testosterone, might play a crucial role in the female pelvic floor and lower urinary tract [41]. In fact, experiments conducted on rats have shown that testosterone exhibits both preventive and curative properties in models of SUI [42]. Recent studies have also revealed that androgen receptors are densely concentrated in the muscles of the pelvic floor. As women age, their serum testosterone levels tend to decline, with the most significant decrease occurring before menopause [43]. Low levels of serum testosterone have been associated with a higher likelihood of stress and mixed incontinence in women [43]. Considering the role of pelvic musculature in maintaining the support of the urethra and the positive impact of androgens on skeletal muscle, more extensive investigations are required to ascertain the exact contribution of androgens in women with UI, pelvic organ prolapse, and other lower urinary tract disorders [44, 45].

Our study presents several strengths. First, it benefits from a substantial sample size and the inclusion of three prominent gynecological clinics situated in distinct regions across the country. Moreover, the utilization of face-to-face interviews and comprehensive gynecological examinations enhances the depth and objectivity of the data collected.

There are certain limitations to our study. The research cohort was drawn from outpatient gynecological clinics at university hospitals and hence may not be representative of the overall peri- and postmenopausal population. Furthermore, the cross-sectional design precludes the discovery of causation. Surgical history was not recorded. Although LUTS may impact women's sexual function, the study design did not incorporate an assessment of sexual function. Additionally, the prevalence of urinary tract infections and their relationship with LUTS was not explored in the current study.

The results of the LADY study and others [30, 31] suggest an interrelation between VVA symptoms and symptoms indicative of urinary atrophy, even prior to the development of clinical signs of VVA. Urinary and/ or vaginal infections are known to be linked to alterations of the urogenital microbiome [46, 47]. The latter is subjected to further modifications triggered by the periand postmenopausal hormone changes, and particularly estrogen deficiency [48, 49]. The time-line of the pathophysiological changes observed in the vaginal and urinary epithelium, during the menopausal transition, has not yet been fully elucidated.

# Conclusion

Lower urinary tract symptoms are highly prevalent in periand postmenopausal women, particularly in women presenting symptoms of VVA. In our study a significantly higher ICIQ-FLUTS score was observed only in women who suffered from irritation, a burning sensation, and pruritus of the vulva or vagina. These findings support the need for a thorough assessment of genitourinary health after the menopausal transition, as these symptoms, if left untreated, compromise the quality of life.

## Declarations

**Conflicts of Interest** The study was sponsored by ITF-Hellas. The company sponsored the collection of data. The company was not involved in the conception, design, data analysis and interpretation or drafting and editing of the manuscript.

# References

- Portman DJ, Gass MLS, Kingsberg S, et al. Genitourinary syndrome of menopause: New terminology for vulvovaginal atrophy from the international society for the study of women's sexual health and the North American Menopause Society. Menopause. 2014;21(10):1063–8. https://doi.org/10.1097/gme.00000000000329.
- Nappi RE, Martini E, Cucinella L, et al. Addressing vulvovaginal atrophy (VVA)/genitourinary syndrome of menopause (GSM) for healthy aging in women. Front Endocrinol (Lausanne). 2019;10:561 https://doi.org/10.3389/fendo.2019.00561.

- Baquedano Mainar L, Sánchez Méndez S, Dieste Pérez P, et al. Women's knowledge about the genitourinary syndrome of menopause: adherence to its treatments in the COVID-19 era in a sample of them: COMEM-GSM study. BMC Womens Health. 2021;21(1):398. https://doi.org/10.1186/S12905-021-01548-2.
- Robinson D, Toozs-Hobson P, Cardozo L. The effect of hormones on the lower urinary tract. Menopause Int. 2013;19(4):155–62. https://doi.org/10.1177/1754045313511398.
- Robinson D, Cardozo LD. The role of estrogens in female lower urinary tract dysfunction. Urology. 2003;62:45–51. https://doi. org/10.1016/S0090-4295(03)00676-9.
- Kupelian V, Wei JT, O'Leary MP, et al. Prevalence of lower urinary tract symptoms and effect on quality of life in a racially and ethnically diverse random sample: the Boston Area Community Health (BACH) Survey. Arch Intern Med. 2006;166(21):2381–7. https://doi.org/10.1001/ARCHINTE.166.21.2381.
- Minassian VA, Yan X, Lichtenfeld MJ, Sun H, Stewart WF. The iceberg of health care utilization in women with urinary incontinence. Int Urogynecol J. 2012;23(8):1087. https://doi.org/10. 1007/S00192-012-1743-X.
- Shaw C, Tansey R, Jackson C, Hyde C, Allan R. Barriers to help seeking in people with urinary symptoms. Fam Pract. 2001;18(1):48–52. https://doi.org/10.1093/fampra/18.1.48.
- Parker WP, Griebling TL. Nonsurgical treatment of urinary incontinence in elderly women. Clin Geriatr Med. 2015;31(4):471–85. https://doi.org/10.1016/J.CGER.2015.07.003.
- Milsom I, Gyhagen M. Does the climacteric influence the prevalence, incidence and type of urinary incontinence? Climacteric. 2023;26(2):75–9. doi:https://doi.org/10.1080/13697137.2022. 2158730.
- Escobar C, Rosenblum N. Vaginal estrogen—what a urologist should know. Urology. 2021;151:37–43. https://doi.org/10.1016/j. urology.2020.05.034.
- Khamis Y, Abdelhakim AM, Labib K, et al. Vaginal CO2 laser therapy versus sham for genitourinary syndrome of menopause management: a systematic review and meta-analysis of randomized controlled trials. Menopause. 2021;28(11):1316–22. https://doi.org/10.1097/GME.00000000001845.
- Page AS, Verbakel JY, Verhaeghe J, Latul YP, Housmans S, Deprest J. Laser versus sham for genitourinary syndrome of menopause: a randomised controlled trial. BJOG. 2023;130(3):312–9. https://doi.org/10.1111/1471-0528.17335.
- Cruff J, Khandwala S. A double-blind randomized sham-controlled trial to evaluate the efficacy of fractional carbon dioxide laser therapy on genitourinary syndrome of menopause. J Sex Med. 2021;18(4):761–9. https://doi.org/10.1016/J.JSXM.2021. 01.188.
- Mension E, Alonso I, Anglès-Acedo S, et al. Effect of fractional carbon dioxide vs sham laser on sexual function in survivors of breast cancer receiving aromatase inhibitors for genitourinary syndrome of menopause: the LIGHT randomized clinical trial. JAMA Netw Open. 2023;6(2):e2255697. https://doi.org/10.1001/jaman etworkopen.2022.55697.
- Athanasiou S, Stavros A, Grigoriadis T, et al. The validation of international consultation on incontinence questionnaires in the Greek language. Neurourol Urodyn. 2012;31(7):1141–4. https:// doi.org/10.1002/nau.22197.
- Brookes ST, Donovan JL, Wright M, Jackson S, Abrams P. A scored form of the Bristol Female Lower Urinary Tract Symptoms questionnaire: data from a randomized controlled trial of surgery for women with stress incontinence. Am J Obstet Gynecol. 2004;191(1):73–82. https://doi.org/10.1016/j.ajog.2003.12.027.
- 18. Nagai K, Homma Y, Ideno Y, Hayashi K. Prevalence and factors associated with overactive bladder and stress urinary incontinence

in the Japan Nurses' Health Study. Menopause. 2021;29(2):129–36. https://doi.org/10.1097/GME.00000000001893.

- Botlero R, Davis SR, Urquhart DM, Shortreed S, Bell RJ. Agespecific prevalence of, and factors associated with, different types of urinary incontinence in community-dwelling Australian women assessed with a validated questionnaire. Maturitas. 2009;62(2):134– 9. https://doi.org/10.1016/J.MATURITAS.2008.12.017.
- Ohta H, Hatta M, Ota K, Yoshikata R, Salvatore S. Online survey of genital and urinary symptoms among Japanese women aged between 40 and 90 years. Climacteric. 2020;23(6):603–7. https:// doi.org/10.1080/13697137.2020.1768236.
- Sartori MGF, Feldner PC, Jarmy-Di Bella ZIK, et al. Sexual steroids in urogynecology. Climacteric. 2011;14(1):5–14. https://doi. org/10.3109/13697137.2010.508542.
- Schreiber Pedersen L, Lose G, Høybye MT, Elsner S, Waldmann A, Rudnicki M. Prevalence of urinary incontinence among women and analysis of potential risk factors in Germany and Denmark. Acta Obstet Gynecol Scand. 2017;96(8):939–48. https://doi.org/ 10.1111/AOGS.13149.
- Wang Q, Que Y, Yang Y, Wan X, Lin C. A population-based cross-sectional survey on the prevalence, severity, risk factors, and self-perception of female urinary incontinence in rural Fujian, China. Int Urogynecol J. 2023;34(9):2089–97. https://doi.org/10. 1007/S00192-023-05518-0.
- Firet L, Teunissen TAM, Kool RB, et al. Usage of a web-based eHealth intervention for women with stress urinary incontinence: mixed methods study. J Med Internet Res. 2022;24(11):e38255 https://doi.org/10.2196/38255.
- Hannestad YS, Rortveit G, Sandvik H, Hunskaar S. A community-based epidemiological survey of female urinary incontinence: the Norwegian EPINCONT Study. J Clin Epidemiol. 2000;53(11):1150–7. https://doi.org/10.1016/S0895-4356(00) 00232-8.
- Jahanlu D, Hunskaar S. The Hordaland Women's Cohort: prevalence, incidence, and remission of urinary incontinence in middleaged women. Int Urogynecol J. 2010;21(10):1223–9. https://doi. org/10.1007/S00192-010-1172-7.
- Waetjen LE, Ye J, Feng WY, et al. Association between menopausal transition stages and developing urinary incontinence. Obstet Gynecol. 2009;114(5):989–98. https://doi.org/10.1097/AOG. 0B013E3181BB531A.
- Chen Y, Yu W, Yang Y, et al. Association between overactive bladder and peri-menopause syndrome: a cross-sectional study of female physicians in China. Int Urol Nephrol. 2015;47(5):743–9. https://doi.org/10.1007/S11255-015-0948-6.
- Maserejian NN, Curto T, Hall SA, Wittert G, McKinlay JB. Reproductive history and progression of lower urinary tract symptoms in women: results from a population-based cohort study. Urology. 2014;83(4):788–94. https://doi.org/10.1016/J.UROLO GY.2013.12.016.
- Cagnacci A, Xholli A, Sclauzero M, Venier M, Palma F, Gambacciani M. Vaginal atrophy across the menopausal age: results from the ANGEL study. Climacteric. 2019;22(1):85–9. https://doi.org/ 10.1080/13697137.2018.1529748.
- Moral E, Delgado JL, Carmona F, et al. Genitourinary syndrome of menopause. Prevalence and quality of life in Spanish postmenopausal women. The GENISSE study. Climacteric. 2018;21(2):167–73. https://doi.org/10.1080/13697137.2017. 1421921.
- Rahkola-Soisalo P, Savolainen-Peltonen H, Gissler M, et al. Increased risk for stress urinary incontinence in women with postmenopausal hormone therapy. Int Urogynecol J. 2019;30(2):251– 6. https://doi.org/10.1007/S00192-018-3682-7.
- Cody JD, Jacobs ML, Richardson K, Moehrer B, Hextall A. Oestrogen therapy for urinary incontinence in post-menopausal

women. Cochrane Database Syst Rev. 2012;(4):CD001405 https:// doi.org/10.1002/14651858.CD001405.PUB3.

- Grodstein F, Lifford K, Resnick NM, Curhan GC. Postmenopausal hormone therapy and risk of developing urinary incontinence. Obstet Gynecol. 2004;103(2):254–60. https://doi.org/10.1097/01. AOG.0000107290.33034.6F.
- Grady D, Brown JS, Vittinghoff E, Applegate W, Varner E, Snyder T. Postmenopausal hormones and incontinence: the Heart and Estrogen/Progestin Replacement Study. Obstet Gynecol. 2001;97(1):116–20. https://doi.org/10.1016/S0029-7844(00) 01115-7.
- Hendrix SL, Cochrane BB, Nygaard IE, et al. Effects of estrogen with and without progestin on urinary incontinence. JAMA. 2005;293(8):935–48. https://doi.org/10.1001/JAMA.293.8.935.
- 37. Matarazzo MG, Caruso S, Giunta G, Valenti G, Sarpietro G, Cianci A. Does vaginal estriol make urodynamic changes in women with overactive bladder syndrome and genitourinary syndrome of menopause? Eur J Obstet Gynecol Reprod Biol. 2018;222:75–9. https://doi.org/10.1016/j.ejogrb.2018.01.002.
- Nelken RS, Özel BZ, Leegant AR, Felix JC, Mishell DR. Randomized trial of estradiol vaginal ring versus oral oxybutynin for the treatment of overactive bladder. Menopause. 2011;18(9):962– 6. https://doi.org/10.1097/GME.0B013E3182104977.
- Tseng LH, Wang AC, Chang YL, Soong YK, Lloyd LK, Ko YJ. Randomized comparison of tolterodine with vaginal estrogen cream versus tolterodine alone for the treatment of postmenopausal women with overactive bladder syndrome. Neurourol Urodyn. 2009;28(1):47–51. https://doi.org/10.1002/NAU.20583.
- Serati M, Salvatore S, Uccella S, Cardozo L, Bolis P. Is there a synergistic effect of topical oestrogens when administered with antimuscarinics in the treatment of symptomatic detrusor overactivity? Eur Urol. 2009;55(3):713–20. https://doi.org/10.1016/J. EURURO.2008.06.051.
- Badawi JK, Bosch R, Djurhuus JC, Hanna-Mitchell AT. Is testosterone important in LUT function in men and women? ICI-RS 2015. Neurourol Urodyn. 2017;36(4):859–62. https://doi.org/10. 1002/NAU.23041.
- 42. Mammadov R, Simsir A, Tuglu I, Evren V, Gurer E, Özyurt C. The effect of testosterone treatment on urodynamic findings and histopathomorphology of pelvic floor muscles in female rats with experimentally induced stress urinary incontinence. Int Urol Nephrol. 2011;43(4):1003–8. https://doi.org/10.1007/S11255-011-9938-5.
- Kim MM, Kreydin EI. The association of serum testosterone levels and urinary incontinence in women. J Urol. 2018;199(2):522– 7. https://doi.org/10.1016/J.JURO.2017.08.093.
- 44. Teleman PM, Persson J, Mattiasson A, Samsioe G. The relation between urinary incontinence and steroid hormone levels in perimenopausal women. A report from the Women's Health in the Lund Area (WHILA) study. Acta Obstet Gynecol Scand. 2009;88(8):927–32. https://doi.org/10.1080/0001634090 3117986.
- Ho MH, Bhatia NN, Bhasin S. Anabolic effects of androgens on muscles of female pelvic floor and lower urinary tract. Curr Opin Obstet Gynecol. 2004;16(5):405–9. https://doi.org/10.1097/00001 703-200410000-00009.
- Musbahi E, Kamp E, Ashraf M, DeGiovanni C. Menopause, skin and common dermatosis. Part III. Genital disorders. Clin Exp Dermatol. 2022;47(12):2123–9. https://doi.org/10.1111/CED. 15400.
- Anglim B, Phillips C, Shynlova O, Alarab M. The effect of local estrogen therapy on the urinary microbiome composition of postmenopausal women with and without recurrent urinary tract infections. Int Urogynecol J. 2022;33(8):2107–17. https://doi.org/10. 1007/S00192-021-04832-9.

- Shardell M, Gravitt PE, Burke AE, Ravel J, Brotman RM. Association of vaginal microbiota with signs and symptoms of the genitourinary syndrome of menopause across reproductive stages. J Gerontol A Biol Sci Med Sci. 2021;76(9):1542–50. https://doi.org/10.1093/GERONA/GLAB120.
- Ammitzbøll N, Bau BPJ, Bundgaard-Nielsen C, et al. Pre- and postmenopausal women have different core urinary microbiota. Sci Reports. 2021 111;11(1):1–10. https://doi.org/10.1038/ s41598-021-81790-8.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.