

**Lichen sclerosis and sexual dysfunction: a systematic review and meta-analysis**

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## **Abstract:**

**Background:** Lichen sclerosis (LS) is a common autoimmune dermatological condition that is often under-diagnosed in women and has been documented to affect quality of life and sexual function. **Aim:** To determine the prevalence of sexual dysfunction among women with vulvar lichen sclerosis. **Methods:** The authors conducted a systematic review and meta-analysis of the existing research on LS and sexual function in database including PubMed using search terms: lichen sclerosis OR vulvar lichen sclerosis OR vulvar lichen sclerosis et atrophicus OR kraurosis vulvae) AND (sexual function OR sexual functions OR sexual disorder OR sexual disorders OR sexual activity OR sexual activities OR sexual dysfunction OR sexual dysfunctions OR dyspareunia OR vaginismus). **Outcomes:** Nearly 60% of women with lichen sclerosis suffer from sexual dysfunction. **Results:** Two hundred and ten studies were initially identified. Twenty-six articles met inclusion criteria and 3 were excluded as they did not relate to sexual function, were regarding a surgical or medical intervention and sexual dysfunction and one was a review article. Therefore, 23 studies were included in the final analysis resulting in a cumulative 486 participants with LS with 208 patients experiencing any kind of sexual dysfunction. Meta-analysis presented prevalence of sexual dysfunction among LS patients as 59% (95% CI: 48% - 70%). Dyspareunia or generalized pain with intercourse was the most commonly reported type of dysfunction. **Clinical Implications:** Discussing sexual concerns with women with LS could empower them to seek treatment. **Strengths and Limitations:** Few articles met criteria for inclusion. **Conclusion:** A large proportion of women with LS experience sexual dysfunction. More research is needed, especially that which includes biopsy-proven LS and validated tools on sexual function.

**Keywords:** lichen sclerosis, sexual dysfunction, vulvar dermatoses, vulvar disorders

## Introduction

Lichen sclerosus (LS) is an autoimmune dermatological condition that affects the vulva and vagina in approximately 1 out of 60 women in gynecological clinics<sup>1</sup>. Onset generally occurs around the age of menopause but may occur in prepubertal children and women at younger ages. Its hallmark characteristics include labia minora flattening and loss of architecture, clitoral fusion, and vulvar atrophy. There is also a small risk that it develops to squamous cell carcinoma. It is commonly associated with burning and pruritis, but those symptoms are not universal. Nevertheless, anatomic changes, inflammation, scarring, and narrowing of the vaginal introitus as well as the presence of erosions and fissures are some of the chronic manifestations that can severely affect one's quality of life. Due to the nature of the condition, women with LS may experience dyspareunia, decreased orgasm, and decreased coital frequency.

The condition appears as white, fragile, skin patches that can have a shiny and smooth surface. If LS is untreated the condition can worsen to include complete fusion of the clitoral prepuce, burying the clitoris, anterior and posterior fourchette fusion, complete resorption of the labia minora, skin erosion and ecchymosis<sup>2</sup>. Unfortunately, LS is a skin disease with no curative treatment and so far the most effective treatments only lessen the symptoms, hopefully causing remission with the mainstay of therapy being high potency topical steroids.

Unfortunately, for many women, in addition to pain with intercourse, they experience an overall negative effect on their intimate relationships due to LS despite treatment and continue to have significant sexual dysfunction<sup>3</sup>. Standard treatments are directed at relieving symptoms, therefore, sexual concerns are not always addressed and side effects from the topical steroids may cause additional problems. There are a multitude of factors affecting women's sexual health and quality of life with LS. This includes distress regarding anticipated vulvar symptoms from having intercourse, dissatisfaction with the appearance of genitalia, and diminished sexual function due to physical changes of the vulvar architecture. However, this topic has been generally under-studied and contributes to the limitations for treatment options, especially for cases refractory to topical steroids.

To date, little research on the impact of LS on sexual function is available. A systematic review investigating the effects of LS on sexual dysfunction in women has yet to be conducted. Understanding the impact of this dermatologic condition in sexual health is necessary to improving treatment outcomes of women with LS. Therefore, this study's objective is to review the literature of LS and sexual function.

## Materials and Methods

### *Literature search strategy and eligibility criteria*

In this study, the methods have been developed according to the Preferred Reporting Items for Systemic Review and Meta-Analyses (PRISMA) statement. Investigators (JIS and MHL) independently searched primarily on PubMed from database inception to 7/31/2021. The articles which assessed sexual dysfunction among the women suffering from LS were selected. Search terms used were (lichen sclerosus OR vulvar lichen sclerosus OR vulvar lichen sclerosus et atrophicus OR kraurosis vulvae) AND (sexual function OR sexual functions OR sexual disorder OR sexual disorders OR sexual activity OR sexual activities OR sexual

dysfunction OR sexual dysfunctions OR dyspareunia OR vaginismus). The investigators consecutively examined the titles and abstracts and then the full-text. Additionally, the investigators manually searched the references of the selected articles to search out for additional eligible studies. Articles were reviewed by investigators and determined for final inclusion by all. If there was a discrepancy, discussion within the investigators and another author (RP) were performed.

We included studies examining the association between LS and sexual dysfunction, including studies focusing on LS patients with sexual dysfunction, studies comparing sexual prevalence in LS group, studies focusing on the surgical or medical treatment among severely progressed LS, and studies comparing LS with other diseases that contribute to sexual dysfunction such as vulvar lichen planus. We did not apply limitations in study design and included clinical trials, observational studies, case series, letters, and interviews. We defined LS as clinically or pathologically diagnosed LS. The definition of sexual dysfunction was based on the definition used in original articles. We compared sexual function tools and scores when possible. We excluded studies that specifically looked at sexual function as an outcome after an intervention such as surgery or treatment. The risk of bias was evaluated using the Newcastle Ottawa Quality Assessment Scale (Table 4).

#### *Data Extraction*

From each eligible article, we extracted the name of the first author, publication year, study design, definition of sexual dysfunction of each articles, and total number of LS patients, and cases suffering from sexual dysfunction, biopsy confirmation of LS diagnosis, usage of Female Sexual Function Index (FSFI) score, usage of Female Sexual Distress Scale (FSDS) score, adjustment of outcome and reference index (Table 1). We performed a meta-analysis to aggregate prevalence of sexual dysfunction within the patients suffering from LS. In calculating prevalence, we excluded studies focusing on the treatment of sexual dysfunction, because all of the LS patients had sexual dysfunction, which would exaggerate the prevalence of sexual dysfunction in LS. We extracted prevalence of sexual dysfunction among LS patients.

#### *Statistical analysis*

From the each included study, we calculated prevalence of sexual dysfunction among the LS patients. In the each study, the prevalence and variance was calculated and meta-analysis was done. The summary prevalence and its 95% confidence interval was estimated. We calculated heterogeneity between the studies by using  $I^2$  value<sup>4</sup>. The software used for the analysis were R ver.4.0.4 and its packages.

### **Results**

A PRISMA diagram of the study process is presented in Figure 1. A total of 210 potentially eligible studies were initially identified. Ten study were excluded due to duplication. 175 studies were excluded due to inappropriate title and abstract and one study was added through additional search. Twenty-six studies met inclusion criteria and 3 were excluded as they did not relate to sexual dysfunction and one was a review article. Therefore, 23 studies were finally eligible, corresponding to 1,524 LS participants.

The definition of LS varied throughout the eligible studies (Table 1). Out of 23 studies, 14

studies were conducted with biopsy-proven LS. In 6 studies<sup>5-10</sup> use of histopathological diagnosis were not mentioned, and the remaining 3 studies<sup>11-13</sup> mainly used clinical diagnosis as their prior method and only used biopsy when necessary.

In the eligible studies, we could only use five studies<sup>6,7,12-14</sup> to calculate the prevalence of sexual dysfunction in the patients suffering from LS. It was not available to use the other 18 studies because of the following reasons: 3 studies<sup>8,10,15</sup> did not have a precise definition of sexual dysfunction, 9 studies<sup>3,5,16-22</sup> were focusing on the surgical or medical treatment of severely progressed LS, such as vulvar adhesion. 5 studies<sup>9,11,23-25</sup> did not present the raw data and remaining one study<sup>26</sup> was a case-control study.

The summary of results and number of patients in those five calculable studies are presented on Table 2. In these five studies, which included a consistent definition of women with sexual dysfunction with the women suffering from LS, the total number of patients with LS is 486 and within those patients, 208 patients presented sexual dysfunction. Meta-analysis was performed among these five studies (Table 3), presenting the prevalence of sexual dysfunction among LS patients. In random effects estimates the prevalence was 0.59 (95% CI: 0.48-0.70), and in fixed effects estimates the prevalence was 0.54 (95% CI: 0.50-0.59). A forest plot was drawn (Figure 2) presenting that about 59% LS patients suffer from any kind of sexual dysfunction. Dyspareunia and generalized pain with intercourse was the most commonly reported dysfunction. Apareunia and difficulty achieving orgasm were also present in LS patients.

Within the included studies, higher quality studies included control groups and used validated measures for sexual function, most commonly the FSFI and FSDS. Beck Anxiety Index (BAI)<sup>25</sup>, Female Genital Self-Image Scale (FGSIS)<sup>25</sup>, Pictorial Representation of Illness and Self Measure (PRISM)<sup>15</sup>, Vulval-disease Quality of Life Index (VLQI)<sup>23</sup> were also used in each of the articles, but these measures were not included in the remaining studies. Unfortunately, there are not enough studies that use the same validated measures in order to combine data for larger power. However for those that did include FSFI, the score of patients suffering from LS were significantly lower than controls<sup>24,25</sup>.

In Yildiz, Cengiz et al.<sup>25</sup>, 59 patients suffering from vulvar LS were included and had a FSFI score of 17.90, which was significantly lower (p value < 0.01) than the score of healthy control group (28.50, n=50). In Van de Nieuwenhof, Meeuwis et al.<sup>24</sup>, 187 patients with LS had a mean total FSFI score of 18.79, which was significantly (p value < 0.001) lower than that of the control group (27.43, n=187). Plus, FSDS score was significantly (p value < 0.001) higher in the LS patient group (mean = 26.08) compared to the control group (mean = 9.97). These results indicate that LS patients have worse sexual function and higher distress compared to the healthy individuals.

Patients suffering from LS also suffered from low quality of life<sup>11,20,21,23,24</sup> and the main reason for the deterioration was due to sexual difficulties and was not because of impact on working or studying<sup>24</sup>. Two studies<sup>11,24</sup> used Dermatologic Life Quality Index (DLQI) score to measure quality of life, which has a high score in patients with low quality of life<sup>24</sup>. Since the scoring system is based on the effect of dermatologic conditions on the quality of life, it is not possible to measure DLQI scores on the healthy control group. In spite of that, LS patients had high DLQI scores of 3.79 (SD: 4.98, n=48)<sup>11</sup> and 11.92 (SD: 6.18, n=215)<sup>24</sup> in the selected studies, indicating LS patients are suffering from low quality of life. One study<sup>21</sup> used Skindex-29 score and Patient Benefit Index (PBI) score, and also suggested that LS patients have problem in

quality of life.

Several studies<sup>5,17-19</sup> focused on surgical treatment to resolve sexual dysfunction among severely progressed LS patients. In those studies surgery of the severe LS with adhesion or phimosis showed high satisfaction among the patients. In those selected patients, LS surgery improved sexual dysfunctions and decreased distress regarding sexual function and most of the patients were satisfied with the effect of the surgery among their sexual dysfunction.

In Brauer, van Lusen et al.<sup>5</sup>, patients with clitoral phimosis was performed with LS surgery, 13 out of 19 LS patients(68.4%) improved from sexual pain after receiving LS surgery. In Chmel, Nováčková et al.<sup>17</sup> 9 patients with severe LS complicated by clitoral phimosis had gone through LS surgery, and after 12 months those patients had significant improvement of FSFI score from  $17.9 \pm 0.9$  to  $26.6 \pm 0.5$ (p value < 0.001). FSDS score were also reduced significantly from  $33.8 \pm 6.9$  to  $21.3 \pm 6.2$ (p value < 0.001). In Lauber, Vaz et al.<sup>19</sup>, 37 out of 41 LS patients receiving perineoplasty had satisfaction from the LS surgery, and there was a significant reduction with dyspareunia. Similar result were shown in Flynn, King et al. 2015<sup>18</sup>. In this study, LS surgery was performed in 25 LS patients suffering from complication of vulvar granuloma fissuratum. 4 to 130 months after the surgery, patients were interviewed by telephone about their satisfaction about their postsurgical state. 11(44%) patients replied as 'Very satisfied' about the surgery, and 10(40%) patients replied 'Satisfied'. Only 4(16%) patients replied they were 'Not satisfied' about the surgery. Of the 25 patients, 21(84%) patients indicated that they will recommend surgery to another women with similar symptoms. In addition, topical laser on the affected area also improves sexual function among the LS patients suffering from sexual dysfunction<sup>22</sup>.

## Discussion

Sexual dysfunction is one of the important symptoms caused by LS. Because of the social taboo regarding sex, and because of other bothersome symptoms such as pruritus and discoloration, patients and researchers tend not to focus on sexual dysfunction. However, upon the interview<sup>5,10</sup>, if physicians ask inquisitively about patients' symptoms, we can see that many LS patients suffer from sexual dysfunction. Sexual dysfunction is a major problem itself, and it can also affect the quality of life and mental health of the patients.

While there are relatively few studies on women with LS and sexual dysfunction, it is clear that a large proportion of women with LS suffer from pain with sexual intercourse among other sexual dysfunctions. From 23 eligible studies, 5 studies were applicable for estimating prevalence of sexual dysfunction among the LS patients. Within those 479 LS patients of 5 studies, 207 patients suffered from sexual dysfunction, and the meta-analysis suggests about 59% of LS patient may suffer from sexual dysfunction. LS patients most commonly suffered from dyspareunia or generalized pain with intercourse.

There were many scoring systems to assess the sexual dysfunction of LS patients throughout the studies. Few papers used the same validated tools, but for those that did, there is clear indication that those with LS have diminished sexual function and increased distress compared to controls. The most commonly used tools were the FSFI and the FSDS. Two studies<sup>24,25</sup> implies LS patients have a significantly lower score of FSFI compared to healthy control group. One study<sup>24</sup>, indicates FSDS score is higher in LS patients than the healthy control group. These

results represent the detrimental effects of LS. Quality of life was also assessed in many studies<sup>11,20,21,23,24</sup>. Many patients suffered from deterioration of quality of life and sexual dysfunction was a major factor for the poor quality of life.

In severe LS with adhesions or phimosis, it is well studied that surgical treatments were highly satisfactory to the patients. In many studies<sup>5,17-19</sup>, surgical treatments improved sexual dysfunction and the quality of life of the patients. Also, the patients were willingly recommend the surgery to the other patients. From the studies above, FSFI score was significantly increased and FSDS score was significantly decreased after the patients received LS surgery. However, one study<sup>20</sup> pointed out that surgical treatment in LS may be good for short term but relapse of the disease is possible.

This study has some limitations. First of all, the number of studies and patients are small and Egger p-value is lower than 0.05, suggesting that there may be a publication bias. Nevertheless, estimating an approximate prevalence would serve as a foundation for future studies. In addition, presenting a solid number instead of ambiguous words such as 'high' or 'moderate' will draw attention from many physicians and patients, which give them a chance to investigate thoroughly about their hidden symptoms. Secondly, few articles specified whether those included had biopsy-proven LS. According to American College of Obstetricians and Gynecologists(ACOG), except in prepubertal child, since other vulvar diseases can mimic LS, a biopsy is necessary to confirm diagnosis of LS<sup>27</sup>. Most of the eligible studies used biopsy-proven LS when entering to their patients group. However some studies did not evince their use of biopsy and some studies only used biopsy when needed. Thirdly, uniform scaling index of sexual dysfunction and distress were not used throughout the study.

In general, due to the scant research but remarkable findings on the negative sexual experience of those with LS, more robust research is needed. Specifically, it would be helpful to include individuals with biopsy-proven LS and to use widely-used validated tools such as FSFI and FSDS in order to compare findings to other studies and continue to learn more about the pathophysiology of the condition in order to eventually reach improved treatment options.

## **Conclusion**

Among the patients suffering from LS, there is a high prevalence (approximately 59%) of sexual dysfunction. The mean FSFI score were lower in LS group compared to healthy control groups and the mean FSDS score were higher in LS group compared to healthy control groups, which indicates that LS is associated with lower sexual function and higher sexual distress. Quality of life was also deteriorated in LS patients and main reason was the sexual dysfunction. In LS patients with vulvar adhesion surgery improved sexual function significantly but may suffer from relapse. We suggest continuing to develop a staging system for LS in order to correlate clinical findings to patient experience such as sexual function and quality of life. We also suggest further research into the mechanism of vulvovaginal changes in order to improve treatment and quality of life of those living with LS.

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**Conflicts of Interest:** The authors declare that there is no conflict of interest.





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## Tables

**Table 1. Characteristics of studies included in the systemic review**

Abbreviations – LS: lichen sclerosus; FSFI: female sexual function index; FSDS: female sexual distress scale.

Study	Study design	Definition of sexual dysfunction	Total number of LS patients	Number of cases with sexual dysfunction	Biopsy status	Single/Multi center	FSFI	FSDS	Adjustment of outcome	Ref
Sadownik et al., 2020	Interview	NA	7	NA	Not mentioned	Single center			NA	10
Brauer et al., 2016	Interview	Sexual pain or decreased sexual activity	19	NA	Not mentioned	Single center			NA	5
Simpkin et al., 2007	Other (consultation and retrospective chart review)	Sexual problems including dyspareunia and apareunia	202	90	Mainly clinical diagnosis, biopsy if needed	Single center			NA	12
Chmel et al., 2019	Prospective cohort study	FSFI score < 26.55	9	NA	Biopsy confirmed	Single center	*	*	NA	17
Burger et al., 2016	Case series	NA	23	NA	Biopsy confirmed	Single center			NA	16
Corazza et al., 2020	Retrospective cohort study	Dyspareunia	90	51	Not mentioned	Single center			NA	6
Dalziel et al., 1995	Survey	Dyspareunia, Reduced frequency of intercourse, Apareunia, Orgasm altered, Relationship affected	45	34	Not mentioned	Single center			NA	7
Yildiz et al., 2020	Prospective cohort study	FSFI score < 26.55	59	NA	Biopsy confirmed	Single center	*		NA	25
Schwegler et al., 2011	Survey	NA	96	NA	Biopsy confirmed	Single center			NA	21
Gordon et al., 2016	Other	FSFI score < 26	16	NA	Not mentioned	Single center	*		NA	8
Richardson et al., 2005	Letter	NA	NA	NA	Not mentioned	Single center			NA	9
Lauber et al., 2021	Retrospective observational study	Dyspareunia, Apareunia, Orgasm altered, Introitus stenosis	41	NA	Biopsy confirmed	Single center			NA	19
Flynn et al., 2015	Retrospective chart review	Low degree of satisfaction and deterioration in sexual	25	NA	Biopsy confirmed	Single center			NA	18

		functioning								
Corazza et al., 2020	Cross-sectional study	NA	87	NA	Biopsy confirmed	Single center			NA	15
Cheng et al., 2017	Prospective cohort study	Low FSFI, FSFD score (cutoff score not clarified)	24	NA	Mainly clinical diagnosis, biopsy if needed	Single center	*	*	NA	11
Skrzypulec et al., 2009	Clinical trial	FSFI score < 26.55, Score in each domain $\leq$ 3.9 (FSFI)	37	NA	Biopsy confirmed	Single center	*		NA	22
Rangatchew et al., 2017	Other	Dyspareunia, Apareunia	38	NA	Biopsy confirmed	Single center			NA	20
Van et al., 2010	Survey	FSFI score < 26.55 FSDS score > 15	215	NA	Biopsy confirmed	Single center	*	*	NA	24
Gutierrez et al., 2019	Letter	FSFI score < 26	20	14	Biopsy confirmed	Single center	*		NA	14
Haefner et al., 2014	Case-control study	Pain and itching, Low sexual activeness, Unsatisfactory sexual activity, Low frequency of orgasm	197	NA	Biopsy confirmed	Single center			NA	26
Burrows et al., 2011	Clinical trial	FSDS score > 15	36	NA	Biopsy confirmed	Single center		*	NA	3
Felmingham et al., 2020	Retrospective chart review	NA	109	NA	Biopsy confirmed	Single center			Age, Duration since the onset of symptoms, Being sexually active	23
Yang et al., 2018	Retrospective chart review	Negative effects on sexual function (varying symptoms)	129	71	Mainly clinical diagnosis, biopsy if needed	Single center			NA	13

**Table 2. Summary of the results of the studies on the prevalence of sexual dysfunction in lichen sclerosis patients**

Abbreviations – SD: standard deviation; LS: lichen sclerosis; FSFI: female sexual function index; FSDS: female sexual distress scale.

Study	Results of the study	Number of patients		Ref
		Sexual dysfunction	LS patients	
Simpkin et al., 2007	101 of 185 patients (56%) with biopsy-confirmed vulval lichen sclerosis were asymptomatic but 22 (12%) continued to have moderate to severe symptoms	90	202	12
Corazza et al., 2020	Dyspareunia occurred in more than half of vulvar lichen sclerosis patients	51	90	6
Dalziel et al., 1995	The majority of women of all ages reported that lichen sclerosis had a detrimental effect on sexual function with problems including dyspareunia, apareunia and difficulty achieving orgasm	34	45	7
Gutierrez et al., 2019	Patients with vulvar LS experience female sexual dysfunction, so it is essential to consider their quality of life related to sexual well-being when devising treatment and care plans for them	14	20	14
Yang et al., 2018	Chinese patients, with a few asymptomatic individuals, follow a normal distribution for the age of onset, with a peak at age 25–30 years, and these patients have less comorbid autoimmune diseases, incidence of dysuria, constipation and squamous cell carcinoma	71	129	13

**Table 3. Summary of the meta-analysis results on the prevalence of sexual dysfunction in lichen sclerosis patients**

	<b>Number of studies</b>	<b>Random effects estimate and 95% confidence interval</b>	<b>Fixed effects estimate and 95% confidence interval</b>	<b>I<sup>2</sup> and p value for Q test</b>	<b>Egger p-value</b>
Proportion of sexual dysfunction among lichen sclerosis patients	5	0.59 (0.48 to 0.70)	0.54 (0.50 to 0.59)	82% (< 0.001)	0.014

Abbreviations –LS: lichen sclerosis

**Table 4. Quality Assessment**

**Newcastle Ottawa scale**

Cohort studies	Selection				Comparability	Outcome			Total quality score	Ref
Author, year	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that the current outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts		
Sadownik et al., 2020		*	*		**	*		*	6	10
Brauer et al., 2016		*	*		**	*			5	5
Simpkin et al., 2007		*	*		**	*			5	12
Chmel et al., 2019		*	*		**	*		*	6	17
Burger et al., 2016		*	*		**	*		*	6	16
Corazza et al., 2020		*	*		**	*			5	6
Dalziel et al., 1995		*	*		*	*			4	7
Yildiz et al., 2020		*	*		**	*			5	25
Schwegler et al., 2011		*	*		**	*			5	21
Gordon et al., 2016		*	*		**	*			5	8
Richardson et al., 2005										9
Lauber et al., 2021		*	*		*	*			4	19
Flynn et al., 2015		*	*		*		*		4	18
Corazza et al., 2020		*	*		**	*			5	15
Cheng et al., 2017		*	*		*	*			4	11
Skrzypulec et al., 2009		*	*		*	*		*	5	22
Rangatchew et al., 2017		*	*		*	*	*		5	20
Van et al., 2010		*	*		**	*			5	24
Gutierrez et al., 2019		*	*		*	*		*	5	14
Haefner et al., 2014		*	*		*	*			4	26
Burrows et al., 2011		*	*		*	*		*	5	3
Felmingham et al., 2020		*	*		**	*			5	23
Yang et al., 2018		*	*		**	*			5	13

