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Characteristics, comorbidities, and treatment practices of lichen planus in Northern Finland: A register-based study among 619 subjects

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Abstract

Background and Aims: Lichen planus (LP) is a common itching skin disease where lesions appear on the skin and mucous membranes. However, the epidemiology of LP is not yet sufficiently understood. The aim of this study was to retrospectively map out the characteristics, comorbidities and treatments of patients diagnosed with LP.

Methods: This is a retrospective hospital patient registry-based study performed between 2009 and 2021 in a secondary care hospital (Oulu University Hospital) in Northern Finland. All patients with recorded diagnosis of LP were included in the study. Characteristics, comorbidities, and treatments of LP patients were studied.

Results: In total, 619 patients were verified from the hospital health records. The mean age of patients was 54.2 years and the majority were female (58.3%). Most of the patients had symptoms in more than two skin areas (mean 2.7 skin areas), lower limbs being the most common site (74.0%). A third of patients (34.7%) had oral LP lesions. Nearly fifth (19.4%) of the subjects had a history of previous LP. Of comorbidities found among LP subjects, obesity (22.5%), malignancies (19.4%), depression (12.8%), and thyroiditis (12.4%) were seen more often than in general Finnish population. The most used form of treatment was topical corticosteroids (97.6%), followed by phototherapy 26.8%. Systemic treatments such as prednisolone and methotrexate had been used in 7.6% and 1.1% of the patients, respectively.

Conclusion: LP patients had a heightened risk for several comorbidities, which should be considered when managing patients with LP.

KEYWORDS

comorbidity, epidemiology, health registry data, lichen planus, treatment

Veera Anttonen and Elia Pöykkö contributed equally to this article.

1 | INTRODUCTION

Lichen planus (LP) is an inflammatory skin disease, which most commonly occurs on the skin and mucous membranes of the mouth. Other locations are, for example, genitals, esophagus, scalp hair follicles, and nails.[1] The clinical presentation of LP is heterogeneous (Figure 1) but it has a uniform histological phenotype,[2,3] and in uncertain cases, clinical diagnosis can be confirmed with a biopsy.[1] The exact prevalence of LP is unknown but the estimated prevalence of LP is reported to vary between 0.2% and 5% worldwide.[4] In a Finnish primary health care data, skin-related conditions were a common cause of physicians's consultation.[5] Of those, LP is one of the most common itching skin disease.[5] LP occurs in people of all ages but it is most common in middle-aged (mean age 45–47 years).[6,7] In children, LP is quite rare, usually reported as accounting for <5% of the total cases.[1,8]

LP is known to be associated with an increased risk of other diseases. Several autoimmune diseases, particularly alopecia areata (AA) and ulcerative colitis, have been reported to occur more frequently in patients with LP than in control populations.[1] In addition, other autoimmune diseases, that is, systemic lupus erythematosus, Sjögren's syndrome, vitiligo, and dermatomyositis, have been reported to associate with LP.[9] In addition, according to a cohort study of 13,100 Finnish women, patients with diagnosed LP have an increased risk of developing several cancers such as esophageal and vulvar cancers.[10] Moreover, hepatitis C virus (HCV) has been found to have a significant association with LP.[1]

Cutaneous LP usually heals on its own in 1–2 years;[2] however, relapses are common. If needed, topical glucocorticoids or ultraviolet therapy are the most common firstline treatment. Secondline therapies (such as acitretin or cyclosporine) can be considered for persistent cases.[11]

The epidemiology of LP is not yet sufficiently understood. The aim of this study was to determine the characteristics of cutaneous LP, its comorbidities, and treatments used in patients diagnosed and treated in Oulu University Hospital (OUH) in Northern Finland.

2 | PATIENTS AND METHODS

2.1 | Patients

All patient records including the International Classification of Diseases 10th revision codes for LP (L43.0, L43.1, L43.3, L43.8,and L43.9) were extracted from the OUH medical records database. Study data were collected and managed by the authors using REDCap electronic data capture tools hosted at the University of Oulu. All records were manually checked by the authors for demographics, clinical picture (Table 1), preselected comorbidities (Figure 2) known to associate with LP according to the previous literature,[1,9,10] and treatments used for LP and collected to the REDCap. All patients who visited the dermatology outpatient clinic with the above-mentioned diagnoses between 2009 and 2021 were included in this study. Those with mistyped code (e.g., true code K43) were excluded. The medical director of OUH approved the study. Ethics committee approval was not required since the study was retrospective and based on medical records only.

2.2 | Statistical analysis

The overall prevalence of LP comorbidities was calculated. Data are presented as means, standard deviation (SD) and range, and as proportions for categorical variables. Pearson's χ^2 test was used to compare the distribution between sexes. All statistical analyses were performed using R software version 4.1.1. R core Team (2020) (R Foundation for Statistical Computing; https://www.R-project.org/). A $p < 0.05$ was considered statistically significant.

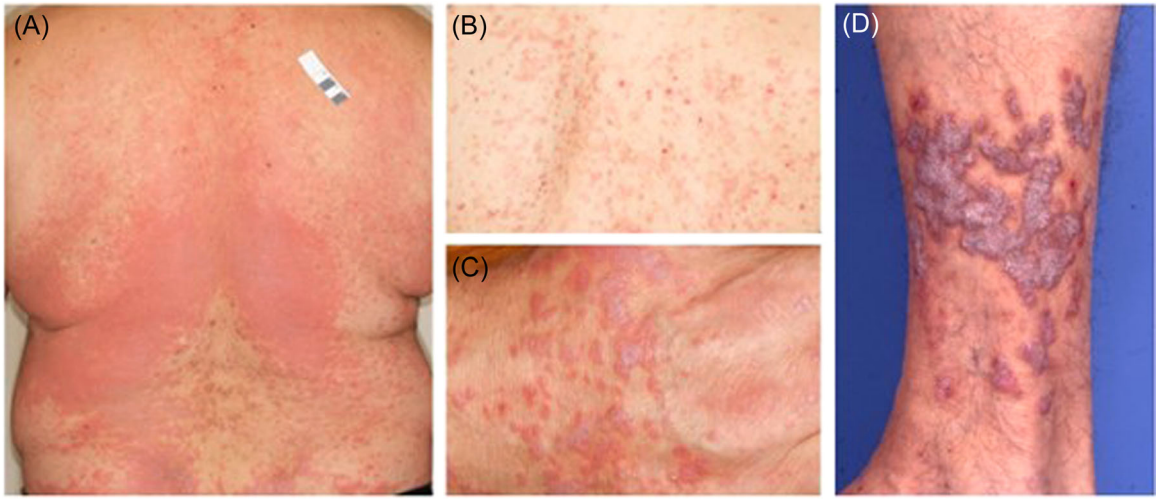

FIGURE 1 Clinical presentation of lichen planus (LP). (A) Widespread papular LP clustering into plaques. (B) Typical slightly shiny LP papules in back. (C) LP on the hand with Wickham's striae. (D) Hyperthrophic LP on shin.

TABLE 1 Baseline characteristics of the study population ($N = 619$).

	Males ($n = 258$)	Females ($n = 361$)	Total ($n = 619$)	p
Age, years, mean (SD)	51.7 (17.7)	56.0 (15.4)	54.2 (16.5)	0.001[a]
Smoking status, *n* (%)				0.001[b]
Smoker	62 (24.0)	58 (16.1)	129 (19.4)	
Nonsmoker	55 (21.3)	137 (38.0)	192 (31)	
Ex-smoker	56 (21.7)	37 (10.2)	93 (15)	
No information[c]	85 (32.9)	129 (35.7)	214 (34.6)	
Duration of symptoms, *n* (%)				0.229[b]
0–3 months	51 (19.8)	64 (17.7)	115 (18.6)	
4–≤12 months	102 (39.5)	156 (43.2)	258 (41.7)	
1–2 years	17 (6.6)	34 (9.4)	51 (8.2)	
2–5 years	26 (10.1)	27 (7.5)	53 (8.6)	
5–10 years	5 (1.9)	10 (2.8)	15 (2.4)	
>10 years	18 (7.0)	12 (3.3)	30 (4.8)	
No information[c]	39 (15.1)	58 (16.1)	97 (15.7)	
Previous record of LP[d] *n* (%)	47 (18.2)	73 (20.2)	120 (19.4)	0.534[b]
Localization, *n* (%)				
Forearms/wrists/hands	153 (59.3)	247 (68.4)	400 (64.6)	
Legs/ankles/feet	179 (69.4)	279 (77.3)	458 (74.0)	
Back	74 (28.7)	144 (39.9)	218 (35.2)	
Fold areas[e]	25 (9.7)	61 (16.9)	86 (13.9)	
Nails	14 (5.4)	14 (3.9)	28 (4.5)	
Scalp	13 (5.0)	30 (8.3)	43 (6.9)	
Genitals	62 (24.0)	64 (17.7)	126 (20.4)	
Front torso	72 (27.9)	121 (33.5)	193 (31.2)	
Face	17 (6.6)	21 (5.8)	38 (6.1)	
Lips	26 (10.1)	26 (7.2)	51 (8.2)	
Oral lesions	72 (27.9)	143 (39.6)	215 (34.7)	
Localization sum, different skin areas, mean (SD)[f]	2.5 (1.3)	2.8 (1.3)	2.7 (1.3)	0.002[a]
Clinical presentation, *n* (%)				
Papular	142 (55.0)	200 (55.4)	342 (55.3)	
Bullotic	6 (2.3)	17 (4.7)	23 (3.7)	
Hypertrophic	54 (20.9)	49 (13.6)	103 (16.6)	
No information/other[g]	86 (33.3)	140 (38.8)	226 (36.5)	

Abbreviations: ANOVA, analysis of variance; LP, lichen planus.

[a]Linear model ANOVA.

[b]Pearson's χ^2 test.

[c]The information was not found in the patient records.

[d]The patient had previously been diagnosed with a separate case of LP.

[e]Groin, crook of the elbow, armpit, back of the knee.

[f]Not including oral lesions.

[g]Unspecified or some other form of clinical presentation, such as annular, erosive, or atrophic.

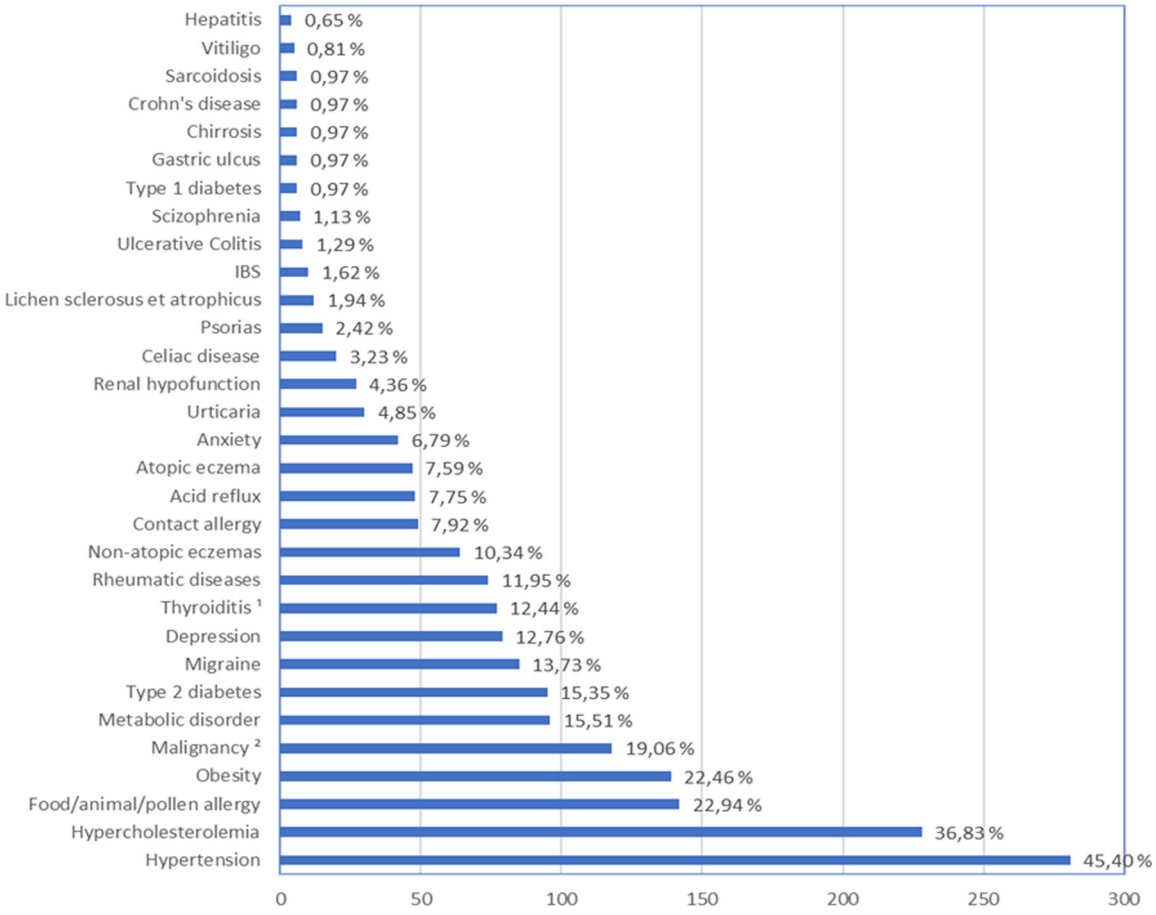

FIGURE 2 The comorbidities of cutaneous lichen planus (LP) in $n = 619$ patients.
[1]Criteria for thyroiditis were either (a) a direct diagnosis for a form of thyroiditis or (b) hypothyroidism without other affecting thyroid diseases or surgical removal of the thyroid.
[2]Patients with solid malignancies $n = 112$, patients with hematologic malignancies $n = 8$. $N = 2$ had both a solid and a hematologic malignancy.
IBS, irritable bowel disease.

3 | RESULTS

We found a total of 619 cases of LP. Of the patients included, 41.7% were male ($n = 258$) and 58.3% female ($n = 361$). Mean age was 54.2 years (51.7 for men and 56.0 [$p = 0.001$] for women, respectively). Of all cases, 13 (2.1%) were children (age < 18 years at the time of diagnosis). Most commonly, the duration of symptoms was 4–12 months (41.7%) before the diagnosis in OUH. Papular LP was the most common clinical presentation of LP (55.3%) and 16.6% of the patients had hypertrophic LP (Table 1).

The most common localizations of LP were "legs/ankles/feet" and "forearms/wrists/hands" (74.0% and 64.6%, respectively). Most patients had symptoms of LP in more than two skin areas (mean 2.7 different skin areas). One-third of the cases (34.7%; $n = 215$) had oral LP symptoms, which were seen more often in females (39.6%) than males (27.9%) ($p = 0.003$). Nearly a fifth of the patients (19.4%) had previously been diagnosed with a distinct case of LP.

Smoking was more common in male subjects with LP than in female cases (24.0% and 16.1%, respectively) ($p < 0.001$). Having quit smoking was also more common among males than females (21.7% and 10.2%, respectively).

3.1 | Comorbidities

The most common comorbidity in all the patients with LP was hypertension (45.4%) followed by hypercholesterolemia (36.8%). The most common autoimmune comorbidity was thyroiditis (17.7% for females, 5.0% for males) ($p < 0.001$). Migraine was more common in females than males (18.3% and 7.4%, respectively) ($p < 0.001$). Of all the LP cases, 18.1% had solid and 1.3% had hematological malignancies. Depression and anxiety were found in 12.8% and 6.8% of the patients, respectively. The comorbidities of LP cases are described in detail in Figure 2.

TABLE 2 Treatments used in cutaneous LP patients.

Treatment	*n* (%)
Topical corticosteroid	604 (97.6)
Topical calcineurin inhibitor	48 (7.8)
Oral prednisolone	47 (7.6)
Hydroxychloroquine	3 (0.5)
Methotrexate	7 (1.1)
Intralesional corticosteroid	2 (0.34)
Phototherapy[a]	166 (26.8)
No treatment	10 (1.7)

Abbreviations: PUVA, psoralen plus ultraviolet-A radiation; UVB, ultraviolet B.

[a]UVB and all forms of PUVA therapy.

3.2 | Treatments

Almost all cases of cutaneous LP were treated with a topical corticosteroid (97.6%). Systemic corticosteroids were used in 7.6% and phototherapy in 26.8% of cases for cutaneous LP. Intralesional corticosteroid injections were used for two cases of hypertrophic cutaneous LP (Table 2).

4 | DISCUSSION

This study evaluated LP comorbidities and treatments in 619 subjects with LP diagnosed in a secondary referral hospital. LP is most prevalent in middle age, as was also seen in the current study (mean age 54.2). However, the age of highest prevalence varies between studies.[6–8] According to a large-scale German retrospective analysis, the highest prevalence of LP for both men and women was seen between 60 and 79 years.[8] Other studies have reported that nearly two-thirds of the patients with LP are 30–60 years.[6,7] In children, LP is less common, seen in under 5% of the cases,[1,8] and our study confirms this finding.

A slight majority of the patients in the present study with cutaneous LP were female (58.3%). However, there is no consensus on whether there is a true female predominance in LP[4] even thought some studies have found a higher prevalence of LP in women, especially in oral LP. Predominance of oral LP in women has speculated to come from hormonal reasons or higher susceptible to immune-mediated inflammatory diseases than men.[12] Nevertheless, the result of our study (female preponderance) may be explained at least partly by the fact that in general, males are less likely to seek medical help.[13]

We found many comorbidities to affect our LP patients of which the hypertension was the most common, affecting 45.4% of the patients. When compared to large-scale studies of the Finnish population, the prevalence of hypertension among LP patients was comparable to that in the general population.[14] In turn, the prevalence of thyroiditis was high in LP patients. This finding aligns with those of previous studies, which have reported an association between thyroiditis and LP.[2,8] Thyroiditis and autoimmune thyroiditis have been observed to be twice more common in LP patients than in controls.[8] When hypothyroidism is used as a proxy for thyroiditis, we see that the prevalence of thyroiditis is significantly higher in the current study population compared to the general Finnish population: the prevalence of hypothyroidism in the Finnish population 50–59 years of age was 8.63% for women and 1.56% for men.[15]

Being in line with previous literature,[10] malignancies were also common in the LP patients in the current study. According to a Finnish Cancer registry study, the total prevalence of cancer in Finland in 2018 was 3.64% for ages 20–69 years and 19.01% for ages 70 years and older.[16] This suggests that our study population with a mean age of 54.2 has higher prevalence of cancer than the general population. In more details, according to a cohort study of women by Halonen et al.,[10] female LP patients are at higher risk of oral, esophageal, laryngeal and vulva cancer, but do not have an increased risk of skin cancer. Their finding of increased overall cancer risk supports the results of the current study.

Previous studies have shown that LP is associated with psychiatric disorders.[17] A systematic review and pooled meta-analyses ($n = 921$) showed that LP patients have a high prevalence of signs of depression (27%) and anxiety (28%); case–control studies showed a strong association between LP and signs of depression, odds ratio (OR) 3.79, 95% confidence interval (CI [2.35; 6.12]) or anxiety, OR 2.54, 95% CI [1.73; 3.72].[17] In the current study, depression was the most common psychiatric comorbidity (12.76%), whereas anxiety occurred in 6.79% of patients. Thus, there was more depression among LP patients than in general Finnish population (12.0% among those aged 45–54 years and 7.0% in those aged 55–64 years, respectively).[18] In addition, our finding about depression and anxiety in LP patients is comparable to psychiatric morbidity overall among adult patients with another itching skin disease, prurigo nodularis, in Finland.[19] However, the prevalences in our study were not as high as in the recent meta-analysis.[17] This can arise, for example, from the different study design and the fact that the meta-analysis also included cases of pure oral LP, and those with oral LP have been described to have higher risk of depression than cases with cutaneous LP.[17]

The pathogenesis of LP remains still partly unknown but it is thought to result from autoimmune reaction and followingly, LP is associated with many autoimmune diseases and viral infections and.[1] In particular, HCV has been found to have a significant association with LP.[1,8,20] In a meta-analysis, the prevalence of LP was higher among patients with HCV (5.4%) than in those without (2.5%).[20] Moreover, Schruf et al.[8] found both HCV and hepatitis B virus infections to be three times more likely in LP patients than in controls. However, HCV was not a frequent comorbidity in the current study, as it was present in only four patients. Recently, many case studies have reported an onset of LP after COVID-19 infection or vaccination.[21] Nevertheless, a general health, comorbidities and immunological status (i.e., factors having an influence on the immune

system) of these people have often been insufficiently described,[22] and thus, more studies are needed to confirm the real relationship between LP and COVID-19 infection or vaccination.

Besides virus infections also the association with autoimmune diseases and LP has been largely reported.[1] For example a case–control study in Taiwan ($n = 12,427$) observed AA to be more than two-fold more common in LP patients.[9] However, in the current study only two LP patients were recorded to have concomitant AA.

In our population, the most common treatments in cutaneous LP included topical corticosteroids, phototherapy, oral prednisolone, and topical calcineurin inhibitors. Topical corticosteroids were used in nearly all the cases (97.6%). This is in line with clinical recommendations, as according to Boch et al.,[11] topical corticosteroids should be used as a first-line treatment in most cases of LP regardless of the anatomical site or severity of the symptoms.

The major strength of the current study is that all the patients included had been evaluated and diagnosed by experienced dermatologists. OUH is the only hospital with a department of dermatology in the Northern Ostrobothnia Hospital District (NOHD), providing special healthcare in dermatology for a Finnish population of 413,830 people. Thus, the current study includes all the dermatological patients with LP treated in NOHD between 2009 and 2021. The current study has some limitations. The study was retrospective and based on medical reports from a university hospital database; information from primary care is thus lacking. Because of this, cases with only mild LP may be missing and information about patients and their treatments was, in some cases, incomplete: for example, the actual number of patients with metabolic diseases is most likely higher than expressed in the results.

This study adds to our knowledge of LP, its treatments, and comorbidities in Finnish population. According to our findings, typical age of LP was in the 5th decade. However, there was also a few children patients. Interestingly, every fifth of our patients had a previously recorded LP in their history and thus, it seems that LP is characterized with relapses. Of note is that a high risk of specific comorbidities such as thyroiditis and malignancies were seen in our study which should be kept in mind when managing patients with LP.

AUTHOR CONTRIBUTIONS

Veera Anttonen: Investigation; writing—original draft. **Elia Pöykkö**: Investigation; writing—original draft. **Eetu Kiviniemi**: Formal analysis; methodology; software. **Jari Jokelainen**: Formal analysis; methodology; software; visualization. **Laura Huilaja**: Conceptualization; data curation; project administration; supervision; writing—review & editing. **Suvi-Päivikki Sinikumpu**: Conceptualization; data curation; project administration; supervision; writing—review & editing.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Our data were retrieved from the OUH patient database. According to Finnish laws and regulations, the data in social welfare are confidential. The Medical Director of the Oulu University Hospital can, on a case-by-case basis, grant permission to use the registers and documents for purposes of scientific research. More information from research authorization applications can be found on www.ppshp.fi. STROBE checklist has been followed when reporting the results of this study.

TRANSPARENCY STATEMENT

The lead author Suvi-Päivikki Sinikumpu affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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