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Evaluation of Serum Uric Acid Levels in Patients with Lichen Planus: A Case-Control Study

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Abstract

BACKGROUND/AIMS: The objective was to assess uric acid (UA) levels in lichen planus (LP) patients and to investigate the impact of oxidative stress in LP etiopathogenesis.

MATERIALS AND METHODS: Fiftieth participants with LP and 50 participants with tinea unguium, all aged 18 years and older, were included as the control group. Sociodemographic data including age, gender, and medical history were documented. In LP patients, disease duration, disease pattern, and severity, current, and past treatments were recorded. UA, total bilirubin, direct bilirubin, indirect bilirubin, were measured for both groups.

RESULTS: This study included 50 LP patients (35 females, 15 males) and 50 patients with tinea unguium (28 females, 22 males) for the control group. The mean age was 52.96±12.84 years for the LP group, compared to 48.44±15.14 for the control group. The difference in age and gender distribution between the LP group and the control group was not statistically significant. Among LP patients, 70% had the localized form, 26% had the oral form, and 4% had the generalized type. Topical corticosteroids were prescribed to 86% of the patients, while 14% received systemic corticosteroids. No significant difference was recorded between the LP group and the control group regarding total, direct, and indirect bilirubin levels, as well as UA levels.

CONCLUSION: No significant difference was reported in total bilirubin, direct and indirect bilirubin, and UA between LP patients and the control group.

Keywords: Bilirubin, lichen planus, oxidative stress, uric acid

INTRODUCTION

Lichen planus (LP) is a skin disease characterized by distinct clinical and histopathological features. It appears as small, shiny, polygonal; mildly erythematous, purplish papules or plaques. Besides affecting the skin and mucous membranes, LP may also involve hair and nails. Clinically, LP presents in different types, such as classic, hypertrophic, bullous, actinic, annular, and follicular types. LP typically occurs between the ages of 30 and 70, with females being affected approximately 1.5 times more often than males.

The exact cause and pathogenesis of LP remain uncertain; it is believed to arise from the attack of cytotoxic T-lymphocytes, which target basal keratinocytes, causing apoptosis. Triggers for this autoimmune reaction

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include microbial antigens, metal ions, and certain medications.[1,2] Some studies have also suggested a potential relationship between hepatitis C virus and LP.[3,4] Recent research has emphasised reactive oxygen species (ROS) in dermatological disorders. In LP, CD4+ T-lymphocytes are one of the sources of ROS which damages endothelial cells, that increases the intercellular adhesion molecule 1, and facilitates T-cell infiltration and exocytosis.[2,5] Oxidative stress, through elevated tumor necrosis factor-alpha, triggers pro- and anti-apoptotic pathways.[6] It also stimulates the release of molecules like perforin and granzyme, exacerbating local tissue destruction.[7]

Uric acid (UA) is a crucial antioxidant that neutralizes ROS and sequesters metal ions.[8-10] Therefore, measuring UA may be important in the clinical management of LP. The objective here is to evaluate UA levels in LP patients and investigate oxidative stress in the etiopathogenesis of LP.

MATERIALS AND METHODS

Fifty LP patients aged 18 and older, all of whom were diagnosed with LP based on clinical presentation and histopathology, were included. The participants were randomly selected from the Clinic of Dermatology and Venereology, University of Health Sciences Türkiye, Ankara Training and Research Hospital between May 2020 and August 2022. Additionally, 50 patients with tinea unguium, all aged 18 and older, were included as the control group. The diagnosis of LP was based on clinical presentation and histopathological confirmation, while tinea unguium was confirmed through clinical examination. Patients were not restricted to newly diagnosed cases and individuals with varying disease durations were included. The control group was selected without specific demographic matching, though efforts were made to ensure a comparable distribution of age and gender. Power analysis was not performed, however, a sample size of 50 patients per group was deemed appropriate based on previous studies examining oxidative stress markers in dermatological conditions and the feasibility of recruitment within the study period. The study received approval from the University of Health Sciences Türkiye, Ankara Training and Research Hospital Ethics Committee (approval number: 978/2022, date: 27.07.2022), and was conducted according to the Declaration of Helsinki and Good Clinical and Laboratory Practices. All participants gave informed consent. Individuals with renal failure, pregnancy, or breastfeeding, as well as those with conditions or medications known to elevate UA levels, were excluded. Patients with congenital, hepatic, cholestatic or hemolytic diseases or medications that could increase bilirubin levels were also excluded. Sociodemographic data including age, gender, and medical history were recorded for both groups. For the LP group, the duration of the disease, treatments received, the extent of the disease, and the pattern of involvement were thoroughly evaluated and documented. Serum UA, total bilirubin, direct and indirect bilirubin levels were measured in the LP group and the control group.

Statistical Analysis

IBM SPSS Statistics 22 software was used for statistical analyses. The normality of data distribution was evaluated with Kolmogorov-Smirnov and Shapiro-Wilk tests. Descriptive statistics (mean, standard deviation, frequency) were used to summarize the data. For comparing quantitative data, Student's t-test and ANOVA were applied to normally distributed parameters, while Mann-Whitney U test and Kruskal-Wallis test were used for non-normally distributed parameters. Qualitative data were analyzed using Fisher's exact chi-square test, Fisher-Freeman-Halton exact chi-square test, and Continuity (Yates) Correction. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 100 patients (50 LP patients and 50 control patients) participated in this study. Among LP patients, 35 were female (70%) and 15 were male (30%), while the control group included 28 females (56%) and 22 males (44%). Gender distribution was not statistically different between the LP group and the control group ($p>0.05$). The age of the LP group varied from 22 to 84 years, with a mean of 52.96±12.84. The age of the control group varied between 20 and 74 years, with a mean of 48.44±15.14. The mean age between the two groups did not show a significant difference ($p>0.05$). 42% of the LP group and 36% of the control group had additional comorbidities, with no significant difference in medical history between the two groups ($p>0.05$) (Table 1).

24% of the LP group had a disease duration of 0 to 6 months, 24% had a disease duration of greater than 6 to 12 months, and 52% had a disease duration of more than one year. In the patient group, 70% were diagnosed with localized LP, 26% with oral LP, and 8% with generalized LP. It was found that 86% received topical corticosteroid treatment, while 14% received systemic corticosteroid treatment (Table 2).

The mean UA level in the LP group was 5.01±1.32, while the mean UA level in the control group was 4.71±1.31. The difference in UA levels between the groups was not statistically significant ($p>0.05$). The median total bilirubin was 0.37 [interquartile range (IQR): 0.22] in the LP group and 0.44 (IQR: 0.28) in the control group. The median direct bilirubin was 0.15 (IQR: 0.08) in the LP group, whereas it was 0.18 (IQR: 0.12) in the control group. The median indirect bilirubin in

Table 1. Demographic characteristics of the patient and control groups

		Patient	Control	p
Gender, n (%)	Female	35 (70%)	28 (56%)	0.214[1]
	Male	15 (30%)	22 (44%)	
Personal history, n (%)	None	29 (58%)	32 (64%)	0.557[2]
	Hypertension	6 (12%)	9 (18%)	
	DM	4 (8%)	2 (4%)	
	HT + DM	1 (2%)	2 (4%)	
	Malignancy	2 (4%)	0 (0%)	
	Other	8 (16%)	5 (10%)	
Age mean ± SD		52.96±12.84	48.44±15.14	0.111[3]

[1]Continuity (Yates's) correction, [2]Fisher-Freeman-Halton exact test, [3]Student's t-test, HT: Hypertension, DM: Diabetes mellitus.

Table 2. Clinical characteristics of the patient group

		n	%
Disease duration	0-6 month	12	24
	>6-12 months	12	24
	>1 year	26	52
Subtype	Localised	35	70
	Oral	13	26
	Generalised	2	4
Treatment	Topical	43	86
	Systemic	7	14
	Total	50	100

the LP group was 0.2 (IQR: 0.17); and 0.25 (IQR: 0.21) in the control group. There was no statistically significant difference in the median total, direct, and indirect bilirubin levels between the LP and the control group (p>0.05). UA, total bilirubin, direct bilirubin and indirect bilirubin levels are shown in Table 3.

UA levels were normal in 41 patients (82%) in the LP group and 39 individuals (78%) in the control group with no significant difference between them (p>0.05). Total and indirect bilirubin levels were within normal reference ranges in all individuals in the LP group, and the control group. Direct bilirubin levels were normal in 47 patients (94%) in the LP group and 49 individuals (98%) in the control group, with no significant difference between the two groups (p>0.05) (Table 4).

UA, total bilirubin, direct bilirubin, and indirect bilirubin values of the different subtypes of LP (localized LP, oral LP, and generalized LP) were compared. No significant difference was observed in UA, total bilirubin, direct bilirubin, and indirect bilirubin levels among patients with localized LP, oral LP, and generalized LP (p>0.05) (Table 5).

DISCUSSION

LP can affect the skin, mucous membranes, hair, and nails.[1,2] Although LP can affect individuals at any age, it is mostly seen in individuals between 30 and 70 years old. The prevalence in the population is thought to range between 0.5% and 1%.[11] Some studies have shown a female predominance in the gender distribution of LP. For instance, McCartan et al.[12] reported a prevalence of 0.96% in males and 1.57% in females. In a study with 1,335 LP patients, 67.5% of the patients were female.[13] Le Cleach and Chosidow[14] reported that 60-70% of oral LP patients were female and had an average age of 50-60 years, while 50% of cutaneous LP patients were female and had an average age of 40-45 years. In a study of 232 LP patients 53.9% of the patients were female and 46.1% were male, with an average age between 40-49 years.[15] In this study, the gender distribution, age of onset, and disease duration were consistent with the literature.

Currently, there is no standardised scoring system to assess the severity of LP. In a study with 444 LP patients, the involvement of a single anatomical region was classified as localized, while involvement of two or more regions was classified as generalized, involvement of only oral, only genital, or both mucosal sites was classified as mucosal, and involvement of only the nails was classified as nail LP. 48% of patients had localized LP, 38% had generalized LP, 13% had mucosal LP, and 1% had nail LP.[16] Similarly, in this study, LP involvement was classified into 3 categories: localized LP for a single anatomical region, generalized LP for two or more regions, and oral LP for cases limited to the oral mucosa. In this study, it was found that 70% of the patients had localized LP, 26% had oral LP, and 4% had generalized LP.

UA is an antioxidant that scavenges free radicals and reduces oxidative stress. LP is an idiopathic disease with autoimmunity, infections, oxidative stress, and dental procedures as triggering factors. Recently, the role of oxidative stress has been emphasised in its disease pathogenesis.[2] However, limited studies have explored the relationship between UA and LP, with most indicating that UA levels are lower in patients with LP. A case-control study involving 58 LP patients diagnosed both clinically and histopathologically examined the relationship between LP and UA. The mean UA in the patient group was significantly lower than in the control group, and a similar decline in UA levels was observed within the patient group as disease severity and duration increased. Therefore, it was concluded that UA has a significant role in antioxidant mechanisms and in the development of LP.[17] In another case-control study involving 39 LP patients, UA levels were notably increased in the control group and during disease remission, implying that UA is an important antioxidant in LP patients.[18] In a study involving 43 oral LP patients, the link between serum and saliva UA levels and psychosocial factors was investigated. The patient group had lower saliva and serum UA levels compared to controls.[19] Additionally, a case-control study by Darczuk et al.[20] involving 40 oral LP patients evaluated the association

Table 3. Uric acid and bilirubin levels of the patient and control groups

	Patient	Control	p
	Mean ± SD/ median (IQR)	Mean ± SD/ median (IQR)	
Uric acid (mean ± SD)	5.01±1.32	4.71±1.31	0.255[1]
Total bilirubin [median, (IQR)]	0.37 (0.22)	0.44 (0.28)	0.113[2]
Direct bilirubin [median, (IQR)]	0.15 (0.08)	0.18 (0.12)	0.113[2]
Indirect bilirubin [median, (IQR)]	0.2 (0.17)	0.25 (0.21)	0.187[2]

[1]Student's t-test, [2]Mann-Whitney U test, IQR: Interquartile range, SD: Standard deviation.

Table 4. Evaluation of uric acid and bilirubin levels of the patient and control groups according to reference values

		Patient	Control	p
		n (%)	n (%)	
Uric acid	Normal	41 (82%)	39 (78%)	0.803[1]
	Out of normal range	9 (18%)	11 (22%)	
Total bilirubin	Normal	50 (100%)	50 (100%)	-
	Out of normal range	0 (0%)	0 (0%)	
Direct bilirubin	Normal	47 (94%)	49 (98%)	0.617[2]
	Out of normal range	3 (6%)	1 (2%)	
Indirect bilirubin	Normal	50 (100%)	50 (100%)	-
	Out of normal range	0 (0%)	0 (0%)	

[1]Continuity (Yates's) correction, [2]Fisher's exact test.

Table 5. Uric acid and bilirubin levels of disease subtype

	Localised lichen planus, (n=35)	Oral lichen planus, (n=15)	Generalised lichen planus, (n=2)	p
	Mean ± SD/ median (IQR)	Mean ± SD/ median (IQR)	Mean ± SD/ median (IQR)	
Uric acid (mean ± SD)	5.15±1.44	4.53±0.96	5.30±0	0.806[1]
Total bilirubin [median, (IQR)]	0.39 (0.19)	0.34 (0.39)	0.34 (-)	0.891[2]
Direct bilirubin [median, (IQR)]	0.15 (0.10)	0.13 (0.07)	0.18 (-)	0.453[2]
Indirect bilirubin [median, (IQR)]	0.24 (0.17)	0.20 (0.32)	0.16 (-)	0.530[2]

[1]ANOVA test, [2]Kruskal-Wallis test, SD: Standard deviation, IQR: Interquartile range.

between UA levels, tyrosine levels, and glutathione peroxidase activity. Consistent with previous findings, all three markers were considerably lower in the patient group. In this study, UA levels of the LP group and the control group were not statistically different from each other. Lower UA levels would be expected in LP, as the condition is thought to be associated with increased oxidative stress. However, higher UA levels in the LP group may be attributed to additional diseases like diabetes and hypertension, which are known to affect UA metabolism. Further studies with larger sample sizes and better control for comorbidities are needed to clarify the relationship between UA and LP.

There are only a few studies investigating serum bilirubin levels in dermatological conditions. In a study with 214 patients diagnosed with psoriasis vulgaris, the association between severity of the disease and serum bilirubin was explored. The study revealed that serum bilirubin levels of the patient group were significantly lower than the control group, and that they showed an inverse correlation with PASI scores.[21] In this study, unlike previous research, differences in bilirubin between LP patients and the control group and among different LP subtypes were not statistically significant. While the role of bilirubin in managing oxidative stress has been highlighted in earlier studies, this was not supported in the current study. Possible explanations for this discrepancy include the small sample size, differences in inclusion and exclusion criteria, additional diseases of both groups, the inclusion of only LP patients who had presented to the clinic in the last two years, and social and genetic variations.

UA and bilirubin are considered to have key roles in the pathogenesis of inflammatory diseases like LP. Measuring their serum levels in such conditions can offer valuable insights into disease prognosis, treatment options, and disease monitoring. Moreover, these tests are quick, simple, and cost-effective.

In our study, UA and bilirubin did not show significant differences between LP patients and the control group. While UA and bilirubin are recognized for their antioxidant functions in LP, research on this topic is limited. Therefore, more comparative studies with larger, more diverse patient groups and longer duration of follow-up are necessary to support this view.

Study Limitations

Possible reasons for the differing results in this study compared to the literature include the small sample size, variations in inclusion and exclusion criteria, additional diseases in the patient and control groups, the focus on patients who visited the clinic in the last two years, as well as social and geographical differences, and irregular clinic attendance during the pandemic.

MAIN POINTS

- Elevated serum UA levels in LP patients suggest that UA can be a clinical marker to assess oxidative stress.
- The results support the idea that oxidative stress may be critical in the etiopathogenesis of LP. This could lead to new possibilities for investigating antioxidant therapies in the management of LP.
- Bilirubin levels, another marker of oxidative stress, did not show significant difference between LP patients and the control group, indicating that not all oxidative stress markers may be elevated in LP.
- Monitoring UA levels in LP patients might help in understanding the disease progression and potentially guide antioxidant-based therapeutic strategies.

ETHICS

Ethics Committee Approval: The study received approval from the University of Health Sciences Türkiye, Ankara Training and Research Hospital Ethics Committee (approval number: 978/2022, date: 27.07.2022).

Informed Consent: All participants gave informed consent.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.K., Concept: D.E., İ.K., Design: D.E., İ.K., N.K., Data Collection and/or Processing: D.E., N.K., Analysis and/or Interpretation: İ.K., Literature Search: D.E., İ.K., N.K., Writing: D.E., İ.K., N.K.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Wagner G, Rose C, Sachse MM. Clinical variants of lichen planus. J Dtsch Dermatol Ges. 2013; 11(4): 309-19.
2. Chakraborti G, Biswas R, Chakraborti S, Sen PK. Altered serum uric Acid level in lichen planus patients. Indian J Dermatol. 2014; 59(6): 558-61.
3. Lodi G, Pellicano R, Carrozzo M. Hepatitis C virus infection and lichen planus: a systematic review with meta-analysis. Oral Dis. 2010; 16(7): 601-12.
4. Rübsam K, Schroll A, Weisenseel P, Multhaup S, Ruzicka T, Prinz JC. Lichen planus and hepatitis virus infections: causal association? J Dtsch Dermatol Ges. 2011; 9(6): 464-8.
5. Sezer E, Ozugurlu F, Ozyurt H, Sahin S, Etikan I. Lipid peroxidation and antioxidant status in lichen planus. Clin Exp Dermatol. 2007; 32(4): 430-4.
6. Shakibaei M, Schulze-Tanzil G, Takada Y, Aggarwal BB. Redox regulation of apoptosis by members of the TNF superfamily. Antioxid Redox Signal. 2005; 7(3-4): 482-96.
7. Hendel A, Hiebert PR, Boivin WA, Williams SJ, Granville DJ. Granzymes in age-related cardiovascular and pulmonary diseases. Cell Death Differ. 2010; 17(4): 596-606.
8. Glantzounis GK, Tsimoyiannis EC, Kappas AM, Galaris DA. Uric acid and oxidative stress. Curr Pharm Des. 2005; 11(32): 4145-51.
9. Feig DI, Kang DH, Johnson RJ. Uric acid and cardiovascular risk. N Engl J Med. 2008; 359(17): 1811-21.
10. Venkateshappa C, Harish G, Mahadevan A, Srinivas Bharath MM, Shankar SK. Elevated oxidative stress and decreased antioxidant function in the human hippocampus and frontal cortex with increasing age: implications for neurodegeneration in Alzheimer's disease. Neurochem Res. 2012; 37(8): 1601-14.

11. 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.

12. McCartan BE, Healy CM. The reported prevalence of oral lichen planus: a review and critique. J Oral Pathol Med. 2008; 37(8): 447-53.

13. Prakash S Mohan R, Ghanta S, Verma S, Agarwal N, Gupta N, et al. Meteorological influences on the incidence of lichen planus in a north Indian population. J Oral Sci. 2013; 55(4): 311-8.

14. Le Cleach L, Chosidow O. Clinical practice. Lichen planus. N Engl J Med. 2012; 366(8): 723-32.

15. Bhattacharya M, Kaur I, Kumar B. Lichen planus: a clinical and epidemiological study. J Dermatol. 2000; 27(9): 576-82.

16. Schwager Z, Stern M, Cohen J, Femia A. Clinical epidemiology and treatment of lichen planus: A retrospective review of 2 tertiary care centers. J Am Acad Dermatol. 2019; 81(6): 1397-9.

17. Kutzing MK, Firestein BL. Altered uric acid levels and disease states. J Pharmacol Exp Ther. 2008; 324(1): 1-7.

18. Gupta A, Mohan RP, Gupta S, Malik SS, Goel S, Kamarthi N. Roles of serum uric acid, prolactin levels, and psychosocial factors in oral lichen planus. J Oral Sci. 2017; 59(1): 139-46.

19. Shaw H, Konidena A, Malhotra A, Yumnam N, Farooq F, Bansal V. Psychological status and uric acid levels in oral lichen planus patients - A case- control study. Indian J Dent Res. 2020; 31(3): 368-75.

20. Darczuk D, Krzyściak W, Bystrowska B, Kęsek B, Kościelniak D, Chomyszyn-Gajewska M, et al. The Relationship between the Concentration of Salivary Tyrosine and Antioxidants in Patients with Oral Lichen Planus. Oxid Med Cell Longev. 2019; 2019: 5801570.

21. Zhou ZX, Chen JK, Hong YY, Zhou R, Zhou DM, Sun LY, et al. Relationship Between the Serum Total Bilirubin and Inflammation in Patients With Psoriasis Vulgaris. J Clin Lab Anal. 2016; 30(5): 768-75.