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Differential Clinical Signatures of Vulvar Lichen Sclerosus, Lichen Planus, and Chronic Lichen Simplex: A Comparative Study in 1355 Patients

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Background: Vulvar lichen sclerosus (VLS), vulvar lichen planus (VLP), and vulvar lichen simplex chronicus (VLSC) are inflammatory dermatoses with overlapping clinical features, posing diagnostic challenges. VLS and VLP carry malignant potential, unlike VLSC. Comparative studies are limited despite frequent misclassification.

Objective: To compare the clinical characteristics of VLS, VLP, and VLSC and identify distinguishing diagnostic features.

Methods: A retrospective study was conducted on clinical data from patients diagnosed with VLS, VLP, or VLSC at the Beijing Hospital Vulvar Clinic (March 2017-August 2024). Epidemiological data, symptoms, and physical findings were compared.

Results: Patients with VLP had a significantly higher median onset age (44 years) than VLS (30 years) or VLSC (34 years) (P<0.001). Diagnostic delay was longest in VLS (median 5 years vs 3 years for VLP/VLSC). Pruritus prevalence and intensity (median Numerical Rating Scale [NRS]) were highest in VLSC (100%; NRS 7), followed by VLS (92%; NRS 5) and VLP (60%; NRS 2). Pain was most frequent in VLP (79%) vs VLS (14%) and VLSC (<1%). VLSC patients reported the highest mean Dermatology Life Quality Index scores (8.67), driven by severe pruritus. Sexual dysfunction was common in both VLS (81%) and VLP (85%). Anatomically, VLS primarily affected the clitoris, labia minora, and interlabial sulci; VLSC predominantly involved the labia majora and perianal region. Vaginal introitus involvement characterized VLP (90%). Lesion morphology differed: VLS featured white patches (84%) and lichenification (61%), VLP erosion (76%), and VLSC marked lichenification (89%).

Conclusion: VLS, VLP, and VLSC exhibit distinct differences in age of onset, clinical manifestations, lesion morphology, and anatomical distribution despite clinical overlap. Recognizing these features facilitates accurate diagnosis, guides individualized treatment, improves long-term outcomes, and enables early detection of malignant potential in VLS/VLP.

Keywords: vulvar lichen sclerosus, vulvar lichen planus, vulvar lichen simplex chronicus

Introduction

Vulvar lichen sclerosus (VLS), vulvar lichen planus (VLP), and vulvar lichen simplex chronicus (VLSC) are the three common inflammatory dermatoses encountered in the field of vulvar dermatology. A population-based descriptive study conducted in Finland revealed that the age-adjusted incidence rate of lichen sclerosus (LS) increased from 14 per 100,000 woman-years in 2003 to 22 per 100,000 woman-years during the period of 2010–2012. The age-specific incidence rate was highest among postmenopausal women, ranging from 24 to 53 per 100,000, while it was also notably elevated in girls aged 5 to 9 years, with an incidence rate of seven per 100,000.[1] There is a lack of extensive population-based studies that provide insights into the epidemiology of VLP. A study conducted at a specialized vulvar clinic over a 13-year period involving 3,350 women revealed that 3.7% of the patients were diagnosed with biopsy-proven VLP.[2]

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Nevertheless, the incidence rate of VLP remains unexamined. There is a lack of epidemiological studies on the incidence of VLSC. A study showed that VLSC comprised up to 35% of patient visits to vulvar specialty clinics.[3] These conditions often present with overlapping clinical features and symptoms, such as local skin changes accompanied by varying degrees of pruritus or pain, which can significantly affect the quality of life of those affected.[3–5] The incidence of overlapping diagnoses is under-researched. There have been reports of cases where VLS coexists with VLP. For instance, Day T et al[6] identified 31 cases of comorbid VLP and VLS over a six-year period using strict criteria at a single pathology service, suggesting that this phenomenon is not uncommon. VLSC can occur as either a primary condition or secondary to other dermatologic diseases, which may lead to clinical overlap with VLS and VLP.[7] Our previous research has detailed the substantial disease burden and impact on quality of life in patients with VLS.[8] Both VLS and VLP carry a potential risk for malignant transformation, whereas VLSC is not associated with an increased risk for squamous cell carcinoma.[7,9,10] Given the differences in disease progression and management among the three diseases, timely and accurate diagnosis is essential for appropriate treatment and improved prognosis.

Previous studies, including our own, have primarily focused on individual disease characteristics, whereas comparative analyses remain limited despite frequent clinical misclassifications due to overlapping manifestations. To the best of our knowledge, only a few studies have comprehensively compared these three conditions. In contrast to our prior work which emphasized the psychosocial burden of VLS, the present study is specifically designed to address the critical challenge of differential diagnosis. This study aimed to delineate the differences in the epidemiological characteristics, clinical symptoms, physical signs, and anatomical distribution among patients with VLS, VLP, and VLSC, thereby providing valuable diagnostic insights for clinical practice.

Materials and Methods

This retrospective study included data from patients diagnosed with VLS, VLP, or VLSC, who presented to the Vulvar Clinic of the Department of Dermatology at Beijing Hospital (Beijing, China) between March 2017 and August 2024. Clinical data were collected at the first visit through physician-administered questionnaires and physical examinations.

The diagnoses of VLS and VLP were based on a detailed medical history and physical examination. Skin biopsy was performed in cases with atypical clinical presentations to confirm the diagnosis.[4,11] Most cases of VLSC are clinically diagnosed based on typical features; biopsies are performed in atypical presentations as an adjunct diagnostic tool.[12] All diagnoses in the present study were confirmed by two experienced dermatologists.

Individuals with missing data exceeding 30%, and those with completely resolved lesions and residual hypopigmentation only, with no further treatment required as judged by the clinician at the first visit, were excluded. Ultimately, data from 1355 patients were included.

Demographic data, age at onset, disease duration, clinical symptoms, physical signs, and lesion distribution were systematically recorded and compared among the three groups. This study was approved by the Ethics Committee of Beijing Hospital (Approval No. 2023BJYYEC-152-01) and was conducted in accordance with the principles of the Declaration of Helsinki. As it was a retrospective analysis of anonymized clinical data, the requirement for written informed consent was waived by the ethics committee. All patient data were de-identified to ensure confidentiality.

Statistical Analysis

Quantitative variables were tested for normality. Non-normally distributed data are expressed as median with interquartile range (IQR), and intergroup differences were assessed using non-parametric rank-sum tests. For significant overall differences, pairwise comparisons were performed using the Bonferroni correction to adjust for multiple comparisons. Categorical variables are expressed as frequency (percentage). The chi-squared test was used for intergroup comparisons when the expected frequencies in all cells met statistical assumptions (ie, no more than 20% of cells had expected counts < 5). Fisher's exact test was applied when > 20% of the expected counts were < 5 or < 1. Post hoc pairwise comparisons of categorical variables were adjusted using Bonferroni correction.

To adjust for potential confounding factors between groups, we employed inverse probability of treatment weighting (IPTW). First, we constructed a three-group variable based on standard diagnoses (VLS, VLP and VLSC). Next, we utilized a multinomial logistic regression model (multinom()) to predict the propensity score for each individual. The

covariates included in the propensity score were age, age at onset, and disease duration. Based on these propensity scores, we calculated inverse probability weights for each patient, applying truncation at the 1st and 99th percentiles to mitigate the influence of extreme weights. In our analysis, for continuous variables, we first calculated the weighted means for each group and conducted between-group comparisons using a weighted generalized linear model (svyglm). For categorical variables, we assessed group differences using a weighted chi-squared test (svychisq). Additionally, pairwise comparisons between groups were performed using the weighted generalized linear model (svyglm). All analyses accounted for sample weights to ensure the robustness and accuracy of our estimates.

For example, for continuous variables (eg, Dermatology Life Quality Index, DLQI), we initially computed the weighted mean for this variable within each group (VLS, VLP, VLSC) using the weighted mean function (svymean). Subsequently, we performed regression analysis with the weighted generalized linear model (svyglm) to evaluate the impact of the diagnostic group on the continuous variable DLQI, followed by an overall test using regTermTest. Finally, for pairwise comparisons, we utilized weighted marginal means (emmeans) to analyze differences among the three groups and extracted p-values for each pair. When handling categorical variables (eg, affect sex), we first employed a weighted frequency table (svytable) and a weighted chi-squared test (svychisq) to investigate distributional differences across the groups (VLS, VLP, VLSC). If the overall test result was significant ($P < 0.05$), we conducted pairwise comparisons using the weighted generalized linear model (svyglm) and subsequently extracted p-values for each comparison. All statistical analyses were performed using R software, version 4.4.0 (R Foundation for Statistical Computing, Vienna, Austria). Differences with $P < 0.05$ were considered to be statistically significant.

Results

General Characteristics

Data from 1355 patients were included in the study: 922 with VLS, 53 with VLP, and 380 with VLSC. The median age at consultation was 41 years (IQR 29–54 years) in the VLS group, 51 years (IQR 37–60 years) in the VLP group, and 39 years (IQR 33–49 years) in the VLSC group (Table 1). Patients with VLP were significantly older at presentation than those with VLS or VLSC ($P < 0.05$), whereas no significant age difference was observed between the VLS and VLSC groups.

The median age at disease onset was 30 years (IQR 22–45 years) for VLS, 44 years (IQR 28–56 years) for VLP, and 34 years (IQR 27–42 years) for VLSC. The age at onset was the highest in the VLP group and the lowest in the VLS group, with statistically significant differences across all pairwise comparisons ($P < 0.05$).

The median disease duration at the time of consultation was 5 years (IQR 1–12 years) for VLS, 3 years (IQR 2–8 years) for VLP, and 3 years (IQR 1–8 years) for VLSC. The overall group comparison revealed significant differences ($P < 0.05$). Further

Table 1 General Characteristics of Patients in the Three Diagnostic Groups Before and After Inverse Probability of Treatment Weighting (IPTW)

Variable	Before IPTW					After IPTW			
	VLS	VLP	VLSC	K-W Test (P)	SMD	VLS	VLP	VLSC	SMD
	(n=922)	(n=53)	(n=380)			(n=923.71)	(n=52.77)	(n=369.73)	
Age	41(29,54)	51(37,60)[a]	39(33,49)[b]	<0.001	0.441	42(30,54)	42(31,54)	39(33,48)	0.136
Age of onset	30(22,45)	44(28,56)[a]	34(27,42)[a,b]	<0.001	0.519	32(23,46)	31(23,45)	32(26,40)	0.091
Duration	5(1,12)	3(2,8)	3(1,8)[a]	0.001	0.27	4(1,10)	4(2,13)	4(2,10)	0.109

Notes: Data are presented as median (IQR). "K–W test (*P*)" refers to the Kruskal–Wallis test comparing the three groups before IPTW. "SMD" denotes the maximum pairwise standardized mean difference among the three groups, before and after IPTW, respectively. After IPTW, the "n" in the table for each group indicates the weighted sample size, which is the total sum of weights for all weighted samples and may be expressed as a decimal. This represents the contribution of the weighted samples rather than merely the count of samples. The decimal representation of the weighted sample size captures the influence of each sample in causal inference. Superscript lowercase letters (a, b) indicate statistically significant pairwise differences between groups before IPTW at $P < 0.05$.

Abbreviations: VLS, vulvar lichen sclerosus; VLP, vulvar lichen planus; VLSC, vulvar lichen simplex chronicus; IQR, interquartile range; IPTW, inverse probability of treatment weighting; SMD, standardized mean difference.

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pairwise comparisons revealed that VLS had a longer disease duration than VLSC ($P < 0.05$), whereas no significant differences were found between VLS and VLP or between VLP and VLSC.

Primary Symptoms and Impact on Quality of Life

Pruritus was a common symptom in all three conditions. All VLSC patients (100%) reported itching, compared with 92.1% (849/922) in the VLS group and 60.4% (32/53) in the VLP group. The prevalence of pruritus differed significantly among the three groups ($P < 0.001$). Post-hoc comparisons revealed that pruritus was most prevalent in the VLSC group, followed by the VLS group, and was least common in the VLP group ($P < 0.05$).

The severity of pruritus, as measured using a median numerical rating scale (NRS), was the highest in the VLSC group (median, 7 [IQR 5–8]), followed by the VLS group (median 5 [IQR 2–8]), and lowest in the VLP group (median, 2 [IQR 0–5]). These differences were statistically significant ($P < 0.001$), with patients with VLSC experiencing more intense pruritus than both those with VLS and VLP.

Pain was another common symptom, most prevalent in patients with VLP (79.2% [42/53]), followed by VLS (14.3% [132/922]), and was rare in those with VLSC (0.3% [1/380]). The differences among the groups were highly significant ($P < 0.001$).

Nighttime sleep disturbances due to discomfort such as pruritus or pain were reported in 64.5% (245/380) of patients with VLSC, 42.4% (390/922) of those with VLS, and 25.0% (13/53) of those with VLP. Pairwise comparisons revealed statistically significant differences among all groups ($P < 0.05$).

Asymptomatic cases were relatively rare, with 5.9% (54/922), 5.7% (3/53), and none (0/380) in the VLS, VLP, and VLSC groups, respectively. The proportion of asymptomatic patients in the VLSC group was significantly lower than those in the VLS and VLP groups, whereas the difference between the VLS and VLP groups was not statistically significant.

Due to the anatomical location, all three conditions affected sexual function to varying degrees. Sexual activity was negatively impacted in 81.2% (592/922) of patients with VLS, 84.8% (39/53) with VLP, and 67.3% (220/380) with VLSC. Intergroup comparisons revealed statistically significant differences ($P < 0.001$), with VLSC exhibiting a significantly lower rate of sexual dysfunction than VLS and VLP. No significant differences were observed between VLS and VLP groups.

The median Dermatology Life Quality Index (DLQI) scores were as follows: 7.5 (IQR 4–12) in the VLSC group, 6 (IQR 3–10) in the VLS group, and 7 (IQR 4–12) in the VLP group. The DLQI score was significantly higher in the VLSC group than in the VLS group ($P < 0.05$) (Table 2).

Table 2 Primary Symptoms and Impact on Quality of Life

Variable	VLS (n=922)	VLP (n=53)	VLSC (n=380)	Unknown	Test Statistic	*P* value	Adjusted *P* value
Asymptomatic (n, %)	54(5.9%)[a]	3(5.7%)[a]	0(0.0%)[b]	0	23.196	<0.001	<0.001
Pruritus (n, %)	849(92.1%)[a]	32(60.4%)[b]	380 (100.0%)[c]	0	117.403	<0.001	<0.001
Pain (n, %)	132(14.3%)[a]	42(79.2%)[b]	1(0.3%)[c]	0	263.02	<0.001	<0.001
Affect sleep (n, %)	390(42.4%)[a]	13(25.0%)[b]	245(64.5%)[c]	4	63.733	<0.001	<0.001
Affect sex (n, %)	592(81.2%)[a]	39(84.8%)[a]	220(67.3%)[b]	253	26.46	<0.001	<0.001
Degree of itching (NRS-ISS)	5(2–8)[a]	2(0–5)[b]	7(5–8)[c]	55	112.696	<0.001	<0.001
DLQI	6(3–10)[a]	7(4–12)[a,b]	7.5(4–12)[b]	150	13.752	0.001	<0.001

Notes: Data are presented as median (IQR) for continuous variables and n (%) for categorical variables. "P value" indicates the overall unadjusted group comparison, whereas "adjusted P value" indicates the overall group comparison after inverse probability of treatment weighting (IPTW) based on age, age at onset, and disease duration. Pairwise group comparisons after IPTW are denoted by supscript lowercase letters (a, b, c); groups sharing the same supscript letter do not differ significantly at the 0.05 level.

Abbreviations: DLQI, Dermatology Life Quality Index; IQR, interquartile range; ISS, itching severity scale; NRS, numerical rating scale.

Lesion Types and Distribution

The most common lesion types in patients with VLSs were white patches (84.1%), lichenification (61.1%), erosion and fissures (30.9%), and labia minora atrophy (14.3%). In the VLP group, erosion and fissures (50.9%), and erythema and edema (41.5%) were the most frequently observed lesions. Among patients with VLSC, lichenification was the predominant lesion type, observed in 82.1% of cases.

White patches and atrophy of the labia minora were significantly more common in the VLS group than in the VLP and VLSC groups ($P < 0.05$). Purpuric lesions were exclusively observed in patients with VLS. Erythema, edema, erosion, and fissures were significantly more prevalent in the VLP group than in the VLS and VLSC groups ($P < 0.05$). Lichenification was significantly more frequent in VLSC than in VLS or VLP ($P < 0.05$). A summary of the lesion types is presented in Table 3.

The most frequently affected sites in patients with VLS were the labia minora (57.4%), interlabial sulci (56.1%), labia majora (49.3%), clitoris (45.1%), and posterior commissure (36.7%). In patients with VLPs, the most commonly involved sites were the labia minora (39.6%) and the vaginal introitus (34.0%). For VLSC, lesions most often involved the labia majora (73.2%), interlabial sulci (26.8%), and perianal region (18.9%).

The clitoris, periclitoral area, labia minora, interlabial sulci, pubic and anterior commissure, posterior commissure, and labial frenulum were significantly more frequently affected in the VLS than in the VLP and VLSC ($P < 0.05$). Perineal involvement was also more common in the VLS group than in the VLP and VLSC group ($P < 0.05$). In contrast, the labia majora and perianal regions were significantly more frequently involved in VLSC than in the other two groups ($P < 0.05$). Vaginal introitus involvement was significantly more prevalent in VLP than in VLS or VLSC ($P < 0.05$).

Extragenital involvement was observed in all three conditions, with a notably higher prevalence in the VLP (35.8% [19/53]) and VLSC (24.7% [94/380]) groups than in the VLS group (1.8% [17/922]) ($P < 0.001$). Eleven patients in the VLP group were diagnosed with vulvovaginal-gingival syndrome. Detailed comparisons are presented in Table 4.

Table 3 Lesion Types

Variable	VLS (n=922)	VLP (n=53)	VLSC (n=380)	Unknown	Test Statistic (χ^2/Fisher)	*P* value	Adjusted *P* value
White patch	775(84.1%)[a]	5(9.4%)[b]	7(1.8%)[c]	0	800.671	<0.001	<0.001
Erythema and edema	106(11.5%)[a]	22(41.5%)[b]	5(1.3%)[c]	0	94.1	<0.001	<0.001
Erosion and fissure	285(30.9%)[a]	27(50.9%)[b]	1(0.3%)[c]	0	166.362	<0.001	<0.001
Lichenification	563(61.1%)[a]	1(1.9%)[b]	312(82.1%)[c]	0	147.206	<0.001	<0.001
Purpura	73(7.9%)[a]	0(0.0%)[b]	0(0.00%)[b]	0	36.235	<0.001	<0.001
Atrophy of labia minora	132(14.3%)[a]	0(0.0%)[b]	0(0.00%)[b]	0	68.682	<0.001	<0.001

Notes: Data are presented as n (%) unless otherwise indicated. "P value" indicates the overall unadjusted group comparison, whereas "adjusted P value" indicates the overall group comparison after inverse probability of treatment weighting (IPTW) based on age, age at onset, and disease duration. Pairwise group comparisons after IPTW are denoted by subscript lowercase letters (a, b, c); groups sharing the same subscript letter do not differ significantly at the 0.05 level.

Table 4 Lesion Distribution

Variable	VLS (n=922)	VLP (n=53)	VLSC (n=380)	Unknown	Test Statistic (χ^2/Fisher)	*P* value	Adjusted *P* value
Clitoris	412(45.1%)[a]	0(0.0%)[b]	2(0.5%)[c]	8	274.717	<0.001	<0.001
Periclitoral area	313(33.9%)[a]	0(0.0%)[b]	9(2.4%)[c]	0	165.321	<0.001	<0.001
Labia minora	518(57.4%)[a]	21(39.6%)[b]	17(4.5%)[c]	21	307.82	<0.001	<0.001
Labia majora	451(49.3%)[a]	6(11.3%)[b]	278(73.2%)[c]	8	103.018	<0.001	<0.001
Interlabial sulci	513(56.1%)[a]	2(3.8%)[b]	102(26.8%)[c]	8	131.991	<0.001	<0.001
Pubic and anterior commissure	177(19.4%)[a]	0(0.00%)[b]	15(3.9%)[c]	8	61.376	<0.001	<0.001

(*Continued*)

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Table 4 (Continued).

Variable	VLS (n=922)	VLP (n=53)	VLSC (n=380)	Unknown	Test Statistic (χ^2/Fisher)	*P* value	Adjusted *P* value
Vaginal introitus	99(10.9%)[a]	18(34.0%)[b]	0(0.0%)[c]	10	84.136	<0.001	<0.001
Posterior commissure	335(36.7%)[a]	5(9.4%)[b]	10(2.6%)[c]	8	169.385	<0.001	<0.001
Labial frenulum	131(14.2%)[a]	1(1.9%)[b]	0(0.0%)[c]	0	65.653	<0.001	<0.001
Perianal region	64(7.0%)[a]	0(0.0%)[b]	72(18.9%)[c]	8	48.388	<0.001	<0.001
Perineum	103(11.2%)[a]	1(1.9%)[b]	9(2.4%)[b]	0	30.284	<0.001	<0.001
Extragenital lesions	17(1.8%)[a]	19(35.8%)[b]	94(24.7%)[b]	0	206.431	<0.001	<0.001

Notes: Data are presented as n (%) unless otherwise indicated. "P value" indicates the overall unadjusted group comparison, whereas "adjusted P value" indicates the overall group comparison after inverse probability of treatment weighting (IPTW) based on age, age at onset, and disease duration. Pairwise group comparisons after IPTW are denoted by supscript lowercase letters (a, b, c); groups sharing the same supscript letter do not differ significantly at the 0.05 level.

Discussion

Vulvar dermatoses often present with overlapping clinical features that pose significant diagnostic challenges in routine practice. VLS, VLP, and VLSC are three representative conditions frequently encountered in vulvar clinics and commonly misdiagnosed or confused with one another. While all three typically manifest as vulvar pruritus, local discomfort, and characteristic mucocutaneous changes, they fundamentally differ in their underlying pathophysiology, clinical distribution patterns, histopathological features, and long-term complications. Accurate differentiation is essential not only for tailoring individualized treatment strategies and optimizing prognosis but also for early recognition and management of potential malignant transformation.

The present study systematically compared the clinical features and lesion characteristics of VLS, VLP, and VLSC to identify diagnostic distinctions that may assist clinicians in differentiating these conditions. This focus on providing clues for differential diagnosis stands in contrast to our previous work, which described the profound disease burden and impact on quality of life in a cohort of patients with VLS.[8] Our findings highlighted clear differences in age distribution and disease duration among the three groups. In a cohort study involving 327 patients, by Cooper et al[13] reported a mean diagnostic delay of approximately 4.6 years for VLS, consistent with our findings. VLP symptoms often begin during the perimenopausal or early menopausal period, with reported average age at onset ranging from 51 to 67 years.[14] In our study, the median age at VLP onset was slightly lower (44 years). In contrast, VLSC predominantly affects younger women 30–50 years of age;[15] in our cohort, the median age was 34 years.

Among the three groups, the VLP group had the highest median age at onset (44 years), which was significantly older than that of the VLS (30 years) and VLSC (34 years) groups. This suggests that age may be a useful clinical indicator of suspected VLP, particularly in older women presenting with new-onset vulvar disease. Additionally, patients with VLSC exhibited the longest median disease duration (five years), which was significantly longer than that of patients with both VLSC and VLP (three years each). This may be attributable to the more insidious onset of VLS symptoms, with a proportion of patients being asymptomatic (minimally 10%),[16] potentially delaying diagnosis and medical consultation.

All three conditions negatively impact the daily lives of those affected. Our previous research documented the significant psychosocial and lifestyle burden, including effects on sexual function and bathing habits, borne by patients with VLS.[8] The current analysis extends this understanding by directly comparing the quality of life impact across the three diseases. VLS can lead to pruritus, pain, and interference with sleep and sexual activities. One study found that nearly 60% of women with VLS experience sexual dysfunction.[17] In contrast, VLP is more frequently characterized by pain. Cheng et al[18] reported that 92% of 72 women with genital lichen planus experienced pain or burning and 50% reported pruritus. Helgesen et al[19] found that 67% of patients with VLP reported dyspareunia.

Previous studies have shown that VLSC is commonly associated with chronic or intermittent pruritus accompanied by intense scratching or friction, which may lead to erosion and localized pain.[20] A five-year cross-sectional study involving 15 patients with VLSC[21] reported that all patients experienced pruritus and 46.7% experienced sexual difficulties.

A comparative study[22] reported mean DLQI scores of 7.18 for erosive vulvovaginal LP, 3.79 for vulvar LS, and 8.67 for vulvar dermatitides, highlighting the significant impact of these conditions on quality of life.

In our study, symptom comparison revealed that pruritus was nearly universal in VLSC (100%), followed by VLS (92.1%) and VLP (60.4%). VLSC also had the highest pruritus intensity (median NRS, 7), significantly exceeding those of VLS (NRS, 5) and VLP (NRS, 2). Thus, severe pruritus (NRS $\geq$ 7) may be a diagnostic clue for VLSC. Conversely, pain was most prevalent in VLP (79.2%), a rate far exceeding that of VLS (14.3%) and VLSC (0.3%), which may strongly suggest a diagnosis of VLP.

Sleep disturbances are the most common in VLSC, likely due to intense pruritus. Sexual dysfunction was more frequently reported in those with VLS (81.2%) and VLP (84.8%) than in VLSC (67.3%), possibly due to the greater propensity of VLS and VLP to affect sensitive structures such as the clitoris and vaginal introitus. VLP can also involve the vaginal mucosa, and both VLS and VLP may lead to introitus stenosis in advanced stages. The DLQI score in the VLSC group was significantly higher than that in the VLS group, likely reflecting more severe pruritus and a greater impact on the activities of daily living of those affected.

Significant differences were also observed in the anatomical distribution of lesions among the three conditions, suggesting that the lesion location may serve as a valuable diagnostic clue. Previous studies have shown that the most commonly affected sites in VLS are the periclitoral hood (70%), perineum (68%), and perianal folds (32%).[23] However, our findings indicated a different distribution, with the labia minora, interlabial sulci, labia majora, and clitoris being the most frequently involved regions in VLS. In VLP, earlier studies have noted that lesions most often involve the introitus (90%), followed by the vagina (20–38%), vulva (37%), and perianal area (8%).[24] Our results similarly showed that the labia minora and vaginal introitus were the predominant sites of involvement in VLP. VLSC typically presents as lichenified plaques, primarily on the labia majora, but may also involve the labia minora and perineum, whereas the vagina is typically spared.[5] Consistent with this, our study found that the labia majora, interlabial sulci, and perianal region were more commonly affected in VLSC.

When comparing the distribution patterns among the three diseases, we found that involvement of the clitoris, periclitoral area, labia minora, interlabial sulci, pubic and anterior commissure, posterior commissure, and labial frenulum was significantly more common in VLS than in VLP or VLSC. Lesions in the labia majora and perianal region are more characteristic of VLSC, whereas the involvement of the vaginal introitus is a hallmark feature of VLP. Although the clinical manifestations of these vulvar dermatoses may overlap, our statistical analysis revealed distinct patterns that supported a differential diagnosis.

In early VLS, lesions typically begin as well-demarcated erythema and edema around the clitoris. Over time, the affected skin becomes fragile and develops fissures, erosions, purpura, and ecchymoses. Without timely treatment, the skin may develop dryness, sclerosis, hypopigmentation, and atrophy, eventually resembling parchment paper. Excessive scarring can lead to loss of labial architecture and clitoral phimosis.[23] In our study, the most common lesion type in VLS was white plaque(s), followed by lichenification, suggesting that most patients presented during the mid-to-late disease course. This may reflect nonspecific or mild symptoms of early stage VLS, which are easily overlooked by both patients and clinicians. Furthermore, early VLS often exhibits subtle histopathological features that may be indistinguishable from those of VLP, such as interface dermatitis and band-like lymphocytic infiltration at the dermoepidermal junction.

D'Souza et al[25] reported that hypopigmentation and atrophy are the key clinical features of VLS, whereas erosions, ulcers, and erythema are characteristic of VLP. Our findings are consistent with this finding, given that the VLP group predominantly exhibited erythema, edema, and erosion. However, similar features may also occur in early VLS, further complicating the differentiation. Therefore, for patients presenting with erythema and edema, clinicians should schedule regular follow-ups to avoid missed or delayed diagnoses.

Notably, 11 patients in the VLP cohort had concurrent gingival involvement. In previous reports, we described cases of vulvar-vaginal-gingival-otic syndrome, in which patients initially sought care from otolaryngology (ie, "ENT") or dental departments and were misdiagnosed with gingivitis or otitis media.[26] These cases often require systemic immunosuppressive therapy rather than topical treatment alone, underscoring the importance of a thorough systemic assessment when diagnosing VLP.

Consistent with the existing literature,[3] the predominant lesion type in our patients with VLPs was erosion. In contrast, VLSC are primarily characterized by lichenification driven by intense pruritus and the resulting itch–scratch–

itch cycle. Although VLS, VLP, and VLSC may present similarly and may even involve extragenital sites, we found that the proportion of extragenital involvement was significantly lower in VLS than in VLP or VLSC.

Importantly, both VLS and VLP carry the risk for malignant transformation and, therefore, require careful monitoring. Studies have shown that women with VLS have an estimated 4–5% lifetime risk for developing vulvar squamous cell carcinoma.[27] Similarly, patients with uncontrolled erosive VLP are at risk, with an estimated malignant transformation rate of 2.3%.[28] Therefore, accurate diagnosis, standardized treatment, and regular follow-up are critical to prevent disease progression and malignancy, especially in patients with VLS or VLP.

Limitations

The present study had several limitations. First, as a single-center study, our work may be subject to selection bias, which may limit the generalizability of the findings; and the retrospective use of routinely recorded clinical information may introduce information bias. Further multicenter prospective studies aimed at validating these findings are warranted. Second, the number of patients in the VLP group was significantly smaller than that in the VLS and VLSC groups. The marked imbalance in sample size across the three groups may have reduced the statistical power to detect true intergroup differences, particularly for small effect sizes, and may thus have introduced additional bias; Future studies should recruit a larger VLP cohort to provide more robust and generalizable evidence.

Conclusions

In summary, this retrospective study systematically compared the clinical characteristics of VLS, VLP, and VLSC. In contrast to prior studies, including our own which focused on the disease burden of VLS alone, this work provides a direct comparative analysis aimed at resolving the common clinical challenge of differential diagnosis. This study highlights significant differences in clinical characteristics and quality of life among patients with VLP, VLS, and VLSC. Notably, patients with VLP presented with a significantly later age of onset and exhibited the highest prevalence of pain, while those with VLSC reported the most severe pruritus and a decrease in quality of life, as evidenced by the mean Dermatology Life Quality Index (DLQI) scores. Additionally, VLS patients experienced the longest diagnostic delays and had a high incidence of sexual dysfunction. Anatomically, the affected areas differ between VLS, VLP and VLSC, and varying lesion morphologies further distinguish these conditions. Recognizing these differences can help avoid misdiagnosis and underdiagnosis in clinical practice and facilitate timely individualized interventions. Ultimately, these efforts could improve patient outcomes and enhance long-term disease management.

Abbreviations

VLS, Vulvar lichen sclerosus; VLP, Vulvar lichen planus; VLSC, Vulvar chronic vulvar simplex lichen; NRS, Numerical Rating Scale; IQR, Interquartile range; DLQI, Dermatology Life Quality Index.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Statement

This study was approved by the Ethics Committee of Beijing Hospital (Approval No. 2023BJYYEC-152-01). As it was a retrospective analysis of anonymized clinical data, the requirement for written informed consent was waived by the ethics committee. All patient data were de-identified to ensure confidentiality.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest.

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