Is urinary incontinence associated with lichen sclerosus in females? A systematic review and cross-sectional study

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Study Synopsis

Title of Study:	Is urinary incontinence associated with lichen sclerosus in females? A systematic review and cross-sectional study
Study Centre:	Data extracted from database at East Lancashire Hospitals NHS Trust
Duration of Study:	12 months
Primary Objective:	This study will investigate if urinary incontinence (UI) is more common in female patients with lichen sclerosus (LS) than patients without LS.
Secondary Objective:	Not applicable
Primary Endpoint:	To determine the odds of UI being present in patients with LS compared with patients without LS.
Rationale:	LS is a scarring chronic inflammatory disease with a predilection for genital skin in both sexes. The aetiology of LS is controversial; increasing evidence suggests that occluded exposure of susceptible epithelium to urine is involved in the pathogenesis of male genital LS. This theory has not yet been investigated in females. A systematic review will be performed to examine all existing evidence available for an association between UI and LS in female patients (adult and paediatric). Data will be extracted for qualitative and quantitative synthesis. A cross-sectional study will be undertaken using anonymised data collected prospectively from adult patients attending a vulval clinic over a 2.5 year period, as part of routine clinical practice. Patients with LS will be compared with controls (patients without LS). Multivariable logistic regression analysis will be used to determine if there is a difference in the odds of UI between the groups.
Methodology:	Cross-sectional
Sample Size:	Approximately 400; 110 cases and 300 controls.
Screening:	All cases entered prospectively at routine clinic attendance.
Registration /Randomisation:	Not applicable
Main Inclusion Criteria:	• Case group: adult females with genital lichen sclerosus • Control group: adult female with alternative genital disorder
Main Exclusion Criteria:	• Age <18
Duration of Treatment:	Not applicable
Statistical Analysis:	Descriptive statistics will be reported to describe the study population. Multivariable analysis using logistic regression will be used to assess and adjust for potential confounding factors. The odds of incontinence being present in patients with LS compared with non-LS patients will be reported. A power calculation has shown that for 90% power and 5% error to detect a 20% difference in the likelihood of LS patients having incontinence compared to non-cases, 110 patients will need to be included per group.

Introduction

Lichen sclerosus (LS) is a scarring chronic inflammatory disease which has a predilection for genital skin in both sexes[1]. The aetiology of LS is controversial and likely multifactorial. Previous evidence has pointed towards autoimmune mechanisms, infections, trauma causing koebnerization and genetics. LS in women is associated with a higher incidence of autoimmune conditions, however, this is not the case in men[2]. HPV infection has also been investigated as a possible causative factor, although infection rates have been found to be higher in men with LS than women with LS[3].

An increasing amount of evidence suggests that occluded exposure of susceptible epithelium to urine is involved in the pathogenesis of LS in men[4,5,6]. Micro-incontinence in men results in 'dribbling' and allows drops of urine to become occluded between the penis and foreskin[7]. This may explain the pattern of LS seen in males – predominantly involving the distal penis and foreskin; involvement of the perianal region is extremely rare. In contrast, LS in women typically has a 'figure of eight' distribution involving the vulva and perianal region, areas which are most likely to be exposed to urine in women[4].

To date, all studies examining the association between urinary incontinence (UI) and genital LS have been retrospective and mostly limited to men. The association of UI with LS has not yet been investigated or quantified in females. Extrapolating established evidence in males to female patients with LS, it is likely that occluded exposure to urine is a trigger factor for LS. Incontinence is likely to be under-reported due to embarrassment and the common misconception that it is untreatable. Therefore, a study with systematically collected, prospective data is needed to establish whether UI is more common in patients with LS than in other genital conditions. Data have been systematically collected and recorded in a computerised database (Microsoft Access) for all new adult patients attending a vulval clinic at the East Lancashire Hospitals NHS Trust over a 2.5 year period. Permission has been granted to use this database for this project.

If the association between UI and LS in females is positive, treatment of incontinence would become an essential part of the management of women with LS and in females who might be at increased risk of LS e.g. those with family members affected. Longer term, this could contribute to an evidence base for ways of preventing LS in a susceptible population. This could be investigated in a cohort study.

Aim/Primary and Secondary Objectives

The primary aim of this study is to determine the odds of UI being present in female patients with LS compared with patients without LS.

Study Design

Cases and controls will be identified from the database held at East Lancashire Hospitals NHS Trust. The case group is adult females with genital LS. The diagnosis in this cohort has been made predominantly on clinical grounds, but many have confirmatory histology. The control group is adult female patients with an alternative genital disorder. The control patients will also be identified from the database. Due to the highly specific and intimate nature of the relevant data collected from the case group, it would not be appropriate to use general dermatology female patients as controls.

Data collected prospectively into the database at the time of clinical contact include:

- Demographic details
- Body mass index (BMI)
- Diagnosis
- Past medical history
- Parity
- Patient reported incontinence (faecal, urinary)
- Family history
- Vulval hygiene practices
- International Consultation of Incontinence Questionnaire (ICIQ) score

Potential confounding factors in the analysis include:

- Age
- Body mass index (BMI)
- Family history of autoimmune disease
- Comorbidities such as autoimmune diseases and parity
- Vulval hygiene practices

We anticipate that some data may be missing. If relevant data are missing in 5% or less of cases, these cases will be excluded. If more than 5% of cases have relevant data missing, statistical techniques such as multiple imputation will be used.

Study Population

Case group: adult female patients (>18) with genital LS.
Control group: adult female patients (>18) with a genital skin condition other than LS.

Inclusion criteria

Case group: adult female patients with genital LS, confirmed clinically or with biopsy. Cases with LS/LP overlap will be included but analysed separately in a sensitivity analysis.

Control group: adult female patients with a genital skin condition other than LS, confirmed clinically or with biopsy.

Exclusion criteria

Case group: none, provided the diagnosis of LS is confirmed either clinically or histologically.

Control group: none; cases with urinary incontinence-associated dermatitis as the sole diagnosis will be analysed separately in a sensitivity analysis.

Identification of participants and consent

Patient details entered in secure database as part of routine clinical practice.

Withdrawal of subjects

Not applicable.

Study Outcome Measures

This study will report odds of UI being present in patients with LS compared with patients without LS. UI will be diagnosed through patient reported presence of UI and quantified by the International Consultation of Incontinence Questionnaire (ICIQ) score.

Assessment of Safety

Not applicable.

Statistics and Data Analysis

Descriptive statistics (percentages and means (standard deviations)) will be used to describe the study population. Multivariable logistic regression will be used to assess and adjust for the potential confounding factors listed above. The 10% rule will be used to compare unadjusted and adjusted odds ratios and identify confounders. The odds of UI being present in patients with LS compared with non-LS patients will be reported. A sensitivity analysis will be conducted for patients with UI-associated dermatitis as the sole diagnosis in the control group. Cases of LS/LP overlap will also be analysed as a sub-group in the case group. A power calculation has shown that for 90% power and 5% error to detect a 20% difference in the likelihood of LS patients having incontinence compared to non-cases, 110 patients will need to be included per group. The database includes approximately 400 patients in total, including over 100 patients with LS. Statistical analysis will be performed using STATA statistical software by Dr Kirby, with support of Dr Gran.

Study closure

Patient details entered in database prior to data extraction (January 2020)

Ethical Consideration

Advice has been sought from the University of Nottingham (base of Dr Simpson, Academic supervisor for this project) regarding Ethical Approval. Research governance coordinator and ethical approval is not required as data will be anonymised and unlinked during data analysis. The data custodian at the collection site has been contacted and has given the necessary permission to use these data in the way described.

Finance and Indemnity

This study is being sponsored by NHS Greater Glasgow & Clyde. Lisa Kirby is supported by the British Skin Foundation/BAD Small Grant Award to undertake this research (reference 010_BSFBAD_19)

Publications

The results of this work will be disseminated to healthcare professionals through publication of the systematic review and cross-sectional study separately in peer reviewed journals. The findings will also be submitted for presentation at clinical conferences; the International Society for the Study of Vulvovaginal Disease (ISSVD), British Association of Dermatologists (BAD) Annual Meeting and the British Society for the Study of Vulval Disease (BSSVD) Annual Scientific Conference.

A lay summary will also be produced, in line with the terms of this grant. To ensure readability, a patient representative will be invited to comment and develop the document. It will be circulated to face-to-face patient groups (such as the Manchester Vulval Support Network) and online support groups with which this research team already have collaborative links.

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