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Evaluation of clinical findings in patients with lichen planus: A retrospective study

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Abstract

Aim: *Lichen planus* is a papulosquamous disease that affects skin and mucous membranes. In this study, we aimed to evaluate the clinical and demographic characteristics, treatment models, and accompanying comorbidities of patients with lichen planus.

Materials and Methods: Our study included 202 patients who were diagnosed with LP clinically and histopathologically between May 2018 and May 2023. Patients' age, gender, involvement features, additional systemic diseases, laboratory findings and applied treatments were recorded retrospectively.

Results: Of the 202 patients in our study, 116 (57.4%) were female and 86 (42.6%) were male. The average age of the patients was 46.42 years (13-84). The average duration of the disease was 10.40 months (1-196). The classic type (120 patients, 64.9%) was observed most typically in skin involvement, while reticular pattern (60 patients, 85.7%) was observed in oral involvement. Skin involvement was detected in 185 (91.6%), oral mucosa involvement in 70 (34.7%), genital involvement in 16 (7.9%), scalp involvement in 30 (14.8%), inverse involvement in 20 (9.9%), palmoplantar involvement in 5 (2.5%) and nail involvement in 21 (10.4%) of the patients, while no ocular involvement was detected. Anti-HCV positivity was found in two (1%) patients. HBsAg positivity was detected in 11 (5.4%) patients. While the most frequent accompanying comorbidity was hypertension with %20.3 (n:41), depression-anxiety was the sequent with 14.4% (n:29). While 154 (76.2%) of the patients received only topical treatment, it was seen that 5 (2.5%) patients were given only systemic treatment. In comparison of the age groups 18-45 and >45, the ratio of DM, hyperlipidemia and hypertension was identified significantly high in the group >45.

Conclusion: Our study shows many similarities with the literature data. However, we believe that prospective cohort studies including more patients are needed to understand LP, whose clinical and epidemiology has not been sufficiently elucidated.

Introduction

Lichen Planus (LP) is an itchy inflammatory disease affecting the skin, mucous membranes, nails, and scalp, the etiology of which is not entirely known. It is seen all over the world and in all races, but its frequency is not known exactly. Since at least two-thirds of the reported cases are between the ages of 30-60, LP is considered a middle-to-older age disease [1]. Although women and men are equally affected by the disease, some studies report that the disease is approximately twice as much in women as in men [2,3]. Although the etiopathogenesis of LP is not entirely known, it is thought that T cell activation plays a key role in its pathogenesis and that LP is a T cell-mediated autoimmune disease. It is thought that viral diseases, autoimmunity, psychological stress, and contact allergens may have a role in etiology and seasonal changes may affect the onset of the disease [1].

Despite all this knowledge, the epidemiological, clinical, and pathogenetic characteristics of the disease have not yet been entirely revealed. In this study, we aimed to evaluate the clinical and demographic characteristics, treatment models, and accompanying comorbidities of patients who applied to our dermatology outpatient clinic and were clinically and histopathologically diagnosed with lichen planus, together with the literature data.

Materials and Methods

In our study the retrospective observatory analysis of 202 patients at the ages of between 0 and 85, who had been followed up as inpatient and/or outpatient with the diag-

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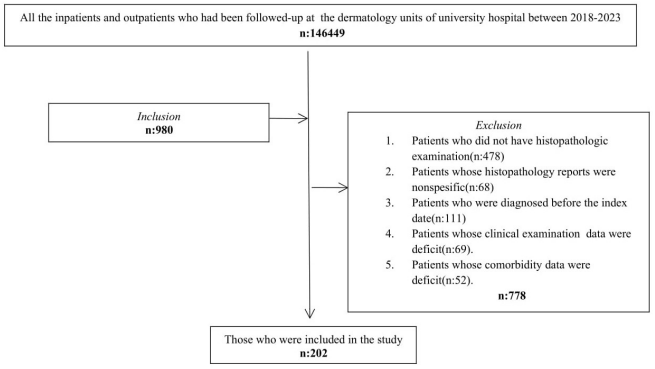

Figure 1. The flowchart of study sample selection.

nosis of LP in the dermatology polyclinics and clinics of Fırat University Medical Faculty Hospital between May 2018 and May 2023, was carried out. The data of this study was obtained by means of carrying out the retrospective analysis of the patients recorded with the diagnosis of LP in the digital patient system of Fırat University Medical Faculty Hospital. Searching was made with the subcodes L43, L43.8 ve L66.1 of the ICD-10 (International Statistical Classification of Diseases and Related Health Problems) code system at the digital patient database of hospital. Of the recorded 980 patients with LP, those who did not have histopathologic examination (n:478), were diagnosed before the index date (n:111); whose histopathology reports were nonspesific (n:68), clinical examination data was deficit (n:69), comorbidity data was deficit (n:52) were excluded in the study (Figure 1). Patients' age, gender, duration of disease, onset time of disease, cutaneous, oral mucosa, and nail and scalp involvement features, additional systemic diseases, hepatitis C virus (HCV) anticore positivity, hepatitis B virus surface antigen (HBsAg) positivity and applied treatments were recorded retrospectively. Cutaneous LP was classified as classic, *lichen planoplaris* (LPP), hypertrophic, pigmented, atrophic, actinic, LP pemphigoides subtypes. Oral LP was classified as reticular, erosive, plaque, bullous, and papular subtypes. The treatments that patients received were classified as topical, systemic, phototherapy and topical-systemic. The patients at the ages between 0 and 85 were involved in the study. Only 1 patient under 18 meeting the conditions was available. Patients were also divided into two age groups as 18-45(n:93) and >45(n:108) and compared in terms of the of clinical and histopathologic features and related factors. Local ethics comittee approval (Fırat University Medical Searching Ethics Comittee, Date 25.05.2023, session no: 2023/ 07 Decision no: 25) was received. The study was carried out upon the decleration of Helsinki.

Statistical analysis

Data analyses were carried out by using SPSS for Windows, version 22.0 (SPSS Inc., Chicago, IL, United States). Whether the distribution of continuous variables was normal or not was determined by the Kolmogorov Smirnov test. Levene test was used for the evaluation of homogeneity of variances. Unless otherwise specified, continuous data were described as median (minimum-maximum value) for skewed distributions. Categorical data were described as the number of cases (%). Statistical analysis differences in not normally distributed variables between two independent groups were compared by Mann Whitney U test. Categorical variables were compared by means of Pearson's chi-square test or fisher's exact test. p-value<0.05 was accepted as a significant level on all statistical analysis.

Table 1. Clinical and demographic findings of lichen planus patients.

Patient (n:202)		Median (min-max)
Age, $\overline{X}$±SD		46.42(13-84)
Disease Duration (months), $\overline{X}$±SD		10.40(1-196)
		n (%)
Gender	Male	86 (42.6%)
	Female	116 (57.4%)
Cutaneous LP	Classical	120 (64.9%)
	LPP	30 (16.2%)
	Hypertrophic	14 (7.6%)
	Pigmented	9 (4.9%)
	Atrophic	7(3.8%)
	Actinic	3 (1.6%)
	LP Pemphigoid	2 (1.1%)
Oral LP	Reticular	60 (85.7%)
	Erosive	7 (10.0%)
	Plaque	2 (2.9%)
	Bullous	1 (1.4%)
	Papular	-
	Atrophic	-
	Hypertrophic	-
Blood Tests	HBsAg(+)	11 (5.4%)
	Anti-HCV(+)	2 (1.0%)
Applied treatments	Topical	154 (76.2%)
	Topical + Systemic	37 (18.3%)
	Systemic	5 (2.5%)
	Phototherapy	6 (3.0%)
Concurrent systemic diseases	HT	41 (20.3%)
	Depression-anxiety	29 (14.4%)
	DM	19 (9.4%)
	Hyperlipidemia	12 (5.9%)
	Hypothyroidism	12 (5.9%)
	Malignancy	7 (3.5%)
	Oral LP+DM+HT (Grinspan Sendromu)	3(1.5%)
	Others	21 (10.4%)

LP: lichen planus, LPP: lichen planopilaris, DM: diabetes mellitus, HT: hypertension, HBsAg: Hepatitis B virus surface antigen, Anti-HCV: hepatitis C virus antibody.

Results

A total of 202 lichen planus patients, including 116 (57.4%) women and 86 (42.6%) men, were included in our study. The average age of the participants was 46.42 years (13-84 years). The average disease duration was 10,40 months

Table 2. Distribution of lichen planus patients according to involvement areas.

Involvement	n (%)
Skin ±oral	185 (91.6%)
Oral	70 (34.7%)
Scalp	30(14.8%)
Oral only	17(9.17%)
Nail	21 (10.4%)
Genital	16 (7.9%)
Inverse	20 (9.9%)
Palmoplantar	5 (2.5%)
Ocular	-
Oral +	
Genital	5 (2.5%)
Nail	9 (4.5%)
Palmoplantar	1 (0.5%)
Genital+ inverse	1(0.5%)
Nail+ inverse	2 (1.0%)
Genital +	
Nail	2 (1.0%)
Palmoplantar	1 (0.5%)
Inverse	4 (2.0%)
Nail +	
Inverse	5 (2.5%)
Scalp +	
Genital	1(6.3%)
Palmoplantar	1(6.3%)

(1-196) (Table 1). In 185 patients (91.6%) skin involvement, in 70 (34.7%) oral mucosa involvement, in 16 (7.9%) genital involvement, in 20 (9.9%) inverse involvement, in 5 (2.5%) palmoplantar involvement, in 30 (14.8%) scalp involvement and in 21 (10.4%) nail involvement were detected while no ocular involvement was detected in any. It was observed that there was also oral involvement in 53 (28.6%) of the patients with skin involvement. Isolated oral involvement was observed in 17 patients (8.5%) (Table 2). In skin involvement, 120 (64.9%) classical LP, 30 (16.2%) lichen planopilaris, 14 (7.6%) hypertrophic LP, 9 (4.9%) pigmented LP, 3 (1.6%) atrophic LP, and 2 (1.1%) LP pemphigoid cases were observed. In oral involvement, 60 (85.7%) reticular pattern, 7 (10%) erosive, 2 (2.9%) plaque, 1 (1.4%) bullous type were observed while papular, atrophic, hypertrophic subtypes were not detected at all. Anti HCV positivity was detected in two (1%) patients. HBsAg positivity was seen in 11 (5.4%) patients. When accompanying additional systemic diseases were evaluated 41 (20.3%) hypertension (HT), 29 (14.4%) depression-anxiety, 19 (9.4%) diabetes mellitus (DM), 12 (5.9%) hypothyroidism, 12 (5.9%) dyslipidemia, 7 (3.5%) malignancy, 3 (1.48%) metabolic syndrome (MS) were detected. There were 3 (1.5%) oral LP+DM+HT (Grinspan Syndrome) cases. When the treatments used by the patients were evaluated, it was seen that 154 (76.2%) patients were given only topical treatment, 37 (18.3%) patients were given systemic and topical treatment, 6 (3%) patients were given phototherapy and 5 (2.5%) patients were given only systemic treatment (Table 1). In comparison of the age groups 18-45 and >45, the ratio of DM, hyperlipidemia and HT was identified significantly high in the group >45. The duration the disease, gender, cutaneous involvement and subspecies frequency, oral involvement and subspecies frequency, the positivity of HBsAg and anti-HCV were not statistically detected different in a significant level in terms of the treatments received by the patients between the age groups of 18-45 and >45 (Table 3).

Discussion

It is stated that the estimated prevalence of cutaneous lichen planus worldwide varies between 0.22% and 5, while oral lesions are observed in 1-4% of the population [4]. In a study by Mc Cartan et al., the prevalence of LP in Sweden was found to be an average of %1.27 (in men: 0.96%, in women: 1.57%), while the incidence in the British population was determined to be between 0.032% and 0.037% [5,6]. Although there is no difference between women and men in the frequency of cutaneous LP, it has been shown that the rate of women in oral LP is higher [3]. In a study by Leasure et al. with 203,813 participants, the female-to-male ratio was determined as 3:1 in 788 diagnosed LP patients [2]. In our study, the female-to-male ratio was found to be 1.34.

In the study by Irvine et al., in the 8 to 12-year follow-up of 214 patients, the age of onset of LP was found to be lower in men than in women (40.3 years in men, 46.4 years in women) [7]. In the study by Leasure et al., most LP cases were reported to be over the age of 55 [2]. In our study, the ages of the patients varied between 13 and 84, similar to the literature, and the average was 46.42 years.

The classic skin lesions of LP are small, shiny, flat-topped, polygonal, and purplish, usually itchy red-purple papules that are single or tend to merge and vary in size from a few mm to 1 cm [1]. In the study of Singh et al. with 441 patients and the epidemiological study of Bhattacharya et al. with 232 patients, the classic type was most frequently seen (74% and 47.4% respectively), followed by hypertrophic (13% and 14.2% respectively) and actinic (7.5% and 4.7% respectively) LP [8,9]. In the epidemiological study of Bhattacharya et al. with 232 patients, the classic type (47.4%) was most frequently seen, followed by hypertrophic (14.2%) and actinic type (4.7%) LP [9]. In the study of Kyriakis et al., while the classic type was most frequently seen, follicular LP was sequently observed [10]. In our study, similarly, classic LP was most frequently observed, followed by LPP and LP pigmentosus. The two most common forms found in our study were compatible with most of the literature data.

Andreasen has divided oral lichen planus (OLP) into six types: reticular, papular, plaque-like, atrophic, erosive, and bullous [11]. Despite different rates reported in the literature regarding oral mucosa involvement, it is observed in an estimated %60-70 of patients with LP and can occur as the only finding in approximately 20-30% of cases [1]. Bhattacharya et al. reported oral mucosa involvement

Table 3. Distribution of lichen planus patients according to age groups.

	18-45(n:93)	>45(n:108)	p
Disease Duration (months), Median (min-max)	4(1-196)	6(120)	0.087
Gender, n(%)			
Male	39(41.9%)	46(42.6%)	0.995
Female	54(58.1%)	62(57.4%)	
Involvement, n(%)			
Oral	31(33.3%)	39(36.1%)	0.641
Ocular	-	-	-
Genital	11(11.8%)	5(4.6%)	0.063
Nail	9(9.6%)	12(11.1%)	0.721
Palmoplantar	2(2.1%)	3(2.8%)	0.999
Inverse	9(9.6%)	11(10.2)	0.885
Scalp	16(17.2%)	14(13.0%)	0.418
Oral LP, n(%)			
Reticular	27(87.1%)	33(84.6%)	
Erosive	3(9.7%)	4(10.3%)	
Atrophic	-	-	
Plaque	1(3.2%)	1(2.6%)	0.981
Papular	-	-	
Bullous	-	1(2.6%)	
Hypertrophic	-	-	
Cutaneous LP, n(%)			
Classical	55(65.1%)	64(65.3%)	
Hypertrophic	6(6.9%)	8(8.2%)	0.993
Atrophic	3(3.4%)	4(4.1%)	
LPP	16(18.6%)	14(14.3%)	
Actinic	1(1.1%)	2(2.0%)	
Pigmented	4(4.6%)	5(5.1%)	
LP Pemphigoid	1(1.1%)	1(1.0%)	
Blood Tests, n(%)			
HBSAg	4(4.3%)	7(6.5%)	0.487
HCV	2(2.1%)	-	0.215
Applied treatments, n(%)			
Topical	73(78.4%)	80(74.1%)	
Systemic	2(2.1%)	3(2.8%)	0.548
Phototherapy	1(1.1%)	5(4.6%)	
Topical + Systemic	17(18.2%)	20(18.5%)	
Concurrent systemic diseases, n(%)			
DM	3(3.2%)	16(14.8%)	**0.005**
Hyperlipidemia	2(2.1%)	10(9.3%)	**0.032**
HT	5(5.3%)	36(33.3%)	**<0.001**
Malignancy	1(1.1%)	6(5.6%)	0.125
Depression-anxiety	11(11.8%)	18(16.7%)	0.316
Hypothyroidism	6(6.4%)	6(5.6%)	0.804
Others	10(10.7%)	11(10.2%)	0.916

Continuous variables are expressed as the median (minimum-maximum value), and categorical variables are expressed as either frequency or percentage. Continuous variables were compared with the mann whitney u test, and categorical variables were compared using Pearson'schi-square test or fisher exact test. Statistically significant p-values are in bold.

in 97 (41.8%) patients in their study. The reticular pattern was most commonly observed in 78 (80.4%) patients, and the erosive form was found in 19 (19.6%) patients [9]. Eisen et al., on the other hand, reported in his study of 723 oral LP patients that the most commonly observed form was the erosive form (40%), followed by reticular

and erythematous forms [12]. In the retrospective study of Yanık et al., the most commonly observed pattern in 63 LP patients with oral involvement was reticular (49.2%), followed by plaque type (31.7%), erosive type (15.9%), and atrophic type (3.2%) [13]. In our study, the reticular pattern was most common, followed by erosive, plaque, and bullous forms. Similar to other studies, the reticular and erosive types stand out in our study as the most commonly observed OLP forms. We believe that the easier clinical diagnosis of these two forms compared to other clinical subtypes plays a significant role in this picture.

Nail involvement in patients with lichen planus is seen in % 1-10 of cases. In %1-2 of cases, nail involvement is observed alone without any skin, mucosal, or scalp involvement [12,14]. In our study, nail involvement was detected in 21 (10.4%) cases, but no case with only nail involvement was observed.

LPP is characterized by follicular keratotic papules and plaques and can be seen alone or with cutaneous and mucosal LP forms [1]. In the study of Kyriakis et al. with 325 patients, classic LP was most commonly seen, followed by LPP with 12% [10]. Yanık et al. observed LPP in 10 (5.2%) patients in their study [13]. In our study, similarly to the literature, LPP was detected in a total of 21 patients (10.4%). Additionally, all the patients that had scalp involvement in our study were those with LPP. The fact that the other patients except for LPP did not have scalp involvement may be due to lack of knowledge.

In male patients, the rate of genital involvement is 25% while it is not known exactly in female patients [12,15]. In our study, genital involvement was detected in 16 (7.9%) patients. Of these patients, 11 were male and 5 were female, and oral mucosal involvement was accompanying in 4 patients.

Gastrointestinal diseases such as viral hepatitis can be seen together with LP. Many studies have examined the relationship between LP and HCV infection, but the results are contradictory. The results of these studies vary according to geographic distribution. For example, a study in Japan reported a 62% HCV positivity rate in patients with LP, while a study in France found this rate to be %4. A study from the UK found no relationship [16,17]. In studies conducted in different regions of our country, HCV antibody positivity is reported to be between 1.8-6.8% among patients with LP [15,18]. In our study, a 1% rate of HCV antibody positivity was detected. Also, only cutaneous involvement was present in both patients with detected HCV antibody positivity. With our current findings, no relationship was found between LP and HCV.

The coexistence of hepatitis B virus infection in patients with LP has also been investigated. In a multicenter study conducted in Italy with 577 LP patients and 1031 controls, HBV positivity was associated with lichen planus [19]. Eisen et al. did not find a relationship between HBV and LP in their study [12]. In our study, HBV (+) was detected in 11 (5.4%) patients. The relationship between LP and many systemic diseases such as alopecia areata, vitiligo, myasthenia gravis, active chronic hepatitis, metabolic syndrome, DM, HT, Sjögren's syndrome, lupus erythematosus, or thyroid pathologies has been investigated. Rey et al. showed in their meta-analysis study that the prevalence of DM in patients with OLP varies between %1.6 and 37.7%, and the prevalence of OLP in patients with DM varies between 0.5% and 6.1%. In the same study, they reported that the risk of developing DM in patients with OLP is 2.43 times higher, and the risk of developing lichen planus in patients with DM is 1,45 times higher [20]. This suggests a relationship between the two diseases. In the meta-analysis study by Mozaffari et al., the relative risk of developing OLP in DM patients was found to be 1.58 [21]. It was found at a rate of 9.4% in our study. In addition, OLP+DM+HT association (Grinspan syndrome) defined by Grinspan et al. [22] was detected in 3 of our patients. As a result, current studies reveal a significant relationship between LP and DM.

It has been suggested that oxidative stress may play a role in the etiopathogenesis of LP, and it has been shown that free oxygen radicals increase in LP [23,24]. Santiago et al. detected higher rates of systolic and diastolic hypertension values in patients with LP compared to controls, but they were not statistically significant [24]. Baykal et al. evaluated values above 140/90 mm/Hg blood pressure as hypertension and found the frequency of hypertension in patients with LP significantly higher compared to the control group [23]. HT was detected as the most common accompanying systemic disease at a rate of 20.3% in our study. According to the results of the retrospective case-control study conducted by Dreiher et al. with 1477 patients diagnosed with LP and a control group of 2856 non-LP individuals aged 20-80; the rate of dyslipidemia in LP was found to be 42.5%, and 37.8% in the control group, with this rate significantly higher in LP [25]. Baykal et al. obtained similar triglyceride, LDL, and HDL values in patients with LP compared to controls, and found no significant difference between the two groups in terms of dyslipidemia [23]. The dyslipidemia rate of 5.9% detected in our study is lower compared to the literature. In comparison of the age groups 18-45 and >45, the ratio of DM, hyperlipidemia and HT was identified significantly high in the group >45.

In Santiago et al.'s study evaluating cardiovascular risk in LP, which included 80 patients and a control group of 80 individuals; MS was encountered at a rate of %27 according to NCEP ATPIII diagnostic criteria in the patient group, while this rate was determined as 20% in the control group; however, no significant difference was found between the two groups [26]. In Baykal et al.'s study consisting of 79 patients with LP and a control group of 79 individuals with similar characteristics in terms of age, gender, abdominal obesity, and smoking; the frequency of MS according to NCEP ATP-III diagnostic criteria was shown to be 26.6% in the patient group and 12.7% in the control group, and a significant difference was found between the two groups in terms of MS risk [23]. In our study, MS was detected at a rate of 1.48%, which is quite low compared to the literature.

It is known that LP imposes a significant burden on patients and is associated with anxiety, stress, and depression. In their studies with 70 LP patients, Tawil et al. reported psychiatric comorbidity and poor quality of life at a rate of 62.9% and also reported 51.4% alexithymia [27]. In the study by Schruf et al., the probability of

depression was found to be 1.4 times higher in LP patients than controls (LP 24.6%; controls 19.4%) [4]. In our study, depression-anxiety requiring treatment was detected in 14.4% of patients.

The relationship between thyroid autoimmunity and LP in different subtypes is more controversial, and the lack of publications does not allow for definitive conclusions. Lavaee and Majd found the frequency of hypothyroidism as 6.7% and 4% respectively in their study with 523 patients with oral LP and the same number of control patients [28]. In their studies with 38 patients who had applied to the dermatology outpatient clinic for two years and had thyroid disease (63% autoimmune thyroiditis, 26.3% multinodular goiter, 10.7% hypothyroidism), Brănişteanu et al. reported LP as the second most common dermatological pathology by succeeding alopecia areata [29]. In our study, hypothyroidism was detected at a rate of 5.9%, similar to the literature.

There are many treatment alternatives for LP, including topical and systemic corticosteroids, retinoids, cyclosporine, methotrexate, hydroxychloroquine, tacrolimus, pimecrolimus. When choosing the treatment to be given to the patient, the patient's age, gender, the severity and prevalence of LP, and the presence of accompanying systemic disease should be taken into account. In cases where the disease is limited and mild, considering that LP is a self-limiting disease with a good prognosis, it will be appropriate to choose topical corticosteroids in treatment.

In cases where the disease is severe and widespread, systemic treatment agents may need to be given [1,15]. In our study, it was observed that the majority of patients used topical corticosteroids (76.2%) and other systemic treatment methods were preferred when topical treatment was insufficient or the disease was widespread.

Conclusion

In conclusion, in our study, similar to the literature, LP is more common in women. While the classic type is most common in cutaneous LP and reticular pattern in oral LP, oral involvement rates have been observed to be lower compared to the literature. The positivity of HBV antigen and anti-HCV antibody is lower than the literature and no association could be established with LP. HT, depression-anxiety, and DM were detected as the most common accompanying comorbidities, and we think that patients with LP should be regularly consulted by psychiatry and internal medicine. The limitations of the study may be ranged in terms of being retrospective, the deficiency in the number of pediatric patients and not being able to evaluate the long term follow-up of the patients. We think that prospective cohort studies with more patients are needed to fully understand the epidemiological, clinical, and pathogenetic features of the disease.

Ethical approval

Ethical approval was received for this study from Fırat University Non-Interventional Clinical Research Ethics Committee (01.06.2023-16310).

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