

# Is urinary incontinence associated with vulval lichen sclerosis in females? A cross-sectional study

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## Funding information

British Skin Foundation (010\_BSFBAD\_19)

## Abstract

**Background:** Lichen sclerosis (LS) is a scarring chronic inflammatory disease affecting mainly genital skin. Increasing evidence suggests that the occluded exposure of susceptible epithelium to urine is implicated in the pathogenesis of male genital LS (1). This theory has not been robustly investigated in females (2).

**Methods:** This study utilised data prospectively entered into the East Lancashire Hospitals NHS Trust vulval dermatology database between 2017 and 2020. Cross-sectional analysis of data for adult female patients was performed to determine the odds of UI in LS compared with other genital conditions. The LS group were adult females with genital LS, diagnosed either clinically or histologically. The non-LS group were adult female patients with a genital condition other than LS, also identified from the database. The primary outcome was the reported presence of UI, screened for using the validated International Consultation of Incontinence Questionnaire Short Form (ICIQ). Multivariable logistic regression was used to assess for confounding and obtain a final model.

**Results:** Data for 384 women were analysed; 126 women with genital LS and 258 with an alternative genital condition. The prevalence of UI was 63% in the LS group and 34% in the non-LS group,  $P < 0.001$ . Women with LS were significantly older (median 62 versus 50,  $P < 0.001$ ), with higher BMI (median 29 versus 26,  $P < 0.001$ ) and parity (median 2, interquartile range 2-3 versus 0-2). The unadjusted OR for UI was 3.85 (95%CI 2.40-6.18),  $P < 0.001$ . The final age-adjusted OR for UI was 2.56 (95%CI 1.55-4.24),  $P < 0.001$ .

**Conclusion:** This study demonstrates that the odds of UI were increased 2.5-fold in women with LS. Large population-based cohort studies are now needed to determine the nature of this association in the female population.

## Introduction

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Identifying potential trigger factors for LS was identified as one of the top 10 questions in the 2018 James Lind Alliance Lichen Sclerosus Priority Setting Partnership. "Trigger factors" include both factors responsible for development of lichen sclerosus and for its flare-ups; for example, irritation from clothing, chemicals or urine, trauma, environmental factors, drugs and medications(1).

In males, an increasing body of evidence supports the theory that occluded exposure of susceptible epithelium to urine can be a trigger for developing LS. In uncircumcised males, tiny droplets of urine can become occluded between the foreskin and the penis(2). This may explain the pattern of LS in males, usually involving the foreskin and distal penis(3) and rarely affecting the peri-anal area(4). This is in contrast to the typical 'figure-of-eight' distribution of LS in women, involving the outer labia majora, labia minora, inter-labial sulci and perineum(5). This pattern corresponds with the areas that would be in prolonged contact with urine if incontinence is present. LS is extremely rare in circumcised men(6), supporting the idea that it is the occluded exposure to urine specifically that is important in the pathogenesis of LS.

Extrapolating established evidence in males to female patients with LS, it is likely that occluded exposure to urine is a trigger factor for LS. The consensus among many specialist clinicians treating women with vulval conditions is that the prevalence of UI is higher in LS than in other vulval conditions. Our recent systematic review found that the prevalence of UI in LS is 35%, which is comparable to the general population. However, the evidence was limited and poor quality. Therefore, a study with systematically collected, prospective data is needed to establish whether urinary incontinence is more common in patients with LS than in other vulval diseases.

## Methods

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### *Study design and setting*

This cross-sectional study utilised data prospectively entered into the East Lancashire Hospitals NHS Trust vulval dermatology database between 2017 and 2020. Data have been systematically collected and recorded for all adult female patients attending a specialist vulval dermatology clinic as part of routine practice. All patients were assessed by a Consultant Dermatologist with a specialist interest in vulval disease.

Patient details were entered in the database at first visit, independent of the clinical diagnosis, and not repeated. Clinical diagnosis (plus histological if available), demographics, body mass index (BMI), parity, hygiene practices and past medical history were recorded. All patients completed an International Consultation on Incontinence Questionnaire Urinary Incontinence Short Form (ICIQ) and the score was recorded. The ICIQ is a validated simple tool for evaluating the frequency, severity and impact on quality of life of urinary incontinence(7). The score range is 0-21, with a higher score indicating greater severity of symptoms.

The database was interrogated at East Lancashire Hospitals Trust on 9<sup>th</sup> January 2020. A data quality check performed separately confirmed all data were extracted correctly. Following advice

from the University of Nottingham Research Governance Office, ethical approval was not required as data were anonymised and unlinked throughout data analysis. The data custodian at the collection site granted permission to use these data in the way described.

### *Study population*

All adult females presenting to the specialist vulval clinic between 2017 and 9<sup>th</sup> January 2020 were included in this study. Patients under 18 were not included; these patients did not have BMI or ICIQ measured. The LS group were women with genital LS, diagnosed clinically and/or histologically. Cases with LS and lichen planus (LP) overlap were included but analysed separately in a sensitivity analysis. There were no exclusions, provided the diagnosis of LS was confirmed either clinically or histologically in the specialist clinic.

The non-LS group were adult female patients with a genital condition other than LS, also identified from the database. Patients with incontinence-associated dermatitis as the sole diagnosis were included in the non-LS group. The clinic letters for all cases of irritant contact dermatitis (ICD) were reviewed by two investigators (L.K. and C.O.) to identify cases of incontinence-associated ICD as the sole diagnosis. These patients were analysed in a sensitivity analysis.

### *Outcomes*

The primary outcome of interest was the reported presence of UI, screened for using the ICIQ score.

### *Clinical diagnosis*

Diagnoses were made predominantly on clinical grounds but where the clinical presentation was atypical or there were concerns about malignancy, biopsy was undertaken.

### *Study size*

A power calculation showed that for 90% power and 5% error to detect a 20% difference in the likelihood of LS patients having incontinence compared to alternate vulval conditions, 110 patients needed to be included per group.

## Statistical methods

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### *Confounders*

Age was identified as an a priori confounder; the prevalence of UI increases with age (up to 50%)(8) and the incidence rate of LS is highest in women 75-79 years of age(9). We identified BMI and parity as additional potential confounders(10-12), as well as washing frequency.

The practice of pre-prayer washing was noted to be common amongst women with irritant contact dermatitis in this clinic. In Islam, Wudhu or Wudu involves washing of the hands, arms, mouth, face, neck and feet before prayer. Ghusl is the 'major ablution' and entails washing the

entire body and genitals. Ghusl is required before prayer in certain circumstances, before touching the Qur'an or reciting its verses and prior to entering a mosque(13).

Autoimmune disease is another potential confounding comorbidity, however due to the 'free text' nature of this part of the database, lack of completion could not be assumed to represent lack of disease. Therefore, history of autoimmune disease was not analysed.

### *Analysis*

The association between potential confounders, the exposure and outcome were analysed using the two-sample t-test for normally distributed continuous data or Mann-Whitney U-test for non-normally distributed continuous data. Pearson's  $\chi^2$ -test was used for categorical data. Univariate logistic regression was conducted to determine the association between LS and UI. Multivariable logistic regression using the 10% change in the adjusted odds ratio (OR) was used to assess for confounding and to obtain a final model. All confounders were included in the final model.

### *Sensitivity analysis*

Participants with LS/LP overlap were included in the LS group. As there were only 8 cases, subgroup analysis was not possible. A sensitivity analysis was conducted by excluding them. Participants with incontinence-associated ICD were included in the non-LS group and analysed in a sensitivity analysis by excluding them. A third sensitivity analysis excluding both LS/LP overlap and incontinence-associated dermatitis was performed.

### *Missing data*

Where baseline data were missing from the database, the clinic letters related to that specific episode were reviewed and missing data added if available. The number of missing variables were reported for each covariate for cases and controls. Complete case analysis was planned if appropriate.

Statistical analysis was performed with Stata/SE 16.1 for Mac (StataCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC).

## **Results**

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The baseline characteristics of all study participants (n=384) are shown in table 1. The presence of urinary incontinence was reported in 63% of women with LS and 34% of the non-LS group,  $P<0.001$ . Women with LS were significantly older (median 62 versus 50,  $P<0.001$ ), had a higher BMI (median 29 versus 26 ( $P<0.001$ )) and higher parity (median 2, interquartile range 2-3 versus 0-2). Women without LS reported significantly higher washing frequency than women with LS (median 1, IQR 1-2 versus 1,  $P=0.047$ ), and the practice of pre-prayer washing was also higher in this group (14% versus 2%,  $P=0.001$ ). The severity of incontinence, quantified by the ICIQ score, was higher in LS than non-LS (median 5 versus 0,  $P<0.001$ ).

Potential confounders which were significantly associated with both LS and UI were age, parity and BMI. Participants with missing data for these variables or the presence of UI were excluded from the final analysis (n=31). The excluded population were not statistically different from the analysed population in terms of key variables.

**Table 1** Baseline characteristics of all study participants

Variable	LS group (n=126)	Missing data (LS)	Non-LS group (n=258)	Missing data (non-LS)	P value
<b>Age</b> (median, IQ range)	62 (55-71)	0	50 (34-64)	0	<0.001
<b>BMI</b> (median, IQ range)	29 (25.5-33)	10	26 (23-32)	12	<0.001
<b>Parity</b> (median, IQ range)	2 (2-3)	2	2 (0-2)	2	<0.001
<b>Self-reported UI</b> (number, %)	n=79 (63%)	2	n=87 (34%)	3	<0.001
<b>ICIQ score</b> (median, IQ range)	5 (0-11)	4	0 (0-5)	5	<0.001
<b>Washing frequency</b> (median, IQ range)	1(1-1)	0	1(1-2)	6	0.047
<b>Pre-prayer washing</b> (number, %)	n=3 (2%)	0	n=35 (14%)	0	0.001

A total of 353 participants were included in the multivariable analysis (LS group n=112, non-LS group n=241), shown in table 2. BMI and parity were not found to be confounders using the 10% rule. The unadjusted OR for UI was 3.85 (95%CI 2.40-6.18),  $P<0.001$ . The final age-adjusted OR for UI was 2.56 (95%CI 1.55-4.24),  $P<0.001$ .

**Table 2** Multivariable logistic regression

Independent variable	Odds ratio	95% CI	Standard error	P value
	3.85 (unadjusted)	2.40 - 6.18	0.93	<0.001
<b>Age</b> (a priori)	2.56	1.55 - 4.24	0.66	<0.001
<b>Age + BMI</b>	2.40	1.44 - 4.01	0.63	<0.001
<b>Age + parity</b>	2.50	1.51 - 4.15	0.64	<0.001

### Sensitivity analyses

Sensitivity analyses were conducted excluding patients with LS/LP overlap from the LS group (n=8) and ICD secondary to UI from the non-LS group (n=19, 2 already excluded due to missing data), shown in table 3. When LS/LP overlap were excluded, the age-adjusted OR was 2.80 (95% CI 1.67-4.70),  $P<0.001$ . This increased to 3.15 (95% CI 1.87-5.30) when incontinence-associated ICD was excluded. Excluding both these groups, the age-adjusted OR was 3.55 (95% CI 2.10- 6.04)  $P<0.001$ .

**Table 3** Sensitivity analysis.

Population	Number of patients	Age-adjusted odds ratio	95% CI	Standard error	P value
All	353	2.56	1.55 - 4.24	0.66	<0.001
LS/LP overlap excluded	345	2.80	1.67 - 4.70	0.74	<0.001
Incontinence-associated ICD excluded	334	3.24	1.93 - 5.45	0.84	<0.001
LS/LP overlap and incontinence-associated ICD excluded	326	3.55	2.10 - 6.04	0.96	<0.001

### Missing data

Missing data for BMI, ICIQ score, parity, presence of UI or washing frequency was present in 55 cases at the point of extraction. No data was missing for other variables. After review of the vulval clinic letters relating to the same episode, 40 patients had missing data (one variable n=36, two variables n=4). Participants with missing data for the significant confounders and UI were excluded from the final analysis (n=31).

### Discussion

This study has demonstrated that UI was more prevalent in women with LS than women with other genital conditions in the population attending the vulval dermatology clinic (63% versus 34%,  $P<0.001$ ). Few studies report prevalence of UI in women with LS. Our recent meta-analysis examined the existing evidence; in this the pooled prevalence was 35% (95% CI 13%-58%) and there was no difference in UI between women with LS and controls (risk ratio 0.97, 95% CI 0.53–1.75)(14). However, the included studies were limited by size and power, with no adjustment for confounding factors in several studies. Few studies used validated tools for screening for UI, further compounded by incomplete or absent reporting on methods used. Several studies failed to provide detail about how cases of LS/LP overlap cases were dealt with. When LS and LP overlap, the condition behaves differently to pure LS, and identifying the predominant condition can be challenging(15). To our knowledge, this is the first study using a

validated screening tool for UI and prospectively collected data, which is powered to determine the odds of UI in women with vulval LS.

There is wide variance in prevalence estimates for UI in the general population, according to population examined, definition of UI and diagnostic methods. A large European study of 29,500 women reported that 35% of women had experienced UI in the preceding 30 days(8). The 34% prevalence amongst the non-LS group in our study is in keeping with these findings.

The characteristics of the LS population in this study are typical; patients with LS were significantly older, had higher BMI and parity than those without LS. A recent Finnish study using population data of 7790 women with LS reported the age-specific incidence of LS was highest in post-menopausal women, with the highest rate (53 per 100,000 woman-years) found in women aged 75-79 years(9). A multi-centre Italian study involving 392 women and 337 men with LS found a significantly higher prevalence ratio of BMI >25kg/m<sup>2</sup> (1.44, 95% CI 1.30–1.59,  $P<0.001$ ) in comparison to the general Italian population(12). Increased age and parity in women with LS compared to other vulval diseases, as well as controls, have been reported in two cross-sectional studies(10, 11), one of which also reported higher BMI(10).

Interestingly, women in the non-LS group reported significantly increased washing frequency and practice of pre-prayer washing. This raises many questions; it seems unlikely that increased washing is protective against development of LS. Potentially women with LS may wash less frequently to avoid irritation due to the condition. This is a complex topic, the scope of which is outside the remit of this paper.

The use of prospectively collected data is a major strength of this study. Data were collected for clinical purposes and the entire adult population was analysed. In order to avoid selection bias, cases of LS/LP overlap and ICD secondary to UI were included but analysed separately in a sensitivity analysis, where they were excluded. Data were entered at the same point for all patients; the first appointment within the period of 2017-2020, and measurements were not repeated. Patients received expert and consistent clinical assessment. Where the clinical presentation was atypical, diagnosis was confirmed with histology. A validated screening questionnaire for UI was consistently used.

All cases of LS/LP overlap (n=8) were confirmed histologically, therefore were able to be analysed separately in this study. Exclusion of LS/LP overlap allowed analysis of cases of pure LS, which increased the odds of UI to 2.80 (95% CI 1.67-4.70). Exclusion of incontinence-associated ICD enabled comparison of LS with diagnoses that are unrelated to UI, further increasing the OR to 3.24 (95% CI 1.93-5.45). Exclusion of both these groups raised the odds of UI to 3.55 (95% CI 2.10-6.04). However, the sensitivity analyses are slightly underpowered in the LS group when LS/LP are excluded.

This study has limitations. Data were collected from a single centre; therefore, the study population, local clinical practice and resources may limit the generalisability of these findings. The setting for this study was a specialist vulval clinic in secondary care; patients who have been referred are likely to represent those with more severe or persistent disease, therefore the findings may not be representative of the general population. As with all screening questionnaires, there is scope for recall bias. Patients may over-report UI symptoms due to perception of treatment gain or under-report due to embarrassment, normalisation of symptoms or cultural beliefs. History of autoimmune disease was not analysed but is an additional potential confounder.

This study provides evidence of a link between UI and vulval LS, an association previously demonstrated in male genital LS. Due to the cross-sectional study design, the outcome (UI) and exposure (LS) were measured at the same timepoint, therefore we cannot determine the direction of association between UI and LS (i.e. which one came first). Large population-based cohort studies are now needed to determine the nature of this association in the female population.

### Conflicts of interest

None to declare

### Acknowledgments

We would like to thank Mr Pete Sagar for the database design and Mr Simon Hill for advice about evaluating urinary incontinence.

### References

- 1.Simpson RC, Cooper SM, Kirtschig G, Larsen S, Lawton S, McPhee M, et al. Future research priorities for lichen sclerosis - results of a James Lind Alliance Priority Setting Partnership. *Br J Dermatol.* 2019;180(5):1236-7.
- 2.Bunker CB, Patel N, Shim TN. Urinary voiding symptomatology (micro-incontinence) in male genital lichen sclerosis. *Acta Derm Venereol.* 2013;93(2):246-8.
- 3.Bunker CB. Re: Sanjay Kulkarni, Guido Barbagli, Deepak Kirpekar, et al. Lichen sclerosis of the male genitalia and urethra: surgical options and results in a multicenter international experience with 215 patients. *Eur Urol.* 2009;55:945-56. *Eur Urol.* 2010;58(6):e55-6; author reply e7-8.
- 4.Bunker CB, Shim TN. Male genital lichen sclerosis. *Indian J Dermatol.* 2015;60(2):111-7.
- 5.Lewis F. Dermatoses of the female genitalia: inflammatory dermatoses of the vulva: lichen sclerosis In: Griffiths CEM BJ, Bleiker T, Chalmers R, Creamer D, editor. *Rook's Textbook of Dermatology.* 3. 9th ed. Chicester: John Wiley & Sons; 2016. p. 112.6-9.
- 6.Mallon E, Hawkins D, Dinneen M, Francics N, Fearfield L, Newson R, et al. Circumcision and genital dermatoses. *Arch Dermatol.* 2000;136(3):350-4.
- 7.Avery K, Donovan J, Peters TJ, Shaw C, Gotoh M, Abrams P. ICIQ: a brief and robust measure for evaluating the symptoms and impact of urinary incontinence. *Neurourol Urodyn.* 2004;23(4):322-30.
- 8.Hunskaar S, Lose G, Sykes D, Voss S. The prevalence of urinary incontinence in women in four European countries. *BJU Int.* 2004;93(3):324-30.
- 9.Halonen P, Jakobsson M, Heikinheimo O, Gissler M, Pukkala E. Incidence of lichen sclerosis and subsequent causes of death: a nationwide Finnish register study. *BJOG.* 2020;127(7):814-9.
- 10.Kennedy CM, Nygaard IE, Bradley CS, Galask RP. Bladder and bowel symptoms among women with vulvar disease are they universal? *Journal of Reproductive Medicine for the Obstetrician and Gynecologist.* 2007;52(12):1073-8.
- 11.Swenson CW, Menees SB, Haefner HK, Berger MB. Lower Urinary Tract and Functional Bowel Symptoms in Women With Vulvar Diseases and Controls. *Female Pelvic Medicine & Reconstructive Surgery.* 2015;21(4):211-4.
- 12.Virgili A, Borghi A, Cazzaniga S, Di Landro A, Naldi L, Minghetti S, et al. New insights into potential risk factors and associations in genital lichen sclerosis: Data from a multicentre Italian study on 729 consecutive cases. *Journal of the European Academy of Dermatology and Venereology.* 2017;31(4):699-704.
- 13.Britannica T. Ghysl. 2013 Available from: <https://www.britannica.com/topic/ghysl>. [Accessed 7 April 2021].
- 14.Kirby L, Gran, S, Kreuser-Genis, I, Owen, C, Simpson, R. Is urinary incontinence associated with lichen sclerosis in females? A systematic review and meta-analysis. *Skin Health Dis.* 2021; 1:e13.
- 15.Day T, Moore S, Bohl TG, Scurry J. Comorbid Vulvar Lichen Planus and Lichen Sclerosis. *J Low Genit Tract Dis.* 2017;21(3):204-8.