Lichen planus in Germany – epidemiology, treatment, and comorbidity. A retrospective claims data analysis

Eva Schruf, Mona HC Biermann*, Josephine Jacob, Dennis Häckl, Maximilian Reinhardt, Michael Hertl, Johannes Wohlrab

(1) Novartis Pharma GmbH, Nürnberg, Germany
(2) InGef-Institute for Applied Health Research Berlin GmbH, Berlin, Germany
(3) WIG2 GmbH, Leipzig, Germany
(4) University Leipzig, Leipzig, Germany
(5) Novartis Pharma AG, Basel, Switzerland
(6) Department of Dermatology and Allergology, Philipps-Universität, Marburg, Germany
(7) University Hospital and Polyclinic for Dermatology and Venerology, Martin Luther University, Halle (Saale), Germany

*The first two authors contributed equally to this work.

Introduction

Lichen planus (LP) is a chronic inflammatory disease involving a T-cell mediated autoimmune response against basal epithelial keratinocytes resulting in lesions of skin, mucosa and/or skin appendages [1, 2]. Based on the morphology and localization of the lesions, LP manifests in different variants, with oral lichen planus (OLP) and cutaneous LP being the most frequent. Middle-aged adults are most affected, and the majority of OLP patients are female [3]. There is evidence that IFN-γ, described as a key proinflammatory cytokine in LP, and IL-21 dominate the inflammatory process in cutaneous lesions [4]. LP has been shown to be characterized by a peripheral blood Th1/Th17-dominated cell response [5]. However, the exact etiology is unclear. As a consequence of its clinical features and the associated pain, itch, stigma and psychological distress, LP has a substantial negative impact on health-related quality of life (QoL) [2, 6, 7].

Estimates of incidence and prevalence of LP vary substantially depending on the investigated study population, subtype and geography. The global prevalence of LP was reported to be in the range between 0.22–5 %, with differences in the respective subtypes [2, 8, 9]. The estimated incidence of LP in the general population ranges from 0.1 to 1.27 % [3].

A European S1 guideline on the management of LP has recently been developed [10]. Current therapies primarily
aim to alleviate symptoms and include a broad spectrum of immunosuppressive or anti-inflammatory agents [11, 12]. However, treatment can often be challenging, especially for patients with moderate to severe LP who are refractory to topical therapies due to a lack of approved, efficacious systemic treatment options [3]. Recently, a case series with biologic therapies targeting the IL-23-Th17 axis showed substantial clinical and molecular response in five steroid-refractory LP patients [13].

Despite its frequency, data on epidemiology and management of LP remain scarce and are based on a few clinical studies [14, 15]. This study sought to expand the evidence on the epidemiology of LP using a large sample size of anonymized German claims data. Moreover, we aimed to assess current treatment patterns of LP in Germany and comorbidity in LP patients.

Material and Methods

Data source

Two separate cohort studies, in 2015 and 2018, were conducted using a research database from the Institute for Applied Health Research Berlin GmbH (InGef), an anonymized healthcare claims database consisting of information from approximately nine million individuals from more than 60 German statutory health insurances (SHIs). Claims data are transferred directly from health care providers to a specialized SHI data center. In the data center, data is anonymized before entering the InGef research database. For this study, a sample representative for the general German population in terms of age and sex, with approximately four million insured individuals per year, was used. The database includes sociodemographic information about outpatient services and diagnoses, hospital and drug prescription data, prescribed aids and remedies, and accrued costs. Diagnoses are documented using the German modified International Statistical Classification of Diseases and Related Health Problems catalogue (ICD-10-GM). Outpatient procedures are billed using the German Uniform Value Scale (EBM [Einheitlicher Bewertungsmaßstab]). The database has been shown to have good external validity [16]. All patient-level and provider-level data in the InGef research database are anonymized to comply with German data protection regulations and German federal law. Hence, approval of an Ethics Committee was not required.

Study population

Individuals were included if continuously insured in the two years preceding the study year and in the respective study year and/or until death during the study year. Analyses on characteristics and prescribed medication were carried out in the study populations. Patients were identified as prevalent LP or lichenoid drug reaction (LDR) cases if they had at least one hospital main discharge diagnosis or two confirmed ambulatory or hospital secondary discharge diagnoses in two different quarters or within one quarter from two different physicians within in the study period. An incident LP or LDR case was assumed if patients additionally had none of the listed ICD-10-GM codes (Online Supplementary Table S1) documented over two years preceding the study year. A total LP population, LP subtypes and LDR were assessed based on the ICD-10-GM codes presented in Online Supplementary Table S1. Insured individuals, who did not fulfill the respective case definition in 2018, were included in a control group which was utilized to compare the frequency of predefined comorbidity between prevalent LP patients and non-diseased controls. To increase precision, five age and sex-matched controls were selected for each LP patient.

Parameters

Treatment and physician specialties

For incident LP cases in 2018, the specialty of the physician treating and documenting the first LP diagnosis and the specialties of physicians treating LP patients in the diagnosis free period of 2016–2017 was assessed (Online Supplementary Table S2). The unique physician identifier number (LANR, Lebenslange Arztnummer) was used to evaluate by which physician specialty incident and prevalent patients were diagnosed with LP and treated during the baseline period and in the 2018 study year. For dentists and orthodontists, only patients with available data in the InGef research database (98.76 %) were included and analyzed based on at least one documented treatment. Diagnoses from dentists/orthodontists could not be included since dentists/orthodontists are not obligated to document diagnoses for reimbursement purposes. For incident and prevalent cases, the specialty of the treating physician in 2018 was identified. If patients were diagnosed by more than one specialty, they were counted in each physician subgroup. Specific therapies and therapy combinations were assessed based on Anatomical Therapeutic Chemical (ATC) and Operation and Procedure (OPS) codes using all prescriptions and treatment episodes in 2018 (Online Supplementary Table S3).

Comorbidity

The frequency of pre-defined comorbidity, previously reported to be associated with LP, was assessed by one confirmed outpatient diagnosis, hospital main or secondary discharge diagnosis defined by ICD-10-GM codes in 2018 (Online Supplementary Table S4). Additionally, a data-driven approach
was used to identify the 30 most common comorbidities based on ICD-10-GM coding.

Statistical Analyses

The incidence and prevalence of LP/LDR by age group (in years: 0–< 18; 18–29; 30–39; 40–49; 50–59; 60–69; 70–79; 80–89; ≥ 90) and sex were calculated by dividing the number of incident and prevalent LP/LDR cases, respectively, by the number of SHI insured persons in the InGef research database in the respective age-sex stratum. Both estimates are presented per 100,000 individuals. In addition, prevalence and incidence were extrapolated to the total German population in the respective study year (reference: German Federal Statistical Office, DESTATIS). The proportion of patients with a specific comorbidity, specific therapy or consulting a specific physician specialty were calculated by dividing the number of LP patients or controls by the number of individuals in the LP or control population. Odds Ratios (OR) were calculated to compare the 30 most frequent comorbidities and specific comorbidities in the LP group to the control group. P values were calculated by inverse-function of confidence intervals [17]. Absolute and relative frequencies (%) for categorical variables, and means, standard deviations and medians for continuous variables, were used for analyses of demographics, comorbidity and physicians' specialties. For data protection reasons regarding sensitive patient health data, no measures were reported for strata with less than five patients (presented as < 5). All analyses were conducted using Microsoft R open software, version 3.5.0.

Results

Epidemiology

Approximately 3.6 million individuals were included in the analysis in 2015 and 2018. In this population, an overall prevalence of LP of 90.3 LP cases per 100,000 individuals in 2015 and 104.4 cases per 100,000 individuals in 2018 was observed in the database. The annual prevalence of LP – normalized to the total German population – was 84.7 and 95.9 per 100,000 individuals in 2015 and 2018, respectively. This corresponded to a total projected number of 69,591 LP cases in Germany in 2015 and 79,605 LP cases in 2018 (Table 1).

The prevalence and incidence of LP in the German population in 2018 stratified by age and sex are shown in Figure 1. Women were affected more frequently, and the highest prevalence was observed between 60 and 79 years of age.

The total incidence of LP – normalized to the German population – was 19.7 per 100,000 individuals in 2015 and 20.1 per 100,000 individuals in 2018. This corresponded to a total number of 16,159 new LP cases in Germany in 2015 and 16,647 new LP cases in 2018. The incidence of LP was highest between the ages of 60 and 79. In contrast, a very low prevalence and incidence were observed in the pediatric population (< 18 years): The annual prevalence of pediatric LP – normalized to the German population - was 3.9 per 100,000 individuals (3.2 per 100,000 in males; 4.5 per 100,000 in females) and the annual incidence was 2.3 per 100,000 (1.9 per 100,000 in males; 2.7 per 100,000 in females) (Figure 1; Online Supplementary Table S5).

The overall prevalence of hypertrophic LP, lichen planus pemphigoides and lichen planopilaris (LPP) extrapolated to the German population was 3.0 per 100,000, 0.4 per 100,000 and 5.2 per 100,000 individuals in 2018. The overall incidence of hypertrophic LP, lichen planus pemphigoides and LPP was 0.6 per 100,000, < 0.1 per 100,000 and 1.6 per 100,000 individuals in 2018, respectively. Most diagnoses were documented as LP without further specification (L43.9 LP, unspecified: > 60 %). Of all prevalent LP patients in 2018, 9.99 % were diagnosed with more than one LP subtype. The overall prevalence of LDR was 0.6 per 100,000 and the overall incidence of LDR was 0.6 per 100,000 individuals.

Table 1 Prevalence and incidence of LP in 2015 and 2018 – InGef database and normalized to the total German population.

|          | 2015         |          | 2018         |          |
|----------|--------------|----------|--------------|----------|
|          | n-DB /100,000-DB | n-GER /100,000-GER | n-DB /100,000-DB | n-GER /100,000-GER |
| n-DB number of patients with diagnosis in InGef database; /100,000-DB prevalence per 100,000 individuals at risk in InGef database; n-GER extrapolated number of patients with diagnosis in Germany; /100,000-GER normalized prevalence per 100,000 individuals at risk in Germany; ICD-10 codes L43.0 (Hypertrophic lichen planus); L43.1 (Lichen planus pemphigoides); L43.3 (Subacute [active] lichen planus); L43.8 (Other lichen planus); L43.9 (Lichen planus, unspecified); L66.1 (Lichen planopilaris) were used to define LP. |
Treating physicians

In most cases, the first diagnosis of LP was documented by a dermatologist (67.6 %) or primary care physician (19.9 %). Following the incident diagnosis, LP patients were mainly treated by dermatologists (85.2 %) and primary care physicians (96.5 %), as well as gynecologists (44.5 %) and internists (36.1 %). A total of 85.2 % of all incident and approximately 60 % of all prevalent LP patients contacted a dermatologist at least once in the year 2018 (Table 2).

Table 2 Physician specialties treating LP patients in different observation periods [%-DB (n-DB)].

|                | Incident patients | Prevalent patients |
|----------------|-------------------|--------------------|
|                | Baseline | Diagnosis quarter | Treating | Treating |
| Dermatologist  | 51.2 (390) | 67.6 (515) | 85.2 (649) | 59.6 (2,230) |
| Primary care physician | 96.7 (737) | 19.8 (151) | 96.5 (735) | 97.9 (3,664) |
| Internist      | 46.6 (355) | 1 (8) | 36.1 (275) | 40.9 (1,529) |
| Pediatrician   | 2 (15) | < 0.6 (< 5)* | 1.8 (14) | 0.7 (25) |
| Gynecologist   | 49.7 (379) | 5.6 (43) | 44.5 (339) | 41 (1,534) |
| Urologist      | 21 (160) | < 0.6 (< 5)* | 17.2 (135) | 18.7 (700) |
| Rheumatologist | 4.7 (36) | < 0.6 (< 5)* | 3.1 (24) | 3.6 (135) |
| Oral, maxillofacial and facial surgery | 2.5 (19) | < 0.6 (< 5)* | 3.1 (24) | 1.9 (70) |
| Ear-Nose-Throat | 40.4 (308) | 2.1 (16) | 31 (236) | 30.2 (1,131) |
| Surgeon        | 37 (282) | 0.8 (6) | 23.9 (182) | 24.5 (916) |
| Neurologist/Psychiatrist/Psychotherapist | 25.3 (193) | < 0.6 (< 5)* | 18.2 (139) | 19.2 (718) |
| Dentist/Orthodontist** | 87.4 (666) | 6.2 (47) | 92.1 (702) | 91.7 (3,432) |
| Other          | 94.4 (719) | 0 () | 84.1 (641) | 84.3 (3,153) |

Unless otherwise indicated % (n) are reported; patients contacting more than one physician within a given period were counted in each category.

*For data protection reasons no cells containing less than five patients are reported.

**At least one visit at the dentist or orthodontist. Only estimated for patients with available data in the InGef research database (98.76 % of insured persons in the InGef research database).
topical vitamin D derivatives (0.6 %). Among the topical corticosteroids, potent substances (ATC group III) were most frequently used to treat LP, followed by very potent substances (ATC group IV), with 28.1 % of prevalent LP patients receiving class III and 15.4 % receiving class IV corticosteroids in 2018 (Table 3). Systemic therapies were prescribed in 25.2 % of incident and in 22.1 % of prevalent LP patients. Systemic corticosteroids were the most frequently prescribed systemic therapy in prevalent patients (17.5 %), while systemic retinoids (2.4 %) and aminochinolines (2.1 %) were only very rarely used. Phototherapies played a minor role in LP routine care, as only 8.4 % of incident and 4.3 % of prevalent patients received phototherapy. No therapy was prescribed to 16.8 % of incident and 40.8 % of prevalent patients.

### Table 3 Treatment of prevalent and incident LP patients in 2018.

| Therapy                          | % of prevalent LP patients | % of incident LP patients |
|----------------------------------|---------------------------|---------------------------|
| **Topical therapy**              |                           |                           |
| Topical corticosteroids          | 48.0 (1,796)              | 75.6 (576)                |
| – weak (group I)                 | 1.0 (37)                  | 1.8 (14)                  |
| – moderately potent (group II)   | 3.9 (145)                 | 6.2 (47)                  |
| – potent (group III)             | 28.1 (1,050)              | 46.5 (354)                |
| – very potent (group IV)         | 15.4 (578)                | 24.5 (187)                |
| – combinations                   | 7.6 (283)                 | 11.4 (87)                 |
| – for local oral treatment       | 7.4 (278)                 | 12.6 (96)                 |
| Topical calcineurin inhibitors   | 4.4 (165)                 | 5.8 (44)                  |
| Topical vitamin D derivatives    | 0.6 (24)                  | 1.2 (9)                   |
| **Systemic therapy**             |                           |                           |
| Systemic corticosteroids         | 17.5 (654)                | 20.2 (154)                |
| Systemic retinoids               | 2.4 (91)                  | 3.1 (24)                  |
| Aminochinolines                  | 2.1 (80)                  | 2.0 (15)                  |
| **UV therapy**                   |                           |                           |
| UVB phototherapy                 | 3.6 (135)                 | 6.8 (52)                  |
| UVA 1 phototherapy               | 1.1 (43)                  | 2.2 (17)                  |
| PUVA (photochemotherapy)         | 0.8 (30)                  | 1.4 (11)                  |
| **No therapy (neither topical, nor systemic, nor UV therapy)** | 40.8 (1,525) | 16.8 (128) |

Unless otherwise indicated % (n) are reported; patients treated with more than one therapy were counted in each category.

The three most frequently prescribed therapies are shown for each treatment category.

Comorbidity

18,710 age and sex-matched controls were selected to compare the frequency of pre-defined comorbidity between prevalent LP patients and a non-diseased control group in 2018 (Table 4). Dyslipidemias (LP 45.0 %; controls 37.3 %; OR 1.37; P < 0.001) and autoimmune thyroiditis (LP 7.6 %; controls 3.9 %; OR 2.0; P < 0.001) occurred more frequently in LP patients than in controls. Though relatively rare, the odds for a hepatitis C virus (HCV) infection (LP 0.64 %; controls 0.21 %; OR 3.0; P < 0.001) or for a hepatitis B virus infection (LP 0.56 %; controls 0.19 %; OR 3.0; P < 0.001) were three times higher in LP patients. The odds for malignant neoplasms of the lip or oral cavity were almost seven times higher in LP patients (LP 0.99 %; controls 0.14 %; OR 6.9; P < 0.001). Alopecia areata was also more commonly diagnosed in LP patients (LP 2 %; controls 0.27 %; OR 7.8; P < 0.001). Psoriasis vulgaris was documented in 5.18 % of LP cases compared to 1.99 % of control cases (OR 2.7; P < 0.001). Lichen planus patients were more frequently affected by candidiasis of the mouth and esophagus (LP 1.95 %; controls 0.56 %; OR 3.6; P < 0.001), of the skin and other locations (LP 1.76 %; controls 0.6 %; OR 3.0;
Table 4  Frequency of comorbidity in prevalent LP patients and an age-sex matched control group in 2018.

| Category               | Disease                                | LP patients | Control group | Odds Ratio | P value |
|------------------------|----------------------------------------|-------------|---------------|------------|---------|
|                        |                                        | n           | n             |            |         |
|                        |                                        | %           | %             |            |         |
| **Liver diseases**     | Autoimmune hepatitis                   | 11          | 16            | 0.29       | 0.09    | 3.4     | 0.0016 |
|                        | acute and chronic Hepatitis B         | 21          | 35            | 0.56       | 0.19    | 3.0     | < 0.001|
|                        | acute and chronic Hepatitis C         | 24          | 40            | 0.64       | 0.21    | 3.0     | < 0.001|
| **Thyroid disorders**  | Autoimmune thyroiditis                | 283         | 722           | 7.56       | 3.86    | 2.0     | < 0.001|
|                        | Thyroiditis                           | 309         | 791           | 8.26       | 4.23    | 2.0     | < 0.001|
|                        | Hypothyroidism                        | 772         | 2,746         | 20.63      | 14.68   | 1.5     | < 0.001|
|                        | Thyrotoxicosis [hyperthyroidism]      | 164         | 664           | 4.38       | 3.55    | 1.2     | 0.014  |
| **Malignancies**       | Malignant neoplasm of the skin        | 243         | 712           | 6.49       | 3.81    | 1.8     | < 0.001|
|                        | Malignant neoplasms of lip, oral cavity| 37          | 99            | 0.99       | 0.14    | 6.9     | < 0.001|
| **Psychiatric conditions** | Depression                         | 920         | 3,626         | 24.59      | 19.38   | 1.4     | < 0.001|
| **Dermatologic conditions** | Alopecia areata                     | 77          | 50            | 2.06       | 0.27    | 7.8     | < 0.001|
|                        | Psoriasis vulgaris                    | 194         | 372           | 5.18       | 1.99    | 2.7     | < 0.001|
|                        | Vitiligo                               | 32          | 56            | 0.86       | 0.3     | 2.9     | < 0.001|
| **Candida infections** | Candidiasis of mouth and esophagus    | 73          | 104           | 1.95       | 0.56    | 3.6     | < 0.001|
|                        | Candidiasis of skin and other locations| 66          | 113           | 1.76       | 0.6     | 3.0     | < 0.001|
|                        | Candidiasis of urogenital sites       | 68          | 136           | 1.82       | 0.73    | 2.5     | < 0.001|
| **Inflammatory bowel diseases** | Ulcerative colitis             | 47          | 139           | 1.26       | 0.74    | 1.7     | 0.0018 |
|                        | Coeliac disease                       | 19          | 33            | 0.51       | 0.18    | 2.9     | < 0.001|
| **Other autoimmune diseases** | Lupus erythematosus           | 32          | 29            | 0.86       | 0.15    | 5.6     | < 0.001|
|                        | Ankylosing spondylitis               | 32          | 81            | 0.86       | 0.43    | 2.0     | 0.0011 |
|                        | Arthropathic psoriasis (psoriatic arthritis) | 37          | 94            | 0.99       | 0.5     | 2.0     | < 0.001|
|                        | Sicca syndrome                       | 121         | 370           | 3.23       | 1.98    | 1.7     | < 0.001|
| **Metabolic syndrome** | Obesity                               | 828         | 3,113         | 22.13      | 16.64   | 1.4     | < 0.001|
|                        | Hypertension                         | 2,223       | 9,854         | 59.41      | 52.67   | 1.3     | < 0.001|
|                        | Pure hyperglyceridemia               | 87          | 246           | 2.32       | 1.31    | 1.8     | < 0.001|
|                        | Mixed hyperlipidemia                 | 272         | 1,029         | 7.27       | 5.5     | 1.3     | < 0.001|
|                        | Elevated blood glucose level          | 89          | 324           | 2.38       | 1.73    | 1.4     | 0.0074 |
| **Other cardiovascular/metabolic conditions** | Disorders of lipoprotein metabolism and other lipidemias | 1,682 | 6,975 | 44.95 | 37.28 | 1.4 | < 0.001|
|                        | Hyperlipidemia, unspecified           | 609         | 2,516         | 16.27      | 13.45   | 1.3     | < 0.001|
|                        | Other hyperlipidemia                 | 62          | 213           | 1.66       | 1.14    | 1.5     | 0.0089 |
|                        | Pure hypercholesterolemia            | 1,016       | 4,188         | 27.15      | 22.38   | 1.3     | < 0.001|
|                        | Type 1 diabetes mellitus             | 96          | 369           | 2.57       | 1.97    | 1.3     | 0.020  |
|                        | Type 2 diabetes mellitus             | 758         | 3,078         | 20.26      | 16.45   | 1.3     | < 0.001|

Unless otherwise indicated % (n) are reported; patients with more than one disease were counted in each disease group.
Most incident patients were diagnosed by dermatologists,\(^*\) in routine clinical practice in a large cohort of patients. The odds for depression were 1.4 times higher in LP patients than in controls (LP 24.6 %; controls 19.4 %; \(P < 0.001\)). Furthermore, the 30 most frequent comorbidities were assessed in prevalent LP patients and the control group. Overall, common comorbidities were fairly consistent between LP and the general population (Online Supplementary Table S6).

**Discussion**

This is the first study to systematically explore LP prevalence and incidence based on representative SHI claims data in Germany. Data from over 3.6 million patients was analyzed with a focus on prevalence of comorbidity as well as treatment regimens and treating physicians prior and after LP diagnosis.

The prevalence of LP in Germany in 2018 was 0.096 %, while the prevalence in 2015 was slightly lower (0.085 %), but in a similar range. Additionally, LP prevalence showed a peak for the age group 60–79 years with a female predominance. Therefore, the higher prevalence in 2018 compared to 2015 might be a consequence of the overall demographic development in Germany, which is characterized by a gradual shift in age distribution towards older age groups more frequently affected by LP. Additional longitudinal analyses over extended time periods might reveal potential trends in LP prevalence over time in the future. Prevalence in children and adolescents was extremely low (0.67 % of all prevalent LP patients), demonstrating that pediatric LP is a very rare condition. Previous estimates of LP prevalence and incidence varied and were reported as 0.22–5 % and 0.14–1.27 % worldwide, respectively [10, 18–20]. However, meta-analyses of previous studies criticized deficiencies in study design, methodology, reporting or inconsistent diagnostic criteria and identified those as the cause for the large deviations [2, 21, 22]. Based on a review of epidemiologic studies on selected patients, Wagner et al. assumed a lower frequency of LP in the total population (0.07–0.84 %) [9]. For OLP, a female predominance has been reported [23–25]. The age of manifestation typically lies between 50 and 60 for OLP and between 40 and 45 for cutaneous LP [19, 23]. Therefore, the results from the present study are in line with those reported in previous epidemiological analyses. LDRs, which can occur as adverse events after exposition to certain drugs (for example, antihypertensives, non-steroidal anti-inflammatory drugs or immune checkpoint inhibitors) and represent an important differential diagnosis of LP, were far less prevalent than LP with 0.0006 % in 2018 [3, 26–28].

To our knowledge, this is the first study to assess LP treatment in routine clinical practice in a large cohort of patients. Most incident patients were diagnosed by dermatologists, who remained the main treating specialty physician following diagnosis. This is in line with recommendations that particularly moderate and severe LP cases should be treated by a specialized dermatologist [1].

The newly established European S1 guideline on the management of LP, which was published in 2020 reviews LP medications and summarizes first, second and third-line treatment modalities [10]. In the current claims database analysis, many patients received the recommended first-line therapy: While 48 % of prevalent patients received topical corticosteroids, only 4.4 % received topical calcineurin inhibitors even though these have been widely explored as potential substitutes for corticosteroids [14, 29]. Potent and very potent corticosteroids (ATC groups III and IV) represented the most frequently used corticosteroid classes, while less than 5 % of prevalent LP patients received topical corticosteroids of weak or moderate potency. Weak or moderate potency corticosteroids were also rarely used in incident LP patients, indicating that treating physicians may generally view LP as a condition resistant to lower potency steroid treatment. Of note, topical calcineurin inhibitors and topical retinoids represent off-label treatment options, while topical corticosteroids are approved for the treatment of LP in Germany [3]. Systemic therapy with corticosteroids or acitretin should be considered for the treatment of severe LP inadequately controlled through topical therapies [10]. A relatively low proportion of only 2.2 % of prevalent patients received acitretin, while 17.5 % of patients received systemic corticosteroids. This indicates that acitretin might be prescribed as a third line option after initial systemic glucocorticoid treatment in clinical practice. Phototherapies including UVB and psoralen plus UVA (PUVA) are recommended as second or third-line treatments in the European S1 guidelines, but the current analysis revealed that they only play a minor role in the management of LP [10]. Strikingly, the data revealed a large group of prevalent patients receiving no prescribed therapy at all. This may be explained as follows: For mild disease, over-the-counter medications might be sufficient. For patients with moderate to severe disease, who are inadequately controlled with topical corticosteroid therapies, only very few approved, systemic treatment options exist. Systemic corticosteroids should not be used long-term due to the well-known side effects of chronic corticosteroid exposure. Beyond that, only acitretin showing an unfavorable safety profile is approved for systemic treatment, highlighting the high unmet need for safe and effective systemic treatment options for patients with moderate to severe LP. Currently, several new compounds for targeted LP treatment are being explored in Ph2 clinical trials (e.g., IL-17A inhibition [NCT04300296], JAK1/2 inhibition [NCT03697460], OSMRβ inhibition [NCT03858634]).

A range of comorbidities have been reported to be associated with LP including autoimmune thyroid disease,
Epidemiology of lichen planus in Germany

Original Article

Dr. Eva Schruf
Novartis Pharma GmbH
Roonstrasse 25
90429 Nürnberg
E-mail: eva.schruf@novartis.com

Correspondence to

References

1. Shavit E, Hagen K, Shear N. Oral lichen planus: a novel staging and algorithmic approach and all that is essential to know. F1000Res 2020; 9: 206.
2. Gorouhi F, Davari P, Fazel N. Cutaneous and mucosal lichen planus: a comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. ScientificWorldJournal 2014; 2014: 742826.
3. Solimani F, Forchhammer S, Schloegl A et al. Lichen planus – a clinical guide. J Dtsch Dermatol Ges 2021; 19: 864–82.
4. Pietschke K, Holstein J, Meier K et al. The inflammation in candidiasis diagnoses might be partly driven by the fact that patients suffering from LP were subject to closer monitoring due to more frequent physician visits than patients from the control group. An association of LP with thyroid disorders has been discussed intensely [32, 47, 48]. Our results confirmed these findings, emphasizing the need for raising awareness of this association among dermatologists as well as endocrinologists. Lichen planus is known to be associated with anxiety, stress, and depression [2, 7]. The present study showed that the odds for depression were increased compared to controls in line with previous findings that LP puts a substantial burden on patients, often translating into psychological distress and psychiatric conditions [2, 6, 49, 50].

This study is subject to a few limitations inherent to claims database studies, such as the reliance on accurate coding and diagnosis. Consequently, the results need to be interpreted with caution. No differentiation between the presence of OLP and/or cutaneous LP was possible due to lack of respective ICD-10 codes. Furthermore, it was not possible to distinguish between underserved patients and patients with disease remission or mild disease course. Finally, no diagnoses from dentists were included since dentists do not document diagnosis for reimbursement purposes, raising the possibility of underestimation of OLP prevalence.

Taken together, the observations in this study may improve our understanding of the epidemiological burden of LP and increase the diagnostic awareness among clinicians to shape future screening, such as testing for HCV, thyroid disorders or malignant transformation, and management strategies.

Conflict of interest

ES and MHCB and are employed by Novartis Pharma GmbH, Nuremberg, Germany. MR is employed by Novartis Pharma AG, Basel, Switzerland. MH has received funding for clinical studies and honoraria from Janssen Cilag and Novartis Pharma GmbH. JW has received fees for lecturing and/or consulting, and/or received funding for scientific projects and clinical studies from Novartis Pharma GmbH. DH is an employee of WIG2 GmbH, which received funding from Novartis Pharma GmbH. The other co-authors declare no conflicts of interest.

Acknowledgements

The analyses presented here were funded by Novartis Pharma GmbH, Germany. The authors thank Marion Ludwig of InGef Institute for Applied Health Research Berlin GmbH, Berlin, Germany for providing medical writing support.

Dr. Eva Schruf
Novartis Pharma GmbH
Roonstrasse 25
90429 Nürnberg
E-mail: eva.schruf@novartis.com

Correspondence to

References

1. Shavit E, Hagen K, Shear N. Oral lichen planus: a novel staging and algorithmic approach and all that is essential to know. F1000Res 2020; 9: 206.
2. Gorouhi F, Davari P, Fazel N. Cutaneous and mucosal lichen planus: a comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. ScientificWorldJournal 2014; 2014: 742826.
3. Solimani F, Forchhammer S, Schloegl A et al. Lichen planus – a clinical guide. J Dtsch Dermatol Ges 2021; 19: 864–82.
4. Pietschke K, Holstein J, Meier K et al. The inflammation in cutaneous lichen planus is dominated by IFN-γ and IL-21-A

Acknowledgements

The analyses presented here were funded by Novartis Pharma GmbH, Germany. The authors thank Marion Ludwig of InGef Institute for Applied Health Research Berlin GmbH, Berlin, Germany for providing medical writing support.

Conflict of interest

ES and MHCB and are employed by Novartis Pharma GmbH, Nuremberg, Germany. MR is employed by Novartis Pharma AG, Basel, Switzerland. MH has received funding for clinical studies and honoraria from Janssen Cilag and Novartis Pharma GmbH. JW has received fees for lecturing and/or consulting, and/or received funding for scientific projects and clinical studies from Novartis Pharma GmbH. DH is an employee of WIG2 GmbH, which received funding from Novartis Pharma GmbH. The other co-authors declare no conflicts of interest.

Dr. Eva Schruf
Novartis Pharma GmbH
Roonstrasse 25
90429 Nürnberg
E-mail: eva.schruf@novartis.com

Correspondence to

References

1. Shavit E, Hagen K, Shear N. Oral lichen planus: a novel staging and algorithmic approach and all that is essential to know. F1000Res 2020; 9: 206.
2. Gorouhi F, Davari P, Fazel N. Cutaneous and mucosal lichen planus: a comprehensive review of clinical subtypes, risk factors, diagnosis, and prognosis. ScientificWorldJournal 2014; 2014: 742826.
3. Solimani F, Forchhammer S, Schloegl A et al. Lichen planus – a clinical guide. J Dtsch Dermatol Ges 2021; 19: 864–82.
4. Pietschke K, Holstein J, Meier K et al. The inflammation in cutaneous lichen planus is dominated by IFN-γ and IL-21-A
basis for therapeutic JAKi inhibition. Exp Dermatol 2021; 30: 262–70.
5 Schmidt T, Solimani F, Pollmann R et al. TH1/TH17 cell recognition of desmoglein 3 and bullous pemphigoid antigen 180 in patients with lichen planus. J Allergy Clin Immunol 2018; 142: 669–72.e7.
6 Balci DD, Inandi T. Dermatology life quality index scores in lichen planus: comparison of psoriasis and healthy controls. Lichen planus dermatologic yasam kalite indeksleri: psoriasis ve saglikli kontrolle rleri karsilastirilir. Turkderm-Turk Arch Dermatol Venereol 2008; 42(4): 127–130.
7 Adamo D, Ruoppo E, Leuci S et al. Sleep disturbances, anxiety and depression in patients with oral lichen planus: a case-control study. J Eur Acad Dermatol Venereol 2015; 29: 291–7.
8 Giuliani M, Troiano G, Cordaro M et al. Rate of malignant transformation of oral lichen planus: A systematic review. Oral Dis 2019; 25: 693–709.
9 Wagner G, Rose C, Sachse MM. Clinical variants of lichen planus. J Dtsch Dermatol Ges 2013; 11: 309–19.
10 Ioannides D, Vakirlis E, Kemeny L et al. European S1 guidelines on the management of lichen planus: a cooperation of the European Dermatology Forum with the European Academy of Dermatology and Venereology. J Eur Acad Dermatol Venereol 2020; 34: 1403–14.
11 Lajevardi V, Ghodsi SZ, Hallaji Z et al. Treatment of erosive oral lichen planus with methotrexate. J Dtsch Dermatol Ges 2016; 14: 286–93.
12 Manousaridis I, Manousaridis K, Peitsch WK, Schneider SW. Individualizing treatment and choice of medication in lichen planus: a step by step approach. J Dtsch Dermatol Ges 2013; 11: 981–91.
13 Solimani F, Pollmann R, Schmidt T et al. Therapeutic Targeting of TH17/TC17 Cells Leads to Clinical Improvement of Lichen Planus. Front Immunol 2019; 10.
14 Thandar Y, Maharajh R, Hafiejee F, Mosam A. Treatment of cutaneous lichen planus (Part 1): A review of topical therapies and phototherapy. Cogent Med 2019; 6: 1582467.
15 Thandar Y, Maharajh R, Hafiejee F, Mosam A. Treatment of cutaneous lichen planus (part 2): a review of systemic therapies. J Dermatolog Treat 2019; 30: 633–47.
16 Andersohn F, Walker J. Characteristics and external validity of the German Health Risk Institute (HRI) Database. Pharmaco-epidemiol Drug Saf 2016; 25: 106–9.
17 Altman DG, Bland JM. How to obtain the P value from a confidence interval. BMJ 2011; 343: d2304.
18 Li C, Tang X, Zheng X et al. Global prevalence and incidence estimates of oral lichen planus: a systematic review and meta-analysis. JAMA Dermatol 2020; 156: 172–81.
19 Arnold DL, Krishnamurthy K. Lichen Planus. StatPearls. Treasure Island (FL): StatPearls Publishing, 2021.
20 Axéll T, Rundquist L. Oral lichen planus – a demographic study. Community Dent Oral Epidemiol 1987; 15: 52–6.
21 Gonzalez-Moles MA, Warnakulasuriya S, Gonzalez-Ruiz I et al. Worldwide prevalence of oral lichen planus: a systematic review and meta-analysis. Oral Dis 2020.
22 McCarten BE, Healy CM. The reported prevalence of oral lichen planus: a review and critique. J Oral Pathol Med 2008; 37: 447–53.
23 Le Cleach L, Chosidow O. Clinical practice. Lichen planus. N Engl J Med 2012; 366: 723–32.
24 Carbone M, Arduin P, Carrozzo M et al. Course of oral lichen planus: a retrospective study of 808 northern Italian patients. Oral Dis 2009; 15: 235–43.
25 Bermejo-Fenoll A, Sánchez-Siles M, López-Jornet P et al. A retrospective clinicopathological study of 550 patients with oral lichen planus in south-eastern Spain: Study of 550 OLP patients in Spain. J Oral Pathol Med 2010; 39: 491–6.
26 Geisler AN, Phillips GS, Barrios DM et al. Immune checkpoint inhibitor-related dermatologic adverse events. J Am Acad Dermatol 2020; 83: 1255–68.
27 Cheraghli S, Levy LL. Fixed drug eruptions, bullous drug eruptions, and lichenoid drug eruptions. Clin Dermatol 2020; 38: 679–92.
28 Alqahtani M, Woods TR, Smith MH et al. Medication use and medical history of 155 patients with oral lichenoid lesions: a retrospective study. Gen Dent 2018; 66: 40–45.
29 Chamani G, Rad M, Zarei MR et al. Efficacy of tacrolimus and clobetasol in the treatment of oral lichen planus: a systematic review and meta-analysis. Int J Dermatol 2015; 54: 996–1004.
30 Hasan S, Ahmed S, Kiran R et al. Oral lichen planus and associated comorbidities: An approach to holistic health. J Family Med Prim Care 2019; 8: 3504–17.
31 Cassol-Spanemberg J, Rodríguez-de Rivera-Campillo M-E, Otero-Rey E-M et al. Oral lichen planus and its relationship with systemic diseases. A review of evidence. J Clin Exp Dent 2018; 10: e938–e44.
32 Li D, Li J, Li C et al. The association of thyroid disease and oral lichen planus: a literature review and meta-analysis. Front Endocrinol (Lausanne) 2017; 8: 310.
33 Arias-Santiago S, Buendia-Eisman A, Aneiros-Fernández J et al. Cardiovascular risk factors in patients with lichen planus. Am J Med 2011; 124: 543–8.
34 Alaizari NA, Al-Maweri SA, Al-Shamiri HM et al. Hepatitis C virus infections in oral lichen planus: a systematic review and meta-analysis. Aust Dent J 2016; 61: 282–7.
35 Shang Q, Peng J, Zhou Y et al. Association of human papillomavirus with oral lichen planus and oral leukoplakia: a meta-analysis. J Evid Based Dent Pract 2020; 20: 101485.
36 Lai YC, Yew YW, Schwartz RA. Lichen planus and dyslipidemia: a systematic review and meta-analysis of observational studies. Int J Dermatol 2016; 55: e295–304.
37 Birkenfeld S, Dreher J, Weitzman D, Cohen AD. A study on the association with hepatitis B and hepatitis C in 1557 patients with lichen planus. J Eur Acad Dermatol Venereol 2011; 25: 436–40.
38 Nagao Y, Sata M. A retrospective case-control study of hepatitis C virus infection and oral lichen planus in Japan: association study with mutations in the core and NS5A region of hepatitis C virus. BMC Gastroenterol 2012; 12: 31.
39 Cornberg M, Razavi HA, Alberti A et al. A systematic review of hepatitis C virus epidemiology in Europe, Canada and Israel. Liver Int 2011; 31(Suppl 2): 30–60.
40 van der Meij EH, van der Waal I. Hepatitis C virus infection and oral lichen planus: a report from The Netherlands. J Oral Pathol Med 2000; 29: 255–8.
41 Yarom N, Dagon N, Shinar E, Gorsky M. Association between hepatitis C virus infection and oral lichen planus in Israeli patients. Isr Med Assoc J 2007; 9: 370–2.
42 Padhi T, Garima. Metabolic syndrome and skin: Psoriasis and beyond. Indian J Dermatol 2013; 58: 299–305.
43 Kumar SA, Krishnam Raju PV, Gopal KVT, Rao TN. Comorbidities in lichen planus: a case–control study in Indian patients. Indian Dermatol Online J 2019; 10: 34–7.
44 Halonen P, Jakobsson M, Heikinheimo O et al. Cancer risk of lichen planus: A cohort study of 13,100 women in Finland. Int J Cancer 2018; 142: 18–22.
45 Chung PI, Hwang CY, Chen YJ et al. Autoimmune comorbid diseases associated with lichen planus: a nationwide case-control study. J Eur Acad Dermatol Venereol 2015; 29: 1570–5.
46 Meinhard J, Stroux A, Lunnemann L et al. Lichen planopilaris: Epidemiology and prevalence of subtypes – a retrospective analysis in 104 patients. J Dtsch Dermatol Ges 2014; 12: 229–35, 29–36.
47 Atanaska Mesinkovska N, Brankov N, Piliang M et al. Association of lichen planopilaris with thyroid disease: a retrospective case-control study. J Am Acad Dermatol 2014; 70: 889–92.
48 Garcia-Pola MJ, Llorente-Pendas S, Seoane-Romero JM et al. Thyroid disease and oral lichen planus as comorbidity: a prospective case-control study. Dermatology 2016; 232: 214–9.
49 Sawant NS, Vanjari NA, Khopkar U, Adulkar S. A study of depression and quality of life in patients of lichen planus. ScientificWorldJournal 2015; 2015: 817481.
50 Nasimi M, Ahangari N, Lajevardi V et al. Quality of life and mental health status in patients with lichen planopilaris based on Dermatology Life Quality Index and General Health Questionnaire-28 questionnaires. Int J Womens Dermatol 2020; 6: 399–403.